Medicinrådet

Bilag til Medicinrådets vurdering af upadacitinib til behandling af kæmpecelle arteritis

Vers. 1.0

Bilagsoversigt

1. Ansøgers notat til Rådet vedr. upadacitinib til behandling af kæmpecelle arteritis
2. Forhandlingsnotat fra Amgros vedr. upadacitinib til behandling af kæmpecelle arteritis
3. Ansøgers endelige ansøgning vedr. upadacitinib til behandling af kæmpecelle arteritis

AbbVies svar på Medicinrådets vurdering af Rinvoq til kæmpecelle arteritis

Abbvie takker for et godt samarbejde med Medicinrådets sekretariat i forbindelse med vurderingen. AbbVie har dog et par punkter vi gerne vil addressere

Off-label komparator
Medicinrådet anbefalede i 2018 tocilizumab til kæmpecelle arteritis (GCA) i off-label dosering. Tocilizumab er godkendt til ugentlig dosering, men Medicinrådet har anbefalet dosering hver anden uge, hvilket betyder at en stor del af de danske GCA patienter får off-label dosering. AbbVie mener ikke det er relevant at anvende en off-label komparator og har derfor valgt at sammenligne med tocilizumab i ugentlig dosering i vores base case, men har samtidig suppleret med en scenarie analyse med en alternativ dosering baseret på danske real world evidence[1]. Denne analyse vælger Medicinrådet at afvise og antager i stedet at næsten alle patienter (90%) får den off-label dosering som Medicinrådet har anbefalet, der henvises ikke til data der underbygger denne antagelse. AbbVie mener at man burde bruge de danske data der er tilgængelige, da det alt andet lige er bedre end Medicinrådets antagelser.

Omkostninger
Medicinrådet har valgt kun at anvende lægemiddelomkostninger i den sundhedsøkonomiske analyse, og antager dermed at administration og monitoreringsomkostninger er identiske for tocilizumab og upadacitinib. AbbVie mener det er en oversimplificeret tilgang til analysen, da der er tydelige forskelle mellem de to lægemidler. F.eks. gives tocilizumab subkutant, mens upadacitinib tages peroralt. Medicinrådet antager da også forskellige omkostninger for JAK hæmmere (tofacitinib og baricitinib) og tocilizumab i arbejdet med behandlingsvejledninger[2], men altså ikke i denne vurdering.

Derudover, så underbygger både produktresuméet for tocilizumab (s. 44 og 78)[3] samt NICE vurderingen af tocilizumab til GCA (s. 168)[4] at der er øget monitorering og dermed omkostninger ved tocilizumab.

Medicinrådet antager også at en andel af tocilizumab patienterne vil få hjælp af en hjemmesygeplejerske (0-5%), men tillægger ikke dette nogen omkostning.

Samlet mener AbbVie at Medicinrådets udeladelse af administrations- og monitoreringsomkostninger medfører en undervurdering af omkostningerne forbundet med tocilizumab, som dermed skævvrider sammenligningen med upadacitinib.

Sikkerhed

Medicinrådet indikerer at man vil fortolke EMA's vurdering af sikkerhed som man har gjort indenfor andre sygdomsområder og "nedgradere" upadacitinib til brug efter tocilizumab. EMA's anbefaling er at JAK-hæmmere ikke anvendes til patienter med visse risikofaktorer, medmindre der ikke findes anden mulig behandling. Indenfor kronisk leddegigt og andre sygdomsområder har Medicinrådet valgt at nedgradere alle JAK-hæmmere for alle patienter, uden individuel vurdering af patienten. AbbVie vil gerne udfordre følgende:

<u>Medicinrådets fortolkning af EMA's anbefaling:</u>

EMA anbefaler at man skal vurdere patientens risikofaktorer. Patienter uden risikofaktorer kan behandles med JAK-hæmmere mens patienter med risikofaktorer kun skal behandles med JAK-hæmmere hvis andre muligheder er udtømt. Denne del har Medicinrådet udbredt til alle patienter uden individuel hensyntagen. AbbVie mener at Medicinrådet bør stole på at lægerne kan træffe et informeret valg på baggrund af en individuel patientvurdering.

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[1] https://pubmed.ncbi.nlm.nih.gov/38981187/
[2] https://medicinraadet.dk/media/a1odikfz/udvidet-sammenligningsgrundlag-version-2-0-kronisk-leddegigt.pdf
[3] https://www.ema.europa.eu/en/documents/product-information/roactemra-epar-product-information_en.pdf
[4] *https://www.nice.org.uk/guidance/ta518/evidence/appraisal-consultation-committee-papers-pdf-10958003965*

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JAK - klasseeffekt

Ikke alle JAK-hæmmere er ens. For eksempel er der ganske betydelige forskelle, når det kommer til farmakokinetikken for de forskellige JAK-hæmmere, der er tilgængelige på markedet. Lægemidlernes metabolisme er forskellig, deres halveringstid varierer og deres kemiske sammensætninger er ikke identisk. Disse forskelle kan føre til til forskelle i effektivitet og sikkerhedsprofiler for de forskellige JAK-hæmmere. Effekt- og sikkerhedsdata fra randomiserede kliniske forsøg i JAK-hæmmerklassen har også vist sig at være forskellige, skønt der ikke kan drages en endelig konklusion, da randomiserede direkte sammenligninger ikke er foretaget.

EMA har en formodning om en klasseeffekt for JAK-hæmmere, der giver øget risiko for blandt andet alvorlige kardiovaskulære hændelser og venøs tromboembolisme (VTE). Denne formodning er primært baseret på sikkerhedsdata for tofacitinib (ORAL surveillance studiet) og der er ikke fundet lignende sikkerhedssignaler for upadicitinib. Et nyligt publiceret studie blandt mere end 4000 patienter behandlet i kliniske forsøg fandt at upadicitinib er sammenlignelig med andre behandlinger (adalimumab og methotrexat) hvad angår forekomst af disse bivirkninger[5].

Tilsvarende fandt et studie blandt patienter i risikogruppen for kardiovaskulære hændelser (≥50 år ≥1 kardiovaskulære risikofaktorer) at patienter behandlet med upadicitinib 15 mg/dag havde sammenlignelig risiko for alvorlige kardiovaskulære hændelser og VTE som patienter behandlet med adalimumab eller methotrexat[6].

Samlet set er der nu sikkerhedsdata på mange tusinde patienter i kliniske trials, og der følges løbende op. Senest er der publiceret en opsamling på upadicitinib patienter indenfor kronisk leddegigt, psoriasisartrit, rygsøjlegigt og atopisk dermatit der samler data på mere end 8500 patienter og mere end 27000 patientår. Studiet finder at upadicitinib generelt er veltolereret og der ikke er nye sikkerhedssignaler [7].

Samlet set er upadicitinib et veltolereret og effektivt lægemiddel og tilbyder en ny behandlingsmulighed til en gruppe af patienter der nu kun kan behandles med tocilizumab.

[5] https://pubmed.ncbi.nlm.nih.gov/37945286/
[6] https://pubmed.ncbi.nlm.nih.gov/37308218/
[7] https://pubmed.ncbi.nlm.nih.gov/40875187/

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DBS, KLE

Forhandlingsnotat

Dato for behandling i Medicinrådet	18.02.2026
Leverandør	Abbvie
Lægemiddel	Rinvoq (upadacitinib)
Ansøgt indikation	Kæmpecellearteritis hos voksne patienter
Nyt lægemiddel / indikationsudvidelse	Indikationsudvidelse

Prisinformation

Amgros har følgende aftalepris på Rinvoq (upadacitinib):

Tabel 1: Aftalepris

Lægemiddel	Styrke (Pakningsstørrelse)	AIP (DKK)	Nuværende SAIP, (DKK)	Nuværende rabat ift. AIP
Rinvoq	15 mg (28 stk., tablet)	5.893,83	[redacted]	[redacted]
Rinvoq	30 mg (28 stk., tablet)	11.787,66	[redacted]	[redacted]
Rinvoq	45 mg (28 stk., tablet)	17.681,49	[redacted]	[redacted]

Aftaleforhold

Amgros har en eksisterende aftale på Rinvoq.
[redacted]

Konkurrencesituationen

[redacted]

Tabel 2 viser lægemiddeludgifter på udvalgte sammenlignelige lægemidler.

Tabel 1: Sammenligning af lægemiddeludgifter pr. patient

Lægemiddel	Styrke (pakningsstørrelse)	Dosering*	Pris pr. pakning (SAIP, DKK)	Lægemiddeludgift pr. år (SAIP, DKK)
Rinvoq (upadacitinib)	15 mg (28 stk., tablet)	15 mg, oralt, dagligt	[redacted]	[redacted]
RoActemra (tocilizumab)	162 mg (4 stk., pen)	162 mg, s.c., hver 2. uge	[redacted]	[redacted]

*Jf. Medicinrådets vurderingsrapport.

Status fra andre lande

Tabel 2: Status fra andre lande

Land	Status	Link
Norge	Ikke anbefalet	Link til beslutning
England	Under vurdering	Link til status
Sverige	Ikke ansøgt	Link til status

Opsummering

[redacted].

Application for the assessment of upadacitinib (RINVOQ)® for treatment of Giant Cell Arteritis

Contact information

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Tables and Figures

Abbreviations

CI	Confidence interval
CRP	C-reactive protein
CS	Corticosteroid
CT	Computed tomography
ESR	Erythrocyte sedimentation rate
GCA	Giant cell arteritis
HR	Hazard ratio
IL	Interleukin
IPD	Individual patient data
ITC	Indirect treatment comparison
JAKi	Janus kinase inhibitor
KM	Kaplan-Meier
MAIC	Matching-adjusted indirect comparison
MRI	Magnetic resonance imaging
OR	Odds ratio
PBO	Placebo
PET	Positron emission tomography
RCT	Randomized clinical trial
PMR	Polymyalgia rheumatica
QW	Every week
Q2W	Every 2 weeks
Q3W	Every 3 weeks
SC	Subcutaneous
SLR	Systematic literature review
TCZQW	Tocilizumab every week
UPA15	Upadacitinib 15 mg

1. Regulatory information on the medicine

Overview of the medicine	
Proprietary name	RINVOQ®
Generic name	upadacitinib
Therapeutic indication as defined by EMA	Rinvoq is indicated for treatment of adult patients with giant cell arteritis (GCA)
Marketing authorization holder in Denmark	AbbVie Deutschland GmbH & Co.
ATC code	L04AF03
Combination therapy and/or co-medication	In GCA, Rinvoq will be administered together with oral corticosteroids.
Date of EC approval	14th April 2025
Has the medicine received a conditional marketing authorization?	No
Accelerated assessment in the European Medicines Agency (EMA)	No
Orphan drug designation (include date)	No
Other therapeutic indications approved by EMA	Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Non-radiographic axial spondylarthritis, Atopic Dermatitis, Ulcerative Colitis, Crohn's disease
Other indications that have been evaluated by the DMC (yes/no)	Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis. Non-radiographic axial spondylarthritis, Atopic Dermatitis, Ulcerative Colitis, Crohn's disease
Joint Nordic assessment (JNHB)	No, different treatment guidelines in the Nordic countries
Dispensing group	BEGR/NBS
Packaging – types, sizes/number of units and concentrations	Rinvoq 15 mg, 28 stk. (blister)

2. Summary table

Summary	
Indication relevant for the assessment	Treatment of Giant Cell Arteritis (GCA) in adult patients.
Dosage regiment and administration	The recommended dose of upadacitinib for GCA is 15 mg once daily.
Choice of comparator	Tocilizumab 162 mg solution for subcutaneous injection in pre-filled pen once every week
Prognosis with current treatment (comparator)	GCA is a chronic immune-mediated disease characterized by the inflammation of medium to large arteries, and there is no curative treatment. There are few treatment options for patients with tocilizumab being the only treatment approved for GCA, in addition to corticosteroid treatment. Treatment usually leads to remission, but later relapses are very common. The morbidity and mortality of patients with GCA is increased, due to the disease itself but also due to the corticosteroid treatment.
Type of evidence for the clinical evaluation	Upadacitinib will be compared to tocilizumab using an indirect treatment comparison. A matching-adjusted indirect comparison (MAIC) was conducted to account for differences in baseline characteristics between the two pivotal trials.
Most important efficacy endpoints (Difference/gain compared to comparator)	The most important efficacy endpoint is difference compared to tocilizumab in the proportion of participants in sustained remission at Week 52, difference in time-to-first flare, and time-to-subsequent flares and HrQoL.
Most important serious adverse events for the intervention and comparator	The most important serious adverse event for both upadacitinib and tocilizumab in GCA is serious infections. Additionally, for upadacitinib JAK inhibitor class-specific risks such as MACE, malignancy, and all-cause mortality in older adults or those with cardiovascular risk factors, while tocilizumab is also associated with complications of diverticulitis and hypersensitivity reactions
Impact on health-related quality of life	Clinical documentation: EuroQol Five Dimensions Five Levels Questionnaire (EQ-5D-5L), SF-36 PCS and FACIT-Fatigue Health economic model: N/A
Type of economic analysis that is submitted	Cost minimization analysis
Data sources used to model the clinical effects	SELECT- GCA phase 3 trial GiACTA phase 3 trial

Summary	
Data sources used to model the health-related quality of life	N/A
Life years gained	Assumed clinical equivalent
QALYs gained	Assumed clinical equivalent
Incremental costs	-28 426 DKK per patient
ICER (DKK/QALY)	N/A
Uncertainty associated with the ICER estimate	Scenario analyses were conducted
Number of eligible patients in Denmark	Incidence: 22 per 100 000 for patients ≥ 50 Prevalence: 127 per 100 000 for patients ≥ 50
Budget impact (in year 5)	-4 724 981,43 DKK

3. The patient population, intervention, choice of comparator(s) and relevant outcomes

3.1 The medical condition

Giant Cell Arteritis (GCA) is an autoimmune disease characterized by granulomatous inflammation of the three-layered vessel wall, involving activated macrophages fused into multinucleated giant cells.(1) GCA is also known as temporal arteritis and most commonly affects the temporal artery, but also other cranial arteries, the aorta and other large arteries. (2–4)

3.1.1 Pathophysiology and etiology

The pathophysiology of GCA is thought to involve a dysregulated and inappropriate immune response to vascular endothelial injury, with autoimmune attacks specifically targeted towards the aorta, extracranial aortic vessel and the upper extremity aortic branch vessel. (1,4)

The cause of GCA is, as for most autoimmunological diseases, multifactorial. Dendritic cells in the arterial wall are activated by an unknown trigger, which may be a microbial antigen or an autoantigen, in turn activating an inflammatory cascade by releasing IFN-γ. The cascade of inflammatory events in GCA leads to activation of macrophages and their fusion into multinucleated giant cells and granuloma formation at the junction between the arterial intima and media layers, leading to arterial wall injury.(5,6) These structural changes in the arterial wall - a breakdown of elastic fibres that weakens the muscular layer of the artery and compromises blood flow to tissues and organs, leading to ischemia. (1)

Some of the key cytokines involved in the signaling and the amplification of the immune response in GCA (i.e., IL-6 and IFN-γ) intracellularly signal through the JAK/STAT pathway. Their signaling induces the production and release of more cytokines, which in turn attract more macrophages, fibroblasts and T cells to the arterial wall, further amplifying the immune response and leading to the persistent effect that characterizes the nature of GCA. (4,5,7)

The etiology of GCA is unclear, with literature suggesting that both genetic and environmental risk factors contribute to the development of GCA.(8) Genotyping studies suggest that there is an association between GCA susceptibility and certain human leukocyte antigen (HLA) class I and class II alleles.(9,10) The involvement of environmental risk factors in the development of GCA is less clear, and the data are limited. A history of smoking has been shown to increase the susceptibility of GCA in women only. (11)

3.1.2 Symptoms and disease progression

The majority of patients, approximately 80%, present with symptoms due to **cranial ischemia** (Figure 1).(12) These include temporal artery thickening, loss of pulse, headache (80%), scalp tenderness (23– 52%), jaw claudication/pain (9– 45%), vision loss (transient: 14%, permanent: 17%), tongue edema/pain (25%), and in some rare cases, tongue necrosis.(2,3,6,13–18) Elevated inflammatory biomarkers (ESR and/or CRP) are also present in a large majority of patients with GCA (>90%). (2)

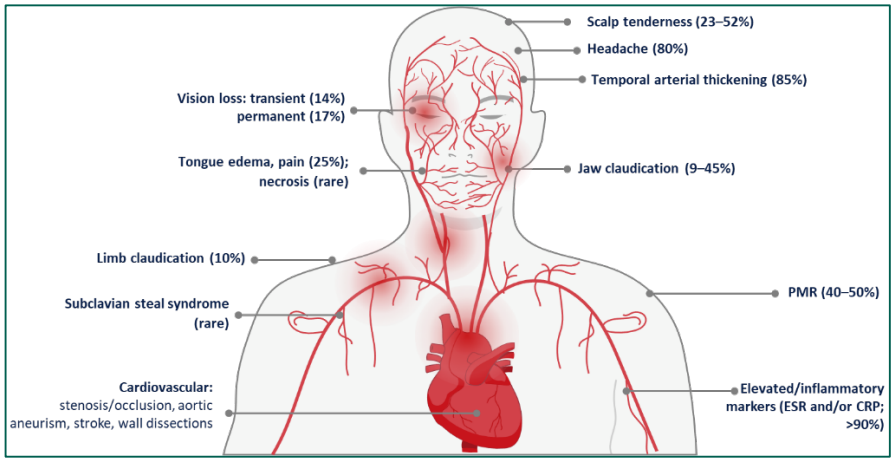


Figure 1. Typical symptoms in GCA patients (2, 5-7, 25, 80)

The most concerning consequence of untreated GCA is irreversible **vision loss** caused by the disease affecting the arteries supplying the optic nerve. Studies report that 8–28% of patients experience vision loss caused largely by ischemic events. (17,19–22)

A distinct subgroup of patients with GCA have **extracranial involvement** where the large vessels (e.g., the aorta and its major branches) are affected; this manifests as limb claudication or subclavian steal syndrome. (12,23,24) **Constitutional symptoms** as a result of extracranial involvement are present in up to 50% of GCA patients. These symptoms include fever, fatigue, night sweats and anorexia/weight loss. (25)

Extracranial stenosis occurring due to untreated GCA results in **cardiovascular complications** such as aortic aneurysms, strokes and wall dissections.(4) Cerebrovascular accidents may occur at GCA disease onset in 2.8–7.2% of patients. (26)

GCA is closely associated with **Polymyalgia rheumatica (PMR)**, which occurs in 40–60% of patients with GCA, see Figure 2. PMR is characterized by body pain and proximal myalgia; pain and stiffness of the neck, shoulders, and pelvic girdle leading to impaired physical functioning.(2,27) Between 16–21% of patients with PMR may develop GCA, particularly if left untreated.(28)

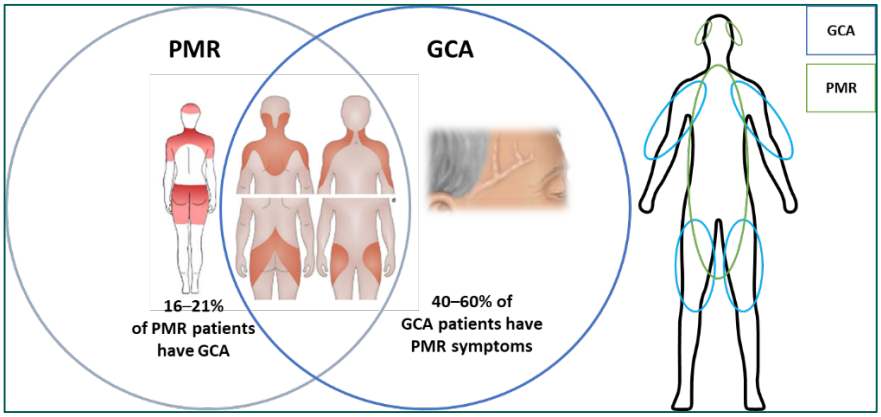


Figure 2. The overlap between GCA and PMR symptoms (left) and the localization of inflammation (right) (2,16,26,29)

Overlapping symptoms between GCA and PMR include constitutional symptoms, headaches, temporal arterial abnormalities, visual disturbance/loss, jaw claudication, tongue pain, bilateral shoulder/hip pain, morning stiffness, peripheral arthritis, limb claudication, bruits, and Reynaud's phenomenon.(16)

Untreated active GCA is an emergency and carries a substantial risk of permanent visual loss and other ischaemic complications.(14) Active GCA is treated to remission. However, relapses to active disease are common and there is no curative treatment for GCA.

3.1.3 Mortality and comorbidities in GCA

Patients with GCA have a higher prevalence of comorbidities compared with the general population.30 A Swedish matched cohort study found that patients with GCA had

statistically significant higher risk of comorbidities, compared to the matched cohort without GCA, as shown in Table 1. In addition, patients with GCA were found to have an increased risk of severe infection, RR 1.85 (95% CI: 1.57 – 2.18, p<0.001) compared to the matched cohort (30)

Table 1. Rates and rate ration of selected comorbidities among 768 patients with GCA and 3066 reference subjects matched for age, sex and date of diagnosis. (30)

Comorbidity	ICD-10 Codes	GCA, n = 768	GCA, Person-yrs	Rate	Reference, n = 3066	Reference, Person-yrs	Rate	Rate Ratio	95% CI	p
Ischemic heart disease[1]	I20–I25	150	4027	37.2	521	16,837	30.9	1.20	1.00–1.44	0.05
Cerebrovascular accident[1]	I60–I69	110	4147	26.5	333	17,636	18.8	1.40	1.12–1.74	0.005
Hypertension	I10–I15	407	2884	141	1421	13,155	108	1.31	1.17–1.46	< 0.001
Diabetes mellitus	E10–E14	133	4006	33.2	431	16,716	25.7	1.29	1.05–1.56	0.01
VTE[1]		46	4364	10.5	82	18,339	4.47	2.36	1.61–3.40	< 0.001
Thyroid diseases	E00–E07	122	3960	30.8	343	17,265	19.8	1.55	1.25–1.91	< 0.001
Dyslipoproteinemias	E78	76	4252	17.8	323	17,495	18.4	0.97	0.74–1.24	0.7
Psychiatric diseases	F00–F99	290	3495	82.9	990	15,284	64.7	1.28	1.12–1.46	0.001
Osteoporosis	M80–M85	188	3722	50.5	313	17,429	17.9	2.81	2.33–3.37	< 0.001
Fractures		185	3744	49.4	528	16,675	31.6	1.56	1.31–1.85	< 0.001

[1] Only inpatient diagnoses; all other diagnoses are for both inpatient and outpatient diagnoses. GCA: giant cell arteritis; ICD-10: International Classification of Diseases, 10th ed; VTE: venous thromboembolic diseases: pulmonary embolus and/or deep vein thrombosis: I260–I269 and/or I800–I809; fractures: M48.4, M48.5, S22.0–S22.3, S32.0–S32.8, S42.2, S42.3, S52.2–S52.6, S72.0–S72.9, S82.1–S82.6.

Similar findings are found in other studies. A matched cohort study conducted in Canada reported that patients with GCA 2.21-fold (95% CI: 1.68–2.91) increased risk for stroke compared to age- sex- and entry-time matched non-GCA cases.(31) Similarly, a study using the UK-based CPRD which identified 9,778 newly diagnosed GCA patients reported that 10-year cumulative incidence rate for stroke from 1990 to 2014 was 11.7 (95% CI: 10.6–12.8) cases per 100 among GCA patients.(32) The study also found other comorbidities with a higher prevalence among GCA patients in comparison to individuals with no GCA include diabetes, hypertension, thromboembolism, aortic aneurysm, dyslipidaemia, depression, psoriasis and rheumatoid arthritis. (32)

Some comorbidities may be exacerbated due to adverse events associated with corticosteroid exposure (especially after long-term use). Corticosteroid use can lead to significantly increased risk of osteoporosis, fractures, hypertension, diabetes, infection and gastrointestinal effects.(18,33)

GCA is associated with an increased all-cause mortality. A high risk of mortality within the first year is likely due to active GCA itself, intensive treatment with corticosteroids, treatment-related AEs and comorbidities related to active disease. (29). In a Danish study, the adjusted RDs and RRs of deaths in the GCA cohort were 2.2% (95% CI: 1.7, 2.7) and 1.49 (95% CI: 1.36, 1.64) after 1 year, and 2.1% (95% CI: 1.0, 3.3) and 1.03 (95% CI: 1.00, 1.05) 10 years after index, compared to a matched reference cohort. GCA patients was found to have a higher risk of death due to infectious, endocrine, cardiovascular and gastrointestinal diseases. Cause-specific mortality indicates that mortality in GCA may in part be due to corticosteroid-related complications. (34)

In summary, patients with GCA have a high disease burden from co-morbidities and increased mortality, caused by the disease itself and by treatment with corticosteroids. There is an unmet need for additional treatment options, both to increase the likelihood of long-term remission and to reduce the cumulative corticosteroid dose.

3.2 Patient population

GCA is most common in the Scandinavian countries and in populations of Scandinavian origin. GCA is most common in patients >70 years and rarely affects individuals <50 years of age. A Danish study reports an average annual incidence rate of GCA among persons aged>50 years of 22.2 (95% CI: 21.8-22.7) per 100,000 aged >50 years, and also the difference in incidence rates depending on patient age, which is shown in Figure 3. (35) The annual incidence rate fluctuated during the study period, but no trend could be seen. A constant incidence rate is assumed over the 5 years in Table 2

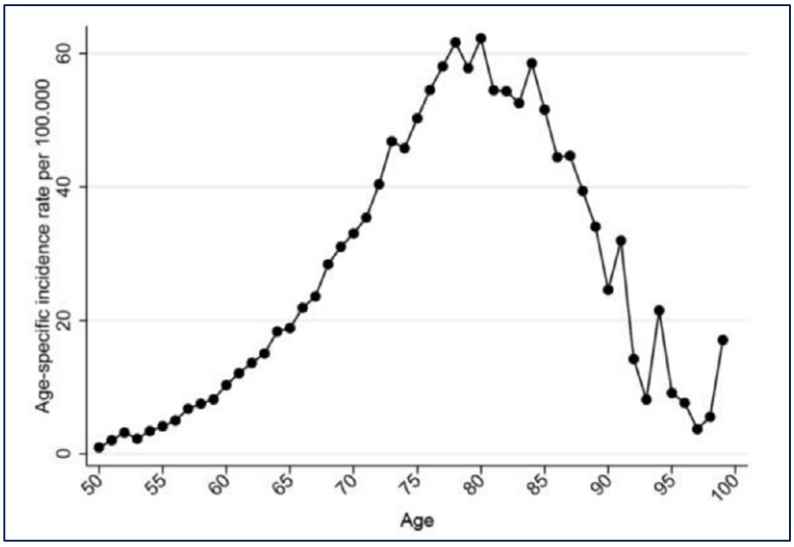


Figure 3. Age specific incidence rates in a Danish cohort (35).

The prevalence of GCA is not as well reported as the incidence, potentially due to the nature of the disease, with many patients achieving remission off treatment and not included in prevalence estimates. (36) No consistent estimation of global prevalence can be made (37) and is reported as not available (NA) in Table 2. An overall point prevalence of biopsy-confirmed GCA of 127 per 100 000 people > 50 has been reported from a Swedish cohort in Skåne. (38). The prevalence of GCA is assumed to be similar between the south of Sweden and Denmark.

This application is for all patients covered by the approved indication for upadacitinib in GCA, adult patients with GCA. Based on the incidence rates in Table 2 (22,2 per 100 000 individuals over age 50), and the number of individuals over age 50 in Denmark (2 438 000 as of April 2025) (39), about 540 patients will be diagnosed with GCA in Denmark every year. As both incidence rates and prevalence rates are stable over time, see Table 2, no increase of eligible patients are assumed over time.

Table 2. Incidence and prevalence in the past 5 years.

Year	2020	2021	2022	2023	2024
Incidence in Denmark (35)	22 per 100 000 for patients ≥ 50	22 per 100 000 for patients ≥ 50	22 per 100 000 for patients ≥ 50	22 per. 100 000 for patients ≥ 50	22 per. 100 000 for patients ≥ 50
Prevalence in Denmark (38)	127 per 100 000 for patients ≥ 50	127 per 100 000 for patients ≥ 50	127 per 100 000 for patients ≥ 50	127 per 100 000 for patients ≥ 50	127 per 100 000 for patients ≥ 50
Global prevalence	NA	NA	NA	NA	NA

NA= Not Available

Given the approved indication for upadacitinib, all these patients are eligible for treatment with upadacitinib, but in clinical practice corticosteroid treatment in monotherapy is expected to continue to be the first line treatment choice for newly diagnosed patients, and for many patients after relapse. (40) 26 % of patients treated with tocilizumab in Denmark are newly-diagnosed (41), the rest of the newly diagnosed patients, 74%, are assumed to be treated with corticosteroids. The relapse rate for GCA patients treated with CS has been found to be about 50 % in a recent meta-analysis. (42) The proportion of patients eligible for treatment with either upadacitinib or tocilizumab based on these assumptions is 26% of newly diagnosed and half of the 74% treated with corticosteroids, a total of 63% of the patients diagnosed with GCA. This corresponds to 340 of the 540 patients diagnosed each year, see Table 3.

Table 3. Estimated number of patients eligible for treatment with upadacitinib or tocilizumab.

Year	Year 1	Year 2	Year 3	Year 4	Year 5
Number of patients diagnosed with GCA in Denmark in the coming years	540	540	540	540	540
Number of patients in Denmark who are eligible for treatment in the coming years	340	340	340	340	340

3.3 Current treatment options

There are several similar guidelines for diagnosis, treatment and clinical pathways for GCA, including guidelines from European Alliance of Associations for Rheumatology (EULAR) and the Danish Rheumatology Association.

GCA is diagnosed using a combination of clinical and laboratory assessments combined diagnostic imaging (PET, MRT, CT or ultrasound). Temporal arterial biopsy (TAB) is recommended when diagnostic imaging is unavailable or to confirm diagnosis if other criteria are uncertain. (40) Typical symptoms and findings upon clinical examinations are summarized in Table 4 below. Please refer to section 3.1.2 for further descriptions of the symptoms of GCA. GCA patients also typically have elevated biomarker levels of C-reactive protein (CRP), and an increased erythrocyte sedimentation rate (ESR) in response to elevated levels of IL-6.

