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17 November 2023

Response to the draft assessment report for bimekizumab for the treatment of ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

UCB has received the draft assessment report for bimekizumab on 8th November 2023 and would like to share the below comments with the Danish Medicines Council (DMC).

UCB has asked for an evaluation by the DMC of bimekizumab as a clinically equivalent treatment alternative to existing standard treatments for AS or nr-axSpA i.e. adalimumab, ixekizumab and secukinumab. Bimekizumab is indicated for 1st line bDMARD[9]-naïve patients and 2nd line bDMARD-experienced patients. Today only a limited number of treatment options are available for patients with AS or nr-axSpA and bimekizumab is a new clinically relevant treatment option for these patients, whether bDMARD-naïve or bDMARD-experienced.

In the Phase 3 studies, BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (AS), bimekizumab has proven clinical efficacy vs placebo in patients with AS or nr-axSpA and shown a tolerability profile consistent with the known tolerability of bimekizumab in other indications. Clinical efficacy was sustained until week 52.[1,12] The proportion of patients who developed uveitis was lower with bimekizumab compared to placebo as described in the SmPC.[1] UCB has ensured that BE MOBILE 1 and BE MOBILE 2 included both bDMARD-naïve and -experienced patients with the aim to study the clinical efficacy and tolerability in both patient populations. As such, the clinical evidence for bimekizumab in AS and nr-axSpA differs from the clinical evidence used for previous DMC recommendations for b/tsDMARDs in AS and nr-axSpA, which were predominantly studies in 100% bDMARD-naïve patients. [2,3,4]

The comparative indirect analyses of bimekizumab vs adalimumab showed no statistically significant differences between bimekizumab and adalimumab for any of the endpoints studied. As in previous DMC assessments,[2,3,4] this allows the conclusion that the treatment effects are equivalent for bimekizumab and adalimumab in AS and nr-axSpA. Similarly, UCB has submitted comparative clinical evidence for the efficacy of bimekizumab vs ixekizumab in bDMARD-naïve patients with AS[5] and comparative clinical evidence vs secukinumab in a mixed population of bDMARD-naïve and -experienced patients with nr-axSpA.[6] For all comparative indirect analyses no statistically significant differences between bimekizumab and comparators were found i.e. equivalent treatment effects of bimekizumab vs ixekizumab and bimekizumab vs secukinumab can be concluded.

UCB concludes that the clinical efficacy of bimekizumab has been established in AS and nr-axSpA using similar methods as in previous DMC assessments. The indirect treatment comparisons have proven clinical equivalence between bimekizumab and current standard treatments (adalimumab, ixekizumab and secukinumab) and the draft assessment report concludes that the tolerability profile of bimekizumab is comparable to those of adalimumab, ixekizumab and secukinumab.

Concerning placebo response rates seen in the indirect comparisons submitted to the DMC, UCB would like to highlight that these are based on subgroups of BE MOBILE 1 and BE MOBILE 2. These placebo response rates are not identical to the mean values in BE MOBILE 1 and BE MOBILE 2, where placebo response rates are comparable to those seen in other recent studies in rheumatology.[7,8]

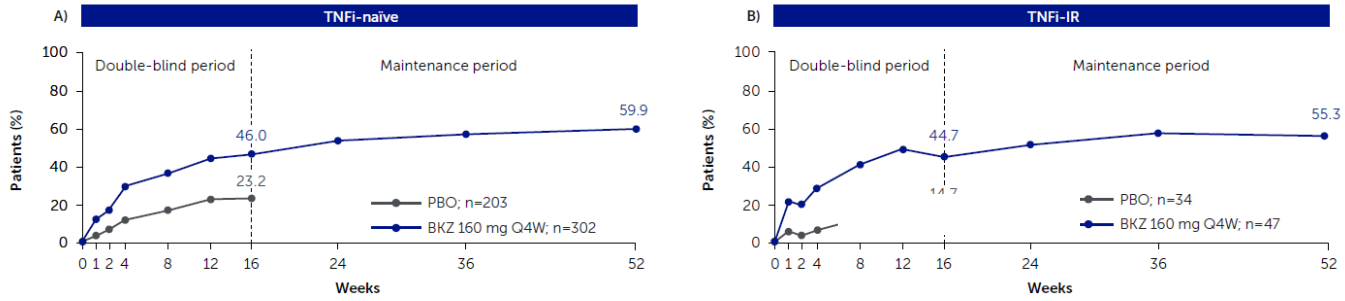
For bDMARD-experienced patients, the bimekizumab SmPC confirms that similar response in ASAS40 was seen in patients regardless of prior anti-TNFα exposure, based on an integrated analysis of BE MOBILE 1 and BE MOBILE 2 .[1] UCB acknowledges the importance of the bDMARD-experienced patient subgroup in the Danish clinical setting where adalimumab is used as the 1st line choice in both AS and nr-axSpA, and as such bimekizumab would likely be considered for treatment of patients previously treated with TNFi[9].

[1] Bimekizumab SmPC. Link: Bimzelx, INN-bimekizumab (europa.eu)
[2] Bilag til Medicinrådets anbefaling vedr. ixekizumab til rygsøjlegigt-vers. 1.0 (medicinraadet.dk);
[3] bilag-til-medicinrådets-anbefaling-vedr-secukinumab-adlegacy.pdf (medicinraadet.dk)
[4] bilag-til-medicinrådets-anbefaling-vedrørende-upadacitinib-til-behandling-af-ankyloserende-spondylitis-version-1-0.pdf (medicinraadet.dk)
[5] Submitted dossier for bimekizumab in AS and nr-axSpA, section 7.2, page 36 (Tables 18, 23, 26, 29 and 32)
[6] Submitted dossier for bimekizumab in AS and nr-axSpA, section 7.6, page 70
[7] Deodhar et al. Improvement of signs and symptoms of nonradiographic axial spondyloarthritis in patients treated with secukinumab: Primary results of a randomised, placebo-controlled phase III study. Arthritis & Rheumatology, Aug 2020; Vol 73, issue 1: 110-120.
[8] Van der Heijde et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS1): a multi-centre, randomised, double-blind, placebo-controlled, phase 2/3 trial. Lancet; Dec 2029; Vol 394: 2108-2117.
[9] TNFi = Tumour Necrosis Factor inhibitors; TNFi-IR = Tumour Necrosis Factor inhibitors inadequate responders; bDMARD=biologic disease-modifying anti-rheumatic drugs

Key results of the integrated analysis of BE MOBILE 1 and BE MOBILE 2 were presented at EULAR 2023[10]:

- At Week 16, the proportion of patients achieving ASAS40 was higher in BKZ-randomised vs placebo-randomised patients, regardless of prior TNFi exposure. Responses in continuous BKZ-treated patients increased to Week 52. Please refer to Figure 1.
- At Week 16, the proportion of patients achieving ASDAS low disease activity (<2.1) was higher in BKZ-randomised vs placebo-randomised patients, regardless of prior TNFi exposure. Responses in continuous BKZ-treated patients increased to Week 52. Figure is available in the reference.

Figure 1: ASAS40 over 52 weeks in pooled A) TNFi-naïve and B) TNFi-experienced patients in BE MOBILE1 &2 (NRI)



Data are pooled from BE MOBILE 1 and 2. Missing data were imputed with NRI. Data from PBO-randomised patients not included from Week 16 onwards. TNFi-IR = TNFi inadequate responders

The integrated analysis showed clinically relevant improvements with bimekizumab in signs and symptoms, disease activity, suppression of inflammation, physical functioning, and health-related quality of life, regardless of prior TNFi i.e. in both bDMARD-naïve and -experienced patients. Results were sustained to week 52. [10]

For comparative analyses in bDMARD-experienced patients, UCB acknowledges the concerns of the DMC about the small subgroups leading to insufficient power for robust statistical testing. To support the clinical equivalence of bimekizumab vs comparators in the indirect treatment comparisons submitted to the DMC, UCB would like to draw attention to the systematic literature review and network meta-analysis for bimekizumab in axSpA published as peer-reviewed manuscript last week, which demonstrates that bimekizumab was comparable with most b/tsDMARDs in AS, including ixekizumab, TNFi and upadacitinib, but achieved higher response rates vs secukinumab.[11] In the subgroup analysis with TNF-experienced patients, observed differences between bimekizumab and active comparators were not statistically significant, confirming previously demonstrated clinical equivalence.[11]

In conclusion, bimekizumab is a clinically relevant treatment for patients with AS or nr-axSpA for which clinical equivalence to current standard treatments has been thoroughly established, regardless of these patients being bDMARD-naïve or bDMARD-experienced. Clinical efficacy with bimekizumab treatment was sustained until week 52[1,12] and the tolerability was consistent with the known profile of bimekizumab.[12,]

The importance of bimekizumab in the axSpA treatment landscape has already been recognized in other countries with positive recommendations e.g. in UK (NICE recommends bimekizumab for use in bDMARD-experienced patients with AS or nr-axSpA; indirect comparison confirmed bimekizumab was as effective as ixekizumab and secukinumab[13]) and in Norway (Norwegian authorities recommend bimekizumab for patients with AS or nr-axSpA irrespective of previous bDMARD use[14]). Finally, UCB would like to mention that bimekizumab is not a new medicinal product and has been recommended since January 2022 as standard treatment for moderate-to-severe psoriasis with actively treated patients in Denmark.[15]

[10] Magrey et al. Bimekizumab achieved sustained improvements in efficacy outcomes in patients with axial spondyloarthritis, regardless of prior TNF inhibitor treatment: week 52 pooled results from two phase 3 studies. EULAR June 2023. Link: POS1107 BIMEKIZUMAB ACHIEVED SUSTAINED IMPROVEMENTS IN EFFICACY OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, REGARDLESS OF PRIOR TNF INHIBITOR TREATMENT: WEEK 52 POOLED RESULTS FROM TWO PHASE 3 STUDIES | Annals of the Rheumatic Diseases (bmj.com)
[11] Deodhar et al. Comparative efficacy and safety of bimekizumab in axial spondyloarthritis: a systematic literature review and network meta-analysis. Rheumatology, 8 Nov 2023: kead598. doi: 10.1093/rheumatology/kead598. Online ahead of print
[12] Baraliakos et al. Bimekizumab treatment in patients with active axial spondyloarthritis: 52 week efficacy and safety from the randomized parallel phase 3 BE MOBILE 1 and BE MOBILE 2 studies. Ann Rheum Dis, October 2023.
[13] NICE. Final draft guidance - bimekizumab for treating axial spondyloarthritis. Link: 1 (nice.org.uk)
[14] Statens Legemiddelverk. Link: Mal for saker til Bestillerforum RHF (nyemetoder.no)
[15] DERMBIO Annual Report 2022. Link: Dermbio_aarsrapport2022_opdateret20230831_godkendt.pdf

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27.11.2023
DBS

Forhandlingsnotat

Dato for behandling i Medicinrådet	November 2023
Leverandør	UCB
Lægemiddel	Bimzelx (Bimekizumab)
Ansøgt indikation	Aksial spondylartrit (rygsøjlegigt)
Nyt lægemiddel/indikationsudvidelse	Indikationsudvidelse

Prisinformation

Amgros har følgende pris på Bimzelx (Bimekizumab):

Tabel 1: Pris oversigt

Lægemiddel	Styrke	Pakningsstørrelse	AIP (DKK)	SAIP (DKK)	Rabatprocent ift. AIP
Bimzelx	160 mg	2 stk.	16.703,31	[redacted]	[redacted]

Aftaleforhold

Bimzelx er en del af det biologiske udbud indenfor psoriasis. Flere af de biologiske lægemidlerne indgår i forskellige behandlingsvejledninger indenfor reumatologien. Alle lægemidlerne er inkluderet i aftaler hvor det er muligt at lave en prisregulering hvert halve år. Den næste prisregulering sker d. 31.03.24 og aftalen gælder d. 30.09.24.

Konkurrencesituationen

Tabel 2 viser lægemiddeludgifter på udvalgte sammenlignelige lægemidler.

Tabel 2: Sammenligning af lægemiddeludgifter pr. patient

Lægemiddel	Styrke	Pakningsstørrelse	Dosering	Pris pr. pakning (SAIP, DKK)	Lægemiddeludgift pr. 18 md (SAIP, DKK)*
Bimzelx	160 mg	2 stk.	160 mg SC hver 4 uge	[redacted]	[redacted]
Cosentyx (secukinumab)	150 mg	2 stk.	150 mg administreres subkutant ved uge 0, 1, 2, 3 og 4 uger, hvorefter behandlingen gentages en gang om måneden	[redacted]	[redacted]
Hyrimoz (adalimumab)	40 mg	2 stk.	40 mg hver anden uge	[redacted]	[redacted]
Taltz (ixekizumab)	80 mg	1 stk.	160 mg (to injektioner af 80 mg) administreres subkutant ved uge 0 efterfulgt af 80 mg hver fjerde uge	[redacted]	[redacted]

*lægemiddeludgifterne er sammenlignet over en periode på 18 måneder jf. Medicinrådets vurderingsrapport. Ikke-diskonterede tal.

Status fra andre lande

Tabel 3: Status fra andre lande

Land	Status	Link
Norge	Godkendt	Link til anbefaling
England	Godkendt	Link til anbefaling

Konklusion

[redacted]

Medicinrådet

Application for the assessment of bimekizumab for adults with active non-radiographic axial spondyloarthritis or active ankylosing spondylitis

Version 1.3

Medicinrådet Dampfærgevej 21-23, 3. sal DK-2100 København Ø +45 70 10 36 00 medicinraadet@medicinraadet.dk www.medicinraadet.dk

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Colour scheme for text highlighting	
Colour of highlighted text	**Definition of highlighted text**
	Confidential information

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1. Basic information

Contact information	
Name	**Janne Riis Treloggen**
Title	Patient Access Lead Denmark
Phone number	31.47.31.53
E-mail	Janne.treloggen@ucb.com

Overview of the pharmaceutical	
Proprietary name	Bimzelx
Generic name	Bimekizumab
Marketing authorization holder in Denmark	UCB Nordic A/S
ATC code	L04AC21
Pharmacotherapeutic group	Immunosuppressants, IL-17 interleukin inhibitor
Active substance(s)	Bimekizumab
Pharmaceutical form(s)	Subcutaneous injection
Mechanism of action	Bimekizumab is the first humanised IgG1/κ monoclonal antibody designed with dual specificity that potently and selectively neutralises the biological function of both IL-17A and IL-17F homodimers (IL-17A/IL-17A and IL-17F/IL-17F) as well as the heterodimer (IL-17A/IL-17F). It has two identical antigen binding regions that selectively bind and neutralise IL-17A, IL-17F, and IL-17AF cytokines, blocking their interaction with the IL-17RA/IL-17RC receptor complex. Elevation of IL-17A and IL-17F levels are drivers of inflammation and new bone formation in models of psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA). Inhibition of both IL-17F and IL-17A, produced via the innate and adaptive immune systems, reduces the expression of inflammation-related genes, production of inflammatory cytokines, and immune cell migration to reduce inflammation in in vitro models of PSA and axSpA
Dosage regimen	*Axial spondyloarthritis (nr-axSpA and AS)* The recommended dose for adult patients with axial spondyloarthritis is 160 mg (given as 1 subcutaneous injection) every 4 weeks. Consideration should be given to discontinuing treatment in patients who have shown no improvement by 16 weeks of treatment.

Overview of the pharmaceutical	
Therapeutic indication relevant for assessment (as defined by the European Medicines Agency, EMA)	*Non-radiographic axial spondyloarthritis (nr-axSpA):* Bimzelx is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs). *Ankylosing spondylitis (AS, radiographic axial spondyloarthritis):* Bimzelx is indicated for the treatment of adults with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy.
Other approved therapeutic indications	*Plaque psoriasis* Bimzelx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy *Psoriatic arthritis (CHMP PO April 26th 2023)* Bimzelx, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).
Will dispensing be restricted to hospitals?	Yes
Combination therapy and/or co-medication	None
Packaging – types, sizes/number of units, and concentrations	Item number: 390221 - Bimzelx 160mg, 2 prefilled syringes, concentration: 1ml (160mg/ml) Item number: 142295 – Bimzelx 160mg, 2 prefilled pens, concentration: 1ml (160mg/ml)
Orphan drug designation	No

2. Abbreviations

Abbreviation	Definition
Approx.	Approximately
AS	Radiographic axial spondyloarthritis

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AxSpA	Axial spondyloarthritis
CDSR	Cochrane Database of Systematic Reviews
CENTRAL	Cochrane Central Register of Controlled Trials
CFS	COVID-19 Free Set
CMA	Cost-minimization analysis
CRP	C-reactive protein
CVD	Cardiovascular disease
DANBIO	Danish Rheumatology Database
DMC	Danish Medicines Council
EAIR	Exposure adjusted incidence rate
ITC	Indirect treatment comparisons
MoA	Mode of Action
MRI	Magnetic resonance imaging
NA	Not applicable
nr-axSpA	Non-radiographic axial spondyloarthritis
NSAID	Non-steroidal anti-inflammatory drug
PsA	Psoriatic Arthritis
PY	Patient years
QoL	Quality of Life
RA	Rheumatoid arthritis
RD	Risk difference
RR	Relative risk
SLR	Systematic literature review

3. Tables and Figures

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4. Summary

Bimekizumab is expected to be used in Danish clinical practice for the treatment of adults with active nr-axSpA with objective signs of inflammation as indicated by elevated CRP and/or MRI who have responded inadequately or are intolerant to NSAIDs and adults with active AS who have responded inadequately or are intolerant to conventional therapy. Bimekizumab can be used in both the first line setting for treatment-naïve patients and in a second-line setting for treatment-experienced patients. Based on the current recommendation in the DMC drug recommendation for the use of biologic treatment of axSpA[1] bimekizumab is expected to be positioned in patients previously treated with adalimumab or another 1st line treatment with an assumed uptake of 10-15% of the patients switching to a different MoA.

The clinical evidence for bimekizumab indicates clinical equivalence to the existing treatments in 1st line in the treatment guideline and drug recommendation for AS and nr-axSpA valid until end-March 2022 such as adalimumab, secukinumab and ixekizumab. However, this treatment guideline and drug recommendation were developed under the framework of Rådet for Anvendelse af Dyr Sygehusmedicin (RADS).[2] Based on feedback and discussions with the DMC secretariat it has been indicated that bimekizumab cannot be assessed via a direct placement process since both treatment guideline and drug recommendation were developed by RADS and as such based on different methodologies than those used by the DMC today.

Since the DMC has decided not to update neither the treatment guideline nor the drug recommendation in the future it will unfortunately not be possible to place bimekizumab directly into the treatment guideline despite the clinical equivalence indicated in the bimekizumab evidence. However current treatments used after adalimumab, and secukinumab have previously been assessed by the DMC to be equivalent with existing biologic treatments[3, 4]. Both ixekizumab and secukinumab are considered to be relevant treatment comparators for bimekizumab as they are both 1st line treatments typically used after adalimumab or after another biological treatment.

UCB has conducted comparisons to these currently approved and recommended treatments via indirect treatment comparisons (ITCs). These ITCs are based on a systematic literature review (SLR). From the global SLR the relevant comparators and studies were selected for the Danish-specific comparisons. The ITCs have been conducted for the endpoints used in the national treatment guideline valid until end-March 2022 for

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the relevant patient populations in AS and nr-axSpA to the extent that data availability allowed. The method used for conducting the ITCs is the Bucher indirect treatment comparison.

The studies included in the ITC analyses for both AS and nr-axSpA are similar in terms of inclusion criteria. Both analyses for AS and nr-axSpA included a mixed set of studies in relation to prior bDMARD experience, as illustrated below. Hence, analyses were carried out for both the ITT population and bDMARD treatment naïve and experienced subgroups if available).

Based on the results of the ITC vs adalimumab, secukinumab and ixekizumab UCB believes that bimekizumab can be considered to be equivalent to the existing biologic treatments recommended in the treatment recommendation for AS and nr-axSpA. UCB acknowledge that bimekizumab is unlikely to replace adalimumab given the availability of biosimilar adalimumab. Bimekizumab will likely replace secukinumab and ixekizumab depending on the ranking in the drug recommendation and as such be used in bDMARD experienced patients.

5. The patient population, the intervention and choice of comparator(s)

5.1 The medical condition and patient population

Unmet need remains for axSpA patients in control of symptoms and improvement of physical functioning as well as the prevention of disease progression and irreversible structural damage
Axial spondyloarthritis (AxSpA) is a chronic, progressive, inflammatory rheumatic disease [5] affecting the spine and sacroiliac joints [6]. AxSpA causes severe chronic inflammatory back pain, fatigue, and loss of physical function [7, 8], and can lead to irreversible structural damage [9, 10], spinal fractures, and severe spinal cord injury [11]. AxSpA is a complex multi-faceted disease associated with a broad range of non-axial manifestations including enthesitis, peripheral arthritis, dactylitis, uveitis, psoriasis - and IBD. [9, 12]. In addition, patients with axSpA are at increased risk of comorbid conditions including cardiovascular disease (CVD), depression, anxiety, fibromyalgia, obesity, and osteoporosis [13].

The umbrella term axSpA encompasses both non-radiographic axial spondyloarthritis (nr-axSpA, previously known as undifferentiated SpA) and radiographic axial spondyloarthritis (previously known as ankylosing spondylitis [AS][5, 14]. These form a continuum of the same disease and are differentiated primarily through the absence or presence of radiographic structural damage of the sacroiliac joints:

Patients with nr-axSpA have no definitive signs of structural damage on an X-ray, although there may be evidence of inflammation of the sacroiliac joint and spine on magnetic resonance imaging (MRI). [15]
Patients with r-axSpA (AS) have definitive radiographic evidence of structural damage to one or both of the sacroiliac joints on X-ray [15], and vertebrae fusion has been reported in ~60% of patients. [8]

Patients with axSpA experience significant disease burden that impacts their daily lives and quality of life (QoL) and leads to a reduction in work productivity [16-18]. Aside from the presence or absence of radiographic structural damage, the symptoms experienced by patients with nr-axSpA and AS are the same. It is important to note that nr-axSpA should not be considered as a mild form of axSpA, as disease activity and burden is similar for both phenotypes despite differences in radiographic findings. However, if

adequately treated, spinal mobility impairment due to inflammation is potentially reversible whereas structural damage once sustained is irreversible [19].

Typically, axSpA affects the younger patient population, with an average age of symptom onset of 28 years[20, 21], but delays in the diagnosis of axSpA are common: it can take up to 10 years from the onset of symptoms to diagnosis [22], leaving a high proportion of patients undiagnosed, and potentially untreated, for extended periods.

Overall, patients with axSpA experience substantial burden of disease that has a negative impact on their daily lives. The physical burden for patients with axSpA occurs in key domains of pain, fatigue, and physical function, which lead to reduced QoL and reduced ability to work. In alignment with the similar burden of disease, the detrimental impact on patient QoL is generally considered comparable between nr-axSpA and AS[23-26], and is comparable to the QoL decrement observed for rheumatoid arthritis (RA) and psoriatic arthritis (PsA)[26, 27].

The incidence of AS and nr-axSpA is respectively approx. 0.5% and 1.5% in Denmark[28]. In DANBIO (Danish Rheumatology Database), at the end of 2019, approx. 4,100 patients were in treatment for axSpA (AS and nr-axSpA), and in 2018 approx. 320 new patients were in treatment[29]. As the incidence and prevalence of axSpA are relatively stable, they will be assumed to be the same throughout the period 2018-2022. At the end of 2019, approx. 2,270 patients were in biological treatment for AS. Data extracts from DANBIO show that approx. 57% of patients have AS, while 43% of patients have nr-axSpA[3].

Table 1 Incidence and prevalence in the past 5 years

Year	2018	2019	2020	2021	2022
Incidence in Denmark	320	320	320	320	320
Prevalence in Denmark	4,100	4,100	4,100	4,100	4,100
Global prevalence *	NA	NA	NA	NA	NA

* For small patient groups, also describe the worldwide prevalence

NA = not applicable

Table 2 Estimated number of patients eligible for treatment

Year	2024	2025	2026	2027	2028
Number of patients in Denmark who are expected to use the pharmaceutical in the coming years	9	20	34	50	66

The estimated number of patients in Denmark who are expected to use bimekizumab for the treatment of AS or nr-axSpA is based on patient statistics in DANBIO[29]. DANBIO shows that approximately 20-50 new patients every year start on treatment with either secukinumab or ixekizumab. Bimekizumab is expected to be a treatment alternative to secukinumab and ixekizumab, and the estimated number of patients expected to use bimekizumab will be highly dependent on the ranking of bimekizumab versus these two comparators. As such the estimated number of patients is based on the assumption that bimekizumab is a cheaper treatment alternative to ixekizumab as it is the case in the drug recommendation for psoriasis today. The estimated number of patients for bimekizumab indicated above is used in the cost-minimisation model.

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5.1.1 Patient populations relevant for this application

Bimekizumab is expected to be used in Danish clinical practice for the treatment of adults with active nr-axSpA with objective signs of inflammation as indicated by elevated c-reactive protein (CRP) and/or MRI who have responded inadequately or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs) and adults with active AS who have responded inadequately or are intolerant to conventional therapy. Bimekizumab can be used in both the 1st line setting for treatment-naïve patients and in a 2nd line setting for treatment-experienced patients. Based on the current recommendation in the Danish Medicines Council (DMC) drug recommendation for the use of biologic treatment of axSpA[1] bimekizumab is expected to be positioned in patients previously treated with adalimumab or another 1st line treatment with an assumed uptake of 10-15% of the patients switching to a different mode of action (MoA).

5.2 Current treatment options and choice of comparator(s)

5.2.1 Current treatment options

New treatment options are required since many axSpA patients fail to achieve remission or low disease activity

The treatment of axSpA aims to control inflammation, reduce symptoms, and prevent progression to structural damage. The ASAS-EULAR and ACR/SPARTAN/SAA treatment goals are centred around maintaining patients´ functioning and maximising long-term quality of life[30, 31]. This includes control of symptoms and inflammation, prevention of progressive structural damage, and preservation of function and social participation/ability to work. The treatment of patients with axSpA should therefore be individualised based on the current signs and symptoms of disease (axial, peripheral, extra-articular manifestations) and patient characteristics, which include comorbidities and psychosocial factors[31].

The current standard treatment in Denmark is governed by the drug recommendation from the DMC for the use of biologic treatment of axSpA[1]. The DMC treatment recommendation splits the patient populations into AS and nr-axSpA and further into subgroups depending on coexisting uveitis or inflammatory bowel disease.

Adalimumab is the current 1st line choice biological drug for both AS and nr-axSpA. Second choice of biological treatment is guided by price and reason for failure on primary treatment. In case of failure of primary therapy (TNFa) a drug with different MoA should be considered. If switch is caused by secondary failure (decreased response to treatment) or toxicity similar MoA can be considered. In August 2021, the DMC decided no longer to update the treatment recommendation for AS/nr-axSpA.

5.2.2 Choice of comparator(s)

The comparators of this intervention are the existing 1st line treatments in the treatment guideline and drug recommendation for AS and nr-axSpA being adalimumab, secukinumab, and ixekizumab.

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5.2.3 Description of the comparator(s)

5.2.3.1 Description of the adalimumab

Information on adalimumab[32] will be provided in the following.

- Generic name(s) (ATC-code): Adalimumab (L04AB04)
- Mode of action: Adalimumab binds specifically to TNF and neutralises the biological function of TNF by blocking its interaction with the p55 and p75 cell surface TNF receptors. Adalimumab also modulates biological responses that are induced or regulated by TNF, including changes in the levels of adhesion molecules responsible for leukocyte migration (ELAM-1, VCAM-1, and ICAM-1 with an IC_{50} of 0.1-0.2 nM).
- Pharmaceutical form: Solution for injection.
- Posology: 40 mg adalimumab administered every other week as a single dose via subcutaneous injection. Available data suggest that the clinical response is usually achieved within 12 weeks of treatment. Continued therapy should be reconsidered in a patient not responding within this time period.
- Method of administration: Subcutaneous injection. After proper training in injection technique, patients may self-inject if their physician determines that it is appropriate and with medical follow-up as necessary.
- Dosing: 40 mg adalimumab administered every other week as a single dose via subcutaneous injection.
- Should the pharmaceutical be administered with other medicines? No
- Treatment duration/criteria for end of treatment: Stopping treatment should be considered if a patient is not responding within 12 weeks of treatment.
- Necessary monitoring, both during administration and during the treatment period: Specialist follow-up and monitoring are necessary during the treatment period.
- Need for diagnostics or other tests (i.e., companion diagnostics): No
- Packaging: One 0.4 ml single dose pre-filled syringe contains 40 mg adalimumab. One 0.4 ml single dose pre-filled pen contains 40 mg adalimumab.

5.2.3.2 Description of the secukinumab

Information on secukinumab[33] will be provided in the following.

- Generic name(s) (ATC-code): Secukinumab (L04AC10)
- Mode of action: Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

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- Pharmaceutical form: Solution for injection
- Posology:
  - Ankylosing spondylitis (AS, radiographic axial spondyloarthritis): The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.
  - Non-radiographic axial spondyloarthritis (nr-axSpA): The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.
- Method of administration: Subcutaneous injection. After proper training in subcutaneous injection technique, patients may self-inject or be injected by a caregiver if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients or caregivers should be instructed to inject the full amount of secukinumab according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.
- Dosing: see posology description above
- Should the pharmaceutical be administered with other medicines? No
- Treatment duration/criteria for end of treatment: available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.
- Necessary monitoring, both during administration and during the treatment period: Specialist follow-up and monitoring are necessary during the treatment period.
- Need for diagnostics or other tests (i.e., companion diagnostics): No
- Packaging:
  - 150 mg solution for injection in pre-filled syringe. Each pre-filled syringe contains 150 mg secukinumab in 1 ml.
  - 300 mg solution for injection in pre-filled syringe. Each pre-filled syringe contains 300 mg secukinumab in 2 ml.
  - 150 mg solution for injection in pre-filled pen. Each pre-filled pen contains 150 mg secukinumab in 1 ml.
  - 300 mg solution for injection in pre-filled pen. Each pre-filled pen contains 300 mg secukinumab in 2 ml.

5.2.3.3 Description of ixekizumab

Information on ixekizumab[34] will be provided in the following.

- Generic name(s) (ATC-code): Ixekizumab (L04AC13)

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- Mode of action: Ixekizumab is an IgG4 monoclonal antibody that binds with high affinity (< 3 pM) and specificity to interleukin 17A (both IL-17A and IL-17A/F). Elevated concentrations of IL-17A have been implicated in the pathogenesis of psoriasis by promoting keratinocyte proliferation and activation, as well as in the pathogenesis of psoriatic arthritis and axial spondyloarthritis by driving inflammation leading to erosive bone damage and pathological new bone formation. Neutralisation of IL-17A by ixekizumab inhibits these actions. Ixekizumab does not bind to ligands IL-17B, IL-17C, IL-17D, IL-17E or IL-17F. In vitro binding assays confirmed that ixekizumab does not bind to human Fcγ receptors I, IIa, and IIIa or to complement component C1q.
- Pharmaceutical form: Solution for injection
- Posology: The recommended dose is 160 mg (two 80 mg injections) by subcutaneous injection at week 0, followed by 80 mg every 4 weeks. Consideration should be given to discontinuing treatment in patients who have shown no response after 16 to 20 weeks of treatment. Some patients with initially partial response may subsequently improve with continued treatment beyond 20 weeks.
- Method of administration: Subcutaneous injection.
- Dosing: The recommended dose is 160 mg (two 80 mg injections) by subcutaneous injection at week 0, followed by 80 mg every 4 weeks.
- Should the pharmaceutical be administered with other medicines? No
- Treatment duration/criteria for end of treatment: Consideration should be given to discontinuing treatment in patients who have shown no response after 16 to 20 weeks of treatment.
- Necessary monitoring, both during administration and during the treatment period:
    - After proper training in subcutaneous injection technique, patients may self-inject Taltz if a healthcare professional determines that it is appropriate. However, the physician should ensure appropriate follow-up of patients. Doses less than 80 mg which require dose preparation should only be administered by a healthcare professional.
    - Doctor or nurse will regularly monitor the patient's condition to check whether the treatment has the desired effect.
- Need for diagnostics or other tests (i.e., companion diagnostics): No
- Packaging: Each pre-filled syringe contains 80 mg ixekizumab in 1 ml.

5.3 The intervention - bimekizumab

Information on how bimekizumab will be used in clinical practice is described below.

- Generic name(s) (ATC-code): bimekizumab (L04AC21)
- Mode of action: see section 1
- Pharmaceutical form: solution for injection
- Posology: see section 1
- Method of administration: Bimekizumab is administered by subcutaneous injection. The pre-filled syringe or pre-filled pen must not be shaken. After proper training in subcutaneous injection technique, patients may self-inject Bimzelx with the pre-filled syringe or pre-filled pen if their physician determines

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that it is appropriate and with medical follow-up as necessary. Patients should be instructed to inject the full amount of Bimzelx according to the instructions for use provided in the package leaflet.

- Dosing: 160 mg solution of bimekizumab for injection in pre-filled syringe or pen every 4 weeks
- Should the pharmaceutical be administered with other medicines? No
- Treatment duration/criteria for treatment discontinuation: Consideration should be given to discontinuing treatment in patients who have shown no improvement by 16 weeks of treatment.
- Necessary monitoring, during administration, during the treatment period, and after the end of treatment:

  After proper training in subcutaneous injection technique, patients may self-inject Bimzelx with the pre-filled syringe or pre-filled pen if their physician determines that it is appropriate and with medical follow-up as necessary.
- Need for diagnostics or other tests (i.e., companion diagnostics): No
- Packaging: One pre-filled syringe contains 160 mg bimekizumab in one mL

Bimekizumab can be used in both the 1st line setting for treatment-naïve patients and in a 2nd line setting for treatment-experienced patients. The current treatment algorithm for treatment-naïve patients is not expected to change.

6. Literature search and identification of efficacy and safety studies

UCB has conducted comparisons to the currently approved and recommended treatments via indirect treatment comparisons (ITCs). These ITCs are based on a global systematic literature review (SLR) from January 2023 of all interventions approved in the EU or US. Embase, MEDLINE (comprising MEDLINE Daily, In-Process & Other Non-indexed citations, and e-pub ahead-of-print), the Cochrane Central Register of Controlled Trials (CENTRAL), and the Cochrane Database of Systematic Reviews (CDSR) were all searched via the Ovid platform. From the global SLR the relevant comparators and studies were selected for the Danish-specific comparisons.

6.1 Identification and selection of relevant studies

The relevant studies identified in the global SLR are listed in Table 3. The Canadian AS trial was considered at the SLR stage but excluded from all analyses due to lack of results being reported and no events regarding the safety outcomes being considered.

6.2 List of relevant studies

Table 3 Relevant studies included in the assessment

Reference (title, author, journal, year)	Trial name	NCT number	Dates of study (start and expected completion date)	Used in comparison of*
Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two	BE MOBILE 1	NCT03928704	Start: April 26, 2019 Expected completion date: June 15, 2023	For nr-axSpA TNF naive and TNF experienced: Bimekizumab vs adalimumab

Reference (title, author, journal, year)	Trial name	NCT number	Dates of study (start and expected completion date)	Used in comparison of*
parallel phase 3 randomised controlled trials, van der Heijde, Ann Rheum Dis, 2023				Bimekizumab vs secukinumab Bimekizumab vs ixekizumab
Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials, van der Heijde, Ann Rheum Dis, 2023	BE MOBILE 2	NCT03928743	Start: April 26, 2019 Completion date: August 8, 2022	For AS TNF naïve and TNF experienced: Bimekizumab vs adalimumab Bimekizumab vs secukinumab Bimekizumab vs ixekizumab
Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. van der Heijde et al. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology* 2006	ATLAS	NCT00085644	Start date: January 2004 Completion date: July 2009	Bimekizumab vs. adalimumab for AS TNF naïve patients
Efficacy and safety of adalimumab in Chinese adults with active ankylosing spondylitis: results of a randomised, controlled trial. Huang et al. *Ann Rheum Dis* 2014	Huang 2013	NCT01114880	Start date: January 2010 Completion date: February 2011	Bimekizumab vs. adalimumab for AS TNF naïve patients
Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial	COAST-V	NCT02696785	Start date: May 2, 2016 Completion date: October 17, 2018	Bimekizumab vs. adalimumab for AS TNF naïve patients

Reference (title, author, journal, year)	Trial name	NCT number	Dates of study (start and expected completion date)	Used in comparison of*
spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. van der Heijde et al. *Lancet* 2018				
Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. Baeten et al. The New England journal of medicine 2015	MEASURE 2	NCT01649375	Start: October 18, 2012 Completion date: September 18, 2018	Bimekizumab vs. secukinumab for AS TNF experienced patients
Evaluation of the nonsteroidal anti-inflammatory drug-sparing effect of secukinumab in patients with ankylosing spondylitis: Multicenter, randomised, double-blind, phase iv study. Kiltz et al. *Arthritis and Rheumatology* 2021	ASTRUM	NCT02763046	Start: May 31, 2016 Completion date: September 24, 2019	Bimekizumab vs. secukinumab for AS TNF experienced patients
Secukinumab provides rapid and significant improvement in the signs and symptoms of ankylosing spondylitis: Primary (16-week) results from a phase 3 china-centric study,	MEASURE 5	NCT02896127	Start: October 18, 2016 Completion date: March 19, 2019	Bimekizumab vs. secukinumab for AS TNF experienced patients

Reference (title, author, journal, year)	Trial name	NCT number	Dates of study (start and expected completion date)	Used in comparison of*
measure 5 [abstract FRI0414]. Huang et al. *Annals of the Rheumatic Diseases* 2019.				
Efficacy and Safety of Secukinumab 150 mg with and Without Loading Regimen in Ankylosing Spondylitis: 104-week Results from MEASURE 4 Study. Kivitz et al. *Rheumatol Ther* 2018	MEASURE 4	NCT02159053	Start: May 18, 2015 Completion date: January 2, 2018	Bimekizumab vs. secukinumab for AS TNF experienced patients
Efficacy and Safety of Ixekizumab in the Treatment of Radiographic Axial Spondyloarthritis: Sixteen-Week Results From a Phase III Randomized, Double-Blind, Placebo-Controlled Trial in Patients With Prior Inadequate Response to or Intolerance of Tumor Necrosis Factor Inhibitors. Deodhar et al. *Arthritis Rheumatol* 2019.	COAST-W	NCT02696798	Start date: April 12, 2016 Completion date: May 3, 2019	Bimekizumab vs. ixekizumab for AS TNF experienced patients
Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). Sieper et al. *Ann Rheum Dis* 2013	ABILITY1	NCT00939003	Start: July 2009 Completion date: August 2013	Bimekizumab vs. adalimumab for nr-AxSpA TNF naïve patients

Reference (title, author, journal, year)	Trial name	NCT number	Dates of study (start and expected completion date)	Used in comparison of*
Improvement of Signs and Symptoms of Nonradiographic Axial Spondyloarthritis in Patients Treated With Secukinumab: Primary Results of a Randomized, Placebo-Controlled Phase III Study. Deodhar et al. *Arthritis and Rheumatology* 2021	PREVENT	NCT02696031	Start: April 29, 2016 Completion date: March 11, 2021	Bimekizumab vs. secukinumab for nr-AxSpA TNF experienced patients
Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial. Deodhar et al. *Lancet* 2020	COAST-X	NCT02757352	Start date: August 2, 2016 Completion date: May 7, 2019	Bimekizumab vs. ixekizumab for nr-AxSpA TNF experienced patients

For detailed information about included studies, refer to appendix B.

7. Efficacy and safety

The clinical evidence for bimekizumab indicates clinical equivalence to the existing treatments in 1st line in the treatment guideline and drug recommendation for AS and nr-axSpA valid until end-March 2022 such as adalimumab, secukinumab and ixekizumab. Current treatments used after adalimumab, such as ixekizumab and secukinumab, have previously been assessed by the DMC to be equivalent with existing biologic treatments[3, 4]. Both ixekizumab and secukinumab are considered to be relevant treatment comparators for bimekizumab as they are both 1st line treatments typically used after adalimumab or after another biological treatment.

In the following subsections bimekizumab will be compared to adalimumab, secukinumab and ixekizumab for AS and nr-axSpA patients, respectively.

The studies included in the analyses within AS for bimekizumab (BE MOBILE 2), adalimumab (ATLAS, Huang 2013, COAST-V, ixekizumab (COAST-W) and secukinumab (ASTRUM, MEASURE 2, MEASURE 4 and MEASURE 5) are similar in terms of inclusion criteria relating to classification criteria as all studies utilized a clinical diagnosis of ankylosing spondylitis (AS) fulfilling ASAS/modified New York criteria, disease activity

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(BASDAI score ≥4 ± spinal pain (BASDAI Q2) score ≥4 ± morning stiffness. Studies were similar in terms of the mean BASDAI, ASDAS, and CRP scores indicating a similar level of disease activity across the trials.

In general, the studies are similar in terms of the main baseline characteristics (if reported [please see appendix C for a full overview of baseline characteristics]), with the following exception noted regarding the mean age of patients in the COAST-W study was higher compared with other studies.

The analyses included a mixed set of studies in relation to prior bDMARD experience:

- One study included 100% bDMARD experienced patients (COAST-W)
- Three studies included 100% bDMARD naive patients: ATLAS, Huang 2013, and COAST-V
- Five studies included some bDMARD experienced patients: MEASURE 2 (39%), MEASURE 4 (~27%), MEASURE 5 (~20.8%), ASTRUM (~28%) and BE MOBILE 2 (~ 16.3%)

The studies included in the analyses within nr-axSpA for bimekizumab (BE MOBILE 1), adalimumab (ABILITY-1), ixekizumab (COAST-X) and secukinumab (PREVENT) are similar in terms of inclusion criteria with exceptions noted below:

- classification criteria: sacroiliitis on the screening magnetic resonance imaging (MRI) and/or elevated CRP (and/or fulfils ASAS criteria)
- disease activity: BASDAI score ≥4 ± spinal pain (BASDAI Q2) score ≥4 ± morning stiffness
- inadequate response ≥1 or ≥2 NSAIDs, ± intolerance or contraindication(s) to NSAIDs

The analyses included a mixed set of studies in relation to prior bDMARD experience:

- Two studies allowed for bDMARD experienced patients to be included in the study (BE MOBILE 1 and PREVENT):
    - A higher % of patients were bDMARD experienced in the PBO arm compared with the active arms in BE MOBILE 1 (12.7% compared with 9.4%).
    - Data in the bDMARD experienced subgroup (9.7%) for PREVENT are not reported in the public domain.
    - Data in the bDMARD experienced subgroup (approx. 10.6%) for BE MOBILE 1 are not reported in the public domain.
- Two studies were 100% bDMARD naïve: ABILITY-1 and COAST-X
    - In addition, data are also available for the bDMARD naïve subgroup of patients for BE MOBILE 1 and PREVENT.

7.1 Efficacy and safety of bimekizumab compared to adalimumab for AS bDMARD naïve patients

7.1.1 Relevant studies

The comparison of bimekizumab versus adalimumab is based on the ATLAS, Huang 2013, COAST-V trials for estimating the effect of adalimumab and the BE MOBILE 2 trial for bimekizumab. All adalimumab studies included a bDMARD naïve population whereas the BE MOBILE 2 consisted of a mixed population with 16.3% being bDMARD experienced patients.

For the analyses presented a subgroup population from the BE MOBILE 2 has been used to match the populations of the adalimumab trials. Analyses of safety outcomes are based on the ITT populations.

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BE MOBILE 2 is a multicentre, Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in study participants with active AS, a sub population of axSpA with r-axSpA. To be eligible to participate in this study, study participants must have been adults with a diagnosis of active AS, determined by documented radiologic evidence (x-ray) fulfilling the modified New York criteria for AS, including at least 3 months of symptoms and age at symptom onset <45 years, and moderate to severe active disease at baseline as defined by: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 and spinal pain ≥4 on a 0 to 10 numeric rating scale (NRS) (from BASDAI Item 2). Subjects had to have either failed to respond to 2 different nonsteroidal anti-inflammatory drugs (NSAIDs) given at the maximum tolerated dose for a total of 4 weeks or have a history of intolerance to or a contraindication to NSAID therapy. Patients who have taken a tumour necrosis factor alpha (TNFα) inhibitor must have experienced an inadequate response or intolerance to treatment given at an approved dose for at least 12 weeks. Eligible study participants were randomized 2:1 to receive 1 of 2 treatments (bimekizumab 160mg sc Q4W or placebo sc Q4W) and remain on their allowable background medication. At the end of the 16-week Double-Blind Treatment Period, study participants receiving placebo were re-allocated to bimekizumab treatment at Week 16 after all assessments had been completed. These study participants received bimekizumab 160mg sc at Week 16 and 160mg sc Q4W thereafter. Starting at Week 20, nonbiologic rescue therapy for axSpA may have been adjusted or added, while continuing bimekizumab.
Interim analyses of all available data (including efficacy, safety, PK, and immunogenicity) were conducted after the planned number of randomized study participants completed 24 weeks and 52 weeks of treatment.

The primary efficacy endpoint for this study was the ASAS40 response at Week 16.
Data for week 52 is presented in appendix K.

ATLAS was a multicentre, randomized (2:1 ratio), double-blind, placebo-controlled study to evaluate a subcutaneous injection of adalimumab, 40 mg every other week, compared with placebo for 24 weeks. Patients were classified as having AS based on the modified New York criteria. All had active disease, defined by fulfilling at two of the following criteria: BASDAI score ≥4, a total back pain score ≥4 by VAS, or a duration of morning stiffness ≥1 hour. Patients who had previously received anti-TNF therapy were excluded. Enrolled patients were randomly assigned in a 2:1 ratio to receive adalimumab 40 mg or placebo every other week for 24 weeks. The primary efficacy end point was the percentage of patients with a 20% response according to ASAS20 at week 12, whereas ASAS40 was reported as secondary endpoint.[35]

Huang 2013 was a placebo-controlled, double-blind, randomised, phase III trial conducted between January 2010 and February 2011 in China (NCT01114880). Eligible patients fulfilled the modified New York criteria, had active disease, as defined by ≥2 of the following: BASDAI ≥4 cm, total back pain VAS ≥4 cm, and ≥1 hour of morning stiffness, and had an inadequate response or were intolerant to ≥1 NSAID. Prior exposure to anti-TNF therapy within 28 days of baseline was not allowed. Following a screening period of up to 4 weeks, participants were centrally randomised using an interactive voice response or web-based system in a 2:1 ratio to receive adalimumab 40 mg or matching placebo subcutaneously every other week during a 12-week double-blind phase. The double-blinded period was followed by a 12-week open-label phase, during which all patients received open-label adalimumab 40 mg Q2W.[36]

COAST-V was a phase 3, randomised, double-blind, placebo-controlled study of ixekizumab. Adult patients with inadequate response or intolerance to non-steroidal anti-inflammatory drugs, an established diagnosis of radiographic axial spondyloarthritis (AS), radiographic sacroiliitis centrally defined by modified New York

criteria, and at least one spondyloarthritis (SpA) feature according to the ASAS criteria, were recruited from 84 sites (12 countries) in Europe, Asia, and North America. Prior or current treatment with bDMARDs was excluded. By use of a computer-generated random sequence, patients were randomly assigned (1:1:1:1) to 80 mg subcutaneous ixekizumab every two (Q2W) or four (Q4W) weeks, 40 mg adalimumab Q2W (active reference group), or placebo. The primary objective was to compare the proportion of patients achieving an ASAS40 response, a composite measure of clinical improvement in axial spondyloarthritis (axSpA), at week 16 for both ixekizumab treatment groups versus the placebo group. The adalimumab reference group was included as an in-study active reference for comparison with placebo to provide additional context to interpretation of the ixekizumab study results.

7.1.2 Efficacy and safety – results per study

7.1.2.1 Efficacy and safety – bimekizumab (BE MOBILE 2)

BE MOBILE 2 met its primary objective and demonstrated that treatment with bimekizumab 160mg Q4W was superior to placebo in providing robust, statistically significant, and clinically meaningful improvements at Week 16 in disease activity as measured by ASAS40 response rate, in study participants with active AS. No impact of the COVID-19 pandemic was observed on ASAS40 response rates; ASAS40 response rates analysed in the COVID-19 Free Set (CFS) or analysed by timing of the Week 16 Visit showed a similar improvement of bimekizumab over placebo as the primary analysis.

BE MOBILE 2 also met all ranked secondary efficacy endpoints. Statistically significant improvements were observed in the bimekizumab 160mg Q4W group compared with the placebo group at Week 16 for ASAS40 response in TNFα inhibitor naïve participants, ASAS20, BASDAI, ASAS-PR, ASDAS-MI, ASAS5/6, BASFI, NSP, ASQoL total score, SF-36 PCS (all comparisons p≤0.001), and BASMI (p=0.006) which resulted in meaningful improvement after bimekizumab treatment.

Following treatment with bimekizumab, improvements over placebo for efficacy endpoints related to the signs and symptoms of AS and their impact on patients' lives were rapid and observed as early as Week 2 (after the first dose of bimekizumab) with continued improvement to Week 16. Improvement across efficacy endpoints was sustained from Week 16 to Week 52 or further improved up to Week 52.

Study participants who switched from placebo to bimekizumab 160mg Q4W at Week 16 showed marked improvement across the spectrum of efficacy endpoints and showed similar levels of efficacy at Week 24 compared with Week 16 or Week 24 for participants randomized to bimekizumab treatment and additional improvement or a sustained response to Week 52.

For endpoints measuring participants' quality of life (SF-36 PCS), greater improvements in the bimekizumab 160mg Q4W group were observed compared with the placebo group up to Week 16.

To match the bDMARD population in scope the ITCs features a subgroup of bDMARD naïve patients from BE MOBILE 2 to compare with the bDMARD naïve comparator studies. The results of the bDMARD naïve subgroup for selected endpoints are provided in Table 4.

Table 4 Results of the bDMARD naïve subgroup at week 16 (from BE MOBILE 2)

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	84	184	22	94	1.95 (1.31; 2.90)	22%	0.22 (0.11; 0.33)

ASDAS< 2.1	Bimekizumab	Placebo	16	86	184	18	94	2.44 (1.57; 3.80)	28%	0.28 (0.17; 0.38)
BASDAI50	Bimekizumab	Placebo	16	90	184	23	94	2.00 (1.36; 2.94)	24%	0.24 (0.13; 0.36)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)

Endpoint	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
SF36-PCS	Bimekizumab	Placebo	16	184	9.7	8.8	94	6	7.4	3.70 (1.62; 5.78)
SF36-MCS	Bimekizumab	Placebo	16	184	2.1	8.3	94	1.4	6.2	0.70 (-1.20; 2.60)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.1.2.2 Efficacy and safety – adalimumab (ATLAS, Huang 2013, and COAST-V)

The following studies of adalimumab are used to inform the indirect comparison: ATLAS, Huang 2013, COAST-V trials All adalimumab studies included a bDMARD naïve population, hence all estimates are derived from the ITT populations. All studies were used to inform a meta-analysis of efficacy and safety of adalimumab.

All studies reported the relevant endpoints except ASDAS<2.1 and SF36-MCS where data only were available from COAST-V (ASDAS<2.1) and ATLAS and Huang 2013 (SF36-MCS), respectively,

Data was not available for serious infections, SF-36 vitality subdomain and discontinuation due to lack of efficacy due to lack of data in the included studies.

The studies demonstrated that adalimumab was superior to placebo in statistically significant, and clinically meaningful improvements at Week 16 across all relevant endpoints.

Table 5 Results for ASAS40 (bDMARD naïve) at week 16

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ATLAS	Adalimumab	Placebo	12	83	208	14	107	3.05 (1.82; 5.11)	27%	0.27 (0.18; 0.36)

Huang 2013	Adalimumab	Placebo	12	102	229	11	115	4.66 (2.61; 8.32)	35%	0.35 (0.27; 0.43)
COAST-V	Adalimumab	Placebo	16	32	90	16	87	1.93 (1.15; 3.26)	17%	0.17 (0.04; 0.30)
Meta-analysis	**Adalimumab**	**Placebo**						**2.93 (2.15; 4.00)**	**29%**	**0.29 (0.23; 0.34)**

Table 6 Results for ASDAS<2.1 (bDMARD naïve) at week 16

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
COAST-V	Adalimumab	Placebo	16	34	90	11	87	2.99 (1.62; 5.51)	25%	0.25 (0.13; 0.37)

Table 7 Results for BASDAI50 (bDMARD naïve) at week 16

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ATLAS	Adalimumab	Placebo	12	94	208	17	107	2.84 (1.79; 4.51)	29%	0.29 (0.20; 0.39)
Huang 2013	Adalimumab	Placebo	12	114	229	19	115	3.01 (1.96; 4.64)	33%	0.33 (0.24; 0.43)
COAST-V	Adalimumab	Placebo	16	29	90	15	87	1.87 (1.08; 3.24)	15%	0.15 (0.02; 0.27)
Meta-analysis	Adalimumab	Placebo						2.62 (2.00; 3.45)	28%	0.28 (0.22; 0.34)

Table 8 Results for SF36-PCS (bDMARD naïve) at week 16

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
Huang 2013	Adalimumab	Placebo	12	229	6.6	6.4	115	4	6.3	2.60 (1.17; 4.03)

ATLAS	Adalimumab	Placebo	12	208	6.9	8.7	107	1.6	8.3	5.30 (3.30; 7.30)
COAST-V	Adalimumab	Placebo	16	90	6.9	6.9	87	3.6	7	3.30 (1.25; 5.35)
Meta-analysis	Adalimumab	Placebo								3.46 (2.45; 4.47)

Table 9 Results for SF36-MCS (bDMARD naïve) at week 16

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
Huang 2013	Adalimumab	Placebo	12	229	5.1	9.9	115	2.8	9.4	2.30 (0.12; 4.48)
ATLAS	Adalimumab	Placebo	12	208	2.7	10	107	2.4	10	0.30 (-2.03; 2.63)
Meta-analysis	Adalimumab	Placebo								1.37 (-0.23; 2.96)

Table 10 Results for discontinuation due to AEs (ITT population) at week 16

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ATLAS	Adalimumab	Placebo	12	2	208	2	107	0.51 (0.07; 3.60)	-1%	-0.01 (-0.04; 0.02)
Huang 2013	Adalimumab	Placebo	12	4.5*	230	0.5*	116	4.54 (0.25; 83.60)	2%	0.02 (0.00; 0.03)
COAST-V	Adalimumab	Placebo	16	1.5*	91	0.5*	88	2.90 (0.12; 70.27)	1%	0.01 (-0.01; 0.03)
Meta-analysis	Adalimumab	Placebo						1.25 (0.30; 5.30)	1%	0.01 (0.00; 0.02)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

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7.1.3 Comparative analyses of efficacy and safety

Method of synthesis

The comparability with respect to baseline characteristics between the relevant studies included in the ITC were qualitatively assessed. Full details on the baseline characteristics of the studies are provided in Appendix B Main characteristics of included studies. The study design (inclusion and exclusion criteria) and patient characteristics were deemed comparable, however reporting of all ITT-analyses were reported at week 16 for the newer studies and at week 12 for the older adalimumab studies. The synthesis by ITC was however deemed feasible given the underlying assumption that the treatment effect had stabilized, and only minor change would be expected. The baseline characteristics were very similar, and overall, the differences were considered minor, therefore justifying an unadjusted indirect treatment comparison using Bucher's method.

The specified endpoints for analyses were ASAS40, BASDAI50, ASDAS<2.1, SF-36 and safety based on previous DMC assessment and protocols within AS and nr-axSpA.[28, 37]

The ITC is a statistical method used to pool results across a number of trials with comparable patient populations linked by common comparators. The technique assumes that, on a suitable scale, one can add and subtract the within study estimates of relative treatment effects. For example, direct data comparing treatment A with C and B with C can be used to indirectly compare A and B. This is under the assumption that the following relationship between the estimated treatment effects holds: (A–B) = (A–C)–(B–C). The underlying methodology for the ITC is the Bucher et al. 1997 method, which is a frequentist approach to evidence synthesis. For this analysis continuous outcomes were assessed in terms of mean difference. Binary outcomes were assessed in terms of relative risk (RR) and risk difference (RD). Significance of treatment effect for the frequentist method was determined by the two-sided 95% CI and tests with two-sided p-values less than 0.05 are referred to as being statistically significant.

Results from the comparative analysis

7.1.3.1 ASAS40 (bDMARD naïve)

Result of the ASAS40 ITC demonstrates that the point estimate did not favour bimekizumab with a non-statistically significant absolute risk difference of -6% (95% CI: -0.19; 0.06) and a risk ratio of 0.67 (95% CI: 0.40;1.10). The results are not statistically significant for ASAS40 and it can be concluded that the treatment effect as measured by ASAS40 can be considered similar for bimekizumab and adalimumab.

Table 11 ASAS40 (Data based on the subgroup of bDMARD naïve patients from BE MOBILE 2 vs adalimumab meta-analysis of bDMARD naïve only)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ATLAS	Adalimumab	Placebo	12	83	208	14	107	3.05 (1.82; 5.11)	27%	0.27 (0.18; 0.36)

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Huang 2013	Adalimumab	Placebo	12	102	229	11	115	4.66 (2.61; 8.32)	35%	0.35 (0.27; 0.43)
COAST-V	Adalimumab	Placebo	16	32	90	16	87	1.93 (1.15; 3.26)	17%	0.17 (0.04; 0.30)
Meta-analysis	**Adalimumab**	**Placebo**						**2.93 (2.15; 4.00)**	**29%**	**0.29 (0.23; 0.34)**
BE MOBILE 2 naive	Bimekizumab	Placebo	16	84	184	22	94	1.95 (1.31; 2.90)	22%	0.22 (0.11; 0.33)
Indirect comparison	**Bimekizumab**	**Adalimumab**						**0.67 (0.40; 1.10)**	**-6%**	**-0.06 (-0.19; 0.06)**

7.1.3.2 ASDAS<2.1 (bDMARD naïve)

Only COAST-V provided data for ASDAS<2.1 to inform the ITC. Result of the ITC demonstrates that the absolute risk difference point estimate favours bimekizumab with 2% although the risk ratio of 0.82 (95% CI: 0.38;1.74) did not favour bimekizumab. The discrepancy is due by the difference in placebo rate which is higher for BE MOBILE hence penalizing BKZ on the relative scale. The results are not statistically significant for ASDAS<2.1 and it can be concluded that the treatment effect as measured by ASDAS<2.1 can be considered similar for bimekizumab and adalimumab.

Table 12 ASDAS<2.1 (Data based on the subgroup of bDMARD naïve patients from BE MOBILE 2 vs adalimumab meta-analysis of bDMARD naïve only)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-V	Adalimumab	Placebo	16	34	90	11	87	2.99 (1.62; 5.51)	25 %	0.25 (0.13; 0.37)
BE MOBILE 2 naive	Bimekizumab	Placebo	16	86	184	18	94	2.44 (1.57; 3.80)	28 %	0.28 (0.17; 0.38)
indirect comparison	**Bimekizumab**	**Adalimumab**						**0.82 (0.38; 1.74)**	**2%**	**0.02 (-0.14; 0.19)**

7.1.3.3 BASDAI50 (bDMARD naïve)

Result of the BASDAI50 ITC demonstrates a marginal absolute risk difference with a point estimate of -3% which do not favour bimekizumab and a risk ratio of 0.76 (95% CI: 0.48; 1.22). The result is not statistically

significant for BASDAI50 and it can be concluded that the treatment effect as measured by BASDAI50 can be considered similar for bimekizumab and adalimumab.

Table 13 BASDAI50 (Data based on the subgroup of bDMARD naïve patients from BE MOBILE 2 vs adalimumab meta-analysis of bDMARD naïve only)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
ATLAS	Adalimumab	Placebo	12	94	208	17	107	2.84 (1.79; 4.51)	29 %	0.29 (0.20; 0.39)
Huang 2013	Adalimumab	Placebo	12	114	229	19	115	3.01 (1.96; 4.64)	33 %	0.33 (0.24; 0.43)
COAST-V	Adalimumab	Placebo	16	29	90	15	87	1.87 (1.08; 3.24)	15 %	0.15 (0.02; 0.27)
Meta-analysis	**Adalimumab**	**Placebo**						**2.62 (2.00; 3.45)**	**28 %**	**0.28 (0.22; 0.34)**
BE MOBILE 2 naive	Bimekizumab	Placebo	16	90	184	23	94	2.00 (1.36; 2.94)	24 %	0.24 (0.13; 0.36)
indirect comparison	**Bimekizumab**	**Adalimumab**						**0.76 (0.48; 1.22)**	**-3%**	**-0.03 (-0.16; 0.10)**

7.1.3.4 SF36-PCS (bDMARD naïve)

For SF36-PCS, the result of the ITC demonstrates that the point estimate favours bimekizumab with a difference in mean change of 0.24 (95% CI: -2.07; 2.55) although the result is not statistically significant for the SF36-PCS domain. The conclusion is that the treatment effect as measured by SF36-PCS can be considered similar for bimekizumab and adalimumab.

Table 14 SF36-PCS (Data based on the subgroup of bDMARD naïve patients from BE MOBILE 2 vs adalimumab meta-analysis of bDMARD naïve only)

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
Huang 2013	Adalimumab	Placebo	12	229	6.6	6.4	115	4	6.3	2.60 (1.17; 4.03)

ATLAS	Adalimumab	Placebo	12	208	6.9	8.7	107	1.6	8.3	5.30 (3.30; 7.30)
COAST-V	Adalimumab	Placebo	16	90	6.9	6.9	87	3.6	7	3.30 (1.25; 5.35)
Meta-analysis	**Adalimumab**	**Placebo**								**3.46 (2.45; 4.47)**
BE MOBILE 2 naive	Bimekizumab	Placebo	16	184	9.7	8.8	94	6	7.4	3.70 (1.62; 5.78)
indirect comparison	**Bimekizumab**	**Adalimumab**								**0.24 (-2.07; 2.55)**

7.1.3.5 SF36-MCS (bDMARD naïve)

For SF36-MCS the result of the ITC demonstrates that the point estimate did not favour bimekizumab with a difference in mean change of -0.67 (95% CI: -3.15; 1.81) although the result is not statistically significant for the SF36-MCS domain. For the interpretation of the results of should be noted that the baseline SF-36 MCS score for BE MOBILE 1 and 2 patients were close to the general population. The conclusion is that the treatment effect as measured by SF36-MCS can be considered similar for bimekizumab and adalimumab.

Table 15 SF36-MCS (Data based on the subgroup of bDMARD naïve patients from BE MOBILE 2 vs adalimumab meta-analysis of bDMARD naïve only)

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
Huang 2013	Adalimumab	Placebo	12	229	5.1	9.9	115	2.8	9.4	2.30 (0.12; 4.48)
ATLAS	Adalimumab	Placebo	12	208	2.7	10	107	2.4	10	0.30 (-2.03; 2.63)
Meta-analysis	**Adalimumab**	**Placebo**								**1.37 (-0.23; 2.96)**
BE MOBILE 2 naive	Bimekizumab	Placebo	16	184	2.1	8.3	94	1.4	6.2	0.70 (-1.20; 2.60)
indirect comparison	**Bimekizumab**	**Adalimumab**								**-0.67 (-3.15; 1.81)**

7.1.3.6 Discontinuation due to AEs (ITT population)

For discontinuation due to AEs, the result of the ITC demonstrates an absolute risk difference point estimate of no difference (0%) between bimekizumab and adalimumab. The risk ratio of 2.82 (95% CI: 0.11; 75.63) did not favour bimekizumab. The results are not statistically significant and should be interpreted with caution given that the number of events is zero in many arms and low in others. In the arms with zero events a continuity correction (+1 for N and +0,5 for n for both arms of the trial) was applied. The conclusion is that discontinuation due to AEs can be considered similar for bimekizumab and adalimumab.

Table 16 Discontinuation due to AEs (Data based on the full population of BE MOBILE 2 vs adalimumab meta-analysis of bDMARD naïve only)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
ATLAS	Adalimumab	Placebo	12	2	208	2	107	0.51 (0.07; 3.60)	-1%	-0,01 (-0,04; 0,02)
Huang 2013	Adalimumab	Placebo	12	4.5*	230	0.5*	116	4.54 (0.25; 83.60)	2%	0.02 (0.00; 0.03)
COAST-V	Adalimumab	Placebo	16	1.5*	91	0.5*	88	2.90 (0.12; 70.27)	1%	0.01 (-0.01; 0.03)
Meta-analysis	**Adalimumab**	**Placebo**						**1.25 (0.30; 5.30)**	**1%**	**0.01 (0.00; 0.02)**
BE MOBILE 2	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
indirect comparison	**Bimekizumab**	**Adalimumab**						**2.82 (0.11; 75.63)**	**0%**	**0.00 (-0.02; 0.02)**

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

For the ITC comparing bimekizumab to adalimumab in AS bDMARD naïve patients, a subgroup of bDMARD naïve patients from BE MOBILE2 for bimekizumab was compared to a meta-analysis of bDMARD naïve patients treated with adalimumab for the efficacy estimates, however for the safety endpoint, the full BE MOBILE 2 patient population for bimekizumab was used including 16% of experienced patients. None of the results from the ITC analysis were statistically significant i.e., based on the available data no differences in efficacy and safety between bimekizumab and adalimumab were identified and clinical equivalence between bimekizumab and adalimumab can be concluded.

Data was not available for serious infections, SF-36 vitality subdomain and discontinuation due to lack of efficacy due to lack of data in the included studies Therefore these endpoints were not possible to include into the ITC.

7.2 Efficacy and safety of bimekizumab compared to ixekizumab for AS bDMARD experienced patients

7.2.1 Relevant studies

Given the positioning of ixekizumab as a subsequent treatment after adalimumab, the main ITC analyses focus on the bDMARD experienced subpopulation (16.3%) of BE MOBILE 2 compared to COAST-W (100% bDMARD experienced). As this comparison limits the number of patients for the bimekizumab arm, and thus increases the uncertainty for the results, analyses for the BE MOBILE 2 ITT population are also provided. For completeness additional sensitivity analyses of the BE MOBILE 2 ITT population compared to the COAST-V trial (100% naïve) are also provided. These analyses have been provided for all endpoints presented below. Analyses of safety outcomes are based on the ITT populations.

BE MOBILE 2 please see study description in section 7.1.1.

COAST-W is a multicentre, phase III, randomized, double-blind, placebo-controlled, parallel-group, outpatient clinical trial. Eligible subjects were age ≥18 years, required to have an established diagnosis of axSpA and fulfilment of ASAS classification criteria for radiographic axSpA (AS) (i.e., radiographic evidence of sacroiliitis according to the modified New York criteria and having ≥1 SpA feature), and required to have a history of back pain for ≥3 months with an age at onset of <45 years. SI joint radiographs were scored by central readers. All patients fulfilling ASAS criteria for radiographic axSpA (AS) also fulfilled the modified New York criteria for AS.

Patients were randomly assigned (1:1:1) to receive subcutaneous administration of ixekizumab 80 mg every 2 weeks (IXEQ2W group), ixekizumab 80 mg every 4 weeks (IXEQ4W group), or matched placebo from week 0 to week 16. Patients randomized to the ixekizumab treatment regimens were randomized (1:1) to receive either an 80-mg or 160-mg starting dose of ixekizumab at week 0. The 2 starting doses were included in order to assess the impact of starting dose on week 16 responses, following regulatory agency feedback. All patients received the same frequency and number of injections regardless of treatment arm or assigned starting dose.

During the double-blinded treatment period (weeks 0–16), site personnel, patients, and the sponsor trial team were blinded with regard to treatment. Randomization to treatment groups was determined using a computer-generated, random-sequence, interactive web-response system with follow-up confirmation by site personnel using the confirmation number present on the investigational product packaging. Randomization of treatment assignment (including starting dose) was stratified by country, high-sensitivity C-reactive protein (CRP) level (≤5 or >5 mg/litre) at screening, and the number of prior TNFi taken (1 or 2) to achieve between-group comparability.

At week 16, patients entered the extended treatment period (weeks 16–52). Patients who were initially assigned to the placebo arm were, for the extended treatment period, randomly reassigned at week 16 to

IXEQ4W or IXEQ2W with a 160-mg starting dose. Patients already receiving ixekizumab remained on their assigned treatment regimens through week 52.

The primary end point of the trial was the proportion of patients achieving an ASAS 40% improvement in disease activity (ASAS40) 22 at week 16, with comparison of each ixekizumab dosing regimen to placebo.

COAST-V please study description in section 7.1.1.

7.2.2 Efficacy and safety – results per study

7.2.2.1 Efficacy and safety – bimekizumab (BE MOBILE 2)

The results of the bDMARD experienced subgroup for selected endpoints are provided in Table 17 and for the ITT population in Table 18

Table 17 Results of the bDMARD experienced subgroup from BE MOBILE 2 at week 16

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	15	37	3	17	2.30 (0.77; 6.89)	23%	0.23 (-0.01; 0.47)
ASDAS< 2.1	Bimekizumab	Placebo	16	7	37	1	17	3.22 (0.43; 24.13)	13%	0.13 (-0.04; 0.30)
BASDAI50	Bimekizumab	Placebo	16	13	37	6	17	1.00 (0.46; 2.17)	0%	0,00 (-0.28; 0.27)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Bimekizumab	Placebo	16	37	7.5	8.1	17	5	10	2.50 (-2.51; 7.51)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

Table 18 Results of the ITT population (16.3% experienced) from BE MOBILE 2 at week 16

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)

ASAS40	Bimekizumab	Placebo	16	99	221	25	111	1.99 (1.37; 2.89)	22%	0.22 (0.12; 0.32)
ASDAS< 2.1	Bimekizumab	Placebo	16	93	221	19	111	2.46 (1.59; 3.81)	25%	0.25 (0.15; 0.35)
BASDAI50	Bimekizumab	Placebo	16	103	221	29	111	1.78 (1.27; 2.51)	20%	0.20 (0.10; 0.31)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Bimekizumab	Placebo	16	221	9.3	8.7	111	5.9	7.9	3.40 (1.48; 5.32)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.2.2.2 Efficacy and safety – ixekizumab COAST-W and COAST-V

The results of the COAST-W study (100% bDMARD experienced) are provided in Table 19 and for COAST-V (100% bDMARD naïve) in Table 20

Table 19 Results of the ITT (100% bDMARD experienced) population from COAST-W at week 16

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Ixekizumab	Placebo	16	29	114	13	104	2.04 (1.12; 3.70)	13%	0.13 (0.03; 0.23)
ASDAS< 2.1	Ixekizumab	Placebo	16	20	114	5	104	3.65 (1.42; 9.37)	13%	0.13 (0.05; 0.21)
BASDAI50	Ixekizumab	Placebo	16	25	114	10	104	2.28 (1.15; 4.52)	12%	0.12 (0.03; 0.22)
Discontinuation due to AEs (ITT	Ixekizumab	Placebo	16	10	114	2	104	4.56 (1.02; 20.34)	7%	0.07 (0.01; 0.13)

population)										
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Ixekizumab	Placebo	16	114	6.3	7.5	104	1.4	8.2	4.90 (2.82; 6.98)

Table 20 Results of the ITT (100% bDMARD naïve) population from COAST-V at week 16

Endpoint	**Intervention**	**Comparator**	**Timepoint**	**n intervention**	**N intervention**	**n comparator**	**N comparator**	**RR (95%CI)**	**ARD**	**ARD (95%CI)**
ASAS40	Ixekizumab	Placebo	16	39	81	16	87	2.62 (1.59; 4.30)	30%	0.30 (0.16; 0.43)
ASDAS< 2.1	Ixekizumab	Placebo	16	35	81	11	87	3.42 (1.86; 6.27)	31%	0.31 (0.18; 0.43)
BASDAI50	Ixekizumab	Placebo	16	34	81	15	87	2.43 (1.44; 4.12)	25%	0.25 (0.11; 0.38)
Discontinuation due to AEs (ITT population)	Ixekizumab	Placebo	16	0	81	0	87	na	0%	0.00 (0.00; 0.00)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Ixekizumab	Placebo	16	81	7.1	7.9	87	3.6	7	3.50 (1.25; 5.75)

7.2.3 Comparative analyses of efficacy and safety

Method of synthesis

The comparability with respect to baseline characteristics between the relevant studies included in the ITC were qualitatively assessed. Full details on the baseline characteristics of the studies are provided in Appendix B Main characteristics of included studies. The study design (inclusion and exclusion criteria) and patient characteristics were deemed comparable. The baseline characteristics were very similar, and

overall, the differences were considered minor, therefore justifying an unadjusted indirect treatment comparison using Bucher's method.

Prior bDMARD experience differed between the studies, as previously described in Section 7, which should be considered when interpreting the results of the ITCs. In previous DMC assessments of secukinumab and ixekizumab within axSpA mixed prior bDMARD experience populations have been used for extrapolating the results onto either bDMARD naïve or experienced patient groups[28, 37]..

The specified endpoints for analyses were ASAS40, BASDAI50, ASDAS<2.1, SF-36 and safety based on previous DMC assessment and protocols within AS and nr-axSpA.[28, 37]

The ITC is a statistical method used to pool results across a number of trials with comparable patient populations linked by common comparators. The technique assumes that, on a suitable scale, one can add and subtract the within study estimates of relative treatment effects. For example, direct data comparing treatment A with C and B with C can be used to indirectly compare A and B. This is under the assumption that the following relationship between the estimated treatment effects holds: (A–B) = (A–C)–(B–C). The underlying methodology for the ITC is the Bucher et al. 1997 method, which is a frequentist approach to evidence synthesis. For this analysis continuous outcomes were assessed in terms of mean difference. Binary outcomes were assessed in terms of relative risk (RR) and risk difference (RD). Significance of treatment effect for the frequentist method was determined by the two-sided 95% CI and tests with two-sided p-values less than 0.05 are referred to as being statistically significant.

Results from the comparative analysis

7.2.3.1 ASAS40 (bDMARD experienced)

For the ASAS40 analysis of the bDMARD experienced patients from BE MOBILE 2 compared to COAST-W (100% experienced) the absolute risk difference point estimate favours bimekizumab (10%) with a risk ratio of 1.13 (95% CI: 0.32; 3.94). None of the results are statistically significant.

As sensitivity analyses, the comparison of the ITT population from BE MOBILE 2 (16.3% experienced) vs COAST-W (100% experienced) shows that the absolute risk difference point estimate favours bimekizumab (9%) with a risk ratio of 0.98 (95% CI: 0.48; 1.98). The comparison of the ITT population from BE MOBILE 2 (83.7% naive) vs COAST-V (100% naive) shows that the point estimate did not favour bimekizumab (-7%) with a risk ratio of 0.76 (95% CI: 0.41; 1.42). None of the results are statistically significant.

The conclusion is that the treatment effect as measured by ASAS40 can be considered similar for bimekizumab and ixekizumab.

Table 21 ASAS40 (Data based on the bDMARD experienced subgroup from BE MOBILE 2 vs experienced population of COAST-W)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)

COAST-W	Ixekizumab Q4W	Placebo	16	29	114	13	104	2.04 (1.12; 3.70)	13 %	0.13 (0.03; 0.23)
BE MOBILE 2 experienced	Bimekizumab	Placebo	16	15	37	3	17	2.30 (0.77; 6.89)	23 %	0.23 (-0.01; 0.47)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**1.13 (0.32; 3.94)**	**10 %**	**0.10 (-0.16; 0.36)**

Table 22 ASAS40 sensitivity analysis (Data based on the ITT population (16.3% experienced from BE MOBILE 2 vs experienced population of COAST-W)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-W	Ixekizumab Q4W	Placebo	16	29	114	13	104	2.04 (1.12; 3.70)	13 %	0.13 (0.03; 0.23)
BE MOBILE 2	Bimekizumab	Placebo	16	99	221	25	111	1.99 (1.37; 2.89)	22 %	0.22 (0.12; 0.32)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.98 (0.48; 1.98)**	**9%**	**0.09 (-0.05; 0.24)**

Table 23 ASAS40 sensitivity analysis (Data based on the ITT population from BE MOBILE 2 (83.7% naive) compared to COAST-V [100% naïve])

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-V	Ixekizumab Q4W	Placebo	16	39	81	16	87	2.62 (1.59; 4.30)	30 %	0.30 (0.16; 0.43)
BE MOBILE 2	Bimekizumab	Placebo	16	99	221	25	111	1.99 (1.37; 2.89)	22 %	0.22 (0.12; 0.32)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.76 (0.41; 1.42)**	**-7%**	**-0.07 (-0.24; 0.09)**

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7.2.3.2 ASDAS<2.1 (bDMARD experienced)

For the ASDAS<2.1 analysis of the bDMARD experienced patients from BE MOBILE 2 compared to COAST-W (100% experienced) the ITCs demonstrates that the absolute risk difference point estimate indicates that bimekizumab is equal to ixekizumab, however with a risk ratio of 0.88 (95% CI: 0.10; 8.16). None of the results are statistically significant for ASDAS<2.1.

For the sensitivity analyses, the comparison of the ITT population from BE MOBILE 2 (16.3% experienced) vs COAST-W (100% experienced) shows that the point estimate favours bimekizumab (12%) with a risk ratio of 0.67 (95% CI: 0.24; 1.91). The comparison of the ITT population from BE MOBILE 2 (83.7% naive) vs COAST-V (100% naïve) shows that the point estimate did not favour bimekizumab (-6%) with a risk ratio of 0.72 (95% CI: 0.34; 1.52). The different results would be expected considering the differences in the patient populations studied. None of the results are statistically significant.

It can be concluded that the treatment effect as measured by ASDAS<2.1 can be considered similar for bimekizumab and ixekizumab.

Table 24 ASDAS<2.1 (Data based on the bDMARD experienced subgroup from BE MOBILE 2 vs experienced population of COAST-W)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-W	Ixekizumab Q4W	Placebo	16	20	114	5	104	3.65 (1.42; 9.37)	13 %	0.13 (0.05; 0.21)
BE MOBILE 2 experienced	Bimekizumab	Placebo	16	7	37	1	17	3.22 (0.43; 24.13)	13 %	0.13 (-0.04; 0.30)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.88 (0.10; 8.16)**	**0%**	**0.00 (-0.18; 0.19)**

Table 25 ASDAS<2.1 (Data based on the ITT population from BE MOBILE 2 (16.3% experienced) vs experienced population of COAST-W)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-W	Ixekizumab Q4W	Placebo	16	20	114	5	104	3.65 (1.42; 9.37)	13 %	0.13 (0.05; 0.21)
BE MOBILE 2	Bimekizumab	Placebo	16	93	221	19	111	2.46 (1.59; 3.81)	25 %	0.25 (0.15; 0.35)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.67 (0.24; 1.91)**	**12 %**	**0.12 (0.00; 0.25)**

Table 26 ASDAS<2.1 (Data based on the ITT population from BE MOBILE 2 (83.7% naive) compared to COAST-V [100% naïve])

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-V	Ixekizumab Q4W	Placebo	16	35	81	11	87	3.42 (1.86; 6.27)	31 %	0.31 (0.18; 0.43)
BE MOBILE 2	Bimekizumab	Placebo	16	93	221	19	111	2.46 (1.59; 3.81)	25 %	0.25 (0.15; 0.35)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.72 (0.34; 1.52)**	**-6%**	**-0.06 (-0.22; 0.10)**

7.2.3.3 BASDAI50 (bDMARD experienced)

For the BASDAI50 analysis of the bDMARD experienced patients from BE MOBILE 2 compared to COAST-W (100% experienced) the result of the ITCs demonstrates that the absolute risk difference point estimate did not favour bimekizumab (-12%) with a risk ratio of 0.44 (95% CI: 0.15; 1.23). None of the results are statistically significant.

The sensitivity analysis comparing the ITT population from BE MOBILE 2 (16.3% experienced) vs COAST-W (100% experienced) shows that the point estimate favours bimekizumab (8%) although the risk ratio of 0.78 (95% CI: 0.36; 1.68) indicates the opposite. Further, the comparison of the ITT population from BE MOBILE 2 (83.7% naïve) vs COAST-V (100% naïve) shows that the point estimate did not favour bimekizumab (-4%) with a risk ratio of 0.73 (95% CI: 0.39; 1.37). None of the results are statistically significant.

It can be concluded that the treatment effect as measured by BASDAI50 can be considered similar for bimekizumab and ixekizumab.

Table 27 BASDAI50 (Data based on the bDMARD experienced subgroup from BE MOBILE 2 vs experienced population of COAST-W)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-W	Ixekizumab Q4W	Placebo	16	25	114	10	104	2.28 (1.15; 4.52)	12 %	0.12 (0.03; 0.22)
BE MOBILE 2 experienced	Bimekizumab	Placebo	16	13	37	6	17	1.00 (0.46; 2.17)	0%	0,00 (-0.28; 0.27)

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indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**				**0.44 (0.15; 1.23)**	**-12 %**	**-0.12 (-0.41; 0.17)**

Table 28 BASDAI50 (Data based on the ITT population from BE MOBILE 2 (16.3% experienced) vs experienced population of COAST-W (100% experienced))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-W	Ixekizumab Q4W	Placebo	16	25	114	10	104	2.28 (1.15; 4.52)	12 %	0.12 (0.03; 0.22)
BE MOBILE 2	Bimekizumab	Placebo	16	103	221	29	111	1.78 (1.27; 2.51)	20 %	0.20 (0.10; 0.31)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.78 (0.36; 1.68)**	**8%**	**0.08 (-0.06; 0.22)**

Table 29 BASDAI50 (Data based on the ITT population from BE MOBILE 2 (83.7% naive) compared to COAST-V [100% naïve])

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-V	Ixekizumab Q4W	Placebo	16	34	81	15	87	2.43 (1.44; 4.12)	25 %	0.25 (0.11; 0.38)
BE MOBILE 2	Bimekizumab	Placebo	16	103	221	29	111	1.78 (1.27; 2.51)	20 %	0.20 (0.10; 0.31)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.73 (0.39; 1.37)**	**-4%**	**-0.04 (-0.21; 0.13)**

7.2.3.4 SF36-PCS (bDMARD experienced)

For SF36-PCS, the result of the ITCs demonstrates that the point estimates did not favour bimekizumab with a difference in mean change of -2.40, -1.50 and -0.10 for the BE MOBILE 2 experienced subgroup vs COAST-W, BE MOBILE2 ITT vs COAST-W and BE MOBILE2 ITT vs COAST-V, respectively. None of the result are statistically significant. The conclusion is that the treatment effect as measured by SF36-PCS can be considered similar for bimekizumab and ixekizumab.

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Table 30 SF-36 PCS (Data based on the bDMARD experienced subgroup from BE MOBILE 2 vs experienced population of COAST-W)

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
COAST-W	Ixekizumab Q4W	Placebo	16	114	6.3	7.5	104	1.4	8.2	4.90 (2.82; 6.98)
BE MOBILE 2 experienced	Bimekizumab	Placebo	16	37	7.5	8.1	17	5	10	2.50 (-2.51; 7.51)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**								**-2.40 (-7.83; 3.03)**

Table 31 SF-36 PCS (Data based on the ITT population from BE MOBILE 2 (16.3% experienced) vs experienced population of COAST-W (100% experienced))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
COAST-W	Ixekizumab Q4W	Placebo	16	114	6.3	7.5	104	1.4	8.2	4.90 (2.82; 6.98)
BE MOBILE 2	Bimekizumab	Placebo	16	221	9.3	8.7	111	5.9	7.9	3.40 (1.48; 5.32)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**								**-1.50 (-4.34; 1.34)**

Table 32 SF-36 PCS (Data based on the ITT population from BE MOBILE 2 (83.7% naive) compared to COAST-V [100% naïve])

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
COAST-V	Ixekizumab Q4W	Placebo	16	81	7.1	7.9	87	3.6	7	3.50 (1.25; 5.75)

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BE MOBILE 2	Bimekizumab	Placebo	16	221	9.3	8.7	111	5.9	7.9	3.40 (1.48; 5.32)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**								**-0.10 (-3.06; 2.86)**

7.2.3.5 Discontinuation due to AEs (ITT population)

For discontinuation due to AEs, the result of the ITC demonstrates that the point estimate of the absolute risk difference favours bimekizumab (-5%) with a risk ratio of 0.77 (95% CI: 0.03; 21.23). The result is not statistically significant. Given that the number of events is zero in many arms and low in others the results should be interpreted with caution. In the arms with zero events a continuity correction (+1 for N and +0,5 for n for both arms of the trial) was applied. It can be concluded that discontinuation due to AEs can be considered similar for bimekizumab and ixekizumab.

Given that the number of events is 0 in all arms of the COAST-V trial no formal ITC is presented.

Table 33 Discontinuation due to AEs (Data based on the full population of BE MOBILE 2 (16.3% experienced) vs COAST-W (100% experienced))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95% CI)
COAST-W	Ixekizumab Q4W	Placebo	16	10	114	2	104	4.56 (1.02; 20.34)	7%	0.07 (0.01; 0.13)
BE MOBILE 2	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.77 (0.03; 21.23)**	**-5%**	**-0.05 (-0.12; 0.01)**

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.2.3.6 Conclusion

For the ITC comparing bimekizumab to ixekizumab in AS bDMARD experienced patients, a subgroup of bDMARD experienced patients from BE MOBILE 2 for bimekizumab was compared to the study COAST-W in 100% bDMARD experienced patients for ixekizumab for the efficacy estimates, however for the safety endpoint, the full BE MOBILE 2 patient population for bimekizumab was used including 16.3% of experienced patients. The ITC analyses proved that overall bimekizumab is favoured by most of the point estimates in the comparisons to ixekizumab, but the differences are not statistically significant. It can be concluded that bimekizumab is clinically equivalent to ixekizumab.

Data was not available for serious infections, SF-36 vitality subdomain, SF-36 mental component summary score and discontinuation due to lack of efficacy due to lack of data in the included studies. Therefore, these endpoints were not possible to include into the ITC.

7.3 Efficacy and safety of bimekizumab compared to secukinumab for AS bDMARD experienced patients

7.3.1 Relevant studies

The comparison of bimekizumab versus secukinumab is based on the ASTRUM, MEASURE 2, 3 and 5 trials for estimating the effect of secukinumab and the BE MOBILE 2 trial for bimekizumab. All secukinumab trials included a mixed bDMARD experienced population of MEASURE 2 (39% experienced), MEASURE 4 (~27% experienced), MEASURE 5 (~20.8% experienced), ASTRUM (~28% experienced) which aligns with the mixed bDMARD experienced population of BE MOBILE 2 for bimekizumab (16.3% experienced).

In the following tables, the main analyses based on the ITT populations i.e., mixed bDMARD experienced patients are presented. Also, sensitivity analyses are presented based on subgroup populations of the bDMARD experienced patients from the trials – this is considered a sensitivity analysis due to the low patient numbers in this subgroup analysis. Analyses of safety outcomes are based on the ITT populations.

BE MOBILE 2 please study description in section 7.1.1.

MEASURE 2 is a randomized, double-blind, placebo-controlled phase 3 trials. Eligible patients were 18 years of age or older and had ankylosing spondylitis (AS) fulfilling the modified New York criteria. They also had a score of 4 or higher on the BASDAI, scores range from 0 to 10, with higher scores indicating more severe disease activity and a score for spinal pain of 4 cm or more on a 10-cm visual analogue scale (with higher numbers indicating greater disease activity), despite treatment with the maximum doses of NSAIDs that were associated with an acceptable side-effects profile. Previous use of DMARDs and anti-TNF agents was allowed. Washout periods for these agents, other than sulfasalazine and methotrexate, were required before initiation of the study treatment. Patients previously treated with not more than one anti-TNF agent could participate if they had an inadequate response to an approved dose for 3 months or more or had unacceptable side effects with at least one dose. Patients could continue to receive the following medications at a stable dose: sulfasalazine (≤3 g per day), methotrexate (≤25 mg per week), prednisone or equivalent (≤10 mg per day), and NSAIDs.

Key exclusion criteria were total spinal ankylosis, evidence of infection or cancer on chest radiography, active systemic infection within 2 weeks before baseline, and previous treatment with cell-depleting therapies or biologic agents other than anti-TNF agents.

Patients were randomly assigned in a 1:1:1 ratio to one of two secukinumab groups or the placebo group. Patients received subcutaneous injections of secukinumab (at a dose of 150 mg or 75 mg) or placebo at baseline; at weeks 1, 2, and 3; and every 4 weeks starting at week 4. At week 16 in both studies, patients in the placebo group were randomly reassigned to receive secukinumab at a dose of 150 mg or 75 mg. Patients continued to receive subcutaneous secukinumab at a dose of 150 mg or 75 mg every 4 weeks from week 16 until the end of the study. Disease activity and efficacy assessments were conducted at baseline and throughout the study, with key assessments at week 16 (primary analysis) and week 52 (follow-up analysis).

In each study, the primary efficacy end point was the proportion of patients who met ASAS20 response criteria at week 16.

MEASURE 4 is a multicentre, randomized, double-blind, placebo-controlled, parallel-group, 2-year study. Patients ≥ 18 years of age, with active AS with prior documented radiological evidence fulfilling the modified New York criteria for AS, a BASDAI score of 4 or higher, and a score for spinal pain of 4 cm or more on a 10-cm VAS were enrolled. Patients previously treated with not more than one TNFi could participate if they had an inadequate response to an approved dosage for ≥ 3 months or were intolerant to at least one dose.
Eligible patients were randomly assigned (1:1:1) by means of an Interactive Response Technology to one of three treatment groups: s.c. secukinumab 150 mg with loading dose (secukinumab 150 mg), s.c. secukinumab 150 mg without loading dose (secukinumab 150 mg no load), or placebo. All patients received s.c. secukinumab 150 mg or placebo at baseline and weeks 1, 2, 3, and every 4 weeks starting at week 4. At week 16, all placebo patients were switched to s.c. secukinumab 150 mg q4w. Thus, starting at week 16, patients in all three arms received secukinumab 150 mg q4w in an open-label fashion, although study participants and investigators remained blinded to the original group assignment. Randomization of patients was stratified according to previous use of TNFi therapy (i.e., patients who were naïve to TNFi therapy versus those who were TNFi-IR).

The primary endpoint was to demonstrate that the efficacy of secukinumab 150 mg, with or without a loading regimen, was superior to placebo based on the proportion of patients achieving an ASAS20 response at week 16. ASAS20 is defined as a relative improvement of ≥ 20% and an absolute improvement of ≥ 1 unit (on a 10-unit scale) in at least three of the four main ASAS domains (patient global assessment of disease activity, back pain, physical function, and inflammation), with no worsening of ≥ 20% and ≥ 1 unit (on a 10-unit scale) in the remaining domain.
Pre-specified subgroup analyses based on previous use of TNFi therapy were performed for key efficacy endpoints.

MEASURE 5 is a 52-week, randomized, double-blind, placebo-controlled, parallel-group, multicentre, Phase III, China-centric study conducted in China, the Czech Republic, Republic of Korea, and the United Kingdom. Patients enrolled in the study were ≥18 years of age and had moderate to severe AS with prior documented radiological evidence fulfilling the modified New York criteria; active AS assessed by BASDAI score of ≥4; spinal pain score ≥4 cm on a 10 cm VAS; and total back pain score ≥40 mm on a 100 mm VAS. Patients should have had an inadequate response to previous treatment with at least two NSAIDs. Patients on scheduled NSAIDs were required to be on a stable dose for at least 2 weeks before randomization. Patients previously treated with TNFi (no more than one) could participate if they had an inadequate response to an approved dosage for ≥3 months or were intolerant to at least one dose (hereafter collectively referred to as TNFi-IR and were included after appropriate washout periods before randomization. Patients could continue to receive the following medications at a stable dose: sulfasalazine (≤3 g/day), methotrexate (≤25 mg/week), glucocorticoids (≤10 mg/day prednisone or equivalent), and NSAIDs.

Key exclusion criteria included total spinal ankylosis, malignancy in the past 5 years, active systemic infection within 2 weeks before randomization, history of ongoing, chronic, or recurrent infectious disease or evidence of tuberculosis infection, known infection with human immunodeficiency viruses, hepatitis B or C at screening or randomization, and previous treatment with cell-depleting therapies or biologic agents other than TNFi.

The primary objective was to demonstrate that the efficacy of s.c. secukinumab 150 mg is superior to placebo based on the proportion of patients achieving an ASAS20 response at Week 16.

ASTRUM is a phase IV, 20-week, randomized, double-blind, 3-arm, placebo-controlled, parallel-group, multicenter study to examine the clinical response of secukinumab treatment in patients with ankylosing spondylitis (AS) as measured by the ASAS20 response and the NSAID-sparing effect. Patients previously treated with a TNFα inhibitor were allowed into the study after an appropriate wash-out period prior to randomization. The study evaluated to which extent NSAID treatment can be reduced between Week 4 and Week 12 in patients randomized to secukinumab 150 mg or placebo following an initial run-in phase of 4 weeks on stable NSAID therapy. Two NSAID tapering approaches were evaluated in this study:

1. an early tapering approach in which NSAID were tapered at the start of secukinumab treatment,
2. a delayed tapering approach in which NSAID were tapered following 4 weeks of secukinumab treatment.

Patients were randomized 1:1:1 to one of the following treatment groups:

- Secukinumab - delayed NSAID tapering: Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering).
- Secukinumab - early NSAID tapering: Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).
- Placebo: Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.

The primary objective of the study was to demonstrate that the efficacy of secukinumab 150 mg subcutaneous (s.c.) injection (with NSAID tapering) is superior to placebo based on the proportion of patients achieving an ASAS20 response at Week 12.

7.3.2 Efficacy and safety – results per study

7.3.2.1 Efficacy and safety – bimekizumab (BE MOBILE 2)

The results for the ITT population for selected endpoints are provided in Table 34 and for the bDMARD experienced subgroup in Table 35

Table 34 Results of the bDMARD ITT population (16.3% experienced) from BE MOBILE 2 at week 16

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	99	221	25	111	1.99 (1.37; 2.89)	22%	0.22 (0.12; 0.32)

ASDAS< 2.1	Bimekizumab	Placebo	16	93	221	19	111	2.46 (1.59; 3.81)	25%	0.25 (0.15; 0.35)
BASDAI50	Bimekizumab	Placebo	16	103	221	29	111	1.78 (1.27; 2.51)	20%	0.20 (0.10; 0.31)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Bimekizumab	Placebo	16	221	9.3	8.7	111	5.9	7.9	3.40 (1.48; 5.32)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

Table 35 Results of the bDMARD experienced subgroup from BE MOBILE 2 at week 16

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	15	37	3	17	2.30 (0.77; 6.89)	23%	0.23 (-0.01; 0.47)
ASDAS< 2.1	Bimekizumab	Placebo	16	7	37	1	17	3.22 (0.43; 24.13)	13%	0.13 (-0.04; 0.30)
BASDAI50	Bimekizumab	Placebo	16	13	37	6	17	1,00 (0,46; 2.17)	0%	0,00 (-0,28; 0.27)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**

SF36-PCS	Bimekizumab	Placebo	16	37	7.5	8.1	17	5	10	2.50 (-2.51; 7.51)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.3.2.2 Efficacy and safety – secukinumab (MEASURE 2, EASURE 4, MEASURE 5 and ASTRUM)

Table 36 ASAS40 (Data based on the ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95% CI)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	31	71	15	70	2.04 (1.21; 3.43)	22 %	0.22 (0.07; 0.37)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	26	72	8	74	3.34 (1.62; 6.88)	25 %	0.25 (0.12; 0.38)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	134	305	26	153	2.59 (1.78; 3.75)	27 %	0.27 (0.19; 0.35)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	45	116	33	117	1.38 (0.95;1.99)	11 %	0.11 (-0.01; 0.23)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**2.01 (1.61; 2.52)**	**22 %**	**0.22 (0.17; 0.28)**

Table 37 ASAS40 (Data based on the bDMARD experienced subgroup meta-analysis for secukinumab)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	7.5	29	0.5	30	15.52 (0.93; 259.52)	25 %	0.25 (0.09; 0.41)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	9	20	5	20	1.80 (0.73; 4.43)	20 %	0.20 (-0.09; 0.49)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	32	65	4	31	3.82 (1.48; 9.84)	36 %	0.36 (0.19; 0.53)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	11	31	8	34	1.51 (0.70; 3.26)	12 %	0.12 (-

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					0.10; 0.34)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**	**2.19 (1.34; 3.57)**	**26 %**	**0.26 (0.16; 0.35)**

BASDAI50 was not reported in the MEASURE 4 and 5 trials, hence only ASTRUM and MEASURE 2 are included for secukinumab. Subgroup data were not available for the secukinumab trials meaning only the results for the ITT-populations are reported.

Table 38 BASDAI50 (Data based on the ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	23	71	16	70	1.42 (0.82; 2.45)	10 %	0.10 (-0.05; 0.24)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	22	72	8	74	2.83 (1.35; 5.93)	20 %	0.20 (0.07; 0.33)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**1.81 (1.16; 2.0)**	**15 %**	**0.15 (0.06; 0.25)**

SF36-PCS was not reported in the ASTRUM trial, hence only the MEASURE trials are included.

Table 39 SF36-PCS (Data based on the ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	72	6.1	7.1	74	1.9	6.0	4.20 (2.07; 6.33)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	305	7.4	6.6	153	4.6	6.6	2.80 (1.52; 4.08)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	116	5.9	7.5	117	4.5	7.5	1.40 (-0.53; 3.33)

Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**								**2.74 (1.78; 3.69)**

Table 40 SF36-PCS (Data based on the bDMARD experienced subgroup of meta-analysis for secukinumab)

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	24	4.5	5.9	23	0.3	5.8	4.20 (0.85; 7.55)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	31	5.2	7.1	34	4.0	7.1	1.20 (-2.26; 4.66)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	65	7.3	6.9	31	3.3	6.2	4.00 (1.14; 6.86)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**								**3.27 (1.43; 5.11)**

Only MEASURE 2 reported SF-36 MCS for secukinumab - and only data for the ITT population is available.

Table 41 SF-36 MCS (Data based on the ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	72	4.04	11.0	74	3.36	11.0	0.68 (-2.89; 4.25)

Table 42 Discontinuation due to AEs (Data based on the ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	5	72	4	74	1.28 (0.36; 4.59)	2%	0.02 (-0.06; 0.09)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	5.5*	72	0.5*	71	10.85 (0.61;	7%	0.07 (0.01; 0.13)

								192.56)		
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	2	305	1	153	1.00 (0.09; 10.98)	0%	0.00 (-0.02; 0.02)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	1	116	1	117	1.01 (0.06; 15.94)	0%	0.00 (-0.02; 0.02)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**1.53 (0.58; 4.08)**	**0%**	**0.00 (-0.01; 0.02)**

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.3.3 Comparative analyses of efficacy and safety

The comparability with respect to baseline characteristics between the relevant studies included in the ITC were qualitatively assessed. Full details on the baseline characteristics of the studies are provided in Appendix B Main characteristics of included studies. The study design (inclusion and exclusion criteria) and patient characteristics were deemed comparable. The baseline characteristics were very similar, and overall, the differences were considered minor, therefore justifying an unadjusted indirect treatment comparison using Bucher's method.

Prior bDMARD experience differed between the studies, as previously described in Section 7, which should be considered when interpreting the results of the ITCs. In previous DMC assessments of secukinumab and ixekizumab within axSpA mixed prior bDMARD experience populations has been used for extrapolating the results onto either bDMARD naïve or experienced patient groups[28, 37].

The specified endpoints for analyses were ASAS40, BASDAI50, ASDAS<2.1, SF-36 and safety based on previous DMC assessment and protocols within AS and nr-axSpA.[28, 37]

The ITC is a statistical method used to pool results across a number of trials with comparable patient populations linked by common comparators. The technique assumes that, on a suitable scale, one can add and subtract the within study estimates of relative treatment effects. For example, direct data comparing treatment A with C and B with C can be used to indirectly compare A and B. This is under the assumption that the following relationship between the estimated treatment effects holds: (A–B) = (A–C)–(B–C). The underlying methodology for the ITC is the Bucher et al. 1997 method, which is a frequentist approach to evidence synthesis. For this analysis continuous outcomes were assessed in terms of mean difference. Binary outcomes were assessed in terms of relative risk (RR) and risk difference (RD). Significance of treatment effect for the frequentist method was determined by the two-sided 95% CI and tests with two-sided p-values less than 0.05 are referred to as being statistically significant.

7.3.3.1 ASAS40 (ITT population)

For ASAS40 the comparison of the ITT populations shows that the absolute risk difference point estimate indicates similarity for bimekizumab and secukinumab (0%) with a risk ratio of 0.99 (95% CI: 0.64; 1.53). The results are not statistically significant.

In the sensitivity analysis based on the subgroup analysis of bDMARD experienced patients, the ITC demonstrates that the absolute risk difference point estimate did not favour bimekizumab (-3%) but the risk ratio of 1.05 (95% CI: 0.32; 3.50) did favour bimekizumab. None of the results are statistically significant.