Table 4. Symptoms and clinical findings used in the diagnosis of GCA. (14)

Symptoms suggestive of GCA	Key findings on clinical examination
• New onset of persistent localized headache, often in the temporal area. • Constitutional symptoms (e.g., weight loss >2 kg, low-grade fever, fatigue, night sweats). • Jaw and/or tongue claudication. • Acute visual symptoms such as amaurosis fugax, acute visual loss, diplopia. • Symptoms of polymyalgia rheumatica. • Limb claudication.	• Tenderness and / or thickening of the superficial temporal arteries with or without reduced pulsation. • Scalp tenderness. • Bruits (particularly in the axilla). • Reduced pulses/blood pressure of the upper limbs. • Pathological findings during ophthalmologic examination including anterior ischemic optic neuropathy, oculomotor cranial nerve palsy/palsies, central retinal artery occlusion, branch retinal artery occlusion and/or choroidal ischemia.

The Danish Rheumatology Association has published a treatment guideline for GCA, including the treatment algorithm in Figure 4. (38)

Depending on whether the patient has newly diagnosed GCA or relapse/refractory disease, and taking the patient´s individual risk for glucocorticoid adverse events into account, an immunosuppressive treatment is chosen:

1. Prednisolone monotherapy with a long 52-week taper regimen, or
2. Prednisolone in a shorter 30-week taper regimen in combination with tocilizumab.

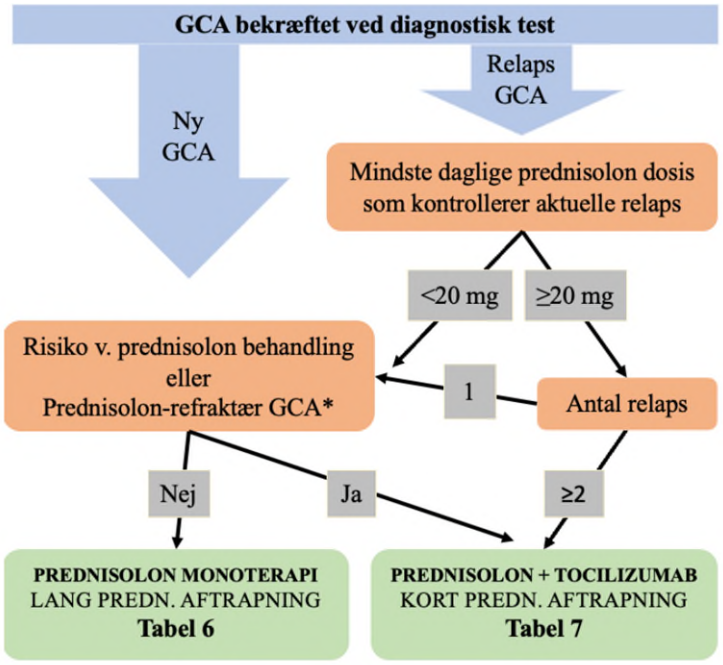


Figure 4. Treatment algorithm for GCA in Denmark (40)

The **risk stratification of the risk with prednisolone treatment** is based on current comorbidities, previous or current prednisolone adverse events and the expected future need for prednisolone. A risk evaluation is especially relevant for patients with:

1. *Established comorbidities and comorbidities* caused by prednisolone: severe cardiovascular disease, osteoporosis, diabetes mellitus, glaucoma or severe psychiatric diseases or other unacceptable adverse events caused by prednisolone treatment.
2. *Relapse GCA or refractory GCA*: expected unacceptable need for prednisolone, for instance recurrent relapses despite 7,5 – 20 mg prednisolone daily and limited likelihood of successful prednisolone taper.(40)

Patients presenting with visual symptoms or jaw claudication should be treated with high dose peroral or intravenous corticosteroid treatment without delay. After the initial high dose treatment, corticosteroids are tapered according to the same principle as for patients without visual symptoms or jaw claudication. (40)

3.3.1 Corticosteroids

The primary treatment for GCA consists of corticosteroids, commonly prednisolone. Early administration of an effective dose of corticosteroids can have a protective effect against the development of comorbidities, especially vision impairment.(43) Corticosteroids inhibit several anti-inflammatory pathways, suppress interleukins transcription, cytokine expression, T-cell activation and promote lymphocyte apoptosis to reduce inflammation in the arteries. (44) This in turn can prevent acute symptoms of GCA.

Despite remaining the gold-standard treatment for GCA, corticosteroids are associated with a high rate of relapse, particularly during or after tapering.(25) Relapses mainly

occur within the first year of diagnosis, often when corticosteroids are tapered to below 10 mg daily (of prednisone or equivalent), or when corticosteroids are tapered too quickly.(21,45) Most patients with GCA treated only with corticosteroids relapse (40–80%), while <20% of patients achieve remission.(45,46) The only randomized clinical trial investigating dosing and tapering of corticosteroid is the GiACTA study, where corticosteroids in 26- and 52 – week tapers were included as comparator arms to tocilizumab. 18% of 51 patients receiving placebo alongside a 52-week corticosteroid taper regimen achieved corticosteroid-free sustained remission at week 52. (45)

Long-term or repeated corticosteroid treatment is used to manage relapses.(14,43) A Danish cohort study show that on average 73%, 47% and 37% of patients with GCA are treated with corticosteroids after 2, 5 and 10 years. The median cumulative corticosteroid dose among patients with a minimum of 2 years follow-up was 11 000 mg (IQE: 6 500 – 18 000 mg)(35) Increased cumulative steroid exposure increases the risk of corticosteroid-related AEs and toxicity, with >85% of patients developing corticosteroid-related AEs. (25,33,46,47)

Common corticosteroid related AE:s are shown in Figure 5. Before treatment initiation with corticosteroids a risk stratification of the risk or adverse events or impact on comorbidities is done, as described above. Treatment with corticosteroids contribute to the increased morbidity and mortality seen in patients with GCA. (30,34)

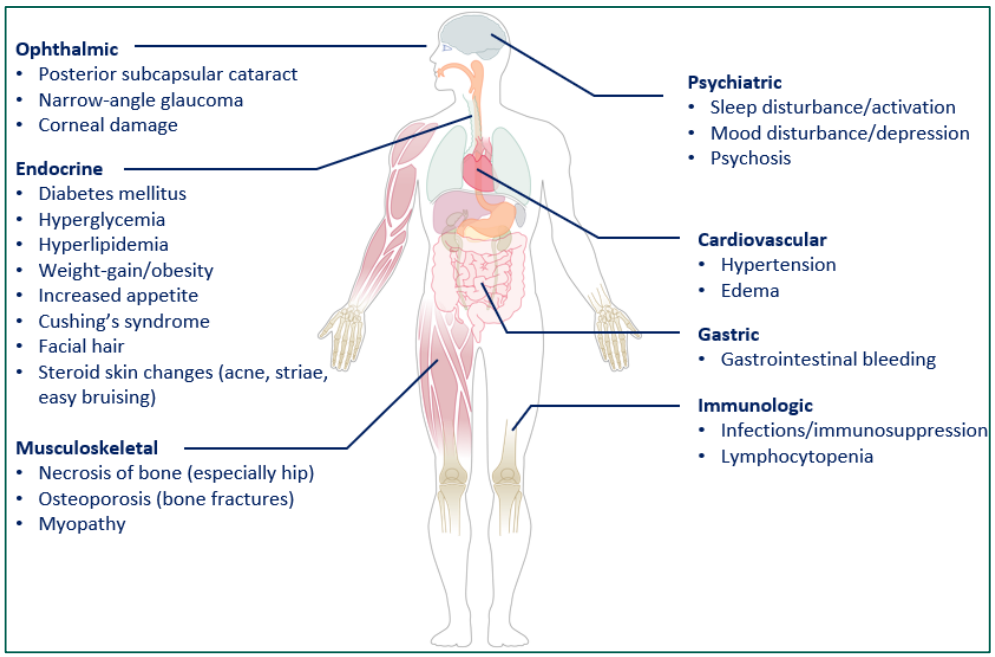


Figure 5. Corticosteroid- related AEs (47,48)

3.3.2 Tocilizumab

Tocilizumab is an IL-6 inhibitor, and the only advanced therapy currently approved to treat GCA. IL-6 participates in the activation of T cells and enables the differentiation of Th17 cells. Tocilizumab blocks IL-6 action and inhibits the downstream inflammatory cascade. (49) It is administered via an subcutaneous injection, with the approved dose of

162 mg weekly, in combination with a tapering course of corticosteroids, or alone following discontinuation of corticosteroids. (50) In the Danish treatment guidelines tocilizumab is recommended as an addition to treatment with prednisolone in patients to reduce cumulative steroid dose and the risk for relapse. (40).

As described in section 3.5, tocilizumab is considered the most relevant comparator to upadacitinib as upadacitinib is expected to be used in a similar way as tocilizumab in clinical practice. Tocilizumab is therefore further described in sections 3.5, 3.6 and 6.

Tocilizumab has been investigated in the GiACTA trial, a Phase III, multicenter, randomized, placebo-controlled, double-dummy, double-blind, parallel-group trial in patients with GCA. A 52-week blinded period (Part-1) was followed by a 104-week open-label period (Part 2), with a total study duration of 156 weeks. In Part 1 of the trial 251 patients were randomized in a 2:1:1:1 ratio to receive the following treatments:

- Group A: 162 mg of subcutaneous (SC) TCZ every week (qw) + 26-week prednisone taper regimen (n = 100)
- Group B: 162 mg of SC TCZ every other week (q2w) + 26-week prednisone taper regimen (n = 50)
- Group C: SC placebo + 26-week prednisone taper regimen (n = 50)
- Group D: SC placebo + 52-week prednisone taper regimen (n = 51)

Sustained remission, defined as remission from week 12 through week 52 while adhering to the corticosteroid (prednisone) taper, was achieved by 53% and 56% of patients receiving 162 mg of tocilizumab subcutaneously once every other week and once weekly, respectively. In comparison, 14% of patients receiving placebo with a 26-week corticosteroid taper regimen and 18% of patients receiving placebo with a 52-week corticosteroid taper regimen, respectively, achieved sustained remission. Tocilizumab also reduced the time to next flare, the proportion of patients experiencing flares and the cumulative corticosteroid exposure compared to placebo.(45)

The Danish treatment guideline recommends 162 mg tocilizumab every other week, despite this not being the approved dose.(40) Patients, both newly diagnosed and with relapsed disease, are however initiated on both doses in Danish clinical practice (41). The treatment guideline recommends an increase to weekly dosing in case of relapse (40). It should be noted that patients with relapsed disease treated with tocilizumab every other week did not have a statistically significant lower risk of flare (relapse) compared to either of the placebo arms in the GiACTA trial (45).

Tocilizumab treatment beyond 12 months of treatment could be discontinued if the patient has been in prednisolone-free remission for at least 3 months prior. (40). According to the SmPC for tocilizumab, the recommended treatment length is 52 weeks. Treatment beyond 52 weeks should be guided by disease activity, physician discretion, and patient choice. (50)

Monitoring for disease activity is done using the same principles used at diagnosis. Normally, the acute phase reactants are very rarely normal during relapse. However, this is not the case during tocilizumab treatment.(40) According to the EULAR guideline, patients treated with tocilizumab may have falsely reassuring normal CRP and/or ESR

values. These are caused by tocilizumab suppressing the synthesis of CRP in the liver, which might result in normal CRP – levels despite active inflammation. (14) During follow-up of clinical response during tocilizumab treatment it is recommended that outcome measures that do not include acute phase reactants be used to evaluate disease activity (51).

A consulted Danish clinician described the issues in clinical practice following treatment with tocilizumab caused by the CRP and/or ESR suppression and the safety profile of tocilizumab:

"These markers can mask ongoing subclinical vasculitis, especially in large vessels or cranial arteries. This phenomenon underscores the risk of irreversible ischemic events, such as vision loss or aortic complications, in patients whose disease is not truly controlled. Thus, while valuable, inflammatory markers must be interpreted cautiously and always considered alongside clinical findings.

Inflammatory markers like CRP and ESR remain crucial for serial assessments, despite their limitations, especially in the context of IL-6 inhibition, where these markers may be suppressed. In particular, patients with cranial manifestations or active aortitis are particularly vulnerable to severe ischemic complications. In these high-risk cases, reliance on inflammatory markers is essential but must be contextualized, as normal values under IL-6 blockade may mislead clinicians. Rigorous clinical monitoring and, where feasible, imaging should complement laboratory data.

Additionally, there may be challenges with IL-6 inhibition in clinical practice. Although IL-6 inhibition has shown efficacy in reducing inflammation and steroid burden, its use presents several clinical challenges. These include an increased risk of neutropenia, elevated liver enzymes, and heightened susceptibility to gastrointestinal complications, notably in patients with diverticulosis. These safety concerns require careful screening and ongoing monitoring.

All the above underscore the urgent need for alternative therapeutic targets that act beyond IL-6 inhibition and for developing more reliable biomarkers to monitor disease activity. Such advancements are critical to improve diagnostic accuracy, guide individualised treatment strategies, and ultimately prevent irreversible complications in patients with GCA "(52)

3.3.3 Additional treatment options

A few additional treatment options are mentioned in the Danish treatment guideline. (40)

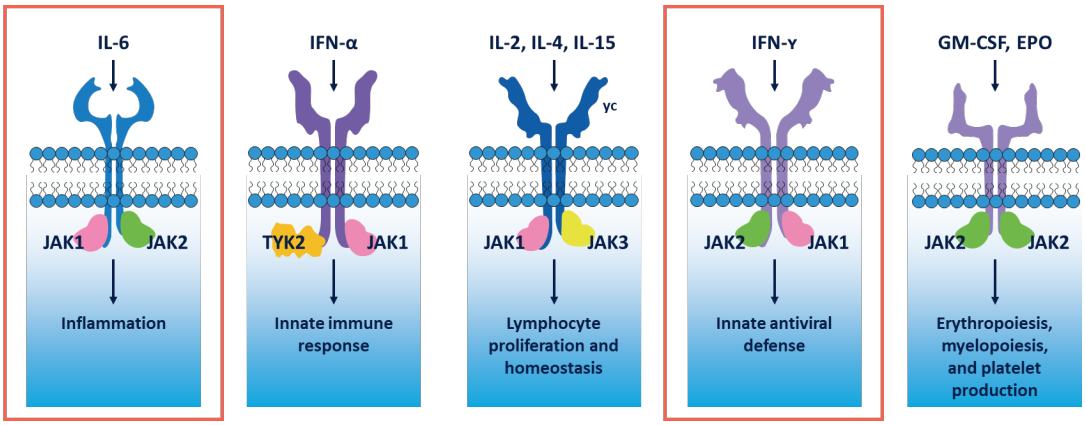
Methotrexate is not recommended as a first line treatment, due to low to moderate evidence of efficacy for treating GCA and is considered an option when tocilizumab can not be used. Leflunomide and abatacept are mentioned as options after treatment failure with other treatments, but there is little scientific evidence. Ciclosporin A, TNF-inhibitors, cyclofosfamid and azatioprin are not recommended for use in GCA in the Danish treatment guideline due to negative outcomes in clinical trials and/or negative safety profiles.

Neither of these treatments are approved for treating GCA. This highlights the need for additional treatment options for patients with GCA, with well- documented efficacy and safety profiles. There are currently no suitable treatment options as alternatives to tocilizumab for patients who need either higher likelihood of remission compared to treatment with corticosteroids alone, or who need to reduce the corticosteroid burden. There is also an unmet need for treatments with additional modes of action for treating GCA, as well as other routes of administration.

3.4 The intervention

Overview of intervention	
Indication relevant for the assessment	Rinvoq is indicated for the treatment of Giant Cell Arteritis (GCA) in adult patients.
ATMP	N/A
Method of administration	Oral tablet
Dosing	The recommended dose of upadacitinib is 15 mg once daily in combination with a 26-week tapering course of corticosteroids. Upadacitinib monotherapy should not be used for the treatment of acute relapses. .
Dosing in the health economic model (including relative dose intensity)	The dosing used in the health economic model is 15 mg as an oral tablet taken once daily.
Should the medicine be administered with other medicines?	In GCA, Rinvoq will be administered together with a 26-week taper regimen with oral corticosteroids.
Treatment duration / criteria for end of treatment	Based upon the chronic nature of giant cell arteritis, upadacitinib 15 mg once daily can be continued as monotherapy following discontinuation of corticosteroids. Treatment beyond 52 weeks should be guided by disease activity, physician discretion, and patient choice
Necessary monitoring, both during administration and during the treatment period	Blood test, liver function test, and lipid panel test
Need for diagnostics or other tests (e.g. companion diagnostics). How are these included in the model?	N/A
Package size(s)	28 tablets pr. package

Targeting the JAK signaling pathway for the treatment of autoimmune diseases such as GCA is supported by the pathogenesis of the disease. As described in section 1.1, the JAK/STAT pathway has a major role in the pathogenesis of GCA, whose main proinflammatory drivers are the cytokines IL-6 and IFN-γ, which as shown in Figure 6 are dependent on JAK1 for signal transduction. The activation of JAK-signaling initiates the expression of survival factors, cytokines, chemokines, and other molecules that facilitate leukocyte trafficking and proliferation and contribute to the pathogenesis of multiple inflammatory and autoimmune diseases. (2)



Abbreviations: EPO: erythropoietin; GSM-CSF: granulocyte macrophage colony-stimulating factor; IFN-γ: interferon gamma; IL: interleukin; JAK/STAT: janus kinase/signal transducer and activator of transcription; TYK: tyrosine kinase

Figure 6. JAK1 affecting downstream processes in cytokine signalling pathways. The most relevant cytokines involved in the pathogenesis of GCA, IL 6 and INF-γ are represented on the highlighted boxes. (53)

Inhibiting both IL-6 and IFN-γ, upadacitinib has a different pharmacological profile compared to tocilizumab which inhibits IL-6 only. Data suggest that a level of subclinical inflammation persists in patients with GCA, driven largely by IFN-γ signalling. (54) Persistent inflammation among GCA patients treated with tocilizumab has been supported by studies that report vasculitis of medium and large vessels upon autopsy despite apparent clinical response to therapy.(55) The IL-6 cytokine pathway is highly responsive to corticosteroids, while the IFN-γ pathway is resistant to corticosteroid-mediated immunosuppression. (56)

3.4.1 The intervention in relation to Danish clinical practice

The SELECT-GCA study included patients with either newly diagnosed or relapsed GCA, comparing upadacitinib in combination with a 26- week taper of corticosteroids, with placebo and a 52- week taper of corticosteroids. Despite upadacitinib demonstrating superior efficacy to corticosteroid treatment and to significantly reduce the cumulative corticosteroid dose, upadacitinib is not expected to replace corticosteroid monotherapy in the treatment algorithm. Rather, upadacitinib will be a treatment alternative to tocilizumab for patients who need to reduce the corticosteroid dose and/or increase the likelihood of sustained remission. The treatment algorithm will not be further altered if upadacitinib is recommended.

3.5 Choice of comparator(s)

Tocilizumab is the only treatment alternative with the approved indication to treat GCA and is used in Danish clinical practice for patients who need to reduce the cumulative corticosteroid dose and/or to improve treatment outcomes. If recommended, upadacitinib is expected to have the same position in the treatment guideline as tocilizumab, which makes tocilizumab the most relevant comparator to upadacitinib.

Overview of comparator	
Generic name	Tocilizumab (RoActemra)
ATC code	L04AC07
Mechanism of action	IL6 – inhibitor
Method of administration	Subcutaneus injection
Dosing	162 mg every week
Dosing in the health economic model (including relative dose intensity)	162 mg every week (base case)
Should the medicine be administered with other medicines?	Yes, tocilizumab is administered with a 26 – week corticoid steroid taper regimen.
Treatment duration/ criteria for end of treatment	Treatment should be discontinued after 1 year for patients in remission.
Need for diagnostics or other tests (i.e. companion diagnostics)	No
Package size(s)	4 pre-filled injection pens

3.6 Cost-effectiveness of the comparator

Tocilizumab has previously been evaluated and recommended by the DMC in 2018, before the DMC evaluated cost-effectiveness. The DMC concluded that the clinical benefit of treatment with tocilizumab would offset the increased costs compared to treatment with prednisone.

3.7 Relevant efficacy outcomes

3.7.1 Definition of efficacy outcomes included in the application

The efficacy endpoints included in the application are listed in Table 5, with the definitions and methods of data collection used in the SELECT-GCA study.

Table 5. Efficacy outcome measures relevant for the application

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
Sustained Remission at Week 52	Week 12 and 52	Absence of GCA signs and symptoms from Week 12 through Week 52 and Adherence to the protocol-defined corticosteroid treatment regimen	**Remission and Flares:** Clinical signs and symptoms of GCA was evaluated at every study visit and entered in the eCRF. After the baseline visit, the study subject, investigator, sponsor and on-site personnel were blinded for the laboratory values as these could result in inadvertent un-blinding. A local Laboratory Assessor was assigned to review the ESR result and advise the investigator of any ESR measurements ≥ 30mm/hr.
Sustained complete remission at Week 52	Week 12 and 52	An absence of GCA signs from Week 12 through Week 52 Normalization of ESR to <30 mm/hour from Week 12 through Week 52, Normalization of high sensitivity CRP (to <1 mg/dL without elevation [on two consecutive visits] to ≥1 mg/dL) from Week 12 through Week 52, and Adherence to the protocol-defined corticosteroid treatment regimen.	
Patients experiencing disease flare	Up to 52 weeks	Experience ≥1 disease flare during the course of blinded treatment, defined as an event determined by the investigator to represent recurrence of GCA signs and/or symptoms or an ESR >30 mm/hr (attributable to GCA) AND requiring an increase in CS dose.	

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
Cumulative CS dose	Up to 52 weeks	Cumulative corticosteroid dose over 52 weeks, measured in mg	The dose and frequency of CS was recorded in the eCRF. Comparisons between the upadacitinib treatment group and the PBO group will be analyzed using a van Elteren test stratified by stratification factors.
Time-to- first flare	TTE, up to 52 weeks	Event determined to represent recurrence of GCA symptoms or an ESR measurement >30 mm/hour attributable to GCA, AND Requiring an increase in corticosteroid dose.	Clinical signs and symptoms of GCA was evaluated at every study visit and entered in the eCRF. After the baseline visit, the study subject, investigator, sponsor and on-site personnel were blinded for the laboratory values as these could result in inadvertent un-blinding. A local Laboratory Assessor was assigned to review the ESR result and advise the investigator of any ESR measurements ≥ 30mm/hr.
Short Form Quality of Life Questionnaire (SF-36	Week 8,12,26 and 52	The SF-36 is a generic health-related quality-of-life instrument that can be used across age, disease and treatment groups and includes 8 domains: physical functioning, role limitations due to physical health problems, role limitations due to emotional health problems, social functioning, pain, energy/fatigue, emotional well-being, and general health problems	Electronic patient reported outcome (ePRO) instruments was administered and collected electronically.
Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue)		The FACIT-Fatigue is a 13-item ePRO measure of fatigue.	

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
EuroQol Five Dimensions Five Levels Questionnaire (EQ-5D-5L)		The EQ-5D-5L questionnaire is a generic questionnaire to measure health-related QoL. It consists of a questionnaire and a visual analogue scale (VAS). The self-assessment questionnaire is a self-reported description of the subject's current health in 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression)	

* Time point for data collection used in analysis (follow up time for time-to-event measures)

Analysis method and handling of missing data

For categorical remission–related end points, upadacitinib groups was compared with the PBO group using the Cochran-Mantel-Haenszel method adjusting for stratification factors. The primary approach for handling missing data was Non-Responder Imputation incorporating multiple imputation (NRI-MI). Subjects with missing data was counted as non-responders, except when missing at random could be reasonably assumed, which was handled by multiple imputation. For example, missing due to COVID-19 logistical restriction or due to political conflict was handled by multiple imputation.

For cumulative CS dose, comparisons between the upadacitinib treatment group and the PBO group was analyzed using a van Elteren test stratified by stratification factors. The time to the first flare of giant-cell arteritis was analyzed with the Kaplan–Meier method.

For the continuous change from baseline endpoint change from baseline EQ-5D-5L comparisons between the upadacitinib treatment groups and the PBO group was carried out using the Mixed-Effect Model Repeat Measurement (MMRM) model with treatment group, visit, treatment-by-visit interaction, and stratification factors as the fixed factors and the corresponding baseline values as the covariates

Validity of outcomes

All measurements included are standard for assessing disease activity in subjects with GCA. All clinical and laboratory procedures in this study are standard and generally accepted.

The categorical remission related end- points (remission, sustained remission and patients experiencing flares) uses symptoms and signs of activity disease that are used in clinical practice, according to the Danish treatment guideline and the EULAR recommendations. All measurements included are standard for assessing disease activity in subjects with GCA. All clinical and laboratory procedures in this study are standard and generally accepted. These end- points was also used in the GiACTA trial for tocilizumab

and have been evaluated by the DMC. The absolute effect for upadacitinib compared to placebo in the SELECT-GCA trial (17 – 30 percent points for these endpoints) was considered clinically relevant by EMA.

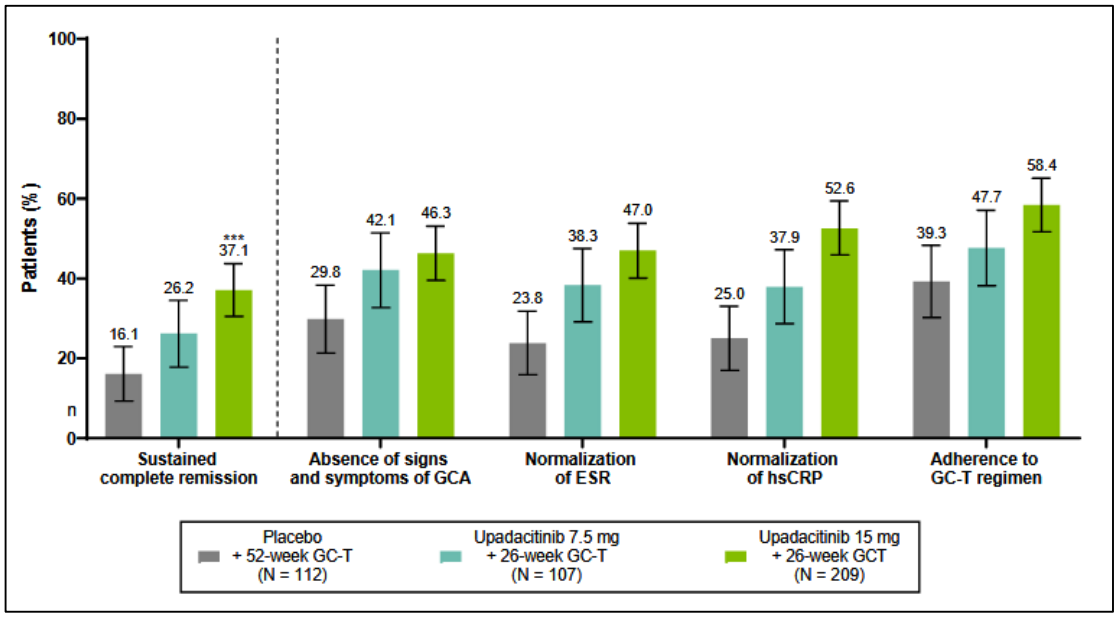
The definition of complete remission and endpoints related to flare include normalization of CRP (complete remission) and ESR (complete remission, definition of flare), though not the primary endpoint of the study. CRP is more commonly used in Danish clinical practice compared to ESR according to feedback from the Medicines Council and the impact of the use of ESR as a measure for acute phase reactants in the endpoints of the clinical studies needs to be considered.

GCA involves granulomatous inflammation of arterial walls, triggering cytokine release, which stimulates liver production of CRP and fibrinogen, which in turn increase ESR. Neither CRP or ESR are specific to GCA and can be elevated in other inflammatory or infectious conditions. (57–59). According to a systematic review and meta-analysis, elevated ESR has a positive likelihood ratio (LR) for GCA, making it a valuable laboratory feature, though not definitive on its own. Similarly, elevated CRP are also informative, while the absence of an elevated ESR or CRP significantly decreases the likelihood of GCA. (60)

CRP rises rapidly, with induction occurring within 6-8 hours and peaking around 48 hours after the initial inflammatory stimulus; the circulating half-life of CRP is consistently reported to be approximately 19 hours. (61) ESR rises more slowly than CRP, typically increasing within 24–72 hours after onset of inflammation due to gradual elevations of fibrinogen and other acute-phase proteins. (62)

An assessment of the components of **sustained complete remission**, shown in Figure 7, that includes both normalization of ESR and CRP.

Figure 7. Assessment of Components of Sustained Complete Remission at Week 52 in the SELECT-GCA Trial. (63)



A slightly higher proportion of patients fulfilled the normalization of CRP component of sustained complete remission, compared to normalization of ESR. Having the outcome for normalisation of CRP only, as suggested is the case in Danish clinical practice, would hypothetically slightly **increase** the proportion of patients in sustained clinical remission. As suggested by the figure, for complete sustained remission, including normalisation of ESR is a more conservative outcome measure compared to including normalisation of CRP alone.

Flare (relapse), of GCA in the SELECT GCA trial is defined as recurrence of GCA signs or symptoms or an elevation of ESR (attributable to GCA) AND requiring an increase in corticosteroid (CS) dose. As described above the major difference between ESR and CRP is the kinetics of the response. CRP elevation is more rapid compared to ESR elevation following an inflammatory response, with CRP peaking within 48 hours and ESR elevation starting within 24 – 72 hours. In theory, using CRP might detect a flare earlier than ESR, if testing was done continuously. However, the recommended frequency of monitoring after initial normalization of CRP/ESR is 4-8 weeks in the Danish clinical guideline for GCA. (40)

For a relapse that occurs between monitoring visits, both CRP and ESR levels are expected to be elevated at the next visit. The margin of error for the time to a flare is larger based on the time between monitoring visits than the shorter difference in time to a detectable CRP and ESR elevation following a relapse. The impact of using CRP in clinical practice for monitoring GCA rather than ESR is not likely to impact the **proportion of patients with flare (relapse)** when comparing the outcomes of the SELECT-GCA trial with Danish clinical practice. Due to the difference in the kinetics of the response, an elevated CRP might occur sooner than an elevation of ESR, making the **time to first flare** shorter if CRP is used to monitor acute phase reactants. The impact of this difference is likely small, again given the frequence of monitoring visits being much longer (days) than the difference in time between CRP and ESR elevation (hours).

The cumulative CS dose and time to first flare are outcomes used in the EULAR recommendation when describing treatment efficacy. The cumulative CS dose has previously been used by the DMC, with a definition of clinically relevant difference of a 25 % reduction in the cumulative CS dose. No further validation of these endpoints is considered necessary.

SF-36 is a generic health-related quality-of-life instrument that can be used across age, disease and treatment groups and includes 8 domains: physical functioning; role limitations due to physical health problems; role limitations due to emotional health problems; social functioning; pain; energy/fatigue; emotional well-being; and general health problems. The summary score PCS is generated based on the eight domains. All items, scales, and summary measures have a score range of 0-100 with higher scores indicating better outcomes. **FACIT-Fatigue** is a 13-item ePRO that evaluates fatigue/tiredness and its impact on daily activities and functioning, which has been validated in the general population and in other chronic diseases. This instrument includes items such as tiredness, weakness, listlessness, lack of energy, and the impact of these feelings on daily functioning (e.g., sleeping, and social activities.

The **EQ-5D-5L** (EuroQol Five Dimensions Five Levels Questionnaire) questionnaire is one of the most used generic questionnaires to measure health-related QoL. It consists of a questionnaire and a visual analogue scale (VAS). The self-assessment questionnaire is a self-reported description of the subject's current health in 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). The subject is asked to grade their own current level of function in each dimension into one of three degrees of disability (severe, moderate or none). Using the VAS, subjects record perceptions of current perceived health status with a grade ranging from 0 (the worst possible health status) to 100 (the best possible health status). The EQ-5D-5L is the preferred HRQoL measurement by the DMC, no further validation is considered necessary.

4. Health economic analysis

4.1 Model structure

A cost-minimization analysis (CMA) model was developed to compare the economic impact of tocilizumab and upadacitinib for the treatment of GCA in a Danish healthcare setting. The model assumes equivalent clinical efficacy between tocilizumab and upadacitinib in achieving sustained remission, based on the results of the indirect treatment comparison described in section 7.

The model reflects the clinical management of patients with GCA over a one-year time horizon. The pathway assumes treatment initiation with either tocilizumab or upadacitinib, followed by continued therapy under clinical remission. Given the CMA framework, the model does not include different health states for response but instead focuses on capturing direct costs associated with treatment.

Included cost components are:

- Drug acquisition
- Mode and frequency of administration
- Monitoring costs
- Patient time and healthcare professional time
- Management of adverse events assumed to be of similar incidence and severity

4.2 Model features

The model features with regards to the population, perspective, half-cycle correction, cycle length discount rate, model structure, comparator, and cost are described in Table 6, along with a justification of chosen features.

Table 6. Features of the economic model.

Model features	Description	Justification
Patient population	Adult patients with giant cell arteritis	According to the approved indication and expected use in Danish clinical practice.
Perspective	Limited societal perspective	According to DMC guidelines
Time horizon	1 year	A one-year time horizon is appropriate as it aligns with the duration of the pivotal clinical trials. This period captures the key cost drivers.
Cycle length	1 week	
Half-cycle correction	No	
Discount rate	3.5 %	The DMC applies a discount rate of 3.5 % for all years
Intervention	Upadacitinib	
Comparator(s)	Tocilizumab	According to national treatment guideline, see section 3.5.
Outcomes	Incremental costs	

5. Overview of literature

A systemic literature review (SLR) was conducted and adapted to the current application by excluding studies with comparators not relevant for the Danish context. The SLR and the adaptation is further described in Appendix H, Appendix I and Appendix J. Literature used for the clinical assessment

The literature used in the clinical assessment is listed in Table 7, and was identified in a SLR. The SLR and the adaptation is further described in Appendix H, Appendix I and Appendix J.

5.1 Literature used for the clinical assessment

The clinical assessment is based on an indirect treatment comparison (ITC) between upadacitinib and tocilizumab, as no head-to-head studies exist. The comparison is based on the two pivotal trials: SELECT-GCA (upadacitinib) and GiACTA (tocilizumab). The studies included in the clinical assessment are listed in Table 7.

Table 7 Relevant literature included in the assessment of efficacy and safety.

Reference (Full citation incl. reference number)*	Trial name*	NCT identifier	Dates of study (Start and expected completion date, data cut-off and expected data cut-offs)	Used in comparison of*
Blockmans D, Penn SK, Setty AR, Schmidt WA, Rubbert-Roth A, Hauge EM, et al. A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis. N Engl J Med. 2025 Apr 2 (63)	SELECT-GCA	NCT03725202	Start: 27/10/2018 Completion: Data cut-off:	Upadacitinib versus tocilizumab
Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, et al. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017 Jul 27;377(4):317–28. (45) Strand V, Dimonaco S, Tuckwell K, Klearman M, Collinson N, Stone JH. Health-related quality of life in patients with giant cell arteritis treated with tocilizumab in a phase 3 randomised controlled trial. Arthritis Res Ther. 2019 Dec;21(1):64	GiACTA	NCT01791153	Start: 12/02/2013 Completion: 06/02/2020 Data cut-off 04/10/2017	Upadacitinib versus tocilizumab

* If there are several publications connected to a trial, include all publications used.

5.2 Literature used for the assessment of health-related quality of life

A targeted literature search was conducted to identify previous HTA evaluations of tocilizumab in GCA from relevant HTA agencies, see Table 71. The purpose of the search was to identify any outcomes for change from baseline for EQ-5D for tocilizumab.

Table 8 Relevant literature included for (documentation of) health-related quality of life (See section 10)

Reference (Full citation incl. reference number)	Health state/Disutility	Reference to where in the application the data is described/applied
CADTH. Clinical Review Report Tocilizumab (SR 0534). CADTH; 2018	EQ-5D Change from baseline.	10. Documentation of health-related quality of life (HRQoL).

5.3 Literature used for inputs for the health economic model

A targeted literature search for was conducted to identify resource use and costs associated with treatment of GCA.

Table 9 Relevant literature used for input to the health economic model

Reference (Full citation incl. reference number)	Input/estimate	Method of identification	Reference to where in the application the data is described/applied
Tocilizumab for treating giant cell arteritis. Technology appraisal guidance TA518 (64)	Assumptions of resorce use.	Targeted search	Section 11

6. Efficacy

6.1 Efficacy of upadacitinib compared to tocilizumab for patients with GCA

6.1.1 Relevant studies

All studies used in the comparison are presented in Table 10. The comparison is done for the full study population, as this population reflects the population expected to be treated in Danish clinical practice, see 6.1.4.

Table 10 Overview of study design for studies included in the comparison

Trial name, NCT-number (reference)	Study design	Study duration	Patient population	Intervention	Comparator	Outcomes and follow-up time
SELECT-GCA (NCT03725202), (63)	Randomized phase III, placebo-controlled, double blind	Period 1: 52 weeks Period 2: 52 week extension	Adult patients with new onset or relapsing active GCA	Upadacitinib 7,5 mg per orally once daily + 26 week taper of prednisone Upadacitinib 15 mg per orally once daily + 26 week taper of prednisone	Placebo + 52 week taper of prednisone	**Primary:** Sustained Remission at Week 52 **Secondary:** Sustained Complete Remission From Week 12 Through Week 52, Cumulative Corticosteroid (CS) Exposure Through Week 52, Time to First Disease Flare Through Week 52, Experience at Least 1 Disease Flare Through Week 52, Percentage of Participants in Complete Remission at Week 52, Percentage of Participants in Complete Remission at Week 24, Change From Baseline in the 36-item Short Form Quality of Life Questionnaire (SF-36) Physical Component Summary (PCS) Score at Week 52, Number of Disease Flares Per Participant Through Week 52, Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) at Week 52, Assessment of Treatment Satisfaction Questionnaire for Medication (TSQM) Patient Global Satisfaction Subscale at Week 52, Rate of Corticosteroid-related Adverse Events Though Week 52
GiACTA (NCT01791153) (45,65)	Randomized phase III, placebo-controlled, double blind	Period 1: 52 weeks Period 2: 52 week extension	Adult patients with new onset or relapsing active GCA	Tocilizumab 162 mg subcutaneously every week (QW) + 26 week taper of prednisone Tocilizumab 162 mg subcutaneously	Placebo + 26 week taper of prednisone Placebo + 52 week taper of prednisone	**Primary:** Sustained Remission at Week 52 (Tocilizumab + 26 Weeks Prednisone Taper Versus Placebo + 26 Weeks Prednisone Taper) **Secondary:** Sustained Remission at Week 52 (Tocilizumab + 26 Weeks Prednisone Taper Versus Placebo + 52 Weeks Prednisone Taper), Time to First GCA Disease Flare, Total Cumulative Prednisone Dose, Change From Baseline in Short Form (SF)-36 Questionnaire Score at Week 52, Change From Baseline in Patient Global Assessment (PGA) of Disease Activity Assessed Using Visual Analogue Scale (VAS) at Week 52, Area Under the Curve From

Trial name, NCT-number (reference)	Study design	Study duration	Patient population	Intervention	Comparator	Outcomes and follow-up time
				every other week (Q2W)+ 26 week taper of prednisone		Time Zero to End of Dosing Interval (AUCtau) at Steady State of Tocilizumab, Maximum Serum Concentration at Steady State (Cmax,ss) of Tocilizumab, Minimum Serum Concentration at Steady State (Cmin,ss) of Tocilizumab, Minimum Observed Serum Concentration (Ctrough) of Tocilizumab, Serum Interleukin-6 (IL-6) Level, Serum Soluble IL-6 Receptor (sIL-6R) Level, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) Level, Percentage of Participants With Anti-Tocilizumab Antibodies

6.1.2 Comparability of studies

GiACTA and SELECT-GCA are both randomised, placebo-controlled, double-blind studies and have similar study designs.

Both studies enrolled patients aged 50 years and older diagnosed with active GCA, including those with elevated ESR or CRP and symptoms of cranial GCA or PMR confirmed by biopsy or imaging. The same definitions of symptoms of GCA are used in the two studies, see Table 11. Each study included patients with new-onset GCA diagnosed within 6 weeks or those with refractory disease.

Table 11. Definition of symptoms of GCA used in the SELECT-GCA and GiACTA trials. (45,63)

SELECT-GCA	GiACTA
• Fever (> 38°C or 100.4°F) • Symptoms of PMR • Localized headache, temporal artery or scalp tenderness. • Visual signs or symptoms such as acute or subacute vision loss due to arteritic anterior ischemic optic neuropathy, transient blurry vision. • Jaw or mouth pain • New or worsened extremity claudication • Other features judged by the Clinical Assessor to be consistent with a GCA or PMR flare.	• Fever (> 38°C or 100.4°F) • Symptoms of PMR • Localized headache, temporal artery or scalp tenderness. • Visual signs or symptoms such as acute or subacute vision loss due to arteritic anterior ischemic optic neuropathy, transient blurry vision. • Jaw or mouth pain • New or worsened extremity claudication • Other features judged by both the clinician-investigator to be consistent with a GCA or PMR flare

The exclusion criteria were similar, focusing on recent surgeries, transplants, certain prior treatments, severe allergies, uncontrolled diseases, active or recurrent infections, immunodeficiency, and recent malignancies.

After screening, patients were randomised to receive either active treatment or placebo. All study arms had a concomitant CS-taper regimen. Tocilizumab and upadacitinib were given with a 26 – week taper. Both studies had a placebo arm with a 52-week corticosteroid taper, that will be used as the anchor of the indirect treatment comparison. The initial 52 – week double-blinded period will be used in this ITC, though both studies had a 52 – week extension after the double-blinded period. In both studies, remission should be induced within the first 12 weeks of the study. Patients who failed to reach remission by week 12 were considered non-responders in the primary analysis

The CS-taper regimens, while generally comparable between the trials, were not entirely identical. In SELECT-GCA, during the open-label taper phase, the initial dose was restricted to standard increments of 20, 30, 40, 50, or 60 mg. Conversely, GiACTA offered greater flexibility by incorporating intermediate doses, such as 25 mg and 35 mg. Moreover, during the blinded taper phase, the daily dose for patients initiating 60 mg/day of corticosteroid was adjusted to 12 mg in SELECT-GCA and 12.5 mg in GiACTA for the second and third taper weeks, followed by identical protocols in the remaining

weeks. **Disease duration** was reported in a potentially heterogeneous way across the included studies. In SELECT-GCA, disease duration was reported as the time since diagnosis, while GiACTA did not specify whether disease duration referred to the time since diagnosis or time since symptom onset.

Neither the difference in CS-taper regimen or in reporting of disease duration are considered large enough to impact the outcome of the indirect treatment comparison.

Escape therapy with corticosteroids was given in both SELECT-GCA and the GiACTA study to patients that experienced a flare OR could not adhere to the corticosteroid taper schedule. The protocols for rescue therapy are very similar between the two studies. If rescue medication was needed in the open-label taper phase, (taper from 60 mg/day to 20 mg/day), patients stopped the CS-taper and were given open-label escape therapy with corticosteroids at the discretion of the investigator. Ongoing CS dose and tapering was at the discretion of the investigator. If rescue medication was needed during the double-blind CS-taper (< 20 mg/day) patients were given escape open label CS therapy, starting with at least 20 mg/day. Ongoing CS use and subsequent tapering will be at the discretion of the investigator. Patients continued to receive blinded study medication during treatment with escape therapy. Patients receiving escape therapy are deemed non-responders in the remission endpoints, in both SELECT-GCA and GiACTA.

In SELECT-GCA, 27.3% of subjects in the UPA 15 group and 43.8% of subjects in the placebo treatment group, and received corticosteroid escape therapy. (66) In the GiACTA trial the proportion of patients who received escape prednisone was 23%, 33%, and 55% in the tocilizumab weekly, tocilizumab biweekly, and placebo (52-week taper) groups, respectively. (67) A similar proportion of patients received escape therapy in the UPA 15 group and the tocilizumab weekly group.

6.1.3 Efficacy and outcome measures

The criteria for sustained remission between week 12 through 52 differed between the two studies. GiACTA allowed for the absence of GCA signs and symptoms (see Table 11 for definition) and/or the presence of elevated ESR (≥30 mm/hr), while SELECT-GCA focused solely on the absence of GCA signs or symptoms (see Table 11 for definition), regardless of ESR level.

Within sustained complete remission with normalization of CRP, GiACTA allowed for more flexibility in the clinical remission criteria, with the possibility of no recurrence of GCA signs or symptoms being coupled with either the presence or absence of ESR levels ≥30 millimetres per hour (mm/hr). In contrast, SELECT-GCA applied a stricter definition, requiring both the absence of GCA signs or symptoms and the absence of ESR levels ≥30 mm/hr simultaneously.

Thera are also differences in handling of missing data and censoring of patients with flare between the studies. Missing data was handled by NRI (non-responder imputation) in the GiACTA trial. In the SELECT-GCA trial study protocol missing data was handled by (NRI-MI non-responder imputation multiple imputation). In the indirect treatment comparison, NRI data is used for SELECT-GCA to mitigate these differences. In the

GiACTA study, patients who did not meet criteria for flare were censored at day 1. In the SELECT-GCA trial study protocol, patients who did not meet criteria for flare were considered to be having a flare at day 1.

The outcomes for SELECT-GCA in Appendix B show both results as per the SELECT-GCA trial protocol, and the analyses done to mitigate the differences with the GiACTA trial.

6.1.3.1 Comparability of patients across studies

A comparison of baseline patient characteristics that are potential treatment-effect modifiers and confounders are presented in Table 12. The comparison shows differences in the baseline characteristics of potential effect modifiers.

Table 12. Baseline patient characteristics of potential effect modifiers.

Study	GiACTA		SELECT-GCA	
Treatment arm	**TCZ QW**	**PBO + 52Wk CS taper**	**PBO + 52Wk CS taper**	**UPA 15**
N	100	51	112	209
Age, years; mean (SE)	69.5 (0.9)	67.8 (1.1)	71.6 (0.7)	70.8 (0.5)
Female (%)	78.0	72.5	68.8	74.6
PMR (%)	59.0	68.6	61.6	52.2
Cranial signs or symptoms (%)	78.0	78.4	83.9	92.8
New-onset GCA (%)	47.0	45.1	67.9	70.8
Relapsing GCA (%)	53.0	54.9	32.1	29.2

To mitigate these differences, a matching-adjusted indirect comparison (MAIC) was performed in addition to the analysis without adjustment. This allows for adjustment for potential bias due to differences across trials regarding treatment effect modifiers.

6.1.4 Comparability of the study population with Danish patients eligible for treatment

The Danish GCA population has been described in a nationwide, population-based cohort study.(35) In addition, patients treated with tocilizumab in Denmark have been described in a retrospective cohort study of patients. (41) The characteristics of the GCA cohorts in these studies is compared with the baseline patient characteristics in the SELECT-GCA trial, see Table 13, in order to evaluate the comparability of the study population with Danish patients eligible for treatment.

Table 13 Characteristics in the relevant Danish population and in the SELECT-GCA trial.

	Value in Danish population (35) N=9908	Value in TCZ treated population in Denmark (41) N=155	SELECT GCA UPA 15	SELECT-GCA Placebo + 52 WK CS taper
Age	73.1 (72.9-73.3) *mean (95% CI)*	69 (63–75) *median (IQR)*	70.8±7.3 *mean(SD)*	71.6±7.3 *mean(SD)*
Female sex – n (%)	6601 (67)	122 (79)	156 (74.6)	77 (68.8)
Glucocorticoid dose — mg, mean (SD)	NA	31 (23)*	34.6±12.7	34.6±11.9
Basis for diagnosis — no. (%)				
- TAB n (%)	6774 (68%)	45 (29%)	86 (41.1)	44 (39.3)
- Imaging n (%)	2380 (29%)	133 (86%)	159 (76.1)	81 (73.0)
PMR n (%)	NA	79 (51)	109 (52.2)	69 (61.6)
New onset GCA n (%)	NA	41 (26)	148 (70.8)	76 (67.9)
Relapsed GCA n (%)	NA	105 (68)	36 (32.1)	61 (29.2)

*at start of tocilizumab treatment

The comparison in Table 12 show that patient characteristics in the SELECT-GCA trial is similar to patients with GCA that are eligible for treatment with upadacitinib in Danish clinical practice with regards to age, gender, proportion of patients with PMR and baseline glucocorticoid dose. There are some differences in basis for diagnosis, which might be explained by changing clinical practice with increasing use of imaging over time. The SELECT-GCA trial was design to include a minimum proportion of patients with new onset disease and has a higher proportion of patients with new onset disease compared to patients treated with tocilizumab. However, subgroup analyses show larger response rates for upadacitinib versus placebo in patients with relapsed disease compared to new-onset in the SELECT-GCA, and outcome of the SELECT-GCA trial is despite these differences in baseline patient characteristics relevant for the patients eligible for treatment in Danish clinical practice.

6.1.5 Efficacy – results of the SELECT-GCA-trial.

Period 1

Efficacy outcomes of the SELECT-GCA trial are shown in Table 14 through week 52 for all patients who underwent randomization and received at least one dose of upadacitinib or placebo in the SELECT-GCA trial. The study met all primary and secondary endpoints, demonstrating statistically significant superior efficacy for upadacitinib 15 mg compared to placebo.

In the SELECT-GCA trial (and in the GiActa trial for tocilizumab), all patients were initially treated to remission. The remission endpoints measure the proportion of patients that had sustained remission between week 12 of the study through week 52. The endpoints relating to flare measures the time to first flare after an initial remission and the proportion of patients with ≥1 disease flare through week 52.

The proportion of patients with at least one flare or relapse was 34,3% (27.4 to 42.4) for patients treated with upadacitinib 15 mg, compared to 55,6 % (42.9 to 69.2) for patients treated with placebo (p 0,001) in period 1 of the SELECT-GCA trial.

Table 14. Primary and Secondary End Points through Week 52 in the SELECT-GCA trial (63)

End Points	Placebo + 52-week GC-T (N = 112)	Upadacitinib 7.5 mg + 26-week GC-T (N = 107)	Upadacitinib 15 mg + 26-week GC-T (N = 209)	P -value for treatment effect, upadacitinib 15 mg
Primary end point	0			0.002
Sustained remission at week 52 — no.(% [95% CI])	33 (29.0 [20.6 to 37.5])	44 (41.1 [31.8 to 50.4])	97 (46.4 [39.6 to 53.2])	
Secondary end points				
Sustained complete remission at week 52 — no. (% [95% CI])	18 (16.1 [9.3 to 22.9])	28 (26.2 [17.8 to 34.5])	78 (37.1 [30.5 to 43.7])	<0.001
Median cumulative glucocorticoid exposure through week 52 (95% CI) — mg†	2882 (2762 to 3253)	1905 (1615 to 2265)	1615 (1615 to 1635)	<0.001
Median time to first disease flare through week 52 (95% CI) — days‡	323 (249 to >365)	>365 (316 to >365)	>365	0.003
≥1 disease flare through week 52 (95% CI) — %§	55.6 (42.9 to 69.2)	41.3 (32.2 to 51.7)	34.3 (27.4 to 42.4)	0.001
Complete remission at week 52 — no. (% [95% CI])	22 (19.6 [12.3 to 27.0])	46 (43.0 [33.6 to 52.4])	105 (50.2 [43.4 to 57.1])	<0.001
Complete remission at week 24 — no. (% [95% CI])	40 (36.1 [27.2 to 45.1])	42 (39.3 [30.0 to 48.5])	120 (57.2 [50.5 to 64.0])	<0.001
Mean no. of disease flares through week 52 per patient-year (95% CI)‖	0.7 (0.5 to 0.9)	0.6 (0.4 to 0.7)	0.4 (0.3 to 0.5)	0.001

† Data were available for 90 patients in the placebo group, 86 patients in the upadacitinib 7.5-mg group, and 180 patients in the upadacitinib 15-mg group. The median of differences in ranked pairs between the upadacitinib and placebo groups is shown, with negative values favoring upadacitinib.
‡ Values indicated as more than 365 days could not be estimated within the first 52-week treatment period. The end point "at least 1 disease flare through week 52," which was calculated with the use of estimates from the analysis of the end point "time to first disease flare through week 52" as (percentage of patients with ≥1 disease flare at week 52) = 1 − (survival probability/percentage of patients without a disease flare at week 52), provides a landmark measure of survival probability at week 52. The treatment effect is shown as the hazard ratio for disease flare.
§ The treatment effect is shown as the odds ratio.
‖ The treatment effect is shown as the rate ratio.

Results for the primary endpoint, sustained remission from week 12 through week 52 , was analysed in prespecified subgroups. Across subgroups defined according to age, sex, new-onset or relapsing giant-cell arteritis, and baseline glucocorticoid dose, treatment with upadacitinib at a dose of 15 mg generally resulted in efficacy consistent with that observed in the overall trial population. Patients with relapsing GCA treated with upadacitinib 15 mg had an absolute response rate of 20.1 point % in the placebo arm, compared to a 15.1 point % for patients with new-onset disease. Additional results for the SELECT-GCA trial are presented in Appendix B.

Period 2

The SELECT-GCA trial continued with a 52-week blinded extension study, period 2 of the study. Patients in remission (absence of the signs or symptoms of GCA and adherence to the protocol-defined GC taper) for ≥ 24 consecutive weeks before the week 52 visit were eligible for inclusion in part 2. Patients originally randomized to upadacitinib 7.5 mg or upadacitinib 15 mg were re-randomized (2:1) to continue the same dose of upadacitinib or to switch to placebo in period 2. Patients originally randomized to placebo continued placebo. (68)

Of the 428 patients randomized and treated in period 1, 181 (42%) achieved ≥ 24 consecutive weeks of sustained remission in period 1 and entered period 2. Most (91%) of these patients completed the study, with 82% remaining on study drug. The results for upadacitinib 15 mg continuous versus switching to placebo are shown inTable 15.

Table 15. Efficacy Results for Patients Who Achieved ≥ 24 Consecutive Weeks of Remission in Period 1 and Entered Period 2 in the SELECT-GCA Trial (68)

	UPA 15 mg + 26-week GC-T to UPA 15 m (N = 68)g	UPA 15 mg + 26-week GC-T to PBO (N = 35)	Response rate difference: UPA 15 mg continuous vs UPA 15 mg to PBO (N = 35)
Maintenance of remission from week 52 through week 104— no. (% [95% CI])	47 (68.6) [57.5, 79.8]	10 (28.6) [13.6, 43.5]	40.3 [22.1, 58.6] p < .0001***
Cumulative GC exposure— median, mg [95% CI]			
Baseline through week 104	1528.0 [1150.0, 1615.0]	2204.2 [1230.0, 3896.3]	p = .001***
Week 52 through week 104	0 [0, 0]	1048.0 [50.0, 2716.0]	p < .0001***
Time to first disease flare from week 52 through week 104— median, weeks [95% CI]	NE [NE, NE]	70.4 [60.1, NE]	p < .0001***

Experienced at least 1 disease flare from week 52 through week 104— % [95% CI]	15.5 [8.4, 34.9]	59.1 [43.2, 75.6]	0.12 [0.05, 0.31] p < .0001***
Complete remission at week 104— no. (% [95% CI])	50 (73.1) [62.5, 83.7]	10 (28.6) [13.6, 43.5]	45.1 [27.9, 62.3] P < .0001***
Number of disease flares per patient per year—no. [95% CI]	0.1 [0.1, 0.3]	0.7 [0.5, 1.0]	0.2 [0.1, 0.4] p < .0001***

From week 52 through week 104, 68.6% of patients on continuous upadacitinib 15mg maintained remission vs 28.6% who switched from upadacitinib 15 mg to placebo. The proportion of patients with a at least 1 flare (relapse) in period 2 was 15,5 % of the patients treated with upadacitinib 15 mg and 59,1 % of patients treated with placebo. The number of disease flares for patients treated with upadacitinib 15 mg were 0.1 [0.1, 0.3] per patient per year in Period 2, compared to 0.7 [0.5, 1.0] per patient per year for patients that were randomized to placebo.

6.1.6 Efficacy – results of the GiACTA- trial.

Part 1

Efficacy outcomes of the GiACTA trial are shown in Table 16 through week 52 for all patients who underwent randomization and received at least one dose of tocilizumab or placebo in the GiACTA trial. Please note that the placebo+52 week taper regimen is the most relevant comparison, as shorter corticosteroid tapering regimens is not recommended. (14) Additional results are presented in Appendix B.

Table 16. Efficacy at Week 52 in the Intention-to-Treat Population in the GiACTA trial (45)

Outcome	Tocilizumab Weekly (N = 100)	Tocilizumab Every Other Week (N = 49)	Placebo + 26-Wk Taper (N = 50)	Placebo + 52-Wk Taper (N = 51)
Sustained remission with adherence to protocol-defined prednisone dose at wk 52				
Patients with sustained remission at wk 52 — no. (%)	56 (56)	26 (53)	7 (14)	9 (18)
Primary outcome: unadjusted difference in rate of sustained remission vs. placebo + 26-wk taper (99.5% CI) — percentage points†	42 (18 to 66) <0.001	39 (12 to 66) <0.001	—	—
Key secondary outcome: unadjusted difference in rate of sustained remission vs. placebo **+ 52-wk taper** (99.5% CI) — percentage points†	38 (18 to 59) <0.001	35 (10 to 60) <0.001	—	—
Patients with sustained remission at wk. 52, excluding normalization of CRP concentration — no. (%)	59 (59)	27 (55)	10 (20)	17 (33)
Sensitivity analyses				

For primary outcome of unadjusted difference in rate of sustained remission vs. placebo + 26-wk taper (99.5% CI) — percentage points†	39 (15 to 63) <0.001	35 (8 to 62) <0.001	—	—
For key secondary outcome of unadjusted difference in rate of sustained remission vs. placebo + 52-wk taper (99.5% CI) — percentage points†	26 (3 to 49) 0.003	22 (−6 to 49) 0.03	—	—
Cumulative prednisone dose				
Expected cumulative dose — mg‡ Median Range	1337 350 to 2632	1442 332 to 2632	1337 952 to 2632	2608 822 to 3902
Actual cumulative dose — mg§ Median Range P value vs. each placebo group	1862 630 to 6602 <0.001	1862 295 to 9912 <0.001	3296 932 to 9778	3818 822 to 10,698

* Values are for the patients who had sustained remission while adhering to the protocol-defined prednisone dose at week 52, except as noted. Patients who had a flare, received escape therapy, withdrew from the trial, did not adhere to the protocol-defined prednisone taper, did not have remission by week 12, or had an elevated concentration of C-reactive protein (CRP) followed by an elevated or missing CRP concentration at the next assessment (except for the sensitivity analyses, from which these patients were excluded) were classified as not having had a response with respect to sustained remission.
† P values were calculated by a Cochran–Mantel–Haenszel test for superiority, with adjustment for the baseline prednisone dose (≤30 mg per day vs. >30 mg per day).
‡ The values for the expected cumulative dose were based on a patient's starting prednisone dose in the taper, assuming that the taper was continued without error.
§ The values for the actual cumulative dose were based on actual records of prednisone taken and included all escape therapy and use of commercial prednisone as well as the prednisone used in the tapering process. P values were calculated by a van Elteren test that was stratified according to the baseline prednisone dose (≤30 mg per day vs. >30 mg per day). For any re- cords of missed tablets from the protocol-defined taper of prednisone, the missed tablets were assumed to be the minimum-dose tablets available from that pack. Patients who received an increased dose of prednisone because they entered escape therapy were included in their originally assigned treatment group.
No imputation of missing data was implemented.

Part 2

Patients who completed the 52-week double-blind part of GiACTA were eligible to enter part two, which was a 104-week, open-label, non-randomised follow-up period. Patients stopped their masked injections at the end of part one, but original treatment assignments remained masked throughout part two. Investigators could adjust patients' treatments at any time during part two, including at the start, and were permitted to treat patients with no treatment, open-label tocilizumab once a week (162 mg), prednisone or methotrexate, or any combination of these, at their discretion. A different definition of remission, **clinical remission**, was used an endpoint in part 2 of the GiACTA Clinical remission was defined as the absence of relapse as determined by the investigator.