It can be concluded that the treatment effect as measured by ASAS40 can be considered similar for bimekizumab and secukinumab.

Table 43 ASAS40 (Data based on the ITT population from BE MOBILE 2 (mixed bDMARD experience) vs ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95% CI)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	31	71	15	70	2.04 (1.21; 3.43)	22 %	0.22 (0.07; 0.37)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	26	72	8	74	3.34 (1.62; 6.88)	25 %	0.25 (0.12; 0.38)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	134	305	26	153	2.59 (1.78; 3.75)	27 %	0.27 (0.19; 0.35)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	45	116	33	117	1.38 (0.95;1.99)	11 %	0.11 (-0.01; 0.23)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**2.01 (1.61; 2.52)**	**22 %**	**0.22 (0.17; 0.28)**
BE MOBILE 2	Bimekizumab	Placebo	16	99	221	25	111	1.99 (1.37; 2.89)	22 %	0.22 (0.12; 0.32)
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**						**0.99 (0.64; 1.53)**	**0%**	**0.00 (-0.12; 0.11)**

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Table 44 ASAS40 (Data based on the bDMARD experienced subgroup from BE MOBILE 2 vs experienced subgroup of meta-analysis for secukinumab)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	7.5	29	0.5	30	15.52 (0.93; 259.52)	25 %	0.25 (0.09; 0.41)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	9	20	5	20	1.80 (0.73; 4.43)	20 %	0.20 (-0.09; 0.49)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	32	65	4	31	3.82 (1.48; 9.84)	36 %	0.36 (0.19; 0.53)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	11	31	8	34	1.51 (0.70; 3.26)	12 %	0.12 (-0.10; 0.34)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**2.19 (1.34; 3.57)**	**26 %**	**0.26 (0.16; 0.35)**
BE MOBILE 2 experienced	Bimekizumab	Placebo	16	15	37	3	17	2.30 (0.77; 6.89)	23 %	0.23 (-0.01; 0.47)
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**						**1.05 (0.32; 3.50)**	**-3%**	**-0.03 (-0.29; 0.23)**

7.3.3.2 BASDAI50 (ITT population)

BASDAI50 was not reported in the MEASURE 4 and 5 trials, hence only ASTRUM and MEASURE 2 are included in the ITC for secukinumab. Subgroup data were not available for the secukinumab trials meaning only the results for the ITT-populations are reported. Result of the ITCs demonstrates that the absolute risk difference point estimate favours bimekizumab (5%) and can be considered equal to secukinumab with a risk ratio of 0.99 (95% CI: 0.57; 1.72). The results are not statistically significant for BASDAI50 and it can be concluded that the treatment effect as measured by BASDAI50 can be considered similar for bimekizumab and secukinumab.

Table 45 BASDAI50 (Data based on the ITT population from BE MOBILE 2 (mixed bDMARD experience) vs ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)

ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	23	71	16	70	1.42 (0.82; 2.45)	10 %	0.10 (-0.05; 0.24)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	22	72	8	74	2.83 (1.35; 5.93)	20 %	0.20 (0.07; 0.33)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**1.81 (1.16; 2.80)**	**15 %**	**0.15 (0.06; 0.25)**
BE MOBILE 2	Bimekizumab	Placebo	16	103	221	29	111	1.78 (1.27; 2.51)	20 %	0.20 (0.10; 0.31)
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**						**0.99 (0.57; 1.72)**	**5%**	**0.05 (-0.09; 0.19)**

7.3.3.3 SF36-PCS (ITT population)

SF36-PCS was not reported in the ASTRUM trial, hence only the MEASURE trials are included in the ITC for secukinumab. Result of the ITC based on the ITT population shows that the difference in change from baseline point estimate favours bimekizumab with a minor difference in mean change of 0.66. The result is not statistically significant.

For the sensitivity analysis based on the subgroup of bDMARD experienced patients, the ITC showed that the point estimate did not favour bimekizumab with a minor difference in mean change of -0.77. This result is not statistically significant.

The conclusion is that the treatment effect as measured by SF36-PCS can be considered similar for bimekizumab and secukinumab.

Table 46 SF36-PCS (Data based on the ITT population from BE MOBILE 2 (mixed bDMARD experience) vs ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	72	6.1	7.1	74	1.9	6	4.20 (2.07; 6.33)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	305	7.4	6.6	153	4.6	6.6	2.80 (1.52; 4.08)

MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	116	5.9	7.5	117	4.5	7.5	1.40 (-0.53; 3.33)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**								**2.74 (1.78; 3.69)**
BE MOBILE 2	Bimekizumab	Placebo	16	221	9.3	8.7	111	5.9	7.9	3.40 (1.48; 5.32)
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**								**0.66 (-1.49; 2.81)**

Table 47 SF36-PCS (Data based on the bDMARD experienced subgroup from BE MOBILE 2 vs experienced subgroup of meta-analysis for secukinumab)

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	24	4.5	5.9	23	0.3	5.8	4.20 (0.85; 7.55)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	31	5.2	7.1	34	4	7.1	1.20 (-2.26; 4.66)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	65	7.3	6.9	31	3.3	6.2	4.00 (1.14; 6.86)
Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**								**3.27 (1.43; 5.11)**
BE MOBILE 2 experienced	Bimekizumab	Placebo	16	37	7,5	8,1	17	5	10	2.50 (-2.51; 7.51)
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**								**-0.77 (-6.11; 4.57)**

7.3.3.4 SF36-MCS (ITT population)

Only MEASURE 2 reported SF-36 MCS for secukinumab - and only data for the ITT population is available. Result of the ITC demonstrates that the point estimate favours bimekizumab with a difference in mean change of 0.02, although the result is not statistically significant for the SF36-MCS domain. The conclusion is

that the treatment effect as measured by SF36-MCS can be considered similar for bimekizumab and secukinumab.

Table 48 SF-36 MCS (Data based on the ITT population from BE MOBILE 2 (mixed bDMARD experience) vs ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in chan (95%CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	72	4.04	11	74	3.36	11	0.68 (-2.89; 4.25
BE MOBILE 2	Bimekizumab	Placebo	16	221	2.5	8.2	111	1.8	6.3	0.70 (-1.04; 2.44
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**								**0.02 (-3.95; 3.99**

7.3.3.5 Discontinuation due to AEs (ITT population)

For discontinuation due to AEs, the result of the ITC demonstrates that the point estimate of the absolute risk difference marginally favours secukinumab (1%) with a risk ratio of 2.31 (95% CI: 0.10; 51.85). The result is not statistically significant. Given that the number of events is zero in some arms and low in others, the results should be interpreted with caution. In the arms with zero events a continuity correction (+1 for N and +0,5 for n for both arms of the trial) was applied. The conclusion is that discontinuation due to AEs can be considered similar for bimekizumab and secukinumab.

Table 49 Discontinuation due to AEs (Data based on the full population of BE MOBILE 2 (mixed bDMARD experience) vs ITT population from meta-analysis for secukinumab (mixed))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95% CI)
MEASURE 2	Secukinumab 150 Q4W SC	Placebo	16	5	72	4	74	1.28 (0.36; 4.59)	2%	0.02 (-0.06; 0.09)
ASTRUM	Secukinumab 150 Q4W SC	Placebo	16	5.5*	72	0.5*	71	10.85 (0.61; 192.56)	7%	0.07 (0.01; 0.13)
MEASURE 5	Secukinumab 150 Q4W SC	Placebo	16	2	305	1	153	1.00 (0.09; 10.98)	0%	0.00 (-0.02; 0.02)
MEASURE 4	Secukinumab 150 Q4W SC	Placebo	16	1	116	1	117	1.01 (0.06; 15.94)	0%	0.00 (-0.02; 0.02)

Meta-analysis	**Secukinumab 150 Q4W SC**	**Placebo**						**1.53 (0.58; 4.08)**	**0%**	**0.00 (-0.01; 0.02)**
BEMOBILE2	Bimekizumab	Placebo	16	3.5*	222	0.5*	112	3.53 (0.18; 67.78)	1%	0.01 (0.00; 0.03)
indirect comparison	**Bimekizumab**	**Secukinumab 150 Q4W SC**						**2.31 (0.10; 51.85)**	**1%**	**0.01 (-0.01; 0.03)**

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.3.3.6 Conclusion

For the ITC comparing bimekizumab to secukinumab in AS bDMARD experienced patients, all studies available for the ITC – both for bimekizumab and secukinumab – were in a mixed bDMARD experienced population. This means that the patient populations for bimekizumab and secukinumab were well-aligned and that the ITC analyses could be done based on the ITT populations for each comparator. In addition, where possible sensitivity analyses based on subgroup populations of bDMARD experienced patients for both bimekizumab and secukinumab were made, however these subgroups were based on small patient numbers leading to a higher degree of uncertainty. The ITC analyses showed that bimekizumab is favoured by most of the point estimates in the comparison to secukinumab, but the differences are not statistically significant. Based on the ITC it can be concluded that the differences are not statistically significant i.e., based on the available data no differences in efficacy and safety between bimekizumab and secukinumab were identified and clinical equivalence between bimekizumab and secukinumab can be concluded.

Data was not available for ASDAS<2.1, serious infections, SF-36 vitality subdomain and discontinuation due to lack of efficacy due to lack of data in the included studies. Therefore, these endpoints were not possible to include into the ITC.

7.4 Efficacy and safety of bimekizumab compared to adalimumab for nr-axSpA bDMARD naïve patients

7.4.1 Relevant studies

The ITC analysis of bimekizumab vs adalimumab in nr-axSpA included a mixed set of studies in relation to prior bDMARD experience. BE MOBILE 1 included 10.6% of patients that were bDMARD experienced, whereas the adalimumab trial ABILITY 1 exclusively included bDMARD naïve patients. In order to match the populations of the two trials, analyses are conducted on a bDMARD naïve subgroup of BE MOBILE 1. Analyses of safety outcomes are based on the ITT populations.

BE MOBILE 1 is AS0010 is a multicenter, Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab compared to placebo in study participants with nr-axSpA. To be eligible to participate in this study, study participants must have had active adult-onset axSpA (BASDAI ≥4 and spinal pain ≥4 on a 0 to 10 numeric rating scale [NRS]) meeting ASAS classification criteria, with inflammatory back pain for at least 3 months prior to the Screening Visit and an age at symptom onset of <45 years. Patients must have had failure to respond to 2 different NSAIDs, or history of intolerance or

contraindication to NSAID therapy. Patients may have been previously treated with anti-TNF agents but must have experienced an inadequate response or been intolerant to treatment.

Eligible study participants were randomized 1:1 to receive 1 of 2 treatments (bimekizumab 160mg sc Q4W or placebo sc Q4W), and remain on allowable background medication, until Week 16. Thereafter, study participants randomized to bimekizumab 160mg Q4W remained on their randomized dose and study participants randomized to placebo were reallocated to receive bimekizumab 160mg Q4W after all Week 16 assessments have been completed.

The primary efficacy endpoint for this study was the ASAS40 response at Week 16.
Data for week 52 is presented in appendix K.

ABILITY-1 is a phase 3, randomised, placebo-controlled, double-blind trial. Eligible patients were randomised 1:1 to receive s.c. injections of adalimumab (N = 91) or matching placebo (N = 94) for 12 weeks during the double-blind period. Patients who completed the double-blind period were eligible to receive open-label adalimumab for up to an additional 144 weeks.

Eligible patients in ABILITY-1 were adult patients who fulfilled the ASAS criteria for axSpA, had a BASDAI score of ≥4,
total back pain score of ≥4 (10 cm VAS) and inadequate response and intolerance or contraindication to NSAIDs.
Patients fulfilling the modified New York criteria for AS were excluded.
Patients could enter the study on concomitant NSAIDs, prednisone (≤10 mg per day), methotrexate (MTX, ≤25 mg per
week), sulfasalazine (≤3 g per day) and/or hydroxychloroquine (≤400 mg per day) or azathioprine (≤150 mg per day,
but not concomitant with any other DMARD) if the doses met the pre-specified stability requirements prior to
randomisation and remained stable during the first 24 weeks.

The primary endpoint was the percentage of patients achieving ASAS40 at week 12.

7.4.2 Efficacy and safety – results per study

7.4.2.1 Efficacy and safety – bimekizumab (BE MOBILE 1)

To match the population in scope (bDMARD naïve) the ITCs features a subgroup of bDMARD naïve patients from BE MOBILE 2 to compare with the bDMARD naïve comparator studies. The results of the bDMARD naïve subgroup for selected endpoints are provided in Table 50.

Table 50 Results of the bDMARD naïve subgroup at 16 weeks from BE MOBILE 1

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)

ASAS40	Bimekizumab	Placebo	16	55	118	25	109	2.03 (1.37; 3.02)	24%	0.24 (0.12; 0.36)
ASDAS< 2.1	Bimekizumab	Placebo	16	53	118	21	109	2.33 (1.51; 3.60)	26%	0.26 (0.14; 0.37)
BASDAI50	Bimekizumab	Placebo	16	56	118	25	108	2.05 (1.38; 3.04)	24%	0.24 (0.12; 0.36)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	2	128	5	126	0.39 (0.08; 1.99)	-2%	-0.02 (-0.06; 0.02)

Endpoint	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
SF36-PCS	Bimekizumab	Placebo	16	118	9.4	7.89	109	5.7	7.74	3.66 (1.63; 5.70)

7.4.2.2 Efficacy and safety – adalimumab (ABILITY 1)

The results of the ABILITY 1 ITT population (100% bDMARD naïve) for selected endpoints are provided in Table 51.

Table 51 Results of the bDMARD naïve ITT population at 12 weeks from ABILITY 1

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	adalimumab	Placebo	12	33	91	14	94	2.43 (1.40; 4.24)	21%	0.21 (0.09; 0.34)
BASDAI50	adalimumab	Placebo	12	32	91	14	94	2.36 (1.35; 4.13)	20%	0.20 (0.08; 0.32)
Discontinuation due to AEs (ITT population)	adalimumab	Placebo	12	1	91	1	94	1.03 (0.07; 16.27)	0%	0.00 (-0.03; 0.03)

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Endpoint	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
SF36-PCS	adalimumab	Placebo	12	91	5.5	8.98	93	2.0	7.04	3.50 (1.17; 5.83)

7.4.3 Comparative analyses of efficacy and safety

Please see section 7.1.3 for more details on methods of synthesis.

7.4.3.1 ASAS40 (bDMARD naïve)

For ASAS40, the result of the ITC demonstrates that the absolute risk difference point estimate of 2% favours bimekizumab, although the risk ratio of 0.83 (95% CI: 0.42; 1.65) did not favour bimekizumab. The result is not statistically significant for ASAS40. The conclusion is that the treatment effect as measured by ASAS40 can be considered similar for bimekizumab and adalimumab.

Table 52 ASAS40 (Data based on bDMARD naïve subgroup population from BE MOBILE 1 vs ABILITY1 (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95%CI)
ABILITY 1	Adalimumab	Placebo	12	33	91	14	94	2.43 (1.40; 4.24)	21 %	0.21 (0.09; 0.34)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	55	118	25	109	2.03 (1.37; 3.02)	24 %	0.24 (0.12; 0.36)
indirect comparison	**Bimekizumab**	**Adalimumab**						**0.83 (0.42; 1.65)**	**2%**	**0.02 (-0.15; 0.19)**

7.4.3.2 BASDAI50 (bDMARD naïve)

For BASDAI50, the result of the ITC demonstrates that the absolute risk difference point estimate of 4% favours bimekizumab, although the risk ratio of 0.87 (95% CI: 0.44; 1.72) did not favour bimekizumab. The result is not statistically significant for BASDAI50 and the conclusion is that the treatment effect as measured by BASDAI50 can be considered similar for bimekizumab and adalimumab.

Table 53 BASDAI50 (Data based on bDMARD naïve subgroup population from BE MOBILE 1 vs ABILITY1 (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95%CI)

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ABILITY 1	Adalimumab	Placebo	12	32	91	14	94	2.36 (1.35; 4.13)	20 %	0.20 (0.08; 0.32)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	56	118	25	108	2.05 (1.38; 3.04)	24 %	0.24 (0.12; 0.36)
indirect comparison	**Bimekizumab**	**Adalimumab**						**0.87 (0.44; 1.72)**	**4%**	**0.04 (-0.13; 0.21)**

7.4.3.3 SF36-PCS (bDMARD naïve)

For SF36-PCS, the result of the ITC demonstrates that the point estimate favours bimekizumab with a difference in mean change of 0.16, although the result is not statistically significant for the SF36-PCS domain. The conclusion is that the treatment effect as measured by SF36-PCS can be considered similar for bimekizumab and adalimumab.

Table 54 SF36-PCS (Data based on bDMARD naïve subgroup population from BE MOBILE 1 vs ABILITY1 (100% naïve))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
ABILITY 1	Adalimumab	Placebo	12	91	5.5	8.98	93	2.0	7.04	3.50 (1.17; 5.83)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	118	9.4	7.89	109	5.7	7.74	3.66 (1.63; 5.70)
indirect comparison	**Bimekizumab**	**Adalimumab**								**0.16 (-2.93; 3.26)**

7.4.3.4 Discontinuation due to AEs (ITT population)

For Discontinuation due to AEs, the result of the ITC demonstrates that the absolute risk difference point estimate of -2% as well as the risk ratio of 0.38 (95% CI: 0.02; 9.33) did favour bimekizumab, although the results are not statistically significant. It can be concluded that discontinuation due to AEs can be considered similar for bimekizumab and adalimumab.

Table 55 Discontinuation due to AEs (Data based on full population from BE MOBILE 1 (10.6% experienced) vs ABILITY1 (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95%CI)

ABILITY 1	Adalimumab	Placebo	12	1	91	1	94	1.03 (0.07; 16.27)	0%	0.00 (-0.03; 0.03)
BE MOBILE 1	Bimekizumab	Placebo	16	2	128	5	126	0.39 (0.08; 1.99)	-2%	-0.02 (-0.06; 0.02)
indirect comparison	**Bimekizumab**	**Adalimumab**						**0.38 (0.02; 9.33)**	**-2%**	**-0.02 (-0.07; 0.03)**

7.4.3.5 Conclusion

For the comparison of bimekizumab vs adalimumab in nr-axSpA bDMARD naïve patients, the ITC analyses were conducted on a bDMARD naïve subgroup of BE MOBILE1 in comparison with ABILITY 1, which was conducted exclusively in bDMARD naïve patients, in order to ensure a match of patient populations.

The ITC analyses showed that bimekizumab is favoured by most of the point estimates in the comparison to adalimumab, but the differences are not statistically significant i.e., based on the available data no differences in efficacy and safety between bimekizumab and adalimumab were identified and clinical equivalence between bimekizumab and adalimumab can be concluded.

Due to lack of data in the included studies, data was not available for ASDAS<2.1, serious infections, SF36 bodily pain subdomain, SF36 physical functioning subdomain and discontinuation due to lack of efficacy. Therefore, these endpoints were not possible to include into the ITC.

7.5 Efficacy and safety of bimekizumab compared to ixekizumab for nr-axSpA bDMARD experienced patients

7.5.1 Relevant studies

Given the positioning of ixekizumab as a subsequent treatment after adalimumab, the main ITC analyses should focus on the bDMARD experienced patients. However, the identified ixekizumab trial (COAST-X) included a purely bDMARD naïve population, whereas BE MOBILE 1 included 10.6% of patients that were bDMARD experienced. The following section presents analyses for the subgroup of bDMARD naïve patients in BE MOBILE 1 compared to the 100% naïve ixekizumab population of COAST-X. This approach is taken to match the two patient populations despite the ideal population being the bDMARD experienced population. Analyses of safety outcomes are based on the ITT populations.

BE MOBILE 1 please study description in section 7.3.1

COAST-X is a multicentre, randomised, double-blind, placebo-controlled, parallel-group, phase 3 trial. Patients were randomly assigned (1:1:1) to receive s.c. 80 mg ixekizumab Q4W (N = 96) or every 2 weeks (Q2W, N = 102), or placebo (N = 105). The starting dose of ixekizumab was either 80 mg or 160 mg at week 0. Changing background medications or switching to open-label ixekizumab Q2W, or both, was allowed after week 16 at the discretion of the investigator. Patients were allocated to treatment by a computer-generated random sequence, with stratification by country and MRI and CRP status at screening (MRI+ and CRP+, MRI+ and CRP–, or MRI– and CRP+).

Eligible participants in COAST-X were adults (aged ≥18 years) with active axSpA without definite radiographic sacroiliitis (nr-axSpA), with objective signs of inflammation (via MRI or CRP), and an inadequate response or intolerance to NSAIDs. Exclusion criteria included previous treatment with bDMARDs. Patients could continue background medications, including NSAIDs, conventional synthetic DMARDs (csDMARDs), glucocorticoids and analgesics. Stable doses of background medications were required during the first 16 weeks of the study.

The primary endpoint was 40% improvement in disease activity according to the ASAS40 criteria at week 16 and week 52. As the posology for nr-axSpA is 160 mg (two 80 mg injections) s.c. injection at week 0 followed by 80 mg Q4W, only data from the Q4W with ixekizumab and the placebo arm are presented. Analyses of ixekizumab Q4W compared with placebo were done without regard to the week 0 starting dose of 80 mg or 160 mg.

7.5.2 Efficacy and safety – results per study

7.5.2.1 Efficacy and safety – bimekizumab (BE MOBILE 1)

Table 56 Results of the bDMARD naïve subgroup at 16 weeks from BE MOBILE 1

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	55	118	25	109	2.03 (1.37; 3.02)	24%	0.24 (0.12; 0.36)
ASDAS< 2.1	Bimekizumab	Placebo	16	53	118	21	109	2.33 (1.51; 3.60)	26%	0.26 (0.14; 0.37)
BASDAI50	Bimekizumab	Placebo	16	56	118	25	108	2.05 (1.38; 3.04)	24%	0.24 (0.12; 0.36)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	2	128	5	126	0.39 (0.08; 1.99)	-2%	-0.02 (-0.06; 0.02)

Endpoint	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
SF36-PCS	Bimekizumab	Placebo	16	118	9.4	7.89	109	5.7	7.74	3.66 (1.63; 5.70)

7.5.2.2 Efficacy and safety – ixekizumab (COAST-X)

Table 57 Results of the ITT (100% bDMARD naïve) population from COAST-X at week 16

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Ixekizumab Q4W	Placebo	16	34	96	20	105	1.86 (1.15; 3.00)	16%	0.16 (0.04; 0.29)
ASDAS< 2.1	Ixekizumab Q4W	Placebo	16	26	96	13	105	2.19 (1.19; 4.01)	15%	0.15 (0.04; 0.26)
BASDAI50	Ixekizumab Q4W	Placebo	16	30	96	15	105	2.19 (1.26; 3.81)	17%	0.17 (0.06; 0.28)
Discontinuation due to AEs (ITT population)	Ixekizumab Q4W	Placebo	16	0.5*	97	2.5*	106	0.22 (0.01; 4.50)	-2%	-0.02 (-0.05; 0.01)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Ixekizumab Q4W	Placebo	16	96	8.06	7.94	105	5.21	8.20	2.85 (0.62; 5.08)

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.5.3 Comparative analyses of efficacy and safety

Please see section 7.1.3 for more details on methods of synthesis.

7.5.3.1 ASAS40 (bDMARD naive)

For ASAS40, the result of the ITC demonstrates that the absolute risk difference point estimate favours bimekizumab (7%) with a risk ratio of 1.09 (95% CI: 0.59; 2.03). The results are not statistically significant. Hence, the treatment effect as measured by ASAS40 can be considered similar for bimekizumab and ixekizumab.

Table 58 ASAS40 (Data based on bDMARD naïve subgroup from BE MOBILE 1 vs COAST-X (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)

COAST-X	Ixekizumab Q4W	Placebo	16	34	96	20	105	1.86 (1.15; 3.00)	16 %	0.16 (0.04; 0.29)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	55	118	25	109	2.03 (1.37; 3.02)	24 %	0.24 (0.12; 0.36)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**1.09 (0.59; 2.03)**	**7%**	**0.07 (-0.10; 0.24)**

7.5.3.2 ASDAS<2.1 (bDMARD naïve)

For ASDAS<2.1, the result of the ITC demonstrates that the absolute risk difference point estimate of 11% favours bimekizumab with a risk ratio of 1.07 (95% CI: 0.51; 2.24). The results are not statistically significant. As such the treatment effect as measured by ASDAS<2.1 can be considered similar for bimekizumab and ixekizumab.

Table 59 ASDAS<2.1 (Data based on bDMARD naive subgroup from BE MOBILE 1 vs COAST-X (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
COAST-X	Ixekizumab Q4W	Placebo	16	26	96	13	105	2.19 (1.19; 4.01)	15 %	0.15 (0.04; 0.26)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	53	118	21	109	2.33 (1.51; 3.60)	26 %	0.26 (0.14; 0.37)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**1.07 (0.51; 2.24)**	**11 %**	**0.11 (-0.05; 0.27)**

7.5.3.3 BASDAI50 (bDMARD naïve)

For BASDAI50 the result of the ITC shows that the absolute risk difference point estimate of 7% favours bimekizumab with a risk ratio of 0.94 (95%C: 0.48; 1.85). The results are not statistically significant. This means that the treatment effect as measured by BASDAI50 can be considered similar for bimekizumab and ixekizumab.

Table 60 BASDAI50 (Data based on bDMARD naive subgroup from BE MOBILE 1 vs COAST-X (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)

COAST-X	Ixekizumab Q4W	Placebo	16	30	96	15	105	2.19 (1.26; 3.81)	17 %	0.17 (0.06; 0.28)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	56	118	25	108	2.05 (1.38; 3.04)	24 %	0.24 (0.12; 0.36)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**0.94 (0.48; 1.85)**	**7%**	**0.07 (-0.09; 0.24)**

7.5.3.4 SF36-PCS (bDMARD naive)

For SF36-PCS, the result of the ITC demonstrates that the point estimate favours bimekizumab with a difference in mean change of 0.81. The result is not statistically significant i.e., the treatment effect as measured by SF36-PCS can be considered similar for bimekizumab and ixekizumab.

Table 61 SF36-PCS (Data based on bDMARD naïve subgroup from BE MOBILE 1 vs COAST-X (100% naïve))

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
COAST-X	Ixekizumab Q4W	Placebo	16	96	8.06	7.94	105	5.21	8.20	2.85 (0.62; 5.08)
BE MOBILE 1 naive	Bimekizumab	Placebo	16	118	9.37	7.89	109	5.71	7.74	3.66 (1.63; 5.70)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**								**0.81 (-2.21; 3.84)**

7.5.3.5 Discontinuation due to AEs (ITT population)

For Discontinuation due to AEs, the result of the ITC demonstrates that the absolute risk difference point estimate of -1% favours bimekizumab although the risk ratio of 1.80 (95% CI: 0.06; 55.69) favours ixekizumab. The results are not statistically significant. Given the very limited number of events the results should be interpreted with caution. In the arms with zero events a continuity correction (+1 for N and +0.5 for n for both arms of the trial) was applied. It can be concluded that discontinuation due to AEs can be considered similar for bimekizumab and ixekizumab.

Table 62 Discontinuation due to AEs (Data based on full population from BE MOBILE 1 (10.6% experienced) vs COAST-X (100% naïve))

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95%CI)

COAST-X	Ixekizumab Q4W	Placebo	16	0,5*	97	2,5*	106	0.22 (0.01; 4.50)	-2%	-0.02 (-0.05; 0.01)
BE MOBILE 1	Bimekizumab	Placebo	16	2	128	5	126	0.39 (0.08; 1.99)	-2%	-0.02 (-0.06; 0.02)
indirect comparison	**Bimekizumab**	**Ixekizumab Q4W**						**1.80 (0.06; 55.69)**	**-1%**	**-0.01 (-0.05; 0.04)**

* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied

7.5.3.6 Conclusion

For the comparison of bimekizumab vs ixekizumab in nr-axSpA bDMARD experienced patients, the ITC analyses were conducted based on a bDMARD naïve subgroup of BE MOBILE1 to match the patient population of the available study for ixekizumab, COAST-X, which included only bDMARD naïve patients. This was done to ensure matching patient populations in the ITC analyses. The results of the ITC analyses showed that the differences are not statistically significant i.e., based on the available data no differences in efficacy and safety between bimekizumab and ixekizumab were identified and clinical equivalence between bimekizumab and ixekizumab can be concluded.
Due to lack of data in the included studies, data was not available for serious infections, SF36 bodily pain subdomain, SF36 physical functioning subdomain and discontinuation due to lack of efficacy. Therefore, these endpoints were not possible to include into the ITC.

7.6 Efficacy and safety of bimekizumab compared to secukinumab for nr-axSpA bDMARD experienced patients

7.6.1 Relevant studies

The two studies included in the ITCs conducted for the comparison of bimekizumab versus secukinumab both allowed for bDMARD experienced patients to be included in the study (BE MOBILE 1 and PREVENT). 10.6% of the patients included in BE MOBILE 1 were bDMARD experienced patients and 9.7% in PREVENT. This means that the patient populations of the two studies are comparable and that the ITC analyses can be conducted based on the ITT populations of the two studies.

BE MOBILE 1 please study description in section 7.3.1

PREVENT is a multicentre, randomised, double-blind, placebo-controlled, parallel-group, phase 3 trial, consisting of a 2-year core phase and a 2-year extension phase. Patients were randomly assigned (1:1:1) to receive 150 mg secukinumab administered s.c. Q4W with a loading dose at week 1, 2 and 3, secukinumab 150 mg s.c. Q4W without a loading dose or placebo (N = 186). Switch to open-label secukinumab or standard of care was permitted after week 20 based on clinical judgement of the disease activity by the investigator and the patient. Starting at week 52, all patients received open-label secukinumab 150 mg s.c. up to week 100. Patients were allocated to treatment via Interactive Response Technology, with stratification by MRI and CRP status at screening (MRI-positive (MRI+) and CRP-positive (CRP+), MRI-positive and CRP-negative (CRP–), or MRI-negative (MRI–) and CRP-positive).

Eligible participants in PREVENT were adults (aged ≥18 years) with active nr-axSpA fulfilling the ASAS classification criteria for axSpA with no radiographic evidence of changes in the sacroiliac joints that would meet the modified New York criteria for AS. Patients enrolled had active disease, defined as a BASDAI score ≥4 and a visual analogue scale (VAS) score for total back pain of ≥40 (on a scale of 0–100 mm) despite current or previous NSAID therapy, and increased CRP and/or evidence of sacroiliitis on MRI.

Patients previously treated with a TNFi (no more than 1) could participate if they had an inadequate response or were intolerant. Patients could continue to receive the following medications at a stable dose: sulfasalazine, methotrexate, corticosteroids and NSAIDs.

The primary endpoint was a 40% improvement in disease activity according to the ASAS40 criteria at week 16 in TNFi-naïve patients. For all other endpoints, the population included both TNFi-naive patients and patients who had previously been treated with TNFi.

As the posology for nr-axSpA is 150 mg secukinumab Q4W with loading (150 mg at week 1, 2 and 3), only data from the treatment arm on secukinumab with LD and the placebo arm are presented.

7.6.2 Efficacy and safety – results per study

7.6.2.1 Efficacy and safety – bimekizumab (BE MOBILE 1)

Table 63 Results of the ITT population at 16 weeks from BE MOBILE 1

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	61	128	27	126	2.22 (1.52; 3.25)	26%	0.26 (0.15; 0.37)
BASDAI50	Bimekizumab	Placebo	16	60	128	27	126	2.19 (1.49; 3.20)	25%	0.25 (0.14; 0.37)
Discontinuation due to AEs (ITT population)	Bimekizumab	Placebo	16	2	128	5	126	0.39 (0.08; 1.99)	-2%	-0.02 (-0.06; 0.02)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Bimekizumab	Placebo	16	128	9.55	8.37	126	5.48	7.75	4.07 (2.09; 6.06)

7.6.2.2 Efficacy and safety – secukinumab (PREVENT)

Table 64 Results of the ITT population at 16 weeks from PREVENT

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Secukinumab 150 mg	Placebo	16	75	184	52	186	1.46 (1.09; 1.95)	13%	0.13 (0.03; 0.22)
BASDAI50	Secukinumab 150 mg	Placebo	16	69	184	39	186	1.79 (1.28; 2.50)	17%	0.17 (0.07; 0.26)
Discontinuation due to AEs (ITT population)	Secukinumab 150 mg	Placebo	20	3	184	3	186	1.01 (0.21; 4.94)	0%	0.00 (-0.03; 0.03)
Endpoint	**Intervention**	**Comparator**	**Timepoint**	**N intervention**	**Mean change**	**SD**	**N comparator**	**Mean change**	**SD**	**Diff in change (95%CI)**
SF36-PCS	Secukinumab 150 mg	Placebo	16	184	5.57	9.36	186	2.93	9.68	2.64 (0.70; 4.58)

7.6.3 Comparative analyses of efficacy and safety

Please see section 7.1.3 for more details on methods of synthesis.

7.6.3.1 ASAS40 (ITT population)

For ASAS40, the result of the ITC demonstrates that the absolute risk difference point estimate of 13% favours bimekizumab with a risk ratio of 1.53 (95% CI: 0.95; 2.46). The results are not statistically significant. Thus, it can be concluded that the treatment effect as measured by ASAS40 can be considered similar for bimekizumab and secukinumab.

Table 65 ASAS40 (Data based on ITT populations from BE MOBILE 1 and PREVENT)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)

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PREVENT	Secukinumab 150mg	Placebo	16	75	184	52	186	1.46 (1.09; 1.95)	13 %	0.13 (0.03; 0.22)
BE MOBILE 1	Bimekizumab	Placebo	16	61	128	27	126	2.22 (1.52; 3.25)	26 %	0.26 (0.15; 0.37)
indirect comparison	**Bimekizumab**	**Secukinumab 150mg**						**1.53 (0.95; 2.46)**	**13 %**	**0.13 (-0.01; 0.28)**

7.6.3.2 BASDAI50 (ITT population)

For BASDAI50, the result of the ITC demonstrates that the absolute risk difference point estimate of 9% favours bimekizumab with a risk ratio of 1.22 (95% CI: 0.74; 2.03). The results are not statistically significant. This leads to the conclusion that the treatment effect as measured by BASDAI50 can be considered similar for bimekizumab and secukinumab.

Table 66 BASDAI50 (Data based on ITT populations from BE MOBILE 1 and PREVENT)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
PREVENT	**Secukinumab** 150mg	Placebo	16	69	184	39	186	1.79 (1.28; 2.50)	17 %	0.17 (0.07; 0.26)
BE MOBILE 1	Bimekizumab	Placebo	16	60	128	27	126	2.19 (1.49; 3.20)	25 %	0.25 (0.14; 0.37)
indirect comparison	**Bimekizumab**	**Secukinumab 150mg**						**1.22 (0.74; 2.03)**	**9%**	**0.09 (-0.06; 0.23)**

7.6.3.3 SF36-PCS (ITT population)

For SF36-PCS, the result of the ITC demonstrates that the point estimates favour bimekizumab with a difference in mean change of 1.43. The result is not statistically significant. It can be concluded that the treatment effect as measured by SF36-PCS can be considered similar for bimekizumab and secukinumab.

Table 67 SF36-PCS (Data based on ITT populations from BE MOBILE 1 and PREVENT)

Trial	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
PREVENT	**Secukinumab** 150mg	Placebo	16	184	5.57	9.36	186	2.93	9.68	2.64 (0.70; 4.58)
BE MOBILE 1	Bimekizumab	Placebo	16	128	9.55	8.37	126	5.48	7.75	4.07 (2.09; 6.06)
indirect comparison	**Bimekizumab**	**Secukinumab 150mg**								**1.43 (-1.34; 4.21)**

7.6.3.4 Discontinuation due to AEs (ITT population)

For Discontinuation due to AEs, the result of the ITC demonstrates that both point estimates favour bimekizumab with an absolute risk difference of -2% and a risk ratio of 0.39 (95% CI: 0.04; 3.77). The results are not statistically significant. Hence, it can be concluded that there is no statistically significant difference in terms of discontinuation due to AEs between bimekizumab and secukinumab.

Table 68 Discontinuation due to AEs (Data based on ITT populations from BE MOBILE 1 and PREVENT)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95% CI)	ARD	ARD (95% CI)
PREVENT	Secukinumab 150mg	Placebo	20	3	184	3	186	1.01 (0.21; 4.94)	0%	0.00 (-0.03; 0.03)
BE MOBILE 1	Bimekizumab	Placebo	16	2	128	5	126	0.39 (0.08; 1.99)	-2%	-0.02 (-0.06; 0.02)
indirect comparison	**Bimekizumab**	**Secukinumab 150mg**						**0.39 (0.04; 3.77)**	**-2%**	**-0.02 (-0.07; 0.02)**

7.6.3.5 Conclusion

For the comparison of bimekizumab vs secukinumab in nr-axSpA bDMARD experienced patients, the ITC analyses were conducted based on ITT populations for both studies, BE MOBILE 1 for bimekizumab and PREVENT for secukinumab since both studies allowed for bDMARD experienced patients to be included in the study and at a similar level. The results of the ITC analyses showed that bimekizumab is favoured by all the point estimates in the comparison to secukinumab, but also that the differences are not statistically significant i.e., based on the available data no differences in efficacy and safety between bimekizumab and secukinumab were identified and clinical equivalence between bimekizumab and secukinumab can be concluded.

Due to lack of data in the included studies, data was not available for ASDAS<2.1, serious infections, SF36 bodily pain subdomain, SF36 physical functioning subdomain and discontinuation due to lack of efficacy. Therefore, these endpoints were not possible to include into the ITC.

7.7 Efficacy and safety of bimekizumab in patients with axial spondyloarthritis with special focus on uveitis

In addition to the axial symptoms of axSpA, acute anterior uveitis is a common extra-musculoskeletal manifestation of axSpA.[38] Limited data are available on biologic treatment for axial spondyloarthritis and uveitis but bimekizumab has demonstrated meaningful clinical benefits in terms of low rates of uveitis flares in BE MOBILE 1 and 2.

7.7.1 Relevant studies

Data presented are pooled from BE MOBILE 1 and 2, please see previous descriptions in earlier sections. Data were pooled separately for patients randomised to bimekizumab or placebo in the double-blind treatment period of BE MOBILE 1 and 2. Uveitis treatment-emergent adverse events (TEAEs) were identified using the preferred terms “autoimmune uveitis”, “iridocyclitis”, “iritis”, and “uveitis”, and were reported as both incidence and exposure adjusted incidence rates (EAIRs) per 100 patient years (PY) for all patients who received ≥1 BKZ dose.[39]

7.7.2 Efficacy and safety – results per study

7.7.2.1 Efficacy and safety – bimekizumab (BE MOBILE 1 & 2)

Baseline characteristics were reflective of a patient population with moderate-to-severe axSpA. In the double-blind treatment period of BE MOBILE 1 and 2, uveitis TEAEs occurred in 11/237 (4.6%; EAIR/100 PY [95% CI]: 15.4 [7.7, 27.5]) and 2/349 (0.6%; 1.8 [0.2, 6.7]) of patients randomised to placebo and bimekizumab (% difference [95% CI]: 4.07 [1.71, 7.60]), respectively. In the 45 placebo-randomised (19.0%) and 52 bimekizumab-randomised (14.9%) patients with history of uveitis, uveitis TEAEs occurred in 20.0% (EAIR/100 PY [95% CI]: 70.4 [32.2, 133.7]) and 1.9% (6.2 [0.2, 34.8]) of patients, respectively. In the pooled ph2b/3 trial data, total bimekizumab exposure was 2,034.4 PY (N=848), 130 (15.3%) pts had history of uveitis. Uveitis TEAEs occurred in 25 (2.9%; EAIR/100 PY [95% CI]: 1.2 [0.8, 1.8]) and 14 (10.8%; 4.6 [2.5, 7.7]) patients overall and with history of uveitis, respectively. All uveitis TEAEs were mild/moderate, one event led to discontinuation.[39]

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7.7.2.2 Conclusion

As mentioned in the bimekizumab SmPC, the incidence rate of uveitis TEAEs was lower at week 16 in axSpA patients randomised to bimekizumab 160 mg Q4W vs placebo. In the largest pool of ph2b/3 data available at the time of this report, the incidence rate of uveitis with bimekizumab 160 mg Q4W remained low at 1.2/100 PY.[39, 40]

7.8 Efficacy and safety of bimekizumab compared to placebo for nr-axSpA bDMARD experienced patients

7.8.1 Relevant studies

In the following section results from the bDMARD experienced subgroup of BE MOBILE 1 (10.6% of the patients included in BE MOBILE 1) are presented. As the sample size of the bDMARD experienced subgroup (n=27) is very limited the analyses should be interpreted with caution.

BE MOBILE 1 please see study description in section 7.3.1

7.8.2 Efficacy and safety – results per study

7.8.2.1 Efficacy and safety – bimekizumab (BE MOBILE 1)

Table 69 Results of the bDMARD experienced subgroup at 16 weeks from BE MOBILE 1

Endpoint	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
ASAS40	Bimekizumab	Placebo	16	6	10	2	17	5.10 (1.26; 20.61)	48%	0.48 (0.14; 0.82)
ASDAS< 2.1	Bimekizumab	Placebo	16	6	10	4	17	2.55 (0.94; 6.90)	36.5%	0.36 (0.00; 0.73)
BASDAI 50	Bimekizumab	Placebo	16	4	10	2	17	3.40 (0.75; 15.34)	28%	0.28 (-0.06; 0.62)
Discontinuation due to AEs	Bimekizumab	Placebo	16	0	10	1	17	0.55 (0.02; 12.25)	-5.9%	-0.06 (-0.17; 0.05)
Discontinuation due to lack of efficacy	Bimekizumab	Placebo	16	0	10	0	17	NA	NA	NA

Endpoint	Intervention	Comparator	Timepoint	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
SF36-PCS	Bimekizumab	Placebo	16	10	11.64	13.25	17	4.09	7.77	7.55 (-0.33; 15.44)

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SF36-bodily pain	Bimekizumab	Placebo	16	10	11.45	10.69	17	6.17	8.32	5.28 (-1.94; 12.50)
SF36-physical functioning	Bimekizumab	Placebo	16	10	12.82	12.44	17	3.21	7.34	9.61 (2.19; 17.02)

7.8.3 Comparative analyses of efficacy and safety

The comparative analyses are solely based on the BE MOBILE 1 study comparison versus placebo and subsequent subgroup analyses.

7.8.3.1 ASAS40 (bDMARD experienced)

For ASAS40, the result of the bDMARD experienced subgroup analyses demonstrates that the absolute risk difference point estimate of 48% favours bimekizumab with a risk ratio of 5.10 (95% CI: 1.26; 20.61). The results are statistically significant, despite the limited sample size, and demonstrates that bimekizumab is superior to placebo in relation to ASDAS40.

Table 70 ASAS40 (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	6	10	2	17	5.10 (1.26; 20.61)	48%	0.48 (0.14; 0.82)

7.8.3.2 ASDAS<2.1 (bDMARD experienced)

For ASDAS<2.1, the result of the bDMARD experienced subgroup analyses demonstrates that the absolute risk difference point estimate of 36.5% favours bimekizumab with a risk ratio of 2.55 (95% CI: 0.94; 6.90). Although, the results are not statistically significant, as can be expected given the sample size, they provide an indication that bimekizumab is associated with better ASDAS<2.1 results versus placebo.

Table 71 ASDAS<2.1 (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	6	10	4	17	2.55 (0.94; 6.90)	36.5%	0.36 (0.00; 0.73)

7.8.3.3 BASDAI50 (bDMARD experienced)

For BASDAI50, the result of the bDMARD experienced subgroup analyses demonstrates that the absolute risk difference point estimate of 28% favours bimekizumab with a risk ratio of 3.40 (95% CI: 0.75; 15.34).

Although, the results are not statistically significant, as can be expected given the sample size, they provide an indication that bimekizumab is associated with better BASDAI50 results versus placebo.

Table 72 BASDAI50 (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Intervention	Comparator	Timepoint	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	4	10	2	17	3.40 (0.75; 15.34)	28%	0.28 (-0.06; 0.62)

7.8.3.4 SF36-PCS (bDMARD experienced)

For SF36-PCS, the result of the bDMARD experienced subgroup analyses demonstrates that the point estimates favour bimekizumab with a difference in mean change of 7.55. Although, the results are not statistically significant, as can be expected given the sample size, they provide an indication that bimekizumab is associated with better SF36-PCS results versus placebo.

Table 73 SF36-PCS (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Intervention	Comparator	Time-point	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	10	11.64	13.25	17	4.09	7.77	7.55 (-0.33; 15.44)

7.8.3.5 SF36 bodily pain (bDMARD experienced)

For SF36 bodily pain, the result of the bDMARD experienced subgroup analyses demonstrates that the point estimates favour bimekizumab with a difference in mean change of 5.28. Although, the results are not statistically significant, as can be expected given the sample size, they provide an indication that bimekizumab is associated with better SF36 bodily pain results versus placebo.

Table 74 SF36 bodily pain (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Intervention	Comparator	Time-point	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	10	11.45	10.69	17	6.17	8.32	5.28 (-1.94; 12.50)

7.8.3.6 SF36 physical functioning (bDMARD experienced)

For SF36 physical functioning, the result of the bDMARD experienced subgroup analyses demonstrates that the point estimates favour bimekizumab with a difference in mean change of 9.61. Although, the results

are not statistically significant, as can be expected given the sample size, they provide an indication that bimekizumab is associated with better SF36 physical functioning results versus placebo.

Table 75 SF36 physical functioning (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Intervention	Comparator	Time-point	N intervention	Mean change	SD	N comparator	Mean change	SD	Diff in change (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	10	12.82	12.44	17	3.21	7.34	9.61 (2.19; 17.02)

7.8.3.7 Discontinuation due to AEs (bDMARD experienced)

For Discontinuation due to AEs, the result of the bDMARD experienced subgroup analyses demonstrates that both point estimates favour bimekizumab with an absolute risk difference of -5.9% and a risk ratio of 0.55 (95% CI: 0.02; 12.25). In the arms with zero events a continuity correction (+1 for N and +0,5 for n for both arms of the trial) was applied. Although, the results are not statistically significant, as can be expected given the sample size, they provide an indication that bimekizumab is associated with better discontinuation due to AEs results versus placebo.

Table 76 Discontinuation due to AEs (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Inter-vention	Comparator	Time-point	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	0	10	1	17	0.55 (0.02; 12.25)	-5.9%	-0.06 (-0.17; 0.05)

7.8.3.8 Discontinuation due to lack of efficacy (bDMARD experienced)

For discontinuation due to lack of efficacy, the result of the bDMARD experienced subgroup analyses showed equivalence between bimekizumab and placebo with no events observed in both arms. Therefore, no formal comparative analysis was conducted for this outcome.

Table 77 Discontinuation due to lack of efficacy (Data based on bDMARD experienced subgroup from BE MOBILE 1)

Trial	Inter-vention	Comparator	Time-point	n intervention	N intervention	n comparator	N comparator	RR (95%CI)	ARD	ARD (95%CI)
BE MOBILE 1	Bimekizumab	Placebo	16	0	10	0	17	NA	NA	NA

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7.8.3.9 Conclusion

For the comparison of bimekizumab vs placebo in nr-axSpA bDMARD experienced patients, the analyses were conducted based on the subgroup in BE MOBILE 1 for both bimekizumab and placebo. The results of the analyses showed that bimekizumab is favoured by all the point estimates in the comparison to placebo. Most of the observed differences are not statistically significant, which can be expected given the small sample size of the subgroup (n=27). Overall, the results indicates that bimekizumab is a superior treatment of nr-axSpA bDMARD experienced patients compared to placebo.

8. Health economic analysis

The health economic analysis is a cost-minimization analysis (CMA) based on the assumption of clinical equivalence, which is in line with previous submissions and assessments for ixekizumab and secukinumab[3, 4].

The patient populations included in the CMA are AS and nr-axSpA and comparators included are adalimumab, ixekizumab and secukinumab.

8.1 Model

As described previously a CMA was chosen based on the assumption of clinical equivalence between bimekizumab and the comparators (adalimumab, ixekizumab and secukinumab). The time horizon of the model is 18 months based on the previous extended basis of comparisons within the therapeutic area and assessment reports.

The discount rate applied in the model is 3.5% as stated in the DMC methods guidance.

8.2 Relationship between the data for relative efficacy, parameters used in the model and relevance for Danish clinical practice

Not applicable

8.2.1 Presentation of input data used in the model and how they were obtained

Not applicable

8.2.2 Relationship between the clinical documentation, data used in the model and Danish clinical practice

Not applicable

8.2.2.1 Patient population

Not applicable

8.2.2.2 Intervention

Bimekizumab is expected to be used in clinical practice in line with the EMA approved posology. Treatment duration is based on previous extended basis of comparisons from the DMC and Amgros (18 months).

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Table 78 Intervention

Intervention	Clinical documentation (including source)	Used in the model (number/value including source)	Expected Danish clinical practice (including source if known)
Posology	160 mg every 4 weeks	160 mg every 4 weeks	160 mg every 4 weeks
Length of treatment (time on treatment) (mean/median)	NA	18 months (based on previous extended basis of comparison)	NA
Criteria for discontinuation	NA	NA	NA

8.2.2.3 Comparators

The latest Danish clinical practice is determined by the DMC treatment recommendation, which recommends adalimumab in first line and ixekizumab and secukinumab in subsequent lines. Please note that the DMC decided in Aug 2021 to no longer to update this treatment recommendation. The posology in clinical practice is expected to be in line with the EMA approved posology for each comparator.

Table 79 Comparator

Comparator	Clinical documentation (including source)	Used in the model (number/value including source)	Expected Danish clinical practice (including source)
Posology (adalimumab)	40 mg once every 2 weeks	40 mg once every 2 weeks	40 mg once every 2 weeks
Posology (ixekizumab)	1st cycle: 160 mg SC (2 injections of 80 mg) week 0, Subsequent cycles: 80 mg every 4 weeks	1st cycle: 160 mg SC (2 injections of 80 mg) week 0, Subsequent cycles: 80 mg every 4 weeks	1st cycle: 160 mg SC (2 injections of 80 mg) week 0, Subsequent cycles: 80 mg every 4 weeks
Posology (secukinumab)	Induction phase: 150 mg week 0, 1, 2, 3, 4. Maintenance phase: Subcutaneously 150 mg every month	Induction phase: 150 mg week 0, 1, 2, 3, 4. Maintenance phase: Subcutaneously 150 mg every month	Induction phase: 150 mg week 0, 1, 2, 3, 4. Maintenance phase: Subcutaneously 150 mg every month
Length of treatment	NA	18 months (based on previous extended basis of comparison)	NA
The comparator's position in the Danish clinical practice	As described in the DMC treatment recommendation	As described in the DMC treatment recommendation	As described in the DMC treatment recommendation

Dosing of secukinumab in clinical practice is suspected to be affected by a substantial proportion of patients being treated with the higher 300 mg dosing rather than the 150 mg dosing. The SmPC of

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secukinumab states that the dose can be increased to 300 mg based on clinical response[33]. This is backed by Norwegian registry data provided in a New Methods input application (Nye Metoder Innspil) for upadacitinib which provide data from the Norwegian Patient Registry (NPR) and Prescription registry illustrating the actual secukinumab dosing between 2018-2021. The mean monthly number of pens/syringes equals 1.41 in the maintenance phase which is considerably higher than the SmPC recommended one pen/syringe per month.[41]

To illustrate the impact of the real-world dosing of secukinumab the economic model includes an analysis based on the Norwegian real-world dosing in clinical practice.

8.2.2.4 Relative efficacy outcomes

Not applicable

8.2.2.5 Adverse reaction outcomes

Not applicable

8.3 Extrapolation of relative efficacy

Not applicable

8.4 Documentation of health-related quality of life (HRQoL)

Not applicable

8.4.1 Health state utility values used in the health economic model

Not applicable

8.5 Resource use and costs

All treatments included in the analyses are administered as subcutaneous injections by the patient or caregivers. As the medicinal products are administered by the patient itself, there are not expected to be relevant differences between the medicinal products for either administration, monitoring, or transport. The cost analysis also includes administration, monitoring, patient, and transport costs in order to give the full overview of the results comparing bimekizumab to the treatments currently included in the DMC treatment recommendation.

A time horizon of 18 months has been chosen as this time horizon is used in the previous DMC treatment recommendations. In a cost minimization analysis, the time horizon is less relevant as no differences in either survival or treatment length are expected between interventions. Ixekizumab and secukinumab have a higher cost in Year 1 than in subsequent years due to increased dosing in the induction phase. Therefore, the results are also presented for year 1 and per subsequent year to give the most accurate results.

All costs reported were in Danish kroner (DKK) and were based on diagnosis-related groups (DRG) tariffs 2023, official unit cost catalogues, and medicinpriser.dk [42-44]. All drug costs were reported as pharmacy purchase prices (PPP), where the lowest cost alternative was used in the health economic assessment. Costs are discounted at 3.5% per year for costs after 1 year according to the DMC guidance.

8.5.1 Drug acquisition cost

The model uses the PPP for all pharmaceuticals utilized in the analysis.

Table 80 Drug acquisition cost

Drug		Mode of administration	Capsules/vials per pack	Vial (mg)	Vial (cost)	Source [43]
Bimekizumab	Bimzelx	SC	2	160	16,703.31 DKK	Medicinpriser.dk (2023)
Adalimumab	Hyrimoz	SC	2	40	4,651.49 DKK	Medicinpriser.dk (2023)
Ixekizumab	Taltz	SC	1	80	7,012.14 DKK	Medicinpriser.dk (2023)
Secukinumab	Cosentyx	SC	2	150	7,710.60 DKK	Medicinpriser.dk (2023)

Abbreviations: IV, intravenous injection; SC, Subcutaneous injections; Search on medicinpriser.dk in April 2023.

8.5.2 Administration costs

Since all medicines are administered subcutaneously, it is assumed that all medicines require training in self-administration. It is assumed that two training visits to the hospital are necessary for administering the drugs, according to Jakobsen. al. 2015[11].

To estimate the cost of each training visit, DRG 2023, 01MA98 MDC01 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DR413A: Amnesi UNS Procedure: BWAA31 Medicingivning ved subkutan injektion. This tariff is DKK 2,321.
The model also allows, as an alternative, to use the DMCs extended basis of comparison for DMARDs for chronic rheumatoid arthritis to estimate administration costs. However, the DRG tariff is used in the base case in accordance with the DMCs guidance.

Table 81 Administration costs

Administration form	Unit cost	Source [42]
SC	2,321 DKK	Interaktiv DRG 2023, 01MA98 MDC01 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DR413A: Amnesi UNS Procedure: BWAA31 Medicingivning ved subkutan injektion

Abbreviations: SC, Subcutaneous injections

8.5.3 Monitoring costs

To estimate the monitoring costs for the medicinal products, the DMCs extended basis of comparison for DMARDs for chronic rheumatoid arthritis has been used. This has been used because monitoring costs for chronic rheumatoid arthritis are expected to be representative of monitoring costs for axSpA when the

dosage of the drugs is similar across therapy areas. Since bimekizumab, ixekizumab and secukinumab are not included in the extended comparison, the monitoring costs for adalimumab are used as a proxy. Since all medicines are administered subcutaneously, this is considered a reasonable assumption. This is supported by the fact that the monitoring costs for all subcutaneous medicinal products in the extended basis of comparison are broadly similar. In the extended basis of comparison, the monitoring costs over 18 months for adalimumab are DKK 1,420.90. In the model, this is converted to a monthly cost of DKK 78.94, which is used for all interventions.

8.5.4 Patient time and transportation costs

To estimate patient costs, the Danish Medicines Council's extended basis of comparison for DMARDs for chronic rheumatoid arthritis (2020) has also been used according to the same method as described above. In the extended basis of comparison, the patient costs over 18 months for adalimumab are DKK 2,255.90. In the model, this is converted into a monthly cost of DKK 125.33, which is used for all interventions.

In order to estimate the transport costs associated with the medicines, the costs associated with the two training visits and each time the patients are dispensed with the medicines are assumed. It is assumed that patients are given the medicines every 8 weeks. It is assumed that the transport costs for each visit are DKK 100 according to the DMCs guidance.

8.6 Results

8.6.1 Base case overview

Table 82 provides an overview of the cost-minimization base case

Table 82 Base case overview

Comparator	Standard care
Type of model	Cost-minimization model
Time horizon	18 months
Treatment line	NA
Measurement and valuation of health effects	NA
Included costs	Pharmaceutical costs Hospital costs Patient costs Transport costs
Dosage of pharmaceutical	Fixed dose based on SmPC
Average time on treatment	18 months

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8.6.2 Base case results

Table 83 shows the total cost of bimekizumab and adalimumab as well as the incremental cost of bimekizumab over an 18-month time horizon. Using AIP, the total cost is DKK 174,470 and DKK 99,095 for bimekizumab and adalimumab, respectively. The pharmaceutical costs, with the base-case assumptions, make up all the incremental costs.

Table 83 Results for the base case bimekizumab versus adalimumab (PPP)

	Bimekizumab	Adalimumab	Incremental costs
Pharmaceutical costs	165.056,14 kr.	89.681,63 kr.	75.374,51 kr.
Administrative costs	4.688,45 kr.	4.688,45 kr.	0,00 kr.
Monitoring costs	1.404,88 kr.	1.404,88 kr.	0,00 kr.
Patient costs	2.230,47 kr.	2.230,47 kr.	0,00 kr.
Transport	1.089,86 kr.	1.089,86 kr.	0,00 kr.
Total	**174.469,80 kr.**	**99.095,28 kr.**	**75.374,51 kr.**

Table 84 shows the total cost of bimekizumab and secukinumab as well as the incremental cost of bimekizumab over an 18-month time horizon. Using AIP, the total cost is DKK 174,470 and DKK 92,855 for bimekizumab and secukinumab, respectively. The pharmaceutical costs, with the base-case assumptions, make up all the incremental costs.

Table 84 Results for the base case bimekizumab versus secukinumab (PPP)

	Bimekizumab	Secukinumab	Incremental costs
Pharmaceutical costs	165.056,14 kr.	83.441,24 kr.	81.614,90 kr.
Administrative costs	4.688,45 kr.	4.688,45 kr.	0,00 kr.
Monitoring costs	1.404,88 kr.	1.404,88 kr.	0,00 kr.
Patient costs	2.230,47 kr.	2.230,47 kr.	0,00 kr.
Transport	1.089,86 kr.	1.089,86 kr.	0,00 kr.
Total	**174.469,80 kr.**	**92.854,90 kr.**	**81.614,90 kr.**

Table 85 shows the total cost of bimekizumab and secukinumab RWE dosing as well as the incremental cost of bimekizumab over an 18-month time horizon. The RWE dosing is based on Norwegian registry data showing a higher average dosing of secukinumab than the SmPC recommended dose (150 mg), which is also used in the current treatment recommendation. Using AIP, the total cost is DKK 174,470 and DKK 119,162 for bimekizumab and secukinumab RWE dosing, respectively. The pharmaceutical costs, with the base-case assumptions, make up all the incremental costs.

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Table 85 Results for the base case bimekizumab versus secukinumab RWE dosing (PPP)

	Bimekizumab	Secukinumab	Incremental costs
Pharmaceutical costs	165.056,14 kr.	109.748,79 kr.	55.307,35 kr.
Administrative costs	4.688,45 kr.	4.688,45 kr.	0,00 kr.
Monitoring costs	1.404,88 kr.	1.404,88 kr.	0,00 kr.
Patient costs	2.230,47 kr.	2.230,47 kr.	0,00 kr.
Transport	1.089,86 kr.	1.089,86 kr.	0,00 kr.
Total	**174.469,80 kr.**	**119.162,44 kr.**	**55.307,35 kr.**

Table 86 shows the total cost of bimekizumab and ixekizumab as well as the incremental cost of bimekizumab over an 18-month time horizon. Using AIP, the total cost is DKK 174,470 and DKK 155,009 for bimekizumab and ixekizumab, respectively. The pharmaceutical costs, with the base-case assumptions, make up all the incremental costs.

Table 86 Results for the base case bimekizumab versus ixekizumab (PPP)

	Bimekizumab	Ixekizumab	Incremental costs
Pharmaceutical costs	165.056,14 kr.	145.595,06 kr.	19.461,08 kr.
Administrative costs	4.688,45 kr.	4.688,45 kr.	0,00 kr.
Monitoring costs	1.404,88 kr.	1.404,88 kr.	0,00 kr.
Patient costs	2.230,47 kr.	2.230,47 kr.	0,00 kr.
Transport	1.089,86 kr.	1.089,86 kr.	0,00 kr.
Total	**174.469,80 kr.**	**155.008,72 kr.**	**19.461,08 kr.**

8.7 Sensitivity analyses

No scenario analyses have been carried out for the cost analysis, as there is no basis for assuming differences in other costs between the medicinal products.

9. Budget impact analysis

Bimekizumab is expected to be placed as clinically equivalent alternative to existing treatments and it is recommended that the Regions use the cheapest treatment. In the current tender set-up, the prices can be regulated every 6 months, so it is not possible to estimate a likely market share or budget impact for the next 5 years. Despite of this UCB have provided an estimate for potential market shares, but it should be noted that bimekizumab approval will only have small impact on the size of the overall budget impact.

A budgetary impact analysis has been prepared comparing regional costs in the current scenario with regional costs in the scenario where bimekizumab is recommended as a possible standard treatment. The budgetary consequences are calculated per year over 5 years and non-discounted values are used.

Number of patients

According to the DMCs previous assessment within axSpA, there are believed to be 2,270 patients potentially relevant for treatment with bimekizumab. In the absence of specific data, it is assumed that the size of the patient population is constant, so there is a fairly stable intake and dropout of patients on biological therapy.
The number of patients increases in year 2 due to the 18 months treatment duration and remains stable in the subsequent years.

Table 87 Number of patients expected to be treated over the next five-year period - if the pharmaceutical is introduced

	Year 1	Year 2	Year 3	Year 4	Year 5
Bimekizumab	9	20	34	50	66
Adalimumab	2111	2111	2111	2111	2111
Secukinumab	114	109	104	98	86
Ixekizumab	36	30	20	11	7
Total number of patients	2270	2270	2270	2270	2270

Table 88 Number of patients expected to be treated over the next five-year period - if the pharmaceutical is NOT introduced

	Year 1	Year 2	Year 3	Year 4	Year 5
Bimekizumab	0	0	0	0	0
Adalimumab	2111	2111	2111	2111	2111
Secukinumab	114	114	114	114	114
Ixekizumab	45	45	45	45	45
Total number of patients	2270	2270	2270	2270	2270

Budget impact

At AIP level, the estimated budget impact of recommending bimekizumab as possible standard treatment is approximately 0,1 MDKK in year 1, 0.4 mDKK in year 2, 0.7 mDKK in year 3, 1.1 mDKK in year 4, and 1.7 mDKK in year 5.

Table 89 Expected budget impact of recommending the bimekizumab for the current indication

	Year 1	Year 2	Year 3	Year 4	Year 5
Bimekizumab is recommended	148.468.525	148.754.918	149.064.923	149.482.707	150.068.826
Bimekizumab is NOT recommended	148.374.079	148.374.079	148.374.079	148.374.079	148.374.079
Budget impact of the recommendation	94.446	380.839	690.844	1.108.628	1.694.747

10. Discussion on the submitted documentation

Based on the results of the ITC vs adalimumab, secukinumab and ixekizumab, UCB believes that bimekizumab can be considered to be equivalent to the existing biologic treatments recommended in the treatment recommendation for AS and nr-axSpA. UCB acknowledge that bimekizumab is unlikely to replace adalimumab given the availability of biosimilar adalimumab. Bimekizumab will likely replace secukinumab and ixekizumab depending on the ranking in the drug recommendation and as such be used in bDMARD experienced patients. Please see below an overview of key results of the ITC.

Table 90 AS ITC analyses results (at 12-16 weeks)

	BKZ vs ADA	BKZ vs SEC	BKZ vs IXE
ASAS40	RR: 0.67 (95% CI: 0.40; 1.10)	RR: 0.99 (95% CI: 0.64; 1.53)	RR: 1.13 (95% CI: 0.32; 3.94)
ASDAS<2.1	RR: 0.82 (95% CI: 0.38; 1.74)	NR	RR: 0.88 (95% CI: 0.10; 8.16)
BASDAI50	RR: 0.76 (95% CI: 0.48; 1.22)	RR: 0.99 (95% CI: 0.57; 1.72)	RR: 0.44 (95% CI: 0.15; 1.23)
SF36-PCS	Diff. mean change: 0.24 (95% CI: -2.07; 2.55)	Diff. mean change: 0.66 (95% CI: -1.49; 2.81)	Diff. mean change: -2.40 (95% CI: -7.83; 3.03)
SF36-MCS	Diff. mean change: -0.67 (95% CI: -3.15; 1.81)	Diff. mean change:0.02 (95% CI: -3.95; 3.99)	NR
Discontinuation due to AEs	RR: 2.82 (95% CI: 0.11; 75.63)	RR: 2.31 (95% CI: 0.10; 51.85)	RR: 0.77 (95% CI: 0.03; 21.23)

RR: risk ratio, AS: ankylosing spondylitis, ASAS: Assessment of Spondyloarthritis International Society, ASDAS: Ankylosing Spondylitis Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Index, SF-36: Short Form 36-item survey, AE: adverse event.

Table 91 nr-axSpA ITC analyses results (at 12-16 weeks)

	BKZ vs ADA	BKZ vs SEC	BKZ vs IXE
ASAS40	RR: 0.83 (95% CI: 0.42; 1.65)	RR: 1.53 (95% CI: 0.95; 2.46)	RR: 1.09 (95% CI: 0.59; 2.03)
ASDAS<2.1	NR	NR	RR: 1.07 (95% CI: 0.51; 2.24)
BASDAI50	RR: 0.87 (95% CI: 0.44; 1.72)	RR: 1.22 (95% CI: 0.74; 2.03)	RR: 0.94 (95% CI: 0.48; 1.85)

SF36-PCS	Diff. mean change: 0.16 (95% CI: -2.93; 3.26)	Diff. mean change: 1.43 (95% CI: -1.34; 4.21)	Diff. mean change: 0.81 (95% CI: -2.21; 3.84)
SF36-bodily pain	NR	NR	NR
Discontinuation due to AEs	RR: 0.38 (95% CI: 0.02; 9.33)	RR: 0.39 (95% CI: 0.04; 3.77)	RR: 1.80 (95% CI: 0.06; 55.69)

RR: risk ratio, nr-axSpA: non-radiographic axial spondyloarthritis, ASAS: Assessment of Spondyloarthritis International Society, ASDAS: Ankylosing Spondylitis Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Index, SF-36: Short Form 36-item survey, AE: adverse event.

In addition to the data presented in the tables above for week 12 and 16 based on ITC, the application also includes data for bimekizumab at week 52 (please see appendix K) to support the long-term effects (from both BE MOBILE1 and BE MOBILE2).

Dual inhibition of IL-17A & F with bimekizumab leads to a marked reduction of inflammation, which is associated with a positive impact on structural disease progression. The available clinical evidence based on ITC for week 12-16 as well as two clinical placebo-controlled RCTs at week 52 (at week 16 patients in the placebo arm were switched to active treatment), show sustained improvements in efficacy outcomes for bimekizumab consistent for both AS and nr-axSpA and as such demonstrates:

- Improvements in ASAS40 with bimekizumab at week 16 with continued improvement until week 52, which specifically means improvements in disease activity, spinal pain, morning stiffness
- Equally high ASAS40 levels of efficacy irrespective of prior TNF use
- Low disease activity with bimekizumab as shown by ASDAS<2.1 at week 16 and sustained at week 52. This means an improvement in spinal pain, morning stiffness, joint pain and swelling, patient global assessment (PGADA) and CRP
- Improvements in patient-reported disease activity and quality of life as measured by BASDAI50 and SF-36. This means an improvement in patient experienced back pain, morning stiffness, fatigue and joint pain and swelling as well as improvement in patient reported quality of life.

In addition, bimekizumab was generally well tolerated in both AS and nr-axSpA patients with low rates of discontinuation.

Based on the comparative ITC evidence in AS, no statistically significant difference where shown, hence we can conclude that the treatments are similar and thus clinical equivalence was established for bimekizumab vs adalimumab in bDMARD naïve patients. Also, clinical equivalence can be concluded for bimekizumab vs ixekizumab in bDMARD experienced patients based on subgroup analysis and confirmed in sensitivity analyses. And finally, clinical equivalence was shown for bimekizumab vs secukinumab in a population of mixed population of bDMARD naïve and experienced patients.

Also, in nr-axSpA, the comparative ITC evidence supported clinical equivalence of bimekizumab vs adalimumab in bDMARD naïve patients as well as vs secukinumab in a mixed population of bDMARD naïve and experienced patients. Finally, clinical equivalence of bimekizumab vs ixekizumab was established based on an analysis of bDMARD naïve as comparative evidence in bDMARD experienced was not available.

In conclusion, bimekizumab can be considered to be equivalent to the existing biologic treatments recommended in the treatment recommendation for AS and nr-axSpA based on the results of the ITC. The pooled, longer-term data also support bimekizumab' s long-term effect, as well as evidence for the low rate of uveitis at week 16.

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Not applicable

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Multicenter Study

Randomized Controlled Trial

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Multicenter Study

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Randomized Controlled Trial

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Appendix A Literature search for efficacy and safety of intervention and comparator(s)

The evidence base for this application was based primarily on previous UCB SLR [45, 46], which consisted of a de novo clinical SLR performed in May 2012, and six subsequent clinical SLR updates, with the most recent performed in October 2020 (please see Figure 1 which shows the PRISMA diagram for the previous SLRs prior to the April 2022 update).

The previous UCB SLR identified 286 publications reporting on 55 RCTs for inclusion in the evidence base. The inclusion and exclusion criteria for the previous SLRs before April 2022 can be found in section "Systematic selection of studies in the global SLRs" and the references included can be found in Table 97. To capture the latest clinical trial evidence in axSpA, including the Phase 3 bimekizumab trials BE MOBILE 1 and BE MOBILE 2, a further clinical SLR update was performed in April 2022. Electronic database searches for this latest update were run on April 27th 2022, using search strings adapted from those utilised in the previous UCB SLR. Embase, MEDLINE (comprising MEDLINE Daily, In-Process & Other Non-indexed citations, and e-pub ahead-of-print), the Cochrane Central Register of Controlled Trials (CENTRAL), and the Cochrane Database of Systematic Reviews (CDSR) were all searched via the Ovid platform. To supplement the electronic database searches, hand-searches were performed of relevant conferences, HTA body websites, clinical trial registries, and the reference lists of other SLRs/NMAs identified during the SLR update. Data from clinical study reports (CSRs) provided by UCB were also eligible for inclusion.

In total, 1,498 publications were identified through the April 2022 electronic database searches. After the removal of 503 duplicates, 995 publications were reviewed based on their titles and abstracts. A total of 698 publications were excluded at the title/abstract review stage, leaving 297 potentially relevant publications that were procured for full-text review. By reviewing the full-text publications, a further 271 publications were excluded. Hand-searching yielded nine additional relevant publications, resulting in a total of 35 unique publications (reporting on 23 unique trials) for final inclusion in the updated review. The flow of publications through the April 2022 SLR clinical update is depicted in the flow diagram in Figure 2.

Of the 35 included publications, 14 were full-text manuscripts, two were errata (reporting corrected numbers for data already in the data extraction table), 17 were conference abstracts or posters, and two were CSRs provided by UCB (reporting on BE MOBILE 1 and BE MOBILE 2, respectively). Overall, 25 of the included publications reported novel data (additional relevant outcomes and/or subgroup analyses) from 16 clinical trials that had already been identified by previous iterations of the clinical SLR, while the remaining 10 included publications reported data from seven more recent clinical trials that had not been published at the time of the previous clinical SLR update in October 2020:

- BE MOBILE 1
- BE MOBILE 2
- SELECT-AXIS 2 (Study 1)
- SELECT-AXIS 2 (Study 2)
- COAST-Y
- ASTRUM
- Wei et al, 2021 (NCT02985983).

An update of the April 2022 SLR was carried out in January 2023, of which the report and results were available late May 2023. The databases selected were consistent with those searched during previous

iterations of the SLR. For the January 2023 database searches, date limits were set to cover the period from January 2022 to the date of search; this overlap with the preceding SLR update was designed to capture any records that had been published but not yet indexed in the electronic databases by April 2022, which otherwise could have been missed.

During the January 2023 clinical SLR update, 862 publications were identified through the electronic database searches. After the removal of 217 duplicates, 645 publications were reviewed based on their titles and abstracts. A total of 586 publications were excluded at the title/abstract review stage, leaving 59 potentially relevant publications that were procured for full-text review. By reviewing the full-text publications, a further 49 publications were excluded; a list of publications excluded at the full-text review stage for all iterations of the SLRs is provided in **Table** 94, Table 95 and Table 96, along with a rationale for their exclusion. Hand-searching yielded 10 additional relevant publications, resulting in a total of 20 publications (reporting on 14 unique trials) for final inclusion in the January 2023 update.

Of the 20 included publications, eight were full-text manuscripts, 11 were conference abstracts or posters, and one was an online clinical trial record. Overall, 16 of the included publications reported novel data (additional relevant outcomes and/or subgroup analyses) from 11 clinical trials that had already been identified by previous iterations of the clinical SLR, while the remaining four included publications reported data from three more recent clinical trials that had not been published at the time of the previous clinical SLR update in April 2022:

- SURPASS
- Li 2022 (ChiCTR20181863)
- Xue 2022 (NCT04285229).

Taken together, the original clinical SLR and eight clinical SLR updates (including the April 2022 and January 2023 updates) identified 341 publications for inclusion, reporting on 65 unique trials. Please refer to Figure 3 for the flow of publications.

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Figure 1 PRISMA flow diagram for all iterations of the clinical SLR prior to the April 2022 update

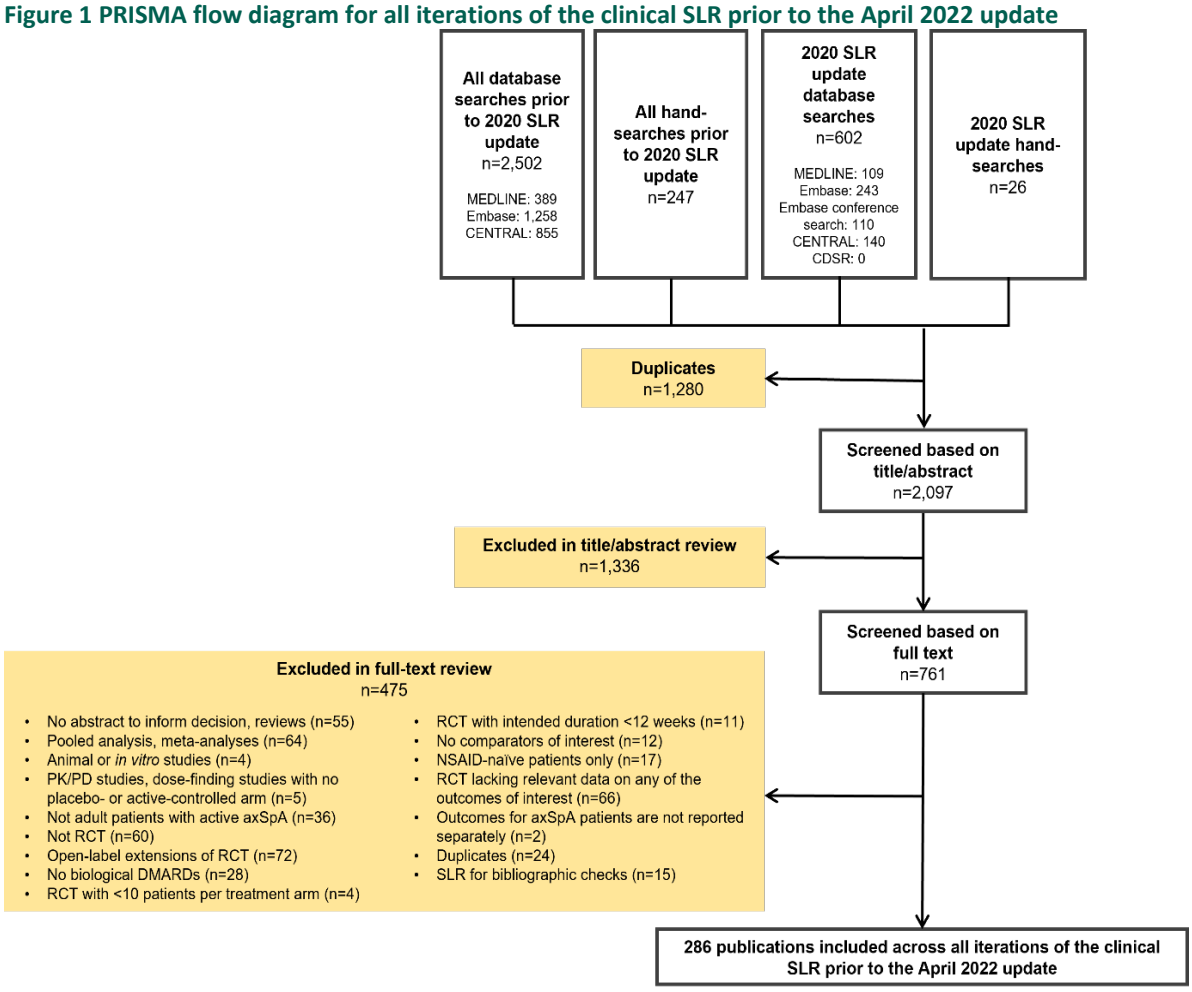
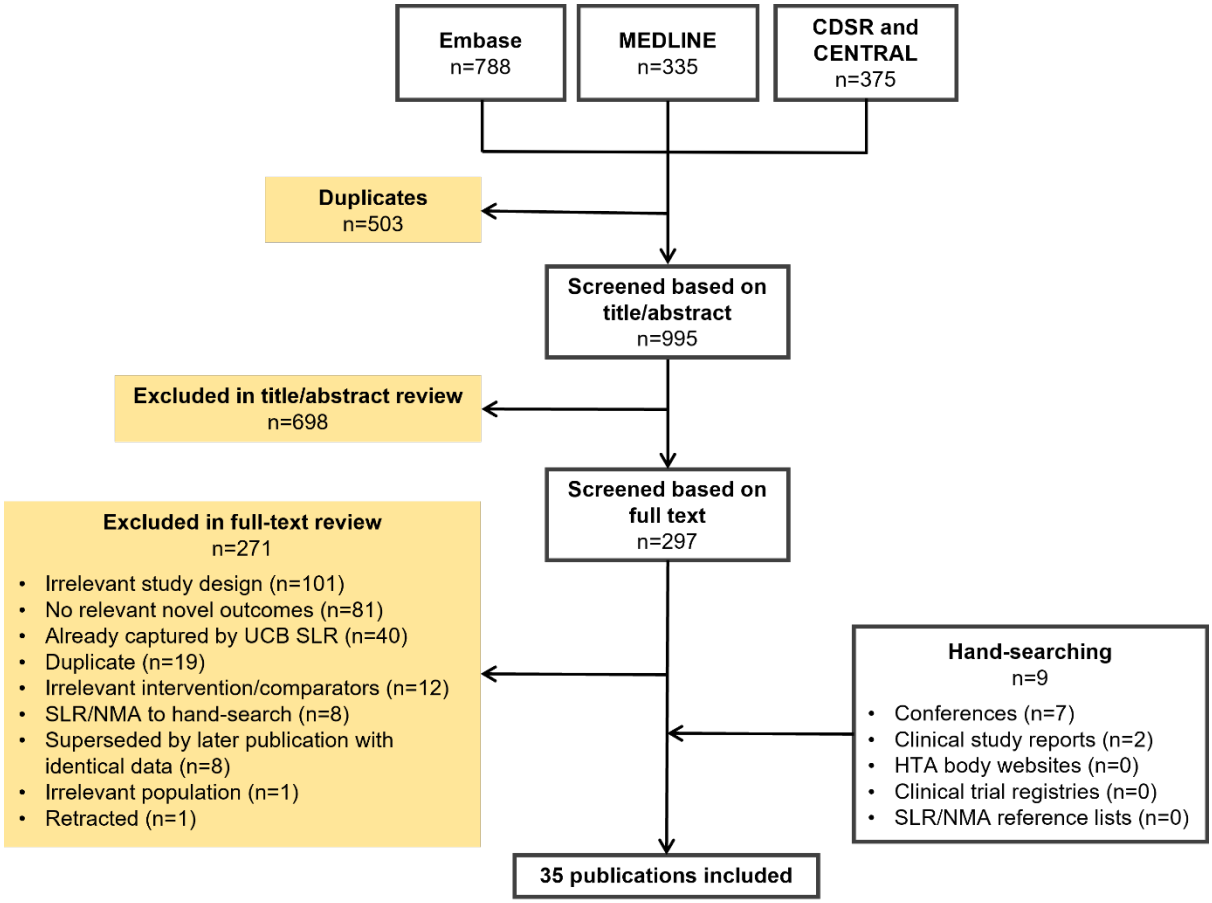
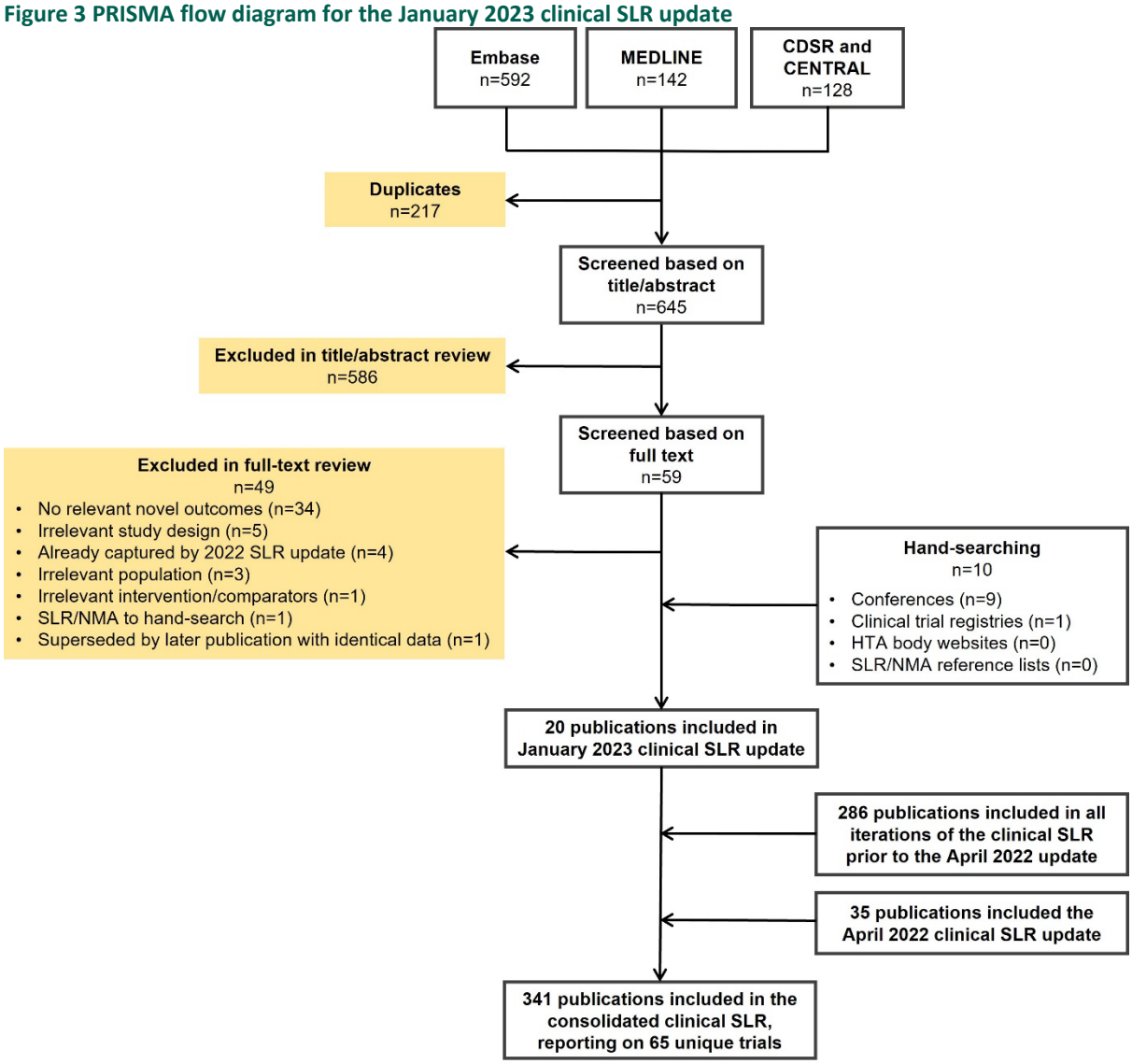


Figure 2 PRISMA flow diagram for April 2022 clinical SLR update, which identified data published between October 27th 2020 and April 27th 2022



Abbreviations: CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; HTA, health technology assessment; NMA, network meta-analysis; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLR, systematic literature review; UCB, Union Chimique Belge.

Figure 3 PRISMA flow diagram for the January 2023 clinical SLR update



Abbreviations: CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; HTA, health technology assessment; NMA, network meta-analysis; SLR, systematic literature review.

Table 92: Bibliographic databases to be included in the clinical SLR update

Database	Platform		Span of search
Embase	Ovid	January 2022† to January 9th 2023 (most recent database update)	January 10th 2023
MEDLINE Daily, In-Process & Other Non-indexed citations, and e-pub ahead-of-print		January 2022† to January 9th 2023 (most recent database update)	
Cochrane library – CENTRAL		January 2022† to December 2022 (most recent database update)	
Cochrane library – CDSR		January 2022† to January 4th 2023 (most recent database update)	

†The database searches for the preceding clinical SLR update were run on April 27th 2022. To avoid missing any records that had been published but not yet indexed by this date, date limits for the January 2023 clinical SLR update searches spanned from January 1st 2022 to the date of search, and any eligible publications already included in the existing SLR were removed manually during screening.
Abbreviations: CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; SLR, systematic literature review.

Hand-searching

Hand-searching was used as a supplementary measure to ensure that all relevant studies are included in the SLR update. The following sources were searched:

- **Conference proceedings**

To identify further studies not captured in the electronic database searches, proceedings of relevant conferences held since the previous clinical SLR update (October 2020 to present) were searched via the conferences' online platforms, or via downloadable abstract books. A record of any conferences for which abstracts cannot be obtained was kept. The following conferences were searched:

- American College of Rheumatology (ACR)
- European League Against Rheumatism (EULAR)
- British Society for Rheumatology (BSR)
- Professional Society for Health Economics and Outcomes Research (ISPOR) International
- ISPOR Europe

- **Health technology assessment submissions**

Previous submission documents from the following HTA agencies were reviewed for relevant data:

  - England: NICE
  - Scotland: Scottish Medicines Consortium (SMC)
  - Canada: Canadian Agency for Drugs and Technologies in Health (CADTH)
  - Australia: Pharmaceutical Benefits Advisory Committee (PBAC)
  - France: Haute Autorité de Santé (HAS)
  - Germany:
    - Institute for Quality and Efficiency in Health Care (IQWiG)
    - Gemeinsamer Bundesausschuss (The Federal Joint Committee [G-BA]).

- **Clinical trial registries**

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To obtain details of potentially relevant published and ongoing trials, the following clinical trial registry databases were accessed:

- World Health Organisation International Clinical Trials Registry Platform (WHO ICTRP): https://www.who.int/ictrp/search/en/)
- United States National Institutes of Health (NIH) trial registry & results database (https://clinicaltrials.gov/).

Search strategy

The database search strings for the SLR update are outlined in the tables below. These search strings have been designed in Embase and translated for the other databases. The searches combine free text and controlled vocabulary terms (Medical Subject He adings [MeSH] in MEDLINE and Emtree terms in Embase).

January 2023 update
Database: Embase
Platform: Ovid
Date last searched: 10/01/2023
Hits: 592
Study design filter: Modified version of Scottish Intercollegiate Guidelines Network (SIGN) [54]

#	Search term group	Searches	Results
1	Population	exp spondylarthritis/	67233
2		exp ankylosing spondylitis/	30668
3		((ankyl$ or axial) adj4 (spondyl$ or SpA)).ti,ab.	31007
4		(ankyl$ adj2 (spine$ or spinal or vertebra$)).ti,ab.	1082
5		((Bechtere$ or Bekhtere$ or Marie Strumpell$ or Marie Struempell$) adj2 (disease or syndrome)).ti,ab.	446
6		(axSpA or ax-SpA or raxSpA or r-axSpA or r-ax-SpA or nraxSpA or nr-axSpA or nr-ax-SpA).ti,ab.	3908
7		((nonradiographic or non-radiographic or radiographic) adj4 (spondyl$ or SpA)).ti,ab.	1948
8		or/1-7	70789
9	Interventions	exp disease modifying antirheumatic drug/ or (DMARD$ or bDMARD$ or disease modifying anti rheumatic drug$ or disease modifying antirheumatic drug$).ti,ab.	33877
10		exp tumor necrosis factor inhibitor/ or (TNF inhibitor$ or anti-TNF$ or TNF-antagonist$ or tumo?r necrosis factor$ or TNFalpha or TNF-alpha or TNFa or TNF-a).ti,ab.	448911
11		exp interleukin 17/ or ((IL17$ or IL-17$ or interleukin17$ or interleukin-17$) adj (inhibitor$ or antagonist$)).ti,ab. or (anti-IL17$ or anti-IL-17$ or anti-interleukin17$ or anti-interleukin-17$).ti,ab.	63443
12		exp bimekizumab/ or (bimekizumab or BKZ or bimzelx or UCB4940 or "UCB 4940" or 1418205-77-2 or cdp4940 or "cdp 4940").ti,ab,rn.	399
13		exp secukinumab/ or (secukinumab or ain457 or "ain 457" or cosentyx or 1229022-83-6 or 875356-43-7 or 875356-44-8).ti,ab,rn.	6518

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14		exp ixekizumab/ or (ixekizumab or taltz or GTPL7541 or ly2439821 or "ly 2439821").ti,ab,rn.	3260
15		exp brodalumab/ or (brodalumab or Siliq or Kyntheum or KHK4827 or "KHK 4827" or AMG827 or "AMG 827" or 1174395-19-7).ti,ab,rn.	1797
16		exp adalimumab/ or (adalimumab or trudexa or humira or amgevita or amjevita or imraldi or solymbic or adalimumab-atto or abp501 or "abp 501" or D2E7 or "D2 E7" or LS-186588 or 331731-18-1).ti,ab,rn.	43571
17		exp etanercept/ or (etanercept or enbrel or altebrel or benepali or embrel or lifmior or erelzi or "tnr 001" or tnr001 or 185243-69-0 or 200013-86-1 or etanercept-szzs or "HSDB 7849" or OP401G7OJC or Recombinant human TNF or Recombinant human dimeric TNF receptor type II-IgG fusion protein or TNF receptor type II-IgG fusion protein or TNFR-Fc or TNFR:Fc or UNII-OP401G7OJC).ti,ab,rn.	37884
18		exp golimumab/ or (golimumab or cnto148 or "cnto 148" or simponi or 476181-74-5 or ACN-040096).ti,ab,rn.	9562
19		exp infliximab/ or (infliximab or remicade or remsima or avakine or flixabi or inflectra or revellex or LS-183368 or LS183368 or 170277-31-3 or CT-P13).ti,ab,rn.	61202
20		exp certolizumab pegol/ or (certolizumab pegol or certolizumab or CZP or cdp870 or "cdp 870" or cimzia or necrosis factor alpha antibody Fab fragment or pha738144 or "pha 738144" or 1132819-27-2 or 339184-10-0 or 428863-50-7 or G6ADW90R16 or "HSDB 7848" or UMD07X179E or UNII-G6ADW90R16 or UNII-UMD07X179E).ti,ab,rn.	9658
21		exp janus kinase inhibitor/ or (janus kinase inhibitor$ or JAK inhibitor$ or JAKinib$).ti,ab.	27327
22		exp tofacitinib/ or (tofacitinib or xeljanz or tasocitinib or jakvinus cp690550 or "cp 690550" or "cp 690 550" or "cp690 550").ti,ab,rn.	8547
23		exp upadacitinib/ or (upadacitinib or rinvoq or abt494 or "abt 494").ti,ab,rn.	1651
24		exp filgotinib/ or (filgotinib or jyseleca or g146034 or "g 146034" or glpg0634 or "glpg 0634" or gs6034 or "gs 6034").ti,ab,rn.	973
25		or/9-24	538211
26	Population + interventions	8 and 25	25842
27	RCT study design filter	exp Clinical Trial/	1764691
28		exp RANDOMIZATION/	96231
29		Single Blind Procedure/	48875
30		Double Blind Procedure/	202431
31		Crossover Procedure/	72608
32		PLACEBO/	390189
33		randomi?ed controlled trial*.tw.	304454
34		rct.tw.	50284
35		(random$ adj3 (allocat$ or assign*)).tw.	224891
36		((singl$ or doubl$ or treb$ or tripl$) adj (blind$ or mask$)).tw.	272095
37		placebo$.tw.	354204

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38		(clinical adj trial*).tw.	659130
39		((phase 1? or phase 2? or phase 3? or phase 4? or phase i? or phase ii? or phase iii? or phase iv?) adj2 (study or studies or trial*)).tw.	232872
40		or/27-39	2675669
41		Case Study/	90828
42		case report.tw.	511718
43		letter/	1175502
44		Editorial.pt.	748576
45		Letter.pt.	1252942
46		Note.pt.	921781
47		or/41-46	3513447
48		40 not 47	2547368
49	Population + interventions + RCTs	26 and 48	7808
50	Removal of animal studies	animal/	1599076
51		nonhuman/	7155450
52		exp animal experiment/	2947864
53		exp experimental animal/	788612
54		animal model/	1623630
55		exp rodent/	3914994
56		(rat or rats or mouse or mice).ti.	1575865
57		or/50-56	9624139
58		human/ and 57	2668525
59		57 not 58	6955614
60		49 not 59	7740
61	Removal of foreign language publications	limit 60 to english language	7553
62	Date limits	limit 61 to dd=20220427-20230110	264
63		limit 61 to dc=20220427-20230110	529
64		limit 61 to yr="2022 - Current"	557
65		or/62-64	592

Database: MEDLINE, incorporating MEDLINE In-Process & Other non-indexed citations, MEDLINE e-pub ahead-of-print, and MEDLINE Daily

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Platform: Ovid
Date last searched: 10/01/2023
Hits: 142
Study design filter: Modified version of Scottish Intercollegiate Guidelines Network (SIGN) [54]

#	Search term group	Searches	Results
1	Population	exp Spondylarthritis/	30093
2		exp Spondylitis, Ankylosing/	16196
3		((ankyl$ or axial) adj4 (spondyl$ or SpA)).ti,ab.	18296
4		(ankyl$ adj2 (spine$ or spinal or vertebra$)).ti,ab.	749
5		((Bechtere$ or Bekhtere$ or Marie Strumpell$ or Marie Struempell$) adj2 (disease or syndrome)).ti,ab.	503
6		(axSpA or ax-SpA or raxSpA or r-axSpA or r-ax-SpA or nraxSpA or nr-axSpA or nr-ax-SpA).ti,ab.	1321
7		((nonradiographic or non-radiographic or radiographic) adj4 (spondyl$ or SpA)).ti,ab.	798
8		or/1-7	34983
9	Interventions	(DMARD$ or bDMARD$ or disease modifying anti rheumatic drug$ or disease modifying antirheumatic drug$).mp.	10173
10		exp tumor necrosis factor inhibitors/ or (TNF inhibitor$ or anti-TNF$ or TNF-antagonist$ or tumo?r necrosis factor$ or TNFalpha or TNF-alpha or TNFa or TNF-a).ti,ab.	276283
11		exp interleukin-17/ or ((IL17$ or IL-17$ or interleukin17$ or interleukin-17$) adj (inhibitor$ or antagonist$)).ti,ab. or (anti-IL17$ or anti-IL-17$ or anti-interleukin17$ or anti-interleukin-17$).ti,ab.	14891
12		(Bimekizumab or BKZ or bimzelx or UCB4940 or "UCB 4940" or 1418205-77-2 or cdp4940 or "cdp 4940").mp.	116
13		(Secukinumab or ain457 or "ain 457" or cosentyx or 1229022-83-6 or 875356-43-7 or 875356-44-8).mp.	1838
14		(Ixekizumab or taltz or GTPL7541 or ly2439821 or "ly 2439821").mp.	932
15		(Brodalumab or Siliq or Kyntheum or KHK4827 or "KHK 4827" or AMG827 or "AMG 827" or 1174395-19-7).mp.	498
16		exp adalimumab/ or (adalimumab or trudexa or humira or amgevita or amjevita or imraldi or solymbic or adalimumab-atto or abp501 or "abp 501" or D2E7 or "D2 E7" or LS-186588 or 331731-18-1).ti,ab,rn.	10324
17		exp etanercept/ or (etanercept or enbrel or altebrel or benepali or embrel or lifmior or erelzi or "tnr 001" or tnr001 or 185243-69-0 or 200013-86-1 or etanercept-szzs or "HSDB 7849" or OP401G7OJC or Recombinant human TNF or Recombinant human dimeric TNF receptor type II-IgG fusion protein or TNF receptor type II-IgG fusion protein or TNFR-Fc or TNFR:Fc or UNII-OP401G7OJC).ti,ab,rn.	9969
18		(Golimumab or cnto148 or "cnto 148" or simponi or 476181-74-5 or ACN-040096).mp.	1568

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19		exp infliximab/ or (infliximab or remicade or remsima or avakine or flixabi or inflectra or revellex or LS-183368 or LS183368 or 170277-31-3 or CT-P13).ti,ab,rn.	16915
20		exp certolizumab pegol/ or (certolizumab pegol or certolizumab or CZP or cdp870 or "cdp 870" or cimzia or necrosis factor alpha antibody Fab fragment or pha738144 or "pha 738144" or 1132819-27-2 or 339184-10-0 or 428863-50-7 or G6ADW90R16 or "HSDB 7848" or UMD07X179E or UNII-G6ADW90R16 or UNII-UMD07X179E).ti,ab,rn.	1739
21		exp janus kinase inhibitors/ or (janus kinase inhibitor$ or JAK inhibitor$ or JAKinib$).ti,ab.	3993
22		(Tofacitinib or xeljanz or tasocitinib or jakvinus cp690550 or "cp 690550" or "cp 690 550" or "cp690 550").mp.	2627
23		(Upadacitinib or rinvoq or abt494 or "abt 494").mp.	445
24		(Filgotinib or jyseleca or g146034 or "g 146034" or glpg0634 or "glpg 0634" or gs6034 or "gs 6034").mp.	247
25		or/9-24	307095
26	Population + interventions	8 and 25	7055
27	RCT study design filter	Randomized Controlled Trials as Topic/	159715
28		randomized controlled trial/	584037
29		Random Allocation/	106898
30		Double Blind Method/	173967
31		Single Blind Method/	32411
32		exp clinical trial/	959595
33		exp Clinical Trials as topic/	379526
34		PLACEBOS/	35924
35		(clinical adj trial*).tw.	459989
36		((singl$ or doubl$ or treb$ or tripl$) adj (blind$ or mask$)).tw.	193913
37		placebo$.tw.	242228
38		(random$ adj2 allocat$).tw.	42401
39		randomi?ed controlled trial*.tw.	235907
40		rct.tw.	29686
41		((phase 1? or phase 2? or phase 3? or phase 4? or phase i? or phase ii? or phase iii? or phase iv?) adj2 (study or studies or trial*)).tw.	111997
42		or/27-41	1786921
43		case report.tw.	381909
44		letter/	1203769
45		historical article/	369005
46		or/43-45	1936205
47		42 not 46	1745625

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48	Population + interventions + RCTs	26 and 47	1851
49	Removal of animal studies	animals/	7216171
50		exp animals, laboratory/	946416
51		exp animal experimentation/	10279
52		exp models, animal/	635962
53		exp rodentia/	3505230
54		(rat or rats or mouse or mice).ti.	1422369
55		or/49-54	7325136
56		humans/ and 55	2177829
57		55 not 56	5147307
58		48 not 57	1849
59	Removal of foreign language publications	limit 58 to english language	1748
60	Date limits	limit 59 to dt=20220427-20230110	71
61		limit 59 to ed=20220427-20230110	77
62		limit 59 to yr="2022 - Current"	141
63		or/60-62	142

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Database: Cochrane - CENTRAL and CDSR
Platform: Ovid
Date last searched: 10/01/2023
Hits: 128

#	Search term group	Searches	Results
1	Population	exp Spondylarthritis/	1512
2		exp Spondylitis, Ankylosing/	752
3		((ankyl$ or axial) adj4 (spondyl$ or SpA)).ti,ab.	2575
4		(ankyl$ adj2 (spine$ or spinal or vertebra$)).ti,ab.	83
5		((Bechtere$ or Bekhtere$ or Marie Strumpell$ or Marie Struempell$) adj2 (disease or syndrome)).ti,ab.	9
6		(axSpA or ax-SpA or raxSpA or r-axSpA or r-ax-SpA or nraxSpA or nr-axSpA or nr-ax-SpA).ti,ab.	574
7		((nonradiographic or non-radiographic or radiographic) adj4 (spondyl$ or SpA)).ti,ab.	418
8		or/1-7	3271
9	Interventions	(DMARD$ or bDMARD$ or disease modifying anti rheumatic drug$ or disease modifying antirheumatic drug$).mp.	4249
10		(tumor necrosis factor inhibitor$ or TNF inhibitor$ or anti-TNF$ or TNF-antagonist$ or tumo?r necrosis factor$ or TNFalpha or TNF-alpha or TNFa or TNF-a).mp.	20650
11		exp interleukin-17/ or ((IL17$ or IL-17$ or interleukin17$ or interleukin-17$) adj (inhibitor$ or antagonist$)).ti,ab. or (anti-IL17$ or anti-IL-17$ or anti-interleukin17$ or anti-interleukin-17$).ti,ab.	706
12		(Bimekizumab or BKZ or bimzelx or UCB4940 or "UCB 4940" or 1418205-77-2 or cdp4940 or "cdp 4940").mp.	151
13		(Secukinumab or ain457 or "ain 457" or cosentyx or 1229022-83-6 or 875356-43-7 or 875356-44-8).mp.	1105
14		(Ixekizumab or taltz or GTPL7541 or ly2439821 or "ly 2439821").mp.	624
15		(Brodalumab or Siliq or Kyntheum or KHK4827 or "KHK 4827" or AMG827 or "AMG 827" or 1174395-19-7).mp.	205
16		(adalimumab or trudexa or humira or amgevita or amjevita or imraldi or solymbic or adalimumab-atto or abp501 or "abp 501" or D2E7 or "D2 E7" or LS-186588 or 331731-18-1).mp.	3790
17		(etanercept or enbrel or altebrel or benepali or embrel or lifmior or erelzi or "tnr 001" or tnr001 or 185243-69-0 or 200013-86-1 or etanercept-szzs or "HSDB 7849" or OP401G7OJC or Recombinant human TNF or Recombinant human dimeric TNF receptor type II-IgG fusion protein or TNF receptor type II-IgG fusion protein or TNFR-Fc or TNFR:Fc or UNII-OP401G7OJC).mp.	2470
18		(Golimumab or cnto148 or "cnto 148" or simponi or 476181-74-5 or ACN-040096).mp.	803
19		(infliximab or remicade or remsima or avakine or flixabi or inflectra or revellex or LS-183368 or LS183368 or 170277-31-3 or CT-P13).mp.	2668

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20		(certolizumab pegol or certolizumab or CZP or cdp870 or "cdp 870" or cimzia or necrosis factor alpha antibody Fab fragment or pha738144 or "pha 738144" or 1132819-27-2 or 339184-10-0 or 428863-50-7 or G6ADW90R16 or "HSDB 7848" or UMD07X179E or UNII-G6ADW90R16 or UNII-UMD07X179E).mp.	816
21		(janus kinase inhibitor$ or JAK inhibitor$ or JAKinib$).mp.	1288
22		(Tofacitinib or xeljanz or tasocitinib or jakvinus cp690550 or "cp 690550" or "cp 690 550" or "cp690 550").mp.	1090
23		(Upadacitinib or rinvoq or abt494 or "abt 494").mp.	603
24		(Filgotinib or jyseleca or g146034 or "g 146034" or glpg0634 or "glpg 0634" or gs6034 or "gs 6034").mp.	338
25		or/9-24	31194
26	Population + interventions	8 and 25	1947
27	Removal of foreign language publications	limit 26 to english language	1908
28	Date limit	limit 27 to yr="2022 -Current"	128

Systematic selection of studies in the global SLRs

The population, intervention, comparator(s), outcomes and study design (PICOS) elements used to assess study eligibility for the April 2022 and January 2023 clinical SLR updates are presented in Table 93. These were developed from the eligibility criteria used in previous iterations of the SLR. The main modifications were:

- Addition of the IL-17 inhibitor brodalumab as a relevant intervention/comparator, based on recent clinical trial evidence that it could be an effective treatment for axSpA.
- Addition of four novel outcomes that were either primary or secondary outcomes in the BE MOBILE 1 and BE MOBILE 2 clinical trials:
  - Enthesitis-free state (i.e. total resolution of enthesitis based on the MASES index in patients with enthesitis at baseline)
  - Tuberculosis reactivation
  - Total treatment-emergent adverse events (TEAEs)
  - Total drug-related TEAEs
- Introduction of date limits to capture records published since the previous clinical SLR update, performed in October 2020.

Table 93 Eligibility criteria (PICOS) – April 2022 and January 2023 clinical SLR updates

Characteristics	Inclusion criteria	Exclusion criteria

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Population	• Adult patients (aged ≥18 years) with either AS/r-axSpA or nr-axSpA, who have:
	  ○ Inadequate response to ≥1 NSAID†, or
	  ○ Intolerance to administration of ≥1 NSAID†, or
	  ○ Contraindication(s) to NSAID therapy†
		• Healthy individuals or patients that do not have axSpA
		• Paediatric/adolescent patients (aged <18 years)
		• Studies explicitly stating that patients are NSAID-naïve or still receiving their first NSAID†
		• Studies with mixed populations (e.g. AS/r-axSpA and nr-axSpA patients) in which outcomes for the subpopulations are not reported separately
		• Studies with patients of mixed ages (e.g. adult and paediatric/adolescent patients) in which outcomes for the age groups are not reported separately

Interventions	• IL-17 inhibitors (bimekizumab, ixekizumab, secukinumab, brodalumab) • TNF-α inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and biosimilars) • JAK inhibitors (tofacitinib, upadacitinib, filgotinib)	• Interventions not listed
Comparators	• IL-17 inhibitors (bimekizumab, ixekizumab, secukinumab, brodalumab) • TNF-α inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and biosimilars) • JAK inhibitors (tofacitinib, upadacitinib, filgotinib) • Conventional DMARDs (cyclosporine, sulfasalazine, methotrexate, leflunomide, hydroxychloroquine) • NSAIDs (celecoxib, etoricoxib, ibuprofen, naproxen, ketoprofen, flurbiprofen, indometacin/indomethacin, etodolac, diclofenac, aceclofenac, sulindac, piroxicam, meloxicam, tenoxicam) • Placebo/usual care/standard-of-care	• Comparators not listed

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Outcomes	• Composite and disease activity outcomes
	  ○ Binomial outcomes
	  ○ ASAS20
	  ○ ASAS40
	  ○ ASDAS-MI
	  ○ BASDAI50
	  ○ ASAS 5/6 response
	  ○ ASAS partial remission (PR)
	  ○ ASDAS <2.1
	  ○ ASDAS-ID
	  ○ ASDAS-CII
	  ○ Continuous outcomes (including pre-, post- and CFB)
	  ○ ASDAS-CRP (sometimes written simply as ASDAS score)
	  ○ BASDAI
	  ○ PtGADA
	  ○ Average of BASDAI Q5–6 concerning morning stiffness‡
	• Enthesitis
	  ○ MASES (including pre-, post- and CFB)
	  ○ Enthesitis-free state/total resolution of enthesitis based on the MASES index in patients with enthesitis at baseline¶
	• Functional capacity or mobility (including pre-, post- and CFB)
	  ○ BASFI
	  ○ BASMI
	  ○ Individual spinal mobility scores (e.g. lumbar flexion and lumbar side flexion)‡
	• Inflammation (including pre-, post- and CFB)
	  ○ SPARCC MRI sacroiliac joint score
	  ○ SPARCC MRI spine score‡
	  ○ CRP level
	  ○ Ankylosing Spondylitis Spine Magnetic Resonance Imaging-Activity (ASspiMRI-a)‡
	• HRQoL (including pre-, post- and CFB)
	  ○ SF-36 PCS
	  ○ SF-36 MCS
	  ○ ASQoL
	  ○ EQ-5D
	• Pain (including pre-, post- and CFB)
		• Outcomes not listed

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	○ Total back/spine pain NRS score ○ Nocturnal back/spine pain NRS score • Fatigue: NRS score from BASDAI Question 1 (including pre-, post- and CFB) • Sleep: Medical Outcomes Study (MOS) sleep scale‡ • Safety and tolerability ○ Mortality ○ Patients experiencing any infections ○ Patients experiencing any malignancies ○ Tuberculosis reactivation¶ ○ Total TEAEs¶ ○ Total serious TEAEs ○ Total drug-related TEAEs¶ ○ Discontinuations ○ Total (for any reason) ○ Due to TEAEs ○ Due to lack of efficacy ○ Patients experiencing flares/not experiencing flares	
Study design	• Placebo or active controlled RCTs with: ○ ≥10 patients per treatment arm ○ Intended treatment duration ≥12 weeks, or crossover occurring after ≥12 weeks	• RCTs with: ○ <10 patients per treatment arm ○ Intended treatment duration <12 weeks, or crossover occurring after <12 weeks • Open label extensions of RCTs • Pooled analyses of RCT data§ • Non-RCTs ○ Single-arm clinical trials ○ Multi-arm non-randomised trials • Real-world evidence ○ Retrospective or prospective observational studies, including cohort studies ○ Medical record review/chart review studies ○ Claims database analyses ○ Patient registry analyses ○ Case series/case studies

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		• Pharmacokinetic or pharmacodynamic studies • Dose-finding studies with no active or placebo comparator • *In vitro*/animal/pre-clinical studies • SLRs/(N)MAs†† • Narrative reviews, guidelines, editorials, commentaries, letters
Date limits	**April 2022 update:** Published October 27th 2020 (date of previous clinical SLR update) to present **January 2023 update:** Published April 27th 2022 (date of previous clinical SLR update) to present	**April 2022 update:** Published prior to October 27th 2020 **January 2023 update:** Published prior to April 27th 2022
Countries	No restrictions	No restrictions
Languages	English language publications (entire publication must be available in English, not just abstract)	Non-English language publications

†Unless the publication explicitly states that patients are NSAID-naïve or still receiving their first NSAID, it was assumed that patients participating in RCTs for IL-17 inhibitors, TNF-α inhibitors or JAK inhibitors had failed at least one NSAID; ‡These outcomes were listed as relevant outcomes in the eligibility criteria table of the previous SLR, but there is no evidence they were ever extracted; where present, they were extracted from publications included in the April 2022 and January 2023 clinical SLR updates; ¶These outcomes are predefined primary or secondary outcomes from the BE MOBILE 1 and BE MOBILE 2 trials, but there is no evidence they were extracted during the previous SLR; where present, they were extracted from publications included in the 2022 clinical SLR update; §Publications pooling data across multiple trials from the same clinical trial programme were eligible for inclusion; ††Relevant SLRs/NMAs were included at the title/abstract screening stage so their bibliographic reference lists could be hand-searched for relevant studies; they were then excluded at the full-text screening stage unless they presented novel data.
Abbreviations: AS, ankylosing spondylitis; ASAS, Assessment of Spondyloarthritis International Society; ASDAS, the ankylosing spondylitis disease activity score; ASDAS-CII, ankylosing spondylitis disease activity score – clinically important improvement; ASDAS-CRP, ankylosing spondylitis disease activity score – C-reactive protein; ASDAS-ID, ankylosing spondylitis disease activity score – inactive disease; ASDAS-MI, ankylosing spondylitis disease activity score – major improvement; ASQoL, ankylosing spondylitis quality-of-life; BASDAI, Bath Ankylosing Spondylitis Disease Activity index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CFB, change from baseline; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drug; HRQoL, health-related quality of life; IL-17, interleukin 17; JAK, janus kinase; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; MCS, mental component summary; MRI, magnetic resonance imaging; NMA, network meta-analysis; nr-axSpA, non-radiographic axial spondyloarthritis; NRS, numerical rating scale; NSAID, non-steroidal anti-inflammatory drug; PCS, physical component summary; PICOS, population, intervention, comparator(s), outcomes and study design; PtGADA, Patient's Global Assessment of Disease Activity; r-axSpA, radiographic axial spondyloarthritis; RCT, randomised controlled trial; SF-36, short form-36; SLR, systematic literature review, SPARCC, Spondyloarthritis Research Consortium of Canada; TEAE, treatment-emergent adverse event; TNF-α, tumour necrosis factor-α.

Table 94 Publications excluded at the full-text screening stage across all iterations of the SLR prior to the April 2022 clinical SLR update (n=475)

#	Citation	Source	Reason for exclusion	SLR iteration
1	Baraliakos X. An immediate decrease in serum-VEGF-levels helps in predicting a major in patients with ankylosing spondylitis who were started on infliximab: results from the ASSERT biomarker study. Abstract THU0496. European League Against Rheumatism Annual European Congress of Rheumatology, 2011.	Hand searches	No outcomes of interest	De novo SLR (May 2012)
2	Bathon JM. Golimumab and cardiovascular disease: carotid artery ultrasound evaluation and cardiovascular adverse events. Abstract 386. American College of Rheumatology Annual Scientific Meeting, 2010.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)

3	Braun J. Clinical efficacy of etanercept versus sulfasalazine in ankylosing spondylitis subjects with peripheral joint involvement. Journal of Rheumatology. 2012. 39(4):836-840.	Database searches	No outcomes of interest	De novo SLR (May 2012)
4	Braun J. Golimumab reduces spinal inflammation in ankylosing spondylitis: MRI results of the randomised, placebo- controlled GO-RAISE study. Annals of the rheumatic diseases. 2012. 71(6):878-84.	Database searches	No outcomes of interest	De novo SLR (May 2012)
5	Braun J. Golimumab, a new human TNF-(alpha) antibody administered subcutaneously every 4 weeks, in ankylosing spondylitis: 104-week efficacy and safety results of the randomized, placebo-controlled go-raise study. Rheumatology. 2010. 49 SUPPL:i59.	Database searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
6	Braun J. Golimumab, a new human TNF-a antibody administered subcutaneously every 4 weeks, in Ankylosing spondylitis: 104-week efficacy and safety results of the randomized, placebo-controlled GO-RAISE study. Abstract 69. British Society of Rheumatology Annual Meeting, 2010.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
7	Braun J. Golimumab, a new, human, TNF-alpha antibody administered subcutaneously every 4 weeks, in ankylosing spondylitis: 104-week efficacy and safety results of the randomized, placebo-controlled GO-RAISE study. Journal of Rheumatology. 2010. 37(6 SUPPL. 2):1323.	Database searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
8	Braun J. Golimumab, a new, human, TNF-antibody administered subcutaneously every 4 weeks, in ankylosing spondylitis (AS): 104-Week efficacy and safety results of the randomized, placebo-controlled GO-RAISE study. Arthritis and rheumatism. 2009. 60 SUPPL:1259.	Database searches	Duplicate	De novo SLR (May 2012)
9	Braun J. Improvement in hemoglobin levels in patients with ankylosing spondylitis treated with infliximab. Arthritis Care and Research. 2009. 61(8):1032-1036.	Database searches	No outcomes of interest	De novo SLR (May 2012)
10	Braun J. Major reduction in spinal inflammation in patients with Ankylosing spondylitis after treatment with infliximab: results of a multicenter, randomized, doubleblind, placebo-controlled magnetic resonance imaging study. Arthritis and rheumatism. 2006. 54(5):1646-52.	Database searches	No outcomes of interest	De novo SLR (May 2012)
11	Braun J. The effect of anti-tumor necrosis factor therapy with two different doses of golimumab on radiographic progression in definite ankylosing spondylitis: 4-year results. Abstract 423. American College of Rheumatology Annual Scientific Meeting, 2011.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
12	Cormier H. The risk of serious infection with and without anti-TNF therapy in rheumatoid arthritis and ankylosing spondylitis: a meta-analysis. Abstract 2245. American College of Rheumatology Annual Scientific Meeting, 2011.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
13	Deng X. Thalidomide delays the rate of relapse in Ankylosing spondylitis after discontinuing etanercept treatment. Arthritis and rheumatism. 2009. 60 SUPPL:1776.	Database searches	No biological DMARDs of interest	De novo SLR (May 2012)
14	Deng XH. Thalidomide delays the rate of relapse in ankylosing spondylitis after discontinuing etanercept treatment. International Journal of Rheumatic Diseases. 2010. 13 SUPPL1:151.	Database searches	No biological DMARDs of interest	De novo SLR (May 2012)
15	Deodhar A. Cost per placebo adjusted response of golimumab, adalimumab, and etanercept in patients with active ankylosing spondylitis. Abstract 922. American College of Rheumatology Annual Scientific Meeting, 2011.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
16	Dougados M. A randomised, multicentre, double-blind, placebocontrolled trial of etanercept in adults with refractory heel enthesitis in spondyloarthritis: The HEEL trial. Annals of the rheumatic diseases. 2010. 69(8):1430-1435.	Database searches	Outcomes for axSpA patients are not reported separately	De novo SLR (May 2012)
17	Dougados M. Achievement of a patient acceptable symptom state (PASS) and of a minimum clinically important improvement (MCII) with etanercept in refractory heel Enthesitis related to spondyloarthritis: Results of a double blind placebo controlled study (HEEL). Arthritis and rheumatism. 2009. 60 SUPPL:1786.	Database searches	Outcomes for axSpA patients are not reported separately	De novo SLR (May 2012)
18	Dougados M. Nonsteroidal anti-inflammatory (NSAIDs) drug-sparing effect and sustained clinical improvement of etanercept in advanced ankylosing spondylitis. Results of an open label extension following a randomized double blind placebo-	Hand searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)

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	controlled study (SPINE). Abstract 1946. American College of Rheumatology Annual Scientific Meeting, 2010.			
19	Dougados M. Nonsteroidal anti-inflammatory (NSAIDs) drug-sparing effect and sustained clinical improvement of etanercept in advanced ankylosing spondylitis. Results of an open label extension following a randomized double blind placebo-controlled study SPINE). Arthritis and rheumatism. 2010. 62 SUPPL:1946.	Database searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
20	Dougados M. Nonsteroidal antiinflammatory drug intake according to the Assessment of SpondyloArthritis International Society Score in clinical trials evaluating tumor necrosis factor blockers: example of etanercept in advanced ankylosing spondylitis. Arthritis care & research. 2012. 64(2):290-294..	Database searches	No outcomes of interest	De novo SLR (May 2012)
21	Dougados M. Predicting clinical outcomes at 24 weeks in patients with Ankylosing spondylitis. Abstract THU0491. European League Against Rheumatism Annual European Congress of Rheumatology, 2011.	Hand searches	No outcomes of interest	De novo SLR (May 2012)
22	Fautrel B. Cost effectiveness of two therapeutic regimens of infliximab in ankylosing spondylitis: economic evaluation within a randomised controlled trial. Annals of the rheumatic diseases. 2010. 69(2):424-7.	Database searches	PK/PD studies; dose-finding studies with no placebo- or active-controlled arm	De novo SLR (May 2012)
23	Furst DE. Improvement & maintenance of hemoglobin levels among rheumatoid arthritis,psoriatic arthritis & ankylosing spondylitis patients with anemia of inflammation after treatment with golimumab:3 year pooled analysis. Abstract 1246. American College of Rheumatology Annual Scientific Meeting, 2011.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
24	Furst DE. Improvement and maintenance of hemoglobin levels among rheumatoid arthritis, psoriatic arthritis & ankylosing spondylitis patients with anemia of inflammation after treatment with golimumab: 3 yr pooled analysis from golimumab rheumatology clinical program. Abstract AB0456. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
25	Garces S. The immunogenicity of infliximab, adalimumab and etanercept in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease and ulcerative colitis - a quantitative and a qualitative review. Abstract 464. American College of Rheumatology Annual Scientific Meeting, 2011.	Hand searches	No abstract to inform decision, narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	De novo SLR (May 2012)
26	Gooch K. Comparison of 3 comorbidity measures affecting physical function and quality of life for patients with ankylosing spondylitis. Value in Health. 2009. 12(3):A64.	Database searches	No outcomes of interest	De novo SLR (May 2012)
27	Hermann KG. The effect of golimumab on structural spinal changes in ankylosing spondylitis: magnetic resonance imaging results of the placebo-controlled GO-RAISE study. Abstract THU0481. European League Against Rheumatism Annual European Congress of Rheumatology, 2011.	Hand searches	No outcomes of interest	De novo SLR (May 2012)
28	Kay J. Golimumab 3-year safety update: an analysis of pooled data from the long term extensions of randomized, double-blind, placebo-controlled studies in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. Abstract 2227. American College of Rheumatology Annual Scientific Meeting, 2011.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
29	Kim SI. Golimumab, a new, human, TNF-(alpha) antibody administered subcutaneously every 4 weeks, in ankylosing spondylitis: 104 week efficacy and safety results of the randomized, placebo-controlled GO-RAISE study. International Journal of Rheumatic Diseases. 2010. 13 SUPPL:152-153.	Database searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
30	Lin Q. Value of the peripheral blood B-cells subsets in patients with ankylosing spondylitis. Chinese medical journal. 2009. 122(15):1784-9.	Database searches	Duration less than 12 weeks	De novo SLR (May 2012)
31	Machado P. Both structural damage and inflammation of the spine contribute to impairment of spinal mobility in patients with ankylosing spondylitis. Annals of the rheumatic diseases. 2010. 69(8):1465-70.	Database searches	Not RCT	De novo SLR (May 2012)
32	Machado P. MRI inflammation and its relation with measures of clinical disease activity and different treatment responses in patients with Ankylosing spondylitis treated with a TNF inhibitor. Abstract FRI0291. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	No outcomes of interest	De novo SLR (May 2012)

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33	Maksymowych W. Predictors of radiographic progression in adalimumab-treated patients with Ankylosing Spondylitis. Arthritis and rheumatism. 2010. 62 SUPPL:1949.	Database searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
34	Maksymowych W. Predictors of radiographic progression in adalimumab-treated patients with Ankylosing spondylitis. Journal of Rheumatology. 2011. 38(6):1161-1162.	Database searches	Open-label extensions of RCT (where randomisation was broken)	De novo SLR (May 2012)
35	Mease P. Efficacy and safety of adalimumab in patients with peripheral spondyloarthritis: results from a phase 3 study. Abstract THU0280. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	Not adult patients with active axSpA	De novo SLR (May 2012)
36	Morency N. Direct imaging evidence that adalimumab induces resolution of inflammatory lesions in AS patients at sites of complete spinal ankylosis. Journal of Rheumatology. 2011. 38(6):1138.	Database searches	No outcomes of interest	De novo SLR (May 2012)
37	Navarro F. A 12-week randomized, double-blind, multicenter study to evaluate the early effect of etanercept (ETN) 100 mg vs 50 mg weekly in subjects with Ankylosing spondylitis (AS). Abstract OP46. British Society of Rheumatology Annual Meeting, 2010.	Hand searches	PK/PD studies; dose-finding studies with no placebo- or active-controlled arm	De novo SLR (May 2012)
38	Ramiro S. Combination therapy for pain management in inflammatory arthritis: a Cochrane systematic review. Abstract OP0260. European League Against Rheumatism Annual European Congress of Rheumatology, 2011.	Hand searches	No abstract to inform decision, narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	De novo SLR (May 2012)
39	Reilly MC. Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. Rheumatology (Oxford, England). 2010. 49(4):812-9.	Database searches	No outcomes of interest	De novo SLR (May 2012)
40	Ritchlin CT. Use of adalimumab for the treatment of enthesitis of the Achilles tendon in patients with spondyloarthritis. Abstract 55. British Society of Rheumatology Annual Meeting, 2010.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
41	Sieper J. A randomized, open-label study to explore whether partial remission can be maintained with naproxen or no treatment in patients with early, active axial spondyloarthritis: preliminary results of INFAST PART II. Abstract THU0276. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	NSAID-naïve patients only	De novo SLR (May 2012)
42	Sieper J. Axial metrology measurement and functional status in ankylosing spondylitis. Arthritis and rheumatism. 2009. 60 SUPPL:1767.	Database searches	No outcomes of interest	De novo SLR (May 2012)
43	Sieper J. Double-blind, placebo-controlled, 28-week trial of efficacy and safety of infliximab plus naproxen vs naproxen alone in patients with early, active axial spondyloarthritis treated with a submaximal dose of NSAIDs: preliminary results of INFAST PART I. Abstract THU0274. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	NSAID-naïve patients only	De novo SLR (May 2012)
44	Sieper J. Week 12 response is a better predictor than baseline disease characteristics of long-term remission in ankylosing spondylitis. Arthritis and rheumatism. 2010. 62 SUPPL:559.	Database searches	No outcomes of interest	De novo SLR (May 2012)
45	Song I. Effects of etanercept vs. sulfasalazine on acute inflammatory lesions as detected by whole body MRI in early axial spondyloarthritis – a 48 week randomized controlled trial. Abstract 2271. American College of Rheumatology Annual Scientific Meeting, 2010.	Hand searches	Duplicate	De novo SLR (May 2012)
46	Song IH. Relationship between active inflammatory lesions in the spine and sacroiliac joints and new development of chronic lesions on whole-body MRI in early axial spondyloarthritis: results of the ESTHER trial at week 48. Annals of the rheumatic diseases. 2011. 70(7):1257-63.	Database searches	No outcomes of interest	De novo SLR (May 2012)
47	Song IH. Relationship between active inflammatory lesions in the spine and sacroiliac joints and new development of fatty infiltration on whole-body MRI in early axial spondyloarthrit is results of the ESTHER trial at week 48. Arthritis and rheumatism. 2010. 62 SUPPL:669.	Database searches	No outcomes of interest	De novo SLR (May 2012)

48	Ubago R. Tumor necrosis factor alpha inhibitors for the treatment of active Ankylosing spondylitis. Abstract PMS1. International Society for Pharmacoeconomics and Outcomes Research Annual European Congress, 2011.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
49	Van Den Bosch F. Randomized double-blind comparison of chimeric monoclonal antibody to tumor necrosis factor alpha (infliximab) versus placebo in active spondylarthropathy. Arthritis and rheumatism. 2002. 46(3):755-65.	Database searches	Fewer than 10 patients per treatment arm	De novo SLR (May 2012)
50	van der Heijde D. Adalimumab effectively reduces the signs and symptoms of active ankylosing spondylitis in patients with total spinal ankylosis. Annals of the rheumatic diseases. 2008. 67(9):1218-21.	Database searches	Fewer than 10 patients per treatment arm	De novo SLR (May 2012)
51	van der Heijde D. Adalimumab effectiveness for the treatment of ankylosing spondylitis is maintained for up to 2 years: long-term results from the ATLAS trial. Annals of the rheumatic diseases. 2009. 68(6):922-9.	Database searches	No outcomes of interest	De novo SLR (May 2012)
52	van der Heijde D. Radiographic findings following two years of infliximab therapy in patients with ankylosing spondylitis. Arthritis and rheumatism. 2008. 58(10):3063-70.	Database searches	Not RCT	De novo SLR (May 2012)
53	van der Heijde D. Radiographic progression of ankylosing spondylitis after up to two years of treatment with etanercept. Arthritis and rheumatism. 2008. 58(5):1324-31.	Database searches	Not RCT	De novo SLR (May 2012)
54	van der Heijde D. The ankylosing spondylitis disease activity score in subjects treated with etanercept (ETN) or sulfasalazine: Comparison with standard efficacy measures. Rheumatology. 2010. 49 SUPPL1:i55.	Database searches	No outcomes of interest	De novo SLR (May 2012)
55	Van Der Heijde DM. Achieving ASDAS-CRP major improvement and inactive disease in patients with ankylosing spondylitis after treatment with golimumab is associated with normalized health related quality of life: two-year results from the GO-RAISE trial. Abstract OP0170. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	No outcomes of interest	De novo SLR (May 2012)
56	Van Der Heijde DM. The Ankylosing spondylitis disease activity score in subjects treated with etanercept (ETN) orsulfasalazine: comparison with standard efficacy measures. Abstract 58. British Society of Rheumatology Annual Meeting, 2010.	Hand searches	No outcomes of interest	De novo SLR (May 2012)
57	van der Heijde DMFM. Is bone formation observed in patients with ankylosing spondylitis related to clinical signs and symptoms? a subanalysis of ATLAS. Arthritis and rheumatism. 2009. 60 SUPPL:1440.	Database searches	No outcomes of interest	De novo SLR (May 2012)
58	Visvanathan S. Inflammatory biomarkers, disease activity and spinal disease measures in patients with ankylosing spondylitis after treatment with infliximab. Annals of the rheumatic diseases. 2008. 67(4):511-7.	Database searches	No outcomes of interest	De novo SLR (May 2012)
59	Wagner C. Serum markers associated with clinical improvement in patients with ankylosing spondylitis treated with golimumab. Annals of the rheumatic diseases. 2012. 71(5):674-80.	Database searches	Not RCT	De novo SLR (May 2012)
60	Weiss A. Comparison of treatment responses to TNF-blockers in axial spondyloarthritis patients with short vs long symptom duration. Abstract AB0847. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	Pooled analysis, meta-analyses	De novo SLR (May 2012)
61	Xu M. The Ankylosing Spondylitis Disease Activity Score is a highly discriminatory measure of disease activity and efficacy following tumour necrosis factor-α inhibitor therapies in ankylosing spondylitis and undifferentiated spondyloarthropathies in China. Rheumatology (Oxford, England). 2011. 50(8):1466-72.	Database searches	Duration less than 12 weeks	De novo SLR (May 2012)
62	Yoo D. A randomized, double-blind, phase 3 study demonstrates clinical equivalence of CT-P13 to infliximab when co-administered with methotrexate in patients with active rheumatoid arthritis. Abstract FRI0143. European League Against Rheumatism Annual European Congress of Rheumatology, 2012.	Hand searches	Not adult patients with active axSpA	De novo SLR (May 2012)
63	Zhang J. A multicenter, double-blind, placebo-controlled, randomized III clinical study of etanercept in the treatment of Chinese subjects with active ankylosing spondylitis. International Journal of Rheumatic Diseases. 2010. 13 SUPPL1:151.	Database searches	Duration less than 12 weeks	De novo SLR (May 2012)

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64	Ash, Z. R., N. Barkham, et al. (2011). "Long term results of a remission induction approach to early axial spondyloarthritis: Still looking for the window of opportunity." Arthritis and Rheumatism 63(10).	Database searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
65	Baraliakos. Long Term Inhibition Of IL-17A With Secukinumab Reduces Spinal Inflammation But Has No Influence On Fatty Lesions As Assessed By Magnetic Resonance Imaging In Patients With Ankylosing Spondylitis. Abstract FRI0420, EULAR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
66	Birbara. Apremilast, An Oral Phosphodiesterase 4 Inhibitor, In Patients With Psoriatic Arthritis Including Current Skin Involvement: Results Of A Phase 3, Randomized, Controlled Trial. Abstract OP0104, EULAR 2013.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
67	Braun, J., D. Van Der Heijde, et al. (2011). "Sustained clinical response with golimumab administered subcutaneously every 4 weeks in ankylosing spondylitis: 104-week results of a randomized, placebo-controlled study." Arthritis and Rheumatism 63(10).	Database searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
68	Burness, C. B. and E. D. Deeks (2012). "Adalimumab: in non-radiographic axial spondyloarthritis." Drugs 72(18): 2385-2395.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	1st update (October 2013)
69	Deodhar. Long-Term Safety And Efficacy Of Golimumab In The Treatment Of Ankylosing Spondylitis: Results Through 5 Years Of The GO-RAISE Trial. Abstract THU0352, EULAR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
70	Emery. Evaluation Of Efficacy And Safety Of Secukinumab In The Treatment Of Patients With Moderate-To-Severe Ankylosing Spondylitis. Abstract O6, BSR 2012.	Hand searches	No biological DMARDs of interest	1st update (October 2013)
71	Gladman. Effect Of Certolizumab Pegol On The Multiple Facets Of Psoriatic Arthritis As Reported By Patients: 24-Week Patient-Reported Outcome Results Of A Phase III Double-Blind Randomized Placebo-Controlled Study. Abstract 285, BSR 2013.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
72	Haibel. Long Term Efficacy Over Five Years Of Adalimumab In Patients With Active Non - Radiographic Axial Spondyloarthritis. Abstract 2466, ACR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
73	Han. Sustained Improvement In Health Related Quality Of Life, Work Productivity, Employability, And Reduced Healthcare Resource Utilization Of Patients With Rheumatoid Arthritis, Psoriatic ArthritisS And Ankylosing Spondylitis Treated With Golimumab: 5yr Results. Abstract THU0513, EULAR 2013.	Hand searches	No outcomes of interest	1st update (October 2013)
74	Huang, F., J. Gu, et al. (2013). "Efficacy and safety of adalimumab in Chinese adults with active ankylosing spondylitis: results of a randomised, controlled trial." Ann Rheum Dis.	Database searches	Duplicate	1st update (October 2013)
75	Kavanaugh. Improvements In Productivity At Paid Work And Within Household, And Increased Participation In Daily Activities After 24 Weeks Of Certolizumab Pegol Treatment Of Patients With Psoriatic Arthritis: Results Of A Phase III Double-Blind Randomized Placebo-Controlled Study. Abstract 286, BSR 2013.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
76	Kavanaugh. Long-Term Radiographic Outcome In Psoriatic Arthritis Patients Treated With Golimumab: 104 Week Results From The GO-REVEAL Study. Abstract O10, BSR 2012.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
77	Kay. Golimumab 3-Year Safety Update: An Analysis Of Pooled Data From The Long Term Extensions Of Randomized, Double-Blind, Placebo-Controlled Studies In Rheumatoid Arthritis, Psoriatic Arthritis, And Ankylosing Spondylitis. Abstract SAT0133, EULAR 2012.	Hand searches	Pooled analysis, meta-analyses	1st update (October 2013)
78	Machado, P., R. Landewe, et al. (2012). "In ankylosing spondylitis, a decrease in MRI spinal inflammation predicts improvement in spinal mobility independently	Database searches	No outcomes of interest	1st update (October 2013)

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	of patient reported symptomatic improvement." Arthritis and Rheumatism 64: S245.			
79	Maksymowych, W. P., N. Morency, et al. (2011). "Multivariate analysis indicates that fat lesions dominate over inflammatory lesions in predicting new bone formation in the spine of patients with ankylosing spondylitis." Arthritis and Rheumatism 63(10).	Database searches	No outcomes of interest	1st update (October 2013)
80	Maksymowych, W., D. Van Der Heijde, et al. (2011). "Predictors of radiographic progression in adalimumab-treated patients with ankylosing spondylitis." Reumatologia Clinica Suplementos 7: 149.	Database searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
81	McInnes. Ustekinumab In Patients With Active Psoriatic Arthritis: Results Of The Phase III, Multicentre, Double-Blind, Placebo-Controlled PSUMMIT I Study. Abstract 287, BSR 2013.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
82	Mease. Effect Of Adalimumab On Physical Function, Health-Related Quality Of Life, And Work Productivity In Patients With Peripheral Spondyloarthritis: Results From The ABILITY-2 Clinical Trial. Abstract OP0105, EULAR 2013.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
83	Mease. Effect Of Certolizumab Pegol On Signs And Symptoms In Patients With Psoriatic Arthritis With Or Without Prior Anti-TNF Exposure: 24-Week Results Of A Phase III Double-Blind Randomized Placebo-Controlled Study. Abstract 284, BSR 2013.	Hand searches	Not adult patients with active axSpA	1st update (October 2013)
84	Morency, N., R. Lambert, et al. (2011). "Direct imaging evidences that adalimumab induces resolution of inflammatory lesions in as patients at sites of complete spinal ankylosis." Reumatologia Clinica Suplementos 7: 5-6.	Database searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
85	Park. A Randomised, Double-Blind, Parallel-Group, Phase 1 Study Comparing The Pharmacokinetics, Safety And Efficacy Of CT-P13 And Infliximab In Patients With Active Ankylosing Spondylitis: 54 Week Results From The PLANETAS Study. Abstract FRI0421, EULAR 2013.	Hand searches	No comparators of interest	1st update (October 2013)
86	Park. A Randomized, DoubleE-Blind, Phase 1 Study Demonstrates Equivalence In Pharmacokinetics, Safety, And Efficacy Of CT-P13 And Infliximab In Patients With Ankylosing Spondylitis. Abstract OP0167, EULAR 2012.	Hand searches	No comparators of interest	1st update (October 2013)
87	Pontes, C. (2012). "Assessment of anti-TNF dose reduction in patients with axial spondyloarthritis: An independent collaborative clinical trial." Basic and Clinical Pharmacology and Toxicology 111: 10.	Database searches	No outcomes of interest	1st update (October 2013)
88	Rudwaleit, M., J. Listing, et al. (2004). "Prediction of a major clinical (BASDAI 50) to tumour necrosis factor (alpha) blockers in ankylosing spondylitis." Annals of the Rheumatic Diseases 63(6): 665-670.	Database searches	Pooled analysis, meta-analyses	1st update (October 2013)
89	Sieper, J., B. Porter-Brown, et al. (2013). "Assessment of short-term symptomatic efficacy of tocilizumab in ankylosing spondylitis: Results of randomised, placebo-controlled trials." Annals of the Rheumatic Diseases.	Database searches	No biological DMARDs of interest	1st update (October 2013)
90	Sieper, J., J. Lenaerts, et al. (2012). "Changes in active inflammatory lesions assessed by magnetic resonance imaging: Results of the infliximab as first line therapy in patients with early active axial spondyloarthritis trial." Arthritis and Rheumatism 64: S338.	Database searches	NSAID -naïve patients only	1st update (October 2013)
91	Sieper. A Randomized, Open-Label Study To Explore Whether Partial Remission Can Be Maintained With Naproxen Or No Treatment In Patients With Early, Active Axial Spondyloarthritis: Preliminary Results Of INFAST Part II. Abstract THU0276, EULAR 2012.	Hand searches	NSAID-naïve patients only	1st update (October 2013)
92	Sieper. Changes in Active Inflammatory Lesions Assessed by Magnetic Resonance Imaging: Results of the Infliximab As First Line Therapy in Patients with Early Active Axial Spondyloarthritis Trial. Abstract 779, ACR 2012.	Hand searches	NSAID-naïve patients only	1st update (October 2013)
93	Sieper. Double-Blind, Placebo-Controlled, 28-Week Trial Of Efficacy And Safety Of Infliximab Plus Naproxen Vs Naproxen Alone In Patients With Early, Active Axial Spondyloarthritis Treated With A Submaximal Dose Of NSAIDs: Preliminary Results Of INFAST Part I. Abstract THU0274, EULAR 2012.	Hand searches	NSAID-naïve patients only	1st update (October 2013)

94	Sieper. Long-Term Maintenance Of Improvements In Patient-Reported Outcomes With Certolizumab Pegol In Patients With Axial SpondyloarthritisS, Including Ankylosing Spondylitis And Non-Radiographic Axial Spondyloarthritis: 48-Week Results Of The RAPID-AXSPA Study. Abstract PMS80, ISPOR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
95	Sieper. Role Of Baseline C-Reactive Protein In Response To Infliximab Plus Naproxen Vs Naproxen Alone In Patients With Axial Spondyloarthritis. Abstract 532, ACR 2013.	Hand searches	NSAID-naïve patients only	1st update (October 2013)
96	Sieper. Sarilumab For The Treatment Of Ankylosing Spondylitis: Results Of A Phase 2, Randomized, Double-Blind, Placebo-Controlled, International Study (ALIGN). Abstract OP0169, EULAR 2012.	Hand searches	No biological DMARDs of interest	1st update (October 2013)
97	Sieper. Sustained Clinical Remission In Patients With Non-Radiographic Axial Spondyloarthritis After Two Years Of Adalimumab Treatment. Abstract 1540, ACR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
98	Sieper. Sustained Clinical Remission In Patients With Non-Radiographic Axial Spondyloarthritis After Two Years Of Adalimumab Treatment. Abstract OP0109, EULAR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
99	Sieper. Sustained Efficacy Of Adalimumab In Patients With Non-Radiographic Axial Spondyloarthritis: Week 68 Results From ABILITY 1. Abstract THU0275, EULAR 2012.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
100	Sieper. Tocilizumab (TCZ) Is Not Effective For The Treatment Of Ankylosing Spondylitis (AS): Results Of A Phase 2, International, Multicentre, Randomised, Double-Blind, Placebo-Controlled Trial. Abstract OP0166, EULAR 2012.	Hand searches	No biological DMARDs of interest	1st update (October 2013)
101	Song, I. H., K. G. Kg, et al. (2012). "Evaluation of the efficacy of Etanercept vs. sulfasalazine on active and chronic inflammatory lesions on magnetic resonance imaging (MRI) in active axial spondyloarthritis." Zeitschrift fur Rheumatologie 71: 10-11.	Database searches	No outcomes of interest	1st update (October 2013)
102	Song. Effective Prevention Of New Osteitis On Magnetic Resonance Imaging In Patients With Early Axial Spondyloarthritis During 3 Years Of Continous Treatment With Etanercept - Data Of The Esther Trial. Abstract 1552, ACR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
103	Song. Stable Clinical and MRI Response In Patients With Early Axial Spondyloarthritis After 3 Years Of Continuous Treatment With Etanercept, Data Of The Esther Trial. Abstract 1526, ACR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
104	Van Der Heijde, D., A. Deodhar, et al. (2013). "Achieving ankylosing spondylitis disease activity score c-reactive protein major improvement and inactive disease in patients with ankylosing spondylitis after treatment with golimumab is associated with normalized health-related quality of life: 2-year results from go-raise." Rheumatology (United Kingdom) 52: i161-i162.	Database searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
105	Van Der Heijde, D., J. Sieper, et al. (2012). "Spinal inflammation in the absence of SI joint inflammation on MRI in patients with active non-radiographic axial spondyloarthritis." Arthritis and Rheumatism 64: S444.	Database searches	No outcomes of interest	1st update (October 2013)
106	Van Der Heijde, D., J. Sieper, et al. (2013). "Spinal inflammation in the absence of SI joint inflammation on mri in patients with active non-radiographic axial spondyloarthritis." Rheumatology (United Kingdom) 52: i53.	Database searches	No outcomes of interest	1st update (October 2013)
107	Van Der Heijde, D., P. Mease, et al. (2012). "Improvement in physical function, health-related quality of life, and work productivity with adalimumab treatment in nonradiographic axial SPA: WK-52 results from ability-1." Arthritis and Rheumatism 64: S583.	Database searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
108	van der Heijde. Achieving ASDAS-CRP Major Improvement And Inactive Disease In Patients With Ankylosing Spondylitis After Treatment With Golimumab Is Associated With Normalized Health Related Quality Of Life: Two-Year Results From The GO-RAISE Trial. Abstract OP0170, EULAR 2012.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)

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109	van der Heijde. Continued Improvements In Workplace And Household Productivity With Certolizumab Pegol Treatment In Axial Spondyloarthritis, Including Ankylosing Spondylitis And Non-Radiographic Axial Spondyloarthritis: 48-Week Results From The RAPID-AXSPA Study. Abstract PMS87, ISPOR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
110	van der Heijde. Relationship Between MRI and Clinical Remission In Patients With Non-Radiographic Axial Spondyloarthritis After Two Years Of Adalimumab Therapy. Abstract 1801, ACR 2013.	Hand searches	Open-label extensions of RCT (where randomisation was broken)	1st update (October 2013)
111	Van Laar. Early Effect Of Secukinumab In Reducing Spinal Inflammation As Detected By Magnetic Resonance Imaging In Patients With Ankylosing Spondylitis. Abstract O11, BSR 2012.	Hand searches	No biological DMARDs of interest	1st update (October 2013)
112	Viapiana. Biophosphonates Versus Infliximab In Ankylosing Spondylitis Treatment. Abstract AB0514, EULAR 2013.	Hand searches	No comparators of interest	1st update (October 2013)
113	Voulgari, P. V., E. Kaltsonoudis, et al. (2012). "Adalimumab in the treatment of rheumatoid arthritis." Expert Opin Biol Ther 12(12): 1679-1686.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	1st update (October 2013)
114	Adelzadeh, L., N. Jourabchi, et al. (2013). "The risk of herpes zoster during biological therapy for psoriasis and other inflammatory conditions." Journal of the European Academy of Dermatology and Venereology.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
115	Al-Mossawi. [THU0503] In-vitro supression of TH17 responses in inflammatory arthritis patients using small molecule ROR-GAMMA-T inhibitors. EULAR 2014.	Hand searches	Animal or in-vitro studies	2nd update (July 2014)
116	Annegret, F., F. Thomas, et al. (2013). "Long-term benefits of radon spa therapy in rheumatic diseases: Results of the randomised, multi-centre IMuRa trial." Rheumatology International 33(11): 2839-2850.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
117	Arreola-Ornelas. PHS41. Economic impact of rheumatic diseases in Mexico. ISPOR (international) 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
118	Baji, P., M. Pentek, et al. (2014). "Comparative efficacy and safety of biosimilar infliximab and other biological treatments in ankylosing spondylitis: systematic literature review and meta-analysis." Eur J Health Econ 15 Suppl 1: 45-52.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
119	Baji, P., M. Pentek, et al. (2014). "Comparative efficacy and safety of biosimilar infliximab and other biological treatments in ankylosing spondylitis: systematic literature review and meta-analysis." The European Journal of Health Economics 16.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
120	Bakshi. 16. Do you recognize this syndrome? BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
121	Bao, C., F. Huang, et al. (2013). "Safety and efficacy of golimumab, a human anti-tnf monoclonal antibody injected subcutaneously every 4 weeks, in chinese patients with active ankylosing spondylitis: One-year results of a phase 3, randomized, placebo-controlled study." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
122	Baraliakos. [AB1023] VEGF and CRP serum levels lack predictive value for outcomes as assessed by conventional radiographs and magnetic resonance imaging in patients with active ankylosing spondylitis treated with the TNF inhibitor golimumab. EULAR 2014.	Hand searches	No outcomes of interest	2nd update (July 2014)
123	Baraliakos. [FRI0155] Persistent fatty lesions in the vertebrae in ankylosing spondylitis favor subsequent new syndesmophytes: imaging results of the GO-RAISE study. EULAR 2014.	Hand searches	No outcomes of interest	2nd update (July 2014)
124	Baraliakos. [SAT0375] The distribution of imflammatory lesions in the anterior and posterior structures of the spine in patients with active ankylosing spondylitis and the effect of TNF-alpha-blockade. EULAR 2014.	Hand searches	No outcomes of interest	2nd update (July 2014)

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125	Bautista-Molano, W., V. Navarro-Compan, et al. (2013). "How well are the asas/omeract core outcome sets for ankylosing spondylitis implemented in randomized clinical trials? A systematic literature review." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
126	Bautista-Molano, W., V. Navarro-Compan, et al. (2013). "How well are the assessment of spondyloarthritis international society (ASAS)/Outcome Measures In Rheumatology (OMERACT) core outcome sets for ankylosing spondylitis implemented in randomized clinical trials? A systematic literature review." Arthritis and Rheumatism 65 SUPPL. 10: S638-S639.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
127	Behrens. [SAT0358] Impact of methotrexate on anti-TNF treatment in psoriatic arthritis? An in-depth analysis of a large prospective observational study with adalimumab. EULAR 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
128	Betts, K. A., A. D. Joshi, et al. (2013). "Cost-per-responder analysis of biological agents for the treatment of active ankylosing spondylitis in Germany." Value in Health 16(7): A562.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
129	Bleil. [SAT0559] High expression of cyclooxygenase-2, prostaglandin E2 and prostaglandin E2 receptor EP4 in zygapophyseal joints of patients with ankylosing spondylitis. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
130	Booth. O30. A nurse led clinic for ankylosing spondylitis improves detection of patients eligible for anti-TNF treatment. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
131	Borazan. [AB0378] Anti-drug antibody (ADAB) differentially affect response among specific TNFI and also among diseases: an SLR and meta-analysis. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
132	Bradley. 208. Plasma microparticle levels are not raised in patients with ankylosing spondylitis. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
133	Braun, J., A. Deodhar, et al. (2008) Efficacy and safety of infliximab in patients with ankylosing spondylitis over a two-year period. Arthritis and rheumatism 1270-1278 DOI: 10.1002/art.24001	Database searches	Duplicate	2nd update (July 2014)
134	Braun, J., D. Van Der Heijde, et al. (2013). "The effect of anti-tumor necrosis factor therapy with golimumab on radiographic progression in definite ankylosing spondylitis: 4-year results." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	No outcomes of interest	2nd update (July 2014)
135	Braun, J., X. Baraliakos, et al. (2014). "The effect of two golimumab doses on radiographic progression in ankylosing spondylitis: results through 4 years of the GO-RAISE trial." Ann Rheum Dis 73(6): 1107-1113.	Database searches	No outcomes of interest	2nd update (July 2014)
136	Bruzzese, V., R. Lorenzetti, et al. (2013). "Anti-TNF therapy and tuberculosis risk in rheumatic diseases, psoriasis, and IBD: A pooled-data analysis of randomized controlled trials." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
137	Callhoff, J., J. Sieper, et al. (2014). "Efficacy of TNFalpha blockers in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis." Ann Rheum Dis.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
138	Callhoff. [SAT0353] Meta-analysis comparing the efficacy of TNF-blockers in AS and NR-AXSPA patients. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
139	Cantini, F., L. Niccoli, et al. (2014). "Adalimumab, etanercept, infliximab, and the risk of tuberculosis: Data from clinical trials, national registries, and postmarketing surveillance." Journal of Rheumatology 41(SUPPL. 91): 47-55.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
140	Cetin. [SAT0361] Short term efficacy of tumor necrosis factor inhibitors in patients with non-radiographic axial spondyloarthritis and ankylosing spondylitis; results from TURKBIO registry. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
141	Choquette, D., D. Sauvageau, et al. (2013). "Retention rate of adalimumab, etanercept and infliximab at 5 years in patients with ankylosing spondylitis: Report from the rhumadata computerized database." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Not RCT	2nd update (July 2014)

142	Choquette. [SAT0335] Use of monotherapy anti-TNF agents in ankylosing spondylitis patients from the RHUMADATA® registry: 8-year comparative effectiveness of adalimumab, etanercept and infliximab. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
143	Ciurea, A., A. Scherer, et al. (2013). "Tobacco smoking is associated with increased disease activity in HLA-B27 positive axial spondyloarthritis patients, but does not alter the course of disease activity." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Not RCT	2nd update (July 2014)
144	Cunha-Miranda. [FRI0209] Nationwide occupational impact of rheumatic diseases: data from EPIREUMA.PT. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
145	Dean. 224. The natural history of ankylosing spondylitis: results from the Scotland and Ireland registry for ankylosing spondylitis. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
146	Deodhar, A., J. Braun, et al. (2013). "Long-term safety and efficacy of golimumab in the treatment of ankylosing spondylitis: Results through 5 years of the go-raise trial." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
147	Dickinson. 222. Current management of ankylosing spondylitis in the UK: the patient perspective. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
148	Diss. 227. Differences in uveitis versus non-uveitis individuals with HLA-B27-positive spondyloarthritis with regard to first presenting symptoms. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
149	Dö nmez. [SAT0369] Do physical therapy modalities have additional benefit over exercise therapy in the management of ankylosing spondylitis? A randomized controlled trial. EULAR 2014.	Hand searches	No biological DMARDs of interest	2nd update (July 2014)
150	Dougados, M., D. Van Der Heijde, et al. (2013). "Clinical and imaging efficacy of etanercept in early non-radiographic axial spondyloarthritis: A 12-week, randomized, double-blind, placebo-controlled trial." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
151	Dougados. [SAT0356] Discriminant capacity of clinical efficacy measures, along or in combination with NSAID intake, in detecting anti-TNF treatment effect in spondyloarthritis. EULAR 2014.	Hand searches	Duration less than 12 weeks	2nd update (July 2014)
152	Dougados. [SAT0357] Evaluation of the nonsteroidal anti-inflammatory drug-sparing effect of etanercept in axial spondyloarthritis: results of the multicenter randomized, double-blind, placebo-controlled SPARSE trial. EULAR 2014.	Hand searches	Duration less than 12 weeks	2nd update (July 2014)
153	Ellis. PMS49. Golimumab utilization patterns and refill adherence in patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. ISPOR (international) 2014.	Hand searches	Not RCT	2nd update (July 2014)
154	Fattah. 29. Complete healing of traumatic multiple spinal fractures in a patient with with ankylosing spondylitis who refused surgical intervention with teriparatide. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
155	Fendri, S., C. Gaujoux-Viala, et al. (2013). "The effect of biological agents on participation in paid work in patients with chronic inflammatory arthritides: A meta-analysis of randomized controlled trials." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
156	Freundlich, B., J. Braun, et al. (2009) Assessment of clinical efficacy in a randomized, double-blind study of etanercept and Sulphasalazine in patients with ankylosing spondylitis [Abstract]. Internal medicine journal A55	Database searches	Duplicate	2nd update (July 2014)
157	Furst, D. E., T. A. Gathany, et al. (2013). "Improvement and maintenance of hemoglobin levels among rheumatoid arthritis, psoriatic arthritis & ankylosing spondylitis patients with anemia of inflammation after treatment with golimumab: 3 yr pooled analysis from golimumab rheumatology clinical program." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
158	Gadsby. I81. An interactive teaching/demonstration of metrology (BASMI) and enthesitis (MASES), a review of outcome measures (BASDAI, BASFI, AS-WIS etc.), and exercises for ankylosing spondylitis patients. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)

159	Gaffne. I73. Recognition of inflammatory back pain and axial spondyloarthritis. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
160	Gaffne. O31. An open label, pilot, multi-centre, sterpdown, randomized controlled trial to examine whether etanercept 25mg once weekly is effective in maintaining a clinical response in patients with ankylosing spondylitis who have responded to 50mg once weekly. BSR 2014.	Hand searches	PK/PD studies; dose-finding studies with no placebo- or active-controlled arm	2nd update (July 2014)
161	Gallinaro, A. L., C. G. S. Saad, et al. (2013). "Benefitial effects of a simple stretching exercise program for patients with ankylosing spondylitis: A randomized controlled trial." Arthritis and Rheumatism 65 SUPPL. 10: S896-S897.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
162	Gao, X., D. Wendling, et al. (2012). "Clinical and economic burden of extra-articular manifestations in ankylosing spondylitis patients treated with anti-tumor necrosis factor agents." Journal of Medical Economics 15(6): 1054-1063.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
163	Garces, S., J. Demengeot, et al. (2013). "Clinical impact of immunogenicity of infliximab, adalimumab and etanercept: A systematic review of the literature with a meta-analysis." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
164	Garces, S., J. Demengeot, et al. (2013). "The immunogenicity of anti-TNF therapy in immune-mediated inflammatory diseases: A systematic review of the literature with a meta-analysis." Annals of the Rheumatic Diseases 72(12): 1947-1955.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
165	Gaydukova, I., A. Akulova, et al. (2014). "Adherence to therapy and results of treatment in patients with the different ways of spondyloarthritis monitoring." Annals of the Rheumatic Disease 73(1): 2014-2002.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
166	Gaydukova. [SAT0348] Efficacy and safety of different schemes of etoricoxib administration in patients with axial spondyloarthritis - results of a 12-week, prospective, open-label study. EULAR 2014.	Hand searches	PK/PD studies; dose-finding studies with no placebo- or active-controlled arm	2nd update (July 2014)
167	Genovese, M. C., P. J. Mease, et al. (2013). "Effect of brodalumab (AMG 827) on pain and physical functioning in patients with psoriatic arthritis." Arthritis and Rheumatism 65 SUPPL. 10: S136.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
168	Georgiou. 226. Intermalleolar distance: measuring on the couch versus measuring on the floor. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
169	Gladman, D. D., P. J. Mease, et al. (2013). "Apremilast, an oral phosphodiesterase 4 inhibitor, is associated with long-term (52-week) improvements in enthesitis and dactylitis in patients with psoriatic arthritis: Pooled results from three phase 3, randomized, controlled trials." Arthritis and Rheumatism 65 SUPPL. 10: S347.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
170	Gu, X., H. Wu, et al. (2013). "Allicin attenuates inflammation and suppresses HLA-B27 protein expression in ankylosing spondylitis mice." Biomed Res Int 2013: 171573.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
171	Gurden. I82. An interactive teaching/demonstration of metrology (BASMI) and enthesitis (MASES), a review of outcome measures (BASDAI, BASFI, AS-WIS etc.), and exercises for ankylosing spondylitis patients. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
172	Haglund. [OP0207-HPR] Gender differences in educational needs to manage the disease in individuals with spondyloarthritis. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
173	Haglund. [OP0207-HPR] Gender differences in educational needs to manage the disease in individuals with spondyloarthritis. EULAR 2014.	Hand searches	Duplicate	2nd update (July 2014)
174	Hamilton. O12. The prevalence of axial spondyloarthropathy in the UK: a cross sectional cohort study in a primary care population. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
175	Hammitzsch. [AB0022] Comparison of in vitro effects of kinase and epigenetic inhibitors on TH17 responses in inflammatory arthritis. EULAR 2014.	Hand searches	Animal or in-vitro studies	2nd update (July 2014)
176	Han, C., A. Kavanaugh, et al. (2013). "Sustained improvement in health related quality of life, work productivity, employability, and reduced healthcare resource utilization of patients with rheumatoid arthritis, psoriatic arthritis and ankylosing	Database searches	Duplicate	2nd update (July 2014)

	spondylitis treated with golimumab:5yr results." Annals of the Rheumatic Diseases 72(3): 2013-2006.			
177	Han, C., A. Kavanaugh, et al. (2013). "Sustained improvement in health-related quality of life, work productivity, employability, and reduced healthcare resource utilization of patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis treated with golimumab: 5-year results from 3 phase iii studies." Arthritis and Rheumatism 65 SUPPL. 10: S137.	Database searches	No outcomes of interest	2nd update (July 2014)
178	Haroon, N. N., J. Srighanthan, et al. (2013). "Effect of TNF inhibitors on BMD in patients with ankylosing spondylitis-a systematic review and meta-analysis." Journal of Bone and Mineral Research 28(1): 2013-2010.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
179	Haroon, N. N., J. Srighanthan, et al. (2013). "Effect of TNF inhibitors on bone mineral density in patients with ankylosing spondylitis-a systematic review and meta-analysis." Arthritis and Rheumatism 65 SUPPL. 10: S657-S658.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
180	Harris. I75. Interactive session to develop the clinical reasoning skills in the recognition of inflammatory back pain. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
181	Hermann, K. G. A., X. Baraliakos, et al. (2013). "Persistent fatty lesions in the vertebrae in ankylosing spondylitis favor subsequent new syndesmophytes: Imaging results of a phase III, randomized, placebo-controlled study." Arthritis and Rheumatism 65 SUPPL. 10: S767-S768.	Database searches	No outcomes of interest	2nd update (July 2014)
182	Hollick. 230. Predictors of driving disability in ankylosing spondylitis: results from the Scotland and Ireland registry for ankylosing spondylitis. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
183	Hoogeboom. [THU0568] The effectiveness of exercise therapy in people with anlylosing spondylitis: a systematic review and meta-analysis. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
184	Horneff, G., S. Fitter, et al. (2012) Double blind, Placebo-controlled randomized trial with Adalimumab for Treatment of Juvenile onset Ankylosing Spondylitis (JoAS): Significant short term improvement. 14, R230	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
185	Hu, Z., M. Xu, et al. (2013). "Adalimumab significantly reduces inflammation in active ankylosing spondylitis: An ultrasound study." Arthritis and Rheumatism 65 SUPPL. 10: S1060.	Database searches	No outcomes of interest	2nd update (July 2014)
186	Huang, F., X. Deng, et al. (2013). "Thalidomide reduces recurrence of ankylosing spondylitis in patients following discontinuation of etanercept." International Journal of Rheumatic Diseases 16 SUPPL. 1: 41-42.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
187	Huang. [FRI0158] Ankylosing spondylitis spinal magnetic resonance imaging activity score is associated with the disease activity of ankylosing spondylitis: a systemiatic literature review with meta-analysis. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
188	Husain. 211. The cost of ankylosing spondylitis to the UK NHS. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
189	Husain. 216. The work-related costs of ankylosing spondylitis in a UK cohort. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
190	Jethwa. O26. Does inflammatory arthritis really improve during pregnancy? A systematic review and meta-analysis. BSR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
191	Ji. [OP0161] A cost-effectiveness model of adalimumab (ADA) in non-radiographic axial spondyloarthritis in Spain. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
192	Kalyoncu. [SAT0347] Patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis had similar TNFI drug survival: HÜR-BIO real life results. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
193	Kang, H. W., Y. J. Lim, et al. (2014). "An experience of anti-TNF biosimilar, CT-P13 use: Clinical efficacy, safety and interchangeability in inflammatory bowel disease; A pilot study." Journal of Crohn's and Colitis 8 SUPPL. 1: S303.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
194	Kay, J., R. Fleischmann, et al. (2013). "Golimumab 3-year safety update: An analysis of pooled data from the long term extensions of randomized, double-	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)

	blind, placebo-controlled studies in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis." Annals of the Rheumatic Disease 71(3): 2012-2006.			
195	Kay. [THU0176] Golimumab 5-year safety: an analysis of pooled data from the long term extensions of randomized, double-blind, placebo-controlled studies in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
196	Kiltz, U., X. Baraliakos, et al. (2013). "Withdrawal of medical therapies in axial spondyloarthritis: What would be the optimal trial design?" Clinical and Experimental Rheumatology 31(SUPPL.78): S47-S50.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
197	Koo, B. S., M. W. So, et al. (2013). "A randomized controlled trial of the efficacy of incentive spirometer exercise on pulmonary functions of patients with ankylosing spondylitis stabilized by tumor necrosis factor inhibitor therapy." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
198	Landewe, R., M. Rudwaleit, et al. (2013). "Effect of certolizumab pegol on signs and symptoms of axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis: 24-week results of rapid-axSpA study." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
199	Lee, J., D. Park, et al. (2014). "Drug survival of anti-tumor necrosis factor therapies in RA and AS." International Journal of Rheumatic Diseases 17 SUPPL. 1: 104.	Database searches	Not RCT	2nd update (July 2014)
200	Lee. 225. Determinants of AS-related fatigue and the risks of its persistence: results from the Scotland and Ireland registry for ankylosing spondylitis. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
201	Lie, E., A. Author, et al. (2013). "Switching TNF-blockers: What is the evidence." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
202	Lin, Z. M., Z. Y. Hu, et al. (2014). "Adalimumab reduces enthesitis in AS patients: An ultrasound study." International Journal of Rheumatic Diseases 17 SUPPL. 1: 79.	Database searches	No outcomes of interest	2nd update (July 2014)
203	Lindström. [SAT0098] Validity of ankylosing spondyloarthritis and spondyloarthritis diagnosis in the Swedish national patient registry. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
204	Lorencetti. [AB1085] Direct and indirect costs of ankylosing spondylitis: a Brazilian public health care perspective. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
205	Machado, P., R. Landewe, et al. (2013). "MRI inflammation and its relation with measures of clinical disease activity and different treatment responses in patients with ankylosing spondylitis treated with a TNF inhibitor." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Duplicate	2nd update (July 2014)
206	Machado. PMS29. Cost of drug therapy for ankylosing spondylitis in the Brazilian public health system. ISPOR (international) 2014.	Hand searches	Not RCT	2nd update (July 2014)
207	Maksymowych. [SP0210] Advanced imaging in clinical trials for spondyloarthritis. EULAR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
208	Manrique, M. G., P. Font, et al. (2013). "Is there a role for etoricoxib in patients with axial ankylosing spondylitis refractory to traditional nsaid?" Arthritis and Rheumatism 65 SUPPL. 10: S1043.	Database searches	Not RCT	2nd update (July 2014)
209	Manrique-Arija, S., I. Urena-Garnica, et al. (2013). "Fulfillment of some GUIPCAR-2007 recommendations for the care of patients with recent-onset reumatoid arthritis in spanish rheumatology centres. EMAR-II study." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Not RCT	2nd update (July 2014)
210	Marin Pedrosa, S., I. Perez Medrano, et al. (2014). "Clinical and epidemiological features of patients with inflammatory bowel disease and extraintestinal manifestations associated." Journal of Crohn's and Colitis 8 SUPPL. 1: S340.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)

211	Martindale. I74. The impact of delay in diagnosing ankylosing spondylitis/axial SpA. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
212	Mease, P. J., S. Rao, et al. (2013). "Effect of adalimumab on physical function, health-related quality of life, and work productivity in patients with peripheral spondyloarthritis: Results from the ability-2 clinical trial." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
213	Mease, P., J. Sieper, et al. (2013). "Efficacy and safety of adalimumab in patients with peripheral spondyloarthritis: Results from a phase 3 study." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
214	Mease. [FRI0128] Utility of enthesitis assessments in peripheral spondyloarthritis – data from the ABILITY-2 trial. EULAR 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
215	Meirinhos, T., R. Aguiar, et al. (2014). "Neuropathic pain in rheumatic diseases: A cross-sectional study." Annals of the Rheumatic Disease 73(1): 2014-2002.	Database searches	Not RCT	2nd update (July 2014)
216	Mennini. PMS28. The economic burden on the social security system pensions for musculoskeletal disorders in Italy. ISPOR (international) 2014.	Hand searches	Not RCT	2nd update (July 2014)
217	Molto, A., S. Paternotte, et al. (2013). "Efficacy of Anti TNF alpha therapy in early axial spondyloarthritis is similar regardless the presence of objective Signs of inflammation or structural damage of the sacroiliac joints. Data from the desir cohort." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Not RCT	2nd update (July 2014)
218	Mouterde, G., P. Aegerter, et al. (2014). "Value of contrast-enhanced ultrasonography for the detection and quantification of enthesitis vascularization in patients with spondyloarthritis." Arthritis Care Res (Hoboken) 66(1): 131-138.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
219	Murdaca, G., F. Spano, et al. (2014). "Efficacy and safety of etanercept in chronic immune-mediated disease." Expert Opin Drug Saf 13(5): 649-661.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
220	Murphy, C. L., M. O'Sullivan, et al. (2013). "Major cost savings associated with reduced biologic dosing frequency in inflammatory arthritis." Arthritis and Rheumatism 65 SUPPL. 10: S79.	Database searches	Not RCT	2nd update (July 2014)
221	Narayanan, S., A. Baskett, et al. (2013). "Disease status, treatments and outcomes of patients with ankylosing spondylitis receiving their first biologic in the United States and European union." Value in Health 16(7): A389.	Database searches	Not RCT	2nd update (July 2014)
222	Narayanan. PMS3. Prevalence of comorbidities among patients with psoriasis(PSO) with and without psoriatic arthritis (PSA) in European Union (EU). ISPOR (international) 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
223	Niedermann, K., E. Sidelnikov, et al. (2013). "Effect of cardiovascular training on fitness and perceived disease activity in people with ankylosing spondylitis." Arthritis Care and Research 65(11): 1844-1852.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
224	Nigil Haroon, N., J. Sriganthan, et al. (2014). "Effect of TNF-alpha inhibitor treatment on bone mineral density in patients with ankylosing spondylitis: A systematic review and meta-analysis." Semin Arthritis Rheum.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
225	Noyes Essex, M., R. Zhang, et al. (2013). "Pooled safety data from elderly arthritis patients in 21 clinical trials." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
226	Nystad, T. W., B. T. S. Fevang, et al. (2013). "Hip replacement surgery in patients with ankylosing spondylitis." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Not RCT	2nd update (July 2014)
227	Paccou, J. and D. Wendling (2014). "Current treatment of psoriatic arthritis: Update based on a systematic literature review to establish French Society for Rheumatology (SFR) recommendations for managing spondyloarthritis." Joint Bone Spine.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
228	Palazzi, C., S. D'Angelo, et al. (2014). "Safety of anti-tumor necrosis factor agents in psoriatic arthritis - an update." Expert Opin Drug Saf 13(2): 191-196.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)

229	Paramarta, J. E., L. De Rycke, et al. (2012). "Efficacy and safety of adalimumab for the treatment of peripheral arthritis in spondyloarthritis patients without ankylosing spondylitis or psoriatic arthritis." Arthritis and Rheumatism 64 SUPPL. 10: S235.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
230	Paramarta. [OP0156] Targeting synovial mast cells in spondyloarthritis: a proof-of-concept study with nilotinib a tyrosine kinase inhibitor. EULAR 2014.	Hand searches	No biological DMARDs of interest	2nd update (July 2014)
231	Park, D. J., K. E. Lee, et al. (2013). "Drug survival rates of anti-tumor necrosis factor therapies in patients with rheumatoid arthritis and ankylosing spondylitis." Arthritis and Rheumatism 65 SUPPL. 10: S1006.	Database searches	Not RCT	2nd update (July 2014)
232	Park, W., P. Miranda, et al. (2013). "Efficacy and safety of CT-P13 (infliximab biosimilar) over two years in patients with ankylosing spondylitis: Comparison between continuing with." Arthritis and Rheumatism 65(12): 3326.	Database searches	Open-label extensions of RCT (where randomisation was broken)	2nd update (July 2014)
233	Park. [OP0157]Clinical response of disease activity, disability and mobility indices in relation to anti-drug antibody in the PLANETAS. EULAR 2014.	Hand searches	No comparators of interest	2nd update (July 2014)
234	Pathan, E., S. Abraham, et al. (2013). "Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in ankylosing spondylitis." Ann Rheum Dis 72(9): 1475-1480.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
235	Pecourneau, V., A. L. Constantin, et al. (2013). "Effectiveness of exercise program in ankylosing spondylitis: Meta-analysis of randomized controlled trials." Arthritis and Rheumatism 65 SUPPL. 10: S1042.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
236	Pedersen, S. J., D. Poddubnyy, et al. (2013). "Inflammation and structural progression in the sacroiliac joints of patients with axial spa treated with adalimumab or placebo as assessed by the berlin and the spondyloarthritis research consortium of canada MRI methods." Arthritis and Rheumatism 65 SUPPL. 10: S1218.	Database searches	No outcomes of interest	2nd update (July 2014)
237	Pedersen, S. J., I. J. Sorensen, et al. (2013). "Efficacy of adalimumab in patients with axial spondyloarthritis: Results of an investigator-initiated 12-weeks randomized double-blind placebo controlled trial with a 12 weeks open-label extension phase." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
238	Pehlivan. 228. Effects of smoking in patients with ankylosing spondylitis and nonradiographic axial spondyloarthritis receiving TNF inhibitors. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
239	Pickles. I83. An interactive teaching/demonstration of metrology (BASMI) and enthesitis (MASES), a review of outcome measures (BASDAI, BASFI, AS-WIS etc.), and exercises for ankylosing spondylitis patients. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
240	Poddubnyy. [OP0155] Ustekinumab effectively reduces active inflammation as detected by magnetic resonance imaging in patients with active ankylosing spondylitis: results of a 28-week, prospective, open-label, proof-of-concept study (TOPAS). EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
241	Ramiro. [FRI0138] A psychometric analysis of outcome measures in trials of peripheral spondyloarthritis. EULAR 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
242	Rat. [SAT0578] Patients with rheumatoid arthritis, spondyloarthritis and psoriatic arthritis treated with biologics use similar coping strategies: a study of 671 patients. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
243	Ren, L., J. Li, et al. (2013). "Efficacy of antitumor necrosis factor((alpha)) agents on patients with ankylosing spondylitis." American Journal of the Medical Sciences 346(6): 455-461.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
244	Ridley. 234. KIR3DL2 binding to HLA-B27 licences pathohenic T-cell differentiation in spondyloarthritis. BSR 2014.	Hand searches	Animal or in-vitro studies	2nd update (July 2014)
245	Roussou. 298. Assessment of the existing criteria for inflammatory back pain among patients with fibromyalgia. BSR 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
246	Rudwaleit. [SAT0355] Observed incidence rates of uveitis following certolizumab pegol treatment in patients with axial spondyloarthritis. EULAR 2014.	Hand searches	No outcomes of interest	2nd update (July 2014)

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247	Ruof, J., O. Sangha, et al. (1999) Evaluation of a German version of the Bath Ankylosing Spondylitis Functional Index (BASFI) and Dougados Functional Index (D-FI). Zeitschrift für Rheumatologie 218-225	Database searches	No biological DMARDs of interest	2nd update (July 2014)
248	Safety and Efficacy of Subcutaneous Golimumab Induction Therapy in Patients with Moderately to Severely Active Ulcerative Colitis AUTHOR ADDRESSES SOURCE Clinical Advances in Hematology and Oncology (2012) 10:10 (25). Date of Publication: Oct 2012 CONFERENCE NAME 47th Annual Meeting of the European Association for the Study of the Liver CONFERENCE LOCATION Barcelona, Spain CONFERENCE DATE 2012-04-18 to 2012-04-22.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
249	Santo. [AB0397] GO.A.RE.L. (GOlimumab in Apulian REal-Life patients) study. Preliminary data from golimumab therapy in patients affected with polyarthritis. A multicenter experience in Apulia (Southern Italy). EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
250	Sari. [FRI0121] The comparative one-year drug survival rate of tumor necrosis factor inhibitors in patients with rheumatoid arthritis and ankylosing spondylitis; results from TURKBIO registry. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
251	Sarzi-Puttini, P., F. Atzeni, et al. (2013). "Analgesic efficacy of ketoprofen vs ibuprofen and diclofenac: A systematic review of the literature and meta-analysis." Regional Anesthesia and Pain Medicine 38(1): 2012-2011.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
252	Sathi. 270. Combination of diagnostic criteria, clinical features and magnetic resonance imaging of the spine with high resolution ultrasound of the wrists and hands: a cost effective clinical approach for the early diagnosis of seronegative spondyloarthritis. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
253	Scaccabarozzi. PSY32. Cost-minimization analysis of anti-TNF biologics in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis under the Brazilian private health care system perspective. ISPOR (international) 2014.	Hand searches	Not RCT	2nd update (July 2014)
254	Scaccabarozzi. PSY34. Cost-minimization analysis of anti-TNF biologics in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis under the Brazilian private health care system (SUS) perspective. ISPOR (international) 2014.	Hand searches	Not RCT	2nd update (July 2014)
255	Schoels, M. M., J. Braun, et al. (2014). "Treating axial and peripheral spondyloarthritis, including psoriatic arthritis, to target: Results of a systematic literature search to support an international treat-to-target recommendation in spondyloarthritis." Annals of the Rheumatic Diseases 73(1): 238-242.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
256	Sieper, J., A. Kivitz, et al. (2013). "Rapid improvements in patient-reported outcomes with certolizumab pegol in patients with axial spondyloarthritis, including ankylosing spondylitis: 24-week results of rapid-axSpA study." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
257	Sieper, J., B. Porter-Brown, et al. (2013). "Tocilizumab (TCZ) is not effective for the treatment of ankylosing spondylitis (AS): Results of a phase 2, international, multicentre, randomised, double-blind, placebo-controlled trial." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
258	Sieper, J., D. L. Baeten, et al. (2013). "Sustained clinical remission in patients with non-radiographic axial spondyloarthritis after two years of adalimumab treatment." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
259	Sieper, J., D. L. Baeten, et al. (2013). "Sustained clinical remission in patients with non-radiographic axial spondyloarthritis after two years of adalimumab treatment." Arthritis and Rheumatism 65 SUPPL. 10: S653-S654.	Database searches	Open-label extensions of RCT (where randomisation was broken)	2nd update (July 2014)
260	Sieper, J., D. Poddubnyy, et al. (2013). "Smoking was not associated with response to adalimumab therapy in patients with non-radiographic axial spondyloarthritis." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	No outcomes of interest	2nd update (July 2014)
261	Sieper, J., D. Poddubnyy, et al. (2013). "Smoking was not associated with response to adalimumab therapy in patients with non-radiographic axial spondyloarthritis." Arthritis and Rheumatism 65 SUPPL. 10: S1042-S1043.	Database searches	Open-label extensions of RCT (where randomisation was broken)	2nd update (July 2014)

262	Sieper, J., D. Van Der Heijde, et al. (2013). "Disease burden is comparable in patients with non-radiographic axial spondyloarthritis and ankylosing spondylitis: Implications for treatment." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	No outcomes of interest	2nd update (July 2014)
263	Sieper, J., D. Van Der Heijde, et al. (2013). "Sustained efficacy of adalimumab in patients with non-radiographic axial spondyloarthritis: Week 68 results from ability 1." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Duplicate	2nd update (July 2014)
264	Sieper, J., J. Braun, et al. (2014). "Sarilumab for the treatment of ankylosing spondylitis: Results of a Phase II, randomised, double-blind, placebo-controlled study (ALIGN)." Annals of the Rheumatic Diseases 18.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
265	Sieper, J., J. Lenaerts, et al. (2013). "Double-blind, placebo-controlled, 28-week trial of efficacy and safety of infliximab plus naproxen vs naproxen alone in patients with early, active axial spondyloarthritis treated with a submaximal dose of NSAIDS: Preliminary results of INFAST part I." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	NSAID-naïve patients only	2nd update (July 2014)
266	Sieper, J., J. Lenaerts, et al. (2013). "Efficacy and safety of infliximab plus naproxen versus naproxen alone in patients with early, active axial spondyloarthritis: Results from the double-blind, placebo-controlled INFAST study, Part 1." Annals of the Rheumatic Diseases 21.	Database searches	NSAID-naïve patients only	2nd update (July 2014)
267	Sieper, J., J. Lenaerts, et al. (2014). "Efficacy and safety of infliximab plus naproxen versus naproxen alone in patients with early, active axial spondyloarthritis: results from the double-blind, placebo-controlled INFAST study, Part 1." Ann Rheum Dis 73(1): 101-107.	Database searches	NSAID-naïve patients only	2nd update (July 2014)
268	Sieper, J., J. Lenaerts, et al. (2014). "Maintenance of biologic-free remission with naproxen or no treatment in patients with early, active axial spondyloarthritis: results from a 6-month, randomised, open-label follow-up study, INFAST Part 2." Ann Rheum Dis 73(1): 108-113.	Database searches	NSAID-naïve patients only	2nd update (July 2014)
269	Sieper, J., M. Rudwaleit, et al. (2013). "Role of baseline c-reactive protein in response to infliximab plus naproxen vs naproxen alone in patients with axial spondyloarthritis in the infast study." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	NSAID-naïve patients only	2nd update (July 2014)
270	Sieper, J., M. Rudwaleit, et al. (2013). "Role of baseline c-reactive protein in response to infliximab plus naproxen vs naproxen alone in patients with axial spondyloarthritis." Arthritis and Rheumatism 65 SUPPL. 10: S233.	Database searches	NSAID-naïve patients only	2nd update (July 2014)
271	Sieper, J., R. D. Inman, et al. (2013). "Sarilumab for the treatment of ankylosing spondylitis: Results of a phase 2, randomized. Double-blind, placebo-controlled, international study (align)." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
272	Sieper, J., S. Srinivasan, et al. (2013). "Comparison of two referral strategies for diagnosis of axial spondyloarthritis: the Recognising and Diagnosing Ankylosing Spondylitis Reliably (RADAR) study." Ann Rheum Dis 72(10): 1621-1627.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
273	Sieper. I59. New biologic treatments for ankylosing spondylitis. BSR 2014.	Hand searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
274	Sifuentes Giraldo, W. A., A. Gonzalez Garcia, et al. (2014). "Colonic perforation secondary to metastatic lung adenocarcinoma during anti-TNF treatment for ankylosing spondylitis." Acta Reumatol Port 39(1): 72-76.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
275	Siu. [OP0277] Effect of disease modifying drugs on bone mineral density in patients with rheumatoid arhtritis, psoriatic arthritis, psoriasis, and ankylosing spondylitis: a meta-analysis. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
276	Song, I. H. and M. Rudwaleit (2013). "Certolizumab pegol in axial spondyloarthritis." Expert Rev Clin Immunol 9(12): 1161-1172.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
277	Stockdale. 218. A qualitative approach: exploring the exercise behavior in ankylosing spondylitis patients on anti-TNF alpha medication. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)

278	Sykes. 209. The clinical spectrum of axial SPA in a UK secondary care cohort. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
279	Sykes. 223. Delay to diagnosis in axial spondyloarthritis: are we improving? BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
280	Syngle. [THU0114] Efficacy and safety of spironolactone in the treatment of rheumatoid arthritis and ankylosing spondylitis. EULAR 2014.	Hand searches	No biological DMARDs of interest	2nd update (July 2014)
281	Tarp, S., U. Tarp, et al. (2013). "Serious adverse events associated with using biological agents to treat rheumatic diseases: Network meta-analysis from a national guideline panel." Arthritis and Rheumatism 65 SUPPL. 10: S997-S998.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
282	Thomas, S., N. Borazan, et al. (2013). "Comparative immunogenicity of tumor necrosis factor inhibitors: Impact on clinical efficacy and tolerability in the management of autoimmune diseases: A systematic review and meta-analysis." Arthritis and Rheumatism 65 SUPPL. 10: S866.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
283	Uddin. [FRI0165] The molecular convergence of non-HLA ankylosing spondylitis risk genes with autoimmune diseases. EULAR 2014.	Hand searches	Animal or in-vitro studies	2nd update (July 2014)
284	Vacca. [THU0061] Vitamin D insufficiency and deficiency in two European cohorts of patients with inflammatory rheumatic disorders. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
285	Van Den Bosch, F., P. Mease, et al. (2013). "Similar levels of disease activity in patients with oligoarticular vs. polyarticular peripheral spondyloarthritis." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
286	Van den Bosch. [SAT0342] Arthritis and enthesitis remission during adalimumab treatment in peripheral spondyloarthritis: year-2 results from ABILITY-2 . EULAR 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
287	Van Der Burg, L., M. Ter Wee, et al. (2013). "The effect of biological therapy on work participation in ankylosing spondylitis patients: A systematic review." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
288	Van Der Heijde, D., A. Deodhar, et al. (2013). "Achieving ASDAS-CRP major improvement and inactive disease in patients with ankylosing spondylitis after treatment with golimumab is associated with normalized health related quality of life: Two-year results from the go-raise trial." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Duplicate	2nd update (July 2014)
289	van der Heijde, D., D. Zack, et al. (2014). "Rates of serious infections, opportunistic infections, inflammatory bowel disease, and malignancies in subjects receiving etanercept vs. controls from clinical trials in ankylosing spondylitis: a pooled analysis." Scand J Rheumatol 43(1): 49-53.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
290	Van Der Heijde, D., J. Braun, et al. (2013). "Improvements in work and household productivity after 24 weeks of certolizumab pegol in treatment of axial spondyloarthritis patients, including patients with ankylosing spondylitis: Results of rapid-axSpA study." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
291	Van Der Heijde, D., J. Sieper, et al. (2013). "Concurrent sacroiliac joint and spinal inflammation on MRI in patients with non-radiographic axial spondyloarthritis." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	No outcomes of interest	2nd update (July 2014)
292	Van Der Heijde, D., W. Maksymowych, et al. (2013). "Relationship between MRI and clinical remission in patients with non-radiographic axial spondyloarthritis after two years of adalimumab therapy." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Open-label extensions of RCT (where randomisation was broken)	2nd update (July 2014)
293	Van Der Heijde, D., W. P. Maksymowych, et al. (2013). "Effect of certolizumab pegol on inflammation of spine and sacroiliac joints in patients with axial spondyloarthritis: 12-week magnetic resonance imaging results of rapid-axSpA study." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	Duplicate	2nd update (July 2014)
294	Van Der Heijde, D., W. P. Maksymowych, et al. (2013). "Relationship between MRI and clinical remission in patients with non-radiographic axial spondyloarthritis after two years of adalimumab therapy." Arthritis and Rheumatism 65 SUPPL. 10: S768.	Database searches	Open-label extensions of RCT (where randomisation was broken)	2nd update (July 2014)

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295	van Hoeven. [FRI0208] The impact of a referral model for axial spondyloarthritis in young patients with chronic low back pain, the design of an impact study. EULAR 2014.	Hand searches	Not adult patients with active axSpA	2nd update (July 2014)
296	Veale, D. J. (2013). "Psoriatic arthritis: recent progress in pathophysiology and drug development." Arthritis Res Ther 15(6): 224.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	2nd update (July 2014)
297	Viapiana, O., E. Fracassi, et al. (2013). "Bisphosphonates versus infliximab in ankylosing spondylitis treatment." Annals of the Rheumatic Diseases 72(3): 2013-2006.	Database searches	No comparators of interest	2nd update (July 2014)
298	Wallis, D., F. D. O'Shea, et al. (2013). "Mechanical back pain demonstrates better response to celecoxib than acetaminophen despite lack of mRI-defined inflammatory changes in the spine." Arthritis and Rheumatism 65 SUPPL. 10: S903-S904.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
299	Wang, H., D. Zuo, et al. (2014). "Randomized, placebo controlled and double-blind trials of efficacy and safety of adalimumab for treating ankylosing spondylitis: a meta-analysis." Int J Rheum Dis 17(2): 142-148.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
300	Weiss, A., I. H. Song, et al. (2013). "Comparison of treatment responses to TNF-blockers in axial spondyloarthritis patients with short vs long symptom duration." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
301	Weiss, A., I. H. Song, et al. (2014). "Good correlation between changes in objective and subjective signs of inflammation in short- but not long-diseased patients with axial spondyloarthritis treated with tumor necrosis factor-blockers." Arthritis Res Ther 16(1): R35.	Database searches	Pooled analysis, meta-analyses	2nd update (July 2014)
302	Williamson. 53. Usability of the modofied Swindon foot and ankle questionnaire. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
303	Winthrop, K. L., T. Momtahen, et al. (2013). "Sarilumab, a subcutaneously administered, fully human monoclonal antibody inhibitor of the IL-6 receptor alpha: 12 week infection rates by level of circulating neutrophils in rheumatoid arthritis and ankylosing spondylitis." Arthritis and Rheumatism 65 SUPPL. 10: S1008.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
304	Wu. [SAT0364] Efficacy and safety of intra-articular therapy with methotraxate in large glucose injection volume on knee synovitis in patients with ankylosing spondylitis. EULAR 2014.	Hand searches	No biological DMARDs of interest	2nd update (July 2014)
305	Yin. 207. Assessing bone density in patients with ankylosing spondylitis using dual energy absorptiometry. BSR 2014.	Hand searches	Not RCT	2nd update (July 2014)
306	Yoo, D., P. Miranda, et al. (2013). "A randomized, double-blind, phase 3 study demonstrates clinical equivalence of CT-P13 to infliximab when co-administered with methotrexate in patients with active rheumatoid arthritis." Annals of the Rheumatic Disease 71(3): 2012-2006.	Database searches	Not adult patients with active axSpA or any of its subpopulations	2nd update (July 2014)
307	Zangi. [SP0216] The evidence for patient education in inflammatory arthritis. EULAR 2014.	Hand searches	Pooled analysis, meta-analyses	2nd update (July 2014)
308	Zhang, J., Y. M. Zhang, et al. (2009) Efficacy of etanercept in patients with ankylosing spondylitis: A double-blind, randomized, placebo controlled trial. [Chinese]. Chinese Journal of New Drugs 1846-1849+1881	Database searches	Duration less than 12 weeks	2nd update (July 2014)
309	Zheng, Y., M. Gu, et al. (2014). "Tomography-guided palisade sacroiliac joint radiofrequency neurotomy versus celecoxib for ankylosing spondylitis: a open-label, randomized, and controlled trial." Rheumatology International.	Database searches	No biological DMARDs of interest	2nd update (July 2014)
310	Zlatkovic-Svenda. [FRI0214] EULAR project: spondyloarthritis prevalence in Serbia. EULAR 2014.	Hand searches	Not RCT	2nd update (July 2014)
311	ASAS40 AND ASDAS RESPONSES ARE ASSOCIATED WITH IMPROVED PHYSICAL FUNCTION, HRQOL, AND WORK PRODUCTIVITY IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS; D. van der Heijde, A. Joshi, M. Mittal, A. Pangan, N. Chen, K. Betts, C. Qi, Y. Bao. EULAR 2014	Hand searches	NSAID-naïve patients only	3rd update (January 2017)

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312	DISCRIMINANT CAPACITY OF CLINICAL EFFICACY MEASURES, ALONE OR IN COMBINATION WITH NSAID INTAKE, IN DETECTING ANTI-TNF TREATMENT EFFECT IN SPONDYLOARTHRITIS; M. Dougados, E. Wood, L. Gossec, D. van der Heijde, A. Dubanchet, I. Logeart. EULAR 2014	Hand searches	Duration less than 12 weeks	3rd update (January 2017)
313	A Multi-Center, Open Label, Randomized Clinical Tries of Etanercept and Celecoxib Alone/Combined Treatment in Effectiveness and Safety of Ankylosing Spondylitis jieruo Gu 1, Liudan Tu2, Minjing Zhao3, Zhiming Lin4, Zetao Liao5, Shuangyan Cao6, Qinghong Yu7 and Zhizhong Ye_ab 736 . ACR 2016	Hand searches	Duplicate of included publication found through database searches	3rd update (January 2017)
314	A Randomized, Clinical Trial to Assess the Relative Efficacy and Tolerability of Two Doses of Etoricoxib in Patients with Ankylosing Spondylitis Eva Balazcs1, Desiree van der Heijde2,Narinder Rawal3,joachim Sieper4, Boyd Scotts, Kara Bickham, Nancy Frontera6, Paul Stryszak6, Dimitris Papanicolaou6, Zoran Popmihajlov6 and Paul Peloso_ab 2845. ACR 2015	Hand searches	Pooled analysis, meta-analyses	3rd update (January 2017)
315	AN OPEN LABEL, PILOT, MULTI-CENTRE, STEPDOWN,RANDOMIZED CONTROLLED TRIAL TO EXAMINE WHETHER ETANERCEPT 25 MG ONCE WEEKLY IS EFFECTIVE IN MAINTAINING A CLINICAL RESPONSE IN PATIENTS WITH ANKYLOSING SPONDYLITIS WHO HAVE RESPONDED TO 50 mg ONCE WEEKLY; Karl Gaffney, , Frances Elender, , Louise Hamilton, Max Yates, Loretta Dean and Helen Doll. BSR 2014	Hand searches	Not adult patients with active axSpA	3rd update (January 2017)
316	Bao, C., F. Huang, et al. (2012). "Golimumab administered subcutaneously every 4 weeks in Chinese patients with active ankylosing spondylitis: Week 24 safety and efficacy results from a randomized, placebo-controlled study." International Journal of Rheumatic Diseases,15: 88.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
317	Baraliakos, X., J. Braun, et al. (2012). "Secukinumab reduces spinal inflammation as early as week 6 in patients with ankylosing spondylitis, as detected by magnetic resonance imaging-results of a double-blind, placebo-controlled, multicenter phase II proof-of-concept study." Dermatology and Therapy,2: S49.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
318	Baraliakos, X., M. Schiff, et al. (2016). "Secukinumab sustains individual clinical responses over time in patients with active ankylosing spondylitis: 2-year results from a phase 3 randomized placebo-controlled trial." Arthritis and Rheumatology,68: 917-918.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
319	Better Health-Related Quality of Life and Work Capacity in Patients Achieving Inactive Disease and Clinical Response in Patients with Non-Radiographic Axial Spondyloarthritis Maxime Dougados1, Desiree van der Heijde2, Wen-Chan Tsai3, Diego Saaibi4, Randi Bonin5, Lisa Marshall6,Heather jones7,Ronald Pedersen8, Bonnie Vlahos9 and Miriam Tarallo . ACR 2016	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
320	Braun, J., J. Davis, et al. (2009). "Golimumab, a new, human, TNFα antibody, in ankylosing spondylitis (AS): 24-Week efficacy and safety results of the go-raise study." Rheumatology,48: i57.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
321	Braun, J., W. P. Maksymowych, et al. (2015). "Achievement of remission of inflammation in the spine and sacroiliac joints measured by magnetic resonance imaging (MRI) in patients with axial spondyloarthritis, and associations between MRI and clinical remission, over 96 weeks of treatment with Certolizumab Pegol." Annals of the Rheumatic Diseases,74: 134-135.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
322	Braun, J.,Baraliakos, X., et al. (2016). "Serum C-reactive Protein Levels Demonstrate Predictive Value for Radiographic and Magnetic Resonance Imaging Outcomes in Patients with Active Ankylosing Spondylitis Treated with Golimumab." Ann Rheum Dis,43(9): 1704-1712.	Database searches	No outcomes of interest	3rd update (January 2017)
323	CERTOLIZUMAB PEGOL FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-AXSPA TRIAL; D. van der Heijde, M. Dougados, R. Landewé, J. Sieper, W.P. Maksymowych, M. Rudwaleit, F. van den Bosch, J. Braun, P.J. Mease, O. Davies, B. Hoepken, L. Peterson, A. Deodhar. EULAR 2016	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)

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324	CLINICAL AND IMAGING EFFICACY OF ETANERCEPT IN EARLY NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 48-WEEK TREATMENT DATA; W. P. Maksymowych, D. van der Heijde, M. Dougados, J. Sieper, J. Braun, G. Citera, C. Miceli-Richard, J. C. C. Wei, R. Pedersen, R. Bonin, I. Logeart, J. Wajdula, M. U. Rahman, B. Vlahos, J. Bukowski. EULAR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
325	CLINICAL CHARACTERISTICS OF ANKYLOSING SPONDYLOARTHRITIS IN REAL CLINICAL PRACTICE IN RUSSIA: RESULTS OF A SINGLE MULTICENTER NON-INTERVENTIONAL STUDY- EPIKA 2 T. Dubinina1, s. Emesl,0. Rumyantseva 1,D. Abdulganieva2,I. Vinogradovw3,L. Evstigneeva",A. Yelonalcov5,E. Otteva6, T. Raskina7, T. SalnikovaB,R. Samigullina9, v. SorotskayaB,L. Shkil1o.1vA Nasonova Research Institute of Rheumatology,Moscow; 2KSMU,Kazan; 3Distrlct Clinical Hospital "1Ullanovsk; 4Distrlct Rheumatology Center, Ekaterinburg; 5MONIKI,Moscow; 6Regional Clinical Hospital "1"named after Prof Sergeev S.I.,Xabarovsk; 7District Clinical Hospital of War Veterans, Kemerovo; 8District Clinical Hospital,Tula; 9NWSMU named after Mechnikov,St. Peterburg; 10MHCI Municipal Clinical Hospital "20"named after Berzon I.S.,Krasnoyarsk, Russian Federation . EULAR 2016	Hand searches	Not RCT	3rd update (January 2017)
326	Clinical Response and Remission in Patients with Non Radiographic Axial Spondyloarthritis after Three Years of Adalimumab Therapy; Desiree M. van der Heijde1,Joachim Sieper2 Walter P. Maksymowych3 Dominique L. Baeten4 Yinglin Xia5,Jaclyn K. Anderson5 and Aileen L. Pangan _ab 562. ACR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
327	CLINICAL RESPONSE AND REMISSION IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AFTER THREE YEARS OF ADALIMUMAB THERAPY; D. van der Heijde, J. Sieper, D. L. Baeten, W. P. Maksymowych, Y. Xia, J. K. Anderson, A. L. Pangan. EULAR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
328	CLINICAL RESPONSES AND IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES ARE ASSOCIATED WITH INCREASED PRODUCTIVITY IN THE WORKPLACE AND AT HOME IN AXIAL SPONDYLOARTHRITIS PATIENTS TREATED WITH CERTOLIZUMAB PEGOL; van der Heijde D, Braun J, Rudwaleit M, Purcaru O, Kavanaugh A. ISPOR EU 2015	Hand searches	No outcomes of interest	3rd update (January 2017)
329	Deodhar, A. A., J. D. Reveille, et al. (2016). "Safety and efficacy of intravenous golimumab in adult patients with active ankylosing spondylitis: Results through week 28." Arthritis and Rheumatology,68: 1370-1371.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
330	Disease Activity and Clinical Response Early in the Course o Treatment Predict Long-Term Outcomes in Axial Spondyloarthritis Patients Treated with Certolizumab Pego Desiree M. van der Heijde1, Atul A. eodhar2, Owen Davies3, Tommi Nurminen4 and Martin Rudwaleit_ab 543. ACR 2014	Hand searches	No outcomes of interest	3rd update (January 2017)
331	Dose Reduction Compared with Standard Dosing for Maintenance of Remission in Patients with Spondyloarthropathies and Clinical Remission with Anti TNF: A Randomised Real-Life Trial jorge Gratacos-Masmitja 1,Caridad Pontes2,Ferran Torres3,Xavier juanola4,Antoni Vallano 5,TC Salman-Monte6, Francisco j. Blanco7,Agusti Sellas-Fernandez 8,Raimon Sanmarti9,Gonzalo Calvo10, Teresa Clavaguera11, Raul Veroz Gonzalez12,juan Carlos Torre Alonso 13,jesus Sanz14,Cristina Avendai'io15,Carlos Rodriguez-Lozano16, Luis Francisco Linares17, Ana Urruticoechea18, Eduardo Collantes-Estevez19, Rosa Moria Novell20, Delia Reina21, Eduardo Cuende22, Pedro Zarco23, Cruz Fernandez-Espartero24, Rosario Garcia-Vicuna25,Carlos Alberto Mantilla Morales26, Eugenio De Miguel27, Roser Vives2 and Mireia Moreno_ab 2149. ACR 2015	Hand searches	Not RCT	3rd update (January 2017)
332	Dougados, M., D. Van Der Heijde, et al. (2016). "Better health-related quality of life and work capacity in patients achieving inactive disease and clinical response in patients with non-radiographic axial spondyloarthritis." Arthritis and Rheumatology,68: 3732-3733.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
333	Dougados, M., D. Van Der Heijde, et al. (2016). "Clinical and imaging efficacy of etanercept in early non-radiographic axial spondyloarthritis: 104-week treatment results." Journal of Rheumatology,43(6): 1232.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)

334	Dougados, M., G. Bergman, et al. (2016). "Baseline demographic and disease characteristics associated with response to golimumab in patients with active non radiographic axial spondyloarthritis." Journal of Rheumatology,43(6): 1180.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
335	Dougados, M., H. Jones, et al. (2014). "Evaluation of extreme enthesitis and/or patientrelated outcome score as potential surrogates for fibromyalgia and as potential confounding factors of anti-TNF response." Clinical and Experimental Rheumatology,32(5): 777.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
336	DRUG SURVIVAL AND CLINICAL EFFICACY OF 7 YEARS ETANERCEPT TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE GLAS COHORT; S. Arends, E. Brouwer, F. Wink, R. Bos, F. Maas, H. Bootsma, E. van der Veer, A. Spoorenberg. EULAR 2015	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
337	Effect of Certolizumab Pegol over 96 Weeks of Treatment on Inflammation of Spine and Sacroiliac joints Measured By Magnetic Resonance Imaging in Patients with Axial Spondyloarthritis; jQrgen Braun , Walter P. Maksymowych , Robert B. M. Landewe , Christian Stach, Owen Davies, Tommi Nurminen and Desiree van der Heijde_ab 565 . ACR 2014	Hand searches	No outcomes of interest	3rd update (January 2017)
338	Effect of secukinumab, an interleukin-17A inhibitor on spinal radiographic changes through 2 years in patients patients with active ankylosing spondylitis:Resukts of the phase 3 study, measure1_ab OP0001 . EULAR 2016	Hand searches	No outcomes of interest	3rd update (January 2017)
339	Effectiveness of different schemes of etoricoxib administration in reduction of active sacroilitis in patients with axial spondyloarthritis-results of a 12 week, prospective, open label study. EULAR 2015	Hand searches	No outcomes of interest	3rd update (January 2017)
340	EFFICACY AND SAFETY OF ADALIMUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS - AN INVESTIGATOR-INITIATED RANDOMIZED PLACEBO-CONTROLLED TRIAL; S. Krabbe, M. Østergaard, I.J. Sørensen, B. Jensen, O.R. Madsen, G.P. Eng, K.H. Asmussen, J. Møller, L. Balding, S.J. Pedersen. EULAR 2016	Hand searches	NSAID-naïve patients only	3rd update (January 2017)
341	EFFICACY AND SAFETY OF GOLIMUMAB IN PATIENTS WITH ACTIVE, VERY EARLY PERIPHERAL SPONDYLOARTHRITIS: FIRST RESULTS FROM THE CRESPA STUDY, A MONOCENTRIC, PLACEBO-CONTROLLED RANDOMIZED TRIAL P. Carron 1,G. Varlcar 2, H. Cypersf,2, L. Van Praet1, D. Elewau 2, F. Van den Bosch 1• 1Rheumatology; 2 VIB inflammation Research Center, Univeristy of Ghent, Gent, Belgium . EULAR 2016	Hand searches	Not adult patients with active axSpA	3rd update (January 2017)
342	Evaluation of the Nonsteroidal Anti-1nflammatory Drug Sparing Effect of Etanercept in Axial Spondyloarthritis: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial Maxime Dougados1, Emily Wood2, Bernard Combe3,Corinne Miceli-Richard4,Francis Berenbaum5, Nandan Koppiker6, Arnaud Dubanchet7 and Isabelle Logeart _ab 581. ACR 2014	Hand searches	Duration less than 12 weeks	3rd update (January 2017)
343	Golimumab Versus Pamidronate for the Treatment of Axial Spondyloarthropathy (SpA): A 48-Week Randomized Controlled Trial Chi Chiu Mok, Angela Li, Kar Li Chan and Ling Yin Ho_ab 854. ACR 2014	Hand searches	No comparators of interest	3rd update (January 2017)
344	GOLIMUMAB VERSUS PAMIDRONATE FOR THE TREATMENT OF AXIAL SPONDYLOARTHROPATHY (SPA): A 48-WEEK RANDOMIZED CONTROLLED TRIAL; C. C. Mok, A. Li, K. L. Chan, L. Y. Ho. EULAR 2014	Hand searches	No comparators of interest	3rd update (January 2017)
345	Goll, G. L., I. C. Olsen, et al. (2016). "Biosimilar infliximab (CT-P13) is not inferior to originator infliximab: Results from a 52-week randomized switch trial in Norway." Arthritis and Rheumatology,68: 4389-4392.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
346	Illness Perceptions and Health-Related Quality of Life in Patients with Axial Spondyloarthritis and Other Forms of Chronic Back Pain in the Spondyloarthritis Caught Early (SPACE)-Cohort Miranda van Lunteren1, Pauline Bakker1, Margreet Scharloo2, Ad Kaptein3, Zineb Ez-Zaitouni1, Camilla Fongen4, Robert Landewe5, Maikel van Oosterhout 6,	Hand searches	Not RCT	3rd update (January 2017)