Consequently, there is not possible to perform an indirect treatment comparison between tocilizumab and upadacitinib, as all treatment arms in part two of GiACTA are a mix of different treatments. No results are available for the proportion of patients that continued tocilizumab according to their randomized treatment in part 1. As the results of part 2 of the GiACTA is not used in any analysis they are not included in this dossier.

7. Comparative analyses of efficacy

7.1.1 Differences in definitions of outcomes between studies

The efficacy outcomes assessed in the comparative analysis of efficacy are described in Table 17, along with definitions of the outcomes.

Table 17. Outcome measures and definitions included in the ITC.

Outcome	Definition	Outcome type
Sustained remission	Absence of signs and/or symptoms of GCA and/or ESR <30 mm/hr following induction of remission within 12 weeks of baseline up to week 52. Patients must have followed and adhered to the protocol-defined CS-tapering regimen.	Binary
Sustained complete remission with normalization of CRP	Absence of signs or symptoms of GCA and/or ESR <30 mm/hr following induction of remission and normalization of the CRP < 1 milligram per deciliter and recurrence within 12 weeks of baseline up to week 52. Patients must have followed and adhered to the protocol-defined CS-tapering regimen.	Binary
Patients experiencing disease flare	Experience ≥1 disease flare during the course of blinded treatment, defined as an event determined by the investigator to represent recurrence of GCA signs and/or symptoms or an ESR >30 mm/hr (attributable to GCA) AND requiring an increase in CS dose.	Binary
Cumulative CS exposure	Cumulative CS dose ≥ 1862 mg	Binary
	Cumulative CS dose (mg)	Continuous
Time-to-first flare	The time until a patient experiences their first disease flare, defined as an event determined by the investigator to represent recurrence of GCA signs and/or symptoms or an ESR >30 mm/hr (attributable to GCA) AND requiring an increase in CS dose.	TTE

Abbreviations: CRP = C-reactive protein; CS = corticosteroid; ESR = erythrocyte sedimentation rate; GCA = giant cell arteritis. TTE = Time To Event

As described in section 6.1.3, there are differences in the definition of remission between SELECT-GCA and GIACTA.

The criteria for **sustained remission** differed between the two studies. GiACTA allowed for the absence of GCA signs and symptoms and/or the presence of elevated ESR (≥30 mm/hr), while SELECT-GCA focused solely on the absence of GCA signs or symptoms, regardless of ESR level.

Within **sustained complete remission with normalization of CRP**, GiACTA allowed for more flexibility in the clinical remission criteria, with the possibility of no recurrence of GCA signs or symptoms being coupled with either the presence or absence of ESR levels ≥30 millimetres per hour (mm/hr). In contrast, SELECT-GCA applied a stricter definition, requiring both the absence of GCA signs or symptoms and the absence of ESR levels ≥30 mm/hr simultaneously.

These differences in definitions of sustained complete remission and sustained remission, together with the suppression of CRP synthesis in the liver caused by tocilizumab, should be considered when interpreting the results of the ITC.

The primary analysis will be of the primary endpoint in the SELECT-GCA trial, sustained remission. This endpoint does not include normalization of CRP and reduces the impact of the suppression of CRP synthesis caused by tocilizumab in the indirect treatment comparison.

7.1.2 Method of synthesis

As described in section 6.1.3 there are differences in the baseline patient characteristics between patients included in the GiACTA trial and the SELECT GCA trial. To adjust for differences in baseline characteristics, patients in the SELECT GCAs with IPD were weighted such that their weighted mean baseline characteristics for the treatment-effect modifiers described above match those reported for the GIACTAs without IPD for analysis such that:

1. the weighted mean baseline characteristics in SELECT GCA exactly matches those reported for patients in GIACTA; and
2. each patient's weight is equal to his/her estimated odds of enrollment in the SELECT GCA versus the GIACTA.

After matching the effective sample size (ESS) was 115 patients in the UPA 15 arm and 71 patients in the placebo arm. The distribution of weights is shown in the histogram in Figure 8.

Figure 8. Histogram for distribution of weights (66).

The baseline characteristics of potential effect modifiers before and after matching are presented in Table 18.

Table 18. Matching of Baseline Characteristics.

Before Matching							After Matching			
Baseline Characteristics	SELECT GCA		GiACTA		P-Value		SELECT GCA		GiACTA	
	UPA15	PBO	TCZQW	PBO	UPA15 vs TCZQW	SELECT GCA PBO vs. GIACTA PBO	UPA15	PBO	TCZQW	PBO
	N = 209	N = 112	N=100	N=51			N = 209	N = 112	N=100	N=51
Age, mean, years	70.8	71.6	69.5	67.8			69.5	67.8	69.5	67.8
Female, %	74.6%	68.8%	78%	73%	0.5151	0.5882	78%	73%	78%	73%
White, %	95.2%	92.0%	96%	96%	0.7524	0.3467	96%	96%	96%	96%
Newly diagnosed GCA (%)	70.80%	67.90%	47%	45%	0.0001*	0.0056*	47%	45%	47%	45%
Relapsing GCA (%)	29.20%	32.10%	53%	55%	0.0001*	0.0056*	53%	55%	53%	55%
Cranial signs or symptoms - %	83.9%	92.8%	78%	78%	0.2074	0.0068*	78%	78%	78%	78%
Symptoms of PMR, %	52.2%	61.6%	59%	68.60%	0.2623	0.39	59%	68.60%	59%	68.60%

Abbreviations: GCA = giant cell arteritis; PMR = polymyalgia rheumatica

Study outcomes in SELECT GCA were assessed in an unweighted (before matching) and weighted sample (after matching). They were compared to published study outcomes in GIACTA using a Z-test. Rate differences and log odds ratio for binary outcomes, and log hazard ratio for time to disease flare outcome between UPA15 and its anchor group, and between TCZQW and its anchor group were reported, as well as 95% confidence intervals (CIs) (Wald confidence limits). Log hazard ratio for time to disease flare in GIACTA trial was estimated from inpatient level data that was digitized from published Kaplan-Curves using methods established by Li et al. The resulting inpatient data for the GiACTA trial is shown under the Kaplan-Maier curves in Figure 10b Further, difference in rate difference, log odds ratio, and log hazard ratio between UPA15 and its anchor group and between TCZQW and its anchor group were calculated, and their 95% CIs were

estimated (assuming normality of difference). Odds ratio (OR) and hazard ratio (HR) and 95% CIs between UPA15 and TCZQW were obtained by exponentiating log OR and log HR. A similar approach was used for outcome comparisons after matching except that weights were used after matching select-GCA patient characteristics to GiACTA patient characteristics. Because naïve estimators for standard error of weighted outcomes after matching are biased, they were estimated using sandwich methods using a general linear model with binomial distribution and identity link.

For cumulative CS dose, median dose was reported in GiACTA trial. Without other distributions such as mean and standard deviation, it was not possible to compare mean cumulative CS dose between UPA15 and TCZQW. As a result, the median dose in the TCZQW arm was converted to a binary outcome which equates to 50% of subjects with cumulative CS dose greater than the median dose reported. Percent of subjects with cumulative CS dose greater than the TCZQW median dose were estimated for the UPA15 arm in the SELECT-GCA study. Because it was not possible to estimate percent of subjects with cumulative CS dose ≥ 1862mg in the GiACTA PBO arm (and median doses in the two arms were different between the treatment and PBO arms), an unanchored MAIC was performed comparing UPA15 to TCZQW for this newly created binary outcome.

7.1.3 Results from the comparative analysis

The results from the comparative analyses are summarized in Table 19 (before matching) and Table 20 (after matching) below. All comparisons are made for the intention-to-treat population – all randomized patients who received at least one dose of the study drug, and include the full study population. The results are further described in the following sections.

Table 19. Results from the comparative analysis of upadacitinib and tocilizumab, before matching of baseline patient characteristics.

Outcome measure	UPA 15 (N= 209)	PBO 52W (N=112)	TCZQW (N=100)	PBO 52W (51)	UPA 15 vs TCZQW OR, (95% CI). P-value
Sustained remission at 52 weeks, n (%)	93 (44.5%)	32 (28.6%)	59 (59%)	17 (33 %)	OR, (95% CI). p-value 0,85 (0.57;1.29), p=0.4500
Sustained remission at 52 weeks, including normalization of CRP, n (%)	74 (35,4 %)	18 (16,1 %)	56 (56%)	9 (18%)	OR, (95% CI). p-value 0.73 (0.48;1.10), p=0.1280
Proportion of patients experiencing at least one flare, n (%)	52 (24,9%) **	44 (39,3%) **	23 (23%)	25 (49%)	OR, (95% CI). p-value 1.24 (0.83;1.87), p=0.2970
Median time to first disease flare (days)	> 365	352**	> 365	295	HR (95% CI) 1.34(0.67,2.69)
Proportion of patients with cumulative CS dose above GiACTA median	40%	-	50%	-	p=0,00974

*For binary outcomes, missing data was handled by NRI (non-responder imputation) to align with the GiACTA trial. In the SELECT-GCA trial study protocol missing data was handled by (NRI-MI non-responder imputation multiple imputation).

**In order to align with the GiACTA study, patients who did not meet criteria for flare were censored at day 1. In the SELECT-GCA trial study protocol, patients who did not meet criteria for flare were considered to be having a flare at day 1. Outcomes will for that reason differ for UPA 15 and placebo in the indirect comparison, compared to the published results.

Table 20. Results from the comparative analysis of upadacitinib and tocilizumab, after matching of baseline patient characteristics*.

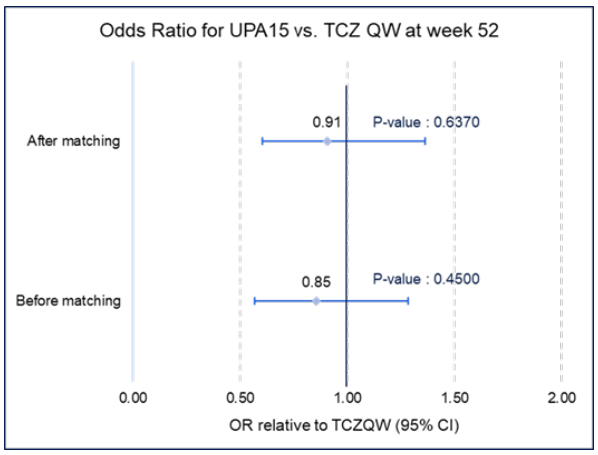
Outcome measure	UPA 15	PBO 52W	TZCQW	PBO 52W	Result
Sustained remission at 52 weeks (%)	47.5%	28.3%	59%	33 %	OR, (95% CI). p-value 0.91 (0.6; 1.36), p=0.6370
Sustained remission at 52 weeks, including normalization of CRP (%)	38.9%	16.6%	56%	18%	OR, (95% CI). p-value 0.77 (0.51, 1.17), p=0.1980
Proportion of patients experiencing at least one flare (%)	23.0%	39.1%	23%	49%	OR, (95% CI). p-value 1.19 (0.79, 1.79), p=0.3980
Time to first flare, days (median)	> 365	> 365	> 365	295	HR (95% CI) 1.34 (0.63, 2.82
Proportion of patients with cumulative CS dose above GiACTA median (%)	31%	-	50%	-	p=0.0010

*No patient numbers (N(n)) are available after matching, as the matching is a weighting of the study population of the SELECT-GCA study to match the GiACTA study population.

7.1.4 Efficacy – results per outcome – Remission endpoints

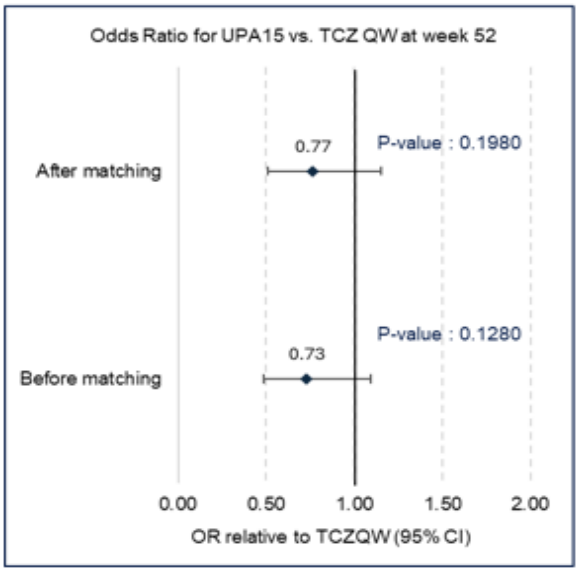
For the primary endpoint in the SELECT-GCA trial, sustained remission at 52 weeks, the results of the ITC before and after matching are shown in Figure 9. Results showed no statistically significant difference between tocilizumab and upadacitinib, with an OR of 0.91 (95% CI: 0.6, 1.36, p=0.6370) after matching.

Figure 9. Forest plot of ORs vs. PBO for sustained remission before and after matching.



Results for sustained complete remission are shown in Figure 10. again showing no statistically significant difference between the treatments, with an OR of 0.77 (95% CI: 0.51, 1.17, p=0.1980) after matching.

Figure 10. Forest plot of ORs vs. PBO for sustained complete remission before and after matching.

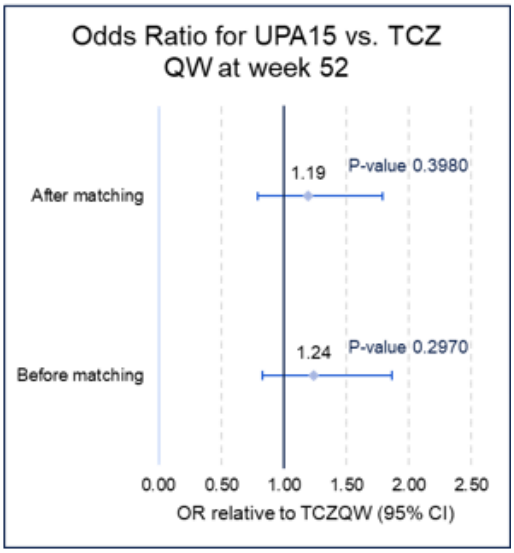


As mentioned above, the results should be interpreted with some caution due to the more stringent definition of remission used in the SELECT-GCA trial which likely result in conservative estimations for upadacitinib.

7.1.5 Efficacy – results per outcome – Flare

The results of the ITC for the proportion of patients experiencing at least one flare before and after matching is shown in Figure 11. After matching, the OR for upadacitinib versus tocilizumab was 1.19 (95% CI: 0.79, 1.79, p=0.3980).

Figure 11. Forest plot of ORs vs. PBO for patients who experienced at least one flare before and after matching.



7.1.6 Efficacy – results per outcome – Time to first flare

Time to first flare was significantly longer for UPA15 and TCZQW when compared to PBO, respectively, and not reached for either upadacitinib or tocilizumab at 52 weeks. The HR (95% CI) for UPA15 vs TCZQW was not statistically significant at 1.34 (0.63, 2.82). Time to first flare KM curves are presented in Figure 12.

Figure 12. Time to first flare KM curve UPA15 vs TCZQW.

a Before Matching

b. After Matching

The median time to first flare before matching was 352 days for PBO52W in SELECT GCA and 295 days in PBO52W in GIACTA. After matching IPD in SELECT GCA to GIACTA the median time to first flare for SELECT GCA was longer than 365 days (trial duration) and so cannot be reported whereas the median time to first flare for PBO52W in GIACTA was 295 days. The difference in the median time for placebo arms in the two trials was more than 57 days.

7.1.7 Efficacy – results per outcome – Cumulative CS exposure

The median cumulative CS dose remained identical for treatment and placebo arms before and after matching. The median CS dose in GIACTA PBO was nearly 1000 mg higher than SELECT GCA PBO (Figure 13). Thus, an unanchored analyses was conducted to determine percent of patients who had cumulative CS dose (mg) ≥ 1862 mg for UPA15 and TCZQW. The analyses showed a significantly lower proportion of patients on UPA15 had cumulative CS dose ≥ 1862 mg after matching (
Figure 14).

Figure 13: Placebo Anchored Analyses for Median Cumulative CS Dose

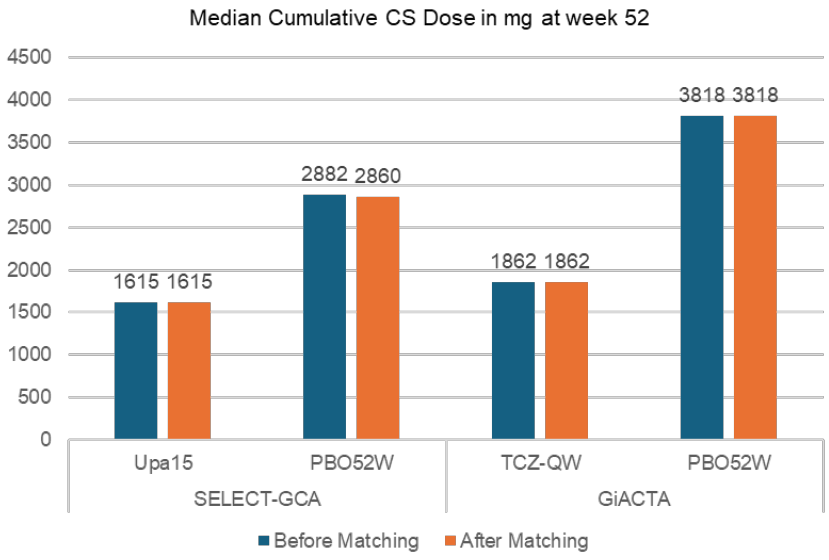
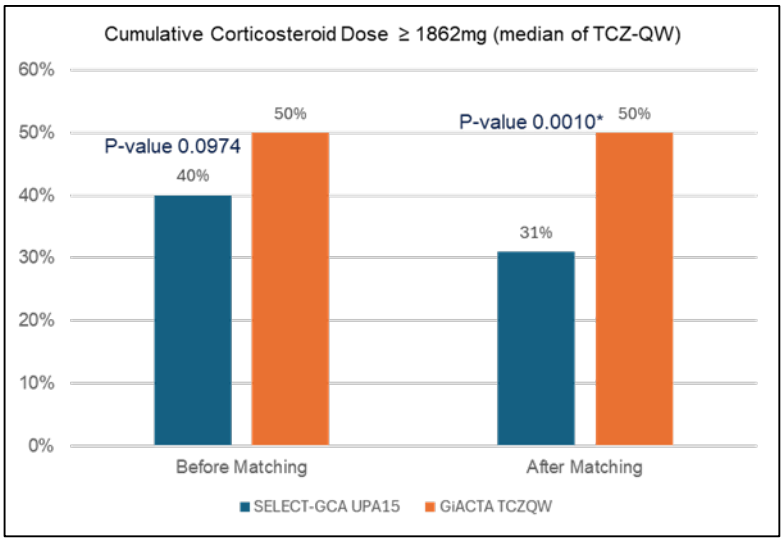


Figure 14: Unanchored Analyses for Cumulative Median CS Dose



7.1.8 Conclusion of the comparison of treatment efficacy

No statistically significant differences between the two treatments were found in the indirect treatment comparison. As described, there are some concerns in the homogeneity assumption in outcome definitions. SELECT-GCA has a more stringent definition of both remission and flare, which means the results of the indirect treatment comparison might be conservative for upadacitinib.

The primary endpoint in the SELECT-GCA study, sustained remission, is also the most suitable outcome measure for the comparison between upadacitinib and tocilizumab as it excludes CRP and eliminates some of the differences in definition of outcomes. It is also the endpoint most similar to how patients treated with tocilizumab are monitored in Swedish clinical practice as CRP according to the clinical guidelines cannot be used as an outcome for patients treated with tocilizumab (43). A majority of the patients treated with upadacitinib in the SELECT-GCA study had a lower cumulative corticosteroid dose compared with patients treated with tocilizumab in the GiACTA trial.

In conclusion, no statistically significant differences between upadacitinib and tocilizumab was demonstrated in the indirect treatment comparison, indicating similar efficacy. This is also in line with the conclusions of the specialist group for Nye Metoder ("New Methods") in Norway, who conducted a preliminary clinical assessment of comparability between the treatments. (69) Furthermore, an ad board with clinical experts in GCA from Sweden, Norway and Denmark reached the same conclusion. When presented with the results from the SELECT-GCA study, their overall expectations for upadacitinib are that the clinical efficacy will be equal to that of tocilizumab.

8. Modelling of efficacy in the health economic analysis

8.1 Presentation of efficacy data from the clinical documentation used in the model

No statistically significant differences in efficacy were found in the indirect treatment comparison, as demonstrated in section 7. Based on the findings in the indirect treatment comparison, a cost – minimization analysis was performed.

Efficacy comparison for the first year of treatment

The cost minimization analysis is performed based on the assumption that for the first year, where there is data for an indirect treatment comparison both upadacitinib and tocilizumab, there are no differences in efficacy between upadacitinib 15 mg and tocilizumab QW, with regards to proportion of patients in remission after 52 weeks, proportion of patients that experience at least one flare (relapse) and time to first flare.

Patients that experience a flare are assumed to continue treatment with either upadacitinib or tocilizumab and re-initiate corticosteroid treatment until they are in a second remission. The corticosteroid dosing and taper schedules for treating a flare are assumed to be the same as those used in the clinical trials, that is a 26-week taper, for both upadacitinib and tocilizumab.

Based in the SmPC: s for upadacitinib and tocilizumab, and the Danish treatment guideline, patients stay on treatment for the first 52 weeks of the model. According to real world evidence from Danish clinical practice, patients who discontinued tocilizumab treatment were treated for a median of 392 days.(41)

8.1.1 Extrapolation of efficacy data

Not applicable

8.1.1.1 Extrapolation of [effect measure 1]

Not applicable

8.1.1.2 Extrapolation of [effect measure 2]

Not applicable

8.1.2 Calculation of transition probabilities

Not applicable

8.2 Presentation of efficacy data from [additional documentation]

Treatment of patients for the second year of treatment

After the first year of treatment patients can either continue or discontinue treatment. The choice is made based on disease activity, treating physicians' assessment and patient preference, according to the SmPC: s of tocilizumab and upadacitinib. In Danish clinical practice, patients stay on treatment, taper the dose of tocilizumab or discontinue treatment.

A Danish study provides data for the proportion of patients treated with tocilizumab that continue treatment without tapering of tocilizumab, discontinue due to lack of response or relapse while on treatment, discontinue after taper or discontinue without taper.(41) The flowchart in the study publication, see Figure 15, has been used to calculate the proportion of all patients, that continue on treatment without taper, discontinue due to relapse/non-response, discontinue in remission or stay on treatment after taper.

Figure 15. Patient flow-chart of patients treated with tocilizumab in Danish clinical practice(41)

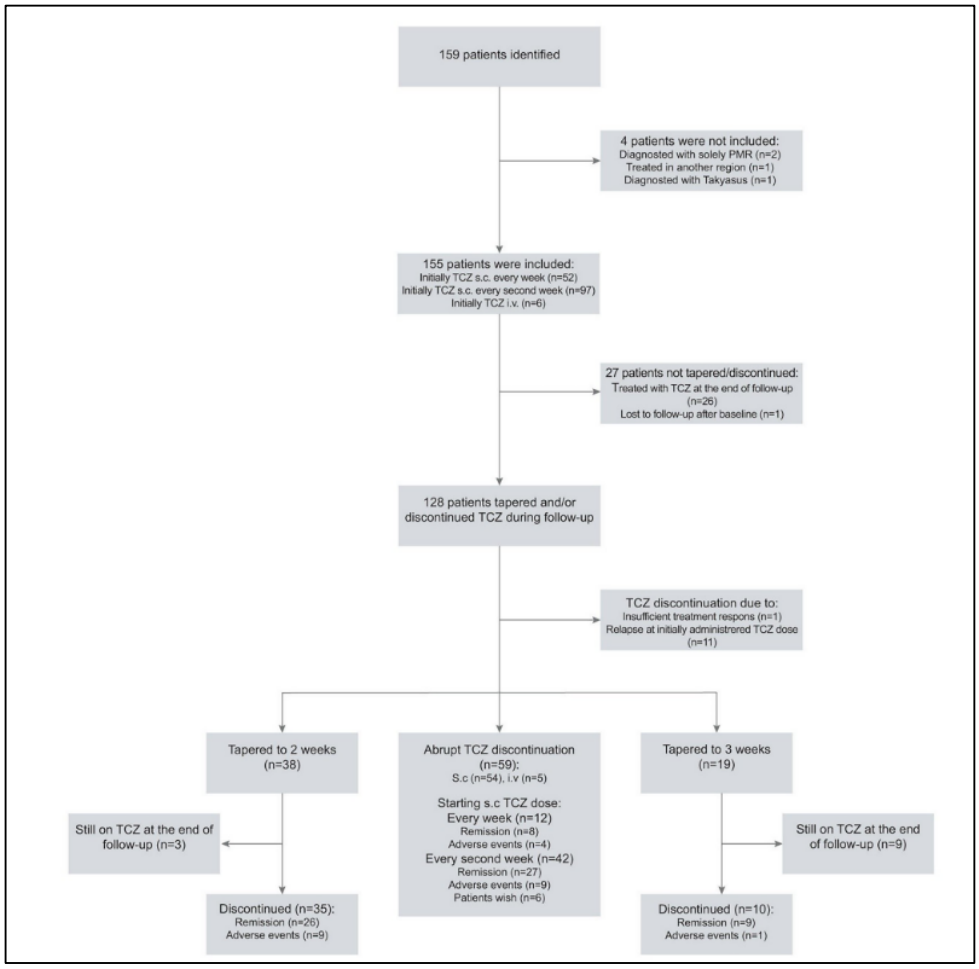


Table 21. Distribution of patients that continue on treatment with tocilizumab, including tapering of dose, and discontinue treatment.

	Patients treated with tocilizumab N=155	Proportion of patients % (n/N)
On treatment, n (%)	39	25%
Without taper	27	17%
After taper from QW to Q2W	3	2%
After taper from Q2W to Q3W	9	6%
Discontinued due to relapse/non-response	12	8%
Discontinued in remission, total	104	67%
Abrupt discontinuation	*59*	38%
After taper from QW to Q2W	*35*	23%
After taper from Q2W to Q3W	*10*	6%

Tapering of tocilizumab is not included in the approved dosing for tocilizumab. No tapering or dose reductions are not included in the SmPC for upadacitinib. The 7,5 mg dose was included in the clinical trial but did not demonstrate superiority compared to placebo and was not approved. Therefore, no dose reductions or tapering is included in the model for upadacitinib. As the clinical decision for treatment with upadacitinib after the first year is expected to be based on the same criteria as for tocilizumab, the same distribution of patients is assumed to continue on treatment, discontinue due to relapse/non-response and discontinue in remission, see Table 22.

Table 22. Assumed distribution of patients treated with upadacitinib, after the first year of treatment.

	Patients treated with upadacitinib N=155	Proportion of patients % (n/N)
On treatment without taper, n (%)	39	25%
Discontinued due to relapse/non-response	12	8%
Discontinued in remission, total	104	67%

Efficacy comparison after the first year of treatment

Data was available for an indirect treatment comparison for 52 weeks of treatment. Both the GiACTA trial and the SELECT GCA studies have a second part, where patients are treated for an additional year – until 104 weeks, see further descriptions in 6.1.5and 6.1.6. However, the second part of the GiACTA trial was not randomized or placebo-controlled, as investigators were permitted to treat patients with no treatment, open-label tocilizumab once a week (162 mg), prednisone or methotrexate, or any combination of these, at their discretion in **all** study arms. The endpoint in this part of the GiACTA trial is **clinical** remission, defined as absence of relapse as determined by the investigator, which differs from the endpoints used in the first part of the study.(70) It is not possible to perform an indirect treatment comparison based on the GiACTA and SELECT GCA trials.

The objective of the Danish RWE study was to compare tapering of tocilizumab with abrupt discontinuation. As demonstrated in Table 21, as only a small proportion of patients stay on treatment after dose tapering, dose tapering seem to be used as a way to reduce the risk of relapse at treatment discontinuation. (41) Please note that the RWE study reflects the clinical setting, where treatment decisions are made based on disease activity, treating physicians' assessment and patient preference as compared to the clinical study setting in SELECT-GCA where the treatment allocation was randomized. In addition, 64% of patients in the RWE study remained in treatment with corticosteroids upon discontinuation with tocilizumab. Patients in the randomized trials were not considered to be in remission if corticosteroids were needed after the initial 26- or 52-week taper.

8.2.1 On treatment

Data from period 2 of the SELECT-GCA trial demonstrate that 68,6 % of patients that continued upadacitinib 15 mg after period 1, maintained in remission through week 104. (68). The Danish RWE study does not report results for the 17% of patients who stay on treatment without tapering or separately for the small proportion of patients in the

study (2% and 6% tapered to Q2W and Q3W respectively) that stay on treatment after dose tapering. (41) The GiACTA study does not report results for the proportion of patients that were treated with tocilizumab in part one of the trial and continued treatment with tocilizumab in part two of the trial, regardless of dose. (70)

Efficacy for tocilizumab will be considered equal to that of upadacitinib for the second year in the model, though the dose (and consequently the costs) will be reduced according to the proportions presented in Table 21, based on the assumption that the similar clinical efficacy demonstrated for year 1 for tocilizumab and upadacitinib will be extrapolated into year two. Assuming equal efficacy of tocilizumab regardless of dosing/taper is a conservative assumption in the model as the approved dose of tocilizumab QW is used in the indirect treatment comparison.

8.2.2 Discontinued due to relapse/non-response

No difference in efficacy is assumed for these patients, based on the indirect treatment comparison in section 7 where no statistically significant differences in efficacy between upadacitinib and tocilizumab was found for the first year of treatment.

8.2.3 Discontinued after remission.

Bearing in mind the limitations that follow the differences in study design and definition of endpoints, there are no results in the GiACTA study that can be compared with results from the SELECT-GCA 104-week data.(70)

In the Danish RWE study, relapse rates after discontinuation of tocilizumab was 46% in the group that discontinued abruptly, and 47 % in the group that discontinued after tapering. However, as described above 64 % of the patients remained in corticosteroid treatment after discontinuation of tocilizumab. (41) Should these relapse rates be used, additional costs for corticosteroid treatment and corticosteroid related adverse events should be included.