	Mariagrazia Lorenzin7, Desiree van der Heijde1 and Floris van Gaalen . ACR 2016			
347	Inman, R., A. Deodhar, et al. (2013). "Achieving ankylosing spondylitis disease activity score-c-reactive protein major improvement and inactive disease in patients with ankylosing spondylitis after treatment with golimumab is associated with normalized health related quality of life: 2-year results from go-raise." Journal of Rheumatology,40(6): 1012.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
348	Li, X., Q. Han, et al. (2016). "Assessment of clinical efficacy of TNF-α inhibitor or thalidomide combined with sulfasalazine on active coxitis in patients with ankylosing spondylitis." International Journal of Rheumatic Diseases,19: 237.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
349	Li, X., Q. Han, et al. (2016). "Radiographic response in patients with ankylosing spondylitis during 2 years of TNF-α blocking combined with Sulfasalazine therapy." International Journal of Rheumatic Diseases,19: 237.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
350	Infliximab Added to Naproxen Does Not Increase Frequency of New Fatty Lesions on MRI of the Sacroiliac joints and of the Spine As Compared to Naproxen Alone in Early Axial Spondyloarthritis Denis Poddubnyy nd Joachim Sieper_ab 2983. ACR 2014	Hand searches	NSAID-naïve patients only	3rd update (January 2017)
351	Long term anti-tnf treatment is asscociated with reduction of progression of radiographic changes in the sacroiliac joints in patients with non-radiographic axial SPA: six year results of ESTHER trial_ ab SAT 0422. EULAR 2016	Hand searches	No outcomes of interest	3rd update (January 2017)
352	LONG-TERM EFFICACY AND TOLERABILITY OF GOLIMUMAB IN ACTIVE NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS OF THE OPEN-LABEL EXTENSION OF A RANDOMIZED, DOUBLE-BLIND STUDY; D. van der Heijde, M. Dougados, W.P. Maksymowych, J. Braun, G. Bergman, S.P. Curtis, A. Tzontcheva, G. Philip, S. Huyck, J. Sieper. EULAR 2016	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
353	LONG-TERM MAINTENANCE OF IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES WITH CERTOLIZUMAB PEGOL IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, INCLUDING ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 96-WEEK RESULTS OF THE RAPID-AXSPA STUDY; Sieper J, Kivitz A, van Tubergen A, Deodhar A, Szegvari B, Nurminen T, Landewé R. ISPOR EU 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
354	LONG-TERM SAFETY AND EFFICACY OF GOLIMUMAB IN THE TREATMENT OF ANKYLOSING SPONDYLITIS: RESULTS THROUGH 5 YEARS OF A RANDOMIZED, PLACEBO-CONTROLLED TRIAL; Atul Deodhar, Jurgen Braun, Robert Inman, Desiree van der Heijde, Yiying Zhou and Ben Hs . BSR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
355	Long-Term Tolerability and Efficacy of Golimumab in Active Nonradiographic Axial Spondyloarthritis: Results from the Open-Label Extension of a Randomized, Double-Blind Study Desiree van der Heijde; Maxime Dougados2, Walter Maksymowych3, Gina Bergman4,Sean P. Curtis4, Anjela Tzontcheva4, George Philip4, Susan Huycand Joachim Sieper _ab2845. ACR 2015	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
356	Maksymowych, W. P., D. Van Der Heijde, et al. (2014). "Clinical and imaging efficacy of etanercept in early non-radiographic axial spondyloarthritis: 48-week treatment data." Clinical and Experimental Rheumatology,32(5): 774.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
357	Maksymowych, W. P., S. Curtis, et al. (2015). "Quality of life in patients with active nonradiographic axial spondyloarthritis after 16 weeks of golimumab treatment." Annals of the Rheumatic Diseases,74: 1151-1152.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
358	Maksymowych, W., A. Tzontcheva, et al. (2016). "Spondyloarthritis research consortium of canada (SPARCC) baseline MRI SI joint score ≥2 better predicts response to golimumab than does assessment of spondyloarthritis international society (ASAS) MRI positivity in nonradiographic axial spondyloarthritis." Arthritis and Rheumatology,68: 905-907.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
359	Maksymowych, W., D. Van Der Heijde, et al. (2013). "Spinal inflammation in the absence of SI joint inflammation on MRI in patients with active non-radiographic axial spondyloarthritis." Journal of Rheumatology,40(6): 989.	Database searches	Narrative reviews, guidelines, commentary,	3rd update (January 2017)

			letters to the editor, conference proceedings	
360	Maksymowych, W., D. Van Der Heijde, et al. (2015). "Clinical and imaging efficacy of etanercept in early non-radiographic axial spondyloarthritis; 48-week treatment data." Journal of Rheumatology,42(7): 1286.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
361	Maksymowych, W., R. Lambert, et al. (2011). "Defining the smallest detectable change for the sparcc spine and sacroiliac joint MRI index for ankylosing spondylitis." Reumatologia Clinica Suplementos,7: 31.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
362	Maksymowych, W., R. Landewe, et al. (2014). "Effect of certolizumab pegol over 48 weeks in patients with axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis." Journal of Rheumatology,41(7): 1495-1496.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
363	Maksymowych, W., S. Curtis, et al. (2016). "Quality of life in patients with active non radiographic axial spondyloarthritis after 16 weeks of golimumab treatment." Journal of Rheumatology,43(6): 1179-1180.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
364	Maksymowych, W., S. Wichuk, et al. (2016). "Modification of structural lesions on magnetic resonance imaging by etanercept: A 12-Week randomized placebo-controlled trial." Journal of Rheumatology,43(6): 1232.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
365	Marzo-Ortega, H., C. W. Legerton, et al. (2016). "Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis: 2-year results from a phase 3 trial with subcutaneous loading and maintenance dosing (MEASURE 2)." Annals of the Rheumatic Diseases,75: 812-813.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
366	Patient-Reported Quality of Life in Patients with Baseline Objective Signs of Inflammation and Active Nonradiographic Axial Spondyloarthritis Treated with Golimumab: Results of the Open-Label Extension of a Randomized, Double-Blind Study Walter Maksymowych 1, Maxime Dougados2,joachim Sieper3,jurgen Braun4, G Bergman5, Sean P. Curtis6, Anjela Tzontcheva6, George Philip6, Susan Huyck6 and Desiree van der Heijde7_ab 710. ACR 2016	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
367	PATIENT-REPORTED QUALITY OF LIFE IN PATIENTS WITH BASELINE OBJECTIVE SIGNS OF INFLAMMATION AND ACTIVE NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH GOLIMUMAB: RESULTS OF THE OPEN-LABEL EXTENSION OF A RANDOMIZED, DOUBLE-BLIND STUDY; W.P. Maksymowych, M. Dougados, J. Sieper, J. Braun, G. Bergman, S.P. Curtis, A. Tzontcheva, G. Philip, S. Huyck, D. van der Heijde. EULAR 2016	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
368	QUALITY OF LIFE WITH ETANERCEPT IN EARLY NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 24 AND 48-WEEK DATA FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL; J. Sieper, E. Drescher, J. Rosa, R. Pedersen, R. Bonin, B. Vlahos, J. Bukowski, S. Kotak. EULAR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
369	REDUCTION IN FATIGUE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF TWO PHASE 3 STUDIES OF SECUKINUMAB; T.K. Kvien, P.G. Conaghan, A. Deodhar, L. Gossec, M. Østergaard, J. Cañete, K. Gandhi, H. Richards, N. Williams, S. Jugl. EULAR 2016	Hand searches	Pooled analysis, meta-analyses	3rd update (January 2017)
370	RELATIONSHIP BETWEEN MRI AND CLINICAL REMISSION IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AFTER TWO YEARS OF ADALIMUMAB THERAPY; Desiree van der Heijde, , Walter P. Maksymowych, Joachim Sieper,Robert G. Lambert, Matthew A. Brown, Suchitrita S. Rathmann,Jaclyn Anderson and Aileen L. Pangan. BSR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
371	Rudwaleit, M., R. Landewé, et al. (2014). "Observed incidence rates of uveitis following certolizumab pegol treatment in patients with axial spondyloarthritis." Clinical and Experimental Rheumatology,32(5): 787.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
372	Safety and Efficacy of Certolizumab Pegol over 204 Weeks in Patients with Axial Spondyloarthritis, Including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis Atul A. Deodhar 1, Maxime Dougados2, Robert	Hand searches	Open-label extensions of RCT (where	3rd update (January 2017)

	Landewe3,Joachim Sieper4, Walter Maksymowych5, Martin Rudwaleit6, Filip van Den Bosch7, Jurgen Braun8, PhilipJ Mease9, Alan Kivitz10,jessica Walsh11, Owen Davies12,Bengt Hoepken13, Luke Peterson14 and Desiree van der Heijde _ab 687. ACR 2016		randomisation was broken)	
373	Safety and Efficacy of Certolizumab Pegol over 96 Weeks in Patients with Axial Spondyloarthritis, Including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis Joachim Sieper, Martin Rudwaleit Desiree M.van der Heijde, Walter P. Maksymowych Maxime Dougados5, Philip j. Mease 6, jurgen Braun7, Atul A. Deodhar 8, Bengt Hoepken9, Tommi Nurminen and Robert B. M. Landewe_ab 852 . ACR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
374	Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Active Psoriatic Arthritis in Anti TNF-Naive Patients and Those Previously Exposed to Anti TNF Therapy: 52-Week Results from a Randomized, Double Blind, Placebo-Controlled Phase 3 Trial with Subcutaneous Dosing Arthur Kavanaugh1, Iain B.Mclnnes 2,Philip J.Mease 3,Stephan Hall4, Hector Chinoy5,Alan J Kivitz6, Manmath atekar7,Zailong Wang8 and Shephard Mpofu . ACR 2015	Hand searches	Not adult patients with active axSpA	3rd update (January 2017)
375	SECUKINUMAB REDUCES SACROILIAC JOINT AND SPINAL INFLAMMATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: MRI DATA FROM A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY (MEASURE 1); X. Baraliakos, J. Braun, J. Sieper, D.L. Baeten, A. Readie, G. Ligozio, H. Richards EULAR 2015	Hand searches	No outcomes of interest	3rd update (January 2017)
376	Sieper, J., A. A. Deodhar, et al. (2016). "Impact of time since diagnosis, age, and number of prior non-steroidal anti-inflammatory drugs on response to adalimumab (humira) in patients with ankylosing spondylitis." Arthritis and Rheumatology,68: 979-980.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
377	Sieper, J., D. Van Der Heijde, et al. (2016). "Efficacy of golimumab for nonradiographic axial spondyloarthritis (nraxspa): Subgroup analysis by baseline MRI and C-reactive protein status." Arthritis and Rheumatology,68: 943-945.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
378	Sieper, J., D. Van Der Heijde, et al. (2016). "Efficacy of golimumab for nonradiographic axial spondyloarthritis: Subgroup analysis by baseline MRI and c-reactive protein status." Annals of the Rheumatic Diseases,75: 813-814.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
379	Sieper, J., E. Drescher, et al. (2014). "Quality of life with etanercept in early non-radiographic axial spondyloarthritis." Clinical and Experimental Rheumatology,32(5): 777.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
380	Sieper, J., J. Braun, et al. (2015). "Secukinumab significantly improves signs and symptoms of active ankylosing spondylitis: 52-week data from measure 2, a randomized, double-blind, placebo-controlled phase 3 trial with subcutaneous loading and maintenance dosing." Annals of the Rheumatic Diseases,74: 132-133.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
381	SUSTAINED AND SIMILAR CLINICAL RESPONSE TO ETANERCEPT AFTER 6 YEARS OF TREATMENT IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND ANKYLOSING SPONDYLITIS: LONG-TERM RESULTS OF THE ESTHER TRIAL; D. Poddubnyy, I.-H. Song, K.-G. Hermann, H. Haibel, J. Callhoff, J. Listing, B. Buss, B. Freundlich, E. Lange, M. Rudwaleit, J. Sieper. EULAR 2015	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
382	SUSTAINED CLINICAL REMISSION IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AFTER TWO YEARS OF ADALIMUMAB TREATMENT; Joachim Sieper, Dominique L. Baeten, Filip Van den Bosch, Suchitrita S. Rathmann, Jaclyn Anderson and Aileen L. Pangan. BSR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
383	Sustained Improvement in Physical Function, Health Related Quality of Life, and Work Productivity with Adalimumab Treatment in Non-Radiographic Axial Spondyloarthritis Desiree van der Heijde ,Manish Mitta , Naijun Chen ,Aileen L. Pangan and Avani D. joshi _ab 552 . ACR 2014	Hand searches	Open-label extensions of RCT (where randomisation was broken)	3rd update (January 2017)
384	SUSTAINED IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE, WORK PRODUCTIVITY, EMPLOYABILITY AND REDUCED HEALTHCARE RESOURCE UTILIZATION OF PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS	Hand searches	Pooled analysis, meta-analyses	3rd update (January 2017)

	AND ANKYLOSING SPONDYLITIS TREATED WITH GOLIMUMAB: 5-YEAR RESULTS FROM THREE PHASE III STUDIES ; Chenglong Han , Arthur Kavanaugh , Mark C. Genovese, Atul Deodhar, Ben Hsu and Elizabeth Hsia . BSR 2014			
385	Sustained improvement in workplkace and household productivity and social participation with certolizumab pegol over 96 weeks in patients with axial spondyloarthritis, including ankylosing spondylitis and non-radiographical axial spondyloarthritis; van der Heijde, Braun J, Ruwaleit M, Purucaru O, Kavanaugh A. ISPOR EU 2014	Hand searches	No outcomes of interest	3rd update (January 2017)
386	The effects of Infliximab treatment on depression, anxiety and sleep disorders in patients with ankylosing spondylitis Bozkirli_ab 0658. EULAR 2014	Hand searches	No comparators of interest	3rd update (January 2017)
387	Treatment with Tofacitinib Is Associated with Clinically Meaningful Reductions in Axial MRIInflammation in Patients with Ankylosing Spondylitis Walter Maksymowych, Desiree van der Heijde2,Xenofon Baraliakos3,Atul A. Deodhar4, Matt Brown5, Sarah Sherlock6, David Li7, Dona Fleishaker8 and Thijs Hendrikx. ACR 2016	Hand searches	No biological DMARDs of interest	3rd update (January 2017)
388	Van Der Heijde, D., J. Braun, et al. (2015). "Clinical responses and improvements in patient-reported outcomes are associated with increased productivity in the workplace and at home in axial spondyloarthritis patients treated with certolizumab pegol." Annals of the Rheumatic Diseases,74: 268-269.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
389	Wei, J. C. C., D. L. Baeten, et al. (2015). "Intravenous loading and subcutaneous maintenance with secukinumab provides sustained improvement in multiple measures of disease activity in subjects with active ankylosing spondylitis: 52-week data from the randomized, double-blind, placebo-controlled, phase 3 measure 1 study." Annals of the Rheumatic Diseases,74: 1146-1147.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
390	Wei, J. C. C., H. Marzo-Ortega, et al. (2016). "Secukinumab improves patient-reported outcomes in active ankylosing spondylitis: 2-Year results from the phase 3 MEASURE 2 study." International Journal of Rheumatic Diseases,19: 233-234.	Database searches	Narrative reviews, guidelines, commentary, letters to the editor, conference proceedings	3rd update (January 2017)
391	Baraliakos, X,Sieper, J,Chen, S,Pangan, Al,Anderson, Jk. Non-radiographic axial spondyloarthritis patients without initial evidence of inflammation may develop objective inflammation over time. Rheumatology (oxford, england). 2017. 56:1162-1166	Database searches	Not RCT	4th update (April 2018)
392	Goll, G. L.,Olsen, I. C.,Jorgensen, K. K.,Lorentzen, M.,Bolstad, N.,Haavardsholm, E. A.,Lundin, K. E. A.,Mork, C.,Jahnsen, J.,Kvien, T. K.. Biosimilar infliximab (CT-P13) is not inferior to originator infliximab: Results from a 52-week randomized switch trial in Norway. Arthritis and Rheumatology. 2016. 68:4389-4392	Database searches	Not adult patients with active axSpA or any of its subpopulations	4th update (April 2018)
393	Krabbe, S.,Ostergaard, M.,Eshed, I.,Sorensen, I. J.,Jensen, B.,Moller, J. M.,Balding, L.,Madsen, O. R.,Asmussen, K.,Eng, G.,Jorgensen, N. R.,Pedersen, S. J.. Whole-body Magnetic Resonance Imaging in Axial Spondyloarthritis: Reduction of Sacroiliac, Spinal, and Entheseal Inflammation in a Placebo-controlled Trial of Adalimumab. J Rheumatol. 2018. #volume#:#pages#	Database searches	Open-label extensions of RCT (where randomisation was broken)	4th update (April 2018)
394	Landewe, Rbm,Sieper, J,Deodhar, Aa,Marzo-Ortega, H,Lambert, Rg,Li, M,Wang, X,Anderson, Jk. Comparison of the clinical and imaging arms of the assessment of spondyloarthritis international society classification criteria and parameters of objective inflammation in patients with non-radiographic axial spondyloarthritis. Arthritis and rheumatology. Conference: american college of rheumatology/association of rheumatology health professionals annual scientific meeting, ACR/ARHP 2017. United states. 2017. 69:#pages#	Database searches	No outcomes of interest	4th update (April 2018)
395	Sieper, J.,Rudwaleit, M.,Lenaerts, J.,Wollenhaupt, J.,Myasoutova, L.,Park, S. H.,Song, Y. W.,Yao, R.,Huyck, S.,Govoni, M.,Chitkara, D.,Vastesaeger, N.. Partial remission in ankylosing spondylitis and nonradiographic axial spondyloarthritis in treatment with infliximab plus naproxen or naproxen alone: Associations between partial remission and baseline disease characteristics. Rheumatology (United Kingdom). 2016. 55:1946-1953	Database searches	NSAID-naïve patients only	4th update (April 2018)
396	A. A. Deodhar, A. Boonen, G. Ferraccioli, F. Van Den Bosch, D. Martinez, B. Porter, A. Shete, N. Scheuer, I. Gilloteau, V. Strand. Secukinumab provides early and sustained improvements in health-related quality of life in patients with	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)

	ankylosing spondylitis: A pooled analysis from the secukinumab phase 3 trial program. Arthritis and Rheumatology. 2018. 70:2883-2884			
397	A. Deodhar, X. Baraliakos, H. Marzo-Ortega, J. Sieper, A. D. Gupta, B. Porter, T. Fox. Secukinumab demonstrates consistent safety over long-term exposure (up to 3 years) in patients with active ankylosing spondylitis: Pooled analysis of three phase 3 studies. Journal of Clinical Rheumatology. 2018. 24:S107	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)
398	A. J. Kivitz, K. Pavelka, E. Dokoupilova, R. Blanco, M. Maradiaga, H. Tahir, Y. Wang, B. Porter, A. Stefanska, S. Rohrer, H. Richards. Sustained improvements in signs and symptoms of active ankylosing spondylitis and reassuring safety with secukinumab 300mg: 3-year results from a phase 3 study. Arthritis and Rheumatology. 2018. 70:2084-2085	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
399	A. R. Cruz-Machado, S. R. Manica, J. L. Silva, F. M. Pimentel-Santos, J. Tavares-Costa, E. Vieira-Sousa. The effect of biologic disease-modifying antirheumatic drugs in targeting disease remission in axial spondyloarthritis (AXSPA): A systematic literature review. Annals of the Rheumatic Diseases. 2018. 77:998-999	Database searches	SLR for bibliography check	5th update (April 2019)
400	A. R. Machado, S. R. Manica, J. L. Silva, F. Pimentel-Santos, J. T. Costa, E. Vieira-Sousa. The effect of biologic disease-modifying antirheumatic drugs in targeting disease remission in axial spondyloarthritis: A systematic literature review. Arthritis and Rheumatology. 2018. 70:2870-2872	Database searches	SLR for bibliography check	5th update (April 2019)
401	B. Bannert, X. Baraliakos, M. Schiff, K. Pavelka, R. Martin, C. Gaillez. Secukinumab sustains individual clinical responses over time in patients with active ankylosing spondylitis: 2-year results from a phase 3 randomized placebocontrolled trial. Swiss Medical Weekly. 2017. 147:9S-10S	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
402	C. Escalas, S. Trijau, M. Dougados. Evaluation of the treatment effect of NSAIDs/TNF blockers according to different domains in ankylosing spondylitis: results of a meta-analysis. Rheumatology. 2010. 49:1317-1325	Database searches	SLR for bibliography check	5th update (April 2019)
403	C. Traverson, A. Tubery, C. Hua, F. Barchechath-Flaisler, C. Lukas, B. Combe, J. Morel, C. Gaujoux-Viala. Impact of biological and targeted synthetic DMARDs on work in patients with chronic inflammatory arthritis : A meta analysis of randomised controlled trials and controlled cohorts. Annals of the Rheumatic Diseases. 2018. 77:597-598	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)
404	C. Wagner, S. Visvanathan, J. Braun, D. van der Heijde, A. Deodhar, B. Hsu, M. Mack, M. Elashoff, R. D. Inman. Serum markers associated with clinical improvement in patients with ankylosing spondylitis treated with golimumab. Annals of the rheumatic diseases. 2012. 71:674-680	Database searches	No outcomes of interest	5th update (April 2019)
405	D. M. Van Der Heijde, J. Sieper, W. P. Maksymowych, D. L. Baeten, Y. Xia, J. K. Anderson, A. L. Pangan. Clinical response and remission in patients with non-radiographic axial spondyloarthritis after three years of adalimumab therapy. Arthritis and rheumatology. 2014. 66:S247-	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
406	D. Van Der Heijde, M. Dougados, R. Landewe, J. Sieper, W. P. Maksymowych, M. Rudwaleit, F. Van Den Bosch, J. Braun, P. J. Mease, O. Davies,et al.. Certolizumab pegol for the treatment of axial spondyloarthritis: 4-year outcomes from the rapid-axSpA trial. Annals of the rheumatic diseases. 2016. 75:803-	Database searches	No comparators of interest	5th update (April 2019)
407	D. Van Der Heijde, W. P. Maksymowych, J. Sieper, R. Lambert, M. A. Brown, S. S. Rathmann, J. K. Anderson, A. L. Pangan. Relationship between MRI and clinical remission in patients with non-radiographic axial spondyloarthritis after two years of adalimumab therapy. Arthritis and rheumatism. 2013. 65:S768-	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
408	G. L. Goll, N. Bolstad, I. Iria, R. A. Klaasen, K. K. Jorgensen, I. C. Olsen, A. Valido, M. J. Saavedra, J. E. Fonseca, K. Lundin,et al.. The fine specificity of anti-drug antibody responses to originator and biosimilar infliximab: analyses across five diseases from the 52-week randomized nor-switch study. Annals of the rheumatic diseases. 2018. 77:852-853	Database searches	Not adult patients with active axSpA or any of its subpopulations	5th update (April 2019)
409	H. Marzo-Ortega, C. W. Legerton, J. Sieper, A. Kivitz, R. Blanco, M. Cohen, J. Zuazo, A. Readie, B. Porter, H. Richards. Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis: 2-year results from a phase 3 trial with subcutaneous loading and maintenance dosing (MEASURE 2). Annals of the rheumatic diseases. 2016. 75:812-813	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)

410	H. Marzo-Ortega, J. Sieper, A. J. Kivitz, R. Blanco, M. Cohen, E. M. Delicha, S. Rohrer, H. Richards. Secukinumab 150 mg provides sustained improvements in the signs and symptoms of active ankylosing spondylitis with consistent safety profile and high retention rate: 4-year results from a phase III trial. Arthritis and Rheumatology. 2018. 70:2846-2847	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
411	H. Marzo-Ortega, J. Sieper, A. Kivitz, R. Blanco, M. Cohen, E. M. Delicha, S. Rohrer, H. Richards. Secukinumab 150 mg provides sustained improvements in the signs and symptoms of active ankylosing spondylitis with high retention Rate: 4-year results from the phase iii trial, measure 2. Annals of the Rheumatic Diseases. 2018. 77:1005	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
412	H. Marzo-Ortega, T. K. Kvien, A. A. Deodhar, L. Gossec, P. G. Conaghan, V. Strand, M. Østergaard, N. Williams, B. Porter, K. Gandi, S. Jugl. Secukinumab provides sustained reduction in fatigue in patients with ankylosing spondylitis through three years: Long-term results of two randomised double-blind placebo-controlled phase III studies. Rheumatology (United Kingdom). 2018. 57:iii112-iii113	Database searches	No outcomes of interest	5th update (April 2019)
413	H. Tahir, H. Marzo-Ortega, C. W. Legerton, J. Sieper, A. Kivitz, R. Blanco, M. Cohen, E. M. Delicha, S. Rohrer, H. B. Richards. Secukinumab 150mg provides sustained improvements in the signs and symptoms of active ankylosing spondylitis with high retention rate: Three-year results from phase 3 trial, measure 2. Rheumatology (United Kingdom). 2018. 57:iii109-iii110	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
414	H. Tahir, W. Maksymowych, E. Choy, Y. Yazici, J. Walsh, H. Thom, C. Kalyvas, T. Fox, K. Gandi, S. Jugl. Comparative effectiveness of secukinumab and golimumab in ankylosing spondylitis assessed by matching-adjusted indirect comparison using pivotal phase III clinical trial data. Rheumatology (united kingdom). 2018. 57:iii110-iii111	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)
415	H. X. Zong, S. Q. Xu, H. Tong, X. R. Wang, M. J. Pan, Y. Z. Teng. Effect of Anti-tumor necrosis factor alpha treatment on radiographic progression in patient with ankylosing spondylitis: A Systematic Review and Meta-Analysis. Mod Rheumatol. 2018. #volume#:1-19	Database searches	Not RCT	5th update (April 2019)
416	J. Braun, X. Baraliakos, A. Deodhar, D. Baeten, J. Sieper, P. Emery, Z. Talloczy, R. Martin, H. B. Richards. Effect of secukinumab, an interleukin-17a inhibitor, on spinal radiographic changes through 2 years in patients with active ankylosing spondylitis: results of the phase 3 study measure. Annals of the rheumatic diseases. 2016. 75:52-	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
417	J. Callhoff, J. Sieper, A. Weiss, A. Zink, J. Listing. Efficacy of TNFα blockers in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis. Annals of the rheumatic diseases. 2014. #volume#:#pages#	Database searches	SLR for bibliography check	5th update (April 2019)
418	J. Chen, C. Liu, J. Lin. Methotrexate for ankylosing spondylitis. Cochrane database of systematic reviews (online). 2006. #volume#:CD004524	Database searches	SLR for bibliography check	5th update (April 2019)
419	J. Chen, C. Liu. Sulfasalazine for ankylosing spondylitis. Cochrane database of systematic reviews (online). 2005. #volume#:CD004800	Database searches	SLR for bibliography check	5th update (April 2019)
420	J. Gratacos, C. Pontes, X. Juanola, J. Sanz, F. Torres, C. Avendano, A. Vallano, G. Calvo, E. de Miguel, R. Sanmarti. Non-inferiority of dose reduction versus standard dosing of TNF-inhibitors in axial spondyloarthritis. Arthritis Res Ther. 2019. 21:11	Database searches	PK/PD studies; dose-finding studies with no placebo- or active-controlled arm	5th update (April 2019)
421	J. Sieper, D. L. Baeten, F. Van Den Bosch, S. S. Rathmann, J. K. Anderson, A. L. Pangan. Sustained clinical remission in patients with non-radiographic axial spondyloarthritis after two years of adalimumab treatment. Arthritis and rheumatism. 2013. 65:S653-S654	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
422	J. Sieper, D. Poddubnyy, A. L. Pangan, S. S. Rathmann, J. K. Anderson. Smoking was not associated with response to adalimumab therapy in patients with non-radiographic axial spondyloarthritis. Arthritis and rheumatism. 2013. 65:S1042-S1043	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
423	J. Wei, D. Baeten, J. Sieper, A. Deodhar, B. Porter, R. Martin, H. Richards. Secukinumab improves signs and symptoms of active ankylosing spondylitis in Asian patients: pooled results from two phase 3 trials. International journal of rheumatic diseases. 2015. 18:25	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)

424	K. Betts, J. Griffith, M. Mittal, K. Hennessey, A. Joshi, A. Ganguli. Indirect treatment comparison of adalimumab, etanercept, certolizumab, golimumab, and infliximab for the treatment of ankylosing spondylitis. Journal of Managed Care and Specialty Pharmacy. 2015. 21:S69	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)
425	K. Gooch, R. Wong. Comparison of 3 comorbidity measures affecting physical function and quality of life for patients with ankylosing spondylitis. Value in health. 2009. 12:A64-	Database searches	No comparators of interest	5th update (April 2019)
426	L. Q. Hou, G. X. Jiang, Y. F. Chen, X. M. Yang, L. Meng, M. Xue, X. G. Liu, X. C. Chen, X. Li. The Comparative Safety of TNF Inhibitors in Ankylosing Spondylitis—a Meta-Analysis Update of 14 Randomized Controlled Trials. Clinical Reviews in Allergy and Immunology. 2018. 54:234-243	Database searches	SLR for bibliography check	5th update (April 2019)
427	M. A. Abad, A. M. Ortiz, E. Loza, J. A. Martinez Lopez, M. P. Rosario, L. Carmona. Can we discontinue anti-TNF therapy in patients with Ankylosing spondylitis and remission? A systematic literature review. Arthritis and rheumatism. 2010. 62:516-	Database searches	SLR for bibliography check	5th update (April 2019)
428	M. Fan, J. Liu, B. Zhao, M. Zhao, X. Wu, J. Gu. Indirect comparison of TNF inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis: meta-analysis of randomized, double-blind, placebo-controlled trials. Annals of the rheumatic diseases. 2016. 75:1131-	Database searches	SLR for bibliography check	5th update (April 2019)
429	N. Kwantra, M. Magrey, P. J. Mease, J. Sieper, R. B. M. Landewé, X. Wang, A. Lertratanakul, J. K. Anderson, N. Mostafa. Adalimumab serum concentration fails to predict achievement of sustained remission or absence of flare for patients with non-radiographic axial spondyloarthritis. Arthritis and Rheumatology. 2018. 70:2868-2869	Database searches	No outcomes of interest	5th update (April 2019)
430	N. V. Kwatra, M. Magrey, P. J. Mease, J. Sieper, R. Landewe, X. Wang, A. Lertratanakul, J. K. Anderson, N. M. Mostafa. Adalimumab serum concentration fails to predict achievement of sustained remission or absence of flare for patients with nonradiographic axial spondyloarthritis in the ability-3 study. Annals of the Rheumatic Diseases. 2018. 77:63	Database searches	No outcomes of interest	5th update (April 2019)
431	P. Emery, D. Baeten, A. Deodhar, A. Wei, P. Geusens, Z. Talloczy, Y. Gong, B. Porter. Secukinumab improves physical function and quality of life in patients with active ankylosing spondylitis: 2-year data from measure 1, a phase 3 randomised trial. Annals of the rheumatic diseases. 2016. 75:818-	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
432	R. Landewe, T. Nurminen, O. Davies, M. Turina, D. Baeten. A single determination of C-reactive protein does not suffice to declare a patient with a diagnosis of axial SPA "CRP-negative". Annals of the rheumatic diseases. 2016. 75:325-	Database searches	No outcomes of interest	5th update (April 2019)
433	S. Bonovas, S. Minozzi, T. Lytras, M. González-Lorenzo, V. Pecoraro, S. Colombo, I. Polloni, L. Moja, M. Cinquini, V. Marino, D. Goletti, A. Matucci, G. Tocci, G. M. Milano, R. Scarpa, F. Cantini. Risk of malignancies using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: A systematic review and meta-analysis. Expert Opinion on Drug Safety. 2016. 15:35-54	Database searches	SLR for bibliography check	5th update (April 2019)
434	S. Juhl Pedersen, I. J. Sørensen, A. G. Loft, J. Hindrup, G. Kollerup, G. Thamsborg, K. Asmussen, O. Hendricks, J. Nørregaard, M. Østergaard. The performance of 12 flare definitions including the assessment of spondyloarthritis international society (ASAS)-endorsed definition of clinically important worsening in ASDAS in patients with axial spondyloarthritis treated with adalimumab for 5 years. Annals of the Rheumatic Diseases. 2018. 77:647-648	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
435	S. Krabbe, I. Eshed, I. J. Sorensen, B. Jensen, J. M. Moller, L. Balding, O. R. Madsen, S. J. Pedersen, M. Ostergaard. Whole-body magnetic resonance imaging inflammation in peripheral joints and entheses in axial spondyloarthritis: Distribution and changes during adalimumab treatment. J Rheumatol. 2019. #volume#:#pages#	Database searches	Not RCT	5th update (April 2019)
436	S. Krabbe, M. Ostergaard, I. J. Sorensen, B. Jensen, O. R. Madsen, G. P. Eng, K. H. Asmussen, J. Moller, L. Balding, S. J. Pedersen. Efficacy and safety of adalimumab in patients with axial spondyloarthritis-an investigator-initiated randomized placebo-controlled trial. Annals of the rheumatic diseases. 2016. 75:1131-1132	Database searches	Duration less than 12 weeks	5th update (April 2019)

437	S. Minozzi, S. Bonovas, T. Lytras, V. Pecoraro, M. González-Lorenzo, A. J. Bastiampillai, E. M. Gabrielli, A. C. Lonati, L. Moja, M. Cinquini, V. Marino, A. Matucci, G. M. Milano, G. Tocci, R. Scarpa, D. Goletti, F. Cantini. Risk of infections using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: A systematic review and meta-analysis. Expert Opinion on Drug Safety. 2016. 15:11-34	Database searches	SLR for bibliography check	5th update (April 2019)
438	S. R. Manica, J. L. Silva, A. R. Machado, C. Coelho, J. Duarte, E. Vieira-Sousa, J. T. Costa, F. Pimentel-Santos. The effect of biologic disease-modifying antirheumatic drugs in patient reported outcomes in axial spondyloarthritis; A systematic literature review and a call for action. Arthritis and Rheumatology. 2018. 70:2904-2906	Database searches	SLR for bibliography check	5th update (April 2019)
439	S. Rodrigues-Manica, J. Leite Silva, A. R. Machado, C. Coelho, J. Duarte, E. Vieira-Sousa, J. Tavares-Costa, F. M. Pimentel-Santos. The effect of biologic disease-modifying antirheumatic drugs patient reported outcomes in patients with axial spondyloarthritis a systematic literature review and a call for action. Annals of the Rheumatic Diseases. 2018. 77:1550-1551	Database searches	SLR for bibliography check	5th update (April 2019)
440	S. Wang, Q. He, Z. Shuai. Risk of serious infections in biological treatment of patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis. Clinical Rheumatology. 2018. 37:439-450	Database searches	SLR for bibliography check	5th update (April 2019)
441	T. K. Kvien, P. G. Conaghan, A. Deodhar, L. Gossec, M. Ostergaard, J. Canete, K. Gandhi, H. Richards, N. Williams, S. Jugl. Reduction in fatigue in patients with active ankylosing spondylitis: results of two phase 3 studies of secukinumab. Annals of the rheumatic diseases. 2016. 75:823-	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)
442	U. Kiltz, D. Van Der Heijde, A. Boonen, L. S. Gensler, T. Hunter, F. Zhao, H. Carlier, J. Braun. Ixekizumab significantly improves self-reported overall functioning and health in patients with active as/radiographic axial spa naive to biologic dmard therapy: 16-week results of a phase 3 randomized, active and placebo-controlled trial. Arthritis and Rheumatology. 2018. 70:2076-2078	Database searches	No outcomes of interest	5th update (April 2019)
443	U. Kiltz, D. Van Der Heijde, A. Boonen, L. S. Gensler, T. Hunter, Y. Dong, K. Wyrwich, H. Carlier, J. Braun. Psychometric properties of the assessment of spa international society health index in patients with active as/radiographic Axial Spa in a phase 3 clinical study. Arthritis and Rheumatology. 2018. 70:1768-1770	Database searches	No outcomes of interest	5th update (April 2019)
444	V. Rios Rodriguez, J. Sieper, K. G. Hermann, H. Haibel, C. Althoff, B. Buss, O. Behmer, D. Poddubnyy. Long-term anti-tnf treatment is associated with reduction of progression of radiographic changes in the sacroiliac joints in patients with non-radiographic axial SpA: six-year results of the esther trial. Annals of the rheumatic diseases. 2016. 75:823-824	Database searches	No comparators of interest	5th update (April 2019)
445	W. P. Maksymowych, S. Wichuk, M. Dougados, H. Jones, A. Szumski, L. Marshall, J. F. Bukowski, R. G. Lambert. Modification of structural lesions on magnetic resonance imaging by etanercept: a 12-week randomized placebo-controlled trial. Annals of the rheumatic diseases. 2016. 75:804-805	Database searches	No outcomes of interest	5th update (April 2019)
446	X. Chen, T. Zhang, W. Wang, J. Xue. Analysis of relapse rates and risk factors of tapering or stopping pharmacologic therapies in axial spondyloarthritis patients with sustained remission. Clin Rheumatol. 2018. 37:1625-1632	Database searches	No comparators of interest	5th update (April 2019)
447	Y. Xia, Y. Liang, S. Guo, J. G. Yu, M. S. Tang, P. H. Xu, F. D. Qin, G. P. Wang. Association between cytokine gene polymorphisms and ankylosing spondylitis susceptibility: A systematic review and meta-analysis. Postgraduate Medical Journal. 2018. 94:508-516	Database searches	Not RCT	5th update (April 2019)
448	Carron, P,Varkas, G,Cypers, H,Praet, L,Elewaut, D,Bosch, F. High drug-free remission in early peripheral spondyloarthritis after induction therapy with golimumab. Annals of the rheumatic diseases. Conference: annual european congress of rheumatology, EULAR 2017. Spain. 2017. 76:62	Database searches	Not adult patients with active axSpA or any of its subpopulations	5th update (April 2019)
449	Emery, P,Halliday, A,Jugl, S,Mokashi, S,Porter, B,Martin, R,Sherif, B,Williams, N,Marzo-Ortega, H. Long-term efficacy of secukinumab conditional on response status at week 12: analysis in tumour necrosis factor a inhibitor-naive and tumour necrosis factor a inhibitor inadequate responder patients with active ankylosing spondylitis. Rheumatology (united kingdom). Conference: rheumatology 2017. United kingdom. 2017. 56:ii91	Database searches	Duplicate	5th update (April 2019)

450	Goll, Gl,Olsen, Ic,Bolstad, N,Jorgensen, Kk,Lorentzen, M,Mork, C,Jahnsen, J,Haavardsholm, Ea,Kvien, Tk. Disease worsening and safety in patients switching from originator infliximab to biosimilar infliximab (CT-P13) in the randomized nor-switch-study: explorative analysis in spa patients. Annals of the rheumatic diseases. Conference: annual european congress of rheumatology, EULAR 2017. Spain. 2017. 76:338-339	Database searches	Not adult patients with active axSpA or any of its subpopulations	5th update (April 2019)
451	Marzo-Ortega, H,Sieper, J,Kivitz, A,Blanco, R,Cohen, M. Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis: 2-year results from a phase 3 trial with subcutaneous loading and maintenance dosing (Measure 2). Rheumatology (united kingdom). Conference: rheumatology 2017. United kingdom. 2017. 56:ii94	Database searches	Open-label extensions of RCT (where randomisation was broken)	5th update (April 2019)
452	Pavelka, K,Kivitz, A,Dokoupilova, E,Blanco, R,Maradiaga, M,Tahir, H,Pricop, L,Andersson, M,Readie, A,Porter, B. Efficacy, safety, and tolerability of secukinumab in patients with active ankylosing spondylitis: a randomized, double-blind phase 3 study, MEASURE 3. Arthritis research & therapy. 2017. 19:#pages#	Database searches	Duplicate	5th update (April 2019)
453	Sieper, J,Deodhar, A,Marzo-Ortega, H,Aelion, Ja,Blanco, R,Jui-Cheng, T,Andersson, M,Porter, B,Richards, Hb. Secukinumab efficacy in anti-TNF-naive and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 Study. Annals of the rheumatic diseases. 2017. 76:571-592	Database searches	Duplicate	5th update (April 2019)
454	Sieper, J,Deodhar, A,Marzo-Ortega, H,Aelion, Ja,Blanco, R,Jui-Cheng, T,Andersson, M,Porter, B,Richards, Hb. Secukinumab efficacy in anti-TNF-naive and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 Study. Annals of the rheumatic diseases. 2017. 76:571-592	Database searches	Duplicate	5th update (April 2019)
455	Sieper, J.,Deodhar, A. A.,Hojnik, M.,Zhang, Y.,Dougados, M.. Impact of time since diagnosis, age, and number of prior non-steroidal anti-inflammatory drugs on response to adalimumab (humira) in patients with ankylosing spondylitis. Arthritis and Rheumatology. 2016. 68:979-980	Database searches	Pooled analysis, meta-analyses	5th update (April 2019)
456	Baraliakos, X, Kruse, et al. Long-term certolizumab pegol treatment of axial spondyloarthritis is associated with rapid and sustained reduction of active inflammation and minimal structural changes in the spine: 4-year MRI results from RAPIDaxSpA. Annals of the rheumatic diseases. 2019;78876-877	Database searches	No outcomes of interest	6th update (October 2020)
457	Behrens, F, Sewerin, et al. Achilles tendon enthesitis and disease burden in psoriatic arthritis and axial spondyloarthritis: Baseline results from a randomized controlled trial. Arthritis and Rheumatology. 2019;71 (Supplement 10)4432-4434	Database searches	No outcomes of interest	6th update (October 2020)
458	Cecena, MM, Kivitz, et al. Sustained improvements in signs and symptoms of active ankylosing spondylitis and reassuring safety with secukinumab 300 mg: 3-year results froma phase3study. Journal of Clinical Rheumatology. 2019;25 (3 Supplement)S4-S5	Database searches	Open-label extensions of RCT (where randomisation was broken)	6th update (October 2020)
459	Deodhar, A, Mease, et al. Ixekizumab improves fatigue, pain, and sleep up to 52 weeks in patients with radiographic axial spondyloarthritis. Arthritis and Rheumatology. 2019;71 (Supplement 10)2667-2671	Database searches	Open-label extensions of RCT (where randomisation was broken)	6th update (October 2020)
460	Dougados, M, Sieper, et al. Ixekizumab: 52-week efficacy and safety in radiographic axial spondyloarthritis patients with prior inadequate response/intolerance to Tumor Necrosis Factor Inhibitors. Arthritis and Rheumatology. 2019;71 (Supplement 10)2647-2648	Database searches	Open-label extensions of RCT (where randomisation was broken)	6th update (October 2020)
461	Kiltz, U, Van Der Heijde, et al. Ixekizumab improves self-reported overall functioning and health as measured by the assessment of spondyloarthritis international Society Health Index in Patients with Active Radiographic Axial Spondyloarthritis: 52-Week Results of Two Phase 3 Randomized Trials. Arthritis and Rheumatology. 2019;71 (Supplement 10)2748-2749	Database searches	No outcomes of interest	6th update (October 2020)
462	Krabbe, S, Eshed, et al. Whole-body magnetic resonance imaging inflammation in peripheral joints and entheses in axial spondyloarthritis: Distribution and changes during adalimumab treatment. Journal of Rheumatology. 2020;4750-58	Database searches	Duration less than 12 weeks	6th update (October 2020)
463	Lopez-Medina, C, Ramiro, et al. Characteristics and burden of disease in patients with radiographic and non-radiographic axial Spondyloarthritis: a comparison by systematic literature review and meta-analysis. RMD Open. 2019;5e001108	Database searches	SLR for bibliography check	6th update (October 2020)

464	Luttringer, O, Fox, et al. Structural damage progression over 4 years of secukinumab treatment in ankylosing spondylitis: Post-hoc analysis of measure-1 trial using a longitudinal bayesian mixture model. Annals of the Rheumatic Diseases. 2019;78 (Supplement 2)1236	Database searches	Open-label extensions of RCT (where randomisation was broken)	6th update (October 2020)
465	Maksymowych, WP, Gallo, et al. Ixekizumab is effective in the treatment of radiographic axial spondyloarthritis regardless of the level of c-reactive protein or magnetic Resonance Imaging Scores. Arthritis and Rheumatology. 2019;71 (Supplement 10)2691-2693	Database searches	Pooled analysis, meta-analyses	6th update (October 2020)
466	Maksymowych, WP, Gallo, et al. Ixekizumab is effective in the treatment of radiographic axial spondyloarthritis regardless of the level of C-reactive protein or magnetic resonance imaging scores: 16-week data from COAST-V and COASTW. Annals of the rheumatic diseases. 2019;78884-885	Database searches	Pooled analysis, meta-analyses	6th update (October 2020)
467	Marcu, IR, Dop, et al. Non-Steroidal Anti-Inflammatory Drug Etoricoxib Facilitates the Application of Individualized Exercise Programs in Patients with Ankylosing Spondylitis. Medicina. 2020;56	Database searches	No biological DMARDs of interest	6th update (October 2020)
468	Marzo-Ortega, H, Mysler, et al. Long-term safety of ixekizumab in patients with radiographic axial spondyloarthritis/ankylosing spondylitis: An integrated analysis of coast-v and coast-w. Annals of the Rheumatic Diseases. 2019;78 (Supplement 2)885-886	Database searches	Pooled analysis, meta-analyses	6th update (October 2020)
469	Pavelka, K, Kivitz, et al. Secukinumab 150/300 mg Provides Sustained Improvements in the Signs and Symptoms of Active Ankylosing Spondylitis: 3-Year Results from the Phase 3 MEASURE 3 Study. ACR Open Rheumatology. 2020;2119-127	Database searches	Open-label extensions of RCT (where randomisation was broken)	6th update (October 2020)
470	Reveille, JD, Chakravarty, et al. Efficacyand safety of intravenous golimumab in ankylosing spondylitis patients with complete ankylosis: Results through week 52 of the go-alive study. Journal of Clinical Rheumatology. 2019;25 (3 Supplement)S64	Database searches	Fewer than 10 patients per treatment arm	6th update (October 2020)
471	Schwartzman, S, Deodhar, et al. Inflammatory bowel disease and anterior uveitis in patients treated with ixekizumab for radiographic axial spondyloarthritis: Results from Two Phase 3 Studies Through 52 Weeks. Arthritis and Rheumatology. 2019;71 (Supplement 10)2694-2695	Database searches	No outcomes of interest	6th update (October 2020)
472	Seven, S, Pedersen, et al. Peripheral Enthesitis Detected by Ultrasonography in Patients With Axial Spondyloarthritis-Anatomical Distribution, Morphology, and Response to Tumor Necrosis Factor-Inhibitor Therapy. Frontiers in Medicine. 2020;7 (no pagination)	Database searches	Duration less than 12 weeks	6th update (October 2020)
473	Webers, C, Stolwijk, et al. Infliximab treatment reduces depressive symptoms in patients with ankylosing spondylitis: An ancillary study to a randomized controlled trial (ASSERT). Arthritis Research and Therapy. 2020;22	Database searches	Fewer than 10 patients per treatment arm	6th update (October 2020)
474	Wei, CC, Gensler, et al. Primary 1-year data of ixekizumab in biologic disease-modifying anti-rheumatic drug-naive patients with radiographic axial Spondyloarthritis Including Data in Patients Rerandomized from Adalimumab to Ixekizumab. Arthritis and Rheumatology. 2019;71 (Supplement 10)2750-2752	Database searches	Open-label extensions of RCT (where randomisation was broken)	6th update (October 2020)
475	Ismail, M, Nader, et al. Exposure-response analyses for upadacitinib efficacy and safety in ankylosing spondylitis-analyses of the select-axis i study. Arthritis and Rheumatology. 2019;71 (Supplement 10)2625-2627	Database searches	No outcomes of interest	6th update (October 2020)

Table 95 Publications excluded at the full-text screening stage in the April 2022 clinical SLR update (n=271)

#	Authors	Title	Year	Reason for exclusion
1	Abidin A.Z.; Snoswell C.L.; Shafiee Hanjani L.; Callaghan G.; Edmonds M.	Infliximab switching from reference product to biosimilar: a review of evidence regarding the clinical efficacy, safety profile and immunogenicity	2021	Irrelevant study design
2	Amarnani R.; Soni A.	The efficacy of biologic treatment in improving fatigue in ankylosing spondylitis: A literature review and implications for clinical practice	2020	Irrelevant study design

3	Anonymous	Correction: Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase llb, randomised, double blind, placebo-controlled, dose-ranging study.	2020	Already captured by 2020 SLR update
4	Anonymous.	Erratum: Association of secukinumab treatment with tuberculosis reactivation in patients with psoriasis, psoriatic arthritis, or ankylosing spondylitis (JAMA Dermatol (2020) DOI: 10.1001/jamadermatol.2020.3257)	2021	Irrelevant study design
5	Aparicio M.; Guillen-Astete C.A.; Lopez-Medina C.; Sastre C.; Rodriguez Martinez F.J.	Evidence for the Use of Secukinumab in Patients with Radiographic and Non-radiographic Axial Spondyloarthritis in the Last 5 Years	2022	SLR/NMA to hand-search
6	Atul D.; Xenofon B.; Iain M.; De Vlam K.; Louis B.; Anna M.; Ralph L.; Christopher S.; Tianming G.; In-Ho S.; Andrew O.	Effect of upadacitinib on reducing pain in patients with active ankylosing spondylitis and inadequate response to nonsteroidal anti-inflammatory drug	2021	Duplicate
7	Azadeh H.; Alizadeh-Navaei R.; Rezaiemanesh A.; Rajabinejad M.	Immune-related adverse events (irAEs) in ankylosing spondylitis (AS) patients treated with interleukin (IL)-17 inhibitors: a systematic review and meta-analysis	2022	SLR/NMA to hand-search
8	Baraliakos X.; Bessette L.; Salvarani C.; Chen N.; Lippe R.; Patel J.; Song I.-H.; Zueger P.; Goupille P.	Association between clinically meaningful back pain improvement and patient-reported outcomes and disease activity in patients with ankylosing spondylitis: Results from a phase 2/3 trial	2021	No relevant novel outcomes
9	Baraliakos X.; Bolce R.; Calderon D.S.; Leage S.L.; Geneus V.; Adams D.; Deodhar A.; Walsh J.; Sieper J.	Clinical features of patients with activeankylosing spondylitis who did not respond toadalimumab but responded to ixekizumab: A posthoc analysis	2021	No relevant novel outcomes
10	Baraliakos X.; Bolce R.; Sandoval D.; Liu-Leage S.; Geneus V.; Adams D.; Deodhar A.; Walsh J.; Sieper J.	Clinical Features of Patients with Active Ankylosing Spondylitis Who Did Not Respond to Adalimumab but Responded to Ixekizumab: A Post-hoc Analysis	2020	Duplicate
11	Baraliakos X.; Deodhar A.; Dougados M.; Oortgiesen M.; De Peyrecave N.; Bauer M.; Vaux T.; Fleurinck C.; Van Der Heijde D.	Bimekizumab Long-Term Efficacy and Safety over 96 Weeks in Patients with Ankylosing Spondylitis: Interim Results from a Phase 2b Open-Label Extension Study	2020	No relevant novel outcomes
12	Baraliakos X.; Deodhar A.; Liu Leage S.; Schymura Y.; Bolce R.; Sandoval D.; Walsh J.A.; Sieper J.	Patients with radiographic axspa who progressed from asas20 at week 16 to asas40 at week 52: Results from coast-w	2021	No relevant novel outcomes
13	Baraliakos X.; Deodhar A.; Ranza R.; Rednic S.; Ciccia F.; Ganz F.; Gao T.; Lertratanakul A.; Song I.-H.; Ostor A.; Coates L.	Comparison of axial and peripheral manifestations in patients with psoriatic arthritis and ankylosing spondylitis in upadacitinib clinical trials	2021	Irrelevant study design
14	Baraliakos X.; Dougados M.; Gaffney K.; Sengupta R.; Magrey M.; De Peyrecave N.; Oortgiesen M.; Vaux T.; Fleurinck C.; Deodhar A.	Bimekizumab shows sustained longterm improvements in patient-reported outcomes and quality of life in ankylosing spondylitis: 3-year results from a phase 2b study	2021	No relevant novel outcomes
15	Baraliakos X.; Gensler L.S.; D'Angelo S.; Iannone F.; Favalli E.G.; de Peyrecave N.; Auteri S.E.; Caporali R.	Biologic therapy and spinal radiographic progression in patients with axial spondyloarthritis: A structured literature review	2020	Irrelevant study design
16	Baraliakos X.; Hermann K.G.A.; Xu S.; Hsia E.C.; Braun J.	Spinal mobility in the cervical and lumbar spine correlates with magnetic resonance imaging findings for inflammatory and structural changes in patients with active ankylosing spondylitis	2020	No relevant novel outcomes
17	Baraliakos X.; Kruse S.; Auteri S.; De Peyrecave N.; Nurminen T.; Kumke T.; Hoepken B.; Braun J.	The impact of persistent inflammatory changes on prevalence of fatty lesions in patients with axial spondyloarthritis treated with certolizumab Pegol: 4-year MRI results from rapid-AXSPA	2020	No relevant novel outcomes
18	Baraliakos X.; Kruse S.; Auteri S.E.; De Peyrecave N.; Nurminen T.; Kumke T.; Hoepken B.; Braun J.	The impact of persistent inflammatory changes on prevalence of fat lesions in patients with axial spondyloarthritis treated with certolizumab pegol: 4-Year MRI results from RAPID-axSpA	2020	No relevant novel outcomes

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19	Baraliakos X.; Kruse S.; Auteri S.E.; de Peyrecave N.; Nurminen T.; Kumke T.; Hoepken B.; Braun J.	Certolizumab Pegol Treatment in Axial Spondyloarthritis Mitigates Fat Lesion Development: 4-Year Post-Hoc MRI Results from a Phase 3 Study	2021	No relevant novel outcomes
20	Baraliakos X.; Kruse S.; Ivanova M.; Auteri S.E.; De Peyrecave N.; Nurminen T.; Kumke T.; Hoepken B.; Braun J.	The impact of persistent inflammatory changes on prevalence of fat lesions in patients with axial spondyloarthritis treated with certolizumab pegol: 4-year MRI results from RA PID-axSpA	2020	No relevant novel outcomes
21	Baraliakos X.; Ostergaard M.; Landewe R.B.M.; Barchuk W.; Liu K.; Tasset C.; Gilles L.; Hendrikx T.; Besuyen R.; Maksymowych W.P.	Effects of filgotinib on spinal lesions in ankylosing spondylitis: Magnetic resonance imaging data from the tortuga trial	2021	No relevant novel outcomes
22	Baraliakos X.; Sewerin P.; De Miguel E.; Pournara E.; Kleinmond C.; Shekhawat A.; Wiedon A.; Behrens F.	Imaging characteristics in patients with spondyloarthritis using a novel heel enthesitis magnetic resonance imaging scoring (hemris) system: Post-hoc analysis of a phase 3 secukinumab trial	2021	Irrelevant population
23	Baraliakos X.; Szumski A.; Kwok K.; Vlahos B.	Temporal Achievement of Clinical Response and Inactive Disease Status in Patients with Axial Spondyloarthritis Treated with Etanercept	2020	Irrelevant study design
24	Barkham N.; Schett G.; Baraliakos X.; Van Den Bosch F.; Deodhar A.; Gensler L.S.; Ostergaard M.; Agawane S.; Das Gupta A.; Mpofu S.; Fox T.; Winseck A.; Shete A.; Porter B.	Secukinumab provides sustained improvement of enthesitis in patients with ankylosing spondylitis: Pooled analysis of four pivotal phase 3 studies	2020	Duplicate
25	Beake J.	Long-term evaluation of secukinumab 150mg in ankylosing spondylitis: 5-year end-of-study efficacy and safety results from a phase 3 trial	2020	Retracted publication
26	Behrens F.; Sewerin P.; de Miguel E.; Patel Y.; Batalov A.; Dokoupilova E.; Kleinmond C.; Pournara E.; Shekhawat A.; Jentzsch C.; Wiedon A.; Baraliakos X.	Efficacy and safety of secukinumab in patients with spondyloarthritis and enthesitis at the Achilles tendon: Results from a Phase 3b trial	2021	No relevant novel outcomes
27	Behrens F.; Sewerin P.; De Miguel E.; Patel Y.; Batalov A.; Dokoupilova E.; Kleinmond C.; Pournara E.; Shekhawat A.; Jentzsch C.; Wiedon A.; Baraliakos X.	Efficacy and Safety of Secukinumab in Patients with Spondyloarthritis and Enthesitis at the Achilles Tendon: 52-weeks Results from a Randomized, Placebo-controlled Phase 3b Trial	2020	Superseded by later publication with identical data
28	Benucci M.; Damiani A.; Gobbi F.L.; Grossi V.; Infantino M.; Manfredi M.; Niccoli L.; Cantini F.	Therapeutic potential of ixekizumab in the treatment of ankylosing spondylitis: A review on the emerging clinical data	2020	Irrelevant study design
29	Braun J.; Blanco R.; Dokoupilova E.; Gensler L.S.; Kivitz A.; Hall S.; Kameda H.; Poddubnyy D.; Van De Sande M.; Van Der Heijde D.; Wiksten A.; Porter B.; Richards H.; Haemmerle S.; Deodhar A.	Secukinumab 150 mg significantly improved signs and symptoms of non-radiographic axial spondyloarthritis: 52-week results from the phase III prevent study	2020	Already captured by 2020 SLR update
30	Braun J.; Blanco R.; Marzo-Ortega H.; Gensler L.; Van Den Bosch F.; Hall S.; Kameda H.; Poddubnyy D.; Van De Sande M.; Van Der Heijde D.; Zhuang T.; Stefanska A.; Readie A.; Richards H.; Deodhar A.	Effect of secukinumab on radiographic progression and inflammation in sacroiliac joints and spine in patients with non-radiographic axial spondyloarthritis: 2-year imaging outcomes from a phase iii randomized trial	2021	No relevant novel outcomes
31	Braun J.; Blanco R.; Marzo-Ortega H.; Gensler L.; Van Den Bosch F.; Kameda H.; Poddubnyy D.; Van De Sande M.; Wiksten A.; Porter B.; Moreno S.; Shete A.; Richards H.; Haemmerle S.; Deodhar A.	Secukinumab Improved Signs and Symptoms in Patients with Non-radiographic Axial Spondyloarthritis: Results from a Randomized Controlled Phase III Study Stratified by Baseline Objective Signs of Inflammation	2020	Already captured by 2020 SLR update

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32	Braun J.; Kiltz U.; Deodhar A.; Tomita T.; Dougados M.; Bolce R.; Sandoval D.; Adams D.; Lin C.Y.; Walsh J.; Nortamo P.	Long-term treatment with ixekizumab in patients with axial spondyloarthritis: Two-year results from COAST-Y	2021	Superseded by later publication with identical data
33	Braun J.; Kiltz U.; Deodhar A.; Tomita T.; Dougados M.; Bolce R.; Sandoval D.; Adams D.; Lin C.Y.; Walsh J.A.	Long-term treatment with ixekizumab in patients with axial spondyloarthritis: Twoyear results from coast-y	2021	Superseded by later publication with identical data
34	Braun, Jurgen; Buehring, Bjoern; Baraliakos, Xenofon; Gensler, Lianne S; Porter, Brian; Quebe-Fehling, Erhard; Haemmerle, Sibylle	Effects of secukinumab on bone mineral density and bone turnover biomarkers in patients with ankylosing spondylitis: 2-year data from a phase 3 study, MEASURE 1.	2021	No relevant novel outcomes
35	Burisch J.; Eigner W.; Schreiber S.; Aletaha D.; Weninger W.; Trauner M.; Reinisch W.; Narula N.	Risk for development of inflammatory bowel disease under inhibition of interleukin 17: A systematic review and meta-analysis	2020	Irrelevant study design
36	Burmester G.; Cohen S.; Winthrop K.; Nash P.; Rubbert-Roth A.; Deodhar A.; Elkayam O.; Mysler E.; Tanaka Y.; Liu J.; Lacerda A.P.; Pierre-Louis B.; Shaw T.; Mease P.	Long-term safety profile of upadacitinib in patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis	2021	Irrelevant study design
37	Burmester G.R.; Gordon K.B.; Rosenbaum J.T.; Arikan D.; Lau W.L.; Li P.; Faccin F.; Panaccione R.	Long-Term Safety of Adalimumab in 29,967 Adult Patients From Global Clinical Trials Across Multiple Indications: An Updated Analysis	2020	Irrelevant study design
38	Bykerk V.P.; Blauvelt A.; Curtis J.R.; Gaujoux-Viala C.; Kvien T.K.; Winthrop K.; Tilt N.; Popova C.; Mariette X.; Haraoui B.	Associations Between Safety of Certolizumab Pegol, Disease Activity, and Patient Characteristics, Including Corticosteroid Use and Body Mass Index	2021	Irrelevant study design
39	Caron, Benedicte; Jouzeau, Jean-Yves; Miossec, Pierre; Petitpain, Nadine; Gillet, Pierre; Netter, Patrick; Peyrin-Biroulet, Laurent	Gastroenterological safety of IL-17 inhibitors: a systematic literature review.	2022	Irrelevant study design
40	Castro A.; Diaz J.; Quiceno G.; Cush J.	Comparative Efficacy of Janus Kinase Inhibitors and TNF Inhibitors in Ankylosing Spondylitis: A Network Meta-Analysis	2020	Irrelevant study design
41	Chaudhury K.; Rahman P.; Sandoval D.; Muram T.; Kronbergs A.; Bolce R.; Geneus V.; Hunter T.; Liu-Leage S.; Rudwaleit M.; Maldonado-Cocco J.; Van Den Bosch F.; Robinson P.	Response to ixekizumab by C-reactive protein level in patients with radiographic axial spondyloarthritis: Results from the COAST-V (biological-naive) and COAST-W (TNF-A inhibitor-experienced) trials at 52 weeks	2021	No relevant novel outcomes
42	Compan V.N.; Redlich K.; Bird P.; Bello N.; Nassab M.H.; Pum G.; Leage S.L.	Ixekizumab significantly improves signs, symptoms and spinal inflammation of active ankylosing spondylitis/radiographic axial spondyloarthritis: 16-week results of a phase 3 randomized, active and placebo-controlled trial	2020	No relevant novel outcomes
43	Cruz-Machado A.R.; Rodrigues-Manica S.; Silva J.L.; Alho I.; Coelho C.; Duarte J.; Florencio C.; Pimentel-Santos F.M.; Tavares-Costa J.; Vieira-Sousa E.	Systematic review and meta analysis Effect of biologic disease-modifying anti-rheumatic drugs targeting remission in axial spondyloarthritis: Systematic review and meta-analysis	2020	Irrelevant study design
44	Cruz-Machado, Ana Rita; Rodrigues-Manica, Santiago; Silva, Joana Leite; Alho, Irina; Coelho, Constanca; Duarte, Joana; Florencio, Claudia; Pimentel-Santos, Fernando M; Tavares-Costa, Jose; Vieira-Sousa, Elsa	Effect of biologic disease-modifying anti-rheumatic drugs targeting remission in axial spondyloarthritis: systematic review and meta-analysis.	2020	Irrelevant study design
45	De Vlam K.; Conaghan P.; Mease P.; Rahman P.; Krishnan V.; Bolce R.; Calderon D.S.; Park S.Y.; Gallo G.; Maksymowych W.	Ixekizumab shows a distinct pattern of pain improvement beyond measurable inflammation as assessed by MRI or CRP or basdai questions 5 & 6 in patients with ankylosing spondylitis	2021	No relevant novel outcomes

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46	De Vlam K.; Gallo G.; Mease P.J.; Rahman P.; Krishnan V.; Sandoval D.; Lin C.Y.; Bolce R.; Conaghan P.G.	Ixekizumab shows a distinct pattern of pain improvement beyond inflammation in radiographic axial spondyloarthritis	2021	No relevant novel outcomes
47	Deodhar A.; Baraliakos X.; McInnes I.; De Vlam K.; Bessette L.; Maniccia A.; Lippe R.; Saffore C.; Gao T.; Song I.H.; Ostor A.	Effect of upadacitinib on reducing pain in patients with active ankylosing spondylitis and inadequate response to nonsteroidal anti-inflammatory drugs	2021	Superseded by later publication with identical data
48	Deodhar A.; Blanco R.; Dokoupilova E.; Van De Sande M.; Hall S.; Wiksten A.; Porter B.O.; Richards H.B.; Haemmerle S.; Braun J.	Secukinumab significantly improved signs and symptoms of non-radiographic axial spondyloarthritis: 16-week results from the phase-iii prevent study	2020	No relevant novel outcomes
49	Deodhar A.; Chakravarty S.D.; Cameron C.; Peterson S.; Hensman R.; Fogarty S.; Spin P.; Kafka S.; Nair S.; Gensler L.S.	A systematic review and network meta-analysis of current and investigational treatments for active ankylosing spondylitis	2020	Irrelevant study design
50	Deodhar A.; Gensler L.; Hall S.; Robinson P.; Hoepken B.; Bauer L.; Kumke T.; Maksymowych W.	Certolizumab Pegol Efficacy in Patients with Non-Radiographic Axial Spondyloarthritis Stratified by Baseline MRI and C-Reactive Protein Status	2020	No relevant novel outcomes
51	Deodhar A.; Gladman D.D.; McInnes I.B.; Spindeldreher S.; Martin R.; Pricop L.; Porter B.; Jorge S.; Shete A.; Bruin G.	Secukinumab Immunogenicity over 52 Weeks in Patients with Psoriatic Arthritis and Ankylosing Spondylitis	2020	Irrelevant study design
52	Deodhar A.; Kafka S.; Hsia E.; Lo K.H.; Lilianne K.; Xu S.; Reveille J.	Efficacy and safety of intravenous golimumab in ankylosing spondylitis patients with early versus late disease through week 52 of go-alive study	2021	Duplicate
53	Deodhar A.; Kafka S.; Hsia E.C.; Hung Lo K.; Kim L.; Xu S.; Reveille J.D.	Efficacy and safety of intravenous golimumab in ankylosing spondylitis patients with early vs late disease through week 52 of go-alive study	2021	Duplicate
54	Deodhar A.; Kafka S.; Hsia E.C.; Lo K.H.; Kim L.; Xu S.; Reveille J.D.	Efficacy and safety of intravenous golimumab in ankylosing spondylitis patients with early vs late disease through week 52 of go-alive study	2021	No relevant novel outcomes
55	Deodhar A.; Mcinnes I.; Baraliakos X.; Reich K.; Gottlieb A.B.; Lebwohl M.; Schreiber S.; Bao W.; Marfo K.; Richards H.; Pricop L.; Shete A.; Safi J.; Mease P.J.	Secukinumab demonstrates a consistent safety profile in patients with psoriasis, psoriatic arthritis and ankylosing spondylitis over long term: updated pooled safety analyses	2020	Irrelevant study design
56	Deodhar A.; Mease P.; Gensler L.; Rahman P.; Navarro-Compan V.; Marzo-Ortega H.; Hunter T.; Sandoval D.; Kronbergs A.; Zhu B.; Leung A.; Strand V.	Impact of Ixekizumab on Work Productivity in Non-Radiographic Axial Spondyloarthritis Patients: Results from the COAST-X Trial at 52 Weeks	2020	Already captured by 2020 SLR update
57	Deodhar A.; Mease P.; Marzo-Ortega H.; Hunter T.; Sandoval D.; Kronbergs A.; Lauzon S.; Leung A.; Navarro-Compan V.	Ixekizumab improves sleep and work productivity in patients with non-radiographic axial spondyloarthritis: results from the COAST-X trial at 52 weeks	2021	No relevant novel outcomes
58	Deodhar A.; Mease P.J.; Gensler L.S.; Rahman P.; Navarro-Compan V.; Marzo-Ortega H.; Hunter T.; Sandoval D.; Kronbergs A.; Zhu B.; Leung A.; Strand V.	Impact of ixekizumab on work productivity in non-radiographic axial spondyloarthritis patients: results from the coast-x trial at 52 weeks	2020	Already captured by 2020 SLR update
59	Deodhar A.; Ostor A.; Maniccia A.; Ganz F.; Gao T.; Chu A.; Poddubnyy D.	Achievement of partial remission and inactive disease in upadacitinib-treated patients with ankylosing spondylitis	2021	Duplicate
60	Deodhar A.; Ostor A.; Maniccia A.; Ganz F.; Gao T.; Chu A.D.; Poddubnyy D.	Achievement of Partial Remission and Inactive Disease in Upadacitinib-Treated Patients with Ankylosing Spondylitis	2020	Already captured by 2020 SLR update

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61	Deodhar A.; Schett G.; Baraliakos X.; Van Den Bosch F.; Gensler L.; Ostergaard M.; Agawane S.; Gupta A.; Mpofu S.; Fox T.; Winseck A.; Porter B.; Shete A.	Secukinumab provides sustained improvement of enthesitis in ankylosing spondylitis patients: A pooled analysis of four pivotal phase 3 trials	2020	Superseded by later publication with identical data
62	Deodhar A.; van der Heijde D.; Gensler L.S.; Kim T.-H.; Maksymowych W.P.; Ostergaard M.; Poddubnyy D.; Marzo-Ortega H.; Bessette L.; Tomita T.; Leung A.; Hojnik M.; Gallo G.; Li X.; Adams D.; Carlier H.; Sieper J.; Morin F.; Rahman P.; Ariel F.; Berman A.; Carrio J.; Lucero E.; Cocco J.M.; Hidalgo R.P.; Velasco J.; Viola D.O.; Grisar J.; Resch H.; Scheinecker C.; Melazzi A.C.; Roimicher L.; Scotton A.S.; Rodriguez A.A.B.; Molina F.F.C.; Barragan S.D.; Skinner C.M.; Tena C.F.P.; Remus C.R.R.; Rodriguez J.C.R.; Hong S.-J.; Kang S.W.; Lee C.K.; Lee E.B.; Lee S.H.; Park M.-C.; Lee S.-H.; Dokoupilova E.; Dvorak Z.; Malcova M.; Pvelka K.; Eklund K.K.; Jarvinen P.; Karjalainen A.; Paimela L.; Taniguchi Y.; Tsuda T.; Tada K.; Dobashi H.; Inui K.; Ueki Y.; Matsumoto Y.; Hatta K.; Atsumi T.; Goto H.; Honjo S.; Matsui K.; Takakubo Y.; Neeck G.; Wagner S.; Braun J.; Blicharshi T.; Dudek A.; Hrycai P.; Plebanski R.; Drabiszcak-Piatkowska J.; Brzezicki J.; Krogulec M.; Opris-Belinski D.; Ramazan A.M.; Tronaru L.; van de Sande M.G.; Matsievskaya G.; Schmidt E.; Stanislav M.; Yakushin S.; Ershova O.; Rebroy A.; Churchill M.A.; Flint K.P.; Greenwald M.; Howell M.P.; Kaine J.L.; Kivitz A.; Klein S.J.; Mueller E.C.; Peters E.A.; Querubin R.; Sayers M.E.; Scoville C.D.; Shanahan J.C.; Roseff R.; Hull J.E.; Mallepalli J.R.; Sebai M.B.; Kimmel S.C.; Goddard D.H.; Mease P.J.; Harris M.D.; Mabaquiao A.R.; Diegel R.J.; Thai C.; Rivera T.L.; Perez-De Jesus A.; Soto-Raices O.; Toro-Torres R.; Pantojas C.	Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial	2020	Already captured by 2020 SLR update
63	Deodhar A.; Van Der Heijde D.; Sieper J.; Van Den Bosch F.; Maksymowych W.; Kim T.-H.; Kishimoto M.; Ostor A.; Combe B.; Sui Y.; Wang X.; Chu A.D.; Song I.-H.	Efficacy and Safety of Upadacitinib in Patients with Active Ankylosing Spondylitis: 1-Year Results from a Randomized, Double-Blind, Placebo-Controlled Study with Open-Label Extension	2020	Already captured by 2020 SLR update
64	Deodhar A.; Van Der Heijde D.; Sieper J.; Van Den Bosch F.; Maksymowych W.P.; Kim T.H.; Kishimoto M.; Ostor A.; Combe B.; Sui Y.; Wang X.; Chu A.; Song I.H.	Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis: 1-year results from a randomized, doubleblind, placebo-controlled study with openlabel extension	2021	Duplicate
65	Deodhar A.A.; Mease P.J.; Rahman P.; Navarro-Compan V.; Strand V.;	Ixekizumab improves spinal pain, function, fatigue, stiffness, and sleep in radiographic axial Spondyloarthritis: COAST-V/W 52-week results	2021	No relevant novel outcomes

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	Hunter T.; Bolce R.; Leon L.; Lauzon S.; Marzo-Ortega H.			
66	Deodhar A.A.; Miceli-Richard C.; Baraliakos X.; Marzo-Ortega H.; Gladman D.D.; Blanco R.; Das Gupta A.; Martin R.; Safi J.; Porter B.; Shete A.; Rosenbaum J.T.	Incidence of Uveitis in Secukinumab-treated Patients With Ankylosing Spondylitis: Pooled Data Analysis From Three Phase 3 Studies	2020	No relevant novel outcomes
67	Diel R.; Schaberg T.; Nienhaus A.; Otto-Knapp R.; Kneitz C.; Krause A.; Fabri M.; Mrowietz U.; Bauer T.; Hacker B.	Joint Statement (DZK, DGRh, DDG) on the Tuberculosis Risk with Treatment Using Novel Non-TNF-Alpha Biologicals	2021	Irrelevant study design
68	Dougados M.; Kiltz U.; Kivitz A.; Pavelka K.; Rohrer S.; McCreddin S.; Quebe-Fehling E.; Porter B.; Talloczy Z.	Nonsteroidal anti-inflammatory drug-sparing effect of secukinumab in patients with radiographic axial spondyloarthritis: 4-year results from the MEASURE 2, 3 and 4 phase III trials	2022	No relevant novel outcomes
69	Dougados, Maxime; van der Heijde, Desiree; Tsai, Wen-Chan; Saaibi, Diego; Marshall, Lisa; Jones, Heather; Pedersen, Ron; Vlahos, Bonnie; Tarallo, Miriam	Relationship between disease activity status or clinical response and patient-reported outcomes in patients with non-radiographic axial spondyloarthritis: 104-week results from the randomized controlled EMBARK study.	2020	Irrelevant study design
70	Dougados, Maxime; Wei, James Cheng-Chung; Landewe, Robert; Sieper, Joachim; Baraliakos, Xenofon; Van den Bosch, Filip; Maksymowych, Walter P; Ermann, Joerg; Walsh, Jessica A; Tomita, Tetsuya; Deodhar, Atul; van der Heijde, Desiree; Li, Xiaoqi; Zhao, Fangyi; Bertram, Clinton C; Gallo, Gaia; Carlier, Hilde; Gensler, Lianne S; COAST-V and COAST-W Study Groups	Efficacy and safety of ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial spondyloarthritis (COAST-V and COAST-W).	2020	Already captured by 2020 SLR update
71	Ducourau E.; Rispens T.; Samain M.; Dernis E.; Le Guilchard F.; Andras L.; Perdriger A.; Lespessailles E.; Martin A.; Cormier G.; Armingeat T.; Devauchelle-Pensec V.; Gervais E.; Le Goff B.; De Vries A.; Piver E.; Paintaud G.; Desvignes C.; Ternant D.; Watier H.; Goupille P.; Mulleman D.	Methotrexate effect on immunogenicity and long-term maintenance of adalimumab in axial spondyloarthritis: a multicentric randomised trial	2020	Irrelevant intervention/comparators
72	Elewaut D.; Braun J.; Anderson J.K.; Arikan D.; Chen S.; Hojnik M.; De Craemer A.-S.; Curtis J.R.	Low Incidence of Inflammatory Bowel Disease Adverse Events in Adalimumab Clinical Trials Across Nine Different Diseases	2021	Irrelevant study design
73	Elewski B.; Baddley J.W.; Deodhar A.; Magrey M.; Rich P.; Soriano E.; Soung J.; Bao W.; Patekar M.; Lebwohl M.; Sharma A.	15261 Lack of tuberculosis reactivation in 12,319 patients with psoriasis, psoriatic arthritis, or ankylosing spondylitis treated with secukinumab: An ad hoc analysis of pooled safety data from 28 clinical trials	2020	Irrelevant study design
74	Elewski B.E.; Baddley J.W.; Deodhar A.A.; Magrey M.; Rich P.A.; Soriano E.R.; Soung J.; Bao W.; Keininger D.; Marfo K.; Patekar M.; Sharma A.; Shete A.; Lebwohl M.G.	Association of Secukinumab Treatment with Tuberculosis Reactivation in Patients with Psoriasis, Psoriatic Arthritis, or Ankylosing Spondylitis	2021	Irrelevant study design
75	Gaffney K.; Aletaha D.; Bradley A.J.; Nassab M.H.; Leage S.L.; Micheroli R.	52-Week efficacy and safety of ixekizumab in r-axspa/as patients naive to biologic treatments or with prior inadequate response/intolerance to tumor necrosis factor inhibitors	2020	Already captured by 2020 SLR update
76	Gaffney K.; Deodhar A.; Gensler L.; Kay J.; Maksymowych W.; Haroon N.; Landewe R.; Rudwaleit M.; Hall	Czp improves work and household productivity and social participation over 1 year of treatment in patients with non-radiographic axspa	2020	Already captured by 2020 SLR update

	S.; Bauer L.; Hoepken B.; De Peyrecave N.; Kumke T.; Van Der Heijde D.			
77	Genovese M.C.; Mysler E.; Tomita T.; Papp K.A.; Salvarani C.; Schwartzman S.; Gallo G.; Patel H.; Lisse J.R.; Kronbergs A.; Leage S.L.; Adams D.H.; Xu W.; Marzo-Ortega H.; Lebwohl M.G.	Safety of ixekizumab in adult patients with plaque psoriasis, psoriatic arthritis and axial spondyloarthritis: data from 21 clinical trials	2020	Irrelevant study design
78	Genovese, Mark C; Mysler, Eduardo; Tomita, Tetsuya; Papp, Kim A; Salvarani, Carlo; Schwartzman, Sergio; Gallo, Gaia; Patel, Himanshu; Lisse, Jeffrey R; Kronbergs, Andris; Leage, Soyi Liu; Adams, David H; Xu, Wen; Marzo-Ortega, Helena; Lebwohl, Mark G	Corrigendum to: Safety of ixekizumab in adult patients with plaque psoriasis, psoriatic arthritis and axial spondyloarthritis: data from 21 clinical trials.	2021	Irrelevant study design
79	Gensler L.; Baraliakos X.; Bauer L.; Hoepken B.; Kumke T.; Kim M.; Landewe R.	Disease activity and inflammation in axial spondyloarthritis patients who did not experience flares following certolizumab pegol withdrawal, dose reduction or dose continuation	2021	No relevant novel outcomes
80	Gensler L.; Deodhar A.; Van Der Heijde D.; Poddubnyy D.; Kivitz A.; Dougados M.; De Peyrecave N.; Oortgiesen M.; Vaux T.; Fleurinck C.; Baraliakos X.	Bimekizumab long-term safety and efficacy in patients with ankylosing spondylitis: Interim results after 3 years of treatment in an ongoing phase 2b study	2021	No relevant novel outcomes
81	Gensler L.S.; Baraliakos X.; Bauer L.; Kumke T.; Kim M.; Landewe R.B.M.	Disease activity and inflammation following withdrawal of certolizumab pegol treatment in axial spondyloarthritis patients who did not experience flares during the C-OPTIMISE study	2021	No relevant novel outcomes
82	Gottlieb A.; Deodhar A.; McInnes I.B.; Baraliakos X.; Reich K.; Schreiber S.; Bao W.; Richards H.B.; Pricop L.; Mease P.J.; Lebwohl M.	25529 Secukinumab demonstrates a consistent safety profile in patients with psoriasis, psoriatic arthritis and ankylosing spondylitis over long term: Updated pooled safety analyses	2021	Irrelevant study design
83	Gottlieb A.B.; Deodhar A.; Mcinnes I.B.; Baraliakos X.; Reich K.; Schreiber S.; Bao W.; Marfo K.; Richards H.B.; Pricop L.; Shete A.; Trivedi V.; Keefe D.; Papavassilis C.C.; Jagiello P.; Papanastasiou P.; Mease P.J.; Lebwohl M.	Long-term Safety of Secukinumab Over Five Years in Patients with Moderate-to-severe Plaque Psoriasis, Psoriatic Arthritis and Ankylosing Spondylitis: Update on Integrated Pooled Clinical Trial and Post-marketing Surveillance Data	2022	Irrelevant study design
84	Harrison S.R.; Marzo-Ortega H.	Ixekizumab: an IL-17A inhibitor for the treatment of axial Spondylarthritis	2021	Irrelevant study design
85	He C.; Xue C.; Zhu G.; Kang P.	Efficacy and safety of interleukin-17 inhibitors in the treatment of chronic rheumatic diseases: A combined and updated meta-analysis	2021	Irrelevant study design
86	Ho A.; Younis I.; Le Q.A.	Impact of biologics on health-related quality of life in patients with Ankylosing spondylitis: A systematic review and meta-analysis of randomized controlled trials	2022	SLR/NMA to hand-search
87	Huang F.; Sun F.; Wan W.-G.; Wu L.-J.; Dong L.-L.; Zhang X.; Kim T.-H.; Sengupta R.; Senolt L.; Wang Y.; Qiu H.-M.; Porter B.; Haemmerle S.	Secukinumab provided significant and sustained improvement in the signs and symptoms of ankylosing spondylitis: results from the 52-week, Phase III China-centric study, MEASURE 5	2020	Already captured by 2020 SLR update
88	Huang J.-X.; Lee Y.-H.; Wei J.C.-C.	Ixekizumab for the treatment of ankylosing spondylitis	2020	Irrelevant study design
89	Huang Y.; Chen Y.; Liu T.; Lin S.; Yin G.; Xie Q.	Impact of tumor necrosis factor alpha inhibitors on MRI inflammation in axial spondyloarthritis assessed by Spondyloarthritis Research Consortium Canada score: A meta-analysis	2020	SLR/NMA to hand-search

90	Husni M.E.; Deodhar A.; Schwartzman S.; Chakravarty S.D.; Hsia E.C.; Leu J.H.; Zhou Y.; Lo K.H.; Kavanaugh A.	Pooled safety results across phase 3 randomized trials of intravenous golimumab in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis	2022	Irrelevant study design
91	Jamaludin A.; Windsor R.; Ather S.; Kadir T.; Zisserman A.; Braun J.; Gensler L.; MacHado P.; Ostergaard M.; Poddubnyy D.; Coroller T.; Porter B.; Mpofu S.; Readie A.	Machine Learning-based Berlin Scoring of Magnetic Resonance Images of the Spine in Patients with Ankylosing Spondylitis: Analysis of Data from a Phase 3 Trial with Secukinumab	2020	No relevant novel outcomes
92	Jamaludin A.; Windsor R.; Ather S.; Kadir T.; Zisserman A.; Braun J.; Gensler L.S.; Machado P.; Ostergaard M.; Poddubnyy D.; Coroller T.; Porter B.; Mpofu S.; Readie A.	Machine learning based berlin scoring of magnetic resonance images of the spine in patients with ankylosing spondylitis from the measure 1 study	2020	No relevant novel outcomes
93	Ji X.; Man S.; Hu L.; Huang F.	Risk of malignancy and tuberculosis of biological and targeted drug in patients with spondyloarthritis: Systematic review and meta-analysis	2020	Irrelevant study design
94	Kaeley G.S.; Kaler J.K.	Peripheral Enthesitis in Spondyloarthritis: Lessons from Targeted Treatments	2020	Irrelevant study design
95	Kameda H.; Poddubnyy D.; Deodhar A.; Baraliakos X.; Blanco R.; Dokoupilova E.; Hall S.; Kivitz A.; Van De Sande M.; Stefanska A.; Pertel P.; Richards H.; Braun J.	Secukinumab provides sustained improvement in Non-radiographic Axial Spondyloarthritis: 2-year data from the PREVENT study	2021	No relevant novel outcomes
96	Karl G.; Daniel A.; Andrew B.; Haschemi N.M.; Soyi L.-L.; Raphael M.	52-week efficacy and safety of ixekizumab in radiographic axial spondyloarthritis/ankylosing spondylitis patients naive to bio-logic treatments or with prior inadequate response/intolerance to tumor necrosis factor inhibitors	2020	No relevant novel outcomes
97	Katsevman G.A.; Mariscal G.; Barrios C.; Domenech-Fernandez P.; Ziembinski C.; Bhatia S.	Efficacy and safety of anti-interleukin-17a monoclonal antibody secukinumab in treatment of ankylosing spondylitis: A meta-analysis	2020	Irrelevant study design
98	Kay J.; Gensler L.S.; Deodhar A.; Maksymowych W.P.; Haroon N.; Stoilov N.; Auteri S.E.; De Peyrecave N.; Kumke T.; Hoepken B.; Bauer L.; Rudwaleit M.	Earlier Treatment of Non-Radiographic Axial Sp ondyloarthritis with Certolizumab Pegol Results in Improved Clinical and Patient-Reported Outcomes	2020	Duplicate
99	Keeling S.; Maksymowych W.P.	JAK inhibitors, psoriatic arthritis, and axial spondyloarthritis: a critical review of clinical trials	2021	SLR/NMA to hand-search
100	Kerschbaumer A.; Smolen J.S.; Nash P.; Doerner T.; Dougados M.; Fleischmann R.; Geissler K.; McInnes I.B.; Takeuchi T.; Trauner M.; Winthrop K.; De Wit M.; Boehncke W.-H.; Falzon L.; Van Der Heijde D.	Points to consider for the treatment of immune-mediated inflammatory diseases with Janus kinase inhibitors: A systematic literature research	2020	Irrelevant study design
101	Khoury G.; Combe B.; Morel J.; Lukas C.	Change in MRI in patients with spondyloarthritis treated with anti-TNF agents: Systematic review of the literature and meta-analysis	2021	Irrelevant study design
102	Kiltz U.; Baraliakos X.; Brandt-Juergens J.; Wagner U.; Lieb S.; Sieder C.; Mann C.; Braun J.	Evaluation of the nonsteroidal anti-inflammatory drug-sparing effect of secukinumab in patients with ankylosing spondylitis: Results of the multicenter, randomised, double-blind, phase iv astrumtrial	2021	Duplicate
103	Kiltz U.; Sieper J.; Deodhar A.; Zueger P.; Song I.H.; Chen N.; Van Der Heijde D.	Improvements in global functioning and health-related quality of life and their association with disease activity and functional improvement in patients with active ankylosing spondylitis treated with upadacitinib: Results from the select-axis 1 trial	2020	Already captured by 2020 SLR update

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104	Kiltz U.; Sieper J.; Deodhar A.; Zueger P.; Song I.-H.; Chen N.; Van Der Heijde D.	Improvements in Global Functioning and Health-related Quality of Life and Their Association with Disease Activity and Functional Improvement in Patients with Active Ankylosing Spondylitis Treated with Upadacitinib	2020	Already captured by 2020 SLR update
105	Kiltz U.; Walsh J.A.; Vargas R.B.; Hunter T.; Bolce R.; Sandoval D.; Liu Leage S.; Leung A.; Li X.; Blue E.; Braun J.	Ixekizumab improves self-reported overall functioning and health as measured by the asas health index in patients with non-radiographic axial spondyloarthritis: 52-week results of a phase 3 randomized, active and placebo-controlled trial (coast-x)	2020	No relevant novel outcomes
106	Kiltz U.; Wei J.C.-C.; van der Heijde D.; van den Bosch F.; Walsh J.A.; Boonen A.; Gensler L.S.; Hunter T.; Carlier H.; Dong Y.; Li X.; Bolce R.; Strand V.; Braun J.	Ixekizumab improves functioning and health in the treatment of radiographic axial spondyloarthritis: Week 52 results from 2 pivotal studies	2021	Irrelevant study design
107	Kim T.-H.; Wei J.C.C.; Kishimoto M.; Jeong H.; Nozaki A.; Kobayashi S.	Efficacy and safety of Brodalumab, Anti-IL-17 receptor A monoclonal antibody, for axial spondyloarthritis, A 68-week result of phase 3 study	2020	Irrelevant study design
108	Kiri S.; Kim M.; Betts M.; Chitnis M.; Fahrbach K.; Tarpey J.; Turner M.	Network Meta-Analysis of Long-Term Efficacy (ASAS40) of Biologic Disease-Modifying Anti-Rheumatic Drugs (bDMARDs) in bDMARD-Naive Patients with Non-Radiographic Axial Spondyloarthritis	2020	Irrelevant study design
109	Kiri S.; Kim M.; Betts M.B.; Chitnis M.K.; Turner M.; Fahrbach K.; Tarpey J.	PBI5 An Indirect Comparison of Sustained Remission and FLARE Rates in Responders with NON-Radiographic Axial Spondyloarthritis (NR-AXSPA)	2020	Irrelevant study design
110	Kishimoto M.; Deodhar A.; Van Der Heijde D.; Sieper J.; Van Den Bosch F.; Maksymowych W.; Kim T.; Ostor A.; Combe B.; Sui Y.; Wang X.; Chu A.; Song I.	Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis: 1 year results from randomized, double-blind, placebocontrolled study with open-label extension	2021	Irrelevant study design
111	Konomi A.; Van Der Heijde D.; Stergaard M.; Reveille J.; Baraliakos X.; Kronbergs A.; Sandoval D.; Li X.; Carlier H.; Adams D.; Maksymowych W.	Evaluation of spinal radiographic progression in patients with radiographic axial spondyloarthritis receiving ixekizumab therapy over 2 years	2021	No relevant novel outcomes
112	Krabbe S.; Eshed I.; Sorensen I.J.; Jensen B.; Moller J.M.; Balding L.; Madsen O.R.; Pedersen S.J.; Ostergaard M.	Whole-body magnetic resonance imaging inflammation in peripheral joints and entheses in axial spondyloarthritis: Distribution and changes during adalimumab treatment	2020	Already captured by 2020 SLR update
113	Kvien T.K.; Conaghan P.G.; Gossec L.; Strand V.; Ostergaard M.; Poddubnyy D.; Williams N.; Porter B.; Shete A.; Gilloteau I.; Deodhar A.	Secukinumab Provides Sustained Reduction in Fatigue in Patients with Ankylosing Spondylitis: Long-term Results of Two Phase III Randomized Controlled Trials	2020	No relevant novel outcomes
114	Kvien, Tore K; Conaghan, Philip G; Gossec, Laure; Strand, Vibeke; Ostergaard, Mikkel; Poddubnyy, Denis; Williams, Nicole; Porter, Brian; Shete, Abhijit; Gilloteau, Isabelle; Deodhar, Atul	Secukinumab and Sustained Reduction in Fatigue in Patients With Ankylosing Spondylitis: Long-Term Results of Two Phase III Randomized Controlled Trials.	2022	No relevant novel outcomes
115	Kwan Y.H.; Lim K.K.; Fong W.; Goh H.; Ng L.; Haaland B.; Phang J.K.; Low L.L.; Yeo J.G.; Huang F.; Leung Y.Y.; Thumboo J.; Ostbye T.	Risk of malignancies in patients with spondyloarthritis treated with biologics compared with those treated with non-biologics: a systematic review and meta-analysis	2020	Irrelevant study design
116	L'Ami M.J.; Ruwaard J.; Kneepkens E.L.; Krieckaert C.L.M.; Nurmohamed M.; Hooijberg F.; Van Denderen J.C.; Van Kuijk A.; Burgemeister L.; Boers M.; Wolbink G.J.	Interval prolongation in etanercepttreated patients with rheumatoid arthritis, ankylosing spondylitis or psoriatic arthritis: An open-label, randomised controlled trial	2020	Irrelevant intervention/comparators

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117	Landewe R.; van der Heijde D.; Dougados M.; Baraliakos X.; Van den Bosch F.; Gaffney K.; Bauer L.; Hoepken B.; de Peyrecave N.; Thomas K.; Gensler L.S.	Induction of Sustained Clinical Remission in Early Axial Spondyloarthritis Following Certolizumab Pegol Treatment: 48-Week Outcomes from C-OPTIMISE	2020	Irrelevant intervention/comparators
118	Landewe R.B.M.; Van Der Heijde D.; Dougados M.; Baraliakos X.; Van Den Bosch F.; Gaffney K.; Bauer L.; Hoepken B.; De Peyrecave N.; Thomas K.; Gensler L.S.	Does gender, age or subpopulation influence the maintenance of clinical remission in axial spondyloarthritis following certolizumab pegol dose reduction?	2020	No relevant novel outcomes
119	Landewe R.B.M.; Van Der Heijde D.; Dougados M.; Baraliakos X.; Van Den Bosch F.E.; Gaffney K.; Bauer L.; Hoepken B.; Davies O.R.; De Peyrecave N.; Thomas K.; Gensler L.	Maintenance of clinical remission in early axial spondyloarthritis following certolizumab pegol dose reduction	2020	Already captured by 2020 SLR update
120	Langley R.; Reich K.; Bissonnette R.; Gottlieb A.; Marzo-ortega H.; Dicomite G.; Aassi M.; Mease P.	Secukinumab provides comprehensive long-term treatment across multiple manifestations of psoriatic disease	2020	Irrelevant study design
121	Lau C.S.; Chen Y.-H.; Lim K.; de Longueville M.; Arendt C.; Winthrop K.	Tuberculosis and viral hepatitis in patients treated with certolizumab pegol in Asia-Pacific countries and worldwide: real-world and clinical trial data	2021	Irrelevant study design
122	Lawson D.O.; Eraso M.; Mbuagbaw L.; Joanes M.; Aves T.; Leenus A.; Omar A.; Inman R.D.	Tumor Necrosis Factor Inhibitor Dose Reduction for Axial Spondyloarthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials	2021	Irrelevant study design
123	Lebwohl M.; Deodhar A.; Griffiths C.E.M.; Menter M.A.; Poddubnyy D.; Bao W.; Jehl V.; Marfo K.; Primatesta P.; Shete A.; Trivedi V.; Mease P.J.	The risk of malignancy in patients with secukinumab-treated psoriasis, psoriatic arthritis and ankylosing spondylitis: analysis of clinical trial and postmarketing surveillance data with up to five years of follow-up	2021	Irrelevant study design
124	Lee Y.H.; Song G.G.	Janus kinase inhibitors for treating active ankylosing spondylitis: a meta-analysis of randomized controlled trials	2022	Irrelevant study design
125	Lee Y.H.; Song G.G.	Comparative efficacy and safety of secukinumab and ixekizumab in patients with active ankylosing spondylitis	2021	Irrelevant study design
126	Li J.; Zhang Z.; Wu X.; Zhou J.; Meng D.; Zhu P.	Risk of Adverse Events After Anti-TNF Treatment for Inflammatory Rheumatological Disease. A Meta-Analysis	2021	Irrelevant study design
127	Li, Shu; Li, Fen; Mao, Ni; Wang, Jia; Xie, Xi	Efficacy and safety of Janus kinase inhibitors in patients with ankylosing spondylitis: A systematic review and meta-analysis.	2022	SLR/NMA to hand-search
128	Macaluso F.S.; Cummings J.R.F.; Atreya R.; Choi J.; Orlando A.	A Systematic Review on Infliximab Biosimilar SB2: From Pre-Clinical Data to Real-World Evidence	2022	Irrelevant study design
129	Magrey M.; De Vlam K.; Bolce R.; Liu-Leage S.; Zhu D.; Hunter T.; Sandoval D.; Van Der Horst-Bruinsma I.	Gender Differences in Baseline Clinical Characteristics among Patients with Ankylosing Spondylitis and Non-radiographic Axial Spondyloarthritis: Data from 3 Randomized Ixekizumab Controlled Trials	2020	No relevant novel outcomes
130	Magrey M.; De Vlam K.; Kronbergs A.; Bolce R.; Sandoval D.; Li X.; Liu Leage S.; Poddubnyy D.	Efficacy of ixekizumab through 52 weeks for improving peripheral joint involvement among patients with radiographic-axial spondyloarthritis	2021	No relevant novel outcomes
131	Magrey M.; Ramiro S.; Pinheiro M.; Gao T.; Ganz F.; Song I.H.; Biljan A.; Haroon N.; Rudwaleit M.	Predictors of 1-year treatment response among upadacitinib-treated patients with ankylosing spondylitis: A post hoc analysis of select-axis 1	2021	No relevant novel outcomes
132	Magrey M.; Ramiro S.; Pinheiro M.M.; Gao T.; Ganz F.; Song I.-H.; Biljan A.; Haroon N.; Rudwaleit M.	Predictors of 1-year treatment response among upadacitinib-treated patients with ankylosing spondylitis: A post hoc analysis	2021	No relevant novel outcomes
133	Magrey M.; Walsh J.A.; Huang F.; Kameda H.; Wang J.; Herrem C.; Pertel P.; Marzo-Ortega H.	Efficacy of secukinumab in tnfi-nalve patients across the axial spondyloarthritis spectrum over 52 weeks: A post hoc analysis of the measure and prevent clinical trials	2021	Irrelevant study design

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134	Magrey M.N.; Ramiro S.; Pinheiro M.M.; Gao T.; Ganz F.; Song I.-H.; Biljan A.; Haroon N.; Rudwaleit M.	Predictors of 1-year treatment response among upadacitinib-treated patients with ankylosing spondylitis: A post hoc analysis of select-axis 1	2021	No relevant novel outcomes
135	Maksymowych W.; Baraliakos X.; Lambert R.; Landewe R.; Calderon D.S.; Carlier H.; Lisse J.; Li X.; Hojnik M.; Ostergaard M.	Effects of ixekizumab treatment on structural changes in the sacroiliac joints based on MRI assessments at 16 weeks in patients with non-radiographic axial spondyloarthritis	2021	No relevant novel outcomes
136	Maksymowych W.; Kumke T.; Auteri S.; Hoepken B.; Bauer L.; Rudwaleit M.	Predictors of Response in Patients with Non-Radiographic Axial Spondyloarthritis Receiving Certolizumab Pegol in the C-axSpAnd Study	2020	No relevant novel outcomes
137	Maksymowych W.; Ostergaard M.; Landewe R.; Barchuk W.; Liu K.; Tasset C.; Gilles L.; Hendrikx T.; Besuyen R.; Baraliakos X.	Effects of Filgotinib on Spinal Lesions in Patients with Ankylosing Spondylitis: Magnetic Resonance Imaging Data from the Placebo-Controlled, Double-Blind, Randomized TORTUGA Trial	2020	No relevant novel outcomes
138	Maksymowych W.; Ostergaard M.; Landewe R.; Barchuk W.; Liu K.; Tasset C.; Gilles L.; Hendrikx T.; Besuyen R.; Baraliakos X.	Impact of Filgotinib on Structural Lesions in the Sacroiliac Joints at 12 Weeks in Patients with Active Ankylosing Spondylitis: Correlation with Clinical Endpoints	2020	Already captured by 2020 SLR update
139	Maksymowych W.; Tian Y.; Xu J.; Barchuk W.; Galien R.; Besuyen R.; Liu Y.; Malkov V.; Hertz A.	Filgotinib treatment results in reduction of inflammatory and matrix remodeling biomarkers associated with disease in patients with ankylosing spondylitis	2021	No relevant novel outcomes
140	Maksymowych W.P.; Kumke T.; Auteri S.; Hoepken B.; Bauer L.; Rudwaleit M.	Predictors of response in patients with non-radiographic axial spondyloarthritis receiving certolizumab pegol in the c-axspand study	2021	No relevant novel outcomes
141	Maksymowych W.P.; Kumke T.; Auteri S.E.; Hoepken B.; Bauer L.; Rudwaleit M.	Predictors of long-term clinical response in patients with non-radiographic axial spondyloarthritis receiving certolizumab pegol	2021	No relevant novel outcomes
142	Maksymowych W.P.; Kumke T.; Auteri S.E.A.; Hoepken B.; Bauer L.; Rudwaleit M.	Predictors of response in patients with non-radiographic axial spondyloarthritis receiving certolizumab pegol in the c-axspand study	2021	No relevant novel outcomes
143	Maksymowych W.P.; Marzo-Ortega H.; Ostergaard M.; Gensler L.S.; Ermann J.; Deodhar A.; Poddubnyy D.; Sandoval D.; Bolce R.; Kronbergs A.; Liu Leage S.; Doridot G.; Geneus V.; Leung A.; Adams D.; Rudwaleit M.	Efficacy of ixekizumab on disease activity and quality of life in patients with active non-radiographic axial spondyloarthritis and objective signs of inflammation, stratified by baseline CRP/sacroiliac joint MRI status	2020	No relevant novel outcomes
144	Maksymowych W.P.; Ostergaard M.; Landewe R.; Barchuk W.; Liu K.; Gilles L.; Hendrikx T.; Besuyen R.; Baraliakos X.	Filgotinib decreases both vertebral body and posterolateral spine inflammation in ankylosing spondylitis: results from the TORTUGA trial	2021	No relevant novel outcomes
145	Maksymowych W.P.; Ostergaard M.; Landewe R.; Barchuk W.; Liu K.; Tasset C.; Gilles L.; Hendrikx T.; Besuyen R.; Baraliakos X.	Impact of filgotinib on sacroiliac joint MRI structural lesions at 12 weeks in patients with active ankylosing spondylitis (TORTUGA trial)	2021	No relevant novel outcomes
146	Maksymowych W.P.; Ostergaard M.; Landewe R.B.M.; Barchuk W.; Liu K.; Tasset C.; Gilles L.; Hendrikx T.; Besuyen R.; Baraliakos X.	Impact of filgotinib on structural lesions in the sacroiliac joints at 12 weeks in patients with active axial spondyloarthritis: magnetic resonance imaging data from the double-blind, randomized Tortuga trial	2020	Already captured by 2020 SLR update
147	Maksymowych W.P.; Tian Y.; Yoon O.K.; Barchuk W.; Galien R.; Besuyen R.; Liu Y.; Mirza A.M.; Malkov V.; Hertz A.	Filgotinib treatment results in reduction of biomarkers associated with disease in patients with ankylosing spondylitis	2020	No relevant novel outcomes
148	Man S.; Hu L.; Ji X.; Wang Y.; Ma Y.; Wang L.; Zhu J.; Huang F.	Risk of Malignancy and Tuberculosis of Biological and Targeted Drug in Patients With Spondyloarthritis: Systematic Review and Meta-analysis of Randomized Controlled Trials	2021	SLR/NMA to hand-search

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149	Marques M.L.; Ramiro S.; MacHado P.M.; Van Der Heijde D.; Van Gaalen F.	No Relationship between Lumbar Bone Mineral Density and Syndesmophyte Formation at the Same Level - A Multilevel Analysis in Patients with Radiographic Axial Spondyloarthritis	2020	No relevant novel outcomes
150	Marques M.L.; Ramiro S.; Machado P.M.; Van Der Heijde D.; Van Gaalen F.A.	No relationship between bone mineral density and syndesmophyte formation at the same level in the lumbar spine of patients with radiographic axial Spondyloarthritis	2020	No relevant novel outcomes
151	Marzo-Ortega H.; Deodhar A.; Blanco R.; Kameda H.; Kivitz A.; Poddubnyy D.; Magrey M.; Wang J.; Haemmerle S.; Shete A.; Braun J.	Secukinumab Improves Pain, Morning Stiffness, Fatigue and Physical Function in Tumor Necrosis Factor Inhibitor-Naive Patients with Non-Radiographic Axial Spondyloarthritis: Results from a Randomized Controlled Phase III Study	2020	Already captured by 2020 SLR update
152	Marzo-Ortega H.; Deodhar A.; Blanco R.A.; Kameda H.; Kivitz A.; Poddubnyy D.; Magrey M.N.; Wang J.; Haemmerle S.; Shete A.; Braun J.	Secukinumab improves back pain, morning stiffness, fatigue and physical function in tumour necrosis factor inhibitor-naive patients with nonradiographic axial spondyloarthritis: Results from a randomised controlled Phase 3 study	2021	No relevant novel outcomes
153	Marzo-Ortega H.; Juanola X.; Okano T.; Schymura Y.; Bradley A.; Gammeltoft Gerwien J.; Monsberger B.; Liu Leage S.; Aletaha D.; Ostergaard M.	CRP normalisation versus individual components of clinical response to ixekizumab at week 16 in patients with ankylosing spondylitis: COAST V	2021	No relevant novel outcomes
154	Marzo-Ortega H.; Juanola X.; Okano T.; Schymura Y.; Bradley A.; Gerwien J.; Monsberger B.; Liu Leage S.; Aletaha D.; Ostergaard M.	Normalization of high sensitivity crp versus clinical response to ixekizumab at week 16 in patients with radiographic & non-radiographic axial spondyloarthritis: Results from the coast studies	2021	No relevant novel outcomes
155	Marzo-Ortega H.; Mease P.J.; Rahman P.; Navarro-Compan V.; Strand V.; Dougados M.; Combe B.; Wei J.C.C.; Baraliakos X.; Hunter T.; Sandoval D.; Li X.; Zhu B.; Bessette L.; Deodhar A.	Impact of ixekizumab on work productivity in patients with ankylosing spondylitis: results from the coast-v and coast-w trials at 52 weeks	2020	Already captured by 2020 SLR update
156	Marzo-Ortega H.; Mease P.J.; Rahman P.; Navarro-Compan V.; Strand V.; Dougados M.; Combe B.; Wei J.C.-C.; Baraliakos X.; Hunter T.; Sandoval D.; Li X.; Zhu B.; Bessette L.; Deodhar A.	Impact of Ixekizumab on Work Productivity in Patients with Ankylosing Spondylitis: Results from the COAST-V and COAST-W Trials at 52 Weeks	2020	Already captured by 2020 SLR update
157	Marzo-Ortega H.; Miceli-Richard C.; Gill S.; Magery M.; Machado P.G.P.; Shete A.; Wang J.; Rohrer S.; Deodhar A.	Subcutaneous secukinumab 150mg provides rapid and sustained relief in total and nocturnal back pain, morning stiffness and fatigue in patients with active as over 4 years	2020	Already captured by 2020 SLR update
158	Marzo-Ortega H.; Perella C.; Poddubnyy D.; Pournara E.; Zielinska A.; Baranauskaite A.; Sadhu S.; Schulz B.; Rissler M.	Secukinumab provides significantimprovement of spinal pain and lowers diseaseactivity in patients with axial spondyloarthritis: 24-week results from a randomised controlled Phase 3btrial	2021	Irrelevant study design
159	Marzo-Ortega H.; Sieper J.; Kivitz A.J.; Blanco R.; Cohen M.; Pavelka K.; Delicha E.M.; Stefanska A.; Richards H.B.; Rohrer S.	5-year efficacy and safety of secukinumab in patients with ankylosing spondylitis: end-of-study results from the phase 3 MEASURE 2 trial	2020	Irrelevant study design
160	Marzo-Ortega H; Deodhar A; Blanco R; Kameda H; Kivitz A; Poddubnyy D; Magrey M; Wang J; Haemmerle S; Shete A; Braun J	Secukinumab Improves Pain, Morning Stiffness, Fatigue and Physical Function in Tumor Necrosis Factor Inhibitor-Naïve Patients with Non-Radiographic Axial Spondyloarthritis: results from a Randomized Controlled Phase III Study	2020	Already captured by 2020 SLR update
161	McInnes I.B.; Baraliakos X.; Deodhar A.; Gottlieb A.B.; Lebwohl M.; Schreiber S.; Marfo K.; Bao W.; Richards H.B.; Pricop L.; Shete A.; Safi J.; Mease P.J.	Secukinumab demonstrates a consistent safetyprofile in patients with psoriasis, psoriatic arthritisand ankylosing spondylitis over long term: Updatedpooled safety analyses	2021	Irrelevant study design

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162	McInnes I.B.; Gladman D.D.; Deodhar A.A.; Miceli-Richard C.; Nash P.; Sattar N.; Mehta N.N.; Wang J.; Pricop L.; di Comite G.	15262 Cardio-metabolic effects of long-term treatment with secukinumab in psoriatic arthritis and ankylosing spondylitis patients: Pooled 3 year analysis	2020	Irrelevant study design
163	McInnes I.B.; Ostor A.J.K.; Mease P.J.; Tillett W.; Baraliakos X.; De Vlam K.; Bessette L.; Lippe R.; Maniccia A.; Feng D.; Gao T.; Zueger P.; Saffore C.; Kato K.; Song I.-H.; Deodhar A.	Effect of upadacitinib on reducing pain in patients with active psoriatic arthritis or ankylosing spondylitis: post hoc analysis of three randomised clinical trials	2022	No relevant novel outcomes
164	Mease P.J.; Deodhar A.; Calheiros R.; Meng X.; Fox T.; Baraliakos X.	Symptoms of peripheral arthritis are significantly improved in patients with ankylosing spondylitis treated with secukinumab	2020	No relevant novel outcomes
165	Mease P.J.; Deodhar A.; Rahman P.; Marzo-Ortega H.; Strand V.; Hunter T.; Adams D.; Sandoval D.; Kronbergs A.; Zhu B.; Leung A.; Liu Leage S.; Navarro-Compan V.	Ixekizumab treatment improves fatigue, spinal pain, stiffness, and sleep in patients with non-radiographic axial spondyloarthritis	2020	No relevant novel outcomes
166	Merola J.; McInnes I.; Deodhar A.; Quebe-Fehling E.; Aassi M.; Peine M.; Mehta N.	Secukinumab effects on cardiometabolic risk and systemic inflammation in patients with psoriasis, psoriatic arthritis and axial spondyloarthritis: results from post hoc analyses of pooled data from 19 phase 3/4 clinical studies	2021	Irrelevant study design
167	Merola J.F.; McInnes I.B.; Deodhar A.A.; Dey A.K.; Adamstein N.H.; Quebe-Fehling E.; Aassi M.; Peine M.; Mehta N.N.	Effect of Secukinumab on Traditional Cardiovascular Risk Factors and Inflammatory Biomarkers: Post Hoc Analyses of Pooled Data Across Three Indications	2022	Irrelevant study design
168	Miceli-Richard C.; Poddubnyy D.; Deodhar A.; Bao W.; Parman C.; Porter B.; Pournara E.	Predictors of Response in Secukinumab-treated Patients with Ankylosing Spondylitis: Logistic Regression and Machine Learning Analyses	2020	No relevant novel outcomes
169	Mladov V.; Sokolova V.; Tolkacheva D.	PBI16 Number Needed to Treat and Incremental Costs per Responder for Biologics in Adult Patients with Active Radiographic Axial Spondyloarthritis in the Russian Federation	2021	Irrelevant study design
170	Ogdie A.; De Vlam K.; McInnes I.B.; Mease P.J.; Baer P.; Lukic T.; Gruben D.; Kwok K.; Wang C.; Hsu M.-A.; Maniccia A.	Efficacy of tofacitinib in reducing pain in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis	2020	Irrelevant study design
171	Olivera P.A.; Lasa J.S.; Bonovas S.; Danese S.; Peyrin-Biroulet L.	Safety of Janus Kinase Inhibitors in Patients With Inflammatory Bowel Diseases or Other Immune-mediated Diseases: A Systematic Review and Meta-Analysis	2020	Irrelevant study design
172	Ortolan A.; Ramiro S.; Sepriano A.; Landewe R.B.M.; Van Der Heijde D.; Navarro-Compan V.	Which response or status criterion discriminates best in axspa?	2020	Irrelevant study design
173	Ostergaard M.; Wu J.; Fallon L.; Sherlock S.P.; Wang C.; Fleishaker D.L.; Kanik K.S.; Maksymowych W.	Effect of tofacitinib on spinal vertebral body and posterolateral element inflammation and structural lesions using the Canada-Denmark MRI scoring system in patients with ankylosing spondylitis: results from a phase 2 study	2021	No relevant novel outcomes
174	Ostor A.; Deodhar A.; Baraliakos X.; McInnes I.; De Vlam K.; Bessette L.; Maniccia A.; Lippe R.; Saffore C.; Gao T.; Song I.-H.	Effect of upadacitinib on reducing pain in patients with active ankylosing spondylitis and inadequate response to nonsteroidal anti-inflammatory drugs	2021	Duplicate
175	Ostor A.; Deodhar A.; Maniccia A.; Ganz F.; Gao T.; Chu A.D.; Poddubnyy D.	Achievement of partial remission and inactive disease in Upadacitinib-treated patients with ankylosing spondylitis	2021	Duplicate
176	Pavelka K.; Kivitz A.J.; Dokoupilova E.; Blanco R.; Maradiaga M.; Tahir H.; Wang Y.; Porter B.O.; Stefanska A.; Richards H.B.; Rohrer S.	Secukinumab 150/300 mg Provides Sustained Improvements in the Signs and Symptoms of Active Ankylosing Spondylitis: 3-Year Results from the Phase 3 MEASURE 3 Study	2020	Already captured by 2020 SLR update

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177	Pinheiro Torres R.; Rodrigues-Manica S.; Pimentel Dos Santos F.	Pharmacological treatment of enthesitis -a systematic review on the efficacy of the available options	2021	Irrelevant study design
178	Poddubnyy D.; Attar S.M.H.; Nissen M.J.; Fillipi E.; Russ H.; Erdogan A.; Schymura Y.; Liu-Leage S.; Collantes-Estevez E.; Ciccia F.	Individual components contributing to the achievement of assessment in spondyloarthritis international society 40 response in biologic naive patients with radiographic axial spondyloarthritis: Results from the coast v trial	2021	Duplicate
179	Poddubnyy D.; Deodhar A.; Baraliakos X.; Blanco R.; Dokoupilova E.; Hall S.; Kivitz A.; Van De Sande M.G.H.; Stefanska A.; Pertel P.; Richards H.; Braun J.	Secukinumab 150 mg provides sustained improvement in signs and symptoms of non-radiographic axial spondyloarthritis: 2-year results from the prevent study	2021	Duplicate
180	Poddubnyy D.; Juanola X.; Prati C.; Hagen R.; Schymura Y.; Liu-Leage S.; Haschemi Nassab M.; Dudler J.	Achievement of low disease activity according to basdai with ixekizumab in patients with axial spondyloarthritis: 16-week results from the COAST trials	2021	Duplicate
181	Poddubnyy D.; Juanola X.; Prati C.; Russ H.; Schymura Y.; Liu-Leage S.; Nassab M.H.; Dudler J.	Achievement of Low Disease Activity According to BASDAI with Ixekizumab in Patients with Axial Spondyloarthritis: 16-Week Results from the COAST Trials	2020	Already captured by 2020 SLR update
182	Poddubnyy D.; Liu Y.; Barchuk W.; Besuyen R.; Galien R.; Tian Y.; Malkov V.; Hertz A.	Whole blood transcriptional changes following treatment with filgotinib in patients with ankylosing spondylitis	2021	No relevant novel outcomes
183	Poddubnyy D.; Pournara E.; Schulz B.; Sadhu S.; Deodhar A.; Baraliakos X.; Marzo-Ortega H.	Efficacy of secukinumab and HLA-B27 subtypes: Results from a phase iiib randomised controlled trial in axial SPA	2021	Irrelevant study design
184	Poddubnyy D.; Pournara E.; Zielinska A.; Baranauskaite A.; Jimenez A.M.; Sadhu S.; Schulz B.; Rissler M.; Perella C.; Marzo-Ortega H.	Rapid improvement in spinal pain in patients with axial spondyloarthritis treated with secukinumab: primary results from a randomized controlled phase-IIIb trial	2021	Irrelevant study design
185	Proft F.; Torgutalp M.; Weis A.; Protopopov M.; Rios Rodriguez V.; Haibel H.; Hermann K.; Althoff C.; Behmer O.; Sieper J.; Poddubnyy D.	Frequency of disease flares under longterm anti-tnf therapy in patients with early axial spondyloarthritis: results from the etanercept versus sulfasalazine in early axial spondyloarthritis trial	2020	Irrelevant study design
186	Proft F.; Torgutalp M.; Weiss A.; Protopopov M.; Rios Rodriguez V.; Haibel H.; Behmer O.; Sieper J.; Poddubnyy D.	Long-term clinical outcome of anti-tnf treatment in patients with early axial spondyloarthritis: 10-year data of the etanercept vs. sulfasalazin in early axial spondyloarthritis trial	2020	Irrelevant study design
187	Proft F.; Weiss A.; Torgutalp M.; Protopopov M.; Rodriguez V.R.; Haibel H.; Behmer O.; Sieper J.; Poddubnyy D.	Sustained clinical response and safety of etanercept in patients with early axial spondyloarthritis: 10-year results of the ESTHER trial	2021	Irrelevant study design
188	Ramiro S.; Bolce R.; Sandoval D.; Kronbergs A.; Park S.Y.; Wu B.; Walsh J.A.	Sustainability of ixekizumab response at the individual patient level over time in radiographic axial spondyloarthritis	2021	No relevant novel outcomes
189	Reich K.; Blauvelt A.; Armstrong A.; Langley R.; Deodhar A.; Gladman D.; Mcinnes I.; Pricop L.; Porter B.; Safi J.; Shete A.; Ren M.; De Vera A.; Spindeldreher S.; Kolbinger F.; Bruin G.	Immunogenicity of secukinumab, a fully human anti-interleukin-17a monoclonal antibody, in patients with psoriasis, psoriatic arthritis, and ankylosing spondylitis during a 52-week treatment period	2020	Irrelevant study design
190	Reveille J.; Deodhar A.; Harrison D.; Hsia E.; Chan E.K.H.; Kafka S.; Lo K.H.; Kim L.; Zazzetti F.; Han C.	Effects of intravenous golimumab, an anti-tnfalpha monoclonal antibody, on health-related quality of life in patients with ankylosing spondylitis: 1-year results ofa phase iii trial	2020	No relevant novel outcomes
191	Reveille J.; Rahman P.; Sandoval D.; Muran T.; Kronbergs A.; Bolce R.; Geneus V.; Hunter T.; Liu-Leage S.; Rudwaleit M.; Maldonado-Cocco J.; Van Den Bosch F.	Response to Ixekizumab by C-reactive Protein Level in Patients with Radiographic Axial Spondyloarthritis: Results from the COAST-V (Biological-Naive) and COAST-W (TNF Inhibitor-Experienced) Trials at 52 Weeks	2020	Already captured by 2020 SLR update

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192	Reveille J.D.; Deodhar A.; Ince A.; Chan E.K.H.; Peterson S.; Li N.; Hsia E.C.; Kim L.; Lo K.H.; Xu S.; Harrison D.D.; Han C.	Effects of Intravenous Golimumab on Health-Related Quality of Life in Patients with Ankylosing Spondylitis: 28-Week Results of the GO-ALIVE Trial	2020	Already captured by 2020 SLR update
193	Reveille J.D.; Hwang M.C.; Danve A.; Kafka S.; Peterson S.; Lo K.H.; Kim L.; Hsia E.C.; Chan E.K.H.; Deodhar A.	The effect of intravenous golimumab on health-related quality of life and work productivity in adult patients with active ankylosing spondylitis: results of the phase 3 GO-ALIVE trial	2021	Already captured by 2020 SLR update
194	Reveille J.D.; Rahman P.; Calderon D.M.S.; Muram T.; Kronbergs A.; Bolce R.; Geneus V.; Hunter T.; Liu-Leage S.; Rudwaleit M.; Maldonado-Cocco J.A.; Van DenBosch F.	Response to ixekizumab by C-reactive proteinlevel in patients with aadiographic axialspondyloarthritis: Results from the COAST-V(biological-naive) and COAST-W (TNF-a inhibitorexperienced) trials at 52 weeks	2021	Duplicate
195	Reveille J; Rahman P; Sandoval D; Muran T; Kronbergs A; Bolce R; Geneus V; Hunter T; Liu-Leage S; Rudwaleit M; Maldonado-Cocco J; Van Den Bosch F	Response to Ixekizumab by C-reactive Protein Level in Patients with Radiographic Axial Spondyloarthritis: results from the COAST-V (Biological-Naïve) and COAST-W (TNF Inhibitor-Experienced) Trials at 52 Weeks	2020	Already captured by 2020 SLR update
196	Reveille, John D; Deodhar, Atul; Caldron, Paul H; Dudek, Anna; Harrison, Diane D; Kim, Lilianne; Lo, Kim Hung; Leu, Jocelyn H; Hsia, Elizabeth C	Safety and Efficacy of Intravenous Golimumab in Adults with Ankylosing Spondylitis: Results through 1 Year of the GO-ALIVE Study.	2019	Already captured by 2020 SLR update
197	Robinson P.; Hall S.; Hoepken B.; Bauer L.; Demas E.; Kim M.; Deodhar A.	Response to certolizumab pegol in patients with non-radiographic axial spondyloarthritis by baseline C-reactive protein cut-offs: Post-hoc analysis from a phase 3 multicenter study	2021	Irrelevant intervention/comparators
198	Robinson P.; Machado P.; Haroon N.; Gensler L.; Reveille J.; Taieb V.; Vaux T.; Fleurinck C.; Oortgiesen M.; De Peyrecave N.; Deodhar A.	Minimal impact of the COVID-19 pandemic on patient-reported disease activity and health-related quality of life in patients with ankylosing spondylitis receiving bimekizumab: Post hoc analyses from a phase 2b study	2021	Irrelevant study design
199	Roche D.; Badard M.; Boyer L.; Lafforgue P.; Pham T.	Incidence of anterior uveitis in patients with axial spondyloarthritis treated with anti-TNF or anti-IL17A: a systematic review, a pairwise and network meta-analysis of randomized controlled trials	2021	Irrelevant study design
200	Rodrigues-Manica S.; Silva J.; Cruz-Machado R.; Coelho C.; Duarte J.; Vieira-Sousa E.; Tavares-Costa J.; Pimentel-Santos F.M.	Biologic disease-modifying anti-rheumatic drugs and patient-reported outcomes in axial SpA: a systematic review and a call for action	2021	Irrelevant study design
201	Rudwaleit M.; Machado P.; Gensler L.; Taieb V.; De Peyrecave N.; Hoepken B.; Van Der Heijde D.	Achievement of stringent thresholds of disease control is associated with reduced burden on work and household productivity in patients with axial spondyloarthritis	2021	Irrelevant study design
202	Rusman T.; Van Der Weijden M.A.C.; Nurmohamed M.T.; Landewe R.B.M.; De Winter J.J.; Boden B.J.H.; Bet P.M.; Van Der Bijl C.M.A.; Van Der Laken C.J.; Van der Horst-Bruinsma I.	Is very early treatment effective? Six months results of the prevas study, a placebo-controlled trial with etanercept in patients suspected of non-radiographic axial spondyloarthritis	2020	Already captured by 2020 SLR update
203	Ruwaard J.; L' Ami M.J.; Kneepkens E.L.; Krieckaert C.L.M.; Nurmohamed M.T.; Hooijberg F.; van Kuijk A.W.R.; van Denderen J.C.; Burgemeister L.; Rispens T.; Boers M.; Wolbink G.J.	Interval prolongation of etanercept in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a randomized controlled trial	2022	Irrelevant intervention/comparators
204	Sayed Abdulla J.; Shi J.; Roy B.S.; Zhanwen Z.; Liu C.	Patients with ankylosing spondylitis treatment by golimumab: a systematic review and meta-analysis	2020	Irrelevant study design
205	Schett G.; Van Den Bosch F.; Baraliakos X.; Sandoval D.; Geneus	Ixekizumab Improves Signs and Symptoms of Patients with Radiographic and Non-radiographic Axial Spondyloarthritis and Extra-articular Manifestation of Enthesitis Through 16 Weeks	2020	Already captured by 2020 SLR update

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	V.; Bolce R.; Liu-Leage S.; Kronbergs A.; Mease P.			
206	Schneeberger E.; Citera G.; De Leon D.P.; Szumski A.; Kwok K.; Cutri M.; Dougados M.	Performance of SASDAS (Simplified Axial Spondyloarthritis Disease Activity Score) versus ASDAS in a Post Hoc Analysis of a Randomized Controlled Clinical Trial	2020	No relevant novel outcomes
207	Schwartzman S.; Deodhar A.; Combe B.; Accioly A.; Kronbergs A.; Janos B.; Zhu D.; Sandoval Calderon D.; Rahman P.; Poddubnyy D.	Safety profile of ixekizumab for the treatment of psoriatic arthritis and axial spondyloarthritis up to 3 years: An updated integrated safety analysis	2021	Irrelevant study design
208	Schwartzman S.; Sandoval D.; Kronbergs A.; Lisse J.; Patel H.; Xu W.; Liu-Leage S.; Magrey M.; Marzo-Ortega H.; Poddubnyy D.	Long-Term Safety Profile of Ixekizumab Treatment in Patients with Axial Spondyloarthritis	2020	No relevant novel outcomes
209	Schymura Y.; Graham-Clarke P.L.; Liu-Leage S.	A systematic literature review and network meta-analysis of the efficacy and safety ofixekizumab versus currently licensed biologics fo versus currently licensed biologics forthe treatment of radiographic axSpA	2021	Irrelevant study design
210	Sengupta R.; Bird P.; Aletaha D.; Magrey M.; Kadono Y.; Soriano E.; Bradley A.J.; LiuLeage S.; Schymura Y.; Nissen M.J.	The impact of peripheral articularmanifestations on the e}cacy of ixekizumab inpatients with radiographic axial spondyloarthritis	2021	No relevant novel outcomes
211	Sengupta R.; Gensler L.; Kay J.; Maksymowych W.; Haroon N.; Bauer L.; Hoepken B.; De Peyrecave N.; Kumke T.; Deodhar A.	Certolizumab pegol-treated patients with non-radiographic axspa demonstrate improvements in sleep quality and other patient reported outcomes	2020	Already captured by 2020 SLR update
212	Shu M.; Chen L.; Gaur P.; Vidya Sagar A.; Ramakrishna G.; Bernice T.	Efficacy and safety of secukinumab for treating ankylosing spondylitis in China, japan, and korea: A systematic literature review	2021	Irrelevant study design
213	Sokolova V.; Mladov V.; Tolkacheva D.	PBI15 Biologics to Treat Adults with Active Radiographic Axial Spondyloarthritis in the Russian Federation: Number Needed to Treat and Cost per Responder	2021	Irrelevant study design
214	Song G.G.; Lee Y.H.	Comparative efficacy and safety of secukinumab 75 mg, 150 mg, and 300 mg in patients with active ankylosing spondylitis	2021	Irrelevant study design
215	Soriano E.R.; Elewski B.; Baddley J.; Deodhar A.; Magrey M.; Rich P.; Soung J.; Sharma A.; Bao W.; Patekar M.; Lebwohl M.	Lack of reactivation of tuberculosis in 12,319 patients with psoriasis, psoriatic arthritis and ankylosing spondylitis treated with secukinumab: An ad hoc analysis of pooled safety data from 28 clinicaltrials	2020	Irrelevant study design
216	Sornasse T.; Song I.H.; Radstake T.; McGonagle D.	Targeted serum proteomic analysis following upadacitinib treatment in ankylosing spondylitis shows robust suppression of innate and adaptive immune pathways with tissue repair modulation	2021	No relevant novel outcomes
217	Sornasse T.; Song I.-H.; Radstake T.; McGonagle D.	Targeted Serum Proteomic Analysis Following Upadacitinib Treatment in Ankylosing Spondylitis Shows Robust Suppression of Innate and Adaptive Immune Pathways with Tissue Repair Modulation	2020	No relevant novel outcomes
218	Su J.; Li M.; He L.; Zhao D.; Wan W.; Liu Y.; Xu J.; Liu H.; Jiang L.; Wu H.; Zuo X.; Huang C.; Li F.; Liu X.; Dong L.; Li T.; Chen H.; Li J.; He D.; Lu X.; Huang A.; Tao Y.; Wang Y.; Zhang Z.; Wei W.; Li X.; Zeng X.	Comparison of the Efficacy and Safety of Adalimumab (Humira) and the Adalimumab Biosimilar Candidate (HS016) in Chinese Patients with Active Ankylosing Spondylitis: A Multicenter, Randomized, Double-Blind, Parallel, Phase III Clinical Trial	2020	Already captured by 2020 SLR update
219	Subramonian, Anusree; Peprah, Kwakye; Picheca, Lory		2020	Irrelevant study design
220	Sun W.-T.; He Y.-H.; Dong M.-M.; Zhang Y.-N.; Peng K.-X.; Zhang Y.-M.; Lin Y.-D.; Yang C.; Peng P.-X.	The comparative safety of biological treatment in patients with axial spondylarthritis: a meta-analysis of randomized controlled trials with placebo	2020	Irrelevant study design
221	Tanaka Y.	A review of upadacitinib in rheumatoid arthritis	2020	Irrelevant study design

222	Tanski W.; Swiatoniowska-Lonc N.; Dudek K.; Jankowska-Polanska B.	Benefit of Biological Drugs for Quality of Life in Patients with Ankylosing Spondylitis: A Systematic Review and Meta-Analysis of Clinical Trials	2021	SLR/NMA to hand-search
223	Tolkacheva D.; Sokolova V.; Mladov V.	PBI2 EFFICACY AND SAFETY OF BIOLOGICS FOR THE TREATMENT OF ADULT PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN RUSSIA: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS	2020	Irrelevant study design
224	Torres R.; Manica S.; Santos F.	Pharmacological treatment of enthesitis-a systematic review on the efficacy of the available options	2021	Irrelevant study design
225	Truong S.L.; Chin J.; Liew D.F.L.; Zahir S.F.; Ryan E.G.; Rubel D.; Radford-Smith G.; Robinson P.C.	Systematic Review and Meta-Analysis of Inflammatory Bowel Disease Adverse Events with Anti-Interleukin 17A Agents and Tumor Necrosis Factor Inhibitors in Rheumatic Disease and Skin Psoriasis	2021	Irrelevant study design
226	Tsai W.; Bao C.; Furtner D.; Hung Lo K.; Zhou Y.; Hsia E.	Improvements in patient-reported outcomes in AS patients treated with golimumab: Sub-analysis of asian patients enrolled in phase III clinical trials	2020	Irrelevant study design
227	Tsai W.C.; Bao C.; Furtner D.; Lo K.H.; Zhou Y.; Hsia E.C.	Improvements in patient-reported outcomes in ankylosing spondylitis patients treated with golimumab: Sub-analysis of asian patients enrolled in phase-3 clinical trials	2021	Irrelevant study design
228	Tseng J.-C.; Wei J.C.-C.; Deodhar A.; Martin R.; Porter B.; McCreddin S.; Talloczy Z.	Secukinumab Demonstrates Sustained Efficacy and Safety in a Taiwanese Subpopulation With Active Ankylosing Spondylitis: Four-Year Results From a Phase 3 Study, MEASURE 1	2020	No relevant novel outcomes
229	Uhrenholt L.; Christensen R.; Dinesen W.K.H.; Liboriussen C.H.; Andersen S.S.; Dreyer L.; Schlemmer A.; Hauge E.-M.; Skrubbeltrang C.; Taylor P.C.; Kristensen S.	Risk of flare after tapering or withdrawal of b-/tsDMARDs in patients with RA or axSpA: A systematic review and meta-analysis	2021	Irrelevant study design
230	Van Den Bosch F.; Nash P.; Wei J.C.-C.; Blanco F.; Tsekouras V.; Zang C.; Graham D.; Arthur E.; Selema P.; Vlahos B.; Deodhar A.	Efficacy Outcomes Following Etanercept Withdrawal by Sustained Remission Status in Patients with Nr-axSpA: Results from RE-EMBARK	2020	Irrelevant intervention/comparators
231	Van Den Bosch F.; Poddubnyy D.; Stigler J.; Ostor A.; D'Angelo S.; Navarro-Compan V.; Song I.-H.; Gao T.; Ganz F.; Gensler L.	Influence of baseline demographics on improvements in disease activity measures in patients with ankylosing spondylitis receiving upadacitinib: A post hoc subgroup analysis	2021	Duplicate
232	Van Den Bosch F.; Wei J.C.-C.; Blanco F.; Selema P.; Graham D.; Arthur E.; Tsekouras V.; Vlahos B.; Zang C.; Deodhar A.; Nash P.	Predictors of Maintaining Inactive Disease after Etanercept Withdrawal, and Regaining Inactive Disease Status after Flare and Retreatment, in Adults with Non-radiographic Axial Spondyloarthritis: Results from RE-EMBARK	2020	Irrelevant intervention/comparators
233	Van Den Bosch F.; Wei J.C.C.; Nash P.; Blanco F.J.; Graham D.; Zang C.; Arthur E.; Borlenghi C.; Vlahos B.; Deodhar A.	Etanercept withdrawal and re-treatment in patients with inactive non-radiographic axial spondyloarthritis at 24 weeks: Results of re-embark, an open-label, phase iv trial	2020	Irrelevant intervention/comparators
234	Van Der Heijde D.; Deodhar A.; Maksymowych W.; Sieper J.; Van Den Bosch F.; Kim T.-H.; Kishimoto M.; Ostor A.; Combe B.; Sui Y.; Duan Y.; Chu A.D.; Song I.-H.	Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis: 2-year results from a randomized, double-blind, placebo-controlled study with open-label extension	2021	No relevant novel outcomes
235	van der Heijde D.; Dougados M.; Maksymowych W.P.; Bergman G.; Curtis S.P.; Tzontcheva A.; Huyck S.; Philip G.; Sieper J.	Long-term tolerability and efficacy of golimumab in active non-radiographic axial spondyloarthritis: results from open-label extension	2022	No relevant novel outcomes
236	Van Der Heijde D.; Gensler L.; Maksymowych W.; Landewe R.; Rudwaleit M.; Bauer L.; Hoepken B.; Kumke T.; Kim M.; Deodhar A.	Long-term safety and efficacy of certolizumab pegol in patients with active non-radiographic axial spondyloarthritis: 3-year results from a phase 3 multicenter study	2021	Superseded by later publication with identical data

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237	Van der Heijde D.; Gensler L.S.; Deodhar	Erratum: Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double blind, placebo-controlled, dose-ranging study (Ann of Rheum Dis (2020	2020	Already captured by 2020 SLR update
238	Van Der Heijde D.; Gensler L.S.; Deodhar A.; Baraliakos X.; Poddubnyy D.; Kivitz A.; Farmer M.K.; Baeten D.; Goldammer N.; Coarse J.; Oortgiesen M.; Dougados M.	Efficacy and safety of bimekizumab in ankylosing spondylitis: 48-week patientreported outcomes from a phase 2b, randomised, double-blind, placebocontrolled, dose-ranging study	2020	Superseded by later publication with identical data
239	Van Der Heijde D.; Gensler L.S.; Deodhar A.; Baraliakos X.; Poddubnyy D.; Kivitz A.; Farmer M.K.; Baeten D.; Goldammer N.; Coarse J.; Oortgiesen M.; Dougados M.	Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: Results from a 48-week phase IIb, randomised, double-blind, placebo-controlled, dose-ranging study	2020	Already captured by 2020 SLR update
240	Van Der Heijde D.; Gensler L.S.; Maksymowych W.P.; Landewe R.; Rudwaleit M.; Bauer L.; Kumke T.; Kim M.; Auteri S.E.; Hoepken B.; Deodhar A.	Long-term safety and clinical outcomes of certolizumab pegol treatment in patients with active non-radiographic axial spondyloarthritis: 3-year results from the phase 3 C-axSpAnd study	2022	Irrelevant study design
241	Van Der Heijde D.; Ostergaard M.; Reveille J.D.; Baraliakos X.; Kronbergs A.; Sandoval D.; Li X.; Carlier H.; Adams D.; Maksymowych W.P.	Evaluation of spinal radiographic progression in patients with radiographic axial spondyloarthritis receiving ixekizumab therapy over 2 years	2021	Duplicate
242	van der Heijde D.; Ostergaard M.; Reveille J.D.; Baraliakos X.; Kronbergs A.; Sandoval D.M.; Li X.; Carlier H.; Adams D.H.; Maksymowych W.P.	Spinal Radiographic Progression and Predictors of Progression in Patients With Radiographic Axial Spondyloarthritis Receiving Ixekizumab Over 2 Years	2022	No relevant novel outcomes
243	Van Der Heijde D.; Ostergaard M.; Reveille J.D.; Baraliakos X.; Kronbergs A.; Sandoval D.M.; Li X.; Carlier H.; Adams D.H.; Maksymowych W.P.; De Lima Tostes C.	Evaluation of spinal radiographic progression in patients with radiographic axial spondyloarthritis receiving ixekizumab therapy over 2 years	2021	Duplicate
244	Van Der Horst-Bruinsma I.; Bolce R.; Hunter T.; Calderon D.S.; Zhu D.; Geneus V.; Lisse J.; Liu-Leage S.; Magrey M.	Baseline characteristics and treatment response to ixekizumab categorised by sex in radiographic and non-radiographic axial spondylarthritis patients through 52 weeks: Data from 3 phase iii, randomized, controlled trials	2021	Duplicate
245	Van Der Horst-Bruinsma I.; Bolce R.; Hunter T.; Sandoval D.; Zhu D.; Geneus V.J.; Lisse J.; Liu Leage S.; Magrey M.	Baseline characteristics and treatment response to ixekizumab categorised by sex in radiographic and non-radiographic axial spondylarthritis patients through 52 weeks: Data from 3 phase iii, randomized, controlled trials	2021	Superseded by later publication with identical data
246	van der Horst-Bruinsma I.; Miceli-Richard C.; Braun J.; Marzo-Ortega H.; Pavelka K.; Kivitz A.J.; Deodhar A.; Bao W.; Porter B.; Pournara E.	A Pooled Analysis Reporting the Efficacy and Safety of Secukinumab in Male and Female Patients with Ankylosing Spondylitis	2021	No relevant novel outcomes
247	van der Horst-Bruinsma I.E.; de Vlam K.; Walsh J.A.; Bolce R.; Hunter T.; Sandoval D.; Zhu D.; Geneus V.; Soriano E.R.; Magrey M.	Baseline Characteristics and Treatment Response to Ixekizumab Categorised by Sex in Radiographic and Non-radiographic Axial Spondylarthritis Through 52 Weeks: Data from Three Phase III Randomised Controlled Trials	2022	No relevant novel outcomes
248	Vinson, D; Molet-Benhamou, L; Degboe, Y; den Broeder, A; Ibrahim, F; Pontes, C; Westhovens, R; Zavada, J; Pham, T; Barnetche, T; Constantin, A; Ruyssen-Witrand, A	Impact of tapering targeted therapies (bDMARDs or JAKis) on the risk of serious infections and adverse events of special interest in patients with rheumatoid arthritis or spondyloarthritis: a systematic analysis of the literature and meta-analysis.	2020	Irrelevant study design

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249	Walsh J.A.; Magrey M.N.; Baraliakos X.; Inui K.; Weng M.-Y.; Lubrano E.; van der Heijde D.; Boonen A.; Gensler L.S.; Strand V.; Braun J.; Hunter T.; Li X.; Zhu B.; Leon L.; Calderon D.M.S.; Kiltz U.	Improvement of Functioning and Health With Ixekizumab in the Treatment of Active Nonradiographic Axial Spondyloarthritis in a 52-Week, Randomized, Controlled Trial	2022	Already captured by 2020 SLR update
250	Wang L.; Ping X.; Chen W.; Xing W.	Performance of Janus kinase inhibitors in psoriatic arthritis with axial involvement in indirect comparison with ankylosing spondylitis: a retrospective analysis from pooled data	2021	Irrelevant study design
251	Wang P.; Zhang S.; Hu B.; Liu W.; Lv X.; Chen S.; Shao Z.	Efficacy and safety of interleukin-17A inhibitors in patients with ankylosing spondylitis: a systematic review and meta-analysis of randomized controlled trials	2021	Irrelevant study design
252	Wang R.; Dasgupta A.; Ward M.	Predicting Major Treatment Response to Tumor Necrosis Factor Inhibitorsin Patients with Ankylosing Spondylitis	2020	Irrelevant study design
253	Wang R.; Dasgupta A.; Ward M.M.	Predicting Probability of Response to Tumor Necrosis Factor Inhibitors for Individual Patients with Ankylosing Spondylitis	2022	Irrelevant study design
254	Webers C.; Stolwijk C.; Schiepers O.; Schoonbrood T.; Van Tubergen A.; Landewe R.; Van Der Heijde D.; Boonen A.	Infliximab treatment reduces depressive symptoms in patients with ankylosing spondylitis: An ancillary study to a randomized controlled trial (ASSERT)	2020	Already captured by 2020 SLR update
255	Wei, James Cheng-Chung; Kim, Tae-Hwan; Kishimoto, Mitsumasa; Ogusu, Naoki; Jeong, Haeyoun; Kobayashi, Shigeto	Response to: 'Correspondence on 'Efficacy and safety of brodalumab, an anti-IL17RA monoclonal antibody, in patients with axial spondyloarthritis: 16-week results from a randomised, placebo-controlled, phase 3 trial'' by Zhao and Huang.	2021	Irrelevant study design
256	Wendling D.	Local sacroiliac injections in the treatment of spondyloarthritis. What is the evidence?	2020	Irrelevant study design
257	Xenofon B.; Atul D.; Roberto R.; Simona R.; Francesco C.; Fabiana G.; Tianming G.; In-Ho S.; Apinya L.; Andrew O.; Laura C.C.	Comparison of axial and peripheral manifestations in patients with psoriatic arthritis and ankylosing spondylitis in upadacitinib clinical trials	2021	Irrelevant study design
258	Yin Y.; Wang M.; Liu M.; Zhou E.; Ren T.; Chang X.; He M.; Zeng K.; Guo Y.; Wu J.	Efficacy and safety of IL-17 inhibitors for the treatment of ankylosing spondylitis: A systematic review and meta-analysis	2020	Irrelevant study design
259	Zhang T.; Zhu J.; He D.; Chen X.; Wang H.; Zhang Y.; Xue Q.; Liu W.; Xiang G.; Li Y.; Yu Z.; Wu H.	Disease activity guided stepwise tapering or discontinuation of rhTNFR:Fc, an etanercept biosimilar, in patients with ankylosing spondylitis: a prospective, randomized, open-label, multicentric study	2020	Already captured by 2020 SLR update
260	Zhao D.; He D.; Bi L.; Wu H.; Liu Y.; Wu Z.; Li Y.; Wang G.; Li X.; Bao C.; Jiang L.; Zhang Z.; Xiao W.; Tong G.; Wang D.; Huang F.	Safety and Efficacy of Prefilled Liquid Etanercept-Biosimilar Yisaipu for Active Ankylosing Spondylitis: A Multi-Center Phase III Trial	2021	Irrelevant intervention/comparators
261	Zhao Y; Huang J-X	Correspondence on a Efficacy and safety of brodalumab, an anti-IL17RA monoclonal antibody, in patients with axial spondyloarthritis: 16-week results from a randomized, placebo-controlled, phase 3 trial'	2021	Irrelevant study design
262	Zhou Y.; Ma J.; Ge J.; Wang B.; Yue D.; Wang W.	Short-term efficacy and safety of secukinumab for ankylosing spondylitis: A systematic review and meta-analysis of RCTs	2020	Irrelevant study design
263	Anonymous	Study to Evaluate the Efficacy and Safety of Filgotinib in Participants With Active Ankylosing Spondylitis Who Have an Inadequate Response to Biologic Disease-Modifying Antirheumatic Drug Therapy	2020	No relevant novel outcomes
264	Anonymous	Study to Evaluate the Efficacy and Safety of Filgotinib in Participants With Active Ankylosing Spondylitis Who Are Naive to Biologic Disease-Modifying Antirheumatic Drug Therapy	2020	No relevant novel outcomes
265	Anonymous	Efficacy and Safety Study of Secukinumab in Chinese Participants With Non-radiographic Axial Spondyloarthritis	2021	Irrelevant study design

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266	Anonymous	Safety and Efficacy Study of Prefilled Liquid Etanercept(Yisaipu) for Active Ankylosing Spondylitis	2020	Irrelevant intervention/comparators
267	Anonymous	Evaluate the Preliminary Efficacy, Safety, and PK of Subcutaneous JS005 in Chinese Adult Patients With Active AS	2022	Irrelevant intervention/comparators
268	Anonymous	Evaluate the Preliminary Efficacy, Safety, and PK of Subcutaneous JS005 in Chinese Adult Patients With Active Nr-axSpA	2022	Irrelevant intervention/comparators
269	Anonymous	A clinical trial to study the safety and efficacy of Biosimilar Adalimumab injection versus HUMIRAÂ® in subjects with active Ankylosing spondylitis	2020	No relevant novel outcomes
270	Anonymous	A Study of Ixekizumab (LY2439821) in Chinese Participants With Radiographic Axial Spondyloarthritis	2020	No relevant novel outcomes
271	Anonymous	Erratum: correction: dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double blind, placebo-controlled, dose-ranging study (Annals of	2020	Already captured by 2020 SLR update

Table 96 Publications excluded at the full-text screening stage in the January 2023 clinical SLR update (n=49)

#	Authors	Title	Year	Reason for exclusion	SLR iteration
1	Baraliakos X.; Deodhar A.; Dougados M.; Gensler L.S.; Molto A.; Ramiro S.; Kivitz A.J.; Poddubnyy D.; Oortgiesen M.; Vaux T.; Fleurinck C.; Shepherd-Smith J.; de la Loge C.; de Peyrecave N.; van der Heijde D.	Safety and Efficacy of Bimekizumab in Patients With Active Ankylosing Spondylitis: Three-Year Results From a Phase IIb Randomized Controlled Trial and Its Open-Label Extension Study	2022	No relevant novel outcomes	8th update (January 2023)
2	Baraliakos X.; Sewerin P.; de Miguel E.; Pournara E.; Kleinmond C.; Shekhawat A.; Jentzsch C.; Wiedon A.; Behrens F.	Magnetic resonance imaging characteristics in patients with spondyloarthritis and clinical diagnosis of heel enthesitis: post hoc analysis from the phase 3 ACHILLES trial	2022	Irrelevant population	8th update (January 2023)
3	Braun J.; Kiltz U.; Deodhar A.; Tomita T.; Dougados M.; Bolce R.; Sandoval D.; Lin C.-Y.; Walsh J.	Efficacy and safety of ixekizumab treatment in patients with axial spondyloarthritis: 2-year results from COAST	2022	No relevant novel outcomes	8th update (January 2023)
4	Burmester G.R.; Cohen S.B.; Winthrop K.; Nash P.; Rubbert-Roth A.; Deodhar A.; Elkayam O.; Mysler E.; Tanaka Y.; Liu J.; Lacerda A.P.; Pierre-Louis B.J.; Shaw T.; Mease P.J.	Long-Term Safety Profile of Upadacitinib in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, or Ankylosing Spondylitis	2022	No relevant novel outcomes	8th update (January 2023)
5	Cao Z.; Guo J.; Li Q.; Li Y.; Wu J.	Optimal Biologic Drugs for the Treatment of Ankylosing Spondylitis: Results from a Network Meta-Analysis and Network Metaregression	2022	Irrelevant study design	8th update (January 2023)
6	Cella, David; Lenderking, William R; Chongpinitchai, Peter; Bushmakin, Andrew G; Dina, Oluwaseyi; Wang, Lisy; Cappelleri, Joseph C; Navarro-Compan, Victoria	Functional Assessment of Chronic Illness Therapy-Fatigue is a reliable and valid measure in patients with active ankylosing spondylitis.	2022	No relevant novel outcomes	8th update (January 2023)
7	Deodhar A.; Akar S.; Curtis J.; Zorkany B.; Magrey M.; Wang C.; Wu J.; Makgoeng S.B.; Vranic I.; Menon S.; Fleishaker D.; Diehl A.; Fallon L.; Yndestad A.; Landewe R.B.M.	INTEGRATED SAFETY ANALYSIS of TOFACITINIB in ANKYLOSING SPONDYLITIS CLINICAL TRIALS	2022	No relevant novel outcomes	8th update (January 2023)
8	Deodhar A.; Chakravarty S.D.; Shiff N.J.; Lo K.H.; Xu S.; Hsia E.C.; Danve A.; Reveille J.D.	Efficacy and Safety of Intravenous Golimumab in Patients With Ankylosing Spondylitis and Complete	2022	Irrelevant population	8th update (January 2023)

		Spinal Ankylosis: Results Through Week 52 of the GO-ALIVE Study			
9	Deodhar A.; Poddubnyy D.; Blanco R.; Hall S.; Magrey M.; Quebe-Fehling E.; Calheiros R.; Pertel P.; Marzo-Ortega H.	EFFICACY of SECUKINUMAB in PATIENTS with NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: ANALYSIS by SYMPTOM DURATION and AGE	2022	No relevant novel outcomes	8th update (January 2023)
10	Deodhar A.; Van Den Bosch F.; Poddubnyy D.; Maksymowych W.P.; Van Der Heijde D.; Kim T.H.; Kishimoto M.; Duan Y.; Li Y.; Pangan A.; Wung P.; Song I.H.	EFFICACY and SAFETY of UPADACITINIB in PATIENTS with ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL	2022	Already captured by 2022 SLR update	8th update (January 2023)
11	Deodhar A.; Van Der Heijde D.; Gensler L.S.; Xu H.; Gaffney K.; Dobashi H.; Maksymowych W.P.; Rudwaleit M.; Magrey M.; Elewaut D.; Oortgiesen M.; Fleurinck C.; Ellis A.; Vaux T.; Smith J.; Baraliakos X.	BIMEKIZUMAB in PATIENTS with ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 24-WEEK EFFICACY & SAFETY from BE MOBILE 1, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED STUDY	2022	Already captured by 2022 SLR update	8th update (January 2023)
12	Deodhar A.A.; Shiff N.J.; Gong C.; Hsia E.C.; Lo K.H.; Kim L.; Xu S.; Reveille J.D.	Efficacy and Safety of Intravenous Golimumab in Ankylosing Spondylitis Patients with Early and Late Disease Through One Year of the GO-ALIVE Study	2022	Irrelevant population	8th update (January 2023)
13	Hansmaennel A.; Gerazime A.; Fakih O.; Chouk M.; Prati C.; Wendling D.; Verhoeven F.	EFFECTS of DISEASE MODIFYING ANTI RHEUMATIC DRUGS on SACROILIAC MRI SCORE in AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW and META-ANALYSIS	2022	Irrelevant study design	8th update (January 2023)
14	Kiprianos A.; Van Der Horst-Bruinsma I.E.; Bolce R.; Hunter T.; Calderon D.M.S.; Zhu D.; Geneus V.; Lisse J.R.; Liu-Leage S.; Magrey M.	BASELINE CHARACTERISTICS AND TREATMENT RESPONSE TO IXEKIZUMAB CATEGORISED BY SEX IN RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLARTHRITIS PATIENTS THROUGH 52 WEEKS: DATA FROM THREE PHASE III, RANDOMIZED, CONTROLLED TRIALS	2022	No relevant novel outcomes	8th update (January 2023)
15	Landewe R.B.M.; Poddubnyy D.; Rahman P.; Bolce R.; Liu Leage S.; Lisse J.; Leung A.; Park S.Y.; Gensler L.S.	RECAPTURE RATES with IXEKIZUMAB after WITHDRAWAL of THERAPY in PATIENTS with AXIAL SPONDYLOARTHRITIS: RESULTS at WEEK 104 from A RANDOMIZED PLACEBO-CONTROLLED WITHDRAWAL STUDY	2022	No relevant novel outcomes	8th update (January 2023)
16	Landewe R.B.M.; Poddubnyy D.; Rahman P.; Van Den Bosch F.E.; Bolce R.; Liu Leage S.; Lisse J.R.; Park S.Y.; Gensler L.	Recapture and retreatment rates with ixekizumab after withdrawal of therapy in patients with axial spondyloarthritis: Results at week 104 from a randomised placebo-controlled withdrawal study	2022	No relevant novel outcomes	8th update (January 2023)
17	Lee Y.H.	Comparative Efficacy and Safety of Janus Kinase Inhibitors and Secukinumab in Patients with Active Ankylosing Spondylitis: A Systematic Review and Meta-Analysis	2022	Irrelevant study design	8th update (January 2023)
18	Macfarlane G.J.; Biallas R.; Dean L.E.; Jones G.T.; Goodson N.; Rotariu O.	THE RISK OF INFLAMMATORY BOWEL DISEASE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH BIOLOGIC AGENTS: DATA FROM THE BSR REGISTRY IN AXIAL SPONDYLOARTHRITIS (BSRBR-AS) AND METAANALYSIS	2022	Superseded by later publication with identical data	8th update (January 2023)
19	Macfarlane G.J.; Biallas R.; Dean L.E.; Jones G.T.; Goodson N.J.; Rotariu O.	The risk of inflammatory bowel disease in patients with axial spondyloarthritis treated with biologic agents: BSRBR-AS and meta-analysis	2022	Irrelevant study design	8th update (January 2023)
20	Magrey M.; Deodhar A.; Mease P.J.; Navarro-Compan V.; Ramiro S.; Rudwaleit M.; de la Loge C.; Fleurinck C.; Taieb V.; Morup M.F.; Oortgiesen M.; Kay J.	PCR196 Association of Clinical Response Criteria and Disease Activity Levels With Physical Function and HRQoL in Patients With Active Axial Spondyloarthritis: 16-Week Results From Two Phase 3 Randomised, Placebo-Controlled Studies	2022	No relevant novel outcomes	8th update (January 2023)

21	Maksymowych W.P.; Baraliakos X.; Lambert R.G.; Landewe R.; Sandoval D.; Carlier H.; Lisse J.; Li X.; Hojnik M.; Ostergaard M.	Effects of ixekizumab treatment on structural changes in the sacroiliac joint: MRI assessments at 16 weeks in patients with non-radiographic axial spondyloarthritis	2022	No relevant novel outcomes	8th update (January 2023)
22	Maksymowych W.P.; Baraliakos X.; Lambert R.G.; Landewe R.B.M.; Sandoval D.; Carlier H.; Lisse J.; Li X.; Hojnik M.; Ostergaard M.	STRUCTURAL OUTCOMES in the SACROILIAC JOINT after IXEKIZUMAB TREATMENT for 16 WEEKS in PATIENTS with ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS STRATIFIED by GENDER, HLA-B27, and BASELINE MRI INFLAMMATION	2022	No relevant novel outcomes	8th update (January 2023)
23	Maksymowych W.P.; Ostergaard M.; Landew R.; Barchuk W.; Liu K.; Tasset C.; Gilles L.; Hendrikx T.; Besuyen R.; Baraliakos X.	Impact of filgotinib on sacroiliac joint magnetic resonance imaging structural lesions at 12 weeks in patients with active ankylosing spondylitis (TORTUGA trial)	2022	No relevant novel outcomes	8th update (January 2023)
24	Maney N.; De Vlam K.; Conaghan P.G.; Mease P.J.; Rahman P.; Krishnan V.; Bolce R.; Calderon D.M.S.; Park S.Y.; Gallo G.; Maksymowych W.	IXEKIZUMAB SHOWS A DISTINCT PATTERN OF PAIN IMPROVEMENT BEYOND MEASURABLE INFLAMMATION AS ASSESSED BY MRI, CRP OR BASDAI QUESTIONS 5 AND 6 IN PATIENTS WITH ANKYLOSING SPONDYLITIS	2022	No relevant novel outcomes	8th update (January 2023)
25	Marzo-Ortega H.; Tsai W.-C.; Kameda H.; Konomi A.; Bradley A.J.; Ng K.J.; Schymura Y.; Liu-Leage S.; Maksymowych W.P.; Ostergaard M.	POST-HOC ANALYSIS OF SPINAL MRI SPARCC INFLAMMATION SCORES IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH IXEKIZUMAB: RESULTS FROM THE COAST-V STUDY AT WEEK 16	2022	No relevant novel outcomes	8th update (January 2023)
26	Merola J.F.; McInnes I.B.; Deodhar A.A.	33257 Secukinumab effects on cardiovascular risk factors in patients with psoriasis, psoriatic arthritis and axial spondyloarthritis: Results from post hoc analyses of pooled data from 19 phase 3/4 clinical studies	2022	No relevant novel outcomes	8th update (January 2023)
27	Nash P.; Burmester G.R.; Cohen S.B.; Winthrop K.; Rubbert-Roth A.; Deodhar A.; Elkayam O.; Mysler E.; Tanaka Y.; Liu J.; Lacerda A.P.; Pierre-Louis B.J.; Shaw T.; Mease P.J.	LONG-TERM SAFETY PROFILE OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR ANKYLOSING SPONDYLITIS	2022	No relevant novel outcomes	8th update (January 2023)
28	Navarro-Compan V.; Reveille J.D.; Rahman P.; Maldonado-Cocco J.; Magrey M.; Bolce R.; Sandoval D.; Park S.Y.; Kronbergs A.; Rudwaleit M.	IXEKIZUMAB IMPROVES SIGNS, SYMPTOMS, and QUALITY of LIFE in PATIENTS with AXIAL SPA IRRESPECTIVE of DISEASE DURATION: RESULTS from the COAST-V, COAST-W and COAST-X TRIALS	2022	No relevant novel outcomes	8th update (January 2023)
29	Navarro-Compan V.; Rudwaleit M.; De Peyrecave N.; Fleurinck C.; Oortgiesen M.; Taieb V.; Baraliakos X.	MAINTENANCE of RESPONSE to BIMEKIZUMAB over 3 YEARS of TREATMENT in PATIENTS with ACTIVE ANKYLOSING SPONDYLITIS: POST HOC ANALYSES from the BE AGILE STUDY and ITS OPEN-LABEL EXTENSION	2022	No relevant novel outcomes	8th update (January 2023)
30	Pinto A.S.; Farisogullari B.; Machado P.M.	Predictors of remission in people with axial spondyloarthritis: A systematic literature review	2022	SLR/NMA to hand-search	8th update (January 2023)
31	Ramiro S.; Lukas C.; Nissen M.J.; Schymura Y.; Ng K.; Bradley A.; Doridot G.; Liu Leage S.; Chan A.; Wei J.C.C.	EFFICACY and IMPROVEMENT in PATIENT-REPORTED OUTCOMES at WEEKS 16 and 52 in IXEKIZUMAB TREATED BIOLOGICAL NAIVE PATIENTS with RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS ACHIEVING CLINICALLY IMPORTANT PAIN at NIGHT REDUCTION at WEEK 16: RESULTS from COAST-V TRIA	2022	No relevant novel outcomes	8th update (January 2023)
32	Rios Rodriguez V.; Torgutalp M.; Haibel H.; Hermann K.G.A.; Proft F.; Protopopov M.; Rademacher J.; Sieper J.; Poddubnyy D.	MRI CHANGE SCORE but NOT the STATUS SCORE IS RELATED to DISEASE ACTIVITY and CLINICAL RESPONSE over TIME in PATIENTS with AXIAL SPONDYLOARTHRITIS: RESULTS from ESTHER STUDY	2022	No relevant novel outcomes	8th update (January 2023)
33	Robinson P.; Maksymowych W.P.; Gensler L.S.; Rudwaleit M.;	LONG-TERM CLINICAL OUTCOMES of CERTOLIZUMAB PEGOL TREATMENT in PATIENTS with ACTIVE NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS	2022	No relevant novel outcomes	8th update (January 2023)

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	Hoepken B.; Bauer L.; Kumke T.; Kim M.; Deodhar A.	STRATIFIED by BASELINE MRI and C-REACTIVE PROTEIN STATUS			
34	Rusman T.; van der Weijden M.A.C.; Nurmohamed M.T.; van Denderen C.J.; Landewe R.B.M.; Bet P.M.; Bijl C.; vander Laken C.J.; van der Horst-Bruinsma I.E.	Does a short course of etanercept influence disease progression and radiographic changes in patients suspected of non-radiographic axial spondyloarthritis? Three -years follow- up of a placebo-controlled trial	2022	No relevant novel outcomes	8th update (January 2023)
35	Schneeberger E.E.; Citera G.; de Leon D.P.; Szumski A.E.; Kwok K.; Cutri M.; Dougados M.	Simplified Ankylosing Spondylitis Disease Activity Score (SASDAS) Versus ASDAS: A Post Hoc Analysis of a Randomized Controlled Trial	2022	No relevant novel outcomes	8th update (January 2023)
36	Shaw T.; Burmester G.R.; Cohen S.B.; Winthrop K.; Nash P.; Rubbert-Roth A.; Deodhar A.; Elkayam O.; Mysler E.; Tanaka Y.; Liu J.; Lacerda A.P.; Pierre-Louis B.J.; Mease P.J.	LONG-TERM SAFETY PROFILE OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR ANKYLOSING SPONDYLITIS	2022	No relevant novel outcomes	8th update (January 2023)
37	Tay T.; Marzo-Ortega H.; Juanola X.; Okano T.; Schymura Y.; Bradley A.; Gerwien J.; Monsberger B.; Liu-Leage S.; Aletaha D.; Ostergaard M.	NORMALISATION OF HIGH SENSITIVITY CRP VERSUS CLINICAL RESPONSE TO IXEKIZUMAB AT WEEK 16 IN PATIENTS WITH RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE COAST-V/W/X STUDIES	2022	No relevant novel outcomes	8th update (January 2023)
38	Tay T.; Schwartzman S.; Deodhar A.; Combe B.; Accioly A.; Kronbergs A.; Janos B.; Zhu D.; Sandoval D.; Rahman P.; Poddubnyy D.	SAFETY PROFILE OF IXEKIZUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS UP TO 3 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS	2022	No relevant novel outcomes	8th update (January 2023)
39	Tiburca L.; Bembea M.; Zaha D.C.; Jurca A.D.; Vesa C.M.; Ratiu I.A.; Jurca C.M.	The Treatment with Interleukin 17 Inhibitors and Immune-Mediated Inflammatory Diseases	2022	Irrelevant study design	8th update (January 2023)
40	Van Der Heijde D.; Baraliakos X.; Dougados M.; Brown M.; Poddubnyy D.; Van Den Bosch F.; Haroon N.; Xu H.; Tomita T.; Gensler L.S.; Oortgiesen M.; Fleurinck C.; Vaux T.; Marten A.; Deodhar A.	BIMEKIZUMAB in PATIENTS with ACTIVE ANKYLOSING SPONDYLITIS: 24-WEEK EFFICACY & SAFETY from BE MOBILE 2, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED STUDY	2022	Already captured by 2022 SLR update	8th update (January 2023)
41	Van Der Heijde D.; Baraliakos X.; Sieper J.; Deodhar A.; Inman R.; Kameda H.; Zeng X.; Sui Y.; Bu X.; Pangan A.; Wung P.; Song I.H.	EFFICACY and SAFETY of UPADACITINIB in PATIENTS with ACTIVE ANKYLOSING SPONDYLITIS REFRACTORY to BIOLOGIC THERAPY: A DOUBLEBLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL	2022	Already captured by 2022 SLR update	8th update (January 2023)
42	Van Der Heijde D.; Deodhar A.; Maksymowych W.P.; Sieper J.; Van Den Bosch F.; Kim T.-H.; Kishimoto M.; Ostor A.; Combe B.; Sui Y.; Duan Y.; Chu A.D.; Song I.-H.	EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 2-YEAR RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY WITH OPEN-LABEL EXTENSION	2022	No relevant novel outcomes	8th update (January 2023)
43	Weinstein C.; Govoni M.; Lin J.; Meehan A.; Qureshi Z.	LONG-TERM GOLIMUMAB PERSISTENCE: 5-YEAR TREATMENT RETENTION DATA POOLED from FIVE PHASE III CLINICAL TRIALS in PATIENTS with RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, and ANKYLOSING SPONDYLITIS	2022	No relevant novel outcomes	8th update (January 2023)
44	Zong H.-X.; Xu S.-Q.; Wang J.-X.; Chu Y.-R.; Chen K.-M.; Wang C.; Tong W.-Q.; Wang X.-L.	Presence of subclinical inflammation in axial spondyloarthritis patients with NSAID/anti-TNF-alpha drug-induced clinical remission	2022	Irrelevant intervention/comparators	8th update (January 2023)
45	Trial record (NCT05303285)	A Study Evaluating the Efficacy of Secukinumab 300mg in Chinese Adults With Active Ankylosing Spondylitis	2022	No relevant novel outcomes	8th update (January 2023)
46	Trial record (KCT0007642)	Evaluation of Efficacy and Safety of Eucept in Subjects with Active Spondyloarthritis	2022	No relevant novel outcomes	8th update (January 2023)

47	Trial record (NCT05527444)	The Clinical Efficacy and the Changes of Immune Cells Subsets With Bioagents in Ankylosing Spondylitis Patients	2022	No relevant novel outcomes	8th update (January 2023)
48	Trial record (KCT0007239)	The prospect, non-inferiority study comparing subcutaneous infliximab and adalimumab by evaluating the recurrence of non-infectious acute anterior uveitis in patients with moderate to severe ankylosing spondylitis patients who had prior acute anterior uve	2022	No relevant novel outcomes	8th update (January 2023)
49	Trial record (CTRI/2022/05/042887)	To look the effectiveness of the tablet "Tofacitinib" in a disease causing back pain "Ankylosing spondylitis" and its correlation with blood test markers causing this disease	2022	No relevant novel outcomes	8th update (January 2023)

Of the 341 publications reporting on 65 trials from the consolidated SLR (all SLRs conducted, as illustrated in Table 97) 37 met the eligibility criteria for the global NMA and ITCs.

Table 97 Publications included across all iterations of the global clinical SLR (n=341)

Trial	Trial identifier	Citation	Source	SLR iteration
ABILITY-1 (2)	NCT00939003	**Sieper J, van der Heijde D, Dougados M, Mease PJ, Maksymowych WP, Brown MA, et al. Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). Ann Rheum Dis. 2013;72(6):815-22.**	Database searches	1st update (October 2013)
		Maksymowych WM, PJ., Rao S, Pangan A, Brown SA, V. Cifaldi, MA. Effect of Adalimumab on Function, Health-Related Quality of Life, Work Productivity, and Daily Activities in Patients with Non-Radiographic Axial Spondyloarthritis. Presentation number: 1312. ACR/ARHP Scientific Meeting. November 7. 2011.	Hand searches	Original SLR (May 2012)
		Sieper J. Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis – results from a phase 3 study. Abstract 2468A. American College of Rheumatology Annual Scientific Meeting. 2011.	Hand searches	Original SLR (May 2012)
		Sieper J. Sustained efficacy of adalimumab in patients with non-radiographic axial spondyloarthritis: week 68 results from ABILITY 1. Abstract THU0275. European League Against Rheumatism Annual European Congress of Rheumatology. 2012.	Hand searches	Original SLR (May 2012)
		Maksymowych, W. P., P. J. Mease, et al. (2011). "Effect of adalimumab on function, health-related quality of life, work productivity, and daily activities in patients with non-radiographic axial spondyloarthritis." Arthritis and Rheumatism 63(10).	Database searches	1st update (October 2013)
		Sieper, J., D. Van Der Heijde, et al. (2011). "Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis results from a phase 3 study." Arthritis and Rheumatism 63(10).	Database searches	1st update (October 2013)
		Sieper, J., D. Van Der Heijde, et al. (2013). "Sustained efficacy of adalimumab in patients with non-radiographic axial spondyloarthritis with positive MRI of the sacroiliac joints or spine or elevated C-reactive protein at baseline." Rheumatology (United Kingdom) 52: i52-i53.	Database searches	1st update (October 2013)
		van der Heijde D, Sieper J, Maksymowych WP, Brown MA, Lambert RG, Rathmann SS, et al. Spinal inflammation in the absence of sacroiliac joint inflammation on magnetic resonance imaging in patients with active nonradiographic axial spondyloarthritis. Arthritis Rheumatol. 2014;66(3):667-73.	Database searches	2nd update (July 2014)
		van Der Heijde D, Mease P, Pangan A, A Rao S, Chen NC, M. Improvement in physical function, health-related quality of life, and work productivity with adalimumab treatment in non-radiographic axial spondyloarthritis. Arthritis and Rheumatism.65:S1052.	Database searches	2nd update (July 2014)

		van der Heijde. Improvement In Physical Function, Health-Related Quality Of Life, and Work Productivity With Adalimumab Treatment In Non-Radiographic Axial Spondyloarthritis. Abstract 2459, ACR 2013.	Hand searches	1st update (October 2013)
		Sieper. Sustained Efficacy Of Adalimumab In Patients With Non-Radiographic Axial Spondyloarthritis With Positive MRI Of The Sacroiliac Joints Or Spine Or Elevated C-Reactive Protein At Baseline. Abstract O56, BSR 2013.	Hand searches	1st update (October 2013)
		van der Heijde. [SAT0339] ASAS40 and ASDAS responses are associated with improved physical function, HRQOL, and work productivity in patients with non-radiographic axial spondyloarthritis. EULAR 2014.	Hand searches	2nd update (July 2014)
		van der Heijde. [SAT0337] Clinical response and remission in patients with non-radiographic axial spondyloarthritis after three years of adalimumab therapy. EULAR 2014.	Hand searches	2nd update (July 2014)
		Sieper J, Baeten DL, Van den Bosch F, Rathmann SS, Anderson J, Pangan AL. 215. Sustained Clinical Remission in Patients with Non-Radiographic Axial Spondyloarthritis after Two Years of Adalimumab Treatment. Rheumatology. 2014;53(suppl_1):i140.	Hand searches	2nd update (July 2014)
		van der Heijde D, Maksymowych WP, Sieper J, Lambert RG, Brown MA, Rathmann SS, et al. 229. Relationship Between MRI AND Clinical Remission in Patients with Non-Radiographic Axial Spondyloarthritis After Two Years of Adalimumab Therapy. Rheumatology. 2014;53(suppl_1):i145.	Hand searches	2nd update (July 2014)
ABILITY-3 (3)	NCT01808118	**Landewe R, Sieper J, Mease P, Inman RD, Lambert RG, Deodhar A, et al. Efficacy and safety of continuing versus withdrawing adalimumab therapy in maintaining remission in patients with non-radiographic axial spondyloarthritis (ABILITY-3): a multicentre, randomised, double-blind study. Lancet. 2018;392(10142):134-44.**	Database searches	5th update (April 2019)
		Landewé RBM, Sieper J, Kiltz U, Wang X, Li M, Anderson JK. Potential Differences in Axial Spondyloarthritis Disease Activity Categorization Using Different Minimum Values for High-Sensitivity CRP in Ankylosing Spondylitis Disease Activity Score Calculation and Different Definitions of Disease Flare [abstract]. Arthritis Rheumatol. 2017;69.	Database searches	4th update (April 2018)
		Landewé RBM, Sieper J, Mease P, Inman RD, Li M, Anderson JK. Efficacy and Safety of Continuing Versus Withdrawing Adalimumab in Maintaining Remission in Patients with Non-Radiographic Axial Spondyloarthritis [abstract]. Arthritis Rheumatol. 2017;69.	Database searches	4th update (April 2018)
		Landewé R, Sieper J, Mease P, Inman R, Wang X, Li M, et al. Efficacy and safety of continuing versus withdrawing adalimumab in maintaining remission in patients with non-radiographic axial spondyloarthritis. Abstracts, 20th PANLAR Meeting: Buenos Aires, April 2018. Journal of Clinical Rheumatology. 2018;24(pS1-pS174).	Database searches	5th update (April 2019)
		Landewé R, Sieper J, Kiltz U, Wang X, Li M, Anderson J. OP0248 Potential differences in axial spondyloarthritis disease activity categorization using different minimum values for high-sensitivity crp in ankylosing spondylitis disease activity score calculation and different definitions of disease flare. Annals of the Rheumatic Diseases. 2018;77(Suppl 2):173-.	Database searches	5th update (April 2019)
		Landewé R, Sieper J, Mease P, Inman R, Wang X, Li M, et al. OP0334 Efficacy and safety of continuing versus withdrawing adalimumab (ADA) in maintaining remission in patients with non-radiographic axial spondyloarthritis (NR-AXSPA). Annals of the Rheumatic Diseases. 2018;77(Suppl 2):213-.	Database searches	5th update (April 2019)
		clinicaltrials.gov. Continuing Versus Withdrawing Adalimumab in Maintaining Remission in Non-Radiographic Axial Spondyloarthritis. Available at: https://clinicaltrials.gov/show/nct01808118. 2013.	Database searches	5th update (April 2019)
		Emery P, Halliday A, Jugl S, Mokashi S, Porter B, Martin R, et al. Week 12 response predicts long-term efficacy of secukinumab in patients with active ankylosing spondylitis independent of previous TNFi exposure. Poster presented at the British Society for Rheumatology; April 2017. Birmingham, United Kingdom. 2017.	Hand searches	5th update (April 2019)
ASART-2 (4)	None	**Denisov L, Shesternya P, Plaksina T, Kropotina T, Soroka N, Kunder E, et al. SAT0267 Efficacy and safety of bcd-055, proposed infliximab biosimilar,**	Database searches	5th update (April 2019)

		compared to infliximab: 54-week results from asart-2 phase 3 clinical study. Annals of the Rheumatic Diseases. 2018;77(Suppl 2):997.		
ASCEND (5)	NCT00247962	**Braun J, van der Horst-Bruinsma IE, Huang F, Burgos-Vargas R, Vlahos B, Koenig AS, et al. Clinical efficacy and safety of etanercept versus sulfasalazine in patients with ankylosing spondylitis: a randomized, double-blind trial. Arthritis Rheum. 2011;63(6):1543-51.**	Database searches	Original SLR (May 2012)
		Freundlich B. Assessment of clinical efficacy in a randomized, double-blind study of etanercept and sulphasalazine in patients with ankylosing spondylitis. Internal Medicine Journal. 2009.39 SUPPL2 A55 (May 2009 C)	Database searches	Original SLR (May 2012)
		Guzman R. Etanercept is significantly more effective than sulfasalazine in patients with Ankylosing spondylitis. Journal of Clinical Rheumatology. 2010. 16 SUPPL:S73.	Database searches	Original SLR (May 2012)
		van der Heijde DM. Clinical improvement with Etanercept versus sulfasalazine treatment in patients with ankylosing spondylitis: Comparative performance of various efficacy measurements (ASCEND). Arthritis and rheumatism. 2010. 62 SUPPL:1927.	Database searches	Original SLR (May 2012)
		van der Horst-Bruinsma IE, Braun J, Huang F, Burgos-Vargas R, Freundlich B, Vlahos B, et al. Assessment of clinical efficacy in a randomized, double-blind study of etanercept and sulphasalazine in patients with ankylosing spondylitis [abstract 85]. Rheumatology. 2009;48:i49-i58.	Database searches	Original SLR (May 2012)
		Damjanov N, Szumski A, Tang B, Kapolika D, Youseif EA, Bananis E, et al. Eastern Europe, Latin America, and Asia efficacy outcomes ofetanercept versus sulfasalazine treatment in patients with ankylosingspondylitis: results of the ASCEND study [abstract 703380]. Int J Rheum Dis. 2012;15:88-91.	Database searches	1st update (October 2013)
		Van Der Heijde D, Braun J, Dougados M, Sieper J, Pedersen R, Szumski A, et al. Sensitivity and discriminatory ability of the Ankylosing Spondylitis Disease Activity Score in patients treated with etanercept or sulphasalazine in the ASCEND trial. Rheumatology. 2012;51(10):1894-905.	Database searches	1st update (October 2013)
		Damjanov N, Shehhi WA, Huang F, Kotak S, Burgos-Vargas R, Shirazy K, et al. Assessment of clinical efficacy and safety in a randomized double-blind study of etanercept and sulfasalazine in patients with ankylosing spondylitis from Eastern/Central Europe, Latin America, and Asia. Rheumatology international. 2016;36(5):643-51.	Database searches	3rd update (January 2017)
		Huang F, Taylor A, Chen S, Schachna L, Braun J, Wishneski C, et al. Etanercept is significantly more effective than sulfasalazine in patients with ankylosing spondylitis [abstract 0270]. International Journal of Rheumatic Diseases. 2010;13:153.	Database searches	Original SLR (May 2012)
		Sieper J, Li W, Koenig AS, Stewart M. THU0488. Relationship between spinal mobility and physical function in ankylosing spondylitis in the ASCEND trial. Annals of the Rheumatic Diseases. 2011;70(341).	Hand searches	Original SLR (May 2012)
		Moots RJ, Ostor AJK, Loft AGR, Järvinen P, Larsson P, Ekelund M, et al. Reduction of direct and indirect costs in patients with AS receiving etanercept: results from an open-label 36-week extension of the ASCEND study in four European countries. Rheumatology. 2011;51(2):393-6.	Hand searches	Original SLR (May 2012)
ASSERT (6)	NCT00207701	**van der Heijde D, Dijkmans B, Geusens P, Sieper J, DeWoody K, Williamson P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis: results of a randomized, placebo-controlled trial (ASSERT). Arthritis Rheum. 2005;52(2):582-91.**	Database searches	Original SLR (May 2012)
		Braun J, Deodhar A, Dijkmans B, Geusens P, Sieper J, Williamson P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis over a two-year period. Arthritis Care & Research. 2008;59(9):1270-8.	Database searches	Original SLR (May 2012)
		van der Heijde D, Han C, DeVlam K, Burmester G, van den Bosch F, Williamson P, et al. Infliximab improves productivity and reduces workday loss in patients with ankylosing spondylitis: results from a randomized, placebo-controlled trial. Arthritis Rheum. 2006;55(4):569-74.	Database searches	Original SLR (May 2012)
ASTRUM (7)	NCT02763046	**Kiltz U, Baraliakos X, Brandt-Jrgens J, Wagner U, Lieb S, Sieder C, et al. Evaluation of the nonsteroidal anti-inflammatory drug-sparing effect of**	Database searches	7th update (April 2022)

		secukinumab in patients with ankylosing spondylitis: Multicenter, randomised, double-blind, phase iv study. Arthritis and Rheumatology. 2021;73(SUPPL 9):1886-8.		
ATLAS (8)	NCT00085644	**van der Heijde D, Kivitz A, Schiff MH, Sieper J, Dijkmans BA, Braun J, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2006;54(7):2136-46.**	Database searches	Original SLR (May 2012)
		Davis JC, Jr., Revicki D, van der Heijde DM, Rentz AM, Wong RL, Kupper H, et al. Health-related quality of life outcomes in patients with active ankylosing spondylitis treated with adalimumab: results from a randomized controlled study. Arthritis Rheum. 2007;57(6):1050-7.	Database searches	Original SLR (May 2012)
		Dougados M, Luo MP, Maksymowych WP, Chmiel JJ, Chen N, Wong RL, et al. Evaluation of the patient acceptable symptom state as an outcome measure in patients with ankylosing spondylitis: data from a randomized controlled trial. Arthritis Rheum. 2008;59(4):553-60.	Database searches	Original SLR (May 2012)
		Kimel M, Thompson C, Gooch K, Fryback D, Feeny D, Revicki D. Norms-Based Assessment of Patient-Reported Outcomes Associated with Adalimumab Monotherapy in Patients with Ankylosing Spondylitis [abstract 1395]. Arthritis & Rheumatism. 2009;60:1135-6.	Database searches	Original SLR (May 2012)
		Maksymowych WP, Gooch K, Dougados M, Wong RL, Chen N, Kupper H, et al. Thresholds of patient-reported outcomes that define the patient acceptable symptom state in ankylosing spondylitis vary over time and by treatment and patient characteristics. Arthritis Care & Research. 2010;62(6):826-34.	Database searches	Original SLR (May 2012)
		Revicki DA, Luo MP, Wordsworth P, Wong RL, Chen N, Davis JC. Adalimumab reduces pain, fatigue, and stiffness in patients with ankylosing spondylitis: results from the adalimumab trial evaluating long-term safety and efficacy for ankylosing spondylitis (ATLAS). The Journal of Rheumatology. 2008;35(7):1346-53.	Database searches	Original SLR (May 2012)
		Van der Heijde D, Sieper J, Brown S, Lavie F, Panagan A. Comparison of ASAS partial remission and low ASDAS as indicators of remission-like states in ankylosing spondylitis. Arthritis Rheum. 2010;62(Suppl 10):S216.	Database searches	Original SLR (May 2012)
		van der Heijde DM, Revicki DA, Gooch KL, Wong RL, Kupper H, Harnam N, et al. Physical function, disease activity, and health-related quality-of-life outcomes after 3 years of adalimumab treatment in patients with ankylosing spondylitis. Arthritis research & therapy. 2009;11(4):1-12.	Database searches	Original SLR (May 2012)
		Wordsworth P, van der Heijde D, Dijkmans B, Schiff M, Kivitz A, de Vlam K, et al. Clinical response and partial remission sustained through 3 years of adalimumab treatment in the ATLAS trial. Rheumatology. 2009;48:I56-I.	Database searches	Original SLR (May 2012)
		van der Heijde D, Breban MA, Halter DG, DiVittorio G, Bratt J, Cantini F, et al. Sustained Improvement of Spinal Mobility, Physical Function, and Quality of Life in Patients with Ankylosing Spondylitis: 5-Year Results. Arthritis & Rheumatism. 2011;63:S205-S6.	Hand searches	Original SLR (May 2012)
Bao 2014 (9)	NCT01248793	**Bao C, Huang F, Khan MA, Fei K, Wu Z, Han C, et al. Safety and efficacy of golimumab in Chinese patients with active ankylosing spondylitis: 1-year results of a multicentre, randomized, double-blind, placebo-controlled phase III trial. Rheumatology (Oxford). 2014;53(9):1654-63.**	Database searches	2nd update (July 2014)
		Bao C, Huang F, Khan MA, Fei K, Wu Z, Hsia EC. Golimumab administered subcutaneously every 4 weeks in Chinese patients with active ankylosing spondylitis: week 24 safety and efficacy results from a randomized, placebo-controlled study [abstract]. Arthritis & Rheumatism. 2012;64:S589.	Database searches	1st update (October 2013)
		Bao C, Huang F, Khan MA, Fei K, Wu Z, Hsia EC. Golimumab administered subcutaneously every 4 weeks in Chinese patients with active ankylosing spondylitis: week 24 safety and efficacy results from a randomized, placebo-controlled study [abstract]. International Journal of Rheumatic Diseases. 2012;15.	Database searches	1st update (October 2013)

		Bao C, Huang F, Khan MA, Fei K, Wu Z, Zhuang Y, et al. Safety and Efficacy Of Golimumab, a Human Anti-Tumor Necrosis Factor Monoclonal Antibody Injected Subcutaneously Every 4 Weeks, In Chinese Patients With Active Ankylosing Spondylitis: 1-Year Results Of a Phase 3, Randomized, Placebo-Controlled Study [abstract 1534]. Arthritis & Rheumatology. 2013.	Hand searches	1st update (October 2013)
		Bao C, Huang F, Khan MA, Fei K, Wu Z, Zhuang Y, et al. Safety and efficacy of golimumab, a human anti-tnf monoclonal antibody injected subcutaneously every 4 weeks, in chinese patients with active ankylosing spondylitis: one-year results of a phase 3, randomized, placebo-controlled study [abstract AB0513]. Annals of the Rheumatic Diseases. 2013;72:A945.	Hand searches	1st update (October 2013)
		Bao C, Huang F, Khan MA, Fei K, Wu Z, Zhuang Y, et al. Safety and Efficacy Of Golimumab, a Human Anti-Tumor Necrosis Factor Monoclonal Antibody Injected Subcutaneously Every 4 Weeks, In Chinese Patients With Active Ankylosing Spondylitis: 1-Year Results Of a Phase 3, Randomized, Placebo-Controlled Study. Arthritis & Rheumatism. 2013;65:S651.	Database searches	2nd update (July 2014)
BE AGILE (10)	NCT02963506	**Van Der Heijde D, Gensler LS, Deodhar A, Baraliakos X, Poddubnyy D, Kivitz A, et al. Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double-blind, placebo-controlled, dose-ranging study. Annals of the rheumatic diseases. 2020;79(5):595-604.**	Database searches	6th update (October 2020)
		van der Heijde D, Gensler LS, Deodhar A, Baraliakos X, Poddubnyy D, Farmer MK, et al. LB0001 Dual neutralisation of il-17a and il-17f with bimekizumab in patients with active ankylosing spondylitis (AS): 12-week results from a phase 2b, randomised, double-blind, placebo-controlled, dose-ranging study. Annals of the Rheumatic Diseases. 2018;77(Suppl 2):70-.	Database searches	6th update (October 2020)
		Van Der Heijde, D, Gensler, et al. Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and quality-of-life outcomes in patients with active ankylosing spondylitis: Results from a phase 2B, randomised, double-blind, placebo-controlled, dose-ranging study. Annals of the Rheumatic Diseases. 2019;78 (Supplement 2)193	Database searches	6th update (October 2020)
		van der Heijde D, Gensler L, Deodhar A, Baraliakos X, Poddubnyy D, Kivitz A, et al. Dual Neutralization of IL-17A and IL-17F with Bimekizumab in Patients with Active Ankylosing Spondylitis: 48-Week Efficacy and Safety Results from a Phase 2b, Randomized, Blinded, Placebo-Controlled, Dose-Ranging Study [abstract 937]. Arthritis & Rheumatology. 2019;71.	Database searches	6th update (October 2020)
		Anonymous. Correction: Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double blind, placebo-controlled, dose-ranging study. Annals of the Rheumatic Diseases. 2020;79e121	Database searches	6th update (October 2020)
		Gensler L, Deodhar A, Baraliakos X, Poddubnyy D, Farmer M, Baeten D, et al. Dual neutralization of IL-17A and IL-17F with bimekizumab in patients with active ankylosing spondylitis (AS): 12-week results from a phase 2b, randomized, double-blind, placebo-controlled, dose-ranging study [abstract AB443]. Journal of the American Academy of Dermatology. 2019;81(4).	Database searches	6th update (October 2020)
		Anonymous. Correction: Dual neutralisation of interleukin-17A and interleukin-17F with bimekizumab in patients with active ankylosing spondylitis: results from a 48-week phase IIb, randomised, double blind, placebo-controlled, dose-ranging study. Annals of the rheumatic diseases. 2021;80(11):e186.	Database searches	7th update (April 2022)
BE MOBILE 1 (11)	NCT03928704	**UCB. Data on file. BE MOBILE 1 (AS0010) Clinical Study Report: Week 24 Interim Analysis, Efficacy and Safety of Bimekizumab in Non-Radiographic axSpA (March 2022).**	Hand searches	7th update (April 2022)
		Deodhar A, Van der Heijde D, Gensler LS, Xu H, Gaffney K, Dobashi H, et al. Bimekizumab in Patients with Active Non-Radiographic Axial Spondyloarthritis: 24-Week Efficacy & Safety from BE MOBILE 1, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):772-3.	Hand searches	7th update (April 2022)

BE MOBILE 2 (12)	NCT03928743	**UCB. Data on file. BE MOBILE 2 (AS0011) Clinical Study Report: Week 24 Interim Analysis, Efficacy and Safety of Bimekizumab in Ankylosing Spondylitis (March 2022).**	Hand searches	7th update (April 2022)
		Van der Heijde D, Baraliakos X, Dougados M, Brown M, Poddubnyy D, Van den Bosch F, et al. Bimekizumab in Patients with Active Ankylosing Spondylitis: 24-Week Efficacy & Safety from BE MOBILE 2, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):12-3.	Hand searches	7th update (April 2022)
		van der Heijde A, Baraliakos X, Dougados M, Brown M, Poddubnyy D, Van Den Bosch F, et al. Bimekizumab Improves Signs and Symptoms Including Inflammation in Patients with Active Ankylosing Spondylitis: 24-Week Efficacy & Safety from a Phase 3, Multicenter, Randomized, Placebo Controlled Study [abstract]. Arthritis & Rheumatology. 2022;74(S9).	Hand searches	8th update (January 2023)
BE MOBILE 1 (11) & BE MOBILE 2 (12)	NCT03928704 & NCT03928743	Baraliakos X, Deodhar A, van der Heijde A, Magrey M, Maksymowych W, Tomita T, et al. Bimekizumab Maintains Improvements in Efficacy Endpoints and Has a Consistent Safety Profile Through 52 Weeks in Patients with Non-Radiographic Axial Spondyloarthritis and Ankylosing Spondylitis: Results from Two Parallel Phase 3 Studies [abstract]. Arthritis & Rheumatology. 2022;74(S9).	Hand searches	8th update (January 2023)
		Dubreuil M, Gaffney K, Gensler L, Kay J, Navarro-Compán V, de la Loge C, et al. Bimekizumab Improves Physical Function and Health-Related Quality of Life in Patients with Axial Spondyloarthritis: Results from Two Phase 3 Studies [abstract]. Arthritis & Rheumatology. 2022;74(S9).	Hand searches	8th update (January 2023)
		Mease P, Deodhar A, Dougados M, Dubreuil M, Magrey M, Marzo-Ortega H, et al. Bimekizumab Improves Key Patient Reported Symptoms of Axial Spondyloarthritis Including Spinal Pain and Fatigue: Results from Two Phase 3 Studies [abstract]. Arthritis & Rheumatology. 2022;74(S9).	Hand searches	8th update (January 2023)
Braun 2002 (13)	None	**Braun J, Brandt J, Listing J, Zink A, Alten R, Golder W, et al. Treatment of active ankylosing spondylitis with infliximab: a randomised controlled multicentre trial. Lancet. 2002;359(9313):1187-93.**	Database searches	Original SLR (May 2012)
Calin 2004 (14)	NCT00421915	**Calin A, Dijkmans BA, Emery P, Hakala M, Kalden J, Leirisalo-Repo M, et al. Outcomes of a multicentre randomised clinical trial of etanercept to treat ankylosing spondylitis. Ann Rheum Dis. 2004;63(12):1594-600.**	Database searches	Original SLR (May 2012)
Canadian AS Trial (15)	NCT00195819	**Lambert RG, Salonen D, Rahman P, Inman RD, Wong RL, Einstein SG, et al. Adalimumab significantly reduces both spinal and sacroiliac joint inflammation in patients with ankylosing spondylitis: a multicenter, randomized, double-blind, placebo-controlled study. Arthritis Rheum. 2007;56(12):4005-14.**	Database searches	Original SLR (May 2012)
		Maksymowych WP, Rahman P, Shojania K, Olszynski WP, Thomson GT, Ballal S, et al. Beneficial effects of adalimumab on biomarkers reflecting structural damage in patients with ankylosing spondylitis. J Rheumatol. 2008;35(10):2030-7.	Database searches	Original SLR (May 2012)
CANDLE (16)	NCT00202865	**Inman RD, Maksymowych WP, Group CS. A double-blind, placebo-controlled trial of low dose infliximab in ankylosing spondylitis. J Rheumatol. 2010;37(6):1203-10.**	Database searches	Original SLR (May 2012)
		Maksymowych WP, Salonen D, Inman RD, Rahman P, Lambert RG, Group CS. Low-dose infliximab (3 mg/kg) significantly reduces spinal inflammation on magnetic resonance imaging in patients with ankylosing spondylitis: a randomized placebo-controlled study. J Rheumatol. 2010;37(8):1728-34.	Database searches	Original SLR (May 2012)
		clinicaltrials.gov. Evaluation of Low Dose Infliximab in Ankylosing Spondylitis (Study P04352). Available at: https://clinicaltrials.gov/show/nct00202865. 2005.	Database searches	5th update (April 2019)
		Sieper J, Landewé R, Magrey M, Anderson J, Zhong S, Wang X, et al. SAT0263 Predictors of remission maintenance and successful therapy discontinuation in patients with non-radiographic axial spondyloarthritis (NR-AXSPA) who achieved sustained remission on open-label adalimumab (ADA) treatment. Annals of the Rheumatic Diseases. 2018;77(Suppl 2):995.	Database searches	5th update (April 2019)
C-axSpAnd (17)	NCT02552212	**Deodhar A, Gensler LS, Kay J, Maksymowych WP, Haroon N, Landewé R, et al. A Fifty-Two–Week, Randomized, Placebo-Controlled Trial of Certolizumab Pegol**	Database searches	5th update (April 2019)

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A. A. Deodhar, L. S. Gensler, J. Kay, W. P. Maksymowych, N. Haroon, R. B. M. Landewé, M. Rudwaleit, S. Hall, L. Bauer, B. Hoepken, N. De Peyrecave, B. Kilgallen, D. Van Der Heijde. Efficacy and safety outcomes in patients with non-radiographic axial spondyloarthritis treated with certolizumab pegol: Results from the first 52-week randomized placebo-controlled study (NCT02552212). Arthritis and Rheumatology. 2018. 70:2082-2083	Database searches	5th update (April 2019)
Kay J, Gensler L, Deodhar A, Maksymowych W, Haroon N, Auteri S, et al. Earlier Treatment of Non-Radiographic Axial Spondyloarthritis with Certolizumab Pegol Results in Improved Clinical and Patient-Reported Outcomes [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
Deodhar A, Gensler LK, J., Maksymowych, W., Haroon, N., Landewé, R., Rudwaleit, M., Hall, S., Bauer, L., Hoepken, B., de Peyrecave, N., Kumke, T., van der Heijde, D. Certolizumab Pegol Improves Work and Household Productivity and Social Participation over 1 Year of Treatment in Patients with Non-Radiographic Axial Spondyloarthritis [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
Gensler L, Kay J, Maksymowych W, Haroon N, Bauer L, Hoepken B, et al. Certolizumab Pegol-Treated Patients with Non-Radiographic Axial Spondyloarthritis Demonstrate Improvements in Sleep Quality and Other Patient Reported Outcomes [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
Rudwaleit M, Gensler LS, Deodhar A, Kay J, Maksymowych WP, Haroon N, et al. Earlier treatment of non-radiographic axial spondyloarthritis with certolizumab pegol results in improved clinical outcomes. Swiss Medical Weekly. 2019;149:17S.	Database searches	6th update (October 2020)
Deodhar A, Gensler L, Kay J, Maksymowych W, Haroon N, Landewé R, et al. Certolizumab pegol versus standard care in treating non-radiographic axial spondyloarthritis: results for Asia-Pacific versus rest of the world from C-axSpAnd. Int J Rheum Dis. 2019;22.	Database searches	6th update (October 2020)
Gaffney K, Deodhar A, Gensler L, Kay J, Maksymowych W, Haroon N, et al. Czp improves work and household productivity and social participation over 1 year of treatment in patients with non-radiographic axspa [abstract]. Rheumatology. 2020;59:ii110-ii1.	Database searches	6th update (October 2020)
Sengupta R, Gensler L, Kay J, Maksymowych W, Haroon N, Bauer L, et al. Certolizumab pegol-treated patients with non-radiographic axSpA demonstrate improvements in sleep quality and other patient reported outcomes [abstract P284]. Rheumatology. 2020;59:111-2.	Database searches	6th update (October 2020)
Deodhar A, Gensler L, Hall S, Robinson P, Hoepken B, Bauer L, et al. Certolizumab Pegol Efficacy in Patients with Non-Radiographic Axial Spondyloarthritis Stratified by Baseline MRI and C-Reactive Protein Status [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
Rudwaleit M, Gensler LS, Deodhar A, Kay J, Maksymowych WP, Haroon N, et al. Earlier treatment of non-radiographic axial spondyloarthritis with certolizumab pegol results in improved clinical outcomes [abstract FRI0408]. Annals of the Rheumatic Diseases. 2019;78.	Database searches	6th update (October 2020)
Robinson P, Hall S, Hoepken B, Bauer L, Kumke T, DePeyrecave N, et al. Response to certolizumab pegol in patients with non-radiographic axial spondyloarthritis by baseline C-reactive protein cut-offs: Post-hoc analysis from C-axSpAnd. International Journal of Rheumatic Diseases. 2020;23(SUPPL 1):67-8.	Database searches	7th update (April 2022)
Robinson P, Maksymowych WP, Gensler LS, Rudwaleit M, Hoepken B, Bauer L, et al. Long-term clinical outcomes of certolizumab pegol treatment in patients with active non radiographic axial spondyloarthritis stratified by baseline MRI and C-reactive protein status. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):774-5.	Hand searches	7th update (April 2022)
Robinson PC, Maksymowych WP, Gensler LS, Hall S, Rudwaleit M, Hoepken B, et al. Certolizumab Pegol Efficacy in Patients With Non-Radiographic Axial Spondyloarthritis Stratified by Baseline MRI and C-Reactive Protein Status: An	Database searches	8th update (January 2023)

		Analysis From the C-axSpAnd Study. ACR Open Rheumatology. 2022;4(9):794-801.		
Chinese University of Hong Kong (Hong Kong, China) (18)	None	**Li EK, Griffith JF, Lee VW, Wang YX, Li TK, Lee KK, et al. Short-term efficacy of combination methotrexate and infliximab in patients with ankylosing spondylitis: a clinical and magnetic resonance imaging correlation. Rheumatology (Oxford). 2008;47(9):1358-63.**	Database searches	Original SLR (May 2012)
COAST-V (19)	NCT02696785	**van der Heijde D, Cheng-Chung Wei J, Dougados M, Mease P, Deodhar A, Maksymowych WP, et al. Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. Lancet. 2018;392(10163):2441-51.**	Database searches	5th update (April 2019)
		Navarro-Compan V, Redlich K, Bird P, Bello N, Pum G, Liu-Leage S, et al. Ixekizumab significantly improves signs, symptoms and spinal inflammation of active ankylosing spondylitis/radiographic axial spondyloarthritis: 16-week results of a phase 3 randomised, active and placebo-controlled trial [abstract P31]. Swiss Medical Weekly. 2019;238:16S-7S.	Database searches	6th update (October 2020)
		Wei JCC, van den Bosch F, Kiltz U, Hunter T, Dong Y, Leung A, et al. Ixekizumab significantly improves selfreported overall health as measured by SF-36 in patients with active ankylosing spondylitis/radiographic axial spondyloarthritis naive to biological therapy: 52 week results of a phase 3 trial [abstract AB0710]. Annals of the Rheumatic Diseases. 2019;78.	Database searches	6th update (October 2020)
		Wei JCC, Gensler LS, Landewé RB, Tomita T, Zhao F, Gallo G, et al. Ixekizumab improves signs and symptoms and spinal inflammation of ankylosing spondylitis/radiographic axial spondyloarthritis through one year of treatment in biologic disease modifying antirheumatic drug-naive patients [abstract AB0711]. Annals of the Rheumatic Diseases. 2019;78.	Database searches	6th update (October 2020)
		van der Heijde D, Wei J, Dougados M, Mease P, Deodhar A, Maksymowych W, et al. Ixekizumab Significantly Improves Signs, Symptoms, and Spinal Inflammation of Active Ankylosing Spondylitis/Radiographic Axial Spondyloarthritis: 16-Week Results of a Phase 3 Randomized, Active and Placebo-Controlled Trial [abstract]. Arthritis Rheumatol. 2018;70.	Database searches	5th update (April 2019)
		Poddubnyy D, Attar S, Nissen MJ, Filippi E, Russ H, Erdogan A, et al. Individual components contributing to the achievement of asas40 response in biologic nalve patients with radiographic axspa: Results from the coast-v trial. Annals of the Rheumatic Diseases. 2021;80(SUPPL 1):1259-60.	Database searches	7th update (April 2022)
COAST-W (20)	NCT02696798	**Deodhar A, Poddubnyy D, Pacheco-Tena C, Salvarani C, Lespessailles E, Rahman P, et al. Efficacy and Safety of Ixekizumab in the Treatment of Radiographic Axial Spondyloarthritis: Sixteen-Week Results From a Phase III Randomized, Double-Blind, Placebo-Controlled Trial in Patients With Prior Inadequate Response to or Intolerance of Tumor Necrosis Factor Inhibitors. Arthritis Rheumatol. 2019;71(4):599-611.**	Database searches	5th update (April 2019)
		Gonzalez C, Aletaha D, Nassab M, Bello N, Pum G, Bradley AJ, et al. Efficacy and safety of ixekizumab in the treatment of radiographic axial spondyloarthritis: 16 week results of a phase 3 randomised, double-blind, placebo-controlled trial in patients with prior inadequate response or intolerance to 1 or 2 tumour necrosis factor inhibitors [abstract P35]. Swiss Medical Weekly. 2019;149:18S.	Database searches	6th update (October 2020)
COAST-V (19) & COAST-W (20)	NCT02696785 & NCT02696798	Wei C, Hunter T, Van den Bosch F, Walsh J, Kiltz U, Dong Y, et al. Ixekizumab Significantly Improves Patient-reported Overall Health as Measured by SF-36 in Patients with Active Ankylosing Spondylitis/Radiographic Axial Spondyloarthritis: 52-Week Results of Two Phase 3 Trials [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
		Walsh JA, Kiltz U, Wei JCC, van den Bosch F, Hunter T, Dong Y, et al. Ixekizumab significantly improves selfreported overall health in patients with active ankylosing spondylitis/radiographic axial spondyloarthritis: Sf-36 results of two phase 3 trials [abstract FRI0420]. Annals of the Rheumatic Diseases. 2019;78.	Database searches	6th update (October 2020)