Part 2 of the SELECT GCA trial includes at study arm that switch from upadacitinib 15 mg to placebo (that is upadacitinib free for period 2). At 104 weeks **28,6 %** of patients in this study arm remained in remission, meaning they had no relapses requiring re-initiation of CS, and were not treated with corticosteroids. (68) Based on these data, we assume that the proportion of patients that discontinue treatment with upadacitinib and tocilizumab after year 1 will have the same likelihood of remaining in remission. In the model, 30 % of patients that discontinue treatment will remain in remission and 70 % of patients will relapse during the second year of treatment.

8.3 Modelling effects of subsequent treatments

Not applicable

8.4 Other assumptions regarding efficacy in the model

Not applicable

8.5 Overview of modelled average treatment length and time in model health state

Not applicable

9. Safety

9.1 Safety data from the clinical documentation

An overview of safety events from the SELECT GCA and GiACTA trials is presented in Table 23 for upadacitinib, tocilizumab and the respective placebo arm with 52- week corticosteroid taper. The table include safety data from the 52 week follow up. The safety population in each study are patients randomized and receiving at least one dose of study medication, including placebo. The table include data on adverse events as reported in the clinical trials, no data on adverse reactions is available for comparison. CTCAE are not applicable to this application and is not included in the table.

In the SELECT-GCA trial investigators who were unaware of the trial group assignments conducted clinical evaluations, reported adverse events, and reviewed laboratory results. Adverse events that emerged during treatment were defined as any event that began or worsened in severity after initiation of upadacitinib or placebo through 30 days after the last dose was received; events were categorized with the use of the Medical Dictionary for Regulatory Activities (MeDRA) (63) In the GiACTA trial safety was assessed as the incidence, nature, and severity of adverse events and laboratory abnormalities in the safety population. Events were categorized with the use of the Medical Dictionary for Regulatory Activities (MeDRA). (45)

Table 23. Overview of safety events, up until 52 weeks follow-up. (45,63)

	UPA 15 (N=209) (63)	Placebo (N=112) (63)	Difference, % (95 % CI)	TCZ QW (N=100) (45)	Placebo (N=51) (45)	Difference, % (95 % CI)
Number and proportion of patients with ≥1 adverse events, n (%)	200 (95.7)	105 (93.8)	1.94% (-3.33; 7.2)	98 (98)	47 (92)	5.84 % (-2.03; 13.7)
Number and proportion of patients with ≥ 1 serious adverse events*, n (%)	47 (22,5%)	24 (21,4%)	1.06% (-8.42; 10.5)	15 (15 %)	13 (25%)	-10.5 % (-24.3; 3.37)

	UPA 15 (N=209) (63)	Placebo (N=112) (63)	Difference, % (95 % CI)	TCZ QW (N=100) (45)	Placebo (N=51) (45)	Difference, % (95 % CI)
Number and proportion of patients who discontinue treatment regardless of reason, n (%)	54 (25.8%)	41 (36.6%)	-10.8 % (-21.5 - 0.054)	15 (15%)	5 (9.8%)	5.20 % (-5.55; 15.9)
Number and proportion of patients who discontinue treatment due to adverse events, n (%)	31 (14.8)	22 (19.6)	-4.81 % (- 13.6 – 3.96)	6 (6%)	0	6 % (1.35; 10.65)

* A serious adverse event is an event or reaction that at any dose results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect (see the ICH's complete definition).

The frequency of all serious adverse events with frequency of ≥ 5% recorded in the 52 week part 1 of the SELECT-GCA trial and the GiACTA trial are listed in Table 24 below. Apart from serious infections, no serious adverse event occurred with a frequency of 5% or above in neither study, for any treatment arm in the comparison. The rates of serious infections were higher in the placebo arms compared to the upadacitinib and tocilizumab arms.

Table 24. Serious adverse events (52 weeks), with a frequency of ≥ 5% in the SELECT-GCA - and GiACTA - trials. (45,63)

Adverse events	UPA 15 (N=209) (63)	Placebo (N=112) (63)	TCZ QW (N=100) (43)	Placebo (N=51) (43)
Serious adverse event, n (%)	47 (22.5)	24 (21.4	15 (15)	13 (25)
Serious infection	12 (5.7)	12 (10.7)	7 (7)	6 (12)

* A serious adverse event is an event or reaction that at any dose results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect (see the ICH's complete definition).

As both tocilizumab and upadacitinib have several approved indications in addition to GCA, which provide additional information from other clinical trials on adverse events. Comparison of the safety – profiles will for that reason be based on the SmPC:s of the respective treatment. (48,54)

Upadacitinib and tocilizumab have similar special warnings and precautions for use. As with treatment with all immunosuppressive agents there is a risk for infections and activation of tuberculosis or viral reactivation with both tocilizumab and upadacitinib. Both agents are also known to elevate hepatic transaminases, which should be considered in patients with hepatic disease, and might increase the risk of diverticulitis and gastrointestinal perforation. Hematological abnormalities and elevations in lipid parameters are seen for both and are monitored at start of treatment.

Considering the increased risk of MACE, malignancies, serious infections, and all-cause mortality in patients 65 years of age and older, as observed in a large, randomised study of tofacitinib (another Janus Kinase (JAK) inhibitor), upadacitinib should only be used in the following patients if no suitable treatment alternatives are available:

- 65 years of age and older;
- patients with history of atherosclerotic cardiovascular disease or other
- cardiovascular risk factors (such as current or past long-time smokers)
- patients with malignancy risk factors (e.g. current malignancy or history of malignancy)

The most commonly reported adverse event reactions for patients treated with upadacitinib are upper respiratory tract infection, bronchitis, cough and elevated hematological, liver and lipid laboratory values. The most common serious adverse event is serious infections. For GCA the overall safety profile is consistent with the known safety profile for upadacitinib, except for headaches which were more common in patients with GCA. 5,7 % of the patients in the upadacitinib 15 mg arm in the SELECT-GCA study reported serious infection.

The most commonly reported adverse event reactions for patients treated with tocilizumab are upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased ALT, while the most serious adverse reactions are serious infections, complications of diverticulitis, and hypersensitivity reactions. For GCA the overall safety profile is consistent with the known safety profile of tocilizumab. The most common adverse event is infections and elevated hematological, liver and lipid laboratory values. The rate of infection/serious infection events was 200.2/9.7 events per 100 patient years in the tocilizumab weekly group in the GiACTA study. (48) For a comparable rate to upadacitinib, 7% in the tocilizumab weekly group reported serious adverse events in the first part of the GiACTA study. (42)

In conclusion, the safety profiles of upadacitinib and tocilizumab are similar. The major difference is primarily the JAKi- class safety concerns for upadacitinib, which need to be considered in the risk-benefit assessment performed by the treating physician before initiation of treatment.

No major differences in the safety profiles of tocilizumab and upadacitinib could be identified based on a comparison of adverse events described in the SELECT-GCA and GiACTA study and the SmPC:s of the products. As a scenario analysis, the adverse events related to JAK-safety are included in the health economic model, see Table 25.

Table 25. Adverse events used in the health economic model

Adverse events	Intervention	Comparator		
	Frequency used in economic	Frequency used in economic	Source	Justification

Adverse events	Intervention	Comparator		
	model for intervention	model for comparator		
Adverse event, n(%)				
MACE (Major adverse cardiovascular events)	0,000115	0	(71)	No major differences in the safety profiles of tocilizumab and upadacitinib could be identified based on a comparison of adverse events described in the SELECT-GCA and GiACTA study and the SmPC:s of the products. As a scenario analysis, the adverse events related to JAK-safety are included in the health economic model
VTE (Venous thromboembolism)	0,000115	0	(71)	

9.2 Safety data from external literature applied in the health economic model

Not applicable

10. Documentation of health-related quality of life (HRQoL)

The DMC methods guide recommends the use of the generic measuring instrument EQ-5D-5L for health-related quality of life.

Table 26 Overview of included HRQoL instruments

Measuring instrument	Source	Utilization
EQ-5D	SELECT-GCA, GiACTA	Clinical effectiveness
SF-36	SELECT-GCA, GiACTA	Clinical effectiveness
FACIT-Fatigue	SELECT-GCA, GiACTA	Clinical effectiveness

10.1 Presentation of the health-related quality of life

10.1.1 Study design and measuring instrument:

EQ-5D-5L.

EQ-5D-5L is included as an outcome measure in the SELECT-GCA trial.

The EQ-5D-5L questionnaire is one of the most used generic questionnaires to measure health-related QoL. It consists of a questionnaire and a visual analogue scale (VAS). The self-assessment questionnaire is a self-reported description of the subject's current health in 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). The subject is asked to grade their own current level of function in each dimension into one of three degrees of disability (severe, moderate or none). Using the VAS, subjects record perceptions of current perceived health status with a grade ranging from 0 (the worst possible health status) to 100 (the best possible health status).

SF-36 PCS

SF-36 is included as an outcome measure in the SELECT-GCA trial.

SF-36 is a generic health-related quality-of-life instrument that can be used across age, disease and treatment groups and includes 8 domains: physical functioning; role limitations due to physical health problems; role limitations due to emotional health problems; social functioning; pain; energy/fatigue; emotional well-being; and general health problems. Summary scores are generated based on the eight domains. All items, scales, and summary measures have a score range of 0-100 with higher scores indicating better outcomes.

FACIT-Fatigue

FACIT-Fatigue is included as an outcome measure in the SELECT-GCA trial.

FACIT-Fatigue is a 13-item ePRO that evaluates fatigue/tiredness and its impact on daily activities and functioning, which has been validated in the general population and in other chronic diseases. This instrument includes items such as tiredness, weakness, listlessness, lack of energy, and the impact of these feelings on daily functioning (e.g., sleeping, and social activities)

10.1.2 Data collection

EQ-5D-5L

EQ-5D-5L was collected electronically at baseline and week 8, 24 and 52. Patients in the study entered data on an electronic device; these data were then uploaded to a server. The data on the server was considered source

If needed for any reason (e.g., vision impairment, literacy issues), site staff could read the ePRO questions aloud and record subject responses. To avoid biasing subject responses, these instruments was completed prior to drug administration and prior to any clinical assessments, discussion of adverse events (AEs) or any review of laboratory findings.

The relevant data collection time points are reported in Table 27 and Table 28, along with missing observations, the number and percentage missing since randomization and the number and percentage completed. Missing data were handled by NRI -MI. Values occurring on or after a subject´s first intercurrent event, usually when participants needed escape therapy, are considered as missing.

Table 27. Pattern of missing data and completion EQ-5D-5L, PBO arm in the SELECT-GCA study.

Time point	HRQoL population	Missing	Expected to complete (Patients on study)	Completion (Data available)
	Number of patients at randomization	Number of patients for whom data is missing (% of patients at randomization)	Number of patients "at risk" at time point X	Number of patients who completed (% of patients expected to complete)
Baseline	112	5 (4.5%)	112	107 (95.5%)
Week 8	112	28 (25.0%)	107	84 (78.5%)
Week 24	112	50 (44.6%)	99	62 (62.6)
Week 52	112	68 (60.7%)	87	44 (50.6)

Table 28. Pattern of missing data and completion EQ-5D-5L, UPA15 arm in the SELECT-GCA study.

Time point	HRQoL population	Missing	Expected to complete (Patients on study)	Completion (Data available)
	Number of patients at randomization	% of patients at randomization	Number of patients "at risk" at time point X	Number of patients who completed (% of patients expected to complete)
Baseline	209	11 (5.3%)	209	198 (94.7%)
Week 8	209	41 (19.6%)	204	168 (82.4%)
Week 24	209	69 (33.0%)	190	140 (73.7%)
Week 52	209	88 (42.1%)	177	121 (68.4%)

SF-36 PCS

SF-36 was collected electronically at baseline and week 8, 12, 24 and 52. Patients in the study entered data on an electronic device; these data were then uploaded to a server. The data on the server was considered source

If needed for any reason (e.g., vision impairment, literacy issues), site staff could read the ePRO questions aloud and record subject responses. To avoid biasing subject responses, these instruments was completed prior to drug administration and prior to any clinical assessments, discussion of adverse events (AEs) or any review of laboratory findings.

The relevant data collection time points are reported in Table 29 and Table 30, along with missing observations, the number and percentage missing since randomization and the number and percentage completed. Missing data were handled by NRI -MI. Values occurring on or after a subject´s first intercurrent event, usually when participants needed escape therapy, are considered as missing.

Table 29. Pattern of missing data and completion SF-36 PCS, PBO arm of the SELECT-GCA study (66)

Time point	HRQoL population	Missing	Expected to complete (Patients on study)	Expected to complete (Patients on study)	Completion (Data available)
	Number of patients at randomizatio n	Number of patients for whom data is missing (% of patients at randomizatio n)	Number of patients "at risk" at time point X		Number of patients who completed (% of patients expected to complete)
Baseline	112	4 (3.6%)	112		108 (96.4%)
Week 8	112	27 (24.1%)	107		85 (79.4%)
Week 12	112	35 (31.3%)	103		77 (74.8%)
Week 24	112	49 (43.8%)	99		63 (63.6%)
Week 52	112	68 (60.7%)	87		44 (50.6%)

Table 30. Pattern of missing data and completion SF-36 PCS, UPA15 arm of the SELECT-GCA (57)

Time point	HRQoL population	Missing	Expected to complete (Patients on study)	Completion (Data available)
	Number of patients at randomization	% of patients at randomization	Number of patients "at risk" at time point X	Number of patients who completed (% of patients expected to complete)
Baseline	209	9 (4.3%)	209	200 (96.2%)
Week 8	209	39 (18.7%)	204	170 (83.3%)
Week 12	209	48 (23.0%)	199	161 (80.9%)
Week 24	209	66 (31.6%)	190	143 (75.3%)
Week 52	209	86 (41.1%)	177	123 (69.5%)

FACIT-Fatigue

FACIT-Fatigue was collected electronically at baseline and week 8, 12, 24 and 52. Patients in the study entered data on an electronic device; these data were then uploaded to a server. The data on the server was considered source

If needed for any reason (e.g., vision impairment, literacy issues), site staff could read the ePRO questions aloud and record subject responses. To avoid biasing subject responses, these instruments was completed prior to drug administration and prior to any clinical assessments, discussion of adverse events (AEs) or any review of laboratory findings.

The relevant data collection time points are reported in Table 31 and Table 32 along with missing observations, the number and percentage missing since randomization and the number and percentage completed. Missing data were handled by NRI -MI. Values occurring on or after a subject´s first intercurrent event, usually when participants needed escape therapy, are considered as missing.

Table 31. Pattern of missing data and completion FACIT-Fatigue, PBO arm of the SELECT-GCA study.(66)

Time point	HRQoL population	Missing	Expected to complete (Patients on study)	Completion (Data available)
	Number of patients at randomization	Number of patients for whom data is missing (% of patients at randomization)	Number of patients "at risk" at time point X	Number of patients who completed (% of patients expected to complete)
Baseline	112	4 (3.6%)	112	108 (96.4%)
Week 8	112	27 (24.1%)	107	85 (79.4%)
Week 12	112	35 (31.3%)	103	77 (74.8%)
Week 24	112	49 (43.8%)	99	63 (63.6%)
Week 52	112	67 (59.8%)	87	45 (51.7%)

Table 32. Pattern of missing data and completion FACIT-Fatigue, UPA15 arm of the SELECT-GCA study (57)

Time point	HRQoL population	Missing	Expected to complete (Patients on study)	Completion (Data available)
	Number of patients at randomization	% of patients at randomization	Number of patients "at risk" at time point X	Number of patients who completed (% of patients expected to complete)
Baseline	209	9 (4.3%)	209	200 (95.7%)
Week 8	209	39 (18.7%)	204	170 (83.3%)
Week 12	209	48 (23.0%)	199	161 (80.9%)
Week 24	209	66 (31.6%)	190	143 (75.3%)
Week 52	209	86 (41.1%)	177	123 (69.5%)

10.1.3 HRQoL results

EQ-5D-5L

Results at baseline and all available data collection timepoints are presented in Table 33 (index score with Danish preference weights) and Table 34 (EQ-VAS). The timepoints were selected to capture relevant changes in clinical efficacy including EQ-5D-5L over time, considering the expected efficacy of upadacitinib and the clinical presentation of the disease. The mean change in HRQoL EQ-5D index (Danish Value Set) and EQ-5D VAS from baseline through the different data collection time points for both the intervention and comparator is displayed in Figure 16 and Figure 17.

Table 33. HRQoL EQ-5D index (Danish Value Set) summary statistics for upadacitinib and placebo in the SELECT-GCA trial.

	UPA 15 + 26 Wk CS Taper			Placebo + 52 Wk CS Taper			Intervention vs. comparator
	N	Visit Mean (SE)	LS Mean (SE)	N	Mean (SE)	LS Mean (SE)	LS Mean Difference (95% CI)
Baseline	198	[redacted]		107	[redacted]	[redacted]	
Week 8	168	[redacted]	[redacted]	84	[redacted]	[redacted]	[redacted]
Week 24	140	[redacted]	[redacted]	62	[redacted]	[redacted]	[redacted]
Week 52	121	[redacted]	[redacted]	44	[redacted]	[redacted]	[redacted]

Figure 16: Figure displaying the mean change in HRQoL EQ-5D index (Danish Value Set) from baseline through the different data collection time points for both the intervention and comparator

Table 34. HRQoL EQ-5D VAS summary statistics for upadacitinib and placebo in the SELECT-GCA trial.

	UPA 15 + 26 Wk CS Taper			Placebo + 52 Wk CS Taper			Intervention vs. comparator
	N	Visit Mean (SE)	LS Mean (SE)	N	Mean (SE)	LS Mean (SE)	LS Mean Difference (95% CI)
Baseline	198	[redacted]		107	[redacted]	[redacted]	[redacted]
Week 8	168	[redacted]	[redacted]	84	[redacted]	[redacted]	[redacted]
Week 24	140	[redacted]	[redacted]	62	[redacted]	[redacted]	[redacted]
Week 52	121	[redacted]	[redacted]	44	[redacted]	[redacted]	[redacted]

Figure 17: Figure displaying the mean change in HRQoL EQ-5D VAS from baseline through the different data collection time points for both the intervention and comparator.

No data is available for a comparison with tocilizumab. Available data is not comparable to data presented for upadacitinib, as no EQ-5D VAS or EQ-5D index score with Danish preference weights is available. For tocilizumab, limited data for EQ-5D is available, see Table 35, from the GiACTA trial. EQ- 5D was measured with EQ-5D-3L as an exploratory

outcome and reported descriptively, with no between-group comparisons in the GiACTA trial. (67)

Table 35. HRQoL EQ-5D Index Score for tocilizumab. (67)

	TCZ QW			Placebo + 52 Wk CS taper			Intervention vs. comparator
	N	Visit Mean	Mean change from baseline (SD)	N	Visit Mean	Mean change from baseline (SD)	LS Mean Difference (95% CI)
Baseline	99	0.74		49	0.66		
Week 52	60	N/A	0.10 (0.20)	17	N/A	-0.02 (0.16)	N/A

SF-36 PCS

Results at baseline and all available data collection timepoints are presented in Table 36. The timepoints were selected to capture relevant changes in clinical efficacy including SF-36, considering the expected efficacy of upadacitinib and the clinical presentation of the disease. The mean change in SF-36 PCS from baseline through the different data collection time points for both the intervention and comparator is displayed in Figure 18.

Table 36. Summary statistics for SF-36 PCS in the SELECT-GCA trial. (66)

	UPA 15 + 26 Wk CS Taper			Placebo + 52 Wk CS Taper			Intervention vs, comparator
	N	Visit Mean (SE)	LS Mean (SE)	N	Mean (SE)	LS Mean (SE)	LS Mean Difference (95% CI) per visit
Baseline	200	[redacted]		108	[redacted]	[redacted]	[redacted]
Week 8	170	[redacted]	[redacted]	85	[redacted]	[redacted]	[redacted]
Week 12	161	[redacted]	[redacted]	77	[redacted]	[redacted]	[redacted]
Week 24	143	[redacted]	[redacted]	63	[redacted]	[redacted]	[redacted]
Week 52	123	[redacted]	[redacted]	45	[redacted]	[redacted]	[redacted]

Figure 18: Figure displaying the mean change SF-36 PCS from baseline through the different data collection time points for both the intervention and comparator

The outcome for SF-36 in the SELECT-GCA trial was the difference in change from baseline between upadacitinib 15 mg and placebo is presented in Table 37. For a comparison to tocilizumab, the same outcome from the GiACTA study is presented in the same table. Both upadacitinib and tocilizumab demonstrated statistically significant improvement in FACIT-Fatigue compared to placebo.

Table 37. HRQoL SF-36 PCS outcomes in the SELECT-GCA trial and the GiACTA trial for upadacitinib and tocilizumab, compared to placebo. (45,63)

	UPA 15		PBO		UPA 15 vs PBO	TCZ QW		PBO		TCZ QW vs PBO
Baseline Mean (SE)	201	44.3±9.3	108	45.0±10.		100	43.10	51	41.12	
Week 52 **LS mean change from baseline**	123	2.5 (1.2; 3.8)	45	−1.3 (−3.3; 0.7)	3.8 (1.4; 6.1) p=0.002	NA	4.10 (NA)	NA	−1.49 (NA)	5.59 (0.86; 10.32) p=0,002)

NA; Not Available

FACIT-Fatigue

Results at baseline and all available data collection timepoints are presented in Table 38. The timepoints were selected to capture relevant changes in clinical efficacy including FACIT-Fatigue over time, considering the expected efficacy of upadacitinib and the clinical presentation of the disease. The mean change in FACIT-Fatigue from baseline through the different data collection time points for both the intervention and comparator is displayed in Figure 19.

Table 38. Summary statistics for FACIT-Fatigue in the SELECT-GCA trial (66)

	UPA 15 + 26 Wk CS Taper			Placebo + 52 Wk CS Taper			Intervention vs. comparator
	N	Visit Mean (SE)	LS Mean (SE)	N	Mean (SE)	LS Mean (SE)	LS Mean Difference (95% CI) per visit
Baseline	200	[redacted]		108	[redacted]	[redacted]	[redacted]
Week 8	170	[redacted]	[redacted]	85	[redacted]	[redacted]	[redacted]
Week 12	161	[redacted]	[redacted]	77	[redacted]	[redacted]	[redacted]
Week 24	143	[redacted]	[redacted]	63	[redacted]	[redacted]	[redacted]
Week 52	123	[redacted]	[redacted]	45	[redacted]	[redacted]	[redacted]

Figure 19. Figure displaying the mean change FACIT-Fatigue from baseline through the different data collection time points for both the intervention and comparator.

The outcome for FACIT-Fatigue in the SELECT-GCA trial was the difference in change from baseline between upadacitinib 15 mg and placebo is presented in Table 39. For comparison to tocilizumab, the same outcome from the GiACTA study is presented in the same table. Both upadacitinib and tocilizumab demonstrated statistically significant improvement in FACIT-Fatigue compared to placebo.

Table 39. HRQoL FACIT-Fatigue outcomes in the SELECT-GCA trial and the GiACTA trial for upadacitinib and tocilizumab, compared to placebo. (63,72)

	UPA 15		PBO		UPA 15 vs PBO	TCZ QW		PBO		TCZ QW vs PBO
	N	Mean (SE)	N	Mean (SE)		N	Mean (SE)	N	Mean (SE)	
Baseline	209	36.0 (11.2)	112	37.5 (11.7)		100	36.1 (11.1)	51	31.4 (13.6)	
Week 52 **LS mean change from baseline**	123	1.7 (0.2; 3.1)	44	−2.4 (−4.7; −0.1)	4.0 (1.3; 6.8) p=0.004	NA	5.3 (CI NA)	NA	-0.42	p<0.001

NA; Not Available

10.1.4 Conclusion of the comparison of impact on HRQoL

Patients with GCA experience impairment to their quality of life, which is driven by physical symptoms, a high prevalence of comorbidities and treatment burden of corticosteroids. (73–75) Upadacitinib and tocilizumab are expected to have similar efficacy on symptoms and corticosteroid burden, drivers of the health-related quality of life impairment or patients with GCA. Available data for EQ-5D, FACIT-Fatigue and SF-36 also suggests that both upadacitinib and tocilizumab improves the health-related quality of life, with comparable efficacy for these outcomes.

10.2 Health state utility values (HSUVs) used in the health economic model

N/A – cost-minimization analysis is the most relevant analysis for this application.

10.3 Health state utility values measured in other trials than the clinical trials forming the basis for relative efficacy

N/A – cost-minimization analysis is the most relevant analysis for this application.

11. Resource use and associated costs

A cost-minimization analysis (CMA) was conducted under the assumption of equivalent efficacy between tocilizumab and upadacitinib in achieving sustained remission in GCA patients, as demonstrated in pivotal clinical trials and the indirect treatment comparison in section 7. The analysis considers the costs associated with drug acquisition, administration, patient time, monitoring, and adverse event management over a one-year time horizon.

- Drug costs were sourced from the Medicines Councils price database Medicinpriser.dk.
- Dosing and administration data were extracted from European Medicines Agency (EMA)-approved SmPCs.
- Resource utilization estimates were informed by the SmPC and costs affiliated with them were extracted from relevant Danish databases.
- Adverse event rates were derived from relevant clinical literature (71)

11.1 Medicines - intervention and comparator

The cost-minimization analysis compares upadacitinib to tocilizumab for the treatment of GCA, see Table 40. Both medicines are included in the health economic model and documented in the 'Key figures including general mortality' Excel file. Waste was modelled in Excel by assuming no vial sharing for tocilizumab, in line with DMC guidelines, and no tablet wastage for upadacitinib due to its fixed oral dosing. Treatment duration for both medicines was assumed to be 52 weeks, reflecting standard practice, and study design.

A scenario analysis was conducted incorporating dosing patterns observed in a real-world study from Denmark (41). The analysis includes dosing frequencies of once weekly and every other week. Initial dosing distributions were presented in the study and applied to our analyses the first 6 months, and then it was assumed that patients experiencing relapse on an every-other-week regimen would escalate to weekly dosing.

Table 40. Medicines used in the model.

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Upadacitinib	15 mg oral tablet	100%	Daily	No
Tocilizumab (RoActemra)	162 mg pre-filled syringe	100%	Every Week	No

11.1.1 Real world dosing scenario 1:

A scenario analysis was conducted incorporating dosing patterns observed in a real-world study from Denmark (41). The analysis includes dosing frequencies of once weekly and every other week. Initial dosing distributions were presented in the study and applied to our analyses the first 6 months, and then it was assumed that patients experiencing relapse on an every-other-week regimen would escalate to weekly dosing.

11.1.2 Real-world dosing scenario 2:

In the real-world dosing scenario 2, we model more stratified between different dosing patterns based on the Danish real world study (41). This was described further in section 8.2.

Tocilizumab – year 2 dosing assumptions in the model

In year 2, patients receiving tocilizumab (TCZ) are distributed across the dosing patterns in Table 41:

Table 41. Tocilizumab dosing assumptions for year two of the model.

	Proportion of patients % (n/N)	Dose and cost assumptions for year 2
On treatment, n (%)	25%	
Without taper	*17%*	We assume the same average dosing as in the second half of year 1, between weekly (QW) and every-other-week (Q2W) dosing (52%/48%) applied throughout year 2. This corresponds to an average of 0.76 injections per week over the full year
After taper from QW to Q2W	*2%*	Among patients remaining on treatment after tapering, we assume that 2/8 receive Q2W and 6/8 receive Q3W dosing for the entire year, corresponding to an average of 0.38 injections per week.
After taper from Q2W to Q3W	*6%*	
Discontinued due to relapse/non-response	8%	For these patients no TCZ dosing or additional costs in year 2 are assumed
Discontinued in remission, total	67%	
Abrupt discontinuation	*38%*	For these patients we assume no TCZ dosing in year 2.

After taper from QW to Q2W	*23%*	Taper to Q2W, then stop: assumed Q2W dosing in the first half of the year and no dosing in the second half (average 0.25 injections per week over the year).
After taper from Q2W to Q3W	*6%*	Taper to Q3W, then stop: assumed Q3W dosing in the first half of the year and no dosing in the second half (average 0.17 injections per week over the year).

Relapse during year 2:
Based on assumptions on sustained remission in section 8.2 70% of patients who discontinue TCZ during year 2 experience a relapse and restart TCZ at weekly dosing (QW) in the second half of the year (0 injections per week in H1, 1 injection per week in H2; average 0.5 injections per week over year 2 for this subgroup).

Combining these patterns gives an overall average TCZ dosing of 0.463 injections per week in year 2 in the model.

Upadacitinib – year 2 dosing assumptions in the model

In the real-world dosing scenario 2, we model more stratified between different dosing patterns based on the Danish real world study (41). This was described further in section 8.2. The distribution of patients into different dosing patterns in the model is described in Table 42.

Table 42. Upadacitinib dosing assumptions for year two of the model.

	Proportion of patients% (n/N)	Dose and cost assumptions for year 2
On treatment without taper, n (%)	25%	Patients are assumed to receive 7 doses per week throughout year 2.
Discontinued due to relapse/non-response	8%	No UPA dosing or other treatment costs are assumed in year 2.
Discontinued in remission, total	67%	For remission-related discontinuations, based on the 104-week results from SELECT-GCA, we assume full-dose UPA (7 doses per week) in the first half of year 2 and no UPA in the second half (average 3.5 doses per week

Relapse during year 2:
Based on assumptions on sustained remission in section 8.2, we assume that 70% of patients who discontinue UPA during year 2 experience a relapse and restart UPA at 7

doses per week in the second half of the year (0 in H1, 7 in H2; average 3.5 doses per week over year 2 for this subgroup).

These assumptions result in an overall average UPA dosing of 5.748 doses per week in year 2 in the model.

11.2 Medicines– co-administration

Prednisolone is part of the standard background therapy for GCA and is assumed to be used similarly in both treatment arms as the recommended taper regimens for upadacitinib and tocilizumab are very similar and not assumed to incur any incremental costs. Therefore, it is not included in the cost-minimization comparison.

11.3 Administration costs

Administration costs used in the model are presented in Table 43. For administration costs for subcutaneous tocilizumab (RoActemra) were assumed that 20% of the patients needed to receive the injection at the hospital. Furthermore, we assumed that all patients received one training session by an HCP for 30 minutes. For oral administration (upadacitinib) we assumed no administration costs.

In addition, and consistent with DMC's prior assessment of RoActemra, we included 15 minutes of nurse time per dispensing event. Tocilizumab is assumed to be dispensed at the hospital every second month, resulting in six dispensing events annually. For upadacitinib, dispensing was assumed to occur monthly, as each package contains 28 tablets.