		Magrey M, Navarro-Compan V, Garces S, Baraliakos X, Salonen D, Lisse J, et al. Infections in Patients with Active Radiographic Axial Spondyloarthritis Treated with Ixekizumab in 2 Phase 3 Clinical Trials [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
		Dougados M, Wei JC, Landewe R, Sieper J, Baraliakos X, Van den Bosch F, et al. Efficacy and safety of ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial spondyloarthritis (COAST-V and COAST-W). Ann Rheum Dis. 2020;79(2):176-85.	Database searches	6th update (October 2020)
		Mease P, Walsh JA, Baraliakos X, Inman R, de Vlam K, Wei JC, et al. Translating Improvements with Ixekizumab in Clinical Trial Outcomes into Clinical Practice: ASAS40, Pain, Fatigue, and Sleep in Ankylosing Spondylitis. Rheumatol Ther. 2019;6(3):435-50.	Database searches	6th update (October 2020)
		Wei JCC, Baraliakos X, Hunter T, Zhu B, Bolce R, Zhao F, et al. Ixekizumab significantly reduced pain, inflammation, and fatigue in patients with radiographic axial spondylarthritis (r-axspa)/ankylosing spondylitis (as) [abstract FRI0421]. Annals of the Rheumatic Diseases. 2019;78.	Database searches	6th update (October 2020)
		Gaffney K, Aletaha D, Bradley AJ, Nassab MH, Leage SL, Micheroli R. 52-Week efficacy and safety of ixekizumab in r-axSpA/AS patients naïve to biologic treatments or with prior inadequate response/intolerance to tumor necrosis factor inhibitors [abstract P281]. Rheumatology. 2020;59.	Database searches	6th update (October 2020)
		Marzo-Ortega H, Mease PJ, Rahman P, Navarro-Compan V, Strand V, Dougados M, et al. Impact of Ixekizumab on Work Productivity in Patients with Ankylosing Spondylitis: Results from the COAST-V and COAST-W Trials at 52 Weeks. Rheumatol Ther. 2020;7(4):759-74.	Database searches	6th update (October 2020)
		Kiltz U, Wei JC, van der Heijde D, van den Bosch F, Walsh JA, Boonen A, et al. Ixekizumab Improves Functioning and Health in the Treatment of Radiographic Axial Spondyloarthritis: Week 52 Results from 2 Pivotal Studies. J Rheumatol. 2021;48(2):188-97.	Database searches	6th update (October 2020)
		Marzo-Ortega H, Mease PJ, Rahman P, Navarro-Compán V, Strand V, Dougados M, et al. Impact of ixekizumab on work productivity in patients with ankylosing spondylitis: results from the coast-v and coast-w trials at 52 weeks [abstract THU0396]. Annals of the Rheumatic Diseases. 2020;79.	Hand searches	6th update (October 2020)
		Reveille J, Rahman P, Sandoval D, Muran T, Kronbergs A, Bolce R, et al. Response to Ixekizumab by C-reactive Protein Level in Patients with Radiographic Axial Spondyloarthritis: Results from the COAST-V (Biological-Naïve) and COAST-W (TNF Inhibitor-Experienced) Trials at 52 Weeks [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		Maksymowych WP, Bolce R, Gallo G, Seem E, Geneus VJ, Sandoval DM, et al. Ixekizumab in radiographic axial spondyloarthritis with and without elevated C-reactive protein or positive magnetic resonance imaging. Rheumatology (Oxford, England). 2022;0:1-11.	Database searches	7th update (April 2022)
		Anonymous. Correction: Efficacy and safety of ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial spondyloarthritis (COAST-V and COAST-W). Annals of the rheumatic diseases. 2020;79(6):e75.	Database searches	7th update (April 2022)
		Reveille JD, Rahman P, Sandoval D, Muram T, Bolce R, Park SY, et al. Ixekizumab improves signs, symptoms and quality of life of ankylosing spondylitis in patients irrespective of hla-b27 status: Pooled results from the coast-v and coast-w trials. Annals of the Rheumatic Diseases. 2021;80(SUPPL 1):714.	Database searches	7th update (April 2022)
COAST-X (21)	NCT02757352	**Deodhar A, van der Heijde D, Gensler LS, Kim TH, Maksymowych WP, Ostergaard M, et al. Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial. Lancet. 2020;395(10217):53-64.**	Database searches	6th update (October 2020)

		Walsh J, Magrey M, Kiltz U, Baraliakos X, Weng M, Hunter T, et al. Ixekizumab Significantly Improves Self-reported Overall Health as Measured by Short-Form-36 in Patients with Active Non-radiographic Axial Spondyloarthritis: 16- and 52-Week Results of a Phase 3 Randomized Trial (COAST-X) [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
		Deodhar A, van der Heijde D, Gensler L, Kim T, Maksymowych W, Østergaard M, et al. Ixekizumab in Non-Radiographic Axial Spondyloarthritis: Primary Results from a Phase 3 Trial [abstract]. Arthritis Rheumatol. 2019;71.	Database searches	6th update (October 2020)
		Maksymowych W, Marzo-Ortega H, Østergaard M, Gensler L, Ermann J, Deodhar A, et al. Efficacy of Ixekizumab on Disease Activity and Quality of Life in Patients with Active Nonradiographic Axial Spondyloarthritis and Objective Signs of Inflammation, Stratified by Baseline CRP/Sacroiliac Joint MRI Status [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		Mease P, Deodhar A, Rahman P, Marzo-Ortega H, Strand V, Hunter T, et al. Ixekizumab Treatment Improves Fatigue, Spinal Pain, Stiffness, and Sleep in Patients with Nonradiographic Axial Spondyloarthritis [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		Deodhar A, Mease P, Gensler L, Rahman P, Navarro-Compan V, Marzo-Ortega H, et al. Impact of Ixekizumab on Work Productivity in Non-Radiographic Axial Spondyloarthritis Patients: Results from the COAST-X Trial at 52 Weeks [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		Deodhar A, Mease P, Gensler L, Rahman P, Navarro-Compan V, Marzo-Ortega H, et al. THU0384 IMPACT OF IXEKIZUMAB ON WORK PRODUCTIVITY IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS: RESULTS FROM THE COAST-X TRIAL AT 52 WEEKS. Ann Rheum Dis. 2020;79:422.	Hand searches	6th update (October 2020)
		Navarro-Compan V, Maldonado-Cocco J, Rahman P, Kronbergs A, Sandoval D, Park S, et al. Response to Treatment with Ixekizumab in Patients with Active Non-Radiographic Axial Spondyloarthritis Based on HLA-B27 Status and Disease Duration [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		Walsh JA, Magrey MN, Baraliakos X, Inui K, Weng MY, Lubrano E, et al. Improvement of Functioning and Health With Ixekizumab in the Treatment of Active Nonradiographic Axial Spondyloarthritis in a 52-Week, Randomized, Controlled Trial. Arthritis Care Res (Hoboken). 2022;74(3):451-60.	Database searches	6th update (October 2020)
		Mease P, Deodhar A, Rahman P, Marzo-Ortega H, Strand V, Hunter T, et al. Ixekizumab Treatment Improves Fatigue, Spinal Pain, Stiffness, and Sleep in Patients with Nonradiographic Axial Spondyloarthritis. Arthritis and Rheumatology. 2020;72(SUPPL 10):1774-6.	Database searches	7th update (April 2022)
		Deodhar A, Mease P, Rahman P, Navarro-Compan V, Marzo-Ortega H, Hunter T, et al. Ixekizumab Improves Patient-Reported Outcomes in Non-Radiographic Axial Spondyloarthritis: Results from the Coast-X Trial. Rheumatology and Therapy. 2021;8(1):135-50.	Database searches	7th update (April 2022)
COAST-V (19), COAST-W (20) & COAST-X (21)	NCT02696785, NCT02696798 & NCT02757352	Schett G, Van den Bosch F, Baraliakos X, Sandoval D, Geneus V, Bolce R, et al. Ixekizumab Improves Signs and Symptoms of Patients with Radiographic and Non-radiographic Axial Spondyloarthritis and Extra-articular Manifestation of Enthesitis Through 16 Weeks [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		Poddubnyy D, Juanola X, Prati C, Russ H, Schymura Y, Liu-Leage S, et al. Achievement of Low Disease Activity According to BASDAI with Ixekizumab in Patients with Axial Spondyloarthritis: 16-Week Results from the COAST Trials [abstract]. Arthritis Rheumatol. 2020;72.	Hand searches	6th update (October 2020)
		European Medicines Agency (EMA). Talz (ixekizumab) CHMP Assessment Report. Available at: https://www.ema.europa.eu/en/documents/assessment-report/taltz-epar-public-assessment-report_en.pdf (Accessed 5th April 2022) 2016.	Hand searches	6th update (October 2020)
COAST-Y (22)	NCT03129100	**Landewe RBM, Gensler LS, Poddubnyy D, Rahman P, Hojnik M, Li X, et al. Continuing versus withdrawing ixekizumab treatment in patients with axial spondyloarthritis who achieved remission: Efficacy and safety results from a placebo-controlled, randomised withdrawal study (COAST-Y). Annals of the Rheumatic Diseases. 2021;80(8):1022-30.**	Database searches	7th update (April 2022)

		Landewé RBM, Poddubnyy D, Rahman P, Bolce R, Liu Leage S, Lisse J, et al. Recapture rates with ixekizumab after withdrawal of therapy in patients with axial spondyloarthritis: results at week 104 from a randomized placebo-controlled withdrawal study. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):10-1.	Hand searches	7th update (April 2022)
		Deodhar A, Poddubnyy D, Rahman P, Bolce R, Liu Leage S, Kronbergs A, et al. SAFETY and EFFICACY of IXEKIZUMAB TREATMENT in PATIENTS with AXIAL SPONDYLOARTHRITIS: 3-YEAR CLINICAL TRIAL RESULTS from the COAST PROGRAMME. Annals of the Rheumatic Diseases. 2022;81(Supplement 1):765.	Database searches	8th update (January 2023)
C-OPTIMISE (23)	NCT02505542	**Landewe RB, van der Heijde D, Dougados M, Baraliakos X, Van den Bosch FE, Gaffney K, et al. Maintenance of clinical remission in early axial spondyloarthritis following certolizumab pegol dose reduction. Ann Rheum Dis. 2020;79(7):920-8.**	Database searches	6th update (October 2020)
DANISH (24)	NCT00477893	**Pedersen SJ, Poddubnyy D, Sorensen IJ, Loft AG, Hindrup JS, Thamsborg G, et al. Course of Magnetic Resonance Imaging-Detected Inflammation and Structural Lesions in the Sacroiliac Joints of Patients in the Randomized, Double-Blind, Placebo-Controlled Danish Multicenter Study of Adalimumab in Spondyloarthritis, as Assessed by the Berlin and Spondyloarthritis Research Consortium of Canada Methods. Arthritis Rheumatol. 2016;68(2):418-29.**	Database searches	3rd update (January 2017)
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		Pedersen SJ, Sørensen IJ, Loft AG, Hindrup JS, Thamsborg G, Asmussen K, et al. THU0366 Efficacy of Adalimumab in Patients with Axial Spondyloarthritis: Results of an Investigator-Initiated 12-Weeks Randomized Double-Blind Placebo Controlled Trial with a 12 Weeks Open-Label Extension Phase. Ann Rheum Dis. 2013;72.	Hand searches	1st update (October 2013)
Davis 2003 (25)	None	**Davis JC, Jr., Van Der Heijde D, Braun J, Dougados M, Cush J, Clegg DO, et al. Recombinant human tumor necrosis factor receptor (etanercept) for treating ankylosing spondylitis: a randomized, controlled trial. Arthritis Rheum. 2003;48(11):3230-6.**	Database searches	Original SLR (May 2012)
		Baraliakos X, Davis J, Tsuji W, Braun J. Magnetic resonance imaging examinations of the spine in patients with ankylosing spondylitis before and after therapy with the tumor necrosis factor alpha receptor fusion protein etanercept. Arthritis Rheum. 2005;52(4):1216-23.	Database searches	Original SLR (May 2012)
		Inman RD, Clegg DO, Davis JC, Whitmore JB, Solinger A. Etanercept in adult patients with early onset ankylosing spondylitis. J Rheumatol. 2006;33(8):1634-6.	Database searches	Original SLR (May 2012)
Davis 2003 (25) & Gorman 2002 (26)	None & none	Davis JC, van der Heijde D, Dougados M, Woolley JM. Reductions in health-related quality of life in patients with ankylosing spondylitis and improvements with etanercept therapy. Arthritis Rheum. 2005;53(4):494-501.	Database searches	Original SLR (May 2012)
Deodhar 2021 (27)	NCT03502616	**Deodhar A, Sliwinska-Stanczyk P, Xu H, Baraliakos X, Gensler LS, Fleishaker D, et al. Tofacitinib for the treatment of ankylosing spondylitis: A phase III, randomised, double-blind, placebo-controlled study. Annals of the Rheumatic Diseases. 2021;80(8):1004-13.**	Database searches	7th update (April 2022)
		Navarro-Compan V, Wei JCC, Van Den Bosch F, Magrey M, Wang L, Fleishaker D, et al. Effect of tofacitinib on patient-reported outcomes in patients with active ankylosing spondylitis: Results from a phase 3 trial. Annals of the Rheumatic Diseases. 2021;80(SUPPL 1):704.	Database searches	7th update (April 2022)

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		Navarro-Compan V, Wei JCC, Van Den Bosch F, Magrey M, Wang L, Fleishaker D, et al. Effect of tofacitinib on pain, fatigue, health-related quality of life and work productivity in patients with active ankylosing spondylitis: results from a phase III, randomised, double-blind, placebo-controlled trial. RMD Open. 2022;8(2):e002253.	Database searches	8th update (January 2023)
		Deodhar A, Marzo-Ortega H, Wu J, Wang C, Dina O, Kanik KS, et al. Efficacy and Safety of Tofacitinib in Patients with Ankylosing Spondylitis by Prior bDMARD Treatment: Analysis of a Phase 3 Trial. Arthritis & Rheumatology [abstract]. 2022;74(S9).	Hand searches	8th update (January 2023)
EMBARK (28)	NCT01258738	**Dougados M, van der Heijde D, Sieper J, Braun J, Maksymowych WP, Citera G, et al. Symptomatic efficacy of etanercept and its effects on objective signs of inflammation in early nonradiographic axial spondyloarthritis: a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheumatol. 2014;66(8):2091-102.**	Database searches	2nd update (July 2014)
		Dougados M, Tsai W, Saaibi DL, Bonin R, Bukowski J, Pedersen R, et al. Patient-Reported Outcomes of Etanercept in Early Non-Radiographic Axial Spondyloarthritis: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Trial. Arthritis & Rheumatism. 2013;65:S656-S7.	Database searches	2nd update (July 2014)
		Dougados M, Van der Heijde D, Sieper J, Braun J, Maksymowych WP, Citera G, et al. Safety and efficacy of etanercept in early non-radiographic axial spondyloarthritis: a randomized, double-blind, placebo-controlled trial at 24 weeks. Arthritis & Rheumatism. 2013;65:S642-S3.	Database searches	2nd update (July 2014)
		Wei J, Tsai W, Citera G, Kotak S, Tang B, Llamado L. Clinical/x-ray efficacy of etanercept in non-radiographic axial SpA. Int J Rheum Dis. 2014;17.	Database searches	2nd update (July 2014)
		Dougados M, Tsai WC, Saaibi DL, Bonin R, Bukowski J, Pedersen R, et al. Evaluation of Health Outcomes with Etanercept Treatment in Patients with Early Nonradiographic Axial Spondyloarthritis. J Rheumatol. 2015;42(10):1835-41.	Database searches	3rd update (January 2017)
		Brown M, Bird P, Robinson P, Mease P, Van den Bosch F, Surian C, et al. Baseline Mri/crp as Predictors of Response to Etanercept in the Management of Patients with Non-Radiographic Axial Spondyloarthritis. Internal Medicine Journal. 2015;45:39.	Database searches	4th update (April 2018)
		Dougados, M.,Van Der Heijde, D.,Sieper, J.,Braun, J.,Citera, G.,Van Den Bosch, F.,Pedersen, R.,Bonin, R.,Jones, H.,Marshall, L.,Kotak, S.,Logeart, I.,Vlahos, B.,Bukowski, J.,Maksymowych, W.. Clinical and imaging efficacy of etanercept in early non-radiographic axial spondyloarthritis: 104-week treatment results. Journal of Rheumatology. 2016. 43:1232	Database searches	4th update (April 2018)
		Dougados M, van der Heijde D, Tsai WC, Saaibi D, Bonin R, Marshall L, et al. Better Health-Related Quality of Life and Work Capacity in Patients Achieving Inactive Disease and Clinical Response in Patients with Non-Radiographic Axial Spondyloarthritis [abstract 2779]. Arthritis Rheumatol. 2016;68.	Database searches	4th update (April 2018)
		Maksymowych, W., Wichuk, S., Dougados, M., Jones, H., Szumski, A., Marshall, L., Bukowski, J., Lambert, R.. Modification of structural lesions on magnetic resonance imaging by etanercept: A 12-Week randomized placebo-controlled trial. Journal of Rheumatology. 2016. 43:1232	Database searches	4th update (April 2018)
		Maksymowych WP, Wichuk S, Dougados M, Jones HE, Pedersen R, Szumski A, et al. Modification of structural lesions on MRI of the sacroiliac joints by etanercept in the EMBARK trial: a 12-week randomised placebo-controlled trial in patients with non-radiographic axial spondyloarthritis. Ann Rheum Dis. 2018;77(1):78-84.	Database searches	4th update (April 2018)
		Dougados M, Tsai WC, Saaibi DL, Bonin R, Bukowski J, Pedersen R, et al. Patient-Reported Outcomes of Etanercept in Early Non-Radiographic Axial Spondyloarthritis: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Trial. Presented at: 2013 ACR/ARHP Annual Meeting. Abstract number 1546. Available at: https://acrabstracts.org/abstract/patient-reported-outcomes-of-	Hand searches	1st update (October 2013)

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		Dougados M, van der Heijde D, Sieper J, Braun J, Maksymowych WP, Citera G, et al. Safety and Efficacy Of Etanercept In Early Non-Radiographic Axial Spondyloarthritis: A Randomized, Double-Blind, Placebo-Controlled Trial At 24 Weeks. Presented at 2013 ACR/ARHP Annual meeting. Abstract number 1516. Available at: https://acrabstracts.org/abstract/safety-and-efficacy-of-etanercept-in-early-non-radiographic-axial-spondyloarthritis-a-randomized-double-blind-placebo-controlled-trial-at-24-weeks/. 2013.	Hand searches	1st update (October 2013)
		Dougados. Clinical and Imaging Efficacy of Etanercept in Early Non-Radiographic Axial Spondyloarthritis: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Trial. Abstract OP0108, EULAR 2013.	Hand searches	1st update (October 2013)
		Maksymowych WP, van der Heijde D, Dougados M, Sieper J, Braun J, Citera G, et al. Clinical and imaging efficacy of etanercept in early non-radiographic axial spondyloarthritis: 48-week treatment data [abstract SAT0372]. Annals of the Rheumatic Diseases. 2014;73:728.	Hand searches	2nd update (July 2014)
		Sieper J, Drescher E, Rosa J, Pedersen R, Bonin R, Vlahos B, et al. Quality of life with etanercept in early non-radiographic axial spondyloarthritis: 24 and 48-week data from a randomized, double-blind, placebo-controlled trial [abstract SAT0350]. Annals of the Rheumatic Diseases. 2014;73:719.	Hand searches	2nd update (July 2014)
		Tam HKJ, Nash P, Robinson PC. The Effect of Etanercept in Nonradiographic Axial Spondyloarthritis by Stratified C-Reactive Protein Levels. ACR Open Rheumatology. 2021;3(10):699-706.	Database searches	7th update (April 2022)
ESTHER (29)	NCT00844142	**Song IH, Hermann K, Haibel H, Althoff CE, Listing J, Burmester G, et al. Effects of etanercept versus sulfasalazine in early axial spondyloarthritis on active inflammatory lesions as detected by whole-body MRI (ESTHER): a 48-week randomised controlled trial. Ann Rheum Dis. 2011;70(4):590-6.**	Database searches	Original SLR (May 2012)
		Song IH. Effects of etanercept vs. sulfasalazine on acute inflammatory lesions as detected by whole body MRI in early axial Spondyloarthritis a 48 week randomized controlled trial. Arthritis and rheumatism. 2010. 62 SUPPL:2271.	Database searches	Original SLR (May 2012)
		Song, I. H., K. G. Hermann, et al. (2011). "Effects of etanercept versus sulfasalazine in early axial spondyloarthritis on active inflammatory lesions as detected by whole-body MRI (ESTHER): A 48-week randomised controlled trial (Annals of the Rheumatic Diseases (2011) 70, (590-596) DOI:10.1136/ard.2010.139667)." Annals of the Rheumatic Diseases 70(7): 1350.	Database searches	1st update (October 2013)
		I. H. Song, K. G. Hermann, H. Haibel, C. Althoff, J. Listing, B. Freundlich, M. Rudwaleit. Relationship between active inflammatory lesions in the spine and sacroiliac joints and new development of fatty infiltration on whole-body MRI in early axial spondyloarthrit is results of the ESTHER trial at week 48. Arthritis and rheumatism. 2010. 62:669-	Database searches	5th update (April 2019)
ETN Study 314 (30)	NCT00418548	**van der Heijde D, Da Silva JC, Dougados M, Geher P, van der Horst-Bruinsma I, Juanola X, et al. Etanercept 50 mg once weekly is as effective as 25 mg twice weekly in patients with ankylosing spondylitis. Ann Rheum Dis. 2006;65(12):1572-7.**	Database searches	Original SLR (May 2012)
		Braun J, McHugh N, Singh A, Wajdula JS, Sato R. Improvement in patient-reported outcomes for patients with ankylosing spondylitis treated with etanercept 50 mg once-weekly and 25 mg twice-weekly. Rheumatology (Oxford). 2007;46(6):999-1004.	Database searches	Original SLR (May 2012)
Giardina 2010 (31)	None	**Giardina AR, Ferrante A, Ciccia F, Impastato R, Miceli MC, Principato A, et al. A 2-year comparative open label randomized study of efficacy and safety of etanercept and infliximab in patients with ankylosing spondylitis. Rheumatol Int. 2010;30(11):1437-40.**	Database searches	Original SLR (May 2012)
GO-AHEAD (32)	NCT01453725	**Sieper J, van der Heijde D, Dougados M, Maksymowych WP, Scott BB, Boice JA, et al. A randomized, double-blind, placebo-controlled, sixteen-week study of subcutaneous golimumab in patients with active nonradiographic axial spondyloarthritis. Arthritis Rheumatol. 2015;67(10):2702-12.**	Database searches	3rd update (January 2017)

		Dougados M, Bergman G, Maksymowych W, Curtis S, Huyck S, Tzontcheva A, et al. Baseline demographic and disease characteristics associated with response to golimumab in patients with active non radiographic axial spondyloarthritis [abstract]. Journal of Rheumatology. 2016;43.	Database searches	4th update (April 2018)
		Maksymowych W, Curtis S, Dougados M, Bergman G, Huyck S, Tzontcheva A, et al. Quality of life in patients with active non radiographic axial spondyloarthritis after 16 weeks of golimumab treatment [abstract]. Journal of Rheumatology. 2016;43:1179-80.	Database searches	4th update (April 2018)
		Maksymowych W, Tzontcheva A, Philip G, Bergman G, Huyck S, Curtis SP. Spondyloarthritis Research Consortium of Canada (SPARCC) Baseline MRI SI Joint Score ≥2 Better Predicts Response to Golimumab Than Does Assessment of Spondyloarthritis International Society (ASAS) MRI Positivity in Nonradiographic Axial Spondyloarthritis [abstract 688]. Arthritis Rheumatol. 2016;68.	Database searches	4th update (April 2018)
		Sieper J, van der Heijde D, Maksymowych W, Braun J, Bergman G, Curtis SP, et al. Efficacy of Golimumab for Nonradiographic Axial Spondyloarthritis: Subgroup Analysis by Baseline MRI and C-Reactive Protein Status [abstract SAT0399]. Annals of the Rheumatic Diseases. 2016;75:813-4.	Database searches	5th update (April 2019)
		Maksymowych W, Curtis S, Dougados M, Bergman G, Huyck S, Tzontcheva A, et al. Quality of life in Patients with Active Nonradiographic Axial Spondyloarthritis After 16 Weeks of Golimumab Treatment [abstract AB0757]. Annals of the Rheumatic Diseases. 2015;74:1151-2.	Hand searches	3rd update (January 2017)
		Sieper J, van der Heijde D, Dougados M, Maksymowych W, Boice JA, Bergman G, et al. A Randomized, Double-Blind, Placebo-Controlled, 16-Week Study of Subcutaneous Golimumab in Patients with Active Nonradiographic Axial Spondyloarthritis [abstract THU0238]. Annals of the Rheumatic Diseases. 2015;74:283.	Hand searches	3rd update (January 2017)
		Efficacy of golimumab for nonradiographic axial spondyloarthritis: subgroup analysis by baseline mri and c-reactive protein status; J. Sieper, D. van der Heijde, W.P. Maksymowych, J. Braun4, G. Bergman, S.P. Curtis, A. Tzontcheva, G. Philip, S. Huyck, M. Dougados. EULAR 2016	Hand searches	3rd update (January 2017)
		Sieper J, van der Heijde D, Dougados M, Maksymowych WP, Boice J, Bergman G, et al. A Randomized, Double-Blind, Placebo-Controlled, 16-Week Study of Subcutaneous Golimumab in Patients with Active Nonradiographic Axial Spondyloarthritis [abstract 2938]. Arthritis and Rheumatol. 2014;66.	Hand searches	3rd update (January 2017)
		Sieper J, van der Heijde D, Maksymowych W, Braun J, Bergman G, Curtis SP, et al. Efficacy of Golimumab for Nonradiographic Axial Spondyloarthritis (nr-axSpA): Subgroup Analysis By Baseline MRI and C-Reactive Protein Status [abstract 712]. Arthritis Rheumatol. 2016;68.	Database searches	4th update (April 2018)
		National Institute for Health and Care Excellence. Golimumab for treating non-radiographic axial spondyloarthritis - technology appraisal guidance [TA497]. Available at: https://www.nice.org.uk/guidance/ta497 (last accessed April 2022). 2018.	Hand searches	4th update (April 2018)
GO-ALIVE (33)	NCT02186873	**Reveille JD, Deodhar A, Caldron PH, Dudek A, Harrison DD, Kim L, et al. Safety and Efficacy of Intravenous Golimumab in Adults with Ankylosing Spondylitis: Results through 1 Year of the GO-ALIVE Study. J Rheumatol. 2019;46(10):1277-83.**	Database searches	5th update (April 2019)
		Deodhar A, Reveille JD, Chan EK, Peterson S, Li N, Hsia E, et al. Improvements in sleep problems and pain in patients with active ankylosing spondylitis treated with intravenous golimumab: 28-week results of the phase iii go-alive trial [abstract THU0360]. Annals of the Rheumatic Diseases. 2017;76:341.	Database searches	5th update (April 2019)
		Deodhar A, Reveille J, Harrison DD, Kim L, Lo KH, Hsia E. Safety and efficacy of intravenous golimumab in adult patients with active ankylosing spondylitis: results through week 28 [abstract THU0348]. Annals of the Rheumatic Diseases. 2017;76:335.	Database searches	5th update (April 2019)
		Deodhar A, Reveille J, Harrison DD, Kim L, Lo KH, Hsia E. Safety and Efficacy of Intravenous Golimumab in Adult Patients with Active Ankylosing Spondylitis: Results through Week 28 [abstract 1043]. Arthritis Rheumatol. 2016;68.	Database searches	5th update (April 2019)

		Reveille JD, Deodhar A, Chan EK, Peterson S, Li N, Hsia E, et al. Effects of intravenous golimumab on patient-reported outcomes in active ankylosing spondylitis: 28-week results of the phase III go-alive trial [abstract AB0692]. Annals of the Rheumatic Diseases. 2017;76:1295-6.	Database searches	5th update (April 2019)
		Reveille JD, Deodhar A, Li N, Han C, Chan E, Hsia EC, et al. The effect of golimumab, an anti-TNFa monoclonal antibody, on general health status, daily activity and work productivity in subjects with active ankylosing spondylitis: 28-week results of the phase III go alive trial [abstract A151]. Value in Health. 2017;20.	Database searches	5th update (April 2019)
		Deodhar AA, Reveille JD, Chan EKH, Peterson S, Li N, Hsia EC, et al. Improvements in Sleep Problems and Pain in Patients with Active Ankylosing Spondylitis Treated with Intravenous Golimumab: 28-Week Results of the Phase III Trial [abstract 1530]. Arthritis Rheumatol. 2017;69.	Database searches	5th update (April 2019)
		Reveille JD, Deodhar A, Chan EK, Peterson S, Li N, Hsia E, et al. Effects of intravenous golimumab on patient-reported outcomes in active ankylosing spondylitis: 28-week results of the phase III go-alive trial [abstract]. Arthritis & Rheumatology. 2017;69.	Database searches	5th update (April 2019)
		Deodhar A, Reveille JD, Harrison DD, Kim L, Lo KH, Leu JH, et al. Safety and Efficacy of Golimumab Administered Intravenously in Adults with Ankylosing Spondylitis: Results through Week 28 of the GO-ALIVE Study. J Rheumatol. 2018;45(3):341-8.	Database searches	5th update (April 2019)
		Reveille JD, Deodhar AA, Harrison DD, Kim L, Lo KH, Hsia EC. Safety and Efficacy of Intravenous Golimumab in Adult Patients with Active Ankylosing Spondylitis: Results through 1 Year [abstract 1532]. Arthritis & Rheumatology. 2017;69.	Database searches	5th update (April 2019)
		Reveille JD, Deodhar A, Harrison D, Hsia EC, Chan EKH, Kafka S, et al. Effects of Intravenous Golimumab, an Anti-TNFalpha Monoclonal Antibody, on Health-Related Quality of Life in Patients with Ankylosing Spondylitis: 1-Year Results of a Phase III Trial [abstract 1258]. Arthritis & Rheumatology. 2029;71:2166-8.	Database searches	6th update (October 2020)
		Reveille JD, Deodhar A, Ince A, Chan EKH, Peterson S, Li N, et al. Effects of Intravenous Golimumab on Health-Related Quality of Life in Patients with Ankylosing Spondylitis: 28-Week Results of the GO-ALIVE Trial. Value Health. 2020;23(10):1281-5.	Database searches	6th update (October 2020)
		Reveille JD, Hwang MC, Danve A, Kafka S, Peterson S, Lo KH, et al. The effect of intravenous golimumab on health-related quality of life and work productivity in adult patients with active ankylosing spondylitis: results of the phase 3 GO-ALIVE trial. Clin Rheumatol. 2021;40(4):1331-41.	Database searches	6th update (October 2020)
		Safety and Efficacy of Intravenous Golimumab in Adult Patients with Active Ankylosing Spondylitis: Results through Week 28 Atul A. Deodhar, John D. Reveille, Diane D. Harrison, Lilianne Kim, Kim Hung Lo and Elizabeth C. Hsia (ab 1043). ACR 2016.	Hand searches	3rd update (January 2017)
GO-RAISE (34)	NCT00265083	**Inman RD, Davis JC, Jr., Heijde D, Diekman L, Sieper J, Kim SI, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomized, double-blind, placebo-controlled, phase III trial. Arthritis Rheum. 2008;58(11):3402-12.**	Database searches	Original SLR (May 2012)
		Braun J, Davis J, van der Heijde D, Deodhar A, Diekman L, Sieper J, et al. TNF(alpha) antibody, in Ankylosing spondylitis (AS): 24-Week efficacy and safety results of the go-raise study [abstract]. Rheumatology. 2009;48:i57.	Database searches	Original SLR (May 2012)
		Braun J. Golimumab, a new, human, a antibody, in ankylosing spondylitis: 24-week efficacy and safety results of the go-raise study. Internal Medicine Journal. 2009. 39 SUPPL(May 2009 C).	Database searches	Original SLR (May 2012)
		Braun J, Deodhar A, Inman RD, van der Heijde D, Mack M, Xu S, et al. Golimumab administered subcutaneously every 4 weeks in ankylosing spondylitis: 104-week results of the GO-RAISE study. Ann Rheum Dis. 2012;71(5):661-7.	Database searches	Original SLR (May 2012)
		Braun J, Inman RD, van der Heijde D, Mack M, Parasuraman S, Buchanan J, et al. Golimumab significantly improves productivity in patients with active ankylosing spondylitis: Results from the phase 3 go-raise study. Value in Health. 2009;12.	Database searches	Original SLR (May 2012)

		Deodhar A, Braun J, Inman RD, Mack M, Parasuraman S, Buchanan J, et al. Golimumab reduces sleep disturbance in patients with active ankylosing spondylitis: results from a randomized, placebo-controlled trial. Arthritis Care Res. 2010;62(9):1266-71.	Database searches	Original SLR (May 2012)
		Genovese M, Deodhar A, Hsia E, Hsu B, Lin Y, Han C. Patients Reported Outcomes in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis Treated With Golimumab: Sub-Analysis of Asia Population Enrolled in Multicentre Phase Iii Clinical Trials [abstract PMS20]. Value in Health. 2012;15(7).	Database searches	1st update (October 2013)
		van der Heijde D, Braun J, Deodhar A, Inman RD, Xu S, Mack ME, et al. Comparison of three enthesitis indices in a multicentre, randomized, placebo-controlled trial of golimumab in ankylosing spondylitis (GO-RAISE). Rheumatology (Oxford). 2013;52(2):321-5.	Database searches	1st update (October 2013)
		van der Heijde D, Deodhar A, Inman RD, Braun J, Hsu B, Mack M. Comparison of three methods for calculating the Bath Ankylosing Spondylitis Metrology Index in a randomized placebo-controlled study. Arthritis Care Res (Hoboken). 2012;64(12):1919-22.	Database searches	1st update (October 2013)
		Braun J, Heijde D, Deodhar A, Diekman L, Sieper J, Kim SI, et al. Golimumab, a new, human, TNF-(alpha) antibody administered subcutaneously every 4 weeks, in ankylosing spondylitis: 104-week efficacy and safety results of the randomized, placebo-controlled go-raise study [abstract]. Scandinavian Journal of Rheumatology. 2010;39.	Database searches	2nd update (July 2014)
		van der Heijde D, Deodhar A, Braun J, Mack M, Hsu B, Gathany TA, et al. The effect of golimumab therapy on disease activity and health-related quality of life in patients with ankylosing spondylitis: 2-year results of the GO-RAISE trial. J Rheumatol. 2014;41(6):1095-103.	Database searches	2nd update (July 2014)
		Lee JS, Song YW, Kim TH, Chung WT, Lee SG, Park SH, et al. Baseline extent of damage predicts spinal radiographic progression in Korean patients with ankylosing spondylitis treated with golimumab. Korean J Intern Med. 2018;33(3):622-8.	Database searches	5th update (April 2019)
		M. Zlnay, D. Zlnay. Efficacy and safety of golimumab in patients with ankylosing spondylitis - Results from go-raise study. Rheumatologia. 2010. 24:49-54	Database searches	5th update (April 2019)
		Braun J. The effect of golimumab on structural spinal changes in ankylosing spondylitis: magnetic resonance imaging results of the randomized, placebo-controlled GO-RAISE study. Abstract L1. American College of Rheumatology Annual Scientific Meeting, 2010.	Hand searches	Original SLR (May 2012)
		Han C, Kavanaugh A, Genovese M, Deodhar A, Hsu B, Hsia E. Sustained Improvement in Health-Related Quality of Life, Work Productivity, Employability and Reduced Healthcare Resource Utilization of Patients with Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis Treated with Golimumab: 5-Year Results from Three Phase III Studies [abstract 50]. Rheumatology. 2014;53:i74.	Hand searches	2nd update (July 2014)
		Deodhar A, Braun J, Inman R, van der Heijde D, Zhou Y, Hsu B. Long-Term Safety and Efficacy of Golimumab in the Treatment of Ankylosing Spondylitis: Results Through 5 Years of a Randomized, Placebo-Controlled Trial [abstract 219]. Rheumatology. 2014;53:i142.	Hand searches	2nd update (July 2014)
Gorman 2002 (26)	None	**Gorman JD, Sack KE, Davis JC, Jr. Treatment of ankylosing spondylitis by inhibition of tumor necrosis factor alpha. N Engl J Med. 2002;346(18):1349-56.**	Database searches	Original SLR (May 2012)
		Wanders AJ, Gorman JD, Davis JC, Landewe RB, van der Heijde DM. Responsiveness and discriminative capacity of the assessments in ankylosing spondylitis disease-controlling antirheumatic therapy core set and other outcome measures in a trial of etanercept in ankylosing spondylitis. Arthritis Rheum. 2004;51(1):1-8.	Database searches	Original SLR (May 2012)
Haibel 2008 (35)	NCT00235105	**Haibel H, Rudwaleit M, Listing J, Heldmann F, Wong RL, Kupper H, et al. Efficacy of adalimumab in the treatment of axial spondylarthritis without radiographically defined sacroiliitis: results of a twelve-week randomized,**	Database searches	Original SLR (May 2012)

		double-blind, placebo-controlled trial followed by an open-label extension up to week fifty-two. Arthritis Rheum. 2008;58(7):1981-91.		
Hu 2012 (36)	None	**Hu Z, Xu M, Li Q, Lin Z, Liao Z, Cao S, et al. Adalimumab significantly reduces inflammation and serum DKK-1 level but increases fatty deposition in lumbar spine in active ankylosing spondylitis. Int J Rheum Dis. 2012;15(4):358-65.**	Database searches	Original SLR (May 2012)
Hu 2012 (36) & ATLAS (8)	None & NCT00085644	Huang F, van der Heijde D, Sieper J, Braun J, Mease P, Pangan A, et al. Comparison of ankylosing spondylitis in Chinese and western patients [abstract APLAR-0080]. International Journal of Rheumatic Diseases. 2014;17:42.	Database searches	2nd update (July 2014)
Huang 2014 (37)	NCT01114880	**Huang F, Gu J, Zhu P, Bao C, Xu J, Xu H, et al. Efficacy and safety of adalimumab in Chinese adults with active ankylosing spondylitis: results of a randomised, controlled trial. Ann Rheum Dis. 2014;73(3):587-94.**	Database searches	2nd update (July 2014)
Huji 2019 (38)	NCT02893254	**Xu H, Li Z, Wu J, Xing Q, Shi G, Li J, et al. IBI303, a biosimilar to adalimumab, for the treatment of patients with ankylosing spondylitis in China: a randomised, double-blind, phase 3 equivalence trial [abstract]. The Lancet Rheumatology. 2019;1:e35-e43.**	Database searches	6th update (October 2020)
		Huji X, Zhijun L, Jian W, Qian X, Shi G, Juan L, et al. Similar Efficacy and Safety of Biosimilar Candidate IBI303 and Reference Products of Adalimumab in Patients with Ankylosing Spondylitis: Results from a Randomized, Double-Blind, Phase III Study. Arthritis Rheumatol. 2018;70.	Database searches	5th update (April 2019)
Leeds ETN Study (39)	None	**Barkham N, Coates LC, Keen H, Hensor E, Fraser A, Redmond A, et al. Double-blind placebo-controlled trial of etanercept in the prevention of work disability in ankylosing spondylitis. Ann Rheum Dis. 2010;69(11):1926-8.**	Database searches	Original SLR (May 2012)
Leeds IFX Study (40)	None	**Barkham N, Keen HI, Coates LC, O'Connor P, Hensor E, Fraser AD, et al. Clinical and imaging efficacy of infliximab in HLA-B27-Positive patients with magnetic resonance imaging-determined early sacroiliitis. Arthritis Rheum. 2009;60(4):946-54.**	Database searches	Original SLR (May 2012)
Li 2022 (41)	ChiCTR20181863	**Li J, Xue Z, Wu Z, Bi L, Liu H, Wu L, et al. Comparison of the efficacy and safety of the adalimumab biosimilar TQ-Z2301 and adalimumab for the treatment of Chinese patients with active ankylosing spondylitis: a multi-center, randomized, double-blind, phase III clinical trial. Clinical Rheumatology. 2022;41(10):3005-16.**	Database searches	8th update (January 2023)
Marzo-Ortega 2005 (42)	None	**Marzo-Ortega H, McGonagle D, Jarrett S, Haugeberg G, Hensor E, O'Connor P, et al. Infliximab in combination with methotrexate in active ankylosing spondylitis: a clinical and imaging study. Ann Rheum Dis. 2005;64(11):1568-75.**	Database searches	Original SLR (May 2012)
MEASURE 1 (43)	NCT01358175	Deodhar AA, Dougados M, Baeten DL, Cheng-Chung Wei J, Geusens P, Readie A, et al. Effect of Secukinumab on Patient-Reported Outcomes in Patients With Active Ankylosing Spondylitis: A Phase III Randomized Trial (MEASURE 1). Arthritis Rheumatol. 2016;68(12):2901-10.	Database searches	3rd update (January 2017)
		Braun J, Baraliakos X, Deodhar A, Baeten D, Sieper J, Emery P, et al. Effect of secukinumab on clinical and radiographic outcomes in ankylosing spondylitis: 2-year results from the randomised phase III MEASURE 1 study. Annals of the Rheumatic Diseases. 2016;76:1070-7.	Database searches	3rd update (January 2017)
		Emery P, Baeten D, Deodhar A, Wei A, Geusens P, Talloczy Z, et al. Secukinumab Improves Physical Function and Quality of Life in Patients with Active Ankylosing Spondylitis: 2-Year Data from Measure 1, A Phase 3 Randomised Trial [abstract SAT0410]. Annals of the Rheumatic Diseases. 2016;75.	Hand searches	3rd update (January 2017)
		Baeten D, Braun J, Baraliakos X, Sieper J, Dougados M, Emery P, et al. Secukinumab, a Monoclonal Antibody to Interleukin-17A, Significantly Improves Signs and Symptoms of Active Ankylosing Spondylitis: Results of a 52-Week Phase 3 Randomized Placebo-Controlled Trial with Intravenous Loading and Subcutaneous Maintenance Dosing [abstract 819]. Arthritis & Rheumatology. 2014.	Hand searches	3rd update (January 2017)
		Deodhar A, Baeten D, Braun J, Baraliakos X, Sieper J, Dougados M, et al. Secukinumab, a Monoclonal Antibody to Interleukin-17A, Significantly Improves Physical Function and Quality of Life in Subjects with Active Ankylosing Spondylitis: Results of a Phase 3 Randomized, Placebo-Controlled Trial with	Hand searches	3rd update (January 2017)

		Intravenous Loading and Subcutaneous Maintenance Dosing [abstract 538]. Arthritis & Rheumatology. 2014.		
		Baeten D, Braun J, Sieper J, Dougados M, Deodhar A, Baraliakos X, et al. Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Active Ankylosing Spondylitis: 2-Year Efficacy and Safety Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial [abstract 2896]. Arthritis & Rheumatology. 2015;67.	Hand searches	3rd update (January 2017)
MEASURE 2 (43)	NCT01649375	Sieper J, Deodhar A, Marzo-Ortega H, Aelion JA, Blanco R, Jui-Cheng T, et al. Secukinumab efficacy in anti-TNF-naive and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 Study. Ann Rheum Dis. 2017;76(3):571-92.	Database searches	5th update (April 2019)
		Baraliakos X, Schiff M, Pavelka K, Widmer A, Porter B, Gaillez C. Secukinumab sustains individual clinical responses over time in patients with active ankylosing spondylitis: 2-year results from a phase 3 trial, measure 2 [abstract]. Annals of the Rheumatic Diseases. 2017;76.	Database searches	5th update (April 2019)
		D. Jean, J. Braun, X. Baraliakos, D. Baeten, M. Dougados, P. Emery, A. Deodhar, B. Porter, M. Andersson, H. Richards. Secukinumab efficacy in anti-TNF-naive patients and patients previously exposed to anti-TNF Therapy: Results of A randomized, double-blind, placebo- controlled phase 3 study (MEASURE 2) in active ankylosing spondylitis. Swiss Medical Weekly. 2016. 146:7S	Database searches	5th update (April 2019)
		Marzo-Ortega H, Miceli-Richard C, Gill S, Magery M, Machado PGP, Shete A, et al. Subcutaneous secukinumab 150 mg provides rapid and sustained relief in total and nocturnal back pain, morning stiffness and fatigue in patients with active AS over 4 years [P248]. Arthritis & Rheumatology. 2020;71:2653-4.	Database searches	6th update (October 2020)
		Marzo-Ortega H, Miceli-Richard C, Gill S, Magery M, Machado PGP, Shete A, et al. Subcutaneous secukinumab 150 mg provides rapid and sustained relief in total and nocturnal back pain, morning stiffness and fatigue in patients with active AS over 4 years [P248]. Rheumatology. 2020;59.	Database searches	6th update (October 2020)
		Marzo-Ortega H, Miceli-Richard C, Gill S, Magrey M, Machado P, Shete A, et al. Subcutaneous Secukinumab 150 Mg Provides Sustained Relief in Total and Nocturnal Back Pain, Morning Stiffness, Fatigue, and Low Disease Activity in Patients with Active Ankylosing Spondylitis: End-of-study (5-year) Data from the MEASURE 2 Trial [abstract]. Arthritis & Rheumatology. 2020;72.	Hand searches	6th update (October 2020)
		Braun J, Sieper J, Aelion J, Emery P, Deodhar A, Porter B, et al. Secukinumab Improves Multiple Parameters of Disease Activity in Subjects with Active Ankylosing Spondylitis Through 52 Weeks of Subcutaneous Therapy: Data From the Phase 3 Measure 2 Study [abstract AB0743]. Annals of the Rheumatic Diseases. 2015;74.	Hand searches	3rd update (January 2017)
		Deodhar A, Sieper J, Emery P, Porter B, Andersson M, Richards H. Secukinumab Significantly Improves Physical Function, Quality of Life, and Work Productivity Through 52 Weeks in Subjects with Active Ankylosing Spondylitis in the Phase 3 Measure 2 Study [abstract AB0736]. Annals of the Rheumatic Diseases. 2015;74.	Hand searches	3rd update (January 2017)
		Sieper J, Braun J, Baraliakos X, Baeten DL, Dougados M, Emery P, et al. Secukinumab Efficacy in Anti-Tnf-Naive Patients and Patients Previously Exposed to Anti-Tnf Therapy: Results of a Randomized, Double-Blind, Placebo-Controlled Phase 3 Study (Measure 2) in Active Ankylosing Spondylitis [abstract THU0210]. Annals of the Rheumatic Diseases. 2015;74.	Hand searches	3rd update (January 2017)
		Sieper J, Braun J, Baraliakos X, Baeten DL, Dougados M, Emery P, et al. Secukinumab Significantly Improves Signs and Symptoms of Active Ankylosing Spondylitis: 52-Week Data from Measure 2, A Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial with Subcutaneous Loading and Maintenance Dosing [abstract OP0168]. Annals of the Rheumatic Diseases. 2015;74.	Hand searches	3rd update (January 2017)
		Marzo-Ortega H, Legerton CW, Sieper J, Kivitz A, Blanco R, Cohen M, et al. Secukinumab Provides Sustained Improvements in The Signs and Symptoms of Active Ankylosing Spondylitis: 2-Year Results from A Phase 3 Trial with Subcutaneous Loading and Maintenance Dosing (Measure 2) [abstract SAT0396]. Annals of the Rheumatic Diseases. 2016;75.	Hand searches	3rd update (January 2017)

		Secukinumab significantly improves physical function, quality of life, fatigue and work productivity in subjects with active ankylosing spondylitis treated for up to 52 weeks in the phase 3 measure 2 study; Paul Emery, Atul Deodhar, Joachim Sieper, Mats Andersson, Hanno Richards. BSR 2016	Hand searches	3rd update (January 2017)
		Sieper J, Braun J, Baraliakos X, Baeten D, Dougados M, Emery P, et al. Secukinumab, a Monoclonal Antibody to Interleukin-17A, Significantly Improves Signs and Symptoms of Active Ankylosing Spondylitis: Results of a Phase 3, Randomized, Placebo-Controlled Trial with Subcutaneous Loading and Maintenance Dosing [abstract 536]. Arthritis & Rheumatology. 2014.	Hand searches	3rd update (January 2017)
		Pavelka K, Kivitz A, Calheiros R, Quebe-Fehling E, Pertel P, Blanco R. MEASURE 2: Secukinumab provides rapid and sustained relief from key clinical symptoms of active ankylosing spondylitis in TNFi-naïve patients through 5 years. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):770-1.	Hand searches	7th update (April 2022)
		Pavelka K, Kivitz A, Calheiros R, Quebe-Fehling E, Pertel P, Blanco R. MEASURE 2: SECUKINUMAB PROVIDES RAPID and SUSTAINED RELIEF from KEY CLINICAL SYMPTOMS of ACTIVE ANKYLOSING SPONDYLITIS in TNFI-NAIVE PATIENTS THROUGH 5 YEARS. Annals of the Rheumatic Diseases. 2022;81(Supplement 1):770-1.	Database searches	8th update (January 2023)
MEASURE 1 & MEASURE 2 (43)	NCT01358175 & NCT01649375	**Baeten D, Sieper J, Braun J, Baraliakos X, Dougados M, Emery P, et al. Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. N Engl J Med. 2015;373(26):2534-48.**	Database searches	3rd update (January 2017)
		Collins A, Baeten D, Braun J, Baraliakos X, Sieper J, Dougados M, et al. Secukinumab, a monoclonal antibody to interleukin-17a, significantly improves signs and symptoms of active ankylosing spondylitis: Results of a 52-week phase 3 randomized placebo-controlled trial with intravenous loading and subcutaneous maintenance dosing [abstract]. Internal Medicine Journal. 2015;45:41.	Database searches	5th update (April 2019)
		Deodhar A, Baeten D, Blanco R, Sieper J, Martin R, Porter B, et al. Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis in anti-TNF-naive patients and those previously exposed to anti-TNF therapy: 52-week results from two international phase 3 trials [abstract]. Journal of Clinical Rheumatology. 2016;22(3):137-8.	Database searches	5th update (April 2019)
		Emery P, Halliday A, Jugl S, Mokashi S, Porter B, Martin R, et al. Long-term efficacy of secukinumab conditional on response status at week 12: Analysis in tumour necrosis factor a inhibitor-naïve and tumour necrosis factor a inhibitor inadequate responder patients with active ankylosing spondylitis [abstract 107]. Rheumatology. 2017;56.	Database searches	5th update (April 2019)
		Kivitz A, Blanco R, Maradiaga M, Sieper J, Tahir H, Andersson M, et al. Secukinumab reduces signs and symptoms of active ankylosing spondylitis: Results from a 16-week, randomized placebo-controlled phase 3 trial [abstract]. Journal of Clinical Rheumatology. 2016;22:141.	Database searches	5th update (April 2019)
		Wylie A, Deodhar A, Baeten D, Braun J, Baraliakos X, Sieper J, et al. Secukinumab, a monoclonal antibody to interleukin-17a, significantly improves physical function and quality of life in subjects with active ankylosing spondylitis: Results of a phase 3 randomized, placebo-controlled trial with intravenous loading and subcutaneous maintenance dosing [abstract]. Internal Medicine Journal. 2015;45:40.	Database searches	5th update (April 2019)
		Pavelka K, Kivitz A, Dokoupilova E, Blanco R, Maradiaga M, Tahir H, et al. Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis: 2-year results from a phase 3 study [abstract]. Arthritis & Rheumatology. 2017;69.	Database searches	5th update (April 2019)
		Pavelka K, Kivitz AJ, Blanco R, Maradiaga M, Tahir H, Slade A, et al. Secukinumab provides sustained improvements in the signs and symptoms of active ankylosing spondylitis: 2-year results from a phase 3 study [abstract]. Journal of Clinical Rheumatology. 2018;24:S107-S8.	Database searches	5th update (April 2019)
		Deodhar A, Conaghan PG, Kvien TK, Strand V, Sherif B, Porter B, et al. Secukinumab provides rapid and persistent relief in pain and fatigue symptoms in patients with ankylosing spondylitis irrespective of baseline C-reactive protein	Database searches	5th update (April 2019)

		levels or prior tumour necrosis factor inhibitor therapy: 2-year data from the MEASURE 2 study. Clin Exp Rheumatol. 2019;37(2):260-9.		
		Baeten D, Blanco R, Geusens P, Sieper J, Jui-Cheng T, Martin R, et al. Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Active Ankylosing Spondylitis in Anti-TNF-Naïve Patients and Those Previously Exposed to Anti-TNF Therapy: 52-Week Results from Two Randomized, Double-Blind, Placebo-Controlled Phase 3 Trials [abstract 2890]. Arthritis & Rheumatology. 2015.	Hand searches	3rd update (January 2017)
		Baraliakos X, Van den Bosch F, Machado PM, Gensler LS, Marzo-Ortega H, Sherif B, et al. Achievement of Remission Endpoints with Secukinumab Over 3 Years in Active Ankylosing Spondylitis: Pooled Analysis of Two Phase 3 Studies. Rheumatology and Therapy. 2021;8(1):273-88.	Database searches	7th update (April 2022)
MEASURE 3 (44)	NCT02008916	**Pavelka K, Kivitz A, Dokoupilova E, Blanco R, Maradiaga M, Tahir H, et al. Efficacy, safety, and tolerability of secukinumab in patients with active ankylosing spondylitis: a randomized, double-blind phase 3 study, MEASURE 3. Arthritis Res Ther. 2017;19(1):285.**	Database searches	5th update (April 2019)
MEASURE 4 (45)	NCT02159053	**Kivitz AJ, Wagner U, Dokoupilova E, Supronik J, Martin R, Talloczy Z, et al. Efficacy and Safety of Secukinumab 150 mg with and Without Loading Regimen in Ankylosing Spondylitis: 104-week Results from MEASURE 4 Study. Rheumatol Ther. 2018;5(2):447-62.**	Database searches	5th update (April 2019)
MEASURE 1-4	NCT01358175, NCT01649375, NCT02008916 & NCT02159053	Schett G, Baraliakos X, van den Bosch F, Deodhar A, Ostergaard M, Gupta AD, et al. Secukinumab efficacy on enthesitis in patients with ankylosing spondylitis: Pooled analysis of four pivotal phase III studies. Journal of Rheumatology. 2021;48(8):1251-8.	Database searches	7th update (April 2022)
		Deodhar A, Mease PJ, Poddubnyy D, Calheiros R, Meng X, Strand V, et al. Impact of hla-b27 status on clinical outcomes among patients with ankylosing spondylitis treated with secukinumab. Annals of the Rheumatic Diseases. 2020;79(SUPPL 1):721.	Database searches	7th update (April 2022)
MEASURE 5 (46)	NCT02896127	**Huang F, Sun F, Wan W, Wu L, Dong L, Zhang X, et al. Secukinumab provides rapid and significant improvement in the signs and symptoms of ankylosing spondylitis: Primary (16-week) results from a phase 3 china-centric study, measure 5 [abstract FRI0414]. Annals of the Rheumatic Diseases. 2019;78.**	Database searches	6th update (October 2020)
		Huang F, Sun F, Wan WG, Wu LJ, Dong LL, Zhang X, et al. Secukinumab provided significant and sustained improvement in the signs and symptoms of ankylosing spondylitis: results from the 52-week, Phase III China-centric study, MEASURE 5. Chin Med J (Engl). 2020;133(21):2521-31.	Database searches	6th update (October 2020)
MEASURE 1-5	NCT01358175, NCT01649375, NCT02008916, NCT02159053 & NCT02896127	Deodhar A, Mease P, Poddubnyy D, Strand V, MacHado P, Shete A, et al. Impact of HLA-B27 Status on Clinical Outcomes in Patients with Ankylosing Spondylitis Treated with Secukinumab. Arthritis and Rheumatology. 2020;72(SUPPL 10):1759-61.	Database searches	7th update (April 2022)
PLANETAS (47)	NCT01220518	**Park W, Hrycaj P, Jeka S, Kovalenko V, Lysenko G, Miranda P, et al. A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis. 2013;72(10):1605-12.**	Database searches	1st update (October 2013)
		Park W, Jaworski J, Brzezicki J, Gnylorybov A, Kadinov V, Sariego IG, et al. A randomised, double-blind, parallel-group, phase 1 study comparing the pharmacokinetics, safety and efficacy of ct-p13 and infliximab in patients with active ankylosing spondylitis: 54 week results from the planetas study [abstract FRI0421]. Annals of the Rheumatic Diseases. 2013;72:A516-A7.	Database searches	2nd update (July 2014)
		Park W, Hrycaj P, Kovalenko V, Miranda P, Gutierrez-Ureña S, Lee Y, et al. A randomized, double-blind, phase 1 study demonstrates equivalence in pharmacokinetics, safety, and efficacy of CT-P13 and infliximab in patients with ankylosing spondylitis [abstract OP0167]. Annals of the Rheumatic Diseases. 2013;71:111.	Database searches	2nd update (July 2014)

PrevAS (48)	EudraCT number 2009-015515-40	**Rusman T, van der Weijden MAC, Nurmohamed MT, Landewe RBM, de Winter JJH, Boden BJH, et al. Is Treatment in Patients With Suspected Nonradiographic Axial Spondyloarthritis Effective? Six-Month Results of a Placebo-Controlled Trial. Arthritis and Rheumatology. 2021;73(5):806-15.**	Database searches	7th update (April 2022)
		Rusman T, Van der Weijden MAC, Nurmohamed MT, Landewe RBM, De Winter JJ, Boden BJH, et al. Is very early treatment effective? Six months results of the prevas study, a placebo-controlled trial with etanercept in patients suspected of non-radiographic axial spondyloarthritis [abstract OP0110]. Annals of the Rheumatic Diseases. 2020;79.	Hand searches	6th update (October 2020)
PREVENT (49)	NCT02696031	**Deodhar A, Blanco R, Dokoupilová E, Hall S, Kameda H, Kivitz AJ, et al. Improvement of Signs and Symptoms of Nonradiographic Axial Spondyloarthritis in Patients Treated With Secukinumab: Primary Results of a Randomized, Placebo-Controlled Phase III Study. Arthritis Rheumatol. 2021;73(1):110-20.**	Database searches	7th update (April 2022)
		Marzo-Ortega H, Deodhar A, Blanco R, Kameda H, Kivitz A, Poddubnyy D, et al. Secukinumab Improves Pain, Morning Stiffness, Fatigue and Physical Function in Tumor Necrosis Factor Inhibitor-Naïve Patients with Non-Radiographic Axial Spondyloarthritis: Results from a Randomized Controlled Phase III Study [abstract]. Arthritis & Rheumatology. 2020;72.	Hand searches	6th update (October 2020)
		Braun J, Blanco R, Marzo-Ortega H, Gensler L, Van den Bosch F, Kameda H, et al. Secukinumab Improved Signs and Symptoms in Patients with Non-radiographic Axial Spondyloarthritis: Results from a Randomized Controlled Phase III Study Stratified by Baseline Objective Signs of Inflammation [abstract]. Arthritis & Rheumatology. 2020;72.	Hand searches	6th update (October 2020)
		Braun J, Blanco R, Dokoupilova E, Gensler LS, Kivitz A, Hall S, et al. Secukinumab 150 mg significantly improved signs and symptoms of non-radiographic axial spondyloarthritis: 52-week results from the phase iii prevent study [abstract OP0106]. Annals of the Rheumatic Diseases. 2020;79.	Hand searches	6th update (October 2020)
		Deodhar A, Blanco F, Dokoupilova E, van de Sande M, Hall S, Wiksten AS, et al. Secukinumab 150 mg Significantly Improved Signs and Symptoms of Non-radiographic Axial Spondyloarthritis: Results from a Phase 3 Double-blind, Randomized, Placebo-controlled Study [abstract L21]. Arthritis & Rheumatology. 2019;71.	Database searches	6th update (October 2020)
		Kameda H, Braun J, Hall S, Poddubnyy D, Van De Sande M, Kivitz A, et al. Secukinumab improves signs and symptoms of non-radiographic axial spondyloarthritis in patients naive to TNF inhibitor: Results from the PREVENT Study. International Journal of Rheumatic Diseases. 2020;23(SUPPL 1):32.	Database searches	7th update (April 2022)
		Braun J, Blanco R, Marzo-Ortega H, Gensler LS, van den Bosch F, Hall S, et al. Secukinumab in non-radiographic axial spondyloarthritis: subgroup analysis based on key baseline characteristics from a randomized phase III study, PREVENT. Arthritis Research and Therapy. 2021;23(1):231.	Database searches	7th update (April 2022)
RAPID-axSpA (50)	NCT01087762	**Landewe R, Braun J, Deodhar A, Dougados M, Maksymowych WP, Mease PJ, et al. Efficacy of certolizumab pegol on signs and symptoms of axial spondyloarthritis including ankylosing spondylitis: 24-week results of a double-blind randomised placebo-controlled Phase 3 study. Ann Rheum Dis. 2014;73(1):39-47.**	Database searches	1st update (October 2013)
		Landewe RBM, Rudwaleit M, van der Heijde D, Dougados M, Maksymowych WP, Braun J, et al. Effect of certolizumab pegol on signs and symptoms of ankylosing spondyltitis and non-radiographic axial spondyloarthritis: 24 week results of a double blind randomized placebo-controlled phase 3 axial spondyloarthritis study [abstract]. Arthritis & Rheumatism. 2012;64:S336-S7.	Database searches	1st update (October 2013)
		Sieper J, Kivitz A, Van Tubergen A, Deodhar A, Coteur G, Woltering F, et al. Rapid improvements in patient-reported outcomes with certolizumab pegol in patients with axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis: 24-week results of a phase 3 double blind randomized placebo-controlled study [abstract]. Value in Health. 2013;16:A227.	Database searches	1st update (October 2013)

Sieper J, Kivitz A, Van Tubergen A, Deodhar A, Coteur G, Woltering F, et al. Rapid improvements in patient-reported outcomes with certolizumab pegol in patients with axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis: 24-week results of a phase 3 double blind randomized placebo-controlled study [abstract THU0360]. Annals of the Rheumatic Diseases. 2013;72:A287.	Database searches	1st update (October 2013)
van der Heijde D, Braun J, Rudwaleit M, Purcaru O, Kavanaugh A. Increased participation in daily activities after 24 weeks of certolizumab pegol treatment of axial spondyloarthritis patients, including patients with ankylosing spondylitis: results of a phase 3 double-blind randomized placebo-controlled Study [abstract]. Arthritis & Rheumatism. 2012;64:S592.	Database searches	1st update (October 2013)
van der Heijde D, Braun J, Rudwaleit M, Purcaru O, Kavanaugh A. Improvements in productivity at paid work and within household, and increased participation in daily activities after 24 weeks of certolizumab pegol treatment of axial spondyloarthritis patients, including patients with ankylosing spondylitis: Results of a phase 3 double-blind randomized placebo-controlled study [abstract PMS59]. Value in Health. 2013;16:A228-A9.	Database searches	1st update (October 2013)
Van Der Heijde, D., W. P. Maksymowych, et al. (2012). "Effect of certolizumab pegol on inflammation of spine and sacroiliac joints in patients with axial spondyloarthritis: 12 week magnetic resonance imaging results of a phase 3 double blind randomized placebo-controlled study." Arthritis and Rheumatism 64: S730.	Database searches	1st update (October 2013)
Sieper J, Kivitz A, van Tubergen A, Deodhar A, Coteur G, Singh P, et al. Long-term maintenance of improvements in patient-reported outcomes with certolizumab pegol in patients with axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis: 48-week results of the rapid-axspa study [abstract PMS80]. Value in Health. 2013;16:A569.	Database searches	2nd update (July 2014)
van der Heijde D, Braun J, Rudwaleit M, Purcaru O, Kavanaugh A. Continued Improvements in Workplace and Household Productivity with Certolizumab Pegol Treatment in Axial Spondyloarthritis, Including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis: 48-Week Results from the Rapid-axSpA Study [abstract]. Value in Health. 2013;16:A570.	Database searches	2nd update (July 2014)
Sieper J, Kivitz A, van Tubergen A, Deodhar A, Coteur G, Woltering F, et al. Impact of Certolizumab Pegol on Patient-Reported Outcomes in Patients With Axial Spondyloarthritis. Arthritis Care Res (Hoboken). 2015;67(10):1475-80.	Database searches	3rd update (January 2017)
Osterhaus JT, Purcaru O. Discriminant validity, responsiveness and reliability of the arthritis-specific Work Productivity Survey assessing workplace and household productivity within and outside the home in patients with axial spondyloarthritis, including nonradiographic axial spondyloarthritis and ankylosing spondylitis. Arthritis Res Ther. 2014;16(4):R164.	Database searches	3rd update (January 2017)
Braun J, Baraliakos X, Hermann KG, Landewe R, Machado PM, Maksymowych WP, et al. Effect of certolizumab pegol over 96 weeks of treatment on inflammation of the spine and sacroiliac joints, as measured by MRI, and the association between clinical and MRI outcomes in patients with axial spondyloarthritis. RMD Open. 2017;3(1):e000430.	Database searches	4th update (April 2018)
van der Heijde DM, Braun J, Rudwaleit M, Purcaru O, Kavanaugh A. Reduction of disease burden on workplace and household productivity in axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis, over 48 weeks of treatment with certolizumab pegol [abstract]. Arthritis & Rheumatism. 2013;65:S644-S5.	Hand searches	1st update (October 2013)
Landewe RBM, Rudwaleit M, van der Heijde DM, Dougados M, Mease PJ, Reveille JD, et al. Effect of certolizumab pegol over 48 weeks in patients with axial spondyloarthritis, including ankylosing spondylitis and non-radiographic axial spondyloarthritis [abstract]. Arthritis & Rheumatism. 2013;65:S767.	Hand searches	1st update (October 2013)
Landewe R, Rudwaleit M, van der Heijde D, Dougados M, Maksymowych WP, Braun J, et al. Effect of Certolizumab Pegol on Signs and Symptoms of Axial Spondyloarthritis, Including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis: 24-Week Results of Rapid-Axspa Study [abstract OP0106]. Annals of the Rheumatic Diseases. 2013;72.	Hand searches	1st update (October 2013)

		van der Heijde D, Braun J, Rudwaleit M, Purcaru O, Kavanaugh A. Improvements in Work and Household Productivity after 24 Weeks of Certolizumab Pegol in Treatment of Axial Spondyloarthritis Patients, Including Patients with Ankylosing Spondylitis: Results of Rapid-Axspa Study [abstract OP0107]. Annals of the Rheumatic Diseases. 2013;72:A87.	Hand searches	1st update (October 2013)
		Sieper. Rapid Improvements In Patient-Reported Outcomes With Certolizumab Pegol In Patients With Axial Spondyloarthritis, Including Ankylosing Spondylitis: 24-Week Results Of RAPID-AXSPA Study. Abstract THU0360, EULAR 2013.	Hand searches	1st update (October 2013)
		Van der Heijde D, Maksymowych WP, Landewé R, Stach C, Hoepken B, Fichtner A, et al. Effect of certolizumab pegol on inflammation of spine and sacroiliac joints in patients with axial spondyloarthritis: 12-week magnetic resonance imaging results of rapid-axspa study [abstract FRI0419]. Annals of the Rheumatic Diseases. 2013;72:A515-A6.	Hand searches	1st update (October 2013)
		Sieper J, Rudwaleit M, van der Heijde D, Maksymowych W, Dougados M, Mease PJ, et al. Long-Term Safety and Efficacy of Certolizumab Pegol in Patients with Axial Spondyloarthritis, Including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis: 96-Week Outcomes of the Rapid-Axspa Trial [abstract SAT0351]. Annals of the Rheumatic Diseases. 2014;73:719-20.	Hand searches	2nd update (July 2014)
		Mease PJ, Dougados M, Davies O, Nurminen T, Sieper J. Certolizumab Pegol Rapidly Reduces Peripheral Enthesitis and the Incidence of Tender and Swollen Joints in Patients with Active Axial Spondyloarthritis, Including Both Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis [SAT0362]. Annals of the Rheumatic Diseases. 2014;73:724-5.	Hand searches	2nd update (July 2014)
		van der Heijde D, Deodhar A, Davies O, Nurminen T, Rudwaleit M. Disease Activity and Clinical Response Early in the Course of Treatment predict Long-Term Outcomes in Axial Spondyloarthritis Patients Treated with Certolizumab Pegol [abstract SAT0338]. Annals of the Rheumatic Diseases. 2014;73:714-5.	Hand searches	2nd update (July 2014)
		van der Heijde D, Maksymowych WP, Landewé R, Stach C, Hoepken B, Fichtner A, et al. Effect of Certolizumab Pegol on Inflammation of Spine and Sacroiliac Joints in Patients with Axial Spondyloarthritis: 12-Week Magnetic Resonance Imaging Results of Rapid-Axspa Study [abstract 213]. Rheumatology. 2014;53:i139.	Hand searches	2nd update (July 2014)
SELECT-AXIS 1 (51)	NCT03178487	**van der Heijde D, Song IH, Pangan AL, Deodhar A, van den Bosch F, Maksymowych WP, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multicentre, randomised, double-blind, placebo-controlled, phase 2/3 trial. Lancet. 2019;394(10214):2108-17.**	Database searches	6th update (October 2020)
		van der Heijde D, Song IH, Pangan A, Deodhar A, Van den Bosch F, Maksymowych WP, et al. Efficacy and safety of upadacitinib in a randomized, double-blind, placebo-controlled, multicenter phase 2/3 clinical study of patients with active ankylosing spondylitis [abstract]. Arthritis & Rheumatology. 2019;71.	Database searches	6th update (October 2020)
		Deodhar A, Baraliakos X, McInnes I, de Vlam K, Bessette L, Maniccia A, et al. Effect of Upadacitinib on Reducing Pain in Patients with Active Ankylosing Spondylitis and Inadequate Response to Nonsteroidal Anti-inflammatory Drugs [abstract]. Arthritis & Rheumatology. 2020;72.	Hand searches	6th update (October 2020)
		Kiltz U, Sieper J, Deodhar A, Zueger P, Song IH, Chen N, et al. Improvements in Global Functioning and Health-related Quality of Life and Their Association with Disease Activity and Functional Improvement in Patients with Active Ankylosing Spondylitis Treated with Upadacitinib [abstract THU0375]. Arthritis & Rheumatology. 2020;72.	Hand searches	6th update (October 2020)
		Deodhar A, Ostor A, Maniccia A, Ganz F, Gao T, Chu A, et al. Achievement of Partial Remission and Inactive Disease in Upadacitinib-Treated Patients with Ankylosing Spondylitis [abstract POS0905]. Arthritis & Rheumatology. 2021;72.	Hand searches	6th update (October 2020)
		Deodhar A, Van der Heijde D, Sieper J, Van den Bosch F, Maksymowych WP, Kim TH, et al. Efficacy and Safety of Upadacitinib in Patients with Active Ankylosing Spondylitis: 1-Year Results from a Randomized, Double-Blind, Placebo-Controlled Study with Open-Label Extension [abstract OP0144]. Arthritis & Rheumatology. 2021;72.	Hand searches	6th update (October 2020)

		Kiltz U, Sieper J, Deodhar A, Zueger P, Song IH, Chen N, et al. Improvements in global functioning and health-related quality of life and their association with disease activity and functional improvement in patients with active ankylosing spondylitis treated with upadacitinib: results from the select-axis 1 trial [abstract THU0375]. Annals of the Rheumatic Diseases. 2020;79:419.	Hand searches	6th update (October 2020)
		Désirée van der Heijde, In Ho Song, Aileen L. Pangan, Atul Deodhar, Filip van den Bosch, Walter P. Maksymowych, Tae Hwan Kim, Mitsumasa Kishimoto, Andrea Everding, Yunxia Sui, Xin Wang, Alvina D. Chu, Joachim Sieper. Efficacy and Safety of Upadacitinib in a Randomized, Double Blind, Placebo Controlled, Multicenter Phase 2/3 Clinical Study of Patients With Active Ankylosing Spondylitis. Presented at the American College of Rheumatology; November 8-13, 2019; Atlanta, GA, USA	Hand searches	6th update (October 2020)
		Van Den Bosch F, Poddubnyy D, Stigler J, Ostor A, D'Angelo S, Navarro-Compan V, et al. Influence of baseline demographics on improvements in disease activity measures in patients with ankylosing spondylitis receiving upadacitinib: A post hoc subgroup analysis of select-axis 1. Annals of the Rheumatic Diseases. 2021;80(SUPPL 1):722-3.	Database searches	7th update (April 2022)
		Deodhar A, van der Heijde D, Sieper J, Van den Bosch F, Maksymowych WP, Kim TH, et al. Safety and Efficacy of Upadacitinib in Patients With Active Ankylosing Spondylitis and an Inadequate Response to Nonsteroidal Antiinflammatory Drug Therapy: One-Year Results of a Double-Blind, Placebo-Controlled Study and Open-Label Extension. Arthritis and Rheumatology. 2022;74(1):70-80.	Database searches	7th update (April 2022)
		Van Der Heijde D, Deodhar A, Maksymowych WP, Sieper J, Van Den Bosch F, Kim TH, et al. Upadacitinib in active ankylosing spondylitis: results of the 2-year, double-blind, placebo-controlled SELECT-AXIS 1 study and open-label extension. RMD Open. 2022;8(2):e002280.	Database searches	8th update (January 2023)
SELECT-AXIS 2 (Study 1) (52)	NCT04169373	**van der Heijde D, Baraliakos X, Sieper J, Deodhar A, Inman RD, Kameda H, et al. Efficacy and safety of upadacitinib for active ankylosing spondylitis refractory to biological therapy: a double-blind, randomised, placebo-controlled phase 3 trial. Annals of the Rheumatic Diseases. 2022;81:1515–23.**	Database searches	8th update (January 2023)
		Van der Heijde D, Baraliakos X, Sieper J, Deodhar A, Inman R, Kameda H, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis refractory to biologic therapy: a double-blind, randomized, placebo-controlled phase 3 trial. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):402-3.	Hand searches	7th update (April 2022)
		Baraliakos X, Ganz F, Kameda H, Walsh J, Jain M, D'Silva K, et al. Efficacy and Safety of Upadacitinib in Patients with Ankylosing Spondylitis with Intolerance to And/or Lack of Efficacy of Prior Biologic Therapy: A Subgroup Analysis [abstract]. Arthritis & Rheumatology. 2022;74(S9)	Hand searches	8th update (January 2023)
SELECT-AXIS 2 (Study 2) (53)	NCT04169373	**Deodhar A, Van Den Bosch F, Poddubnyy D, Maksymowych W, van der Heijde D, Kim TH, et al. Upadacitinib for the treatment of active non-radiographic axial spondyloarthritis (SELECT-AXIS 2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400(10349):369-79.**	Database searches	8th update (January 2023)
		Deodhar A, Van den Bosch F, Poddubnyy D, Maksymowych WP, Van der Heijde D, Kim TH, et al. Efficacy and safety of upadacitinib in patients with active non-radiographic axial spondyloarthritis: a double-blind, randomized, placebo-controlled phase 3 trial. Annals of the Rheumatic Diseases. 2022;81(Suppl 1):9-10.	Hand searches	7th update (April 2022)
		Maksymowych W, Baraliakos X, Deodhar A, Poddubnyy D, Ganz F, Gao T, et al. Efficacy of Upadacitinib in Patients with Non-Radiographic Axial Spondyloarthritis Stratified by Objective Signs of Inflammation at Baseline [abstract]. Arthritis & Rheumatology. 2022;74(S9).	Hand searches	8th update (January 2023)
SPAXIM (54)	NCT00507403	**Mulleman D, Lauferon F, Wendling D, Ternant D, Ducourau E, Paintaud G, et al. Infliximab in ankylosing spondylitis: alone or in combination with methotrexate? A pharmacokinetic comparative study. Arthritis Res Ther. 2011;13(3):R82.**	Database searches	Original SLR (May 2012)
SPINE (55)	NCT00420238	**Dougados M, Braun J, Szanto S, Combe B, Elbaz M, Geher P, et al. Efficacy of etanercept on rheumatic signs and pulmonary function tests in advanced**	Database searches	Original SLR (May 2012)

		ankylosing spondylitis: results of a randomised double-blind placebo-controlled study (SPINE). Ann Rheum Dis. 2011;70(5):799-804.		
		Dougados M. Efficacy of etanercept on rheumatic signs and pulmonary function tests in advanced Ankylosing spondylitis. Results of a randomized double blind placebo-controlled study (SPINE). Arthritis and rheumatism. 2009;60 SUPPL:524.	Database searches	Original SLR (May 2012)
Su 2020 (56)	ChiCTR1900022520	**Su J, Li M, He L, Zhao D, Wan W, Liu Y, et al. Comparison of the Efficacy and Safety of Adalimumab (Humira) and the Adalimumab Biosimilar Candidate (HS016) in Chinese Patients with Active Ankylosing Spondylitis: A Multicenter, Randomized, Double-Blind, Parallel, Phase III Clinical Trial. BioDrugs. 2020;34(3):381-93.**	Database searches	6th update (October 2020)
		Su J, Mengtao L, Zeng X. Efficacy, pharmacokinetics, safety and immunogenicity of the biosimilar HS016 in comparison with adalimumab in chinese patients with ankylosing spondylitis: A multicenter, randomized, double-blind, parallel-group, phase 3 trial [abstract FRI0413]. Annals of the Rheumatic Diseases. 2019;78.	Database searches	6th update (October 2020)
		Su J, Li M, He L, Zhao D, Wan W, Liu Y, et al. Evaluation of adalimumab biosimilar candidate (HS016) in Chinese patients with active ankylosing spondylitis based on a health survey: sub-analysis of a phase 3 study. Clinical Rheumatology. 2022;41(3):731-9.	Database searches	7th update (April 2022)
		Su J, Li M, He L, Zhao D, Wan W, Liu Y, et al. Changes in Efficacy Indicators for Adalimumab Biosimilar Candidate (HS016) for the Treatment of Active Ankylosing Spondylitis at Various Time Points. Frontiers in Pharmacology. 2020;11:606497.	Database searches	7th update (April 2022)
SURPASS (57)	NCT03259074	**Baraliakos X, Østergaard M, Poddubnyy D, van der Heijde D, Deodhar A, Machado PM, et al. Effect of Secukinumab versus Adalimumab Biosimilar on Radiographic Progression in Patients with Radiographic Axial Spondyloarthritis: A Randomized Phase IIIb Study [abstract]. Arthritis & Rheumatology. 2022;74(S9).**	Hand searches	8th update (January 2023)
Tam 2014 (58)	NCT01212653	**Tam LS, Shang Q, Kun EW, Lee KL, Yip ML, Li M, et al. The effects of golimumab on subclinical atherosclerosis and arterial stiffness in ankylosing spondylitis-a randomized, placebo-controlled pilot trial. Rheumatology (Oxford). 2014;53(6):1065-74.**	Database searches	2nd update (July 2014)
		Tam LS, Shang Q, Kun EW, Lee VK, Yip ML, Li M, et al. The effects of golimumab on the progression of subclinical atherosclerosis and arterial stiffness in patients with ankylosing spondylitis–a randomized, placebo-controlled trial [abstract FRI0412]. Annals of the Rheumatic Diseases. 2013;72:A513.	Database searches	2nd update (July 2014)
TORTUGA (59)	NCT03117270	**van der Heijde D, Baraliakos X, Gensler LS, Maksymowych WP, Tseluyko V, Nadashkevich O, et al. Efficacy and safety of filgotinib, a selective Janus kinase 1 inhibitor, in patients with active ankylosing spondylitis (TORTUGA): results from a randomised, placebo-controlled, phase 2 trial. Lancet. 2018;392(10162):2378-87.**	Database searches	6th update (October 2020)
		Maksymowych W, Østergaard M, Landewé R, Barchuk W, Liu K, Tasset C, Gilles L, Hendrikx T, Besuyen R, Baraliakos X. Effects of Filgotinib on Spinal Lesions in Patients with Ankylosing Spondylitis: Magnetic Resonance Imaging Data from the Placebo-Controlled, Double-Blind, Randomized TORTUGA Trial [abstract]. Arthritis Rheumatol. 2020; 72 (suppl 10)	Hand searches	6th update (October 2020)
		Maksymowych WP, Østergaard M, Landewé RBM, Barchuk W, Liu K, Tasset C, et al. Impact of filgotinib on structural lesions in the sacroiliac joints at 12 weeks in patients with active axial spondyloarthritis: magnetic resonance imaging data from the double-blind, randomized tortuga trial [abstract]. Arthritis & Rheumatology. 2020;72.	Hand searches	6th update (October 2020)
		Maksymowych WP, Østergaard M, Landewé RBM, Barchuk W, Liu K, Tasset C, et al. Impact of filgotinib on structural lesions in the sacroiliac joints at 12 weeks in patients with active axial spondyloarthritis: magnetic resonance imaging data from the double-blind, randomized tortuga trial [abstract]. Annals of the Rheumatic Diseases. 2020;79.	Hand searches	6th update (October 2020)
Tu 2019 (60)	2015L05751	**Tu L, Wei Q, Xie Y, Shi G, Liu H, Huang Q, et al. Biosimilar Bat1406 versus adalimumab therapy on active ankylosing spondylitis: a randomized, double-**	Database searches	6th update (October 2020)

		blinded, multicenter, controlled phase 3 trial [abstract FRI0415]. Annals of the Rheumatic Diseases. 2019;78:895.		
Tu 2022 (61)	NCT01934933	**Tu L, Zhao M, Wang X, Kong Q, Chen Z, Wei Q, et al. Etanercept/celecoxib on improving MRI inflammation of active ankylosing spondylitis: A multicenter, open-label, randomized clinical trial. Frontiers in Immunology. 2022;13.**	Database searches	8th update (January 2023)
		Gu J, Tu L, Zhao M, Lin Z, Liao Z, Cao S, et al. A multi-center, open label, randomized clinical tries of etanercept and celecoxib alone/combined treatment in effectiveness and safety of ankylosing spondylitis [abstract]. Arthritis & Rheumatology. 2016;68.	Database searches	5th update (April 2019)
van der Heijde 2017 (62)	NCT01786668	**van der Heijde D, Deodhar A, Wei JC, Drescher E, Fleishaker D, Hendrikx T, et al. Tofacitinib in patients with ankylosing spondylitis: a phase II, 16-week, randomised, placebo-controlled, dose-ranging study. Ann Rheum Dis. 2017;76(8):1340-7.**	Database searches	6th update (October 2020)
		Maksymowych WP, van der Heijde D, Baraliakos X, Deodhar A, Sherlock SP, Li D, et al. Tofacitinib is associated with attainment of the minimally important reduction in axial magnetic resonance imaging inflammation in ankylosing spondylitis patients. Rheumatology (Oxford). 2018;57(8):1390-9.	Database searches	6th update (October 2020)
		Maksymowych W, van der Heijde D, Baraliakos X, Deodhar AA, Brown M, Sherlock S, et al. Treatment with tofacitinib is associated with clinically meaningful reductions in axial MRI inflammation in patients with ankylosing spondylitis [abstract]. Arthritis & Rheumatology. 2016;68.	Database searches	6th update (October 2020)
		Maksymowych WP, van der Heijde D, Baraliakos X, Deodhar A, Brown M, Sherlock SP, et al. Tofacitinib treatment is associated with attainment of the minimally important reduction in axial mri inflammation in patients with ankylosing spondylitis [abstract THU0352]. Annals of the Rheumatic Diseases. 2017;76.	Database searches	6th update (October 2020)
		van der Heijde D, Deodhar A, Wei JC, Drescher E, Fleishaker D, Hendrikx T, et al. Tofacitinib in Patients with Ankylosing Spondylitis: A Phase 2, 16-Week, Randomised, Placebo-Controlled, Dose-Ranging Study [abstract OP0002]. Annals of the Rheumatic Diseases. 2016;75.	Database searches	6th update (October 2020)
		van der Heijde, D, Deodhar, et al. Tofacitinib in patients with ankylosing spondylitis: a phase II, 16-week, randomised, placebo controlled, dose-ranging study. Annals of the rheumatic diseases. 2017;27.	Database searches	6th update (October 2020)
		Van Der Heijde, D, Deodhar, et al. Tofacitinib in patients with ankylosing spondylitis: A phase 2, 16-week, randomized, placebo-controlled, dose-ranging study. Arthritis and Rheumatology. 2015;67.	Database searches	6th update (October 2020)
Wei 2021 (63)	NCT02985983	**Wei JC-C, Kim T-H, Kishimoto M, Ogusu N, Jeong H, Kobayashi S, et al. Efficacy and safety of brodalumab, an anti-IL17RA monoclonal antibody, in patients with axial spondyloarthritis: 16-week results from a randomised, placebo-controlled, phase 3 trial. Annals of the rheumatic diseases. 2021;80:1014–21.**	Database searches	7th update (April 2022)
		Kim TH, Kishimoto M, Wei JCC, Jeong H, Nozaki A, Kobayashi S. Brodalumab, an anti-interleukin-17 receptor A monoclonal antibody, in axial spondyloarthritis: 68-week results from a phase 3 study. Rheumatology. 2022:1-9.	Database searches	8th update (January 2023)
Xue 2022 (64)	NCT04285229	**Xue Y, Hu J, Liu D, Li J, Wu H, Tan C, et al. Efficacy and Safety of Ixekizumab in Chinese Patients with Radiographic Axial Spondyloarthritis: 16-Week Results from a Phase 3 Study [abstract]. Arthritis & Rheumatology [abstract]. 2022;74(S9).**	Hand searches	8th update (January 2023)
		NCT record: https://clinicaltrials.gov/ct2/show/NCT04285229	Hand searches	8th update (January 2023)
Zhang 2020 (65)	NCT03880968	**Zhang T, Zhu J, He D, Chen X, Wang H, Zhang Y, et al. Disease activity guided stepwise tapering or discontinuation of rhTNFR:Fc, an etanercept biosimilar, in patients with ankylosing spondylitis: a prospective, randomized, open-label, multicentric study. Ther Adv Musculoskelet Dis. 2020;12:1759720X20929441.**	Database searches	6th update (October 2020)

Citations highlighted in bold denote the primary publication for each trial.

Inclusion and exclusion of studies in the DMC application

Of the 341 publications reporting on 65 trials from the consolidated SLR (all SLRs conducted, as illustrated in Table 97) 37 met the eligibility criteria for the global NMA and ITCs. Of the 37 studies included in the global NMA further 24 publications were excluded to adapt the global material to fit to comparators included in the scope of the DMC treatment guideline. In total 52 publications were excluded, as detailed in the Table 98, and 13 studies were included in the ITCs for the DMC application.

Figure 4 PRISMA flow diagram for the local adaptation

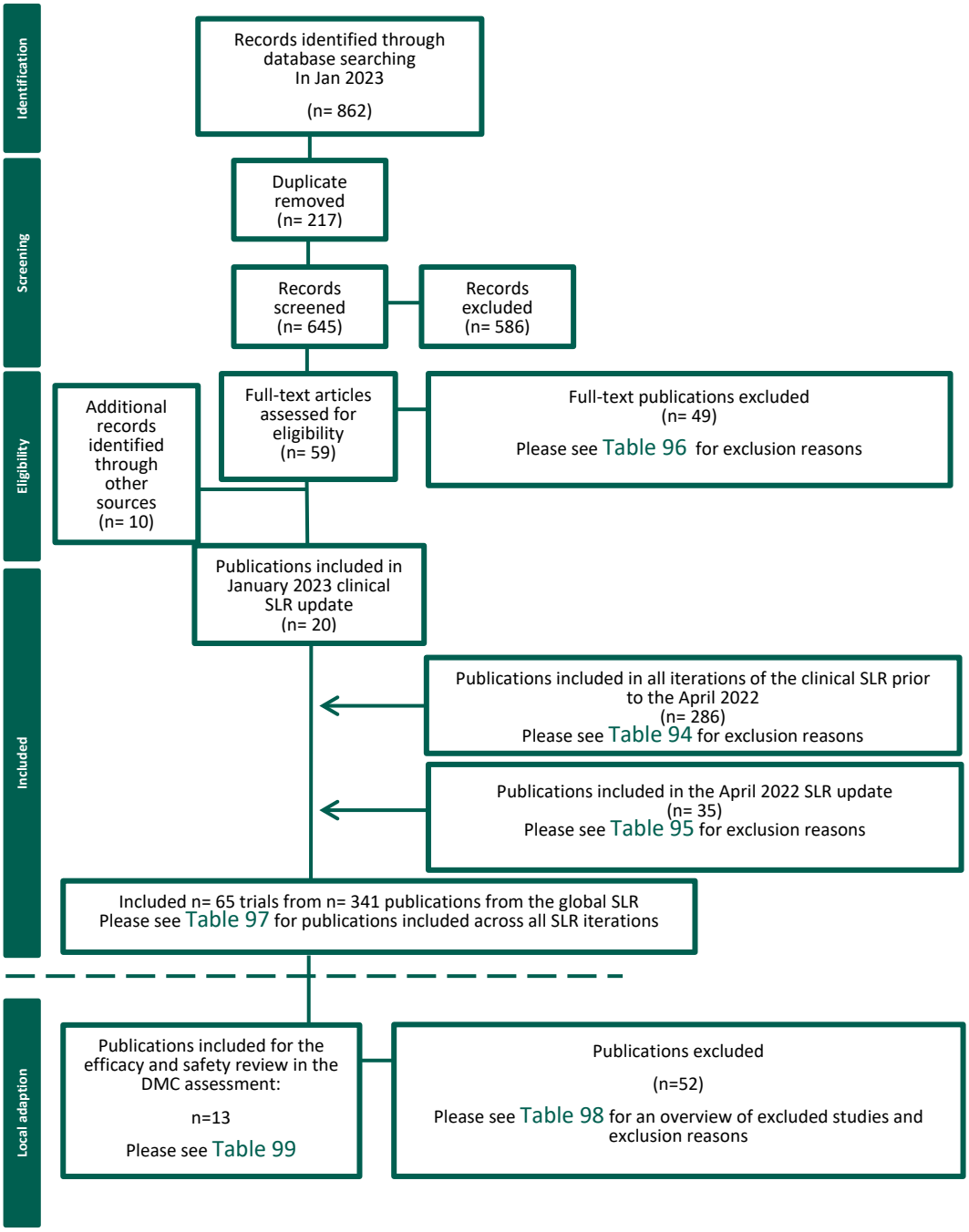

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Table 98 Studies excluded for the ITC and for the DMC treatment guideline adaptation across all iterations of the global SLR (n=52)

#	Citation	Reason for exclusion
1	Haibel 2008 [63]	Patients had unclear biologic exposure and was therefore not considered comparable to the target population
2	c-axSpAnd [64]	No comparator of interest (certolizumab)
3	RAPID-axSpA [65]	No comparator of interest (certolizumab)
4	EMBARK [66]	No comparator of interest (etanercept)
5	GO-AHEAD [67]	No comparator of interest (golimumab)
6	BE AGILE [68]	Study design (dose ranging phase II study)
7	Xue 2022 [69]	Population (Chinese study population)
8	Deodhar 2021 [70]	No comparator of interest (tofacitinib)
9	van der Heijde 2017 [71]	No comparator of interest (tofacitinib)
10	SELECT-AXIS 1 [72]	No comparator of interest (updacitinib)
11	SELECT-AXIS 2 (Study 1) [49]	No comparator of interest (updacitinib)
12	SELECT-AXIS 2 (Study 2) [50]	No comparator of interest (updacitinib)
13	Canadian AS Trial [73]	Initially considered relevant but excluded due to lack of reported results for relevant endpoints and safety outcomes
14	Hu 2012 [74]	Population (Chinese study population)
15	Calin 2004 [75]	No comparator of interest (etanercept)
16	Davis 2003 [76]	No comparator of interest (etanercept)
17	ETN Study 314 [77]	No comparator of interest (etanercept)
18	Gorman 2002 [78]	No comparator of interest (etanercept)
19	Leeds ETN Study [79]	No comparator of interest (etanercept)
20	SPINE [80]	No comparator of interest (etanercept)
21	GO-ALIVE [81]	No comparator of interest (golimumab)
22	Bao 2014 [82]	No comparator of interest (golimumab)
23	GO-RAISE [83]	No comparator of interest (golimumab)
24	ASSERT [84]	No comparator of interest (infliximab)
25	ABILITY-3 [85]	Initial single-arm ADA open-label phase (28 weeks); only patients who achieved sustained remission during that phase were enrolled in the subsequent double-blind phase of 40 weeks

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26	ASCEND [86]	Non-useful analysis bridge as SSZ was not comparator of interest for the NMA
27	ASART-2 [87]	Biosimilar treatment, not of interest for NMA
28	Braun 2002 [88]	Treatment was up to 6 weeks only
29	CANDLE [89]	Unapproved dose (low dose 3 mg/kg, licensed dose 5 mg/kg)
30	Chinese University of Hong Kong (Hong Kong, China) [90]	Non-relevant study design (RCT initiated with PBO vs MTX, IFX was added to both PBO and MTX arms at Week 16)
31	C-OPTIMISE [91]	Not comparable study designs (sustained remission), given the substantial differences in inclusion criteria, timing, and outcome definitions
32	COAST-Y [92]	Lead-in period (24 week), only patients in sustained remission were randomised to treatment arms at the end of this time
33	DANISH [93]	Not comparable axSpA population as used the ESSG classification criteria rather than the ASAS classification criteria for inclusion
34	ESTHER [94]	Not comparable axSpA population as patients had to have active inflammatory lesions on whole-body MRI in sacroiliac joints or the spine
35	Giardina 2010 [95]	No placebo control group, so unsuitable for inclusion in placebo-controlled NMA analyses
36	Tu 2022 (NCT01934933) [96]	Does not meet eligibility criteria for NMA; recruits patients responsive to NSAIDs that may not have already tried NSAIDs
37	Huji 2019 [97]	Biosimilar treatment, not of interest for NMA
38	Leeds IFX Study [98]	Not comparable axSpA population as patients had to have MRI evidence of sacroiliitis
39	Li 2022 (ChiCTR20181863) [99]	Biosimilar treatment, not of interest for NMA
40	Marzo-Ortega 2005 [100]	Non-useful analysis bridge
41	MEASURE 1 [58]	IV load not within marketing authorisation
42	MEASURE 3 [101]	IV load not within marketing authorisation
43	PLANETAS [102]	Biosimilar treatment, not of interest for NMA
44	PrevAS [103]	Not comparable axSpA population Patients were suspected of nr-axSpA, ≥1 axSpA feature fulfilling ESSG criteria: HLA–B27 positive with ≥1 axSpA feature, or HLA-B27 negative with ≥2 axSpA-features
45	SPAXIM [104]	Non-useful analysis treatment bridge

46	Su 2020 [105]	Biosimilar treatment, not of interest for NMA
47	SURPASS [106]	Biosimilar treatment, not of interest for NMA
48	Tu 2019 [107]	Biosimilar treatment, not of interest for NMA
49	TORTUGA [108]	Treatment no longer under investigation in AS
50	Tam 2014 [109]	Time point (24 weeks) not of interest for current analysis
51	Wei 2021 (NCT02985983) [110]	Not yet licensed for axSpA, only psoriasis
52	Zhang 2020 [111]	Not comparable study designs (sustained remission), given the substantial differences in inclusion criteria, timing, and outcome definitions

Table 99 Summary of studies included in the feasibility assessment (n=13)

Study	Trial identifier	Classification	Age at onset; Symptom duration	Disease activity at baseline	Previous treatment	Prior TNFi
IL-17A/IL-17Fs -	bimekizumab					
BE MOBILE 1 [47]	NCT03928704	nr-axSpA: no sacroiliitis fulfilling mNY criteria on x-ray; sacroiliitis on the screening MRI and/or elevated CRP	<45 years; ≥3 months	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, intolerance or contraindication(s) to ≥2 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance
BE MOBILE 2 [48]	NCT03928743	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	<45 years; ≥3 months	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, intolerance or contraindication(s) to ≥2 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance
IL-17As -	ixekizumab					
COAST-V [55]	NCT02696785	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria & ≥1 SpA feature	<45 years; ≥3 months	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, intolerance or contraindication(s) to ≥2 NSAIDs	No, study excluded patients with prior history of TNFi therapy

COAST-W [56]	NCT02696798	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria & ≥1 SpA feature	<45 years; ≥3 months	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, intolerance or contraindication(s) to ≥2 TNFi	Yes, study only enrolled patients that had received 1 or 2 prior TNFi
COAST-X [57]	NCT02757352	nr-axSpA: no sacroiliitis fulfilling mNY criteria on x-ray; sacroiliitis on the screening MRI and/or elevated CRP	<45 years; ≥3 months	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, or intolerance to ≥2 NSAIDs	No, study excluded patients with prior history of TNFi therapy
IL-17As -	secukinumab					
MEASURE 2 [58]	NCT01649375	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, or intolerance to ≥1 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance
MEASURE 4 [59]	NCT02159053	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, or intolerance to ≥1 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance
MEASURE 5 [60]	NCT02896127	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, or intolerance to ≥2 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance
PREVENT [61]	NCT02696031	nr-axSpA: no sacroiliitis fulfilling mNY criteria on x-ray; sacroiliitis on the screening MRI	NR	BASDAI and spinal pain (BASDAI Q2)	Inadequate response, or intolerance to ≥2 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance

		and/or elevated CRP		scores ≥4		
ASTRUM [52]	NCT02763046	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4; total back pain (VAS ≥ 40 mm)	Inadequate response, or intolerance to ≥2 NSAIDs	Yes, ≤1 TNFi discontinued after inadequate response, intolerance
TNFi	adalimumab					
ABILITY-1 [62]	NCT00939003	nr-axSpA: fulfilling the ASAS classification criteria; sacroiliitis on the screening MRI and/or elevated CRP	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4	Inadequate response, or intolerance or contraindication to ≥1 NSAIDs	No, study excluded patients with prior history of bDMARD therapy including TNFi
ATLAS [35]	NCT00085644	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4, morning stiffness ≥1 hour	Inadequate response, or intolerance to ≥1 NSAIDs	Yes but no TNFi within 1 month prior to baseline
Huang 2014 [36]	NCT01114880	r-axSpA: clinical diagnosis of AS fulfilling mNY criteria	NR	BASDAI and spinal pain (BASDAI Q2) scores ≥4, morning stiffness ≥1 hour	Inadequate response, or intolerance or contraindication to ≥1 NSAIDs	Yes but no TNFi within 1 month prior to baseline

Quality assessment

The global literature search performed adhere to the normal SLR quality standards. The global SLR was restricted to the interventions included in the DMC treatment recommendations.

Unpublished data

The submitted unpublished data are derived from the BE MOBILE 1 & 2 as all endpoints for specified subgroups haven't been published.

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Appendix B Main characteristics of included studies

Table 100 BE MOBILE 1

Trial name: BE MOBILE 1 (AS0010; nr-axSpA)	NCT number: NCT03928704
Objective	The purpose of the study is to demonstrate the efficacy, safety and tolerability of bimekizumab administered subcutaneously (sc) compared to placebo in the treatment of subjects with active non-radiographic axial spondyloarthritis (nr-axSpA).
Publications – title, author, journal, year	Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials, van der Heijde, Ann Rheum Dis, 2023 https://ard.bmj.com/content/annrheumdis/early/2023/01/16/ard-2022-223595.full.pdf
Study type and design	Multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of bimekizumab administered subcutaneously compared with placebo for the treatment of patients with active non-radiographic axial spondyloarthritis[112]
Sample size (n)	N=254

Main inclusion and exclusion criteria	**Inclusion:**
	• ≥18 years
	• Patient with nr-axSpA with all of the following criteria:
	  ○ Adult-onset axSpA meeting ASAS classification criteria
	  ○ Inflammatory back pain for ≥3 months prior to screening
	  ○ Age at symptom onset of <45 years
	  ○ No sacroiliitis as defined by mNY criteria (based on central reading)
	• Active nr-axSpA at screening and baseline, defined as
	  ○ BASDAI ≥4
	  ○ Spinal pain ≥4 on 0–10 NRS
	• Sacroiliitis on the screening MRI and/or elevated CRP
	• Failure to respond to 2 different NSAIDs, or history of intolerance or contraindication to NSAID therapy
	• Patients may have been previously treated with anti-TNF agents but must have experienced an inadequate response or been intolerant to treatment.
	
	Exclusion:
	• Fibromyalgia or osteoarthritis symptoms which, in the Investigator's opinion, could interfere with efficacy assessments
	• Acute anterior uveitis within 6 weeks prior to baseline
	• Diagnosis of inflammatory condition other than axSpA, including active IBD
	• Previously received >1 anti-TNF and/or >2 additional non-anti-TNF biologics, or any anti-IL17 biologics
	• Previous participation in a bimekizumab clinical trial, including those on placebo
	• Received any live vaccinations within 8 weeks prior to baseline or BCG vaccination within a 1 year prior to baseline.

Intervention	Bimekizumab 160 mg every fourth week (Q4W) (n=128)

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Trial name: BE MOBILE 1 (AS0010; nr-axSpA)	NCT number: NCT03928704
Comparator(s)	Placebo during the double-blind treatment period and will receive bimekizumab during the maintenance period (n=126)
Follow-up time	The duration of study for each participant will include evaluation of the primary endpoint at week 16 in the double-blind period. Patients will be followed in a maintenance period until week 52.
Is the study used in the health economic model?	No

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Trial name: BE MOBILE 1 (AS0010; nr-axSpA)	NCT number: NCT03928704

Primary, secondary and exploratory endpoints

Primary endpoint(s):

- Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response at Week 16

Secondary endpoints:

- ASAS40 response in anti-TNF naïve patients
- Change from baseline in BASDAI
- ASAS20 response
- ASAS-PR
- ASDAS-MI
- ASAS5/6 response
- Change from baseline in BASFI
- Change from baseline in nocturnal spinal pain
- Change from baseline in ASQoL
- Change from baseline in SF-36 PCS
- Change from baseline in BASMI
- Change from baseline in MASES in patients with enthesitis at baseline
- Enthesitis-free state in patients with enthesitis at baseline
- Incidence of TEAEs
- Incidence of treatment-emergent SAEs
- TEAEs leading to withdrawal

Exploratory endpoints:

- Change from baseline in ASAS components over time
- Change from baseline in ASDAS-CRP and absolute values over time
- ASDAS states over time
- ASDAS <2.1 response over time
- ASDAS-ID response over time
- BASDAI50
- Change from baseline in SPARCC SIJ score at Week 16 and 52
- Change from baseline in ASspiMRI-a in the Berlin Modification score at Week 16 and 52
- hs-CRP levels over time
- ASAS40 response at Week 16 by patient subgroups
- Change from baseline in FACIT-Fatigue over time
- Change from baseline in WPAI-SHP: Overall Work Impairment over time

Endpoints included in this application:

- ASAS40) response at Week 16.
- ASDAS<2.1
- BASDAI50
- SF-36 PCS
- Safety (TEAEs leading to withdrawal)

Other endpoints:

Not applicable

Trial name: BE MOBILE 1 (AS0010; nr-axSpA)	NCT number: NCT03928704
Method of analysis	Sample size calculations were based on testing of bimekizumab vs placebo for ASAS40 response at week 16. Efficacy results are reported at week 16 with summary data up to week 24 for each trial. All analyses were performed on the randomised set. For binary response endpoints (including the primary endpoint), missing data were treated as non-response. For continuous ranked endpoints reported at week 16, missing data to week 16 were imputed with reference-based multiple imputation, with the multiple imputation (MI) model based on placebo group data only. Missing data for non-ranked continuous endpoints and continuous ranked endpoints before and beyond week 16 were handled with MI using data from both bimekizumab and placebo groups. All between-group differences are adjusted risk differences from the logistic regression model for binary endpoints or mean differences vs placebo from the analysis of covariance (ANCOVA) model for continuous endpoints, with associated p values and 95% confidence intervals (CIs).
Subgroup analyses	No apriori subgroup analyses but post-hoc subgroup analyses have been made for ITC purposes
Other relevant information	

Table 101 BE MOBILE 2

Trial name: BE MOBILE 2 (AS0011; AS)	NCT number: NCT03928743
Objective	The purpose of the study is to demonstrate the efficacy, safety and tolerability of bimekizumab administered subcutaneously (sc) compared to placebo in the treatment of subjects with active ankylosing spondylitis (AS).
Publications – title, author, journal, year	Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials, van der Heijde, Ann Rheum Dis, 2023. https://ard.bmj.com/content/annrheumdis/early/2023/01/16/ard-2022-223595.full.pdf
Study type and design	A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Bimekizumab in Subjects With Active Ankylosing Spondylitis
Sample size (n)	N=332

Trial name: BE MOBILE 2 (AS0011; AS)	NCT number: NCT03928743

Main inclusion and exclusion criteria	**Inclusion:** • Male or female patients at least 18 years of age • Subject has ankylosing spondylitis (AS) as per the Modified New York (mNY) criteria with documented radiologic evidence, and at least 3 months of symptoms with age at symptom onset less than 45 years • Subjects has moderate-to-severe active disease defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) >=4 AND spinal pain >=4 on a 0 to 10 Numeric Rating Scale • Subjects had to have either failed to respond to 2 different nonsteroidal anti-inflammatory drugs (NSAIDs) given at the maximum tolerated dose for a total of 4 weeks or have a history of intolerance to or a contraindication to NSAID therapy • Patients who have taken a tumor necrosis factor alpha (TNFα) inhibitor must have experienced an inadequate response or intolerance to treatment given at an approved dose for at least 12 weeks • Patients currently taking NSAIDs, cyclooxygenase 2 (COX-2) inhibitors, analgesics, corticosteroids, methotrexate (MTX), leflunomide (LEF), sulfasalazine (SSZ), hydroxychloroquine (HCQ) AND/OR apremilast can be allowed if they fulfil specific requirements prior to study entry • Age at symptom onset of <45 years **Exclusion:** • Total ankylosis of the spine • Treatment with more than 1 TNFα inhibitor and/or more than 2 additional non-TNFα biological response modifiers, or any interleukin (IL)-17 biological response modifier at any time are excluded • Active infection or history of recent serious infections • Viral hepatitis B or C or human immunodeficiency virus (HIV) infection • Any live (includes attenuated) vaccination within the 8 weeks prior to entering the study or TB (Bacillus Calmette-Guerin) vaccination within 1 year prior entering the study • Known tuberculosis (TB) infection, at high risk of acquiring TB infection, or current or history of nontuberculous mycobacterium (NTMB) infection • Subject has any active malignancy or history of malignancy within 5 years prior to the Screening Visit EXCEPT treated and considered cured cutaneous squamous or basal cell carcinoma or in situ cervical cancer • Diagnosis of inflammatory conditions other than AxSpA, e.g., rheumatoid arthritis. Patients with a diagnosis of Crohn's disease, ulcerative colitis, or other inflammatory bowel disease (IBD) are allowed as long as they have no active symptomatic disease when entering the study. • Presence of active suicidal ideation, or moderately severe major depression or severe major depression • Female patients who are breastfeeding, pregnant, or planning to become pregnant during the study • Subject has a history of chronic alcohol or drug abuse within 6 months prior to Screening
Intervention	Bimekizumab 160 mg every fourth week (Q4W) (n=221)
Comparator(s)	Placebo during the double-blind treatment period and will receive bimekizumab during the maintenance period (n=111)
Follow-up time	The duration of study for each participant will include evaluation of the primary endpoint at week 16 in the double-blind period. Patients will be followed in a maintenance period until week 52.

Trial name: BE MOBILE 2 (AS0011; AS)	NCT number: NCT03928743
Is the study used in the health economic model?	No
Primary, secondary and exploratory endpoints	**Primary endpoint(s):** • ASAS40 response at Week 16 **Secondary endpoints:** • ASAS40 response in anti-TNF naïve patients • ASAS20 response • Change from baseline in BASDAI total score • ASAS-PR response • ASDAS-MI response • ASAS-5/6 response • Change from baseline in BASFI • Change from baseline in nocturnal spinal pain score (NRS) • Change from baseline in ASQoL total score • Change from baseline in SF-36 PCS score • Change from baseline in BASMI • Change from baseline in MASES in patients with enthesitis at baseline • Enthesitis-free state (MASES) response in patients with enthesitis at baseline • Incidence of TEAEs • Incidence of treatment-emergent SAEs • TEAEs leading to withdrawal **Exploratory endpoints:** • Change from baseline in ASDAS-CRP over time • Change from baseline in ASAS components over time • Change from baseline in ASspiMRI-a in the Berlin Modification score at Week 16 and Week 52 • Change from baseline in SPARCC SIJ score at Week 16 and Week 52 • hs-CRP levels over time • ASAS40 response by patient subgroups at Week 16 • Change from baseline in FACIT-Fatigue over time • Change from baseline in WPAI-SHP: Overall Work Impairment over time • Change from baseline in ASAS components over time • Change from baseline in ASDAS-CRP and absolute values over time • Change from Baseline in BASDAI total score BASDAI50 response **Endpoints included in this application:** • ASAS40 response at Week 16 • ASDAS<2.1 • Change from baseline in SF-36 PCS score • SF36-MCD • BASDAI50 response • Safety (TEAEs leading to withdrawal)

Trial name: BE MOBILE 2 (AS0011; AS)	NCT number: NCT03928743
Method of analysis	Sample size calculations were based on testing of bimekizumab vs placebo for ASAS40 response at week 16. Efficacy results are reported at week 16 with summary data up to week 24 for each trial. All analyses were performed on the randomised set. For binary response endpoints (including the primary endpoint), missing data were treated as non-response. For continuous ranked endpoints reported at week 16, missing data to week 16 were imputed with reference-based multiple imputation, with the multiple imputation (MI) model based on placebo group data only. Missing data for non-ranked continuous endpoints and continuous ranked endpoints before and beyond week 16 were handled with MI using data from both bimekizumab and placebo groups. All between-group differences are adjusted risk differences from the logistic regression model for binary endpoints or mean differences vs placebo from the analysis of covariance (ANCOVA) model for continuous endpoints, with associated p values and 95% confidence intervals (CIs).
Subgroup analyses	No a priori subgroup analyses but post-hoc subgroup analyses have been made for ITC purposes
Other relevant information	

Table 102 ATLAS

Trial name: ATLAS	NCT number: NCT00085644
Objective	Evaluate the safety and efficacy of adalimumab 40 mg given every other week (eow) in subjects with active ankylosing spondylitis (AS) who have had an inadequate response to, or who are intolerant to, treatment with at least 1 nonsteroidal anti-inflammatory drug (NSAID) and who may have also failed treatment with at least 1 disease-modifying antirheumatic drug (DMARD).

Trial name: ATLAS	NCT number: NCT00085644
Publications – title, author, journal, year	Maintenance of improvement in spinal mobility, physical function and quality of life in patients with ankylosing spondylitis after 5 years in a clinical trial of adalimumab. van der Heijde et al. Rheumatology (Oxford). 2015 Norms-based assessment of patient-reported outcomes associated with adalimumab monotherapy in patients with ankylosing spondylitis. Kimel et al. Clin Exp Rheumatol. 2011 Psychometric characteristics of the short form 36 health survey and functional assessment of chronic illness Therapy-Fatigue subscale for patients with ankylosing spondylitis. Revicki et al. Health Qual Life Outcomes. 2011 Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. Reilly et al. Rheumatology (Oxford). 2010 Assessment of radiographic progression in the spines of patients with ankylosing spondylitis treated with adalimumab for up to 2 years. van der Heijde D et al. Arthritis Res Ther. 2009 Physical function, disease activity, and health-related quality-of-life outcomes after 3 years of adalimumab treatment in patients with ankylosing spondylitis. van der Heijde et al. Arthritis Res Ther. 2009 Adalimumab effectiveness for the treatment of ankylosing spondylitis is maintained for up to 2 years: long-term results from the ATLAS trial. van der Heijde et al. Ann Rheum Dis. 2009 Evaluation of the patient acceptable symptom state as an outcome measure in patients with ankylosing spondylitis: data from a randomized controlled trial. Dougados et al. Arthritis Rheum. 2008 Adalimumab effectively reduces the signs and symptoms of active ankylosing spondylitis in patients with total spinal ankylosis. van der Heijde et al. Ann Rheum Dis. 2008
Study type and design	Double-blinded randomised placebo-controlled phase 3 study. Subjects were randomized 2:1 to receive either 40 mg adalimumab subcutaneous (sc) every other week (eow) or matched placebo for the 24-week double-blind placebo-controlled period of the study. After 12 weeks, subjects without a reduction of signs and symptoms in ankylosing spondylitis (ASAS 20) were considered for open-label adalimumab treatment. The study was completed in December 2004.
Sample size (n)	315

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Trial name: ATLAS	NCT number: NCT00085644
Main inclusion and exclusion criteria	Inclusion Criteria: • Subjects must be >= 18 years of age • meet Modified NY Criteria definition of ankylosing spondylitis (AS) • have diagnosis of active AS based on protocol specified criteria • inadequate response or intolerance to >= 1 nonsteroidal anti-inflammatory drug (NSAID) • be able and willing to learn to self-administer subcutaneous (SC) injections Exclusion Criteria: • Active tuberculosis, listeriosis,or hepatitis B, or any history of hepatitis C • History of demyelinating disease, multiple sclerosis, cancer, or lymphoproliferative disease • Previous anti-tumor necrosis factor therapy • Treatment with disease-modifying antirheumatic drugs (DMARDs - other than methotrexate, hydroxychloroquine, and sulfasalazine) • Treatment with intra-articular corticosteroid joint injections within 4 weeks of study dosing • Biologic or investigational therapy within 6 weeks of study dosing • Treatment with intravenous (IV) antibiotics within 30 days of study dosing • Treatment with oral antibiotics within 14 days of study dosing
Intervention	Adalimumab 40 mg every other week, subcutaneous. 208 patients received the intervention.
Comparator(s)	Subjects on placebo treatment received SC injection of matched placebo every other week. 107 patients received the comparator.
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Primary, secondary and exploratory endpoints	Primary endpoints: • Number of Responders With a Reduction of Signs and Symptoms of Ankylosing Spondylitis (AS) as Measured With ASAS International Working Group Response Criteria (ASAS 20) [Time Frame: Week 12] • Mean Change in the Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) Compared Against a Historical Control Group (Outcomes in Ankylosing Spondylitis International Study [OASIS]) Using the ANCOVA Model Adjusting for Baseline mSASSS Score [Time Frame: Week 104] Secondary endpoints: • Number of Subjects With a Reduction of Signs and Symptoms as Measured in Assessments of Ankylosing Spondylitis (ASAS) 20 - Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Number of Subjects With a Reduction of Signs and Symptoms as Measured in Assessments of Ankylosing Spondylitis (ASAS) 50 - Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Number of Subjects With a Reduction of Signs and Symptoms as Measured in Assessments of Ankylosing Spondylitis (ASAS) 70 - Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Mean Change in Patient's Global Assessment of Disease Activity in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Number of Subjects With a Reduction of Signs and Symptoms as Measured in Patient's Global Assessment of Disease Activity (an Individual Component of ASAS 20) Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Mean Change in the Bath Ankylosing Spondylitis Functional Index (BASFI) in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Number of Subjects With a Reduction of Signs and Symptoms as Measured in BASFI (an Individual Component of ASAS 20) Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Mean Change in Total Back Pain Visual Analog Scale (VAS) in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Number of Subjects With a Reduction of Signs and Symptoms as Measured in Total Back Pain (an Individual Component of ASAS 20) Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260] • Mean Change in Inflammation (Mean of BASDAI Questions 5 and 6) in Subjects With Adalimumab Exposure Through Week 260

[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]

- Number of Subjects With a Reduction of Signs and Symptoms as Measured in Inflammation (Individual Component of ASAS 20) (Mean of BASDAI Questions 5 and 6) Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Number of Subjects With a Reduction of Signs and Symptoms as Measured in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 20 Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Number of Subjects With a Reduction of Signs and Symptoms as Measured in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Number of Subjects With a Reduction of Signs and Symptoms as Measured in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 70 Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in BASDAI in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in C-Reactive Protein (CRP) (mg/dL) in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Number of Subjects With a Disease Controlling Clinical Response From Adalimumab as Measured in Assessments of Ankylosing Spondylitis (ASAS) 40 - Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Number of Subjects With a Disease Controlling Clinical Response From Adalimumab as Measured in Assessments of Ankylosing Spondylitis Ankylosing Spondylitis (ASAS) 5/6 in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Number of Subjects With a Disease Controlling Clinical Response From Adalimumab as Measured by ASAS Partial Remission Response in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in the Bath Ankylosing Spondylitis Metrology Index (BASMI) in Subjects With Adalimumab Exposure Through Week 260
[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in Chest Expansion (CE) in Subjects With Adalimumab Exposure Through Week 260 [[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) in Subjects With Adalimumab Exposure Through Week 260

[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]

- Mean Change in the Bath Ankylosing Spondylitis Global Index (BAS-G) in Subjects With Adalimumab Exposure Through Week 260
[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in Swollen Joint Count for 44 Joints (44 SJC) in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Mean Change From Baseline in the Tender Joint Count for 46 Joints (TJC 46) in Subjects With Adalimumab Exposure Through Week 260
[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Mean Change in Physician's Global Assessment of Disease Activity in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in Nocturnal Pain in Subjects With Adalimumab Exposure Through Week 260 [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 220, 232, 244, and 260]
- Mean Change in the SF-36 Health Survey Index Physical Component Summary (PCS) Through Week 260 of Adalimumab Exposure [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Number of Subjects With SF-36 Physical Component Summary (PCS) of Minimal Clinically Important Difference (MCID) Response Through Week 260 of Adalimumab Exposure [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Mean Change in the SF-36 Health Survey Index Mental Component Summary (MCS) Through Week 260 of Adalimumab Exposure [Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Number of Subjects With SF-36 Mental Component Summary (MCS) of Minimal Clinically Important Difference (MCID) Response Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Mean Change in Health Utilities Index-3 (HUI-3) Through Week 260 of Adalimumab Exposure [Time Frame: Baseline, Weeks 24, 52, 104, 128, 156, 180, 208, 232, and 260]
- Mean Change in the Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) in Subjects Through Week 260 of Adalimumab Exposure
[Time Frame: Baseline, Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]
- Number of Subjects With Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) MCID Response (MCID <= -1.8 Points) Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260]

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Trial name: ATLAS	NCT number: NCT00085644
	• Number of Subjects Achieving the Patient Acceptable Symptoms State Through Week 260 of Adalimumab Exposure [Time Frame: Weeks 12, 24, 52, 76, 104, 128, 156, 180, 208, 232, and 260] **Endpoints included in this application:** ASAS40, BASDAI50, SF36-PCS, SF36-MCS, discontinuation due to AEs
Method of analysis	ITT analysis was conducted to assess the efficacy and safety of adalimumab in all randomized patients who received at least one dose of the study drug and had at least one post-baseline efficacy measurement. ANCOVA was used to analyze the primary and secondary efficacy endpoints. ANCOVA is a statistical technique that adjusts for baseline differences between treatment groups and provides a more accurate estimate of the treatment effect. Logistic regression analysis was used to analyze the dichotomous endpoints such as ASAS20 and ASAS40 response rates. Logistic regression is a statistical method used to model the relationship between a dichotomous outcome variable and one or more independent variables. Descriptive statistics such as means, standard deviations, and percentages were used to describe the baseline characteristics of the study population and the safety outcomes. Adverse events were summarized using descriptive statistics, including the number and percentage of patients who experienced adverse events, the severity of adverse events, and the relationship of adverse events to the study drug.
Subgroup analyses	None
Other relevant information	NA

Table 103 Huang 2013

Trial name: Huang 2013	NCT number: NCT01114880
Objective	To study of the efficacy and safety of adalimumab compared with placebo in adult Chinese participants with ankylosing spondylitis (AS) who have had an inadequate response to or who are intolerant to one or more nonsteroidal anti-inflammatory drugs (NSAIDs)
Publications – title, author, journal, year	Efficacy and safety of adalimumab in Chinese adults with active ankylosing spondylitis: results of a randomised, controlled trial, Huang et al., Annals of the Rheumatic Diseases, 2014
Study type and design	Double-Blinded, randomised placebo-controlled phase 3 study. Adults with active ankylosing spondylitis (AS) were randomized in a 2:1 ratio to receive treatment with adalimumab 40 mg every other week (eow) or matching placebo, given subcutaneously (SC), in the 12-week double-blind (DB) phase. The study was completed in September 2010.
Sample size (n)	344

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Trial name: Huang 2013	NCT number: NCT01114880

Main inclusion and exclusion criteria*	Inclusion Criteria:
	• Age 18 through 65 years
	• Has a diagnosis of ankylosing spondylitis (AS) based on the Modified New York Criteria
	• Has active AS, as defined by fulfillment of at least 2 of the following 3 conditions at both Screening and Baseline visits:
	  ○ BASDAI score at least 4 cm
	  ○ Total back pain on a visual analog scale (VAS) at least 40 mm
	  ○ Morning stiffness at least 1 hr
	• Has inadequate response to or intolerance to one or more non-steroidal anti-inflammatory drugs (NSAIDs) as defined by the Investigator
	Exclusion Criteria:
	• Has total spinal ankylosis (bamboo spine)
	• Has undergone spinal surgery or joint surgery involving joints assessed within 2 months prior to Baseline
	• Has extra-articular manifestations (i.e., psoriasis, uveitis, inflammatory bowel disease) that is not clinically stable, as defined by the Investigator's best clinical judgment, for at least 28 days prior to Baseline
	• Has received intra-articular joint injection(s), spinal or paraspinal injection(s) with corticosteroids within 28 days prior to Baseline
	• Has prior exposure to any biologic therapy with potential therapeutic impact on AS, including anti-TNF (tumor necrosis factor) therapy

Intervention	Prefilled syringe, 40 mg/0.8 mL administered subcutaneously every other week. 229 patients.
Comparator(s)	Prefilled syringe, matching placebo administered subcutaneously every other week. 115 patients.
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Primary, secondary and exploratory endpoints	Primary endpoint: Number of Participants Meeting the Assessment of Spondyloarthritis International Society (ASAS) ASAS20 Response Criteria [Time Frame: Week 12] Secondary endpoints: • Number of Participants Meeting the ASAS20 Response Criteria [Time Frame: Week 24] • Number of Participants Meeting the ASAS40 Response Criteria [Time Frame: Week 12] • Number of Participants Meeting the ASAS40 Response Criteria [Time Frame: Week 24] • Number of Participants Meeting the ASAS5/6 Response Criteria [Time Frame: Week 12] • Number of Participants Meeting the ASAS5/6 Response Criteria [Time Frame: Week 24] • Number of Participants With ASAS Partial Remission [Time Frame: Week 12] • Number of Participants With ASAS Partial Remission [Time Frame: Week 24] • Change From Baseline in Patient Global Assessment of Disease Activity [Time Frame: Baseline and Week 12] • Change From Baseline in Patient Global Assessment of Disease Activity [Time Frame: Baseline and Week 24] • Change From Baseline in Total Back Pain Score [Time Frame: Baseline and Week 12] • Change From Baseline in Total Back Pain Score [Time Frame: Baseline and Week 24] • Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) Score [Time Frame: Baseline and Week 12] • Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) Score [Time Frame: Baseline and Week 24] • Change From Baseline in Inflammation Score [Time Frame: Baseline and Week 12] • Change From Baseline in Inflammation Score [Time Frame: Baseline and Week 24] • Number of Participants Meeting the Bath Ankylosing Spondyloarthritis Disease Activity Index (BASDAI) BASDAI50 Response Criteria [Time Frame: Week 12] • Number of Participants Meeting the Bath Ankylosing Spondyloarthritis Disease Activity Index (BASDAI) BASDAI50 Response Criteria [Time Frame: Week 24] • Change From Baseline in High-sensitivity C-Reactive Protein (Hs-CRP) [Time Frame: Baseline and Week 12]

Trial name: Huang 2013	NCT number: NCT01114880
	• Change From Baseline in High-sensitivity C-Reactive Protein (Hs-CRP) [Time Frame: Baseline and Week 24] • Change From Baseline in 36-item Short Form Questionnaire Version 2 (SF-36v2) Physical Component Summary Score [Time Frame: Baseline and Week 12] • Change From Baseline in 36-item Short Form Questionnaire Version 2 (SF-36v2) Physical Component Summary Score [Time Frame: Baseline and Week 24] **Endpoints included in this application:** ASAS40, BASDAI50, SF36-PCS, SF36-MCS, discontinuation due to AEs
Method of analysis	The primary analysis of the ASAS20 response rate at week 12 in the adalimumab group versus the placebo group was performed using the two-sided Pearson $\chi 2$ test with α=0.05. Analysis of the primary endpoint was conducted for various subgroups to assess the impact of baseline variables on treatment response. A logistic model with treatment and a prespecified subgroup in the model was performed to assess the treatment by subgroup interaction. If the treatment by subgroup interaction was significant ($p \leq 0.10$), then treatment effect was assessed for components of the subgroup. For the primary endpoint and other categorical variables, a non-responder imputation approach was done at week 12 for missing data. Patients without data at week 12 were treated as non-responders. For continuous variables at week 12, missing data were imputed using the last observation carried forward. Differences from baseline between adalimumab and placebo groups were compared using an analysis of covariance method, adjusting for the baseline score. Open-label extension data at week 24 were summarised descriptively. All efficacy variables were analysed for the intent-to-treat (ITT) population, defined as all randomised patients who received ≥1 double-blind dose of study drug. The safety population consisted of all patients who received ≥1 dose of study drug.
Subgroup analyses	NA
Other relevant information	NA

Table 104 COAST-V

Trial name: COAST-V	NCT number: NCT02696785
Objective	The main purpose of this study is to evaluate the safety and efficacy of the study drug known as ixekizumab in biological disease-modifying anti-rheumatic drugs (bDMARDs)-naive participants with radiographic axial spondyloarthritis (rad-axSpA).

Trial name: COAST-V	NCT number: NCT02696785
Publications – title, author, journal, year	Baseline Characteristics and Treatment Response to Ixekizumab Categorised by Sex in Radiographic and Non-radiographic Axial Spondylarthritis Through 52 Weeks: Data from Three Phase III Randomised Controlled Trials. van der Horst-Bruinsma et al. Adv Ther. 2022 Ixekizumab in radiographic axial spondyloarthritis with and without elevated C-reactive protein or positive magnetic resonance imaging. Maksymowych et al. Rheumatology (Oxford). 2022 Spinal Radiographic Progression and Predictors of Progression in Patients With Radiographic Axial Spondyloarthritis Receiving Ixekizumab Over 2 Years. van der Heijde et al. J Rheumatol. 2022 Ixekizumab improves spinal pain, function, fatigue, stiffness, and sleep in radiographic axial Spondyloarthritis: COAST-V/W 52-week results. Deodhar et al. BMC Rheumatol. 2021 Efficacy and safety of ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial spondyloarthritis (COAST-V and COAST-W). Dougados et al. Ann Rheum Dis. 2020 Translating Improvements with Ixekizumab in Clinical Trial Outcomes into Clinical Practice: ASAS40, Pain, Fatigue, and Sleep in Ankylosing Spondylitis. Mease et al. Rheumatol Ther. 2019
Study type and design	Double-Blinded, randomised placebo-controlled study. Both placebo and adalimumab were used as comparators. The study was completed December 8, 2017.
Sample size (n)	341

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Trial name: COAST-V	NCT number: NCT02696785
Main inclusion and exclusion criteria*	Inclusion Criteria: • Are ambulatory. • Diagnosis of radiographic axial spondyloarthritis (rad-xSpA) with sacroiliitis defined radiographically according to the modified New York criteria. • Participants have a history of back pain ≥3 months with age at onset <45 years. • In the past had an inadequate response to at least 2 non-steroidal anti-inflammatory drugs (for duration 4 weeks) or cannot tolerate NSAIDS. • If taking NSAIDS be on a stable dose for at least 2 weeks prior to randomization. • Have a history of prior therapy for axSpA for at least 12 weeks prior to screening. Exclusion Criteria: • Have total ankylosis of the spine. • Have received any prior, or are currently receiving, treatment with biologics, tumor necrosis factor inhibitors or other immunomodulatory agents. • Have recently received a live vaccine within 12 weeks or have had a vaccination with Bacillus Calmette-Guerin (BCG) within the past year. • Have an ongoing or serious infection within the last 12 weeks or evidence of active tuberculosis. • Have a compromised immune system. • Have any other serious and/or uncontrolled diseases. • Have either a current diagnosis or a recent history of malignant disease. • Have had major surgery within 8 weeks of baseline, or will require surgery during the study. • Are pregnant or breastfeeding.
Intervention	IXE80Q2W/IXE80Q2W: Participants (n=83) received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection during blinded & extension treatment period. Participants did not receive any intervention during follow-up period. IXE80Q4W/IXE80Q4W: Participants (n=81) received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection during blinded & extension treatment period. Participants did not receive any intervention during follow-up period.

Trial name: COAST-V	NCT number: NCT02696785
Comparator(s)	PBO/IXE: • 87 participants • Blinded Treatment Period: Participants received placebo every two weeks by subcutaneous injection. • Extended Treatment Period: Participants received starting dose of 160mg Ixekizumab at week 16 followed by 80mg Ixekizumab either every two weeks (Q2W) or every four weeks (Q4W) by subcutaneous (SC) injection during extended treatment period. • Participants did not receive any intervention during follow-up period. ADA/PBO/IXE: • 90 participants • Blinded Treatment Period: Participants received 40mg Adalimumab every two weeks by SC injection. • Washout Period: Participants received placebo for 6 weeks. • Extended Treatment Period:Participants received 80mg Ixekizumab either Q2W or Q4W by SC injection during extension treatment period. • Participants did not receive any intervention during follow-up period.
Follow-up time	24 weeks
Is the study used in the health economic model?	No

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Primary, secondary and exploratory endpoints	Primary endpoint: Percentage of Participants Achieving an Assessment of Spondyloarthritis International Society 40 (ASAS40) Response [Time Frame: Week 16] Secondary endpoints: • Percentage of Participants Achieving an ASAS20 Response [Time Frame: Week 16] • Change From Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) [Time Frame: Baseline, Week 16] • Percentage of Participants Achieving Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) Response [Time Frame: Week 16] • Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) [Time Frame: Baseline, Week 16] • Percentage of Participants Achieving ASDAS Inactive Disease [Time Frame: Week 16] • ASDAS is a composite index to assess disease activity in AS. The parameters used for the ASDAS (with CRP as acute phase reactant) are the following: • Change From Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Ankylosing Spondylitis Spinal Magnetic Resonance Imaging [ASSpiMRI] - Berlin Score) [Time Frame: Baseline, Week 16] • Change From Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores [Time Frame: Baseline, Week 16] • Change From Baseline in ASAS Health Index (ASAS HI) [Time Frame: Baseline, Week 16] • Change From Baseline in the Measure of High Sensitivity C-Reactive Protein (CRP) [Time Frame: Baseline, Week 16] • Change From Baseline in Mobility on the Bath Ankylosing Spondylitis Metrology Index (BASMI) [Time Frame: Baseline, Week 16] • Change From Baseline in Chest Expansion [Time Frame: Baseline, Week 16] • Change From Baseline in Occiput to Wall Distance [Time Frame: Baseline, Week 16] • Change From Baseline in MRI Sacroiliac Joint(s) (SIJ) Spondyloarthritis Research Consortium of Canada (SPARCC) Score [Time Frame: Baseline, Week 16] • Change From Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) [Time Frame: Baseline, Week 16] • Change From Baseline in SPARCC Enthesitis Score [Time Frame: Baseline, Week 16] • Change From Baseline in Severity of Peripheral Arthritis by Tender (TJC) [Time Frame: Baseline, Week 16] • Number of Participants With Anterior Uveitis or Uveitis Flares [Time Frame: Baseline through Week 16]

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Trial name: COAST-V	NCT number: NCT02696785
	• Change From Baseline in the Fatigue Numeric Rating Scale (NRS) Score [Time Frame: Baseline, Week 16] • Change From Baseline in the Jenkins Sleep Evaluation Questionnaire (JSEQ) [Time Frame: Baseline, Week 16] • Change From Baseline in the Work Productivity Activity Impairment Spondyloarthritis (WPAI-SpA) Scores [Time Frame: Baseline, Week 16] • Change From Baseline in ASAS-Nonsteroidal Anti-Inflammatory Drug (NSAID) Score [Time Frame: Baseline, Week 52] • Number of Participants With Anti Ixekizumab Antibodies [Time Frame: Week 16] • Pharmacokinetics: Trough Ixekizumab Concentration at Steady State (Ctrough ss) [Time Frame: Week 16] • Change From Baseline in Severity of Peripheral Arthritis by Swollen Joint Count (SJC) [Time Frame: Baseline, Week 16] • Change From Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Spondyloarthritis Research Consortium of Canada [SPARCC] Score) [Time Frame: Baseline, Week 16] **Endpoints included in this application:** ASAS40, ASDAS<2.1, BASDAI50, SF36-PCS, discontinuation due to AEs
Method of analysis	Efficacy and health outcomes during the blinded treatment dosing period were analyzed for all randomized patients according to the treatment to which they were assigned (intention-to-treat population). The primary outcome (ASAS40) was also analyzed for the per-protocol set, defined as all randomized patients who were compliant with therapy, who did not have a subset of important protocol deviations that could impact the primary efficacy endpoint, and whose investigator site did not have significant good clinical practice issues that required a report to regulatory agencies prior to Week 16. Categorical efficacy outcomes and health outcomes variables were analyzed using logistic regression with nonresponder imputation for missing data. With the exception of MRI spine and SIJ, continuous efficacy and health outcomes variables were analyzed using a mixed-effects model of repeated measures. SPARCC MRI spine and SIJ scores were analyzed using analysis of covariance based on observed case. Analyses of the ixekizumab Q2W and Q4W treatment groups were performed without regard to the Week 0 starting dose of 80 mg or 160 mg. In COAST-V, adalimumab represents an active reference arm for comparison to placebo. The study was not designed to test equivalence or non-inferiority of active treatment arms to each other. Safety was assessed in a blinded fashion for all randomized patients receiving at least one dose of study drug.
Subgroup analyses	NA
Other relevant information	NA

Table 105 MEASURE 2

Trial name: MEASURE 2	NCT number: NCT01649375
Objective	The purpose of the study is to assess the efficacy and safety of secukinumab in patients with active ankylosing spondylitis who were tolerant to or had an inadequate response to NSAIDs, DMARDs and / or TNFα inhibitor.
Publications – title, author, journal, year	Nonsteroidal anti-inflammatory drug-sparing effect of secukinumab in patients with radiographic axial spondyloarthritis: 4-year results from the MEASURE 2, 3 and 4 phase III trials. Dougados et al. Rheumatol Int. 2022 A Pooled Analysis Reporting the Efficacy and Safety of Secukinumab in Male and Female Patients with Ankylosing Spondylitis. van der Horst-Bruinsma et al. Rheumatol Ther. 2021 Secukinumab Efficacy on Enthesitis in Patients With Ankylosing Spondylitis: Pooled Analysis of Four Pivotal Phase III Studies. Schett et al. J Rheumatol. 2021 Achievement of Remission Endpoints with Secukinumab Over 3 Years in Active Ankylosing Spondylitis: Pooled Analysis of Two Phase 3 Studies. Baraliakos et al. Rheumatol Ther. 2021 The societal impact of a biologic treatment of ankylosing spondylitis: a case study based on secukinumab. Himmler et al. J Comp Eff Res. 2021 Secukinumab and Sustained Reduction in Fatigue in Patients With Ankylosing Spondylitis: Long-Term Results of Two Phase III Randomized Controlled Trials. Kvien et al. Arthritis Care Res (Hoboken). 2022 Incidence of Uveitis in Secukinumab-treated Patients With Ankylosing Spondylitis: Pooled Data Analysis From Three Phase 3 Studies. Deodhar et al. ACR Open Rheumatol. 2020 Secukinumab Immunogenicity over 52 Weeks in Patients with Psoriatic Arthritis and Ankylosing Spondylitis. Deodhar et al. J Rheumatol. 2020 MEASURE 1 and MEASURE 2 study groups. Impact of baseline C-reactive protein levels on the response to secukinumab in ankylosing spondylitis: 3-year pooled data from two phase III studies. Braun et al. RMD Open. 2018 Efficacy and safety of secukinumab in Asian patients with active ankylosing spondylitis: 52-week pooled results from two phase 3 studies. Wei et al. Int J Rheum Dis. 2017 Measure 2 Study Group. Secukinumab and Sustained Improvement in Signs and Symptoms of Patients With Active Ankylosing Spondylitis Through Two Years: Results From a Phase III Study. Marzo-Ortega et al. Arthritis Care Res (Hoboken). 2017 Secukinumab efficacy in anti-TNF-naive and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 Study. Sieper et al. Ann Rheum Dis. 2017 Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. Baeten et al. N Engl J Med. 2015
Study type and design	Double-blinded randomized placebo-controlled phase 3 study. The study was completed September 18, 2018.

Trial name: MEASURE 2	NCT number: NCT01649375
Sample size (n)	219
Main inclusion and exclusion criteria*	Inclusion Criteria: • Male or non-pregnant, non-lactating female patients • Diagnosis of moderate to severe AS with prior documented radiologic evidence (x-ray) fulfilling the Modified New York criteria for AS (1984) • Patients should have been on NSAIDs with an inadequate response • Patients who were regularly taking NSAIDs as part of their AS therapy are required to be on a stable dose • Patients who had been on an anti-TNFα agent (not more than one) must have experienced an inadequate response Exclusion Criteria: • Chest X-ray (or MRI) with evidence of ongoing infectious or malignant process • Patients with total ankylosis of the spine • Patients previously treated with any biological immunomodulating agents except for those targeting TNFα • Previous treatment with any cell-depleting therapies
Intervention	Secukinumab 75 mg: • 73 participants • Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks. Secukinumab 150 mg: • 72 participants • Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks

Trial name: MEASURE 2	NCT number: NCT01649375
Comparator(s)	Placebo: • 74 participants • Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16 Placebo - Secukinumab 75 mg • 32 participants (Week 16 up to Week 260) • Placebo patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16. Placebo - Secukinumab 150 mg • 34 participants (Week 16 up to Week 260) • Placebo patients re-randomized to secukinumab 150 mg subcutaneous injection every 4 weeks starting from week 16.
Follow-up time	Not reported
Is the study used in the health economic model?	No
Primary, secondary and exploratory endpoints	Primary endpoints: Percentage of Participants Achieving ASAS 20 (SpondyloArthritis International Society Criteria) Response at Week 16 [Time Frame: Baseline up to 16 weeks] Secondary endpoints: • Percentage of Participants Achieving ASAS 40 (SpondyloArthritis International Society Criteria) Response [Time Frame: Baseline up to 16 weeks] • Change From Baseline at Week 16 in Serum hsCRP [Time Frame: Baseline up to 16 weeks] • Percentage of Participants Achieving ASAS 5/6 (SpondyloArthritis International Society Criteria) Response at Week 16 [Time Frame: Baseline up to 16 weeks] • Change From Baseline at Week 16 for Total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [Time Frame: Baseline up to 16 weeks] • Change From Baseline at Week 16 in Physical Function Component Summary (PCS) of the Medical Outcomes Study Questionnaire Short-form Health Survey (SF-36) [Time Frame: Baseline up to 16 weeks] • Change From Baseline at Week 16 in ASQoL [Time Frame: Baseline up to 16 weeks] • Percentage of Participants Achieving ASAS Partial Remission at Week 16 [Time Frame: Baseline up to 16 weeks] **Endpoints included in this application:** ASAS40, BASDAI50, SF36-PCS, SF36-MCS, discontinuation due to AEs

Trial name: MEASURE 2	NCT number: NCT01649375
Method of analysis	Analyses of primary and secondary efficacy end points at week 16 included all patients according to the treatment assigned at randomization. The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate. Missing values, including those due to discontinuation of the study treatment, were imputed as nonresponses. Between-group differences in continuous variables were evaluated with the use of a mixed-model repeated-measures (MMRM) approach, with missing data assumed to be missing at random and with study group, assessment visit, and anti-TNF response status as factors. Weight and baseline values of the end points were included in the model as continuous covariates. Interaction terms included study group and baseline value according to assessment visit. For the change in the high-sensitivity CRP level, the loge ratio of the post-baseline value to the baseline value was used to normalize the distribution of the high-sensitivity CRP level at each assessment. The end points assessed at week 16 were analyzed descriptively with the use of observed values from week 20 onward. In a separate analysis of these end points from week 20 onward, missing values for binary variables were imputed as nonresponses, and missing values for continuous variables were imputed with the use of MMRM analysis. Safety end points were evaluated for all patients who received at least one dose of the study drug; these end points were summarized descriptively. A data and safety monitoring committee reviewed unblinded safety data at regular intervals
Subgroup analyses	NA
Other relevant information	NA

Table 106 ASTRUM

Trial name: ASTRUM	NCT number: NCT02763046
Objective	The purpose of the study is to assess the clinical Assessment of SpondyloArthritis international Society (ASAS) 20 response to secukinumab and evaluate to which extent concomitant nonsteroidal anti-inflammatory drug (NSAID) treatment can be reduced in patients treated with secukinumab or placebo following an initial run-in phase of stable NSAID therapy.
Publications – title, author, journal, year	Results not published but available via Clinicaltrials.gov
Study type and design	Double-blinded randomized placebo-controlled phase IV study. Patients were randomized 1:1:1 to one of the following treatment groups: Secukinumab - delayed NSAID tapering, Secukinumab - early NSAID tapering, and Placebo. The study was completed September 24, 2019.
Sample size (n)	211

Trial name: ASTRUM	NCT number: NCT02763046

Main inclusion and exclusion criteria*

Key Inclusion Criteria:

- Diagnosis of active AS with prior documented radiologic evidence fulfilling the Modified New York criteria for AS
- Active AS assessed by total BASDAI ≥ 4 (0-10) at baseline
- Spinal pain as measured by BASDAI Question 2 ≥ 4 cm on a 0-10 cm numeric rating scale at baseline
- Total back pain as measured by VAS ≥ 40 mm (0-100 mm) at baseline
- Patients should have been on at least 2 different NSAIDs at the highest recommended dose for at least 4 weeks prior to randomization, with an inadequate response or failure to respond, or less if therapy had to be reduced due to intolerance, toxicity or contraindications
- Patients must report regular intake of NSAIDs of at least 50% of the highest recommended dose at Screening.
- Patients with prior TNFα inhibitor therapy must report regular intake of NSAIDs of at least 50% of the highest recommended dose at baseline after the appropriate washout
- Patients are required to be on a stable dose of NSAIDs for at least 2 weeks before randomization
- Patients who have previously been on a TNFα inhibitor will be allowed entry into study after an appropriate wash-out period prior to randomization
- Patients who have been on a TNFα inhibitor (not more than two) must have experienced an inadequate response to previous or current treatment given at an approved dose for at least 3 months prior to randomization or have been intolerant to at least one administration of an anti-TNFα agent.
- Patients taking MTX or sulfasalazine are allowed to continue their medication and must have taken it for at least 3 months and be on a stable dose for at least 4 weeks prior to randomization

Key Exclusion Criteria:

- Chest X-ray or MRI with evidence of ongoing infectious or malignant process.
- Previous exposure to Secukinumab or any other biologic drug directly targeting IL-17 or IL-17 receptor
- Patients previously treated with any biological immunomodulating agents, except those targeting TNFα
- Patients who have taken more than two anti-TNFα agents
- Pregnant or nursing (lactating) women.
- History of ongoing, chronic or recurrent infectious disease or evidence of tuberculosis infection.
- Patients who are intolerant to NSAIDs

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Trial name: ASTRUM	NCT number: NCT02763046
Intervention	Secukinumab - Delayed NSAID Tapering: • 71 participants • Induction with secukinumab 150 mg s.c. once per week (Week 0, 1, 2, 3 and 4) followed by maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 8, 12, 16 and 20), with intermittent placebo injections at Week 5, 6, 7, 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (delayed tapering). Secukinumab - Early NSAID Tapering: • 70 participants • Placebo at weeks 0, 1, 2, 3 to maintain the blind; followed by induction with secukinumab 150 mg s.c. once per week (Week 4, 5, 6, 7, 8) and maintenance with secukinumab 150 mg s.c. every 4 weeks (Week 12, 16 and 20), with intermittent placebo injections at Week 17, 18 and 19 to maintain the blind. NSAID tapering allowed from Week 4 (early tapering).
Comparator(s)	Placebo: • 70 participants • Placebo s.c. at Week 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12. After the Week 16 assessments of the secondary endpoint had been performed, these patients received weekly doses of secukinumab 150 mg s.c. (Week 16, 17, 18, 19 and 20). NSAID tapering allowed from Week 4.
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Trial name: ASTRUM	NCT number: NCT02763046
Primary, secondary and exploratory endpoints	Primary endpoints: Proportion of Patients Who Achieved ASAS20 Response in the Pooled Secukinumab Group Compared With the Placebo Group at Week 12 [Time Frame: Baseline, Week 12] Secondary endpoints: • Proportion of Patients Who Achieved ASAS20 Response in Each Secukinumab Group (Delayed NSAID Tapering and Early NSAID Tapering) Compared With the Placebo Group [Time Frame: Baseline, Week 12, Week 16] • Mean Change From Baseline in ASAS-NSAID Score at Week 12 [Time Frame: Baseline, Week 12] • Mean Change From Baseline in ASAS-NSAID Score in Each Secukinumab Group After 12 Weeks of Exposure (at Week 12 in the Secukinumab-delayed NSAID Tapering Group and at Week 16 in the Secukinumab-early NSAID Tapering Group) [Time Frame: Baseline, Week 12 (delayed NSAID tapering), Week 16 (early NSAID tapering)] • Mean Change From Baseline in the BASDAI Total Score [Time Frame: Baseline, Week 12, Week 16] • Mean Change From Baseline in Health-related Quality of Life as Measured by the Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) Score [Time Frame: Baseline, Week 12] **Endpoints included in this application:** ASAS40, BASDAI50, discontinuation due to AEs
Method of analysis	Not reported
Subgroup analyses	NA
Other relevant information	NA

Table 107 MEASURE 5

Trial name: MEASURE 5	NCT number: NCT02896127
Objective	The purpose of this trial is to demonstrate the clinical efficacy at week 16; and to demonstrate safety and tolerability of secukinumab compared to placebo in patients with ankylosing spondylitis at week 16 and long term safety up to Week 52.

Trial name: MEASURE 5	NCT number: NCT02896127
Publications – title, author, journal, year	Effect of Secukinumab on Traditional Cardiovascular Risk Factors and Inflammatory Biomarkers: Post Hoc Analyses of Pooled Data Across Three Indications. Merola et al. Rheumatol Ther. 2022 A Pooled Analysis Reporting the Efficacy and Safety of Secukinumab in Male and Female Patients with Ankylosing Spondylitis. van der Horst-Bruinsma et al. Rheumatol Ther. 2021 Secukinumab provided significant and sustained improvement in the signs and symptoms of ankylosing spondylitis: results from the 52-week, Phase III China-centric study, MEASURE 5. Huang et al. Chin Med J (Engl). 2020
Study type and design	Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study. The study was completed March 19, 2019.
Sample size (n)	458

Main inclusion and exclusion criteria*	Inclusion Criteria:
	• Male or non-pregnant, non-lactating female patients at least 18 years of age
	• Diagnosis of moderate to severe AS with prior documented radiologic evidence (x-ray or radiologist's report) fulfilling the Modified New York criteria for AS:
	  ○ Active AS assessed by BASDAI ≥4 (0-10) at Baseline
	  ○ Spinal pain as measured by BASDAI question #2 ≥ 4 cm (0-10 cm) at Baseline
	  ○ Total back pain as measured by VAS ≥ 40 mm (0-100 mm) at Baseline Patients should have had inadequate response or failure to respond to at least 2 NSAIDs at an approved dose for a minimum of 4 weeks in total and a minimum of 2 weeks for each NSAID prior to randomization, or less than 4 weeks if therapy had to be withdrawn due to intolerance, toxicity or contraindications Patients who are regularly taking NSAIDs (including COX-1 or COX-2 inhibitors) as part of their AS therapy are required to be on a stable dose for at least 2 weeks before randomisation Patients who have been on a TNFα inhibitor (not more than one) must have experienced an inadequate response to previous or current treatment given at an approved dose for at least 3 months prior to randomization or have been intolerant to at least one administration of an anti-TNFα agent
	
	Exclusion Criteria:
	• Chest X-ray or MRI with evidence of ongoing infectious or malignant process
	  ○ Patients taking high potency opioid analgesics
	  ○ Previous exposure to secukinumab or any other biologic drug directly targeting IL-17 or IL-17 receptor
	  ○ Pregnant or nursing (lactating) women

Trial name: MEASURE 5	NCT number: NCT02896127
Intervention	Drug: Secukinumab • 305 participants • Induction: 4x 150 mg Secukinumab s.c. weekly • Maintenance: 150 mg Secukinumab s.c. monthly • All Subjects received blinded treatment weekly starting at baseline, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4 until Week 16. At Week 16, Group 1 patients continued using secukinumab 150 mg and Group 2 patients started receiving secukinumab 150 mg dosing every four weeks. Treatment was provided open-label from Week 16 onward, as all patients took 150 mg s.c. every 4 weeks; however, subjects, investigators, and site staff remained blinded to initial randomized group assignment.
Comparator(s)	Placebo: • 153 participants • Induction: 4x placebo s.c. weekly • Maintenance: placebo s.c. monthly
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Trial name: MEASURE 5	NCT number: NCT02896127

Primary, secondary and exploratory endpoints

Primary endpoints: The Proportion of Participants Who Achieve an ASAS 20 Response (Assessment of SpondyloArthritis International Society Criteria) [Time Frame: Week 16]

Secondary endpoints:

- The Proportion of Participants Who Achieve an ASAS40 Response [Time Frame: The secondary outcome analysis occurred only at Week 16. Thus, while data were collected beyond week 16, they were not part of the secondary outcomes.]
- Change in hsCRP Over Time [Time Frame: Change from baseline to Week 16. The secondary outcome analysis occurred only at Week 16. Thus, while data were collected beyond week 16, they were not part of the secondary outcomes.]
- Percentage of Participants Who Achieve an ASAS 5/6 at Week 16 [Time Frame: Week 16: The secondary outcome analysis occurred only at Week 16. Thus, while data were collected beyond week 16, they were not part of the secondary outcomes.]
- Participants With BASDAI Response at 16 Weeks [Time Frame: The secondary outcome analysis occurred only at Week 16. Thus, while data were collected beyond week 16, they were not part of the secondary outcomes.]
- Change in Short Form (36) - PCS Responders (Improvement of >= 2.5 Points) at Week 16 [Time Frame: The secondary outcome analysis occurred only at Week 16. Thus, while data were collected beyond week 16, they were not part of the secondary outcomes.]
- Change in ASQoL Score Over Time [Time Frame: change from baseline to Week 16]
- The Proportion of Patients Who Achieve an ASAS Partial Remission [Time Frame: Week 16]

Endpoints included in this application:

ASAS40, SF-36PCS, discontinuation due to AEs

Trial name: MEASURE 5	NCT number: NCT02896127
Method of analysis	The primary endpoint was analyzed using a logistic regression model with treatment and randomization stratum (region) as factors and weight as a covariate. Odds ratios and 95% confidence intervals were calculated to compare secukinumab 150 mg with placebo. Statistical analyses were based on logistic regression for binary efficacy variables (eg, ASAS20/40) and a mixed-effects repeated measures model (MMRM) for continuous variables (eg, hsCRP) with treatment, analysis visit, and TNFi use as factors, and baseline score and weight as covariates. Treatment and baseline score by analysis visit were included as interaction terms in the model. For the change in hsCRP level, the loge ratio of the post-baseline value to the baseline value was used to normalize the distribution of the hsCRP level at each assessment time point. For the primary analysis, a missing response was considered as a non-responder and discontinued patients were considered non-responders for all subsequent visits after the time of discontinuation. A sensitivity analysis was performed using multiple imputation to handle missing responses; continuous endpoints were analyzed via MMRM analysis with a missing at random assumption to Week 52. The safety analysis included all patients who received at least 1 dose of secukinumab. AEs are reported as exposure-adjusted incidence rates (EAIR) per 100 patient-years over the entire treatment period, which refers to the cumulative treatment period (ie, events started after the first dose of study treatment or events present before the first dose of study treatment but which increased in severity based on preferred term and events that had an onset on or before the last dose date plus 84 days). Safety results were summarized using descriptive statistics.
Subgroup analyses	NA
Other relevant information	NA

Table 108 MEASURE 4

Trial name: MEASURE 4	NCT number: NCT02159053
Objective	The purpose of this study is to provide 16-week efficacy, safety and tolerability data versus placebo to support the use of secukinumab 150 mg by subcutaneous (s.c.) self-administration with or without a loading regimen and maintenance dosing using pre-filled syringe (PFS) and to assess efficacy, safety and tolerability up to 2 years in subjects with active AS despite current or previous NSAID, non-biologic DMARD, or biologic anti-TNFα therapy.

Trial name: MEASURE 4	NCT number: NCT02159053
Publications – title, author, journal, year	Effect of Secukinumab on Traditional Cardiovascular Risk Factors and Inflammatory Biomarkers: Post Hoc Analyses of Pooled Data Across Three Indications. Merola et al. Rheumatol Ther. 2022 Nonsteroidal anti-inflammatory drug-sparing effect of secukinumab in patients with radiographic axial spondyloarthritis: 4-year results from the MEASURE 2, 3 and 4 phase III trials. Dougados et al. Rheumatol Int. 2022 A Pooled Analysis Reporting the Efficacy and Safety of Secukinumab in Male and Female Patients with Ankylosing Spondylitis. van der Horst-Bruinsma et al. Rheumatol Ther. 2021 Secukinumab Efficacy on Enthesitis in Patients With Ankylosing Spondylitis: Pooled Analysis of Four Pivotal Phase III Studies. Schett et al. J Rheumatol. 2021 Secukinumab Immunogenicity over 52 Weeks in Patients with Psoriatic Arthritis and Ankylosing Spondylitis. Deodhar et al. J Rheumatol. 2020 Efficacy and Safety of Secukinumab 150 mg with and Without Loading Regimen in Ankylosing Spondylitis: 104-week Results from MEASURE 4 Study. Kivitz et al. Rheumatol Ther. 2018
Study type and design	Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study. Eligible subjects are randomized to each of the three treatment arms in a 1:1:1 ratio. The three treatment arms are Secukinumab 150 mg s.c. with loading, Secukinumab 150 mg s.c. without loading, and Placebo. The study was completed January 2, 2018.
Sample size (n)	350
Main inclusion and exclusion criteria*	Inclusion criteria: • moderate to severe AS • prior radiographic evidence according to the Modified NY Criteria (1984) • inadequate response to NSAIDs. Exclusion criteria: • pregnancy or lactation • on-going infectious or malignant process on a chest X-ray or MRI • previous exposure to IL-17 or IL-17R targeting therapies • previous exposure to any biological immunomodulating agent excluding TNF antagonists • previous cell depleting therapy. Other protocol-defined inclusion/exclusion criteria do apply.

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Trial name: MEASURE 4	NCT number: NCT02159053
Intervention	Secukinumab 150 mg With Loading Dose • Participants (n=116) were subcutaneously (s.c.) administered with 150 milligrams (mg) of secukinumab at baseline, Weeks 1, 2, and 3, followed by dosing every four weeks starting at Week 4. Secukinumab 150 mg Without Loading Dose • Participants (n=117) were s.c. administered with 150 mg of secukinumab at baseline, followed by dosing every four weeks starting at Week 4, and with Placebo at Weeks 1, 2, and 3.
Comparator(s)	Placebo: Participants (n=117) were s.c. administered with placebo matching to secukinumab at baseline, Weeks 1, 2, 3, 4, 8, and 12. Participants were further administered with 150 mg of secukinumab every four weeks starting at Week 16.
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Trial name: MEASURE 4	NCT number: NCT02159053

Primary, secondary and exploratory endpoints

Primary endpoints: Percentage of Participants Responded for Assessment of Spondyloarthritis International Society 20 Criteria (ASAS20) at 16 Weeks [Time Frame: 16 Weeks]

Secondary endpoints:

- Percentage of Participants Responded for ASAS 40 Response at 16 Weeks [Time Frame: 16 Weeks]
- Change From Baseline in Serum High Sensitivity C-reactive Protein (hsCRP) at 16 Weeks [Time Frame: Baseline, 16 Weeks]
- Percentage of Participants Responded for ASAS 5/6 Response at 16 Weeks [Time Frame: 16 Weeks]
- Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at 16 Weeks [Time Frame: Baseline, 16 Weeks]
- Change From Baseline in Physical Function Component Summary (PCS) of the Medical Outcomes Study Questionnaire Short-form Health Survey (SF-36) [Time Frame: Baseline, 16 Weeks]
- Change From Baseline in Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) at 16 Weeks [Time Frame: Baseline, 16 Weeks]
- Number of Participants With Adverse Events (AEs), Deaths, Serious Adverse Events (SAEs) and Related Discontinuations at 104 Weeks [Time Frame: 104 Weeks]
- Percentage of Participants Responded for ASAS 20 at Week 4 [Time Frame: Week 4]
- Percentage of Participants Responded for ASAS 40 Response at Week 4 [Time Frame: Week 4]

Endpoints included in this application:

ASAS40, SF-36PCS, discontinuation due to AEs

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Trial name: MEASURE 4	NCT number: NCT02159053
Method of analysis	Analyses of primary and secondary efficacy endpoints at week 16 included all patients according to the treatment assigned at randomization. Closed testing procedures were used to maintain a family-wise error rate of 5% across the secukinumab groups and endpoints. The hypotheses for the primary objective in either secukinumab treatment group versus placebo were tested simultaneously at the 0.025 level. Based on the rejection of one or both of these hypotheses, analyses of the secondary endpoints were completed according to a pre-specified hypothesis testing hierarchy in the sequence described in Fig. S2 of the Supplementary Appendix. Adjusted *P* values are presented unless otherwise stated. Comparative efficacy analyses (i.e., inferential efficacy comparisons versus placebo) were performed on the full analysis set, which was comprised of all patients who were randomized. The primary endpoint and other binary endpoints were evaluated using logistic regression, with treatment and TNFi use as factors and weight as a covariate. Missing values, including those due to discontinuation of study treatment, were imputed as non-response. Between-treatment differences in continuous variables were evaluated using a mixed-effect model repeated-measures (MMRM) approach, which is valid under the missing at random assumption. Treatment, analysis visit, and TNFi use were used as factors, with baseline score and weight as covariates. Treatment and baseline score by analysis visit were included as interaction terms in the model. For the change in hsCRP level, the $\log_e$ ratio of the post-baseline value to the baseline value was used to normalize the distribution of the hsCRP level at each assessment time point. Interactions between treatment and baseline demographics or disease characteristics for ASAS20 response at week 16 were evaluated using a logistic regression model. Safety assessment included all patients who received at least one dose of the study drug; AE rates were summarized descriptively.
Subgroup analyses	NA
Other relevant information	NA

Table 109 COAST-W

Trial name: COAST-W	NCT number: NCT02696798
Objective	The main purpose of this study is to evaluate the efficacy and safety of ixekizumab in tumor necrosis factor (TNF) inhibitor-experienced participants with radiographic axial spondyloarthritis (rad-axSpA).

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Trial name: COAST-W	NCT number: NCT02696798
Publications – title, author, journal, year	Baseline Characteristics and Treatment Response to Ixekizumab Categorised by Sex in Radiographic and Non-radiographic Axial Spondylarthritis Through 52 Weeks: Data from Three Phase III Randomised Controlled Trials. van der Horst-Bruinsma et al. Adv Ther. 2022 Ixekizumab in radiographic axial spondyloarthritis with and without elevated C-reactive protein or positive magnetic resonance imaging. Maksymowych et al. Rheumatology (Oxford). 2022 Spinal Radiographic Progression and Predictors of Progression in Patients With Radiographic Axial Spondyloarthritis Receiving Ixekizumab Over 2 Years. van der Heijde et al. J Rheumatol. 2022 Ixekizumab improves spinal pain, function, fatigue, stiffness, and sleep in radiographic axial Spondyloarthritis: COAST-V/W 52-week results. Deodhar et al. BMC Rheumatol. 2021 Efficacy and safety of ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial spondyloarthritis (COAST-V and COAST-W). Dougados et al. Ann Rheum Dis. 2020 Translating Improvements with Ixekizumab in Clinical Trial Outcomes into Clinical Practice: ASAS40, Pain, Fatigue, and Sleep in Ankylosing Spondylitis. Mease et al. Rheumatol Ther. 2019 Efficacy and Safety of Ixekizumab in the Treatment of Radiographic Axial Spondyloarthritis: Sixteen-Week Results From a Phase III Randomized, Double-Blind, Placebo-Controlled Trial in Patients With Prior Inadequate Response to or Intolerance of Tumor Necrosis Factor Inhibitors. Deodhar et al. Arthritis Rheumatol. 2019
Study type and design	Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study. The study was completed May 3, 2019.
Sample size (n)	316

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Trial name: COAST-W	NCT number: NCT02696798
Main inclusion and exclusion criteria*	Inclusion Criteria: • Are ambulatory. • Have an established diagnosis of radiographic axial spondyloarthritis (rad-xSpA) with sacroiliitis defined radiographically according to the modified New York criteria. • Participants have a history of back pain ≥3 months with age at onset <45 years. • Have had prior treatment with at least 1 and not more than 2 TNF inhibitors. • Must have had an inadequate response to 2 or more NSAIDs at the therapeutic dose range for a total duration of at least 4 weeks OR have a history of intolerance to NSAIDs. • Have a history of prior therapy for axSpa for at least 12 weeks prior to screening. Exclusion Criteria: • Have total ankylosis of the spine. • Have never taken a TNF inhibitor medication or have taken more than 2. • Have recently received a live vaccine within 12 weeks or have had a vaccination with Bacillus Calmette-Guerin (BCG) within the past year. • Have an ongoing or serious infection within the last 12 weeks or evidence of active tuberculosis. • Have a compromised immune system. • Have any other serious and/or uncontrolled diseases. • Have either a current diagnosis or a recent history of malignant disease. • Have had major surgery within 8 weeks of baseline, or will require surgery during the study. • Are pregnant or breastfeeding.

Trial name: COAST-W	NCT number: NCT02696798
Intervention	IXE80Q2W/IXE80Q2W • 98 participants • Blinded Treatment Dosing Period: Participants received starting dose of 80 or 160 milligrams (mg) ixekizumab given subcutaneously (SC) at baseline followed by 80 mg ixekizumab given SC every two weeks (Q2W) up to week 16. • Extended Treatment Period: Participants received 80 mg ixekizumab given SC Q2W from week 16 to week 52. • Post-treatment Follow-up Period: Participants did not receive any intervention during Follow-up period IXE80Q4W/IXE80Q4W • 114 participants • Blinded Treatment Dosing Period: Participants received starting dose of 80 or 160 mg ixekizumab given SC at baseline followed by 80 mg ixekizumab given SC every four weeks (Q4W) up to week 16. • Extended Treatment Period: Participants received 80 mg ixekizumab given SC Q4W from week 16 to week 52. • Post-treatment Follow-up Period: Participants did not receive any intervention during Follow-up period
Comparator(s)	PBO/IXE • 104 participants • Blinded Treatment Dosing Period: Participants received placebo (PBO) every two weeks (Q2W) by subcutaneous (SC) injection during Week 0 to 16. • Extended Treatment Period: Participants who received Placebo in blinded treatment period were re-randomized to receive ixekizumab (IXE) 80 mg every four weeks (Q4W) or 80 mg Q2W at a 1:1 ratio with starting dose of 160 mg. • Post-treatment Follow-up Period: Participants did not receive any intervention during Follow-up period
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Primary, secondary and exploratory endpoints	Primary endpoints: Percentage of Participants Achieving an Assessment of Spondyloarthritis International Society 40 (ASAS40) Response [Time Frame: Week 16] Secondary endpoints: • Percentage of Participants Achieving an ASAS20 Response [Time Frame: Week 16] • Change From Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) [Time Frame: Baseline, Week 16] • Percentage of Participants Achieving Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) Response [Time Frame: Week 16] • Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [Time Frame: Baseline, Week 16] • Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) [Time Frame: Baseline, Week 16] • Percentage of Participants Achieving ASDAS Inactive Disease [Time Frame: Week 16] • Percentage of Participants Achieving ASDAS <2.1 [Time Frame: Week 16] • Change From Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores [Time Frame: Baseline, Week 16] • Change From Baseline in ASAS Health Index (ASAS HI) [Time Frame: Baseline, Week 16] • Change From Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Ankylosing Spondylitis Spinal Magnetic Resonance Imaging [ASSpiMRI] - Berlin Score) [Time Frame: Baseline, Week 16] • Change From Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Spondyloarthritis Research Consortium of Canada [SPARCC] Score) [Time Frame: Baseline, Week 16] • Change From Baseline in the Measure of High Sensitivity C-Reactive Protein (CRP) [Time Frame: Baseline, Week 16] • Change From Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) [Time Frame: Baseline, Week 16] • Change From Baseline in Chest Expansion [Time Frame: Baseline, Week 16] • Change From Baseline in Occiput to Wall Distance [Time Frame: Baseline, Week 16] • Change From Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) [Time Frame: Baseline, Week 16] • Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Score [Time Frame: Baseline, Week 16] • Change From Baseline in Severity of Peripheral Arthritis by Tender Joint Count (TJC) Scores [Time Frame: Baseline, Week 16]

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Trial name: COAST-W	NCT number: NCT02696798
	• Change From Baseline in Severity of Peripheral Arthritis by Swollen Joint Count (SJC) Scores [Time Frame: Baseline, Week 16] • Percentage of Participants With Anterior Uveitis [Time Frame: Week 16] • Change From Baseline in the Fatigue Numeric Rating Scale (NRS) Score [Time Frame: Baseline, Week 16] • Change From Baseline in the Jenkins Sleep Evaluation Questionnaire (JSEQ) [Time Frame: Baseline, Week 16] • Change From Baseline in the Work Productivity Activity Impairment Spondyloarthritis (WPAI-SpA) Scores [Time Frame: Baseline, Week 16] • Change From Baseline in ASAS-Nonsteroidal Anti-Inflammatory Drug (NSAID) Score [Time Frame: Baseline, Week 52] • Percentage of Participants With Anti-Ixekizumab Antibodies [Time Frame: Week 16] • Pharmacokinetics (PK): Trough Ixekizumab Concentration at Steady State (Ctrough ss) [Time Frame: Week 16] **Endpoints included in this application:** ASAS40, ASDAS<2.1, BASDAI50, SF-36PCS, discontinuation due to AEs
Method of analysis	Efficacy analyses for the blinded treatment dosing period included all randomized patients according to the treatment to which they were assigned. Analyses of the IXEQ2W and IXEQ4W treatment groups were performed without regard to the starting dose. Missing values (including for those patients who discontinued trial treatment) were imputed as nonresponders using nonresponder imputation for categorical variables; continuous variables were analyzed using a mixed-effects model of repeated measures (MMRM) without imputation for missing values. The primary analysis method for categorical outcome variables was logistic regression with treatment, geographic region, baseline CRP status (≤5 versus >5 mg/liter), and the number of prior TNFi taken included in the model. Secondary analysis of categorical outcomes was performed using Fisher's exact test when the logistic model did not converge due to sparse data. The primary analysis method for continuous outcomes, except SPARCC MRI index scores, was MMRM with treatment, geographic region, baseline CRP level, the number of prior TNFi taken, baseline value, visit, baseline value–by-visit, and treatment-by-visit interaction as fixed factors. The primary analysis method for SPARCC MRI index scores was analysis of covariance (ANCOVA) with observed case analysis, with inclusion only of patients with both baseline (between 42 days prior to and 14 days after the first injection) and week 16 (injection date at week 16 [±14 days]) SPARCC MRI index scores. The ANCOVA included treatment, geographic region, baseline CRP level, number of prior TNFi taken, and baseline value.
Subgroup analyses	NA

Trial name: COAST-W	NCT number: NCT02696798
Other relevant information	NA

Table 110 ABILITY1

Trial name: ABILITY1	NCT number: NCT00939003
Objective	This study will evaluate how well adalimumab works in the short and long term in patients with axial spondyloarthritis who are not diagnosed as having either ankylosing spondylitis or psoriatic arthritis.
Publications – title, author, journal, year	Clinical and MRI remission in patients with nonradiographic axial spondyloarthritis who received long-term open-label adalimumab treatment: 3-year results of the ABILITY-1 trial. van der Heijde et al. Arthritis Res Ther. 2018 Spinal inflammation in the absence of sacroiliac joint inflammation on magnetic resonance imaging in patients with active nonradiographic axial spondyloarthritis. van der Heijde et al. Arthritis Rheumatol. 2014 Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). Sieper et al. Ann Rheum Dis. 2013
Study type and design	Randomized, Double-blind, Placebo-controlled, Phase III Multicenter Study. The study was completed August 2013.
Sample size (n)	192

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Trial name: ABILITY1	NCT number: NCT00939003
Main inclusion and exclusion criteria*	Inclusion Criteria: • Adult patients with inadequate response to >/= 1 non-steroidal anti-inflammatory drugs (NSAIDs) • Chronic back pain with onset < 45 years of age • Magnetic resonance imaging (MRI) indicating active sacroiliitis or positive human leukocyte antigen-B27 (HLA-B27) blood test in addition to meeting spondyloarthritis clinical criteria • Negative purified protein derivative (PPD) test and chest x-ray performed at Baseline visit must be negative • Ability to administer subcutaneous injections • General good health otherwise Exclusion Criteria: • Prior anti-tumor necrosis factor (TNF) therapy • Psoriasis or psoriatic arthritis • Fulfillment of modified New York criteria for ankylosing spondylitis • Recent infection requiring treatment • Significant medical events or conditions that may put patients at risk for participation • Females who are pregnant or breast-feeding or considering becoming pregnant during the study • History of cancer, except successfully treated skin cancer • Recent history of drug or alcohol abuse
Intervention	Participants(n=95) received adalimumab 40 mg subcutaneously every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.
Comparator(s)	Participants (n=97) received placebo every other week for 12 weeks during the double-blind period and then received adalimumab 40 mg subcutaneously every other week for up to 144 weeks during the open-label period.
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Trial name: ABILITY1	NCT number: NCT00939003

Primary, secondary and exploratory endpoints

Primary endpoints: Number of Participants Achieving an Assessment of Spondyloarthritis International Society (ASAS) 40 Response [Time Frame: Baseline and Week 12]

Secondary endpoints:

- Number of Participants Achieving an Assessment of Spondyloarthritis International Society (ASAS) 20 Response [Time Frame: Baseline and Week 12]
- Number of Participants Achieving a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 Response [Time Frame: Baseline and Week 12]
- Change From Baseline in Short Form-36 (SF-36) Physical Component Summary Score [Time Frame: Baseline and Week 12]
- Number of Participants Achieving ASAS Partial Remission [Time Frame: Week 12]
- Number of Participants Achieving an ASAS5/6 Response [Time Frame: Baseline and Week 12]
- Change From Baseline in Disability Index of Health Assessment Questionnaire Modified for the Spondyloarthropathies (HAQ-S) [Time Frame: Baseline and Week 12]
- Change From Baseline in High-Sensitivity C-Reactive Protein (hsCRP) [Time Frame: Baseline and Week 12]
- Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Score for Sacroiliac Joints [Time Frame: Baseline and Week 12]
- Change From Baseline in SPARCC MRI Score for the Spine [Time Frame: Baseline and Week 12]

Endpoints included in this application:

ASAS40, BASDAI50, SF-36PCS, discontinuation due to AEs

Trial name: ABILITY1	NCT number: NCT00939003
Method of analysis	Efficacy variables were analysed for all randomised patients who received at least one dose of blinded study medication but excluding seven patients from one site due to investigator noncompliance. The safety population consisted of all patients who received at least one dose of study medication. For categorical variables, patients with missing data at week 12 were considered to be non- responders using non-responder imputation (NRI). Last observation carried forward imputed values were used for continuous variables. Analysis of covariance (ANCOVA) adjusting for the baseline score was used to compare change from baseline at week 12 between adalimumab and placebo treatment groups. VAS data were collected on 0-100 mmscales and reported as 0-10 cmdata for consistency. To evaluate the impact of baseline demographics and disease conditions on the primary efficacy endpoint, ASAS40 response at week 12 was summarised by subgroups of sex (male, female), race (white, non-white), age (<40, 2:40 years), weight (<70, 2:70 kg), symptom duration (<5, 2:5 years), baseline C-reactive protein (CRP) (normal, elevated), concomitant baseline NSAID use (yes, no) or DMARD use (yes, no), history of inflammatory bowel disease (yes, no) or uveitis (yes, no), baseline HLA-827 status (positive, negative), past or current MRI evidence of inflammation of the SI joints according to the local radiologist/rheumatologist (positive, negative) and baseline SPARCC SI joint score (<2, 2:2). For subgroup analyses, a logistic model was used to assess treatment and subgroup interaction, with a significant interaction defined as pS0.10. AEs were summarised as the number and percentage of patients experiencing AEs using Medical Dictionary for Regulatory Activities (MedDRA, V.13.1) system organ classes and preferred terms
Subgroup analyses	NA
Other relevant information	NA

Table 111 PREVENT

Trial name: PREVENT	NCT number: NCT02696031
Objective	The purpose of this study was to demonstrate the clinical efficacy, safety and tolerability of secukinumab compared to placebo in patients with nr-axSpA at Week 16 as well as Week 52 and long term efficacy and safety up to Week 104 (core phase) followed by an optional extension phase consisting of a 16-week randomized dose escalation treatment period and a continuous treatment period for up to Week 208.

Trial name: PREVENT	NCT number: NCT02696031
Publications – title, author, journal, year	Effect of Secukinumab on Traditional Cardiovascular Risk Factors and Inflammatory Biomarkers: Post Hoc Analyses of Pooled Data Across Three Indications. Merola et al. Rheumatol Ther. 2022 Secukinumab in non-radiographic axial spondyloarthritis: subgroup analysis based on key baseline characteristics from a randomized phase III study, PREVENT. Braun et al. Arthritis Res Ther. 2021 Improvement of Signs and Symptoms of Nonradiographic Axial Spondyloarthritis in Patients Treated With Secukinumab: Primary Results of a Randomized, Placebo-Controlled Phase III Study. Deodhar et al. Arthritis Rheumatol. 2021
Study type and design	Randomized, Double-blind, Placebo-controlled, Phase III Study. Approximately 555 patients were randomized to one of three treatment groups (secukinumab 150 mg Load, secukinumab 150 mg No Load or placebo in a ratio of 1:1:1). The study was completed March 11, 2021.
Sample size (n)	555

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Trial name: PREVENT	NCT number: NCT02696031
Main inclusion and exclusion criteria*	Inclusion Criteria: • Male or non-pregnant, non-nursing female patients at least 18 years of age • Diagnosis of axial spondyloarthritis according to Ankylosing SpondyloArthritis International Society (ASAS) axial spondyloarthritis criteria • objective signs of inflammation (magnetic resonance imaging (MRI) or abnormal C-reactive protein) • active axial spondyloarthritis as assessed by total Bath Ankylosing Spondylitis Disease Activity Index >=4 cm • Spinal pain as measured by Bath Ankylosing Spondylitis Disease Activity Index question #2 ≥ 4 cm (0-10 cm) at baseline • Total back pain as measured by Visual Analogue scale ≥ 40 mm (0-100 mm) at baseline • Patients should have been on at least 2 different non-steroidal anti-inflammatory drugs with an inadequate response • Patients who have been on a Tumor Necrosis Factor (TNF) α inhibitor (not more than one) must have experienced an inadequate response Exclusion Criteria: • Patients with radiographic evidence for sacroiliitis, grade ≥ 2 bilaterally or grade ≥ 3 unilaterally • Inability or unwillingness to undergo MRI • Chest X-ray or MRI with evidence of ongoing infectious or malignant process • Patients taking high potency opioid analgesics • Previous exposure to secukinumab or any other biologic drug directly targeting interleukin-17 (IL-17) or IL-17 receptor • Pregnant or nursing (lactating) women
Intervention	AIN457 (other name for Secukinumab) 150 mg s.c. load, Core Phase. 185 participants. AIN457 150 mg s.c. no load, Core Phase. 184 participants.
Comparator(s)	Placebo s.c., Core Phase (186 participants) AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg in the Extension phase (from Week 104 to week 208). 147 participants in Extension Phase From wk 104 to wk 208 AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg in the Extension phase (from Week 104 to week 208). 147 participants in Extension Phase From wk 104 to wk 208 AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to the 300 mg Open Label in the Extension phase (from Week 104 to week 208). 78 participants in Extension Phase From wk 104 to wk 208

Trial name: PREVENT	NCT number: NCT02696031
Follow-up time	Not reported
Is the study used in the health economic model?	No

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Primary, secondary and exploratory endpoints	Primary endpoints: • The Number and Percentage of TNF Naive Participants Who Achieved an Assessment of Spondylo Arthritis International Society (ASAS) 40 Response at Week 16 [Time Frame: Week 16] • The Number and Percentage of TNF Naive Participants Who Achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 Response at Week 52 [Time Frame: Week 52] Secondary endpoints: • The Number and Percentage of Participants Who Achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 Response [Time Frame: Week 16 and week 52] • The Number and Percentage of Participants Who Achieved an Assessment of SpondyloArthritis International Society (ASAS) 20 Response [Time Frame: Week 16] • The Number and Percentage of Participants Who Achieved an Assessment of SpondyloArthritis International Society (ASAS) 5/6 Response [Time Frame: Week 16] • The Number and Percentage of Participants Who Achieved an Assessment of SpondyloArthritis International Society Partial Remission (ASAS PR) [Time Frame: Week 16] • Change in Bath Ankylosing Spondylitis Functional Index (BASFI) [Time Frame: Baseline and Week 16] • The Number and Percentage of Patients to Achieve a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 Response [Time Frame: Week 16 and 52] • Change in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [Time Frame: Baseline and Week 16] • Change in Ankylosing Spondylitis Quality of Life (ASQoL) Scores at Week 16 [Time Frame: Baseline and Week 16] • Change in Ankylosing Spondylitis Quality of Life (ASQoL) Scores at Week 52 [Time Frame: Baseline and Week 52] • The Number and Percentage of Patients Who Achieved an Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) Inactive Disease [Time Frame: Week 52] • Change in High Sensitivity C-reactive Protein [Time Frame: Baseline and Week 16] • Change in Short Form-36 Physical Component Summary (SF-36 PCS) [Time Frame: Baseline and Week 16] • Change in Sacroiliac Joint Edema - Week 16 [Time Frame: Baseline and Week 16] • Change in Sacroiliac Joint Edema - Week 52 [Time Frame: Baseline and Week 52] **Endpoints included in this application:**

Trial name: PREVENT	NCT number: NCT02696031
	ASAS40, BASDAI50, SF-36PCS, discontinuation due to AEs
Method of analysis	Efficacy analyses were performed on the full analysis set, which comprised all patients who were randomised and had study treatment assigned. Primary and secondary end points were analysed according to a predefined statistical hierarchy. End points are shown in the order of the testing strategy. The family-wise Type I error rate was set to 5% and was controlled with the applied sequential testing strategy. All end points are shown with unadjusted P values with statistical significance only claimed for end points within the predefined hierarchy which met significance based on adjusted P values corrected for multiplicity of testing. For all exploratory end points unadjusted P values are shown. The primary analysis in the TNFi-naive population was conducted via logistic regression with treatment group and stratification (CRP level or MRI} as factors and weight as a covariate. Missing values were imputed as nonresponders (by nonresponder imputation (NRI)) for binary variables and via a mixed-effects model repeated measures (MMRM; valid under the missing at random assumption) for continuous variables up to week 20. MMRM analysis included treatment group, CRP level or MRI stratification group, TNFi therapy status, and analysis visit as factors and baseline score of the respective end point and weight as continuous covariates. Treatment-by-analysis visit and baseline score-by-analysis visit were included as interaction terms in the model. An unstructured covariance structure was assumed for the model. The significance of treatment effect for the secukinumab regimens was determined from the pairwise comparisons performed between secukinumab regimens and placebo at week 16. For the change in hsCRP level, the log(e) ratio of the post-baseline value to the baseline value was used to normalise the distribution of the hsCRP level at each assessment time point. Safety analyses included all patients who received 1 dose of study medication. AEs are reported as exposure-adjusted incidence rates (EAIR} per 100 patient-years over the entire treatment period, which refers to the cumulative treatment period (i.e., events started after the first dose of study treatment or events present prior to the first dose of study treatment but increased in severity based on preferred term and on or before last dose plus 84 days). Patients switching to standard of care were counted in their previous treatment until the end of the washout phase.
Subgroup analyses	NA
Other relevant information	NA

Table 112 COAST-X

Trial name: COAST-X	NCT number: NCT02757352
Objective	The main purpose of this study is to evaluate the safety and efficacy of the study drug known as ixekizumab in biologic disease modifying antirheumatic drug (bDMARD) naïve participants with nonradiographic axial spondyloarthritis (nonrad-axSpA).

Trial name: COAST-X	NCT number: NCT02757352
Publications – title, author, journal, year	Baseline Characteristics and Treatment Response to Ixekizumab Categorised by Sex in Radiographic and Non-radiographic Axial Spondylarthritis Through 52 Weeks: Data from Three Phase III Randomised Controlled Trials. van der Horst-Bruinsma et al. Adv Ther. 2022 Ixekizumab improves sleep and work productivity in patients with non-radiographic axial spondyloarthritis: results from the COAST-X trial at 52 weeks. Deodhar et al. BMC Rheumatol. 2021. Ixekizumab Improves Patient-Reported Outcomes in Non-Radiographic Axial Spondyloarthritis: Results from the Coast-X Trial. Deodhar et al. Rheumatol Ther. 2021 Improvement of Functioning and Health With Ixekizumab in the Treatment of Active Nonradiographic Axial Spondyloarthritis in a 52-Week, Randomized, Controlled Trial. Arthritis Care Res (Hoboken). Walsh et al. 2022 Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial. Deodhar et al. Lancet. 2020
Study type and design	Randomized, Double-blind, Placebo-controlled, Multicenter Phase III Study. The study was completed May 7, 2019.
Sample size (n)	303

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Trial name: COAST-X	NCT number: NCT02757352

Main inclusion and exclusion criteria*

Inclusion Criteria:

- Are ambulatory.
- Diagnosis of nonradiographic axial spondyloarthritis (nr-axSpA) and fulfilling the 2009 Assessment of Spondyloarthritis International Society (ASAS) classification criteria.
- Have a history of back pain ≥3 months with age at onset <45 years.
- Have active nr-axSpA defined as BASDAI ≥4 and total back pain ≥4 on a numeric rating scale (NRS) at screening and baseline.
- Have objective signs of inflammation by presence of sacroiliitis on MRI and/or presence of elevated C-reactive protein (CRP).
- In the past had an inadequate response to at least 2 non-steroidal anti-inflammatory drugs (NSAIDS) for duration of 4 weeks or cannot tolerate NSAIDS.
- If taking NSAIDS be on stable dose for at least 2 weeks prior to randomization.
- Have a history of prior therapy for axSpA for at least 12 weeks prior to screening.

Exclusion Criteria:

- Have radiographic sacroiliitis fulfilling the 1984 modified New York criteria.
- Have received any prior, or are currently receiving treatment with biologics, tumor necrosis factor inhibitors or other immunomodulatory agents.
- Have received a live vaccine within 12 weeks or have had a vaccination with Bacillus Calmette-Guerin (BCG) within the past year.
- Have an ongoing or serious infection within the last 12 weeks or evidence of active tuberculosis.
- Have a compromised immune system.
- Have any other serious and/or uncontrolled diseases.
- Have either a current diagnosis or a recent history of malignant disease.
- Have had major surgery within 8 weeks of baseline, or will require surgery during the study.
- Are pregnant or breastfeeding.
- Have evidence of active anterior uveitis (an acute episode) within the last 42 days prior to baseline randomization.

Trial name: COAST-X	NCT number: NCT02757352
Intervention	Ixekizumab 80 mg Q4W (IxeQ4W) Double-Blind Period: Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52. 96 participants. Ixekizumab 80 mg Q2W (IxeQ2W) Double-Blind Period: Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC (Q2W) to week 52. 102 participants. Ixekizumab 80 mg Q4W IR (Ixe80Q4WIR)/Ixe80Q2W-Open Label: Participants who received ixekizumab 80 mg Q4W in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label. 40 participants. Ixekizumab 80 mg Q2W IR (Ixe80Q2WIR)/Ixe80Q2W-Open Label: Participants who received ixekizumab 80 mg Q2W in double blind period and were inadequate responders as determined by investigators continued on the same regimen of ixekizumab 80 mg Q2W open label. 42 participants. Ixekizumab 80 mg Q4W Post Treatment Follow-Up Period: Participants discontinued the study early and entered the post-treatment follow-up period. Participants received ixekizumab 80 mg Q4W immediately prior to entering the post-treatment follow-up period. 5 participants. Ixekizumab 80 mg Q2W Post Treatment Follow-Up Period: Participants discontinued the study early and entered the post-treatment follow-up period. Participants received ixekizumab 80 mg Q2W immediately prior to entering the post-treatment follow-up period. 28 participants.
Comparator(s)	Placebo Double-Blind Period: Participants received placebo (PBO) as 2 subcutaneous (SC) injections every two weeks (Q2W) to week 52. 105 participants. PBO IR/Ixe80Q2W-Open Label: Participants who received placebo in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label. 62 participants. Placebo Post Treatment Follow-Up Period: Participants discontinued the study early and entered the post-treatment follow-up period. Participants received placebo immediately prior to entering the post-treatment follow-up period. 3 participants Other Biologic Treatment Group: Participants who discontinued study treatment and were on other biologic therapy prior to entering follow-up period. 5 participants.
Follow-up time	Not reported
Is the study used in the health economic model?	No

Primary, secondary and exploratory endpoints	Primary endpoints: • Percentage of Participants Achieving an Assessment of Spondyloarthritis International Society 40 (ASAS40) Response [Time Frame: Week 16] • Percentage of Participants Achieving an ASAS40 Response [Time Frame: Week 52] Secondary endpoints: • Change From Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) [Time Frame: Baseline, Week 16] • Change From Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) [Time Frame: Baseline, Week 52] • Number of Participants Without Clinically Meaningful Changes in Background Therapy [Time Frame: Baseline through Week 52] • Change From Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score [Time Frame: Baseline, Week 16] • Change From Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score [Time Frame: Baseline, Week 52] • Percentage of Participants Achieving ASDAS Low Disease Activity [Time Frame: Week 16] • Percentage of Participants Achieving ASDAS Low Disease Activity [Time Frame: Week 52] • Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [Time Frame: Baseline, Week 16] • Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [Time Frame: Baseline, Week 52] • Change From Baseline in Magnetic Resonance Imaging (MRI) of the Sacroiliac Joint (SIJ) Spondyloarthritis Research Consortium of Canada (SPARCC) Score [Time Frame: Baseline, Week 16] • Change From Baseline in SPARCC Enthesitis Score [Time Frame: Baseline, Week 52] • Change From Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) [Time Frame: Baseline, Week 52] • Percentage of Participants Achieving ASDAS Inactive Disease [Time Frame: Week 52] • Change From Baseline in the Measure of High Sensitivity C-Reactive Protein (CRP) [Time Frame: Baseline, Week 52] • Change From Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) [Time Frame: Baseline, Week 52] • Change From Baseline in Chest Expansion [Time Frame: Baseline, Week 52] • Change From Baseline in Occiput to Wall Distance [Time Frame: Baseline, Week 52]

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Trial name: COAST-X	NCT number: NCT02757352

- Change From Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) [Time Frame: Baseline, Week 52]
- Change From Baseline in Severity of Peripheral Arthritis by Tender (TJC) and Swollen Joint Count (SJC) Scores of 44 Joints [Time Frame: Baseline, Week 52]
- Number of Participants With Anterior Uveitis [Time Frame: Baseline through Week 52]
- Change From Baseline in the Fatigue Numeric Rating Scale (NRS) Score [Time Frame: Baseline, Week 52]
- Change From Baseline in ASAS Health Index (ASAS HI) [Time Frame: Baseline, Week 52]
- Change From Baseline in the Jenkins Sleep Evaluation Questionnaire (JSEQ) [Time Frame: Baseline, Week 52]
- Change From Baseline in the Work Productivity Activity Impairment Spondyloarthritis (WPAI-SpA) Scores [Time Frame: Baseline, Week 52]
- Change From Baseline in ASAS-Nonsteroidal Anti-Inflammatory Drug (NSAID) Score [Time Frame: Baseline, Week 52]
- Number of Participants With Treatment Emergent (TE) Anti-Ixekizumab Antibodies [Time Frame: Week 52]
- Pharmacokinetics (PK): Trough Concentration at Steady State (Ctrough ss) [Time Frame: Week 52]

Endpoints included in this application:

ASAS40, ASDAS<2.1, BASDAI50, SF-36PCS, discontinuation due to AEs

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Trial name: COAST-X	NCT number: NCT02757352
Method of analysis	Efficacy analyses for the blinded treatment dosing period were done on the intention-to-treat population, defined as all patients randomly assigned to treatment. Analyses of the ixekizumab Q4W and ixekizumab Q2W treatment groups were done regardless of the starting dose. The composite strategy, which was applied to categorical efficacy and health outcome variables, indicated that any intercurrent events-e.g., discontinuing treatment or switching to open-label treatment-were to be assigned unfavourable values (i.e., non-responder). Thus, patients were considered non-responders at timepoints when they did not meet the clinical response criteria or when they had missing clinical response data. Patients who discontinued the masked study treatment to which they were originally assigned and switched to open-label ixekizumab Q2W were considered non-responders after switching. We repeated our analysis of ASAS40 in the per-protocol population, defined as all patients who were compliant with therapy and did not have significant protocol deviations. For patients who switched to open-label ixekizumab Q2W, the requirements for per-protocol population only applied during the treatment period before they took open-label ixekizumab. The primary analysis method for categorical outcome variables was logistic regression with treatment, geographical region, and MRI and CRP status at screening included in the model. Because the mixed-effects model of repeated measures (MMRM) is a robust method even when the data are not missing at random, the primary analysis method for most continuous outcomes was the MMRM with treatment, geographical region, MRI and CRP status at screening, baseline value, visit, baseline value or visit interaction, and treatment or visit interaction as fixed factors. The MMRM model for CRP included treatment, geographical region, MRI and CRP status at screening, visit, and treatment or visit interaction as fixed factors. The primary analysis method for MRI sacroiliac joints SPARCC scores was ANCOVA with observed case analysis. The ANCOVA included treatment, geographical region, MRI and CRP status at screening, and baseline MRI score. The assumptions for the MMRM model and ANCOVA were assessed via residual plots and no serious violations were found. We used a graphical multiple testing strategy for primary and major secondary endpoints to control the overall familywise type I error rate at a two-sided a level of 0·05. Two testing schemes were executed independently, with one focused on the 16-week data (12 group comparisons) and the other on the 52-week data (14 group comparisons; appendix pp 33-34). We ordered the comparisons by relative importance to the disease and the magnitude of the estimated effect size. We optimised the a allocations in a simulation study. We started with testing the first outcomes at the top of the hierarchy. If the null hypothesis of an outcome was not rejected, then the a allocated to this endpoint was considered spent and could not be passed to other outcomes below. Thus, testing would end at that outcome for that group. If the null hypothesis was rejected, then the testing continued for the remaining outcomes.
Subgroup analyses	NA
Other relevant information	NA

Appendix C Baseline characteristics of patients in studies used for the comparative analysis of efficacy and safety

Table 113 Baseline characteristics for studies used in the comparative analysis with adalimumab (AS TNF naïve population)

Study	Tx Arm	N, ITT	Age, mean (SD)	Male %	HLA-B27 positive %	CRP mg/L mean (SD)	BASDAI, mean (SD)	ASDAS-CRP, mean (SD)	Total Spine pain, mean (SD)	Prior bDMARDs %
BE MOBILE 2 [48]	BKZ-160 Q4W	221	41 (12.1)	72.4%	86.4%	8.2†	6.5 (1.3)	3.7 (0.8)	7.1 (1.6)	16.7%
BE MOBILE 2 [48]	PBO	111	39.2 (12.6)	72.1%	83.8%	6.3†	6.5 (1.3)	3.7 (0.8)	7.2 (1.2)	15.3%
ATLAS [35]	ADA-40 Q2W	208	41.7 (11.69)	75.5%	78.4%	18 (22)	6.3 (1.7)	NR	64.4 (20.9)	0%
ATLAS [35]	PBO	107	43.4 (11.32)	73.8%	79.4%	22 (29)	6.3 (1.7)	NR	67.2 (21.5)	0%
COAST-V [55]	PBO	87	42.7 (12)	83%	89%	16 (21)	6.8 (1.2)	3.9 (0.7)	NR	0%
COAST-V [55]	ADA-40 Q2W	90	41.8 (11.4)	81%	91%	12.5 (17.6)	6.7 (1.5)	3.7 (0.8)	NR	0%
COAST-V [55]	IXE-80 Q4W	81	41 (12.1)	84%	93%	12.2 (13.3)	6.8 (1.3)	3.7 (0.7)	NR	0%
Huang 2014 [36]	PBO	115	29.6 (7.5)	82.6%	94.8%	23 (30)	6.2 (1.4)	3.7 (1)	6.7 (1.6)	NR
Huang 2014 [36]	ADA-40 Q2W	229	30.1 (8.7)	80.8%	95.6%	22.4 (24)	6 (1.4)	3.7 (0.9)	6.8 (1.5)	NR

Abbreviations: ADA, adalimumab; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; BKZ, bimekizumab; CRP, C-reactive protein; ITT, intention-to-treat; IXE, ixekizumab; PBO, placebo; Q2W, once every two weeks; Q4W, once every four weeks; AS, ankylosing spondylitis; SD, standard deviation; Tx, treatment.
†Median

Table 114 Baseline characteristics for studies used in the comparative analysis with secukinumab (AS TNF experienced population)

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Study	Tx Arm	N, ITT	Age, mean (SD)	Male %	HLA-B27 positive %	CRP mg/L mean (SD)	BASDAI, mean (SD)	ASDAS-CRP, mean (SD)	Total Spine pain, mean (SD)	Prior bDMARDs %
BE MOBILE 2 [48]	BKZ-160 Q4W	221	41 (12.1)	72.4%	86.4%	8.2†	6.5 (1.3)	3.7 (0.8)	7.1 (1.6)	16.7%
BE MOBILE 2 [48]	PBO	111	39.2 (12.6)	72.1%	83.8%	6.3†	6.5 (1.3)	3.7 (0.8)	7.2 (1.2)	15.3%
ASTRUM [52]	SEC-150 Q4W	71	NR	NR	NR	NR	6.0 (1.4)	3.4 (0.7)	NR	NR
ASTRUM [52]	PBO	70	NR	NR	NR	NR	6.2 (1.3)	3.4 (0.7)	NR	NR
MEASURE 2 [58]	SEC-150 Q4W	72	41.9 (12.5)	64%	79%	25.8 (50.088)	6.59 (1.5)	3.73 (0.89)	66.2 (16.7)	38.9%
MEASURE 2 [58]	PBO	74	43.6 (13.2)	76%	78%	15.71 (18.498)	6.78 (1.3)	3.82 (0.76)	69.2 (18.8)	39.2%
MEASURE 4 [59]	SEC-150 Q4W	116	44.5 (11.62)	69.8%	86.2%	6.25†	7 (1.23)	NR	74.9 (13.07)	26.7%
MEASURE 4 [59]	SEC-150 Q4W	117	41.2 (11.07)	70.9%	84.6%	6.2†	7.0 (1.31)	NR	74.2 (14.18)	27.3%
MEASURE 4 [59]	PBO	117	43.4 (12.46)	65%	79.5%	5.4†	7.1 (1.27)	NR	75 (13.8)	29%
MEASURE 5 [60]	SEC-150 Q4W	305	35.1 (10.38)	82.6%	90.5%	7.5†	6.91 (1.38)	NR	71.6 (14.51)	NR
MEASURE 5 [60]	PBO	153	33 (10.02)	86.3%	92.8%	7.8†	6.87 (1.25)	NR	70.5 (13.44)	NR

Abbreviations: ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; BKZ, bimekizumab; CRP, C-reactive protein; ITT, intention-to-treat; PBO, placebo; Q4W, once every four weeks; SD, standard deviation; SEC, secukinumab; Tx, treatment.
†Median

Table 115 Baseline characteristics for studies used in the comparative analysis with Ixekizumab (AS TNF experienced population)

Study	Tx Arm	N, ITT	Age, mean (SD)	Male %	HLA-B27 positive %	CRP mg/L mean (SD)	BASDAI, mean (SD)	ASDAS-CRP, mean (SD)	Total Spine pain, mean (SD)	Prior bDMARDs %
BE MOBILE 2 [48]	BKZ-160 Q4W	221	41 (12.1)	72.4%	86.4%	8.2†	6.5 (1.3)	3.7 (0.8)	7.1 (1.6)	16.7%
BE MOBILE 2 [48]	PBO	111	39.2 (12.6)	72.1%	83.8%	6.3†	6.5 (1.3)	3.7 (0.8)	7.2 (1.2)	15.3%
COAST-W [56]	PBO	104	46.6 (12.7)	83.7%	NR%	NR	7.3 (1.3)	4.1 (0.8)	NR	100%
COAST-W [56]	IXE-80 Q4W	114	47.4 (13.4)	79.8%	NR%	NR	7.5 (1.3)	4.2 (0.9)	NR	100%
COAST-V [55]	PBO	87	42.7 (12)	83%	89%	16 (21)	6.8 (1.2)	3.9 (0.7)	NR	0%
COAST-V [55]	ADA-40 Q2W	90	41.8 (11.4)	81%	91%	12.5 (17.6)	6.7 (1.5)	3.7 (0.8)	NR	0%
COAST-V [55]	IXE-80 Q4W	81	41 (12.1)	84%	93%	12.2 (13.3)	6.8 (1.3)	3.7 (0.7)	NR	0%

Abbreviations: ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; BKZ, bimekizumab; CRP, C-reactive protein; ITT, intention-to-treat; IXE, ixekizumab; PBO, placebo; Q4W, once every four weeks; SD, standard deviation; Tx, treatment.
†Median

Table 116 Baseline characteristics for studies used in the comparative analysis with adalimumab (nr-AxSpA TNF naïve)

Study	Tx Arm	N, ITT	Age, mean (SD)	Male %	HLA-B27 positive %	CRP mg/L mean (SD)	BASDAI, mean (SD)	ASDAS-CRP, mean (SD)	Total Spine pain, mean (SD)	Prior bDMARDs %
BE MOBILE 1 [47]	BKZ-160 Q4W	128	39.5 (11.1)	57%	80.5%	6.1†	6.9 (1.2)	3.7 (0.8)	7.3 (1.5)	7.8%
BE MOBILE 1 [47]	PBO	126	39.4 (11.8)	51.6%	74.6%	6.5†	6.7 (1.3)	3.7 (0.8)	7.1 (1.6)	13.5%

ABILITY-1 [62]	ADA-40 Q2W	95	37.6 (11.3)	46.3%	82%	6.8 (11.8)	6.4 (1.5)	3.2 (0.8)	6.9 (1.8)	0%
ABILITY-1 [62]	PBO	97	38.4 (10.4)	41.2%	74%	7.6 (10.2)	6.5 (1.6)	3.4 (0.8)	7 (1.7)	0%

Abbreviations: ADA, adalimumab; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; CRP, C-reactive protein; ITT, intention-to-treat; nr-axSpA, non-radiographic axial spondyloarthritis; PBO, placebo; Q2W, once every two weeks; Q4W, once every four weeks; SD, standard deviation; Tx, treatment.
†Median.