Table 43. Administration costs used in the model

Administration type	Frequency	Unit cost [DKK]	Cost pr. year	Reference
Upadacitinib **Oral administration**	0	1684 (Nurse 30 min)	0	Assumption
Tocilizumab, subcutaneous administration	Every week for 20% of the patients	1684 (Nurse 30 min)	17573,74	DRG takster 2025; MDC08 - dagsgruppe, pat. mindst 7 år
Upadacitinib, drug dispensing	Every month	115,5	1506,66	Rigshospitalet price list, adjusted for inflation using Statistics Denmark
Tocilizumab, drug dispensing	Every second month	115,5	753,3	Rigshospitalet price list, using Statistics Denmark

11.4 Disease management costs

The frequency of monitoring costs were allocated to each treatment based on the summary of product characteristics for upadacitinib and the NICE assessment TA518 for tocilizumab, see Table 44.(64) The costs were sourced from Amgros' valuation of unit costs. The costs of liver function tests and lipid panels are assumed to be the same as for blood test.

Since upadacitinib and tocilizumab are considered clinically equivalent, it can be inferred that the disease management costs associated with other factors, such as corticosteroids, are comparable between the treatments. As a result, these costs have been deemed equal and thus excluded from the cost-minimization analysis.

Furthermore, according to expert input to the analysis we have included costs of follow up monitoring for tocilizumab. As a result of the CRP/ESP masking that occurs with IL-6 treatments, these patients often require additional testing during diagnosis and monitoring of remission. According to the Danish expert providing insights on clinical practice for this application (52), additional application of diagnostic tools are required when treating with a IL-6, these tools include ultrasound, magnetic resonance angiography (MR) and PET-CT depending on GCA type. We assume that the patient undergoes either ultrasound, MRI, or PET-CT at the monitoring visit. We assign a weight of 50% to ultrasound, with MRI and PET-CT each receiving a weight of 25%. We assign three ultrasound/PET-CT/MR monitoring visits each year.

Table 44. Disease management costs used in the model.

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
Blood test (upadacitinib)	0,08 weekly	47,23	-	https://www.amgros.dk/media/2223/amgros-vaerdisaetning-af-enhedsomkostninger.pdf
Liver function test (upadacitinib)	0,08 weekly	47,23	-	Assume same costs as blood test, https://www.amgros.dk/media/2223/amgros-vaerdisaetning-af-enhedsomkostninger.pdf
Lipid panel	0,08 weekly	47,23	-	Assume same costs as blood test, https://www.amgros.dk/media/2223/amgros-vaerdisaetning-af-enhedsomkostninger.pdf
Blood test (tocilizumab)	0,17 weekly	47,23	-	https://www.amgros.dk/media/2223/amgros-vaerdisaetning-af-enhedsomkostninger.pdf
Liver function test	0,17 weekly	47,23	-	Assume same costs as blood test, https://www.amgros.dk/media/2223/amgros-vaerdisaetning-af-enhedsomkostninger.pdf

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
(tocilizumab)				
Lipid panel (tocilizumab)	0,17 weekly	47,23	-	Assume same costs as blood test, https://www.amgros.dk/media/2223/amgros-vaerdisaetning-af-enhedsomkostninger.pdf
Ultra sound		1684	BLNJ33	https://casemix360.solutions.iqvia.com/Interactive Prod Valgte Diagnoser (Valgte Diagnoser: A (DM316A)Arteritis temporalis uden reumatisk polymyalgi - Valgte Procedurer: P (BLNJ33)Ultralydbehandling - A (DM316A)Arteritis temporalis uden reumatisk polymyalgi - Valgte Procedurer: P (BLNJ33)Ultralydbehandling
PET	0,06 weekly	4565	(WMBPSXYBH)	https://casemix360.solutions.iqvia.com/Interactive Prod - Valgte DiagnoserA (DM316A)Arteritis temporalis uden reumatisk polymyalgi - Valgte Procedurer - P (WMBPSXYBH)PET Thorax på PET/CT, breath hold
MR		2408	UXMH00	https://casemix360.solutions.iqvia.com/Interactive Prod. Gjennomsnitt av Valgte Procedurer P (UXMH00)MR-skanning af hele kroppen og P (UXMA05)MR-skanning af kranieknogler

11.5 Costs associated with management of adverse events

Tocilizumab and upadacitinib are both associated with acceptable safety profiles. Based on the assumption of equivalent clinical efficacy, a similar incidence and profile of adverse events for the two treatments is expected. Likewise, comparable reduction in corticosteroid use is anticipated, suggesting a similar risk of steroid-related adverse events. As a result, adverse event costs have been excluded from the base case analysis. However, to enhance transparency, selected adverse events have been included in scenario analyses. Given their limited impact on total costs, the analysis includes only on the most serious adverse events associated with JAK inhibitors—namely, major adverse cardiovascular events (MACE) and venous thromboembolism (VTE). This is a conservative approach as it only assigns costs to upadacitinib.

Cost estimates for treating the relevant adverse events were incorporated into the model based on Danish Diagnosis Related Group rates (DRG-rates), see Table 45. Costs were allocated on a weekly basis by considering both the risk of adverse events (AEs) per week and the associated costs of those AEs.

Table 45. Cost associated with management of adverse events.

	DRG code	Unit cost/DRG tariff
MACE (Major adverse cardiovascular events)	DRG tariffs 2025 DRG 05MP32 - 05MP37 (mean) (Akut myokardieinfarkt med ST-segment elevation)	72 537,00
VTE (Venous thromboembolism)	DRG tariffs 2025, DRG 04MA04 and 05MA12 (mean) (Lungeemboli; Perifer karsygdom)	31 010,00

11.6 Subsequent treatment costs

N/A

11.7 Patient costs

Patient costs used in the model are presented in Table 46. Patients receiving tocilizumab are assumed to come into hospital or specialist to administer their treatment (52 visits per year), as described at section 11.3. Each visit involves an estimated time commitment of 0.5 hours, and the travel costs are based on DMCs catalogue of unit costs. Patients receiving upadacitinib are assumed to take the drug orally at home, requiring no visits for administration. Consequently, there are no administration-related patient costs for upadacitinib.

For tocilizumab, patients are assumed to collect the drug every two months (6 visits per year), with each visit requiring 0.25 hours and travel costs based on DMCs catalogue of unit costs. For upadacitinib, monthly dispensing (12 visits per year) is assumed, also with 0.25 hours per visit, and travel costs (see section 11.3 for further description).

Monitoring requirements for patients receiving upadacitinib include routine blood tests, liver function tests, and lipid panel assessments. Each monitoring visit is assumed to take approximately 1 hour, with associated travel costs of DKK 140. Visit frequencies for upadacitinib are based on the product summary for Rinvoq, while frequencies for tocilizumab are derived from NICE Technology Appraisal TA518. For the 20% of patients receiving tocilizumab administration at the hospital, it is assumed that all required monitoring tests, and the follow-up monitoring for tocilizumab are performed during these visits.

Table 46. Patient costs used in the model.

Activity	Time spent [minutes, hours, days]
Administration and monitoring (Tocilizumab)	10,44 hours for visits, with DMCs specified rate applied for travel expenses per visit
Administration (Upadacitinib)	0 hours due to oral administration
Drug dispensing (Tocilizumab)	1,5 Hours for visits, with DMCs specified rate applied for travel expenses per visit
Drug dispensing (Upadacitinib)	3 Hours for visits, with DMCs specified rate applied for travel expenses per visit
Monitoring costs (Upadacitinib)	4,16 hours for visits, with DMCs specified rate applied for travel expenses per visit

11.8 Other costs (e.g. costs for home care nurses, out-patient rehabilitation and palliative care cost)

N/A

12. Results

12.1 Base case overview

An overview of the base case including the central aspects is presented in Table 47.

Table 47. Base case overview.

Feature	Description
Comparator	Tocilizumab
Type of model	Cost minimization analysis
Time horizon	1 year
Treatment line	1st line. Subsequent treatment lines not included.
Measurement and valuation of health effects	N/A
Costs included	Medicine costs Hospital costs Monitoring costs Costs of adverse events Patient & travel costs
Dosage of medicine	Fixed dosage
Average time on treatment	Intervention: 52 weeks Comparator: 52 weeks
Parametric function for PFS	N/A
Parametric function for OS	N/A
Inclusion of waste	No
Average time in model health state	N/A

12.1.1 Base case results

The base case results for the cost minimization analysis are presented in Table 48. The base case shows lower medicines costs, administration costs, disease management costs as well as patient costs for upadacitinib compared to tocilizumab.

Table 48 Base case results, discounted estimates

	Upadacitinib	Tocilizumab	Difference
Medicine costs	78 532	93 179	-14 647
Medicine costs – co-administration	N/A	N/A	N/A
Administration	1 507	20 011	-18 504,41
Disease management costs	616	9014	-8 398
Costs associated with management of adverse events	0	0	0
Subsequent treatment costs	N/A	N/A	N/A
Patient costs	3 613	7 106	-3 493
Palliative care costs	N/A	N/A	N/A
Total costs	**84 268**	**129 311,09**	**-45 043,03**
Total life years	**Assumed clinical equivalent**	**Assumed clinical equivalent**	**Assumed clinical equivalent**
Total QALYs	**Assumed clinical equivalent**	**Assumed clinical equivalent**	**Assumed clinical equivalent**
Incremental costs per life year gained		**Assumed clinical equivalent**	
Incremental cost per QALY gained (ICER)		**Assumed clinical equivalent**	

12.2 Sensitivity analyses

12.2.1 Deterministic sensitivity analyses

The results obtained from deterministic one-way sensitivity analysis are presented in Table 49.

Table 49. One-way sensitivity analyses results.

Change	Reason / Rational / Source	Incremental cost (DKK)	Incremental benefit (QALYs)	ICER (DKK/QALY)
Base case	Cost-min model	-45 043,03	N/A	N/A
Real world dosing – Scenario 1*	Cost-min model	-18 696,58	N/A	N/A
Scenario 2*	Cost-min model (weighted year 1 & 2)	-7 275,8	N/A	N/A
Including safety costs	Cost-min model	--44 410,10	N/A	N/A

*The real-world dosing scenarios are presented in chapter 11.1

12.2.2 Probabilistic sensitivity analyses

We conducted a probabilistic sensitivity analysis to quantify uncertainty in key model inputs related to dosing patterns and serious adverse events. Uncertainty was incorporated for the dosing proportions for tocilizumab in both Year 1 and Year 2, as well as for upadacitinib in Year 2 in scenario 2. The proportion for upadacitinib in the first year was treated as fixed because the SPC specifies a strict once-daily dosing regimen throughout the first treatment year, leaving no meaningful uncertainty to model.

Uncertainty in the rates of major adverse cardiovascular events (MACE) and venous thromboembolism (VTE) was also included in the PSA. These rates were modelled using lognormal distributions. This choice reflects that event rates are positive and often right-skewed, making the lognormal distribution an appropriate representation. We therefore estimated the mean and standard deviation of the log-transformed rates using the study-reported confidence intervals. After sampling from the lognormal distributions, the resulting annual rates were converted into weekly probabilities to align with the cycle structure of the model.

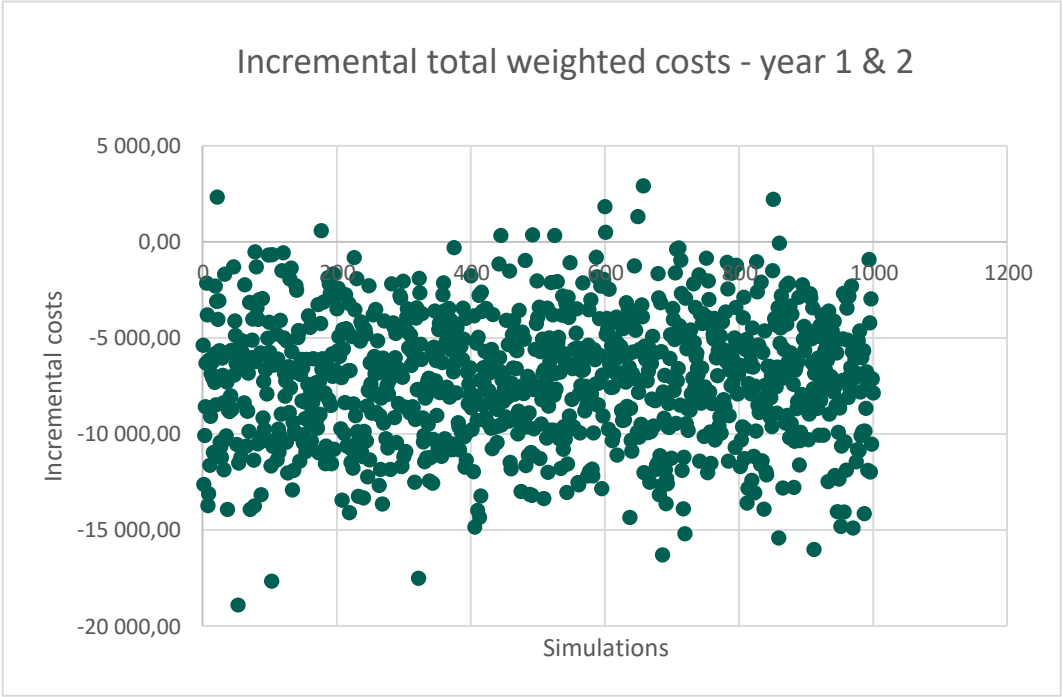
For the proportions related to the dosing regimens, we used beta distributions. This is consistent with standard practice because the beta distribution is defined on the [0,1] interval and accommodates uncertainty based on observed sample sizes. The shape parameters for each beta distribution were derived from the number of patients and observed proportions in the clinical trial. Each dosing proportion was therefore represented by its own beta distribution.

The PSA consisted of 1000 iterations. In each iteration, new parameter values were drawn from the distributions described above, and the full model was run to generate total costs and outcomes for each treatment strategy. The resulting simulations provide

the basis for estimating the uncertainty around the incremental costs of treatment with upadacitinib.

PSA results indicate incremental weighted costs of −7,403.34 across years 1 and 2, consistent with the DSA, and the PSA plot in Figure 20 shows that nearly all iterations fall below zero.

Figure 20. PSA plot.



13. Budget impact analysis

Number of patients (including assumptions of market share)

The number of patients expected to be treated with upadacitinib over the next five-year period is presented in Table 50. As described in section 3.2, about 540 patients are diagnosed with GCA in Denmark every year, based on incidence data. Approximately 340 of these patients are estimated to be treated with tocilizumab. As upadacitinib and tocilizumab have equal clinical efficacy, upadacitinib is expected to have 50% of the market shares for this population. No additional patient groups are expected to be treated because of the introduction of upadacitinib. Treatment length is assumed to be 52 weeks, as in the cost-minimization, leading to the same number of patients being treated every year.

Table 50. Number of new patients expected to be treated over the next five-year period if the medicine is introduced (adjusted for market share).

	Year 1	Year 2	Year 3	Year 4	Year 5
			Recommendation		
upadacitinib	170	170	170	170	170
tocilizumab	170	170	170	170	170
			Non-recommendation		
upadacitinib	0	0	0	0	0
tocilizumab	340	340	340	340	340

Budget impact:

The expected budget impact of recommending upadacitinib for GCA is presented in Table 51.

Table 51. Expected budget (DKK) impact of recommending the medicine for the indication.

	Year 1	Year 2	Year 3	Year 4	Year 5
The medicine under consideration is recommended	36 416 053	36 416 053	36 416 053	36 416 053	36 416 053
The medicine under consideration is NOT recommended	43 965 770	43 965 770	43 965 770	43 965 770	43 965 770
Budget impact of the recommendation	-7 549 717	-7 549 717	-7 549 717	-7 549 717	-7 549 717

Budget impact with real-world dosing scenario 2:

Table 52. Expected budget (DKK) impact of recommending the medicine for the indication in real-world dosing scenario 2.

	Year 1	Year 2	Year 3	Year 4	Year 5
The medicine under consideration is recommended	27 059 860	25 574 944	25 574 944	25 574 944	25 574 944
The medicine under consideration is NOT recommended	26 481 860	26 481 860	26 481 860	26 481 860	26 481 860
Budget impact of the recommendation	**577 999**	**-906 915**	**-906 915**	**-906 915**	**-906 915**

In real-world dosing scenario 2, we assume a two-year patient journey with costs allocated separately to each year.

14. List of experts

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15. References

1. Weyand CM, Goronzy JJ. Immunology of Giant Cell Arteritis. Circulation Research. 2023 Jan 20;132(2):238–50.

2. Borchers AT, Gershwin ME. Giant cell arteritis: A review of classification, pathophysiology, geoepidemiology and treatment. Autoimmunity Reviews. 2012 May 1;11(6):A544–54.

3. Savage COS, Harper L, Cockwell P, Adu D, Howie AJ. ABC of arterial and vascular disease.

4. Koster MJ, Matteson EL, Warrington KJ. Large-vessel giant cell arteritis: diagnosis, monitoring and management. Rheumatology. 2018 Feb 1;57(suppl_2):ii32–42.

5. Ly KH, Régent A, Tamby MC, Mouthon L. Pathogenesis of giant cell arteritis: More than just an inflammatory condition? Autoimmunity Reviews. 2010 Aug 1;9(10):635–45.

6. Stamatis P, Turesson C, Michailidou D, Mohammad AJ. Pathogenesis of giant cell arteritis with focus on cellular populations. Front Med [Internet]. 2022 Nov 17 [cited 2025 Mar 24];9. Available from: https://www.frontiersin.org/journals/medicine/articles/10.3389/fmed.2022.1058600/full

7. Hartmann B, Mohan SV, Goronzy JJ, Weyand CM. Abstract 14947: JAK/STAT-Signaling in Giant Cell Arteritis. Circulation. 2013 Nov 26;128(suppl_22):A14947–A14947.

8. Gonzalez-Gay MA, Miranda-Filloy JA, Lopez-Diaz MJ, Perez-Alvarez R, Gonzalez-Juanatey C, Sanchez-Andrade A, et al. Giant Cell Arteritis in Northwestern Spain: A 25-Year Epidemiologic Study. Medicine. 2007 Mar;86(2):61.

9. Koster MJ, Warrington KJ. Giant cell arteritis: pathogenic mechanisms and new potential therapeutic targets. BMC Rheumatol. 2017 Dec;1(1):2.

10. Samson M, Corbera-Bellalta M, Audia S, Planas-Rigol E, Martin L, Cid MC, et al. Recent advances in our understanding of giant cell arteritis pathogenesis. Autoimmunity Reviews. 2017 Aug 1;16(8):833–44.

11. Duhaut P, Pinede L, Demolombe-Rague S, Loire R, Seydoux D, Ninet J, et al. Giant cell arteritis and cardiovascular risk factors: A multicenter, prospective case-control study. Arthritis & Rheumatism. 1998;41(11):1960–5.

12. Castañeda S, Prieto-Peña D, Vicente-Rabaneda EF, Triguero-Martínez A, Roy-Vallejo E, Atienza-Mateo B, et al. Advances in the Treatment of Giant Cell Arteritis. Journal of Clinical Medicine. 2022 Jan;11(6):1588.

13. Sánchez-Costa JT, Melero González RB, Fernández-Fernández E, Silva MT, Belzunegui Otano JM, Moriano C, et al. POS0795 EPIDEMIOLOGY, DIAGNOSIS AND

CLINICAL CHARACTERISTICS OF GIANT CELL ARTERITIS IN PATIENTS INCLUDED IN THE ARTESER MULTICENTER STUDY. Annals of the Rheumatic Diseases. 2022 Jun 1;81:685–6.

14. Hellmich B, Agueda A, Monti S, Buttgereit F, De Boysson H, Brouwer E, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Annals of the Rheumatic Diseases. 2020 Jan;79(1):19–30.

15. Watts RA, Hatemi G, Burns JC, Mohammad AJ. Global epidemiology of vasculitis. Nat Rev Rheumatol. 2022 Jan;18(1):22–34.

16. Dejaco C, Duftner C, Buttgereit F, Matteson EL, Dasgupta B. The spectrum of giant cell arteritis and polymyalgia rheumatica: revisiting the concept of the disease. Rheumatology. 2016 Aug 1;kew273.

17. Hemmig AK, Aschwanden M, Seiler S, Berger CT, Köhn P, Kyburz D, et al. Long delay from symptom onset to first consultation contributes to permanent vision loss in patients with giant cell arteritis: a cohort study. RMD Open. 2023 Jan;9(1):e002866.

18. Petri H, Nevitt A, Sarsour K, Napalkov P, Collinson N. Incidence of Giant Cell Arteritis and Characteristics of Patients: Data-Driven Analysis of Comorbidities. Arthritis Care & Research. 2015 Mar;67(3):390–5.

19. Chen JJ, Leavitt JA, Fang C, Crowson CS, Matteson EL, Warrington KJ. Evaluating the Incidence of Arteritic Ischemic Optic Neuropathy and Other Causes of Vision Loss from Giant Cell Arteritis. Ophthalmology. 2016 Sep 1;123(9):1999–2003.

20. Vodopivec I, Rizzo JF. Ophthalmic manifestations of giant cell arteritis. Rheumatology. 2018 Feb 1;57(suppl_2):ii63–72.

21. Ponte C, Grayson PC, Robson JC, Suppiah R, Gribbons KB, Judge A, et al. 2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis. Annals of the Rheumatic Diseases. 2022 Dec;81(12):1647–53.

22. Luqmani R, Lee E, Singh S, Gillett M, Schmidt WA, Bradburn M, et al. The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study. Health Technol Assess. 2016 Nov;20(90):1–238.

23. de Boysson H, Lambert M, Liozon E, Boutemy J, Maigné G, Ollivier Y, et al. Giant-cell arteritis without cranial manifestations: Working diagnosis of a distinct disease pattern. Medicine. 2016 Jun;95(26):e3818.

24. Ponte C, Rodrigues AF, O'Neill L, Luqmani RA. Giant cell arteritis: Current treatment and management. World J Clin Cases. 2015 Jun 16;3(6):484–94.

25. Lyons HS, Quick V, Sinclair AJ, Nagaraju S, Mollan SP. A new era for giant cell arteritis. Eye. 2020 Jun;34(6):1013–26.

26. Dejaco C, Ramiro S, Bond M, Bosch P, Ponte C, Mackie SL, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice: 2023 update. Annals of the Rheumatic Diseases. 2024 Jun 1;83(6):741–51.

27. Sheth S, Solomon A, Antiochos B, Evans N, Ratchford EV. Vascular Disease Patient Information Page: Giant cell (temporal) arteritis. Vasc Med. 2022 Oct;27(5):521–4.

28. Li KJ, Semenov D, Turk M, Pope J. A meta-analysis of the epidemiology of giant cell arteritis across time and space. Arthritis Res Ther. 2021 Mar 11;23(1):82.

29. Ness T, Bley TA, Schmidt WA, Lamprecht P. The Diagnosis and Treatment of Giant Cell Arteritis. Deutsches Ärzteblatt international [Internet]. 2013 May 24 [cited 2025 Mar 24]; Available from: https://www.aerzteblatt.de/10.3238/arztebl.2013.0376

30. Mohammad AJ, Englund M, Turesson C, Tomasson G, Merkel PA. Rate of Comorbidities in Giant Cell Arteritis: A Population-based Study. J Rheumatol. 2017 Jan;44(1):84–90.

31. Amiri N, De Vera M, Choi HK, Sayre EC, Avina-Zubieta JA. Increased risk of cardiovascular disease in giant cell arteritis: a general population–based study. Rheumatology. 2016 Jan;55(1):33–40.

32. Li L, Neogi T, Jick S. Giant cell arteritis and vascular disease—risk factors and outcomes: a cohort study using UK Clinical Practice Research Datalink. Rheumatology. 2017 Jan 11;kew482.

33. Broder MS, Sarsour K, Chang E, Collinson N, Tuckwell K, Napalkov P, et al. Corticosteroid-related adverse events in patients with giant cell arteritis: A claims-based analysis. Seminars in Arthritis and Rheumatism. 2016 Oct;46(2):246–52.

34. Therkildsen P, Nielsen BD, De Thurah A, Hansen IT, Nørgaard M, Hauge EM. All-cause and cause-specific mortality in patients with giant cell arteritis: a nationwide, population-based cohort study. Rheumatology. 2022 Mar 2;61(3):1195–203.

35. Therkildsen P, De Thurah A, Hansen IT, Nørgaard M, Nielsen BD, Hauge EM. Giant cell arteritis: A nationwide, population-based cohort study on incidence, diagnostic imaging, and glucocorticoid treatment. Seminars in Arthritis and Rheumatism. 2021 Apr;51(2):360–6.

36. Richard A. Watts, Gulen Hatemi, Jane C. Burns and Aladdin J. Mohammad. Global epidemiology of vasculitis | Nature Reviews Rheumatology. Nature Reviews Reumatology. 2022;18:22–34.

37. Sharma A, Mohammad AJ, Turesson C. Incidence and prevalence of giant cell arteritis and polymyalgia rheumatica: A systematic literature review. Seminars in Arthritis and Rheumatism. 2020 Oct;50(5):1040–8.

38. Stamatis P, Turkiewicz A, Englund M, Turesson C, Mohammad AJ. Epidemiology of biopsy-confirmed giant cell arteritis in southern Sweden—an update on incidence and first prevalence estimate. Rheumatology. 2022 Jan 1;61(1):146–53.

39. Statistics Denmark. Population Figures. [cited 2025 May 12]. Population figures. Available from: https://www.dst.dk/en/Statistik/emner/borgere/befolkning/befolkningstal

40. Hansen IT, Masic D, Chrysidis S, Gade KH. National behandlingsvejledning. Dansk Rheumatologisk Selskab.

41. Nielsen MK, Nielsen AW, Donskov AO, Hansen IT, Nielsen BD, Mørk C, et al. Taper versus discontinuation of tocilizumab in patients with giant cell arteritis: Real-world experience from a tertiary center. Seminars in Arthritis and Rheumatism. 2024 Oct;68:152508.

42. Mainbourg S, Addario A, Samson M, Puéchal X, François M, Durupt S, et al. Prevalence of Giant Cell Arteritis Relapse in Patients Treated With Glucocorticoids: A Meta-Analysis. Arthritis Care & Research. 2020 Jun;72(6):838–49.

43. Knight, Börjesson, Larsson, Turesson. Riktlinjer för utredning, behandling och uppföljning av jättecellsarterit. Svensk Reumatologisk Förening; 2023.

44. Cain DW, Cidlowski JA. Immune regulation by glucocorticoids. Nat Rev Immunol. 2017 Apr;17(4):233–47.

45. Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, et al. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017 Jul 27;377(4):317–28.

46. Unizony SH, Bao M, Han J, Luder Y, Pavlov A, Stone JH. Treatment failure in giant cell arteritis. Annals of the Rheumatic Diseases. 2021 Nov 1;80(11):1467–74.

47. Gale S, Wilson JC, Chia J, Trinh H, Tuckwell K, Collinson N, et al. Risk Associated with Cumulative Oral Glucocorticoid Use in Patients with Giant Cell Arteritis in Real-World Databases from the USA and UK. Rheumatol Ther. 2018 Dec 1;5(2):327–40.

48. Yasir M, Goyal A, Sonthalia S. Corticosteroid Adverse Effects. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Mar 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK531462/

49. Unizony SH, Dasgupta B, Fisheleva E, Rowell L, Schett G, Spiera R, et al. Design of the Tocilizumab in Giant Cell Arteritis Trial. International Journal of Rheumatology. 2013;2013:1–10.

50. European Medicines Agency. Summary of Product Characteristics RoActemra.

51. Aletaha D, Kerschbaumer A, Kastrati K, Dejaco C, Dougados M, McInnes IB, et al. Consensus statement on blocking interleukin-6 receptor and interleukin-6 in inflammatory conditions: an update. Annals of the Rheumatic Diseases. 2023 Jun;82(6):773–87.

52. Stavros Chrysidis. Expert Opinion: Clinical evaluation and unmet need in GCA.

53. Taylor PC, Choy E, Baraliakos X, Szekanecz Z, Xavier RM, Isaacs JD, et al. Differential properties of Janus kinase inhibitors in the treatment of immune-mediated inflammatory diseases. Rheumatology. 2024 Feb 1;63(2):298–308.

54. Unizony S, Arias-Urdaneta L, Miloslavsky E, Arvikar S, Khosroshahi A, Keroack B, et al. Tocilizumab for the treatment of large-vessel vasculitis (giant cell arteritis, Takayasu arteritis) and polymyalgia rheumatica. Arthritis Care & Research. 2012 Nov;64(11):1720–9.

55. Xenitidis T, Horger M, Zeh G, Kanz L, Henes JC. Sustained inflammation of the aortic wall despite tocilizumab treatment in two cases of Takayasu arteritis. Rheumatology. 2013 Sep 1;52(9):1729–31.

56. Weyand CM, Younge BR, Goronzy JJ. IFN-γ and IL-17: the two faces of T-cell pathology in giant cell arteritis. Current Opinion in Rheumatology. 2011 Jan;23(1):43–9.

57. Szekeres D, Al Othman B. Current developments in the diagnosis and treatment of giant cell arteritis. Front Med [Internet]. 2022 Dec 13 [cited 2025 Nov 19];9. Available from: https://www.frontiersin.org/journals/medicine/articles/10.3389/fmed.2022.1066503/full

58. The Role of 18F-FDG PET/CT in Large-Vessel Vasculitis: Appropriateness of Current Classification Criteria? - Balink - 2014 - BioMed Research International - Wiley Online Library [Internet]. [cited 2025 Nov 19]. Available from: https://onlinelibrary.wiley.com/doi/10.1155/2014/687608

59. Allam MN, Ali NB, Mahmoud AK, Scalia IG, Farina JM, Abbas MT, et al. Multi-Modality Imaging in Vasculitis. Diagnostics [Internet]. 2024 Apr 18 [cited 2025 Nov 19];14(8). Available from: https://www.mdpi.com/2075-4418/14/8/838

60. van der Geest KSM, Sandovici M, Brouwer E, Mackie SL. Diagnostic Accuracy of Symptoms, Physical Signs, and Laboratory Tests for Giant Cell Arteritis: A Systematic Review and Meta-analysis. JAMA Intern Med. 2020 Oct 1;180(10):1295–304.