Table 117 Baseline characteristics for studies used in the comparative analysis with secukinumab (nr-AxSpA TNF experienced)

Study	Tx Arm	N, ITT	Age, mean (SD)	Male %	HLA-B27 positive %	CRP mg/L mean (SD)	BASDAI, mean (SD)	ASDAS-CRP, mean (SD)	Total Spine pain, mean (SD)	Prior bDMARDs %
BE MOBILE 1 [47]	BKZ-160 Q4W	128	39.5 (11.1)	57%	80.5%	6.1†	6.9 (1.2)	3.7 (0.8)	7.3 (1.5)	7.8%
BE MOBILE 1 [47]	PBO	126	39.4 (11.8)	51.6%	74.6%	6.5†	6.7 (1.3)	3.7 (0.8)	7.1 (1.6)	13.5%
PREVENT [61]	SEC-150 Q4W	185	39.1 (11.5)	43.2%	73.5%	13.17 (27.21)	7.08 (1.33)	3.7 (0.87)	7.33 (1.30)	11.4%
PREVENT [61]	SEC-150 Q4W	184	39.8 (11.68)	45.7%	63.6%	9.67 (15.82)	6.93 (1.45)	3.59 (0.78)	7.2 (1.45)	9.8%
PREVENT [61]	PBO	186	39.3 (11.5)	48.9%	69.4%	10.76 (21.34)	6.76 (1.24)	3.49 (0.81)	7.1 (1.25)	8.1%

Abbreviations: ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; CRP, C-reactive protein; ITT, intention-to-treat; nr-axSpA, non-radiographic axial spondyloarthritis; PBO, placebo; Q4W, once every four weeks; SD, standard deviation; SEC, secukinumab; Tx, treatment.
†Median.

Table 118 Baseline characteristics for studies used in the comparative analysis with ixekizumab (nr-AxSpA TNF experienced)

Study	Tx Arm	N, ITT	Age, mean (SD)	Male %	HLA-B27 positive %	CRP mg/L mean (SD)	BASDAI, mean (SD)	ASDAS-CRP, mean (SD)	Total Spine pain, mean (SD)	Prior bDMARDs %

BE MOBILE 1 [47]	BKZ-160 Q4W	128	39.5 (11.1)	57%	80.5%	6.1†	6.9 (1.2)	3.7 (0.8)	7.3 (1.5)	7.8%
BE MOBILE 1 [47]	PBO	126	39.4 (11.8)	51.6%	74.6%	6.5†	6.7 (1.3)	3.7 (0.8)	7.1 (1.6)	13.5%
COAST-X [57]	IXE-80 Q4W	96	40.9 (14.5)	52%	75%	12.4 (18)	7 (1.5)	3.8 (0.8)	NR	0%
COAST-X [57]	PBO	105	39.9 (12.4)	42%	74%	14.3 (24.4)	7.2 (1.5)	3.8 (0.9)	NR	0%

Abbreviations: ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; CRP, C-reactive protein; ITT, intention-to-treat; IXE, ixekizumab; nr-axSpA, non-radiographic axial spondyloarthritis; PBO, placebo; Q4W, once every four weeks; SD, standard deviation; Tx, treatment.
†Median.

Comparability of patients across studies

As described in the main text the main difference between the studies are the proportions of bDMARD treatment experienced.

Comparability of the study populations with Danish patients eligible for treatment

Given the comparable efficacy and safety profile of bimekizumab to the current recommended treatments UCB aims for a direct placement of BKZ into the latest treatment guidance and have submitted evidence for both treatment naïve and treatment experienced patients as per latest DMC treatment guidance.

Appendix D Efficacy and safety results per study

Definition, validity and clinical relevance of included outcome measures

The outcome measures included in the analyses and presented in the following sections are based on the DMC treatment guideline for AS and nr-axSpA. Hence, it is assumed to be the most clinically relevant outcomes.

Results per study

Table A3a Results of BE MOBILE 1 (NCT03928704) week 16

				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40 (ITT)	BKZ	128	47.7% (61/128)	26.2%	15.0; 37.5	NR	RR: 2.22	1.52; 3.25	NR	A logistic regression model was used to assess the treatment effect on ASAS40 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	126	21.4% (27/126)								
ASAS40 (naïve)	BKZ	118	46.6% (55/118)	23.7%	11.7; 35.6	NR	RR: 2.03	1.37; 3.02	NR	Data based on the subgroup of patients naïve to biologic. A logistic regression model was used to assess the treatment effect on ASAS40 response at Week 16. The model included	
	PBO	109	22.9% (25/109)								

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Table A3a Results of BE MOBILE 1 (NCT03928704) week 16

										fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
ASDAS<2.1 (ITT)	BKZ	128	46.1% (59/128)	25.5%	14.3; 36.6	NR	RR: 2.23	1.51; 3.30	NR	A logistic regression model was used to assess the treatment effect on ASDAS<2.1 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	126	20.6% (26/126)								
ASDAS<2.1 (naïve)	BKZ	118	44.9% (53/118)	25.6%	14.0; 37.3	NR	RR: 2.33	1.51; 3.60	NR	A logistic regression model was used to assess the treatment effect on ASDAS<2.1 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	109	19.3% (21/109)								
BASDAI50 (ITT)	BKZ	128	46.9% (60/128)	25.4%	14.2; 36.7	NR	RR: 2.19	1.49; 3.20	NR	A logistic regression model was used to assess the treatment effect on BASDAI response at Week 16. The model included fixed effects for treatment and stratification endpoints of	
	PBO	126	21.4% (27/126)								

Table A3a Results of BE MOBILE 1 (NCT03928704) week 16

										MRI/CRP classification and region	
BASDAI50 (naïve)	BKZ	118	47.5% (56/118)	24.3%	12.3; 36.3	NR	RR: 2.05	1.38; 3.04	NR	Data based on the subgroup of patients naïve to biologic. A logistic regression model was used to assess the treatment effect on ASAS40 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	109	23.1% (25/108)								
SF36-PCS (ITT)	BKZ	128	Mean change: 9.55 (SD: 8.37)	4.07	2.09; 6.06	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region as fixed effects and the baseline value as covariate	
	PBO	126	Mean change: 5.48 (SD: 7.75)								
SF36-PCS (naïve)	BKZ	118	Mean change: 9.4 (SD: 7.89)	3.66	1.63; 5.70	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment,	
	PBO	109	Mean change: 5.7 (SD: 7.74)								

Table A3a Results of BE MOBILE 1 (NCT03928704) week 16

										MRI/CRP classification, region as fixed effects and the baseline value as covariate	
Discontinuation due to AEs (ITT)	BKZ	128	1.6% (2/128)	-2.4%	-6.4; 1.6	NR	RR: 0.39	0.08; 1.99	NR	Safety for the placebo-controlled, double-blind treatment period (weeks 0–16) was summarised by treatment group for patients who had ≥1 dose of bimekizumab or placebo, respectively (safety set)	
	PBO	126	4.0 (5/126)								

Table A3b Results of BE MOBILE 2 (NCT03928743) week 16

				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40 (ITT)	BKZ	221	44.8% (99/221)	22.3%	12.1; 32.4	NR	RR: 1.99	1.37; 2.89	NR	A logistic regression model was used to assess the treatment effect on ASAS40 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	111	22.5% (25/111)								

Table A3b Results of BE MOBILE 2 (NCT03928743) week 16											
ASAS40 (naïve)	BKZ	184	45.7% (84/184)	22.2%	11.1; 33.4	NR	RR: 1.95	1.31; 2.90	NR	A logistic regression model was used to assess the treatment effect on ASAS40 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	94	23.4% (22/94)								
ASAS40 (experienced)	BKZ	37	40.5% (15/37)	22.9	-1.2; 46.9	NR	RR: 2.30	0.77; 6.89	NR	A logistic regression model was used to assess the treatment effect on ASAS40 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	17	17.6% (3/17)								
ASDAS<2.1 (ITT)	BKZ	221	42.1% (93/221)	25.0%	15.4; 34.5	NR	RR: 2.46	1.59; 3.81	NR	A logistic regression model was used to assess the treatment effect on ASDAS<2.1 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	111	17.1% (19/111)								
ASDAS<2.1 (naïve)	BKZ	184	46.7% (86/184)	27.6%	16.9; 38.3	NR	RR: 2.44	1.57; 3.80	NR	A logistic regression model was used to assess the treatment	

Table A3b Results of BE MOBILE 2 (NCT03928743) week 16											
	PBO	94	19.1% (18/94)							effect on ASDAS<2.1 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
ASDAS<2.1 (experienced)	BKZ	37	18.9% (7/37)	13.0%	-3.8; 29.9	NR	RR: 3.22	0.43; 24.13	NR	A logistic regression model was used to assess the treatment effect on ASDAS<2.1 response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	17	5.9% (1/17)								
BASDAI50 (ITT)	BKZ	221	46.6% (103/221)	20.5%	10.0; 31.0	NR	RR: 1.78	1.27; 2.51	NR	A logistic regression model was used to assess the treatment effect on BASDAI response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	111	26.1% (29/111)								
BASDAI50 (naïve)	BKZ	184	48.9% (90/184)	24.4%	13.1; 35.7	NR	RR: 2.00	1.36; 2.94	NR	A logistic regression model was used to assess the treatment effect on BASDAI response at Week 16. The model included fixed effects for treatment and	
	PBO	94	24.5% (23/94)								

Table A3b Results of BE MOBILE 2 (NCT03928743) week 16

										stratification endpoints of MRI/CRP classification and region	
BASDAI50 (experienced)	BKZ	37	35.1% (13/37)	-0.2%	-27.6; 27.3	NR	RR: 1.00	0.46; 2.17	NR	A logistic regression model was used to assess the treatment effect on BASDAI response at Week 16. The model included fixed effects for treatment and stratification endpoints of MRI/CRP classification and region	
	PBO	17	35.3 (6/17)								
SF36-PCS (ITT)	BKZ	221	Mean change: 9.3 (SD: 8.7)	3.40	1.48; 5.32	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region as fixed effects and the baseline value as covariate	
	PBO	111	Mean change: 5.9 (SD: 7.9)								
SF36-PCS (naïve)	BKZ	184	Mean change: 9.7 (SD: 8.8)	3.7	1.62; 5.78	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region	
	PBO	94	Mean change: 6.0 (SD: 7.4)								

Table A3b Results of BE MOBILE 2 (NCT03928743) week 16

										as fixed effects and the baseline value as covariate
SF36-PCS (experienced)	BKZ	37	Mean change: 7.5 (SD: 8.1)	2.50	-2.51; 7.51	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region as fixed effects and the baseline value as covariate
	PBO	17	Mean change: 5.0 (SD: 10.0)							
SF36-MCS (ITT)	BKZ	221	Mean change: 2.5 (SD: 8.2)	0.7	-1.04; 2.44	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region as fixed effects and the baseline value as covariate
	PBO	111	Mean change: 1.8 (SD: 6.3)							
SF36-MCS (naïve)	BKZ	184	Mean change: 2.1 (SD: 8.3)	0.7	-1.20; 2.60	NR	NA	NA	NA	Reference-based multiple imputation analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region
	PBO	94	Mean change: 1.4 (SD: 6.2)							

Table A3b Results of BE MOBILE 2 (NCT03928743) week 16											
										as fixed effects and the baseline value as covariate	
Discontinuation due to AEs (ITT)	BKZ	221	1.4% (3/221)	1.4%	-0.2; 2.9	NR	RR: 3.53*	0.18; 67.78*	NR	Safety for the placebo-controlled, double-blind treatment period (weeks 0–16) was summarised by treatment group for patients who had ≥1 dose of bimekizumab or placebo, respectively (safety set). * Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied	
	PBO	111	0.0% (0/111)								

Table A3c Results of ATLAS (NCT00085644) week 12 ITT											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40	ADA	208	39.9% (83/208)	26.8%	17.6; 36.0	NR	RR: 3.05	1.82; 5.11	NR	Response rates between groups were compared using Pearson's chi-square test.	[35]
	PBO	107	13.1% (14/107)								[35]

Table A3c Results of ATLAS (NCT00085644) week 12 ITT											
BASDAI50	ADA	208	45.2% (94/208)	29.3%	19.6; 39.0	NR	RR: 2.84	1.79; 4.51	NR	Response rates between groups were compared using Pearson's chi-square test.	35
	PBO	107	15.9% (17/107)								35
SF36-PCS	ADA	208	Mean change: 6.9 (SD: 8.7)	5.30	3.30; 7.30	NR	NA	NA	NA	Last observation carried forward analysis was used for continuous end points.	35
	PBO	107	Mean change: 1.6 (SD: 8.3)								35
SF36-MCS	ADA	208	Mean change: 2.7 (SD: 10)	0.30	-2.03; 2.63	NR	NA	NA	NA	Last observation carried forward analysis was used for continuous end points.	35
	PBO	107	Mean change: 2.4 (SD: 10)								35
Discontinuation due to AEs	ADA	208	1.0% (2/208)	-0.9%	-3.8; 2.0	NR	RR: 0.51	0.07; 3.60	NA	Fischer's exact test was used for comparisons between treatment groups	35
	PBO	107	1.9% (2/107)								35

Abbreviations: ADA, adalimumab; AE, adverse event; ASAS40, ASAS at least 40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NA, not applicable; PBO, placebo; RR, relative risk; SD, standard deviation

ASDAS<2.1 was not reported in ATLAS

Table A3d Results of Huang 2013 (NCT01114880) week 12 ITT

				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40	ADA	229	44.5% (102/229)	35.0%	26.6; 43.4	NR	RR: 4.66	2.61; 8.32	NR		[36]
	PBO	115	9.6% (11/115)								[36]
BASDAI50	ADA	229	49.8% (114/229)	33.3%	23.9; 42.6	NR	RR: 3.01	1.96; 4.64	NR		[36]
	PBO	115	16.5% (19/115)								[36]
SF36-PCS	ADA	229	Mean change: 6.6 (SD: 6.4)	2.60	1.17;4.03	NR	NA	NA	NA		[36]
	PBO	115	Mean change: 4.0 (SD: 6.3)								[36]
SF36-MCS	ADA	229	Mean change: 5.1 (SD: 9.9)	2.30	0.12; 4.48	NR	NA	NA	NA		[36]
	PBO	115	Mean change: 2.8 (SD: 9.4)								[36]
	ADA	229	1.7% (4/229)	1.7%	0.0; 3.4	NR	RR: 4.54*	0.25; 83.60*	NR		[36]

Table A3d Results of Huang 2013 (NCT01114880) week 12 ITT					
Discontinuation due to AEs	PBO	115	0.0% (0/115)	* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied	[36]

Abbreviations: ADA, adalimumab; AE, adverse event; ASAS40, ASAS at least 40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NA, not applicable; PBO, placebo; RR, relative risk; SD, standard deviation.

ASDAS<2.1 was not reported in Huang 2013.

Table A3e Results of COAST-V (NCT02696785) week 16 ITT											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40	ADA	90	35.6% (32/90)	17.2%	4.4; 30.0	NR	RR: 1.93	1.15; 3.26	NR	Adalimumab represents an active reference arm for comparison to placebo. The study was not designed to test equivalence or non-inferiority of active treatment arms to each other. Analyzed using logistic regression with treatment, geographic region, and baseline CRP status (≤ or > 5 mg/L) in the model with	[55]
	PBO	87	18.4% (16/87)								[55]

Table A3e Results of COAST-V (NCT02696785) week 16 ITT											
										nonresponder imputation for missing data.	
ASDAS<2.1	ADA	90	37.8% (34/90)	25.1%	12.9; 37.3	NR	RR: 2.99	1.62; 5.51	NR	Adalimumab represents an active reference arm for comparison to placebo. The study was not designed to test equivalence or non-inferiority of active treatment arms to each other. Analyzed using logistic regression with treatment, geographic region, and baseline CRP status (≤ or > 5 mg/L) in the model with nonresponder imputation for missing data.	55
	PBO	87	12.6% (11/87)								55
BASDAI50	ADA	90	32.2% (29/90)	15.0%	2.5; 27.5	NR	RR: 1.87	1.08; 3.24	NR	Adalimumab represents an active reference arm for comparison to placebo. The study was not designed to test equivalence or non-inferiority of active treatment arms to each other. Analyzed using logistic regression with treatment, geographic region, and baseline CRP status (≤ or > 5 mg/L) in the model with nonresponder imputation for missing data.	55
	PBO	87	17.2% (15/87)								55

Table A3e Results of COAST-V (NCT02696785) week 16 ITT											
SF36-PCS	ADA	90	Mean change: 6.9 (SD: 6.9)	3.30	1.25; 5.35	NR	NA	NA	NR	Continuous efficacy and health outcome variables were analyzed using a mixed-effects model of repeated measures, which included treatment, geographic region, baseline CRP status (≤ or > 5 mg/L), baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction in the model.	55
	PBO	87	Mean change: 3.6 (SD: 7.0)								55
Discontinuation due to AEs	ADA	90	1.1% (1/90)	1.1%	-1.1; 3.3	NR	RR: 2.90*	0.12; 70.27*	NR	* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied	55
	PBO	87	0.0% (0/87)								55

Abbreviations: ADA, adalimumab; AE, adverse event; ASAS40, ASAS at least 40% improvement; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NA, not applicable; PBO, placebo; RR, relative risk; SD, standard deviation.

SF-36-MCS was not reported in COAST-V.

Table A3f Results of ABILITY1 (NCT00939003) week 12 ITT											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		

Table A3f Results of ABILITY1 (NCT00939003) week 12 ITT											
ASAS40	ADA	91	36.3% (33/91)	21.4%	9.1; 33.6	NR	RR: 2.43	1.40; 4.24	NR	For categorical variables, patients with missing data at week 12 were considered to be non- responders using non-responder imputation (NRI). Analysis of covariance (ANCOVA) adjusting for the baseline score was used to compare change from baseline at week 12 between adalimumab and placebo treatment groups	62
	PBO	94	14.9% (14/94)								62
BASDAI50	ADA	91	35.2% (32/91)	20.3%	8.1; 32.4	NR	RR: 2.36	1.35; 4.13	NR	For categorical variables, patients with missing data at week 12 were considered to be non- responders using non-responder imputation (NRI). Analysis of covariance (ANCOVA) adjusting for the baseline score was used to compare change from baseline at week 12 between adalimumab and placebo treatment groups	62
	PBO	94	14.9% (14/94)								62
SF36-PCS	ADA	91	Mean change: 5.5 (SD: 8.98)	3.50	1.17; 5.83	NR	NA	NA	NR	Last observation carried forward imputed values	62

Table A3f Results of ABILITY1 (NCT00939003) week 12 ITT

	PBO	94	Mean change: 2.0 (SD: 7.04)							were used for continuous variables. Analysis of covariance (ANCOVA) adjusting for the baseline score was used to compare change from baseline at week 12 between adalimumab and placebo treatment groups	62
Discontinuation due to AEs	ADA	91	1.1% (1/91)	0.0%	-2.9; 3.0	NR	RR: 1.03	0.07; 16.27	NR		62
	PBO	94	1.1% (1/94)								62

Abbreviations: ADA, adalimumab; AE, adverse event; ASAS40, ASAS at least 40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NA, not applicable; PBO, placebo; RR, relative risk; SD, standard deviation.

ASDAS<2.1 and SF-36-MCS was not reported in ABILITY1.

Table A3g Results of PREVENT (NCT02696031) week 16 ITT

				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40	SEC	184	40.8% (75/184)	12.8%	3.2; 22.4	NR	RR: 1.46	1.09; 1.95	NR	Proportions and 95% CIs were found as exact	61

Table A3g Results of PREVENT (NCT02696031) week 16 ITT											
	PBO	186	28.0% (52/186)							Clopper-Pearson intervals, whereas CIs for risk differences were derived directly as Newcombe intervals	61
BASDAI50	SEC	184	37.5% (69/184)	16.5%	7.4; 25.7	NR	RR: 1.79	1.28; 2.50	NR	Proportions and 95% CIs were found as exact Clopper-Pearson intervals, whereas CIs for risk differences were derived directly as Newcombe intervals	61
	PBO	186	21.0% (39/186)								61
SF36-PCS	SEC	184	Mean change: 5.57 (SD: 9.36)	2.64	0.70; 4.58	NA	NA	NA	NA	Proportions and 95% CIs were found as exact Clopper-Pearson intervals, whereas CIs for risk differences were derived directly as Newcombe intervals	61
	PBO	186	Mean change: 2.93 (SD: 9.68)								61
Discontinuation due to AEs	SEC	184	1.6% (3/184)	0.0%	-2.6; 2.6	NR	RR: 1.01	0.21; 4.94	NR	Proportions and 95% CIs were found as exact Clopper-Pearson intervals, whereas CIs for risk differences were derived directly as Newcombe intervals	61
	PBO	186	1.6% (3/186)								61

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Abbreviations: AE, adverse event; ASAS40, ASAS at least 40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NA, not applicable; PBO, placebo; RR, relative risk; SD, standard deviation; SEC, secukinumab.
ASDAS<2.1 and SF36-MCS are not reported in PREVENT.

Table A3h Results of COAST-X (NCT02757352) week 16 ITT

				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40	IXE Q4W	96	35.4% (34/96)	16.4%	4.2; 28.5	NR	RR: 1.86	1.15; 3.00	NR	Logistic regression with treatment, geographical region, and MRI and CRPstatus at screening included in the model	[57]
	PBO	105	19.0% (20/105)								[57]
ASDAS<2.1	IXE Q4W	96	27.1% (26/96)	14.7%	3.8; 25.6	NR	RR: 2.19	1.19; 4.01	NR	Logistic regression with treatment, geographical region, and MRI and CRPstatus at screening included in the model	[57]
	PBO	105	12.4% (13/105)								[57]
BASDAI50	IXE Q4W	96	31.3% (30/96)	17.0%	5.5; 28.4	NR	RR: 2.19	1.26; 3.81	NR	Logistic regression with treatment, geographical region, and MRI and CRPstatus at screening included in the model	[57]
	PBO	105	14.3% (15/105)								[57]

Table A3h Results of COAST-X (NCT02757352) week 16 ITT											
SF36-PCS	IXE Q4W	96	Mean change: 8.06 (SD: 7.94)	2.85	0.62; 5.08	NA	NA	NA	NA	Logistic regression with treatment, geographical region, and MRI and CRPstatus at screening included in the model	57
	PBO	105	Mean change: 5.21 (SD: 8.20)								57
Discontinuation due to AEs	IXE Q4W	97	0.0% (0/96)	-1.9%	-4.5; 0.7	NR	RR: 0.22*	0.01-4.50*	NR	* Continuity correction (+1 for N and +0,5 for n for both arms of the trial) applied	57
	PBO	106	1.9% (2/105)								57

Abbreviations: AE, adverse event; ASAS40, ASAS at least 40% improvement; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IXE, Ixekizumab; NA, not applicable; PBO, placebo; Q4W, once every four weeks; RR, relative risk; SD, standard deviation.
SF36-MCS is not reported in COAST-X.

Table A3i Results of MEASURE 2 (NCT01649375) week 16 ITT											
				Estimated absolute difference in effect			**Estimated relative difference in effect**			**Description of methods used for estimation**	**References**
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40 (ITT)	SEC	72	36.1% (26/72)	25.3%	12.1; 38.5	NR	RR: 3.34	1.62; 6.88	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF	
	PBO	74	10.8% (8/74)								

Table A3i Results of MEASURE 2 (NCT01649375) week 16 ITT										
										response status as factors and weight as a covariate
ASAS40 (experienced)	SEC	28	25.0% (7.5/29)	25.0%	9.0; 41.0	NR	RR: 15.52*	0.93; 259.52 *	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate. *Continuity correction applied due to missing events.
	PBO	29	0.0% (0.5/30)							
BASDAI50 (ITT)	SEC	72	30.6% (22/72)	19.7%	7.0; 32.5	NR	RR: 2.83	1.35; 5.93	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate
	PBO	74	10.8% (8/74)							
SF36-PCS (ITT)	SEC	72	Mean change: 6.1 (SD: 7.1)	4.2	2.07; 6.33	NR	NA	NA	NA	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate
	PBO	74	Mean change: 1.9 (SD: 6.0)							

Table A3i Results of MEASURE 2 (NCT01649375) week 16 ITT										
SF36-PCS (experienced)	SEC	24	Mean change: 4.5 (SD: 5.9)	4.2	0.85; 7.55	NR	NA	NA	NA	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate
	PBO	23	Mean change: 0.3 (SD: 5.8)							
SF36-MCS (ITT)	SEC	72	Mean change: 4.04 (SD: 11.0)	0.68	-2.89; 4.25	NR	NA	NA	NA	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate
	PBO	74	Mean change: 3.36 (SD: 11.0)							
Discontinuation due to AEs (ITT)	SEC	72	6.9% (5/72)	1.5%	-6.3; 9.4	NR	RR: 1.28	0.36; 4.59	NR	Safety assessment included all patients who received at least one dose of the study drug; AE rates were summarized descriptively. Continuity correction applied due to missing events
	PBO	74	5.4% (4/74)							

ASDAS<2.1 is not reported in MEASURE 2.

Table A3j Results of MEASURE 4 (NCT02159053) week 16 ITT

				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
ASAS40 (ITT)	SEC	116	38.8% (45/116)	10.6%	-1.5; 22.6	NR	RR: 1.38	0.95;1.99	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate	
	PBO	117	28.2% (33/117)								
ASAS40 (experienced)	SEC	31	35.5% (11/31)	12.0%	-10.1; 34.0	NR	RR: 1.51	0.70; 3.26	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate.	
	PBO	34	23.5% (8/34)								
BASDAI50 (ITT)	SEC	116	Not reported	NR	NR	NR	NR	NR	NR		
	PBO	117	Not reported								
SF36-PCS (ITT)	SEC	116	Mean change: 5.9 (SD: 7.5)	1.4	-0.53; 3.33	NR	NA	NA	NA	Between-treatment differences in continuous	

Table A3j Results of MEASURE 4 (NCT02159053) week 16 ITT											
	PBO	117	Mean change: 4.5 (SD: 7.5)							variables were evaluated using a mixed-effect model repeated-measures (MMRM) approach, which is valid under the missing at random assumption.	
SF36-PCS (experienced)	SEC	31	Mean change: 5.2 (SD: 7.1)	1.2	-2.26; 4.66	NR	NA	NA	NA	Between-treatment differences in continuous variables were evaluated using a mixed-effect model repeated-measures (MMRM) approach, which is valid under the missing at random assumption.	
	PBO	34	Mean change: 4.0 (SD: 7.1)								
Discontinuation due to AEs (ITT)	SEC	116	0.9% (1/116)	0.0%	-2.4; 2.4	NR	RR: 1.01	0.06; 15.94	NR	Safety assessment included all patients who received at least one dose of the study drug; AE rates were summarized descriptively	
	PBO	117	0.9% (1/117)								

ASDAS<2.1 and SF36-MCS are not reported in MEASURE 4.

Table A3k Results of MEASURE 5 (NCT02896127) week 16 ITT											
				Estimated absolute difference in effect			**Estimated relative difference in effect**			**Description of methods used for estimation**	**References**

Table A3k Results of MEASURE 5 (NCT02896127) week 16 ITT

Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value	
ASAS40 (ITT)	SEC	305	43.9% (134/305)	26.9%	18.8; 35.1	NR	RR: 2.59	1.78; 3.75	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate
	PBO	153	17.0% (26/153)							
ASAS40 (experienced)	SEC	65	49.2% (32/65)	36.3%	19.4; 53.3	NR	RR: 3.82	1.48; 9.84	NR	The primary end point and other binary end points were evaluated by means of logistic regression with treatment and anti-TNF response status as factors and weight as a covariate.
	PBO	31	12.9% (4/31)							
BASDAI50 (ITT)	SEC	305	Not reported	NR	NR	NR	NR	NR	NR	
	PBO	153	Not reported							
SF36-PCS (ITT)	SEC	305	Mean change: 7.4 (SD: 6.6)	2.8	1.52; 4.08	NR	NA	NA	NA	Between-treatment differences in continuous variables were evaluated using a mixed-effect model repeated-measures (MMRM) approach, which
	PBO	153	Mean change: 4.6 (SD: 6.6)							

Table A3k Results of MEASURE 5 (NCT02896127) week 16 ITT											
										is valid under the missing at random assumption.	
SF36-PCS (experienced)	SEC	65	Mean change: 7.3 (SD: 6.9)	4.0	1.14; 6.86	NR	NA	NA	NA	Between-treatment differences in continuous variables were evaluated using a mixed-effect model repeated-measures (MMRM) approach, which is valid under the missing at random assumption.	
	PBO	31	Mean change: 3.3 (SD: 6.2)								
Discontinuation due to AEs (ITT)	SEC	305	0.7% (2/305)	0.0%	-1.6; 1.6	NR	RR: 1.00	0.09; 10.98	NR	Safety assessment included all patients who received at least one dose of the study drug; AE rates were summarized descriptively	
	PBO	153	0.7% (1/153)								

ASDAS<2.1 and SF36-MCS are not reported in MEASURE 5.

Table A3l Results of ASTRUM (NCT02763046) week 16 ITT											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		

Table A3l Results of ASTRUM (NCT02763046) week 16 ITT											
ASAS40 (ITT)	SEC	71	43.7% (31/71)	22.2%	7.2; 37.2	NR	RR: 2.04	1.21; 3.43	NR	Not reported	
	PBO	70	21.4% (15/70)								
ASAS40 (experienced)	SEC	20	45.0% (9/20)	20.0%	-8.9; 48.9	NR	RR: 1.80	0.73; 4.43	NR	Not reported	
	PBO	20	25.0% (5/20)								
BASDAI50 (ITT)	SEC	71	32.4% (23/71)	9.5%	-5.1; 24.2	NR	RR: 1.42	0.82; 2.45	NR	Not reported	
	PBO	70	22.9% (16/70)								
SF36-PCS (ITT)	SEC	71	Not reported	NR	NR	NR	NR	NR	NR	Not reported	
	PBO	70	Not reported								
Discontinuation due to AEs (ITT)	SEC	71	7.0% (5/72)	7.0%	1.1; 13.0	NR	RR: 10.85*	0.61; 192.56*	NR	Not reported. *Continuity correction applied due to missing events.	
	PBO	70	0% (0/71)								

ASDAS<2.1 and SF36-MCS are not reported in ASTRUM.

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Appendix E Safety data for intervention and comparator(s)

Safety data are available in the respective SmPCs. The safety profiles of all included treatments are well known. Below is a summary of the safety profile for bimekizumab:

A total of 4821 patients have been treated with bimekizumab in blinded and open-label clinical studies in plaque psoriasis, psoriatic arthritis and axial spondyloarthritis (nr-axSpA and AS) representing 8733.0 patient-years of exposure. Of these, over 3900 patients were exposed to bimekizumab for at least one year. Overall, the safety profile of bimekizumab is consistent across all indications.

The most frequently reported adverse reactions were upper respiratory tract infections (14.5%, 14.6%, 16.3% in plaque psoriasis (PSO), PsA and axSpA, respectively) and oral candidiasis (7.3%, 2.3%, 3.7% in PSO, PsA and axSpA, respectively).

12.1 Description of selected adverse reactions

Approximately 57% of patients with nr-axSpA treated with bimekizumab up to 52 weeks at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, approximately 44% (25% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing.

Approximately 44% of patients with AS treated with bimekizumab up to 52 weeks at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, approximately 44% (20% of all patients treated with bimekizumab) had antibodies that were classified as neutralizing.

Across indications, no clinically meaningful impact on clinical response was associated with anti-bimekizumab antibodies development and an association between immunogenicity and treatment emergent adverse events has not been clearly established.

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Appendix F Comparative analysis of efficacy and safety

The ITC is a statistical method used to pool results across a number of trials with comparable patient populations linked by common comparators. The technique assumes that, on a suitable scale, one can add and subtract the within study estimates of relative treatment effects. For example, direct data comparing treatment A with C and B with C can be used to indirectly compare A and B. This is under the assumption that the following relationship between the estimated treatment effects holds: (A–B) = (A–C)–(B–C). The underlying methodology for the ITC is the Bucher et al. 1997 method, which is a frequentist approach to evidence synthesis. For this analysis continuous outcomes were assessed in terms of mean difference. Binary outcomes were assessed in terms of relative risk (RR) and risk difference (RD). Significance of treatment effect for the frequentist method was determined by the two-sided 95% CI and tests with two-sided p-values less than 0.05 are referred to as being statistically significant.

Table A4a Meta-analysis of studies comparing bimekizumab to adalimumab for AS bDMARD naïve patients

Outcome	Studies included in the analysis	Absolute difference in effect			Relative difference in effect			Method used for quantitative synthesis	Result used in the health economic analysis?
		Difference	CI	*P* value	Difference	CI	*P* value		
ASAS40	4	-6%	-18.9; 6.1	NA	RR: 0.67	0.40; 1.10	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No

Table A4a Meta-analysis of studies comparing bimekizumab to adalimumab for AS bDMARD naïve patients									
ASDAS<2.1	2	2%	-13.8; 18.7	NA	RR: 0.82	0.38; 1.74	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No
BASDAI50	4	-3%	-16.0; 9.5	NA	RR: 0.76	0.48; 1.22	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No
SF36-PCS	4	0.24	-2.07; 2.55	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No
SF36-MCS	3	-0.67	-3.15; 1.81	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No
Discontinuation due to AEs (ITT)	4	0.28%	-1.67; 2.23	NA	RR: 2.82	0.11; 75.63	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method. Data for the ITT population.	No

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Table A4b Meta-analysis of studies comparing bimekizumab to ixekizumab for AS bDMARD experienced patients									
Outcome	Studies included in the analysis	Absolute difference in effect			Relative difference in effect			Method used for quantitative synthesis	Result used in the health economic analysis?
		Difference	CI	*P* value	Difference	CI	*P* value		
ASAS40	2	10.0%	-16.2; 36.1	NA	RR: 1.13	0.32; 3.94	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No
ASDAS<2.1	2	0.3%	-18.4; 19.0	NA	RR: 0.88	0.10; 8.16	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No
BASDAI50	2	-12.5%	-41.5; 16.6	NA	RR: 0.44	0.15; 1.23	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No
SF36-PCS	2	-2.40	-7.83; 3.03	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No

Table A4b Meta-analysis of studies comparing bimekizumab to ixekizumab for AS bDMARD experienced patients									
Discontinuation due to AEs (ITT)	2	-5.5%	-11.5; 0.5	NA	RR: 0.77	0.03; 21.23	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No

Table A4c Meta-analysis of studies comparing bimekizumab to secukinumab for AS bDMARD experienced patients									
Outcome	**Studies included in the analysis**	**Absolute difference in effect**			**Relative difference in effect**			**Method used for quantitative synthesis**	**Result used in the health economic analysis?**
		Difference	**CI**	***P* value**	**Difference**	**CI**	***P* value**		
ASAS40	5	-0.2%	-11.8; 11.4	NA	RR: 0.99	0.64; 1.53	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No
BASDAI50	3	5.1%	-9.1; 19.4	NA	RR: 0.99	0.57; 1.72	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No

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Table A4c Meta-analysis of studies comparing bimekizumab to secukinumab for AS bDMARD experienced patients									
SF36-PCS	4	0.66	-1.49; 2.81	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No
SF36-MCS	2	0.02	-3.95; 3.99	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No
Discontinuation due to AEs (ITT)	5	1.0%	-0.98; 2.98	NR	RR: 2.31	0.10; 51.85	NR	The RRs for the included studies were synthesized using random effects meta-analysis (DerSimonian–Laird). Indirect comparison was based on the Bucher method	No

Table A4d Meta-analysis of studies comparing bimekizumab to adalimumab for nr-axSpA bDMARD naïve patients									
Outcome	**Studies included in the analysis**	**Absolute difference in effect**			**Relative difference in effect**			**Method used for quantitative synthesis**	**Result used in the health economic analysis?**
		Difference	**CI**	***P* value**	**Difference**	**CI**	***P* value**		
ASAS40	2	2.3%	-14.8; 19.4	NA	RR: 0.83	0.42; 1.65	NR	Indirect comparison was based on the Bucher method	No

Table A4d Meta-analysis of studies comparing bimekizumab to adalimumab for nr-axSpA bDMARD naïve patients									
BASDAI50	2	4.0%	-13.1; 21.1	NA	RR: 0.87	0.44; 1.72	NR	Indirect comparison was based on the Bucher method	No
SF36-PCS	2	0.16	-2.93; 3.26	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No
Discontinuation due to AEs (ITT)	2	-2.4%	-7.45; 2.57	NR	RR: 0.38	0.02; 9.33	NR	Indirect comparison was based the Bucher method	No

Table A4e Meta-analysis of studies comparing bimekizumab to ixekizumab for nr-axSpA bDMARD experienced patients									
Outcome	**Studies included in the analysis**	**Absolute difference in effect**			**Relative difference in effect**			**Method used for quantitative synthesis**	**Result used in the health economic analysis?**
		Difference	**CI**	***P* value**	**Difference**	**CI**	***P* value**		
ASAS40	2	7.3%	-9.8; 24.4	NA	RR: 1.09	0.59; 2.03	NR	Indirect comparison was based on the Bucher method	No
ASDAS<2.1	2	10.9%	-5.0; 26.9	NA	RR: 1.07	0.51; 2.24	NR	Indirect comparison was based on the Bucher method	No
BASDAI50	2	7.3%	-9.2; 23.9	NA	RR: 0.94	0.48; 1.85	NR	Indirect comparison was based on the Bucher method	No

Table A4e Meta-analysis of studies comparing bimekizumab to ixekizumab for nr-axSpA bDMARD experienced patients									
SF36-PCS	2	0.81	-2.21; 3.84	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No
Discontinuation due to AEs (ITT)	2	-0.5%	-5.30; 4.30	NR	RR: 1.80	0.06; 55.69	NR	Indirect comparison was based the Bucher method	No

Table A4f Meta-analysis of studies comparing bimekizumab to secukinumab for nr-axSpA bDMARD experienced patients									
Outcome	**Studies included in the analysis**	**Absolute difference in effect**			**Relative difference in effect**			**Method used for quantitative synthesis**	**Result used in the health economic analysis?**
		Difference	**CI**	***P* value**	**Difference**	**CI**	***P* value**		
ASAS40	2	13.4%	-1.3; 28.2	NA	RR: 1.53	0.95; 2.46	NR	Indirect comparison was based on the Bucher method	No
BASDAI50	2	8.9%	-5.6; 23.4	NA	RR: 1.22	0.74; 2.03	NR	Indirect comparison was based on the Bucher method	No
SF36-PCS	2	1.43	-1.34; 4.21	NR	NA	NA	NA	HRQoL results for the included studies were synthesized using the standardized mean difference (SMD).	No

Table A4f Meta-analysis of studies comparing bimekizumab to secukinumab for nr-axSpA bDMARD experienced patients									
Discontinuation due to AEs (ITT)	2	-2.42%	-7.20; 2.36	NR	RR: 0.39	0.04; 3.77	NR	Indirect comparison was based the Bucher method	No

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Appendix G Extrapolation

NA

Appendix H – Literature search for HRQoL data

NA

Appendix I Mapping of HRQoL data

NA

Appendix J Probabilistic sensitivity analyses

NA

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Appendix K BE MOBILE 1 & 2 week 52 data

1.1 BE MOBILE 1 in nr-axSpA

Following treatment with bimekizumab, improvements over placebo for efficacy endpoints related to the signs and symptoms of axSpA and their impact on patients' lives were rapid and observed as early as Week 1 (after the first dose of bimekizumab) with continued improvement to Week 16. Improvement across efficacy endpoints was sustained from Week 16 or further improved up to Week 52.

Study participants who switched from placebo to bimekizumab 160mg Q4W at Week 16 showed marked improvement across the spectrum of other efficacy endpoints, and showed similar levels of efficacy at Week 24 compared with Week 16 or Week 24 for participants randomized to bimekizumab treatment and additional improvement or a sustained response up to Week 52.

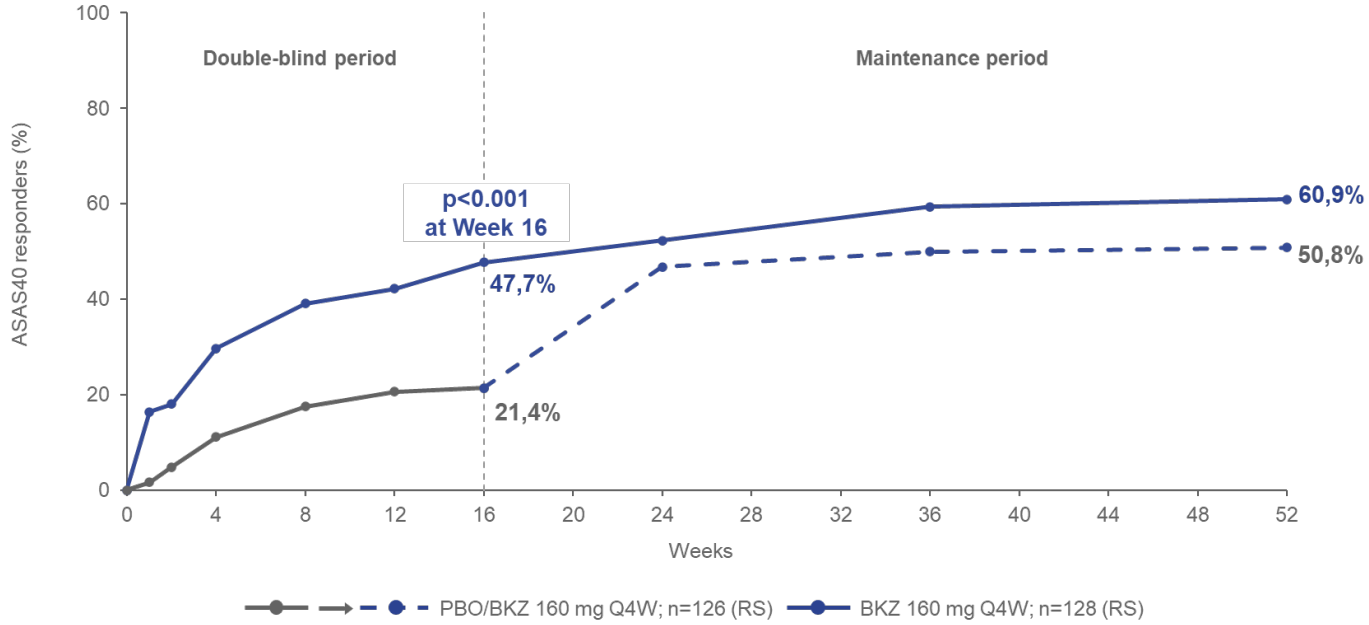
Bimekizumab, at a dose of 160mg Q4W, was well tolerated in study participants with active nr-axSpA, and the safety profile was consistent with studies in the AS population. A favourable safety profile was established with this pivotal study with continued exposure and the overall incidence of study discontinuations due to TEAEs was low (2.5%).[113]

1.1.1 ASAS40

The ASAS40 response rate for study participants in the bimekizumab 160mg Q4W group increased up to Week 16, and the ASAS40 response rate was higher in the bimekizumab 160mg Q4W group (47.7%) compared with the placebo group (21.4%) at Week 16. The ASAS40 response rate further increased from Week 16 (47.7%) to Week 52 (60.9%) for participants in the bimekizumab 160mg Q4W group.

In participants who switched from placebo to bimekizumab 160mg Q4W, the ASAS40 response rate markedly increased from Week 16 (21.4%) to Week 24 (46.8%) and was further increased slightly to Week 52 (50.8%).[113]

Figure 5 ASAS40 Over Time to Week 52 (NRI)

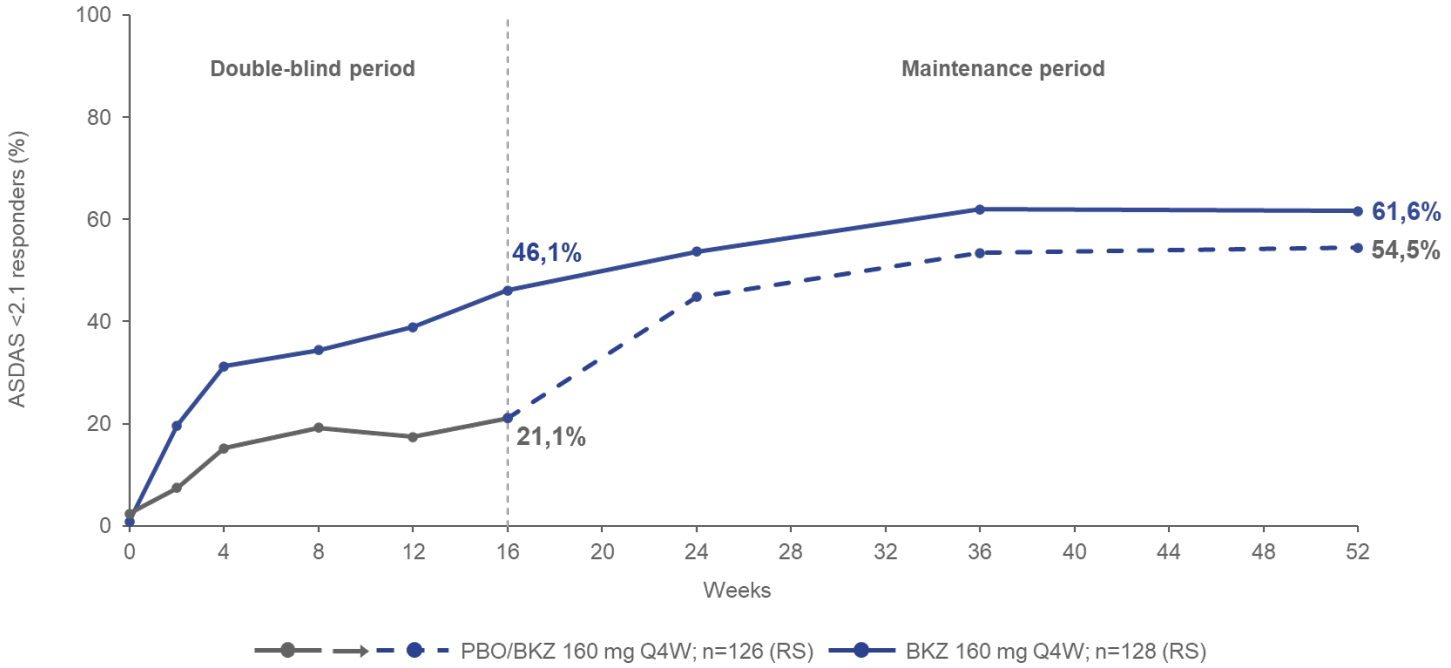


p value was calculated using logistic regression with treatment, MRI/CRP classification and region as factors. ASAS: Assessment in Spondyloarthritis International Society; BKZ: bimekizumab; CRP: C-reactive protein; MRI: magnetic resonance imaging; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q4W: every 4 weeks; RS: randomized set

1.1.2 ASDAS<2.1

ASDAS<2.1 improved over time from week 24 to 52, as illustrated in Figure 10.[113]

Figure 6 ASDAS <2.1 Response Over Time to Week 52 (MI)



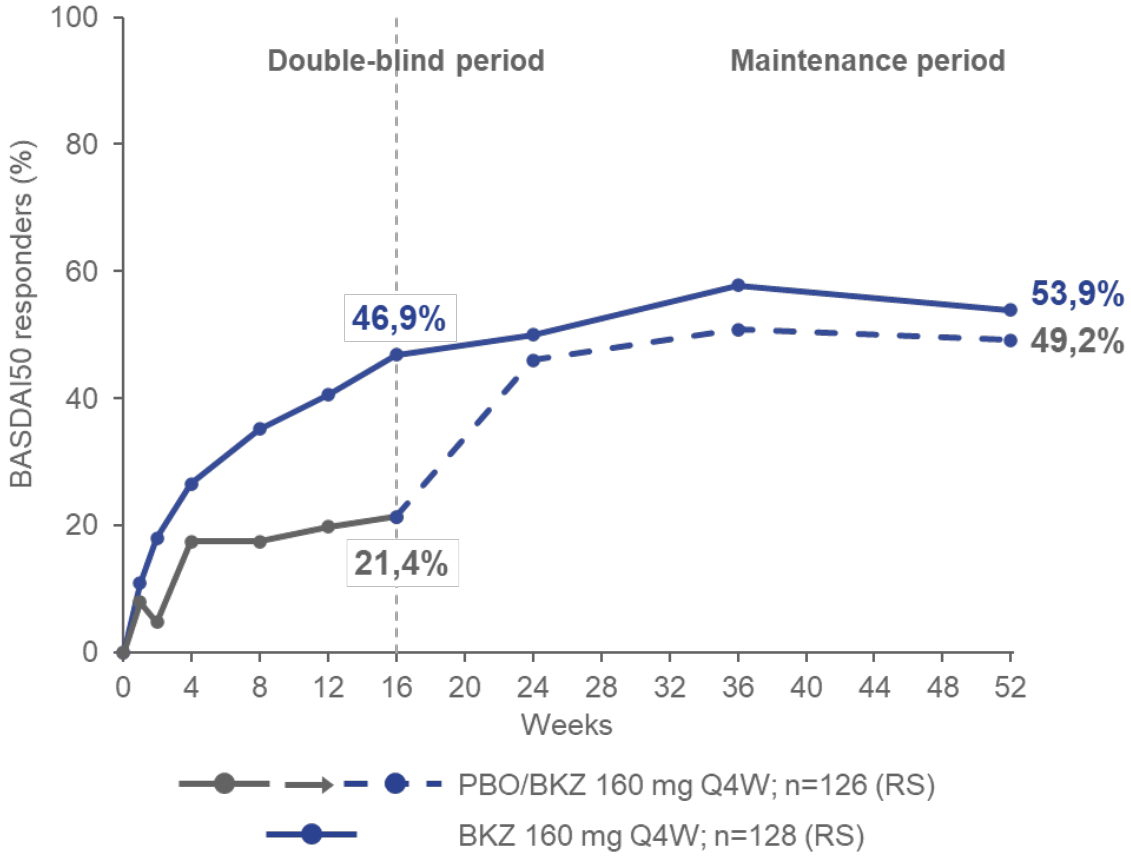
Data are manually calculated from ASDAS disease state response rates. ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; HD: high disease; ID: inactive disease; LD: low disease; MI: multiple imputation; PBO: placebo;
Q4W: every 4 weeks; RS: randomized set; VHD: very high disease.

1.1.3 BASDAI50

The BASDAI50 response rate for study participants in the bimekizumab 160mg Q4W group increased up to Week 16, and the BASDAI50 response rate was greater in the bimekizumab 160mg Q4W group (46.9%) compared with the placebo group (21.4%) at Week 16. The BASDAI50 response rates further increased from Week 16 (46.9%) to Week 52 (53.9%) for participants in the bimekizumab 160mg Q4W group.

In participants who switched from placebo to bimekizumab 160mg Q4W, the BASDAI50 response rate markedly increased from Week 16 (21.4%) to Week 24 (46.0%) and was further increased slightly to Week 52 (49.2%). [113]

Figure 7 BASDAI50 Over Time to Week 52 (NRI)

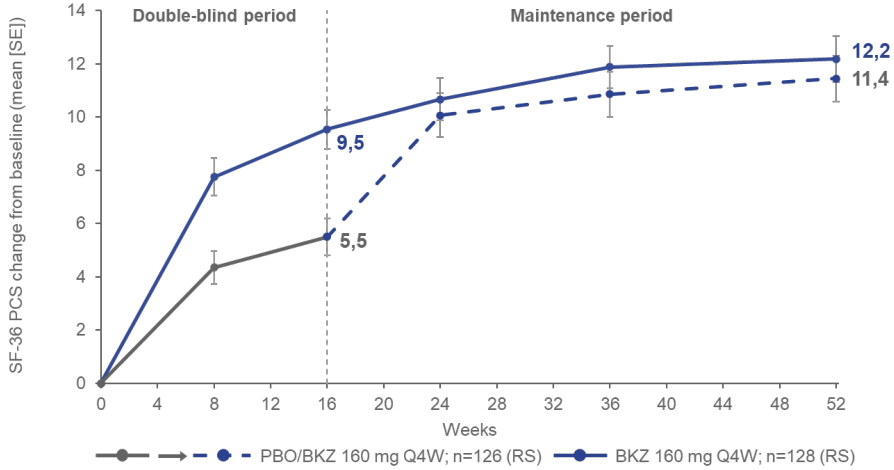


1.1.4 SF-36 PCS

The SF-36 PCS mean change from Baseline in the bimekizumab 160mg Q4W group compared with the placebo group was greater at Week 8 (first time point assessed) (7.752 vs 4.347, respectively), and at Week 16 (9.536 vs 5.494, respectively). The SF-36 PCS mean change from Baseline further increased from Week 16 (9.536) to Week 52 (12.175) for study participants in the bimekizumab 160mg Q4W group.

In participants who switched from placebo to bimekizumab 160mg Q4W, the change from Baseline in SF-36 PCS score markedly increased from Week 16 (5.494) to Week 24 (10.067) and further increased slightly to Week 52 (11.443). [113]

Figure 8 SF-36 PCS Change from Baseline Over Time to Week 52 (MI)



A higher SF-36 score reflects better physical function and the scale is normalised to a general US population, with a mean of 50 (standard deviation: 10).

p value from RBMI analysis as this was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, MRI/CRP classification, region as fixed effects and

the baseline value as covariate. ANCOVA: analysis of covariance. BKZ: bimekizumab; CRP: C-reactive protein; MI: multiple imputation; MRI: magnetic resonance imaging; PBO: placebo; PCS: Physical Component Summary; Q4W: every 4 weeks; RBMI: reference-based multiple imputation; RS: randomized set; SE: standard error; SF-36: Short-Form 36-item Health Survey.

[redacted]

1.1.5 Overall summary of TEAEs

During the Double-Blind Treatment Period, TEAEs were reported at a slightly higher incidence in the bimekizumab 160mg Q4W group (80 study participants [62.5%]) compared with the placebo group (71 study participants [56.3%]). There were no serious TEAEs in the bimekizumab 160mg Q4W group and only 1 serious TEAE reported by 1 participant (0.8%) in the placebo group. [redacted] Very few participants discontinued due to TEAEs: 2 study participants

(1.6%) discontinued due to TEAEs in the bimekizumab 160mg Q4W group and 5 study participants (4.0%) discontinued due to TEAEs in the placebo group. Drug-related TEAEs (as determined by the Investigator) were reported at a higher incidence in the bimekizumab 160mg Q4W group (33 study participants [25.8%]) compared with the placebo group (17 study participants [13.5%]). There were no severe TEAEs in the bimekizumab 160mg Q4W group and only 1 severe TEAE reported by 1 participant (0.8%) in the placebo group. No deaths due to AEs or TEAEs were reported during the Double-Blind Treatment Period.[113]

Table 119 Overall summary of TEAEs – Double-Blind Treatment Period (SS)

Category	PBO N=126 n (%) [#]	BKZ 160mg Q4W N=128 n (%) [#]
Any TEAEs	71 (56.3) [redacted]	80 (62.5) [redacted]
Serious TEAEs	1 (0.8) [redacted]	0
[redacted]	[redacted]	[redacted]
Study participant discontinuations due to TEAEs [b]	5 (4.0) [redacted]	2 (1.6) [redacted]
Permanent withdrawal of IMP due to TEAEs	5 (4.0) [redacted]	2 (1.6) [redacted]
Drug-related TEAEs	17 (13.5) [redacted]	33 (25.8) [redacted]
Severe TEAEs	1 (0.8) [redacted]	0
All deaths (AEs leading to death)	0	0
Deaths (TEAEs leading to death)	0	0

AE=adverse event; BKZ=bimekizumab; IA=interim analysis; IMP=investigational medicinal product; MedDRA=Medical Dictionary for Regulatory Activities; PBO=placebo; Q4W=every 4 weeks; SMQ=standardized MedDRA query; SS=Safety Set; TEAE=treatment-emergent adverse event. Note: n=number of study participants who reported at least 1 TEAE in that category. Note: [#] is the number of individual occurrences of the TEAE in that category. [redacted]

[redacted] [b] Included study participant discontinuations due to TEAEs that occurred after the completion of the Double- Blind Treatment Period and prior to the start of the Maintenance Period (2 study participants in the PBO group) and TEAEs that started in the Double-Blind Treatment Period with the discontinuation occurring in the Maintenance Period (1 study participant in the BKZ

1.1.6 Serious infections

During the Double-Blind Treatment Period, there were no incidences of serious infection TEAEs in the bimekizumab 160mg Q4W group or the placebo group. During the Overall Period, the incidence of serious infection TEAEs was low (4 study participants [1.6%]). [redacted]

Table 120 Incidence of serious infection TEAEs by HLT and PT for the Double-Blind Treatment Period and Overall Period (SS)

	Double-Blind Treatment Period (SS)		Overall Period (SS)
MedDRA V19.0 HLT PT	Placebo N=126 100 participant- years=0.38 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W N=128 100 participant- years=0.40 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W total N=244 100 participant- years=2.08 n (%) [#] Incidence (95% CI)
Any serious infection TEAEs	0	0	4 (1.6) [4] [redacted]

[redacted]	[redacted]	[redacted]	[redacted]
Appendicitis	0	0	2 (0.8) [2]
[redacted]	[redacted]	[redacted]	[redacted]
Tonsillitis bacterial	0	0	1 (0.4) [1]
[redacted]	[redacted]	[redacted]	[redacted]
Erysipelas	0	0	1 (0.4) [1]

BKZ=bimekizumab; CI=confidence interval; HLT=high level term; MedDRA=Medical Dictionary for Regulatory Activities; NEC=not elsewhere classified; PT=preferred term; Q4W=every 4 weeks; SS=Safety Set; TEAE=treatment-emergent adverse event. Note: n=number of study participants reporting at least 1 TEAE within HLT/PT. Note: [#] is the number of individual occurrences of the TEAE. Note: Incidence=Exposure-adjusted event rate per 100 study participant-years and associated 95% CI.

1.1.6.1 Opportunistic infections

During the Double-Blind Treatment Period, 1 study participant (0.8%) reported an opportunistic infection TEAE in the bimekizumab 160mg Q4W group, and no study participants reported an opportunistic infection TEAE in the placebo group. In the bimekizumab 160mg Q4W group, 1 opportunistic infection TEAE of oropharyngeal candidiasis was reported.

The incidence of opportunistic infection TEAEs was low in the Overall Period (5 study participants [2.0%]): 4 study participants (1.6%) had opportunistic infection TEAEs of oropharyngeal candidiasis and 1 study participant (0.4%) had an opportunistic infection TEAE of oropharyngitis fungal.

Overall, all opportunistic infection TEAEs were localized mucocutaneous fungal infections, mild in severity, nonserious, were considered related (except for 1 event), and none led to study discontinuation.

No cases of active TB were reported during the study.

Table 121 Incidence of opportunistic infection TEAEs by HLT and PT for the Double-Blind Treatment Period and Overall Period (SS)

	Double-Blind Treatment Period (SS)		Overall Period (SS)
MedDRA V19.0 HLT PT	Placebo N=126 100 participant- years=0.38 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W N=128 100 participant- years=0.40 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W total N=244 100 participant- years=2.08 n (%) [#] Incidence (95% CI)
Any opportunistic infection TEAEs	0	1 (0.8) [redacted]	5 (2.0) [redacted]
[redacted]	0	[redacted]	[redacted]
Oropharyngeal candidiasis	0	1 (0.8) [redacted]	4 (1.6) [redacted]
[redacted]	[redacted]	[redacted]	[redacted]
Oropharyngitis fungal	0	0	1 (0.4) [redacted]

Any opportunistic infection TEAEs	0	1 (0.8) [redacted]	5 (2.0) [redacted]
[redacted]	[redacted]	[redacted]	[redacted]

BKZ=bimekizumab; CI=confidence interval; HLT=high level term; MedDRA=Medical Dictionary for Regulatory Activities; NEC=not elsewhere classified; PT=preferred term; Q4W=every 4 weeks; SS=Safety Set; TEAE=treatment-emergent adverse event. Note: n=number of study participants reporting at least 1 TEAE within HLT/PT. Note: [#] is the number of individual occurrences of the TEAE. Note: Incidence=Exposure-adjusted event rate per 100 study participant-years and associated 95% CI. Note: Includes events identified using UCB-defined search criteria for opportunistic infections. Note: There were no opportunistic infections other than localized mucocutaneous fungal events that were classified as opportunistic by internal UCB conventions.

1.1.7 Discontinuation due to lack of efficacy

During the Double-Blind Treatment Period study participants were randomized 1:1 to bimekizumab 160mg sc Q4W or placebo sc Q4W. Study participants were stratified by region, and by the presence of sacroiliitis on MRI and elevated CRP to ensure balanced treatment allocation across the 3 MRI/CRP classification levels. A total of 254 study participants were randomized and started the Double-Blind Treatment Period as follows: 128 study participants in the bimekizumab 160mg Q4W group and 126 study participants in the placebo group.

The percentages of study participants who completed the Double-Blind Treatment Period were similar in the bimekizumab 160mg Q4W group (98.4%) and the placebo group (93.7%). The frequency of study discontinuation was low in the All study participants group (10 study participants [3.9%]) and in each of the treatment groups in the Double-Blind Treatment Period (1.6% and 6.3% in the bimekizumab 160mg Q4W and the placebo groups, respectively). The most common primary reasons for discontinuation during the Double-Blind Treatment Period were due to withdrawal by study participant (4 study participants [1.6%]) and an AE (4 study participants [1.6%]). In the bimekizumab 160mg Q4W group, no study participants discontinued due to withdrawal by study participant, and 4 study participants (3.2%) discontinued due to withdrawal by study participant in the placebo group. In the bimekizumab 160mg Q4W group, 1 study participant (0.8%) discontinued due to an AE, and 3 study participants (2.4%) in the placebo group discontinued due to an AE. A summary of study participant disposition and discontinuation reasons during the Double-Blind Treatment Period is presented in table below.

Table 122 Disposition and study discontinuation reasons – Double-Blind Treatment Period (RS)

Disposition	PBO N=126 n (%)	BKZ 160mg Q4W N=128 n (%)	All study participants N=254 n (%)
Started Double-Blind Treatment Period	126 (100)	128 (100)	254 (100)
Completed Double-Blind Treatment Period	118 (93.7)	126 (98.4)	244 (96.1)
Completed Double-Blind Treatment Period not on randomized treatment	0	0	0
Discontinued during Double-Blind Treatment Period	8 (6.3)	2 (1.6)	10 (3.9)
Primary reason for study discontinuation			
AE	3 (2.4)	1 (0.8)	4 (1.6)
Lack of efficacy	1 (0.8)	0	1 (0.4)
Protocol violation	0	0	0
Lost to follow up	0	0	0
Withdrawal by study participant	4 (3.2)	0	4 (1.6)
Other	0	1 (0.8)	1 (0.4)

AE=adverse event; BKZ=bimekizumab; IMP=investigational medicinal product; PBO=placebo; Q4W=every 4 weeks; RS=Randomized Set. Note: Started a period was based on treatment information. Note: A study participant was considered as completing a study period if she/he had completed the last scheduled study visit for that period. Study participants who withdrew from the IMP but returned for all scheduled visits up to the last scheduled study visit for that period were considered as having completed the study period. Note: Study participants were summarized according to randomized treatment at Baseline in the Double-Blind Treatment Period. After the Double-Blind Treatment Period, study participants randomized to PBO switched to BKZ 160mg Q4W at Week 16.

A total of 242 study participants entered the Maintenance Period as follows: 126 study participants in the bimekizumab 160mg Q4W group and 116 study participants in the placebo/bimekizumab 160mg Q4W group. At the time of this Week 52 data cut-off date (01 July 2022), 220 study participants (86.6%) had completed the 36-week Maintenance Period, [redacted] The percentages of study participants who completed the Maintenance Period were 87.5% in the bimekizumab 160mg Q4W group and 85.7% in the placebo/bimekizumab 160mg Q4W group.

At the time of the Week 52 data cut-off date, the most common primary reasons for discontinuation during the Maintenance Period were withdrawal by study participant (12 study participants [4.7%]), due to an AE (5 study participants [2.0%]), and due to lack of efficacy (4 study participants [1.6%]). In the bimekizumab 160mg Q4W group, 8 study participants (6.3%) discontinued due to withdrawal by study participant and 4 study participants (3.2%) in the placebo/bimekizumab 160mg Q4W group discontinued due to withdrawal by study participant. Three study participants (2.3%) in the bimekizumab 160mg Q4W group and 2 study participants (1.6%) in the placebo/bimekizumab 160mg Q4W group discontinued due to an AE. Two study participants (1.6%) in the bimekizumab 160mg Q4W group and 2 study participants (1.6%) in the placebo/bimekizumab 160mg Q4W group discontinued due to lack of efficacy.

A summary of study participant disposition and discontinuation reasons during the Maintenance Period at the time of the Week 52 data cut-off date is presented in table below.

Table 123 Disposition and study discontinuation reasons – Maintenance Period at the time of the Week 52 data cut-off date (RS)

	PBO	BKZ 160mg Q4W	All study participants
Disposition	**N=126**	**N=128**	**N=254**
	n (%)	**n (%)**	**n (%)**

Completed the Double-Blind Treatment Period and did not enter the Maintenance Period	2 (1.6)	0	2 (0.8)

Primary reason for study discontinuation			
AE	2 (1.6)	0	2 (0.8)
Lack of efficacy	0	0	0
Protocol violation	0	0	0
Lost to follow-up	0	0	0
Withdrawal by study participant	0	0	0
Other	0	0	0

Table 124 Disposition and study discontinuation reasons – Maintenance Period at the time of the Week 52 data cut-off date (RS)

Disposition	PBO N=126 n (%)	BKZ 160mg Q4W N=128 n (%)	All study participants N=254 n (%)
Started 36-week Maintenance Period	116 (92.1)	126 (98.4)	242 (95.3)
Completed the 36-week Maintenance Period	108 (85.7)	112 (87.5)	220 (86.6)

Completed the 36-week Maintenance Period while not on randomized treatment	0	0	0
Discontinued during the 36-week Maintenance Period	8 (6.3)	14 (10.9)	22 (8.7)
Primary reason for study discontinuation			
AE	2 (1.6)	3 (2.3)	5 (2.0)
Lack of efficacy	2 (1.6)	2 (1.6)	4 (1.6)
Protocol violation	0	0	0
Lost to follow up	0	1 (0.8)	1 (0.4)
Withdrawal by study participant	4 (3.2)	8 (6.3)	12 (4.7)
Other	0	0	0
[redacted]	[redacted]	[redacted]	[redacted]

AE=adverse event; BKZ=bimekizumab; IMP=investigational medicinal product; PBO=placebo; Q4W=every 4 weeks; RS=Randomized Set; SFU=Safety Follow-Up. Note: Started a period was based on treatment information. Note: A study participant was considered as completing a study period if she/he had completed the last scheduled study visit for that period. Study participants who withdrew from the IMP but returned for all scheduled visits up to the last scheduled study visit for that period were considered as having completed the study period. Note: After the Double-Blind Treatment Period, study participants randomized to PBO switched to Q4W at Week 16.

1.2 BE MOBILE 2 in AS

Following treatment with bimekizumab, improvements over placebo for efficacy endpoints related to the signs and symptoms of axSpA and their impact on patients' lives were rapid and observed as early as Week 2 (after the first dose of bimekizumab) with continued improvement to Week 16. Improvement across efficacy endpoints was sustained from Week 16 to Week 52 or further improved up to Week 52.

Study participants who switched from placebo to bimekizumab 160mg Q4W at Week 16 showed marked improvement across the spectrum of efficacy endpoints and showed similar levels of efficacy at Week 24 compared with Week 16 or Week 24 for participants randomized to bimekizumab treatment and additional improvement or a sustained response to Week 52.

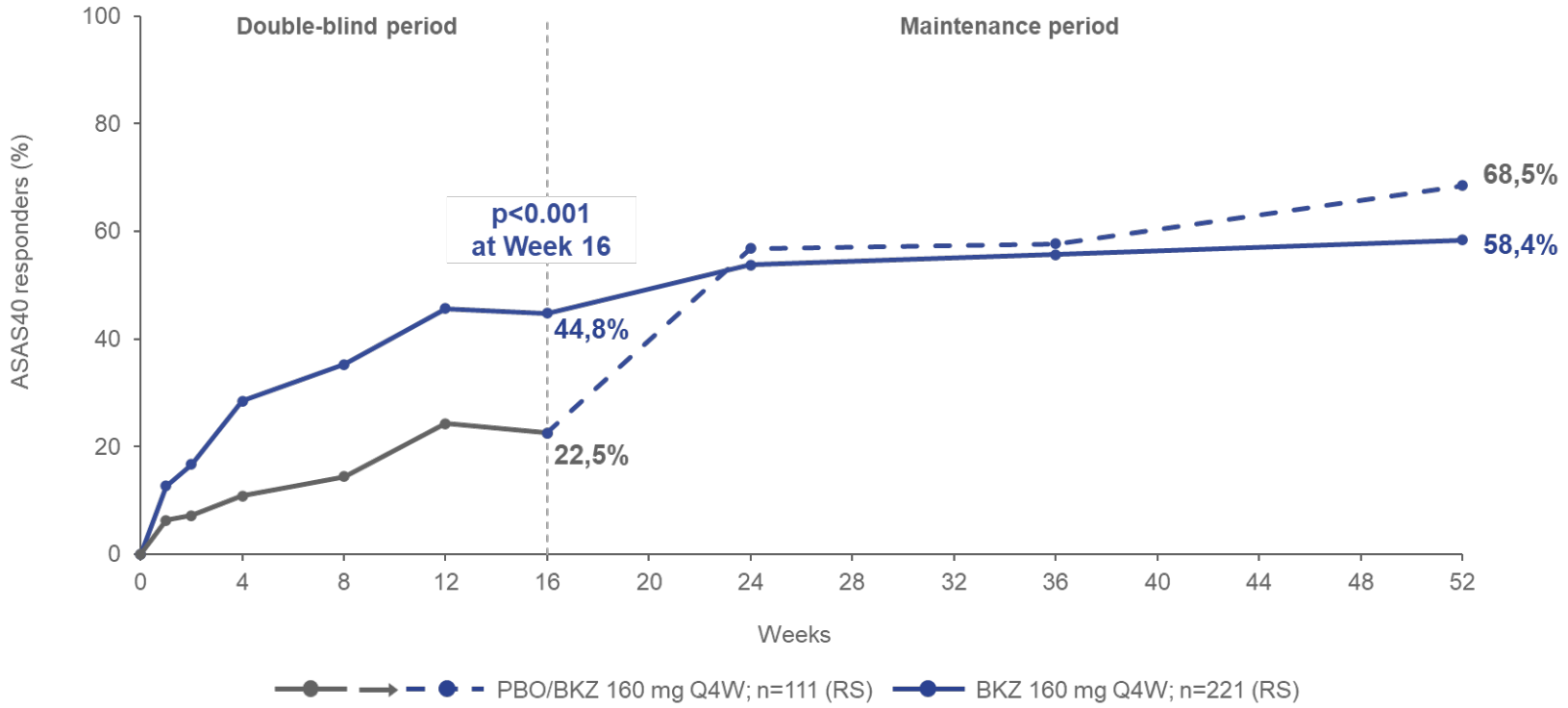
Bimekizumab, at a dose of 160mg Q4W, was well tolerated in study participants with active AS, and the safety profile was consistent with the Phase 2 study in AS. The safety profile remained unchanged with continued exposure and the overall incidence of study discontinuations due to TEAEs was low (4.5%).[113]

1.2.1 ASAS40

The ASAS40 response rate for study participants in the bimekizumab 160mg Q4W group increased up to Week 16, and the ASAS40 response rate was higher in the bimekizumab 160mg Q4W group (44.8%) compared with the placebo group (22.5%) at Week 16. The ASAS40 response rate for study participants in the bimekizumab 160mg Q4W group further increased from Week 16 (44.8%) to Week 52 (58.4%).

In participants who switched from placebo to bimekizumab 160mg Q4W, the ASAS40 response rate markedly increased from Week 16 (22.5%) to Week 24 (56.8%) and further increased to Week 52 (68.5%).[113]

Figure 9 ASAS40 Over Time to Week 52 (NRI)

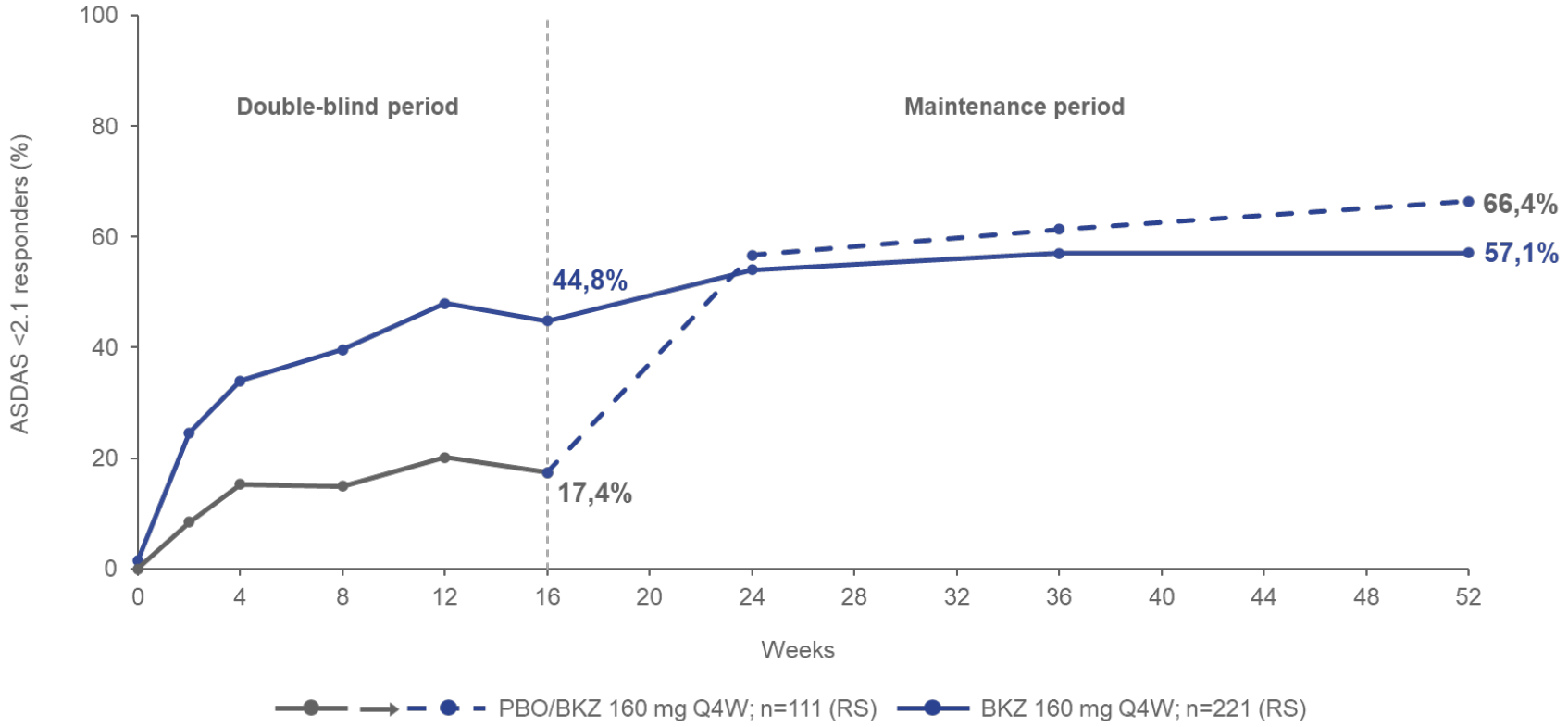


p value was calculated using logistic regression with treatment, prior anti-TNF exposure and region as factors. ASAS: Assessment of Spondyloarthritis International Society; BKZ: bimekizumab; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q4W: every 4 weeks; RS: randomized set; TNF: tumour necrosis factor.

1.2.2 ASDAS<2.1

ASDAS<2.1 improved over time from week 24 to 52, as illustrated in Figure 10.[113]

Figure 10 ASDAS <2.1 Response Over Time to Week 52 (MI)



Data are manually calculated from ASDAS disease state response rates. ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; HD: high disease; ID: inactive disease; LD: low disease; MI: multiple imputation; PBO: placebo; Q4W: every 4 weeks; RS: randomized set; VHD: very high disease.

1.2.3 BASDAI50

The BASDAI50 response rate for study participants in the bimekizumab 160mg Q4W group increased up to Week 16, and the BASDAI50 response rate was greater in the bimekizumab 160mg Q4W group (46.6%) compared with the placebo group (26.1%) at Week 16. The BASDAI50 response rates further increased from Week 16 (46.6%) to Week 52 (53.8%) for study participants in the bimekizumab 160mg Q4W group.

In participants who switched from placebo to bimekizumab 160mg Q4W, the BASDAI50 response rate markedly increased from Week 16 (26.1%) to Week 52 (62.2%).[113]

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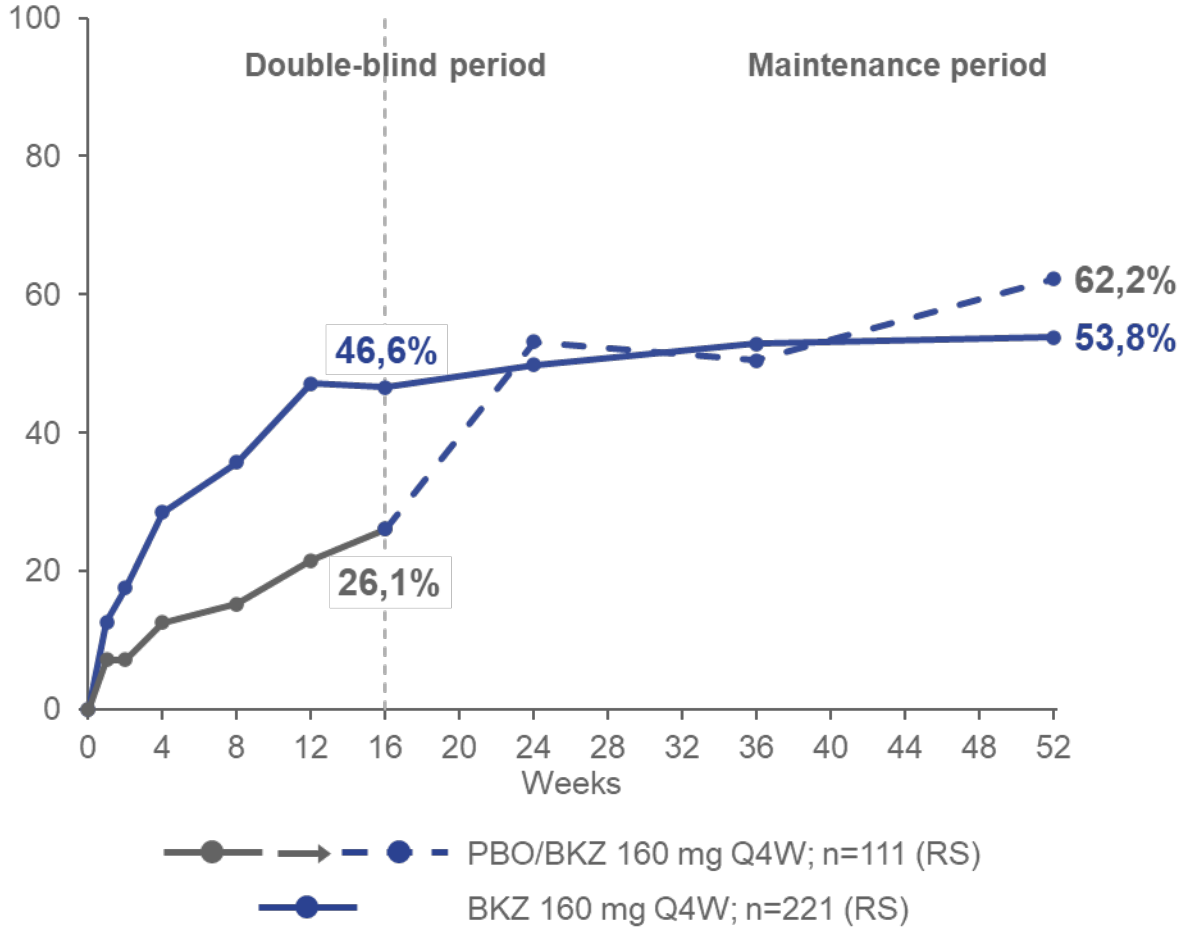
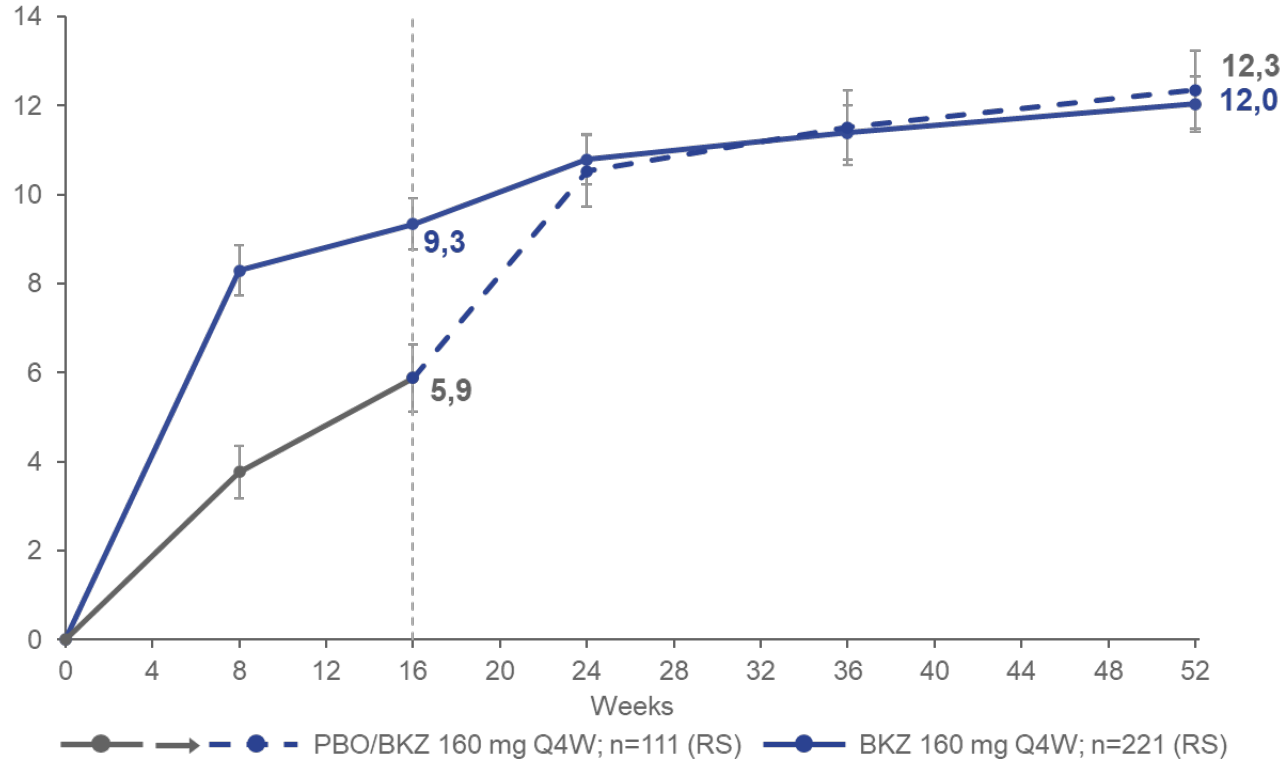
Figure 11 BASDAI50 Over Time to Week 52 (NRI)



1.2.4 SF-36 PCS

By Week 52, SF-36 PCS improved from 34.6/34.4 (PBO/BKZ) at baseline to 47.0 and 46.4 by patients who switched from placebo to bimekizumab and the original bimekizumab arm.

Figure 12 SF-36 PCS Change from Baseline Over Time to Week 52 (MI)



A higher SF-36 score reflects better physical function and the scale is normalised to a general US population, with a mean of 50 (standard deviation: 10). p value from RBMI analysis as is was the primary analysis method for continuous variables. p value was obtained from ANCOVA with treatment, prior anti-TNF exposure and region as fixed effects, and baseline values as covariate. ANCOVA: analysis of covariance; BKZ: bimekizumab; MI: multiple imputation; PBO: placebo; PCS: Physical Component Summary; Q4W: every 4 weeks; RBMI: reference-based multiple imputation; RS: randomized set;
SE: standard error; SF-36: Short-Form 36-item Health Survey; TNF: tumour necrosis factor

[redacted]

1.2.7 Overall summary of TEAEs

During the Double-Blind Treatment Period, TEAEs were reported at a higher incidence in the bimekizumab 160mg Q4W group (120 study participants [54.3%]) compared with the placebo group (48 study participants [43.2%]) (Table 11–3). The incidence of serious TEAEs was low in both treatment groups; 5 study participants (2.3%) in the bimekizumab 160mg Q4W group and 1 study participant (0.9%) in the placebo group. [redacted] In the bimekizumab 160mg Q4W group, 6 study participants (2.7%) discontinued due to TEAEs, and no study participants in the placebo group discontinued due to TEAEs. Drug-related TEAEs (as determined by the Investigator) were reported at a higher incidence in the bimekizumab 160mg Q4W group (65 study participants [29.4%]) compared with the placebo group (19 study participants [17.1%]). In the bimekizumab 160mg Q4W group, 4 study participants (1.8%) had a severe TEAE, and no study participant in the placebo group has a severe TEAE. No deaths due to AEs or TEAEs were reported during the Double-Blind Treatment Period.

Table 125 Overall summary of TEAEs – Double-Blind Treatment Period (SS)

Category	PBO N=111 n (%) [#]	BKZ 160mg Q4W N=221 n (%) [#]
Any TEAEs	48 (43.2) [redacted]	120 (54.3) [redacted]
Serious TEAEs	1 (0.9) [redacted]	5 (2.3) [redacted] a
Safety topics of interest TEAEs	7 (6.3) [redacted]	39 (17.6) [redacted]
Study participant discontinuations due to TEAEs [b]	0	6 (2.7) [redacted]

Permanent withdrawal of IMP due to TEAEs	0	7 (3.2) [redacted] [c]
Drug-related TEAEs	19 (17.1) [redacted]	65 (29.4) [redacted]
Severe TEAEs	0	4 (1.8) [redacted] a
All deaths (AEs leading to death)	0	0
Deaths (TEAEs leading to death)	0	0

AE=adverse event; BKZ=bimekizumab; ICF=Informed Consent Form; IMP=investigational medicinal product; PBO=placebo; PT=preferred term; Q4W=every 4 weeks; SS=Safety Set; TEAE=treatment-emergent adverse event. Note: n=number of study participants who reported at least 1 TEAE in that category. Note: [#] is the number of individual occurrences of the TEAE in that category. [a] One TEAE of cholelithiasis that was serious and severe was reported in the Maintenance Period in the Week 24 CSR. After the Week 24 data cutoff, it was determined that the site entered the incorrect date for the start of this TEAE; therefore, the occurrence of this TEAE was corrected to be reported in the Double-Blind Treatment Period in the Week 52 CSR. [b] Included study participant discontinuations due to TEAEs that occurred after the completion of the Double-Blind Treatment Period and prior to the start of the Maintenance Period (1 study participant in the BKZ 160mg Q4W group) and TEAEs that started in the Double-Blind Treatment Period with the discontinuation occurring in the Maintenance Period (2 study participants in the BKZ 160mg Q4W group). Refer to Section 11.5.1 for additional details. [c] One study participant permanently withdrew from IMP due to a TEAE, by PT, of colitis ulcerative that did not lead to discontinuation; this study participant discontinued during the Maintenance Period due to ICF

1.2.8 Serious infections

During the Double-Blind Treatment Period, the incidence of serious infection TEAEs was low and similar in the bimekizumab 160mg Q4W group (1 study participants [0.5%]) and the placebo group (1 study participants [0.9%]). [redacted]

[redacted]

During the Overall Period, the incidence of serious infections TEAEs was low (6 study participants [1.8%]. [redacted]

Table 126 Incidence of serious infection TEAEs by HLT and PT for the Double-Blind Treatment Period and Overall Period (SS)

	Double-Blind Treatment Period (SS)		Overall Period (SS)
MedDRA V19.0 HLT PT	PBO N=111 100 participant- years=0.35 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W N=221 100 participant- years=0.68 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W Total N=330 100 participant- years=2.91 n (%) [#] Incidence (95% CI)
Any serious infections	1 (0.9) [redacted]	1 (0.5) [redacted]	6 (1.8) [redacted]
Abdominal and gastrointestinal infections	0	0	[redacted]
Diverticulitis	0	0	1 (0.3) [1] [redacted]
[redacted]	[redacted]	[redacted]	[redacted]

Cellulitis	0	0	1 (0.3) [1]
[redacted]	[redacted]	[redacted]	[redacted]
Otitis media	0	0	1 (0.3) [1]
Hepatitis viral infections	0	1 (0.5) [redacted]	1 (0.3) [redacted]
Hepatitis A	0	1 (0.5) [redacted]	1 (0.3) [redacted]
[redacted]	[redacted]	[redacted]	[redacted]
Infectious pleural effusion	0	0	1 (0.3) [1]
[redacted]	[redacted]	[redacted]	[redacted]
Erysipelas	0	0	1 (0.3) [1]
Viral infections NEC	1 (0.9) [1]	0	0
Viral infection	1 (0.9) [1]	0	0

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BKZ=bimekizumab; CI=confidence interval; HLT=high level term; MedDRA=Medical Dictionary for Regulatory Activities; NEC=necrotizing enterocolitis; PBO=placebo; PT=preferred term; Q4W=every 4 weeks; query; SS=Safety Set; TEAE=treatment-emergent adverse event. Note: n=number of study participants reporting at least 1 TEAE within HLT/PT. Note: [#] is the number of individual occurrences of the TEAE. Note: Incidence=Exposure adjusted event rate per 100 study participant-years and associated 95% CI. Note: Included all serious TEAEs that coded to the system organ class"Infections and infestations."

1.2.8.1 Opportunistic infections

Overall, the incidence of opportunistic infection TEAEs was low and only reported in the Overall Period (3 study participants [0.9%]). [redacted]

Overall, all opportunistic infection TEAEs were localized mucocutaneous fungal infections, were mild or moderate in severity, nonserious, and were considered related. In the bimekizumab 160mg Q4W group, 1 opportunistic infection TEAE of oesophageal candidiasis led to discontinuation.

No cases of active TB were reported during the study.

Table 127 Incidence of opportunistic infection TEAEs by HLT and PT for the Double-Blind Treatment Period and Overall Period (SS)

	Double-Blind Treatment Period (SS)		Overall Period (SS)
MedDRA V19.0 HLT PT	Placebo N=111 100 participant- years=0.35 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W N=221 100 participant- years=0.68 n (%) [#] Incidence (95% CI)	BKZ 160mg Q4W total N=330 100 participant- years=2.91 n (%) [#] Incidence (95% CI)
Any opportunistic infection TEAEs	0	0	3 (0.9) [redacted]
[redacted]	[redacted]	[redacted]	[redacted]

Oesophageal candidiasis	0	0	1 (0.3) [1] [redacted]
Oropharyngeal candidiasis	0	0	1 (0.3) [2] [redacted]
[redacted]	[redacted]	[redacted]	[redacted]
Fungal oesophagitis	0	0	1 (0.3) [1] [redacted]

BKZ=bimekizumab; CI=confidence interval; HLT=high level term; MedDRA=Medical Dictionary for Regulatory Activities; NEC=necrotizing enterocolitis; PBO=placebo; PT=preferred term; Q4W=every 4 weeks; query; SS=Safety Set; TEAE=treatment-emergent adverse event. Note: n=number of study participants reporting at least 1 TEAE within HLT/PT. Note: [#] is the number of individual occurrences of the TEAE. Note: Incidence=Exposure adjusted event rate per 100 study participant-years and associated 95% CI. Note: Included events identified using UCB-defined search criteria for opportunistic infections. Note: There were no opportunistic infections other than localized mucocutaneous fungal events that were istic by internal UCB conventions.

1.2.9 Discontinuation due to lack of efficacy

A total of 332 study participants were randomized and started the Double-Blind Treatment Period as follows: 221 study participants in the bimekizumab 160mg Q4W group and 111 study participants in the placebo group.

The percentages of study participants who completed the Double-Blind Treatment Period were similar in the bimekizumab 160mg Q4W group (96.4%) and the placebo group (98.2%). The frequency of study discontinuation during the Double-Blind Treatment Period was low between the treatment groups (3.6% and 1.8% in the bimekizumab 160mg and the placebo groups, respectively).

During the Double-Blind Treatment Period, the discontinuation rate was low (10 study participants [3.0%]). The most common primary reasons for discontinuation during the Double-Blind Treatment Period were due to withdrawal by study participant (4 study participants [1.2%]) and an AE (3 study participants [0.9%]). In the bimekizumab 160mg Q4W group, 3 study participants (1.4%) discontinued due to withdrawal by study participant, and in the placebo group 1 study participant (0.9%) discontinued due to withdrawal by study participant. In the bimekizumab 160mg Q4W group, 3 study participants (1.4%) discontinued due to an AE, and no study participants in the placebo group discontinued due to AE.

Table 128 Disposition and study discontinuation reasons – Double-Blind Treatment Period (RS)

Disposition	PBO N=111 n (%)	BKZ 160mg Q4W N=221 n (%)	All study participants N=332 n (%)
Started Double-Blind Treatment Period	111 (100)	221 (100)	332 (100)
Completed Double-Blind Treatment Period	109 (98.2)	213 (96.4)	322 (97.0)
Completed Double-Blind Treatment Period not on randomized treatment	0	0	0
Discontinued during Double-Blind Treatment Period	2 (1.8)	8 (3.6)	10 (3.0)
Primary reason for study discontinuation			
AE	0	3 (1.4)	3 (0.9)
Lack of efficacy	0	1 (0.5)	1 (0.3)
Protocol violation	0	0	0
Lost to follow up	0	0	0
Withdrawal by study participant	1 (0.9)	3 (1.4)	4 (1.2)
Other	1 (0.9)	1 (0.5)	2 (0.6)

AE=adverse event; BKZ=bimekizumab; IMP=investigational medicinal product; PBO=placebo; Q4W=every 4 weeks; RS=Randomized Set. Note: Started a period was based on treatment information. Note: A study participant was considered as completing a study period if she/he had completed the last scheduled study visit for that period. Note: Study participants who withdrew from the IMP but returned for all scheduled visits up to the last scheduled study visit for that period were considered as having completed the study period. Note: Study participants were summarized according to randomized treatment at Baseline in the Double-Blind Treatment Period. After the Double-Blind Treatment Period, study participants randomized to placebo switched to BKZ 160mg Q4W at Week 16.

During the Maintenance Period study participants in the bimekizumab 160mg Q4W group continued to receive bimekizumab 160mg Q4W and study participants in the placebo group received bimekizumab 160mg sc Q4W starting at Week 16.

Of the 322 study participants who completed the Double-Blind Treatment Period, 3 study participants in the bimekizumab 160mg Q4W group discontinued the study at Week 16 and did not enter the Maintenance Period. The primary reasons for discontinuation in the bimekizumab 160mg Q4W group between the Double-Blind Treatment Period and Maintenance Period were due to withdrawal by study participant (2 study participants [0.9%]) and due to an AE (1 study participant [0.5%]). No study participant in the placebo/bimekizumab 160mg Q4W group discontinued between the Double-Blind Treatment Period and the Maintenance Period.

A total of 319 study participants entered the Maintenance Period as follows: 210 study participants in the bimekizumab 160mg Q4W group and 109 study participants in the placebo/bimekizumab 160mg Q4W group.
At the time of the Week 52 data cut-off date (31 May 2022), all study participants had completed the 36-week Maintenance Period, if they did not discontinue early. The percentages of study participants who completed the Maintenance Period were similar between the bimekizumab 160mg Q4W group (88.7%) and the placebo/bimekizumab 160mg Q4W group (91.9%). [redacted] At the time of the Week 52 data cut-off date, the most common reason for discontinuation during the Maintenance Period was due to an AE (11 study participants [3.3%]) (Table 7–2). In the bimekizumab 160mg Q4W group, 7 study participants (3.2%) discontinued due an AE, and 4 study participants (3.6%) in the placebo/bimekizumab 160mg Q4W group discontinued due to an AE.

Table 129 Disposition and study discontinuation reasons – Maintenance

	PBO	BKZ 160mg Q4W	All study participants
Disposition	**N=111**	**N=221**	**N=332**
	n(%)	**n (%)**	**n (%)**

Completed the Double-Blind Treatment Period and did not enter the Maintenance Period	0	3 (1.4)	3 (0.9)
Primary reason for study discontinuation			
AE	0	1 (0.5)	1 (0.3)
Lack of efficacy	0	0	0
Protocol violation	0	0	0
Lost to follow up	0	0	0
Withdrawal by study participant	0	2 (0.9)	2 (0.6)
Other	0	0	0

Table 130 Disposition and study discontinuation reasons – Maintenance

Disposition	PBO N=111 n (%)	BKZ 160mg Q4W N=221 n (%)	All study participants N=332 n (%)
Started 36-week Maintenance Period	109 (98.2)	210 (95.0)	319 (96.1)
Completed the 36-week Maintenance Period	102 (91.9)	196 (88.7)	298 (89.8)
Completed the 36-week Maintenance Period while not on randomized treatment	0	0	0

Discontinued during the 36-week Maintenance Period	7 (6.3)	14 (6.3)	21 (6.3)
Primary reason for study discontinuation			
AE	4 (3.6)	7 (3.2)	11 (3.3)
Lack of efficacy	1 (0.9)	2 (0.9)	3 (0.9)
Protocol violation	0	0	0
Lost to follow up	0	2 (0.9)	2 (0.6)
Withdrawal by study participant	2 (1.8)	2 (0.9)	4 (1.2)
Other	0	1 (0.5)	1 (0.3)
[redacted]	[redacted]	[redacted]	[redacted]

AE=adverse event; BKZ=bimekizumab; IMP=investigational medicinal product; PBO=placebo; Q4W=every 4 weeks; RS=Randomized Set; SFU=Safety Follow-Up. Note: Started a period was based on treatment information. Note: A study participant was considered as completing the study if she/he had completed the last scheduled study visit (Week 52), not including the SFU Visits. Note: A study participant was considered as completing a study period if she/he had completed the last scheduled study visit for that period. Note: Study participants who withdrew from the IMP but returned for all scheduled visits up to the last scheduled study visit for that period were considered as having completed the study period. Note: After the Double-Blind Treatment Period, study participants randomized to placebo switched to BKZ W at Week 16.

At the time of the Week 52 data cut-off date, 298 study participants (89.8%) had completed the study (ie, completed the Week 52 Visit), 34 study participants (10.2%) had discontinued the study, [redacted]

At the time of the Week 52 data cut-off date, the most common primary reason for study discontinuation was due to an AE (15 study participants [4.5%]), including 11 study participants (5.0%) in the bimekizumab 160mg Q4W group and 4 study participants (3.6%) in the placebo/bimekizumab 160mg Q4W group.

Table 131 Disposition and study discontinuation reasons – Overall Period at the time of the Week 52 data cutoff date (RS)

Disposition	PBO/BKZ 160mg Q4W N=111	BKZ 160mg Q4W N=221	All study participants N=332

	n (%)	n (%)	n (%)
Randomized in study	111 (100)	221 (100)	332 (100)
Completed study	102 (91.9)	196 (88.7)	298 (89.8)
Discontinued	9 (8.1)	25 (11.3)	34 (10.2)
Primary reason for study discontinuation			
AE	4 (3.6)	11 (5.0)	15 (4.5)
Lack of efficacy	1 (0.9)	3 (1.4)	4 (1.2)
Protocol violation	0	0	0
Lost to follow up	0	2 (0.9)	2 (0.6)
Withdrawal by study participant	3 (2.7)	7 (3.2)	10 (3.0)
Other	1 (0.9)	2 (0.9)	3 (0.9)
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

AE=adverse event; BKZ=bimekizumab; COVID-19=coronavirus disease 2019; IMP=investigational medicinal product; OLE=open-label extension; PBO=placebo; Q4W=every 4 weeks; RS=Randomized Set; SFU=Safety Follow-Up. Note: Started a period was based on treatment information. Note: A study participant was considered as completing the study if she/he had completed the last scheduled study visit (Week 52), not including the SFU Visits. Note: A study participant was considered as completing a study period if she/he had completed the last scheduled study visit for that period. Note: Study participants who withdrew from the IMP but returned for all scheduled visits up to the last scheduled study visit for that period were considered as having completed the study period. Note: After the Double-Blind Treatment Period, study participants randomized to placebo switched to BKZ 160mg Q4W at Week 16. Note: One study participant had an AE of pneumonia between Week 48 and Week 52 that prevented the study participant from entering the extension study. When the AE had resolved and there was no concern for the study participant to roll over into the extension study, the SFU Visit was already completed. In the table, the study participant is only categorized under 'Entered extension study' because, per protocol requirement, the SFU Period is only derived for completed study participants who did not enter the extension study. Note: The Week 52 data cutoff date was 31 May 2022 [redacted]