61. Enocsson H, Karlsson J, Li HY, Wu Y, Kushner I, Wetterö J, et al. The Complex Role of C-Reactive Protein in Systemic Lupus Erythematosus. Journal of Clinical Medicine [Internet]. 2021 Dec 13 [cited 2025 Nov 19];10(24). Available from: https://www.mdpi.com/2077-0383/10/24/5837

62. Carvajal Alegria G, Nicolas M, van Sleen Y. Biomarkers in the era of targeted therapy in giant cell arteritis and polymyalgia rheumatica: is it possible to replace acute-phase reactants? Front Immunol [Internet]. 2023 Jun 15 [cited 2025 Nov 19];14. Available from: https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2023.1202160/full

63. Blockmans D, Penn SK, Setty AR, Schmidt WA, Rubbert-Roth A, Hauge EM, et al. A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis. N Engl J Med. 2025 Apr 2;NEJMoa2413449.

64. NICE. Tocilizumab for treating giant cell arteritis. Technology appraisal guidance. 2018 Apr 18;TA518.

65. Hoffmann-La Roche. A Phase III, Multicenter, Randomized, Double-Blind Placebo-Controlled Study to Assess the Efficacy and Safety of Tocilizumab in Subjects With Giant Cell Arteritis [Internet]. clinicaltrials.gov; 2020 Feb [cited 2025 May 12]. Report No.: NCT01791153. Available from: https://clinicaltrials.gov/study/NCT01791153

66. AbbVie, Data on File. SELECT-GCA.

67. CADTH. Clinical Review Report Tocilizumab (Actemra) [Internet]. CADTH; 2018 [cited 2025 May 20]. Available from: https://www.cda-amc.ca/sites/default/files/cdr/clinical/SR0534_ActemraGCA_CL_Report.pdf

68. Efficacy and Safety of Upadacitinib in Giant Cell Arteritis: 2-Year Results From the Re-Randomized, Double-Blind SELECT-GCA Phase 3 Trial [Internet]. ACR Meeting Abstracts. [cited 2025 Nov 19]. Available from: https://acrabstracts.org/abstract/efficacy-and-safety-of-upadacitinib-in-giant-cell-arteritis-2-year-results-from-the-re-randomized-double-blind-select-gca-phase-3-trial/

69. Nye Metoder. Upadacitinib (Rinvoq) ID2025_003 [Internet]. [cited 2025 May 27]. Available from: https://www.nyemetoder.no/metoder/id2025_003/

70. Stone JH, Han J, Aringer M, Blockmans D, Brouwer E, Cid MC, et al. Long-term effect of tocilizumab in patients with giant cell arteritis: open-label extension phase of the Giant Cell Arteritis Actemra (GiACTA) trial. The Lancet Rheumatology. 2021 May 1;3(5):e328–36.

71. Cohen SB, van Vollenhoven RF, Winthrop KL, Zerbini CAF, Tanaka Y, Bessette L, et al. Safety profile of upadacitinib in rheumatoid arthritis: integrated analysis from the SELECT phase III clinical programme. Ann Rheum Dis. 2021 Mar;80(3):304–11.

72. Strand V, Dimonaco S, Tuckwell K, Klearman M, Collinson N, Stone JH. Health-related quality of life in patients with giant cell arteritis treated with tocilizumab in a phase 3 randomised controlled trial. Arthritis Res Ther. 2019 Dec;21(1):64.

73. Kermani T, Sreih A, Tomasson G, Cuthbertson D, Borchin R, Carette S, et al. 148. SHORT-FORM 36 AS A MEASURE OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH GIANT CELL ARTERITIS. Rheumatology [Internet]. 2019 Mar 1 [cited 2025 Mar 24];58(Supplement_2). Available from: https://academic.oup.com/rheumatology/article/doi/10.1093/rheumatology/kez059.025/5421868

74. Robson JC, Almeida C, Dawson J, Bromhead A, Dures E, Guly C, et al. Patient perceptions of health-related quality of life in giant cell arteritis: international development of a disease-specific patient-reported outcome measure. Rheumatology. 2021 Oct 2;60(10):4671–80.

75. Hellmann DB, Uhlfelder ML, Stone JH, Jenckes MW, Cid MC, Guillevin L, et al. Domains of health-related quality of life important to patients with giant cell arteritis. Arthritis Care & Research. 2003;49(6):819–25.

76. AbbVie. A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Upadacitinib in Subjects With Giant Cell Arteritis: SELECT-GCA [Internet]. clinicaltrials.gov; 2025 Mar [cited 2025 Apr 1]. Report No.: NCT03725202. Available from: https://clinicaltrials.gov/study/NCT03725202

Appendix A. Main characteristics of studies included

[Complete Table 53 for each study included. Comply with section 3 of the methods guide.]

Table 53 Main characteristic of studies included

Trial name: SELECT-GCA	**NCT number: NCT03725202**
Objective	Evaluate the safety and efficacy of upadacitinib in individuals with giant cell arteritis.
Publications – title, author, journal, year	Title: A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis Authors: Daniel Blockmans, M.D., Ph.D., Sara K. Penn, M.D., Arathi R. Setty, M.D., M.P.H., Wolfgang A. Schmidt, M.D., M.A.C.R., Andrea Rubbert-Roth, M.D. https://orcid.org/0000-0002-9016-2833, Ellen M. Hauge, M.D., Ph.D., Helen I. Keen, M.B., B.S., Ph.D., Tomonori Ishii, M.D., Ph.D., Nader Khalidi, M.D., Christian Dejaco, M.D., Ph.D., Maria C. Cid, M.D., Bernhard Hellmich, M.D., Meng Liu, Ph.D., Weihan Zhao, Ph.D., Ivan Lagunes, M.D., Ana B. Romero, M.D., Peter K. Wung, M.D., M.H.S., and Peter A. Merkel, M.D., M.P.H., for the SELECT-GCA Study Group. Journal: The New England Journal of Medicine April 2025
Study type and design	The trial was conducted at 100 sites in 24 countries and included two 52-week periods: a randomized, double-blind treatment period followed by an extension period. Randomization was performed with the use of an interactive-response system. The patients were randomly assigned, in a 2:1:1 ratio, to receive upadacitinib at a dose of 15 mg or 7.5 mg once daily in combination with a prespecified 26-week glucocorticoid taper or placebo with a prespecified 52-week glucocorticoid taper (Table S1). The glucocorticoid taper regimen was open-label until the dose reached 20 mg per day, after which it was blinded. The glucocorticoid taper regimens were tailored to each patient on the basis of the starting dose, with the patients in the upadacitinib groups discontinuing by week 26 and those in the placebo group discontinuing by week 52.
Sample size (n)	Original enrollment (estimated): 420 Enrollment (Actual): 438
Main inclusion criteria	• Diagnosis of giant cell arteritis (GCA) according to the following criteria:

Trial name: SELECT-GCA		NCT number: NCT03725202
	○ History of erythrocyte sedimentation rate (ESR) >= 50 mm/hour or high sensitivity C-reactive protein (hsCRP)/CRP >=1.0 mg/dL ○ Presence of at least one of the following: Unequivocal cranial symptoms of GCA or Unequivocal symptoms of polymyalgia rheumatica (PMR) ○ Presence of at least one of the following: temporal artery biopsy revealing features of GCA or evidence of large vessel vasculitis by angiography or cross-sectional imaging such as ultrasound, magnetic resonance imaging (MRI), computed tomography (CT) or positron emission tomography (PET). • Active GCA, either new onset or relapsing, within 8 weeks of Baseline.	
Main exclusion criteria	• Prior exposure to any Janus Kinase (JAK) inhibitor. • Treatment with an interleukin-6 (IL-6) inhibitor within 4 weeks of study start, or prior treatment with an IL-6 inhibitor and experienced a disease flare during treatment.	
Intervention	**Upadacitinib 7.5 mg** (n = 107) is administered orally once daily for 52 weeks. **Upadacitinib 15 mg** (n = 209) is administered orally once daily for 52 weeks. The treatment is combined with corticosteroid dosing according to a tapering schedule over 26 weeks, administered orally (CS).	
Comparator(s)	Placebo + CS tapering (n = 112) Placebo for upadacitinib is administered daily, along with a 52-week corticosteroid tapering regimen.	
Follow-up time	52 weeks for all patients (fixed treatment period)	
Is the study used in the health economic model?	Yes	
Primary, secondary and exploratory endpoints	[State all primary, secondary and exploratory endpoints of the study, regardless of whether results are provided in this application. Definition of included outcomes and results must be provided in Appendix D.] **Endpoints included in this application:** The **primary endpoint** was sustained remission at Week 52, defined as the absence of signs and symptoms of giant cell arteritis (GCA) from	

Trial name: SELECT-GCA	NCT number: NCT03725202

Week 12 to Week 52, and adherence to the protocol-specified glucocorticoid taper regimen.

Secondary endpoints (current):

- Percentage of participants achieving sustained complete remission from Week 12 through Week 52
- Defined as sustained remission plus normalization of ESR and CRP (hs-CRP).
- Cumulative corticosteroid exposure through Week 52
- Time to first disease flare through Week 52
- Flare defined as recurrence of GCA symptoms or ESR >30 mm/hr (attributable to GCA), requiring increased CS dose.
- Percentage of participants with at least 1 disease flare through Week 52
- Percentage of participants in complete remission at Week 52
- Percentage of Participants in Complete Remission at Week 24
- Defined as absence of GCA symptoms, ESR <30 mm/hr, hs-CRP <1 mg/dL, and adherence to CS taper.
- Change from baseline in SF-36 Physical Component Summary (PCS) score at Week 52
- Number of disease flares per participant through Week 52
- Change from baseline in FACIT-Fatigue score at Week 52
- TSQM Global Satisfaction subscale score at Week 52
- Rate of corticosteroid-related adverse events through Week 52

Method of analysis	[State the method of analysis, i.e. intention-to-treat or per-protocol. E.g.: All efficacy analyses were intention-to-treat analyses. We used the Kaplan–Meier method to estimate rates of progression-free survival and overall survival, and a stratified log-rank test for treatment comparisons. Hazard ratios adjusted for XX and YY were estimated with Cox proportional hazards regression. The proportional hazards assumption was assessed by looking for trends in the scaled Schoenfeld residuals.] The trial was powered to test for superiority. An overall sample size of 420 was planned to provide at least 90% power to detect an absolute difference of 20 percentage points between the 15-mg upadacitinib group and the placebo group in sustained remission at week 52, at a two-sided alpha level of 0.05. The overall type I error rate of the primary and secondary end points was controlled for multiplicity at the 0.05 level with the use of a graphical multiplicity-adjustment method (Section S3). We began the hierarchical multiplicity-control approach by

testing the primary end point in the 15-mg upadacitinib group using an alpha of 0.05, followed by sequentially testing the first seven multiplicity-controlled secondary end points using a prespecified alpha transfer path. To test the results in the 7.5-mg upadacitinib group before completing all end-point analyses for the 15-mg group, the alpha was divided to assess the results for the primary end point in the 7.5-mg group and a group of four end points in the 15-mg group. We used the Cochran–Mantel–Haenszel test with the nonresponder imputation approach (incorporating multiple imputation) to analyze categorical remission–related end points. Continuous end points were calculated with the use of a mixed-effects model for repeated measures, except for cumulative glucocorticoid exposure, which was assessed with the use of the van Elteren test. The time to the first flare of giant-cell arteritis was analyzed with the Kaplan–Meier method. Count-based end points were compared between the upadacitinib groups and the placebo group with the use of Poisson regression models. Post hoc analyses were conducted to evaluate the cumulative glucocorticoid dose administered above the amount expected with the prespecified glucocorticoid taper through 52 weeks. The widths of the confidence intervals were not adjusted for multiplicity and should not be used in place of hypothesis testing. Safety data were summarized descriptively. Additional details on statistical methods are provided in Section S4.

Subgroup analyses

[For each analysis, provide the following information:

- characteristics of included population

- method of analysis

- was it pre-specified or post hoc?

- assessment of validity, including statistical power for pre-specified analyses.]

All subgroups were prespecified for the primary endpoint of sustained remission, except for history of polymyalgia rheumatica, which was evaluated post hoc. Results are based on the Cochran-Mantel-Haensel test. Nonresponder imputation incorporating multiple imputation was used to handle missing data. Response rate, adjusted difference of response rate, and its associated confidence intervals are synthetic results from multiple imputation if there was missing data due to COVID-19 logistical restrictions or data were obtained after a patient received more than 100 mg daily systemic glucocorticoids (prednisone or equivalent) for a non-GCA indication. Confidence interval widths were not adjusted for multiplicity and should not be used in place of hypothesis testing.

Sex

- Male
- Female

Trial name: SELECT-GCA	NCT number: NCT03725202

Age group (years)

- < 65
- ≥ 65 to < 75
- ≥ 75

Race group

- White
- Non-White

Geographic region

- North America
- Western Europe
- Eastern Europe
- Asia
- Oceania

Body mass index group (kg/m²)

- < 25
- ≥ 25 to < 30
- ≥ 30

Nicotine user

- Current
- Former
- Never

Baseline disease status

- New-onset giant-cell arteritis
- Relapsing giant-cell arteritis

Prior use of IL-6 inhibitor

- Yes
- No

Baseline glucocorticoid dose

- ≤ 30 mg
- 30 mg

History of polymyalgia rheumatica

- Yes

Trial name: SELECT-GCA	NCT number: NCT03725202
	• No **Ischemia-related vision loss** • Yes • No
Other relevant information	

Trial name:GiACTA	NCT number: NCT01791153
Objective	The objective of the GiACTA trial was to evaluate the efficacy and safety of tocilizumab in participants with GCA.
Publications – title, author, journal, year	Stone JH, Spotswood H, Unizony SH, Aringer M, Blockmans D, Brouwer E, Cid MC, Dasgupta B, Rech J, Salvarani C, Spiera R, Bao M. New-onset versus relapsing giant cell arteritis treated with tocilizumab: 3-year results from a randomized controlled trial and extension. Rheumatology (Oxford). 2022 Jul 6;61(7):2915-2922. doi: 10.1093/rheumatology/keab780. Unizony SH, Bao M, Han J, Luder Y, Pavlov A, Stone JH. Treatment failure in giant cell arteritis. Ann Rheum Dis. 2021 Nov;80(11):1467-1474. doi: 10.1136/annrheumdis-2021-220347. Epub 2021 May 28. Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, Brouwer E, Cid MC, Dasgupta B, Rech J, Salvarani C, Schulze-Koops H, Schett G, Spiera R, Unizony SH, Collinson N. Glucocorticoid Dosages and Acute-Phase Reactant Levels at Giant Cell Arteritis Flare in a Randomized Trial of Tocilizumab. Arthritis Rheumatol. 2019 Aug;71(8):1329-1338. doi: 10.1002/art.40876. Epub 2019 Jul 3. Strand V, Dimonaco S, Tuckwell K, Klearman M, Collinson N, Stone JH. Health-related quality of life in patients with giant cell arteritis treated with tocilizumab in a phase 3 randomised controlled trial. Arthritis Res Ther. 2019 Feb 20;21(1):64. doi: 10.1186/s13075-019-1837-7. Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, Brouwer E, Cid MC, Dasgupta B, Rech J, Salvarani C, Schett G, Schulze-Koops H, Spiera R, Unizony SH, Collinson N. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017 Jul 27;377(4):317-328. doi: 10.1056/NEJMoa1613849.
Study type and design	The GiACTA trial is a multicentre, randomized, double-blind, placebo-controlled, parallel-group phase 3 study. No cross-over occurred. Enrolled patients were randomly assigned in a 2:1:1:1 ratio to one of four groups. The study consists of 2 parts: a 52-week double-blind treatment period (Part 1) followed by a 104-week open label long-term follow-up period (Part 2). In Part 1 of the study eligible participants was

Trial name:GiACTA		NCT number: NCT01791153
	randomized to receive either tocilizumab every week (qw) or every 2 weeks (q2w) or placebo for 52 weeks, with tapering oral daily doses of prednisone. After Week 52, participants in remission stopped study treatment and entered long-term follow-up, whereas participants with disease activity or flares received open-label tocilizumab or other treatment at the discretion of the investigator for a maximum period of 104 weeks.	
Sample size (n)	251	
Main inclusion criteria	• Diagnosis of GCA classified according to age >/=50 years; history of ESR >/=50 mm/hr or history of CRP >/=2.45 mg/dL; and at least one of the following: unequivocal cranial symptoms of GCA or symptoms of polymyalgia rheumatica [PMR]; and at least one of the following: temporal artery biopsy revealing features of GCA or evidence of large-vessel vasculitis by angiography or cross-sectional imaging • New onset (diagnosis within 6 weeks of baseline) or refractory (diagnosis greater than [>] 6 weeks before baseline and previous treatment with >/= 40 milligrams per day prednisone [or equivalent] for at least 2 consecutive weeks at any time) GCA • Active disease (presence of clinical signs and symptoms [cranial or PMR] and ESR >/=30 mm/hour or CRP >/=1 mg/dL) within 6 weeks of baseline visit	
Main exclusion criteria	• Major surgery within 8 weeks prior to screening or planned within 12 months after randomization • Transplanted organs (except corneas with transplant performed >3 months prior to screening) • Major ischemic event, unrelated to GCA, within 12 weeks of screening • Prior treatment with any of the following: investigational agent within 12 weeks (or 5 half-lives of the investigational drug, whichever is longer) of screening; cell-depleting therapies including investigational agent; intravenous (IV) gamma globulin or plasmapheresis within 6 months of baseline; alkylating agents or with total lymphoid irradiation; tocilizumab; hydroxychloroquine, cyclosporine A, azathioprine, or mycophenolate mofetil within 4 weeks of baseline; etanercept within 2 weeks of baseline; infliximab, certolizumab, golimumab, abatacept, or adalimumab within 8 weeks of baseline; anakinra within 1 week of baseline; tofacitinib; cyclophosphamide within 6 months of baseline; >100 milligrams of daily IV methylprednisolone within 6 weeks of baseline	

Trial name:GiACTA		NCT number: NCT01791153
	• Participants requiring systemic glucocorticoids for conditions other than GCA, which, in the opinion of the investigator, would interfere with adherence to the fixed glucocorticoid taper regimen and/or to assessment of efficacy in response to the test article • History of severe allergic reactions to monoclonal antibodies or to prednisone • Evidence of serious uncontrolled concomitant disease (for example, cardiovascular, respiratory, renal, endocrine, psychiatric, corneal ulcers/injuries, or gastrointestinal [GI] disease) • Current liver disease, as determined by the investigator • History of diverticulitis, inflammatory bowel disease, or other symptomatic GI tract condition that might predispose to bowel perforation • Known active or history of recurrent bacterial, viral fungal, mycobacterial, or other infection • Primary or secondary immunodeficiency • Evidence of malignancies diagnosed within previous 5 years (except basal and squamous cell carcinoma of the skin or carcinoma in situ of the cervix uteri that have been excised and cured) • Inadequate hematologic, renal or liver function • Positive for hepatitis B or hepatitis C infection	
Intervention	1. Tocilizumab 162 mg weekly (QW)+ 26 weeks prednisone taper, n= 100. 2. Tocilizumab 162 mg bi-weekly (Q2W)+ Tocilizumab placebo Q2W+ 26 weeks prednisone taper, n=50.	
Comparator(s)	1. Placebo + 26 weeks prednisone taper, n= 50. 2. Placebo + 52 weeks prednisone taper, n=51.	
Follow-up time	52 weeks (part 1), 104 weeks (part 2)	
Is the study used in the health economic model?	No, the study is used for indirect treatment comparison to upadacitinib.	
Primary, secondary and exploratory endpoints	**Endpoints included in this application:** *Primary endpoint:*	

Trial name:GiACTA	NCT number: NCT01791153
	• Sustained Remission at Week 52 (Tocilizumab + 26 Weeks Prednisone Taper Versus Placebo + 26 Weeks Prednisone Taper) *Secondary endpoint:* • Sustained Remission excluding normalization of CRP concentration at Week 52 (Tocilizumab + 26 Weeks Prednisone Taper Versus Placebo + 52 Weeks Prednisone Taper), • Time to First GCA Disease Flare • Total Cumulative Prednisone Dose **Other endpoints (not included in this application):** • Change From Baseline in Short Form (SF)-36 Questionnaire Score at Week 52 • Change From Baseline in Patient Global Assessment (PGA) of Disease Activity Assessed Using Visual Analogue Scale (VAS) at Week 52, • Area Under the Curve From Time Zero to End of Dosing Interval (AUCtau) at Steady State of Tocilizumab, • Maximum Serum Concentration at Steady State (Cmax,ss) of Tocilizumab, • Minimum Serum Concentration at Steady State (Cmin,ss) of Tocilizumab, • Minimum Observed Serum Concentration (Ctrough) of Tocilizumab, Serum Interleukin-6 (IL-6) Leve • Serum Soluble IL-6 Receptor (sIL-6R) Level, • Erythrocyte Sedimentation Rate (ESR), • C-Reactive Protein (CRP)Level, • Percentage of Participants With Anti-Tocilizumab Antibodies
Method of analysis	Results are presented for the Intent-to-treat (ITT) population including all participants randomized into the study who received at least one administration of study drug. For the categorical endpoints, the treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (less than or equal to [</=] 30 mg/day, greater than [>] 30 mg/day). For time to flare, the treatment groups were compared using a Cox proportional hazards model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Trial name:GiACTA	NCT number: NCT01791153
	For the median total cumulative prednisone dose, the treatment groups were compared using a Van Elteren's test stratified by starting prednisone dose (<=30 mg/day, > 30 mg/day).
Subgroup analyses	No results for subgroups are presented in this dossier. The following subgroups were pre-specified in the GiACTA study protocol: • Disease onset at baseline (new-onset, refractory/relapsing). Starting prednisone dose (5 mg intervals) will also be summarized descriptively • Starting prednisone dose (≤ 30 mg/day, > 30 mg/day) • Previous history of remission, refractory patients only (yes, no) • Positive imaging AND negative/no Temporal Artery Biopsy (TAB) AND no cranial symptoms at diagnosis (yes, no) • GCA diagnosis meets the ACR criteria (yes, no). Where ACR 1990 criteria for diagnosis of GCA defined as having 3 out of the following 5 symptoms: aged ≥ 50 years, ESR ≥ 50 mm/hour, new onset localized headache, temporal artery abnormality, abnormal artery biopsy (i.e., positive TAB). • Musculoskeletal morbidities that may mimic polymyalgia rheumatica (PMR) or GCA (yes, no) • TCZ Serum Concentration Quartiles. TCZ concentration at Week 52 will also be summarized descriptively
Other relevant information	-

Appendix B. Efficacy results per study

Results per study

Table 54. Results per study – SELECT- GCA

Results of SELECT -GCA(NCT03725202)											
				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**		
Sustained remission at week 52	UPA 15mg	209	46.4 (39.6 - 53.2)	17.1	(6.3 - 27.8)	0.002	1.58	1,1 – 2,1	0,006	The Cochran–Mantel–Haenszel test with the non-responder imputation approach (incorporating multiple imputation)	(63)
	Placebo + 52 week taper	112	29.0 (20.6 - 37.5)								
Sustained complete remission at week 52	UPA 15mg	209	37.1 (30.5 - 43.7)	20.7	(11.3 to 30.2)	<0.001	2,32	1,5-3,7	<0.001		
	Placebo + 52 week taper	112	16.1 (9.3 - 22.9)								
≥1 disease flare through week 52	UPA 15mg	209	34.3 (27.4 to 42.4)	-21,3	-32,5 - - 10,1	0.04	0.47	0.29 - 0.74	0.001	Poisson regression model with baseline GC dose and disease status as covariates, adjusted by the duration of study participation.	
	Placebo + 52 week taper	112	55.6 (42.9 to 69.2)								
	UPA 15mg	209	>365	-	-	-	0.57		0.003		

Results of SELECT -GCA(NCT03725202)											
				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		
Median time to first disease flare through week 52 (Days)	Placebo + 52 week taper	112	323 (249 - >365)					(0.40 to 0.83)		The time to the first flare of giant-cell arteritis was analyzed with the Kaplan–Meier method.	
Median cumulative glucocorticoid exposure through week 52	UPA 15mg	209	1615 (1615 - 1635)	−1267	(−1587 - −1133)	<0.001	-	-	-	Cumulative glucocorticoid exposure was assessed with the use of the van Elteren test.	
	Placebo + 52 week taper	112	2882 (2762 - 3253)								
LS mean change from baseline in SF-36 PCS score at	UPA 15mg	209	2.5 (1.2 - 3.8)	3.8	(1.4 - 6.1)	0.002	-	-	-	Mixed models for repeated measures (MMRM), analysis was conducted using mixed-effects models including	
	Placebo + 52 week taper	112	−1.3 (−3.3 - 0.7)								

Results of SELECT -GCA(NCT03725202)											
				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**		
week 52 (95% CI)										observed measurements at all visits.	
LS mean change from baseline in FACIT-Fatigue score at week 52	UPA 15mg	209	1.7 (0.2 - 3.1)	4.0	(1.3 - 6.8)3	0.04	-	-	-		
	Placebo + 52 week taper	112	−2.4 (−4.7 - −0.1)								

Table 55. Results per study - GiACTA

Results of GiACTA (NCT01791153)											
				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**		
Sustained remission	TCZ QW	100	56%	38	18 – 59	<0.001	RR: 3.11	1.7 – 5.8	<0.001	The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (less than or equal to [</=] 30 mg/day, greater than [>] 30 mg/day.	(45)
	Placebo + 52 Wk CS taper	51	18%								
Sustained remission excl. normalisation of CRP	TCZ QW	100	59%	26	3 - 49	<0.003	RR:1.77	1.2 – 2.7	0.008	The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (less than or equal to [</=] 30 mg/day, greater than [>] 30 mg/day.	
	Placebo + 52 Wk CS taper	51	33%								

Results of GiACTA (NCT01791153)											
				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**		
Proportion of patients experiencing at least one flare.	TCZ QW	100	23%	-26	-42 – - 10	NA	RR: 0.47	0.30 -0.74	0.125	The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (less than or equal to [</=] 30 mg/day, greater than [>] 30 mg/day.	
	Placebo + 52 Wk CS taper	51	49%								
Median time to first disease flare (days)	TCZ QW	100	NE	NA	NA	NA	HR: 0.39	(0.18 – 0.82)	P=0.0001		
	Placebo + 52 Wk CS taper	51	295 (168 – NE)								
Cumulative prednisone dose (mg) median (range) median)	TCZ QW	100	1862 (630 – 6602)	-1956 mg	NA	<0.001	-	-	-	For the median total cumulative prednisone dose, the treatment groups were compared using a Van Elteren's test stratified by starting prednisone dose (<=30 mg/day, > 30 mg/day).	
	Placebo + 52 Wk CS taper	51	3818 (822 – 10 698)								
	TCZ QW	100	5,3	NR	NR	p<0.001	-	-	-		(72)

Results of GiACTA (NCT01791153)											
				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**		
FACIT-Fatigue Week 52 LS mean change from baseline	Placebo + 52 Wk CS taper	51	-0,42							Quality-of-life end points were analysed with the use of repeated-measures analysis, with adjustment for baseline stratification factors, in which data obtained after the use of escape therapy were considered to be missing.	
SF-36 PCS Week 52 LS mean change from baseline	TCZ QW	100	4,10	5,59	0,86 – 10,32	P=0,002	-	-	-		(45)
	Placebo + 52 Wk CS taper	51	-1,49								

*CI not reported in the GiACTA publication

Appendix C. Comparative analysis of efficacy

Study outcomes in SELECT GCA were assessed in an unweighted (before matching) and weighted sample (after matching). They were compared to published study outcomes in GIACTA using a Z-test. Rate differences and log odds ratio for binary outcomes, and log hazard ratio for time to disease flare outcome between UPA15 and its anchor group, and between TCZQW and its anchor group were reported, as well as 95% confidence intervals (CIs) (Wald confidence limits). Log hazard ratio for time to disease flare in GIACTA trial was estimated from inpatient level data that was digitized from published Kaplan-Curves using methods established by Li et al. Further, difference in rate difference, log odds ratio,

and log hazard ratio between UPA15 and its anchor group and between TCZQW and its anchor group were calculated, and their 95% CIs were estimated (assuming normality of difference). Odds ratio (OR) and hazard ratio (HR) and 95% CIs between UPA15 and TCZQW were obtained by exponentiating log OR and log HR. A similar approach was used for outcome comparisons after matching except that weights were used after matching select-GCA patient characteristics to GiACTA patient characteristics. Because naïve estimators for standard error of weighted outcomes after matching are biased, they were estimated using sandwich methods using a general linear model with binomial distribution and identity link.

For cumulative CS dose, median dose was reported in GiACTA trial. Without other distributions such as mean and standard deviation, it was not possible to compare mean cumulative CS dose between UPA15 and TCZQW. As a result, the median dose in the TCZQW arm was converted to a binary outcome which equates to 50% of subjects with cumulative CS dose greater than the median dose reported. Percent of subjects with cumulative CS dose greater than the TCZQW median dose were estimated for the UPA15 arm in the SELECT-GCA study. Because it was not possible to estimate percent of subjects with cumulative CS dose ≥ 1862mg in the GiACTA PBO arm (and median doses in the two arms were different between the treatment and PBO arms), an unanchored MAIC was performed comparing UPA15 to TCZQW for this newly created binary outcome.

Table 56. Results from the comparative analysis of upadacitinib and tocilizumab, before matching of baseline patient characteristics.

Outcome measure	UPA 15 (N= 209)	PBO 52W (N=112)	TCZQW (N=100)	PBO 52W (51)	UPA 15 vs TCZQW OR, (95% CI). P-value
Sustained remission at 52 weeks, n (%)	93 (44.5%)	32 (28.6%)	59 (59%)	17 (33 %)	OR, (95% CI). p-value 0,85 (0.57;1.29), p=0.4500
Sustained remission at 52 weeks, including normalization of CRP, n (%)	74 (35,4 %)	18 (16,1 %)	56 (56%)	9 (18%)	OR, (95% CI). p-value 0.73 (0.48;1.10), p=0.1280
Proportion of patients experiencing at least one flare, n (%)	52 (24,9%) **	44 (39,3%) **	23 (23%)	25 (49%)	OR, (95% CI). p-value 1.24 (0.83;1.87), p=0.2970
Median time to first disease flare (days)	> 365	352**	> 365	295	HR (95% CI) 1.34(0.67,2.69)

Outcome measure	UPA 15 (N= 209)	PBO 52W (N=112)	TCZQW (N=100)	PBO 52W (51)	UPA 15 vs TCZQW OR, (95% CI). P-value
Proportion of patients with cumulative CS dose above GiACTA median	40%	-	50%	-	p=0,00974

*For binary outcomes, missing data was handled by NRI (non-responder imputation) to align with the GiACTA trial. In the SELECT-GCA trial study protocol missing data was handled by (NRI-MI non-responder imputation multiple imputation).
**In order to align with the GiACTA study, patients who did not meet criteria for flare were censored at day 1. In the SELECT-GCA trial study protocol, patients who did not meet criteria for flare were considered to be having a flare at day 1. Outcomes will for that reason differ for UPA 15 and placebo in the indirect comparison, compared to the published results.

Table 57. Results from the comparative analysis of upadacitinib and tocilizumab, after matching of baseline patient characteristics*.

Outcome measure	UPA 15	PBO 52W	TZCQW	PBO 52W	Result
Sustained remission at 52 weeks (%)	47.5%	28.3%	59%	33 %	OR, (95% CI). p-value 0.91 (0.6; 1.36), p=0.6370
Sustained remission at 52 weeks, including normalization of CRP (%)	38.9%	16.6%	56%	18%	OR, (95% CI). p-value 0.77 (0.51, 1.17), p=0.1980
Proportion of patients experiencing at least one flare (%)	23.0%	39.1%	23%	49%	OR, (95% CI). p-value 1.19 (0.79, 1.79), p=0.3980
Time to first flare, days (median)	> 365	> 365	> 365	295	HR (95% CI) 1.34 (0.63, 2.82
Proportion of patients with cumulative CS dose above GiACTA median (%)	31%	-	40%	-	p=0.0010

*No patient numbers (N(n)) are available after matching, as the matching is a weighting of the study population of the SELECT-GCA study to match the GiACTA study population.

Appendix D. Extrapolation

Not applicable – no extrapolations are included in the application

D.1 Extrapolation of [effect measure 1]

D.1.1 Data input

D.1.2 Model

D.1.3 Proportional hazards

[If the extrapolation model relies on proportional hazards, provide a plot with Schoenfeld residuals and a log-cumulative hazard plot.]

D.1.4 Evaluation of statistical fit (AIC and BIC)

[Provide a table with the AIC and BIC and discuss the statistical fit.]

D.1.5 Evaluation of visual fit

D.1.6 Evaluation of hazard functions

[Provide a plot of the hazard function of the effect measure. The plots must be presented in separate figures for the intervention and comparator, respectively, and must include the estimated hazard for the observed data (if applicable). The plot must be discussed in the context of chosen the distribution for extrapolating the data of the effect measure.]

D.1.7 Validation and discussion of extrapolated curves

D.1.8 Adjustment of background mortality

D.1.9 Adjustment for treatment switching/cross-over

D.1.10 Waning effect

D.1.11 Cure-point

Appendix E. Serious adverse events

All serious adverse events observed in part 1 of the SELECT-GCA and GiACTA studies are listed in Table 58 and Table 59 respectively.

Table 58. All serious adverse events observed in part 1 of the SELECT-GCA trial, listed per study arm. (76)

	Placebo + 52-week CS Taper	7.5 mg Upadacitinib + 26-week CS Taper	15 mg Upadacitinib + 26-week CS Taper
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	24/112 (21.43%)	14/107 (13.08%)	50/210 (23.81%)
Blood And Lymphatic System Disorders			
Anaemia†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Cardiac Disorders			
Atrial Fibrillation†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Cardiac Failure†1	0/112 (0.00%)	1/107 (0.93%)	1/210 (0.48%)
Cardiac Failure Congestive†1	0/112 (0.00%)	0/107 (0.00%)	2/210 (0.95%)
Endocarditis Fibroplastica†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Mitral Valve Incompetence†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Myocardial Ischaemia†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Tricuspid Valve Incompetence†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Ear And Labyrinth Disorders			
Vertigo†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)

Eye Disorders			
Diplopia†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Glaucoma†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Macular Oedema†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Retinal Detachment†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Gastrointestinal Disorders			
Colitis Ischaemic†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Colitis Ulcerative†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Diarrhoea†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Gastrointestinal Angiodysplasia†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Mallory-Weiss Syndrome†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Pancreatitis†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Pancreatitis Acute†1	2/112 (1.79%)	0/107 (0.00%)	0/210 (0.00%)
Vomiting†1	0/112 (0.00%)	1/107 (0.93%)	1/210 (0.48%)
General Disorders			
Death†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Fatigue†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Oedema Peripheral†1	1/112 (0.89%)	0/107 (0.00%)	1/210 (0.48%)
Hepatobiliary Disorders			
Cholecystitis Chronic†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Hepatitis Acute†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)

Immune System Disorders			
Drug Hypersensitivity†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Infections And Infestations			
Aspergillus Infection†1	0/112 (0.00%)	0/107 (0.00%)	0/210 (0.00%)
Covid-19†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Covid-19 Pneumonia†1	0/112 (0.00%)	0/107 (0.00%)	2/210 (0.95%)
Cystitis†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Device Related Infection†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Diverticulitis†1	0/112 (0.00%)	0/107 (0.00%)	0/210 (0.00%)
Erysipelas†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Febrile Infection†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Gastroenteritis Clostridial†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Genitourinary Tract Infection†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Intervertebral Discitis†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Ophthalmic Herpes Zoster†1	0/112 (0.00%)	0/107 (0.00%)	3/210 (1.43%)
Pneumocystis Jirovecii Pneumonia†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Pneumonia†1	5/112 (4.46%)	3/107 (2.80%)	0/210 (0.00%)
Pneumonia Bacterial†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Pseudomonal Bacteraemia†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Respiratory Syncytial Virus Infection†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Respiratory Tract Infection†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)

Salmonellosis†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Sepsis†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Septic Arthritis Streptococcal†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Staphylococcal Sepsis†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Urinary Tract Infection†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Urosepsis†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Wound Infection†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Injury, Poisoning And Procedural Complications			
Fall†1	1/112 (0.89%)	0/107 (0.00%)	1/210 (0.48%)
Foot Fracture†1	0/112 (0.00%)	0/107 (0.00%)	0/210 (0.00%)
Head Injury†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Hip Fracture†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Infusion Related Reaction†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Patella Fracture†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Radius Fracture†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Road Traffic Accident†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Spinal Fracture†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Thoracic Vertebral Fracture†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Investigations			
Blood Alkaline Phosphatase Increased†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Gamma-Glutamyltransferase Increased†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)

Troponin T Increased†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Metabolism And Nutrition Disorders			
Hypokalaemia†1	0/112 (0.00%)	2/107 (1.87%)	0/210 (0.00%)
Hyponatraemia†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Musculoskeletal And Connective Tissue Disorders			
Back Pain†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Intervertebral Disc Protrusion†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Lumbar Spinal Stenosis†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Meniscal Degeneration†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Osteoarthritis†1	1/112 (0.89%)	0/107 (0.00%)	2/210 (0.95%)
Vertebral Foraminal Stenosis†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)			
Malignant Neoplasm Of Ampulla Of Vater†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Prostate Cancer†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Squamous Cell Carcinoma Of Lung†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Squamous Cell Carcinoma Of Skin†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Tongue Neoplasm Malignant Stage Unspecified†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Tonsil Cancer Metastatic†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Nervous System Disorders			
Cerebellar Ataxia†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Cerebral Amyloid Angiopathy†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)

Cerebral Infarction†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Cerebrospinal Fistula†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Cerebrovascular Accident†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Headache†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Quadrantanopia†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Sciatica†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Syncope†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Psychiatric Disorders			
Substance-Induced Psychotic Disorder†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Renal And Urinary Disorders			
Acute Kidney Injury†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Reproductive System And Breast Disorders			
Cervical Dysplasia†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Respiratory, Thoracic And Mediastinal Disorders			
Haemothorax†1	0/112 (0.00%)	1/107 (0.93%)	0/210 (0.00%)
Pulmonary Embolism†1	2/112 (1.79%)	1/107 (0.93%)	5/210 (2.38%)
Vascular Disorders			
Aortic Dissection†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Aortic Thrombosis†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Arteriosclerosis†1	1/112 (0.89%)	0/107 (0.00%)	0/210 (0.00%)
Deep Vein Thrombosis†1	0/112 (0.00%)	0/107 (0.00%)	3/210 (1.43%)

Giant Cell Arteritis†1	1/112 (0.89%)	1/107 (0.93%)	4/210 (1.90%)
Haematoma†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Peripheral Arterial Occlusive Disease†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)
Peripheral Embolism†1	0/112 (0.00%)	0/107 (0.00%)	1/210 (0.48%)

† Indicates events were collected by systematic assessment
1 Term from vocabulary, MedDRA 26.1

Table 59. All serious adverse events observed in part 1 of the GiACTA trial, listed per study arm. (65)

	Part 1: Tocilizumab qw + 26 Weeks Prednisone Taper		Part 1: Tocilizumab q2w + 26 Weeks Prednisone Taper		Part 1: Placebo + 26 Weeks Prednisone Taper		Part 1: Placebo + 52 Weeks Prednisone Taper	
	Affected / at Risk (%)		Affected / at Risk (%)		Affected / at Risk (%)		Affected / at Risk (%)	
Total	**15/100 (15.00%)**		**7/49 (14.29%)**		**11/50 (22.00%)**		**13/51 (25.49%)**	
Cardiac disorders								
Aortic valve stenosis*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Cardiac failure*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Cardiac failure chronic*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Supraventricular tachycardia*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Tachyarrhythmia*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Eye disorders								
Glaucoma*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)

Cataract*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Gastrointestinal disorders								
Gastritis erosive*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Stomatitis*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Diarrhoea*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Immune system disorders								
Drug hypersensitivity*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Hypersensitivity*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Infections and infestations								
Erysipelas*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Pneumonia*1	1	100 (1.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Gastroenteritis*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	2	51 (3.92%)
Genital herpes zoster*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Herpes zoster*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	2	51 (3.92%)
Respiratory tract infection*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Cellulitis*1	1	100 (1.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Chronic sinusitis*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Pneumonia haemophilus*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Pyelonephritis*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Urinary tract infection*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Urosepsis*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)

Cholangitis infective*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Injury, poisoning and procedural complications								
Postoperative wound complication*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Alcohol poisoning*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Laceration*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Tendon rupture*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Meniscus injury*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Investigations								
Hepatic enzyme increased*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Troponin increased*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Metabolism and nutrition disorders								
Hypokalaemia*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Hyponatraemia*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Musculoskeletal and connective tissue disorders								
Arthralgia*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Fibromyalgia*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Osteoarthritis*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Tendon pain*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Breast cancer*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Malignant melanoma*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)

Ovarian adenoma*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Nervous system disorders								
Paraesthesia*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Syncope*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Transient ischaemic attack*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Headache*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Thrombotic stroke*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Psychiatric disorders								
Anxiety*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Stress*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Renal and urinary disorders								
Renal impairment*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Respiratory, thoracic and mediastinal disorders								
Nasal inflammation*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Oropharyngeal pain*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Asthma*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Dyspnoea exertional*1	0	100 (0.00%)	0	49 (0.00%)	0	50 (0.00%)	1	51 (1.96%)
Pleural effusion*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Pulmonary embolism*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Dyspnoea*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)
Vascular disorders								

Hypertension*1	0	100 (0.00%)	0	49 (0.00%)	1	50 (2.00%)	0	51 (0.00%)
Temporal arteritis*1	1	100 (1.00%)	1	49 (2.04%)	1	50 (2.00%)	1	51 (1.96%)
Deep vein thrombosis*1	1	100 (1.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Hypertensive crisis*1	2	100 (2.00%)	0	49 (0.00%)	0	50 (0.00%)	0	51 (0.00%)
Dry gangrene*1	0	100 (0.00%)	1	49 (2.04%)	0	50 (0.00%)	0	51 (0.00%)

*Indicates events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA v19.0

Appendix F. Health-related quality of life

N/A

Appendix G. Probabilistic sensitivity analyses

N/A

Table 60. Overview of parameters in the PSA

Input parameter	Point estimate	Lower bound	Upper bound	Probability distribution
Probabilities				
Efficacy Outcome A	0.72			Beta
HSUV				
State A	0.79			Beta
Costs				
Hospitalization	20000			Gamma

Appendix H. Literature searches for the clinical assessment

H.1 Efficacy and safety of the intervention and comparator(s)

A clinical SLR was conducted with the objective to identify and review existing clinical evidence to support a quantitative evidence synthesis assessing the relative treatment effect of UPA versus other available treatments for GCA, including TCZ.

Bibliographic database searches for the clinical SLR were conducted in April 2024 and supplemental searches were carried out in April, May, and August 2024. Updated database and supplemental searches were carried out in February 2025. Results from this updated search were de-duplicated against references that had been identified in the 2024 searches. Consequently, only records incremental to the 2024 searches were considered during the 2025 update.

Table 61. Bibliographic databases included in the literature search

Database	Platform/source	Relevant period for the search	Date of search completion
MEDLINE (all)	Ovid	1946 to February 17, 2024	February 18, 2025
Embase	Ovid	1974 to 2025 February 17	February 18, 2025
PsycINFO	Ovid	1806 to February 2025 Week 2	February 18, 2025
Central	Ovid	Until December, 2024	February 18, 2025
CDSR	Ovid	2005 to February 12, 2025	February 18, 2025
PubMed	Ovid	1981 to February 17, 2025	February 18, 2025
DARE	Ovid	From 1st Quarter 2016	February 18, 2025
Northern Light	Ovid	2019 - 2025 Week 06	February 18, 2025

Abbreviations: The Database of Abstracts of Reviews of Effects (DARE); Cochrane Database of Systematic Reviews (CDSR)

Table 62. Clinical trial registries.

Registry	Study records returned

	(February 2025)
ClinicalTrials.gov	163
WHO ICTRP	264
NIHR UK Research Registry	4
Health Canada's Clinical Trials Database	7
EU CTR	23
EU CTIS	15
Total	476

Table 63. Conference material included in the literature search, including search results

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search	Hits
International Vasculitis Workshop	Abstracts of the 19th 20th and 21st International Vasculitis and ANCA Workshop	Manual search:	Giant Cell Arteritis	April 5, 2024	150
British Society for Rheumatology Annual Conference	British Society for Rheumatology Annual Conference Abstracts	Manual search:	Giant Cell Arteritis	August 5, 2024	105

H.1.1 Search strategies

- Bibliographic databases were searched from database inception using predefined search strategies. The search strategy for the clinical SLR was designed as follows:

  ((search terms and alternative names for Giant Cell Arteritis) AND (search terms, synonyms, and serial/chemical abstract numbers for interventions) AND (search terms for: randomised or controlled studies or clinical studies or observational studies or prospective or retrospective studies) AND (search terms for efficacy or safety or HRQoL outcomes of interest))

- Proceedings from two conferences, which were not indexed through Northern Light at the time of search, were searched using "giant cell arteritis" as a keyword.

- Clinical trial registries were searched using “giant cell arteritis” as a keyword to identify potentially relevant studies.

Table 64. Clinical SLR – Medline search, February 2025

Search String	Search Terms	Hits
1	giant cell arteritis.mp. or Giant Cell Arteritis/ or (giant adj2 cell adj2 arteritis).ti,ab,kw,ot,kf.	9,684
2	(cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).ti,ab,kw,ot,kf.	2,903
3	1 or 2	10,104
4	(Upadacitinib or Rinvoq or ABT 494 or ABT494 or 1310726-60-3).ti,ab,kw,ot,kf.	1,235
5	(Tocilizumab or Actemra or tocilizumab-bavi or Tofidence or Tyenne or RoActemra or Lusinex or TCZ or Atlizumab or MRA or MSB 11456 or MSB11456 or R 1569 or R1569 or RG 1569 or RG1569 or RHPM 1 or RHPM1 or RO 4877533 or RO4877533).ti,ab,kw,ot,kf.	18,153
6	(Secukinumab or Cosentyx or AIN 457 or AIN457 or AIN 457A or AIN457A).ti,ab,kw,ot,kf.	2,359
7	(Guselkumab or Tremfya or CNTO 1959 or CNTO1959).ti,ab,kw,ot,kf.	808
8	(steroid* or corticosteroid* or CS or prednisone or placebo).ti,ab,kw,ot,kf.	759,617
9	4 or 5 or 6 or 7 or 8	778,506
10	3 and 9	2,260
11	limit 10 to humans	1,957
12	limit 11 to (address or autobiography or bibliography or biography or classical article or comment or consensus development conference or consensus development conference, nih or dictionary or directory or editorial or "expression of concern" or guideline or interactive tutorial or interview or lecture or legal case or legislation or letter or news or newspaper article or patient education handout or periodical index or personal narrative or portrait or practice guideline or video-audio media or webcast)	113
13	11 not 12	1,844
14	exp Randomized Controlled Trial/	633,723
15	exp Randomized Controlled Trials as Topic/	182,839
16	exp Clinical Trial/	1,016,331
17	exp Random Allocation/	108,126
18	exp Double-Blind Method/	182,701
19	exp Single-Blind Method/	34,603
20	exp Clinical Trials as Topic/	403,501
21	(control* adj3 (study or studies or trial* or group*)).ti,ab,kw,ot,kf,pt.	1,363,906
22	((random or randomi#ed) adj2 control* adj2 (trial* or study or studies)).ti,ab,kw,ot,kf,pt.	384,729
23	((Nonrandom* or non-random* or quasirandom* or quasi-random* or single arm or pragmatic or equivalence or open-label or noninferiority or non-inferiority) adj3 (trial* or study or studies)).ti,ab,kw,ot,kf,pt.	98,132
24	(allocat* or double blind or single blind).ti,ab,kw,ot,kf,pt.	351,183
25	(clinical adj2 (trial* or study or studies)).ti,ab,kw,ot,kf,pt.	788,473
26	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25	2,975,233
27	exp Observational Study/	168,748
28	exp Case-Control Studies/	1,577,399
29	exp Cohort Studies/	2,708,655
30	observational.ti,ab,kw,ot,kf,pt.	317,443
31	((observational or cohort or case control) adj3 (study or studies)).ti,ab,kw,ot,kf,pt.	782,046
32	(prospective or retrospective).ti,ab,kw,ot,kf,pt.	1,616,269
33	27 or 28 or 29 or 30 or 31 or 32	3,704,842
34	Systematic review/ or meta analysis/	371,429
35	(systematic review or systematic literature review or SLR or meta analys#s or NMA).ti,ab,kw,ot,kf,pt.	541,556
36	34 or 35	541,556
37	13 and 26	252
38	13 and 33	514
39	13 and 36	43

40	remission.ti,ab,kw,ot,kf.	152,623
41	((corticosteroid* or steroid* or prednisone) adj4 (cumulative or expos* or dose)).ti,ab,kw,ot,kf.	24,205
42	(disease adj3 flare*).ti,ab,kw,ot,kf.	2,998
43	(36 item Short Form Quality of Life or SF 36 or SF36 or Physical Component Score or PCS).ti,ab,kw,ot,kf.	48,598
44	(Functional Assessment of Chronic Illness Therapy or FACIT).ti,ab,kw,ot,kf.	1,907
45	(Treatment Satisfaction Questionnaire for Medication or TSQM).ti,ab,kw,ot,kf.	400
46	(adverse event* or (adverse adj3 event*) or serious adverse event* or (serious adj3 adverse adj3 event*)).ti,ab,kw,ot,kf.	298,022
47	withdrawal.ti,ab,kw,ot,kf.	111,151
48	(safety or efficacy or effectiveness).ti,ab,kw,ot,kf.	2,269,801
49	40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48	2,679,726
50	37 and 49	150
51	38 and 49	241
52	39 and 49	21
53	50 or 51 or 52	324

Table 65. Clinical SLR – Embase search, February 2025

Search String	Search Terms	Hits
1	giant cell arteritis.mp. or Giant Cell Arteritis/ or (giant adj2 cell adj2 arteritis).ti,ab,kw,ot,kf.	12,658
2	(cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).ti,ab,kw,ot,kf.	3,381
3	1 or 2	14,472
4	exp upadacitinib/ or (Upadacitinib or Rinvoq or ABT 494 or ABT494 or 1310726-60-3).ti,ab,kw,ot,kf.	4,065
5	exp tocilizumab/ or (Tocilizumab or Actemra or tocilizumab-bavi or Tofidence or Tyenne or RoActemra or Lusinex or TCZ or Atlizumab or MRA or MSB 11456 or MSB11456 or R 1569 or R1569 or RG 1569 or RG1569 or RHPM 1 or RHPM1 or RO 4877533 or RO4877533).ti,ab,kw,ot,kf.	51,631
6	exp secukinumab/ or (Secukinumab or Cosentyx or AIN 457 or AIN457 or AIN 457A or AIN457A).ti,ab,kw,ot,kf.	9,082
7	exp guselkumab/ or (Guselkumab or Tremfya or CNTO 1959 or CNTO1959).ti,ab,kw,ot,kf.	3,262
8	exp corticosteroid therapy/ or exp corticosteroid/ or (corticosteroid* or steroid* or prednisone or CS or placebo).ti,ab,kw,ot,kf.	1,973,784
9	4 or 5 or 6 or 7 or 8	2,012,937
10	3 and 9	7,702
11	limit 10 to human	7,259
12	limit 11 to (books or chapter or editorial or letter or short survey)	793
13	11 not 12	6,466
14	exp randomized controlled trial/	866,609
15	exp "randomized controlled trial (topic)"/	288,341
16	exp randomization/	100,532
17	exp equivalence trial/	227
18	exp non-inferiority trial/	2,943
19	exp pragmatic trial/	3,144
20	exp controlled study/	11,140,092
21	exp double blind procedure/	227,723
22	single blind procedure/	58,048
23	exp placebo/	421,783
24	exp control group/	109,439
25	(control* adj3 (study or studies or trial* or group*)).ti,ab,kw,ot,kf,pt.	1,884,467
26	((random or randomi#ed) adj2 control* adj2 (trial* or study or studies)).ti,ab,kw,ot,kf,pt.	504,825
27	((Nonrandom* or non-random* or quasirandom* or quasi-random* or single arm or pragmatic or equivalence or open-label or noninferiority or non-inferiority) adj3 (trial* or study or studies)).ti,ab,kw,ot,kf,pt.	158,098

Search String	Search Terms	Hits
28	(allocat* or double blind or single blind).ti,ab,kw,ot,kf,pt.	470,903
29	(clinical adj2 (trial* or study or studies)).ti,ab,kw,ot,kf,pt.	1,127,585
30	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	12,794,783
31	exp observational study/ or exp case control study/ or exp cohort analysis/	1,813,493
32	observational.ti,ab,kw,ot,kf,pt.	491,055
33	((observational or cohort or case control) adj3 (study or studies)).ti,ab,kw,ot,kf,pt.	1,142,862
34	(prospective or retrospective).ti,ab,kw,ot,kf,pt.	2,555,681
35	31 or 32 or 33 or 34	3,861,442
36	systematic review (topic)/ or "systematic review"/ or meta analysis/	680,494
37	(systematic review or systematic literature review or SLR or meta analys#s or NMA).ti,ab,kw,ot,kf,pt.	627,551
38	36 or 37	818,056
39	13 and 30	1,932
40	13 and 35	1,442
41	13 and 38	251
42	exp remission/	276,453
43	remission.ti,ab,kw,ot,kf.	262,070
44	((corticosteroid* or steroid* or prednisone) adj4 (cumulative or expos* or dose)).ti,ab,kw,ot,kf.	46,597
45	(disease adj3 flare*).ti,ab,kw,ot,kf.	6,573
46	(36 item Short Form Quality of Life or SF 36 or SF36 or Physical Component Score or PCS).ti,ab,kw,ot,kf.	78,349
47	(Functional Assessment of Chronic Illness Therapy or FACIT).ti,ab,kw,ot,kf.	4,563
48	(Treatment Satisfaction Questionnaire for Medication or TSQM).ti,ab,kw,ot,kf.	970
49	(adverse event* or (adverse adj3 event*) or serious adverse event* or (serious adj3 adverse adj3 event*)).ti,ab,kw,ot,kf.	519,018
50	withdrawal.ti,ab,kw,ot,kf.	160,510
51	(safety or efficacy or effectiveness).ti,ab,kw,ot,kf.	3,175,027
52	42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51	3,918,412
53	39 and 52	944
54	40 and 52	658
55	41 and 52	122
56	53 or 54 or 55	1,204

Table 66. Clinical SLR – PsycINFO search, April 2025

Search String	Search Terms	Hits
1	((giant adj2 cell adj2 arteritis) or cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).ti,ab.	118
2	(Upadacitinib or Rinvoq or ABT 494 or ABT494 or 1310726-60-3).ti,ab.	0
3	(Tocilizumab or Actemra or tocilizumab-bavi or Tofidence or Tyenne or RoActemra or Lusinex or TCZ or Atlizumab or MRA or MSB 11456 or MSB11456 or R 1569 or R1569 or RG 1569 or RG1569 or RHPM 1 or RHPM1 or RO 4877533 or RO4877533).ti,ab.	510
4	(Secukinumab or Cosentyx or AIN 457 or AIN457 or AIN 457A or AIN457A).ti,ab.	6
5	(Guselkumab or Tremfya or CNTO 1959 or CNTO1959).ti,ab.	3
6	(corticosteroid* or CS or steroid* or prednisone or placebo).ti,ab.	71,909
7	2 or 3 or 4 or 5 or 6	72,392
8	1 and 7	40

Table 67. Clinical SLR – CENTRAL search, February 2025

Search String	Search Terms	Hits
1	exp Giant Cell Arteritis/	152

Search String	Search Terms	Hits
2	((giant adj2 cell adj2 arteritis) or cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).ti,ab.	328
3	1 or 2	368
4	(Upadacitinib or Rinvoq or ABT 494 or ABT494 or 1310726-60-3).ti,ab.	878
5	(Tocilizumab or Actemra or tocilizumab-bavi or Tofidence or Tyenne or RoActemra or Lusinex or TCZ or Atlizumab or MRA or MSB 11456 or MSB11456 or R 1569 or RG 1569 or R1569 or RG1569 or RHPM 1 or RO 4877533 or RHPM1 or RO4877533).ti,ab.	2,807
6	(Secukinumab or Cosentyx or AIN 457 or AIN457 or AIN 457A or AIN457A).ti,ab.	1,233
7	(Guselkumab or Tremfya or CNTO 1959 or CNTO1959).ti,ab.	711
8	(corticosteroid* or steroid* or CS or prednisone or placebo).ti,ab.	432,031
9	4 or 5 or 6 or 7 or 8	434,419
10	3 and 9	293

Table 68. Clinical SLR – CDSR search, February 2025

Search String	Search Terms	Hits
1	(giant cell arteritis or cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).ti,ab.	4

Table 69. Clinical SLR – DARE search, February 2025

Search String	Search Terms	Hits
1	(giant cell arteritis or cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).mp. [mp=title, full text, keywords]	10

Table 70. Clinical SLR – Northern Light search, February 2025

Search String	Search Terms	Hits
1	exp Giant Cell Arteritis/	2,483
2	((giant adj2 cell adj2 arteritis) or cranial arteritis or granulomatous arteritis or temporal arteritis or Horton's disease).ti,ab.	1,666
3	1 or 2	2,560
4	(Upadacitinib or Rinvoq or ABT 494 or ABT494 or 1310726-60-3).ti,ab.	910
5	(Tocilizumab or Actemra or tocilizumab-bavi or Tofidence or Tyenne or RoActemra or Lusinex or TCZ or Atlizumab or MRA or MSB 11456 or MSB11456 or R 1569 or R1569 or RG 1569 or RG1569 or RHPM 1 or RHPM1 or RO 4877533 or RO4877533).ti,ab.	5,033
6	(Secukinumab or Cosentyx or AIN 457 or AIN457 or AIN 457A or AIN457A).ti,ab.	1,304
7	(Guselkumab or Tremfya or CNTO 1959 or CNTO1959).ti,ab.	698
8	(corticosteroid* or CS or steroid* or prednisone or placebo).ti,ab.	80,733
9	4 or 5 or 6 or 7 or 8	87,777
10	3 and 9	516
11	(control* adj3 (study or studies or trial* or group*)).ti,ab.	80,161
12	((random or randomi#ed) adj2 control* adj2 (trial* or study or studies)).ti,ab.	33,707
13	((Nonrandom* or non-random* or quasirandom* or quasi-random* or single arm or double arm or pragmatic or equivalence or open-label or noninferiority or non-inferiority) adj3 (trial* or study or studies)).ti,ab.	11,914
14	(allocat* or double blind or single blind).ti,ab.	22,639
15	(clinical adj2 (trial* or study or studies)).ti,ab.	95,076
16	11 or 12 or 13 or 14 or 15	192,413
17	10 and 16	68
18	limit 17 to yr="2019 -Current"	32

Table 71. Clinical SLR – PubMed search, February 2025

Search String	Search Terms	Hits
1	giant cell arteritis[MeSH Terms] OR "giant cell arteritis"[Title/Abstract] OR "cranial arteritis"[Title/Abstract] OR "granulomatous arteritis"[Title/Abstract] OR "temporal arteritis"[Title/Abstract] OR "Horton's disease"[Title/Abstract]	10,091
2	"Upadacitinib"[Title/Abstract] OR "Rinvoq"[Title/Abstract] OR "ABT-494"[Title/Abstract] OR "ABT494"[Title/Abstract] OR "1310726-60-3"[Title/Abstract] OR "Tocilizumab"[Title/Abstract] OR "Actemra"[Title/Abstract] OR "tocilizumab-bavi"[Title/Abstract] OR "Tofidence"[Title/Abstract] OR "Tyenne"[Title/Abstract] OR "RoActemra"[Title/Abstract] OR "Lusinex"[Title/Abstract] OR "TCZ"[Title/Abstract] OR "Atlizumab"[Title/Abstract] OR "MRA"[Title/Abstract] OR "MSB-11456"[Title/Abstract] OR "MSB11456"[Title/Abstract] OR "R-1569"[Title/Abstract] OR "R1569"[Title/Abstract] OR "RG-1569"[Title/Abstract] OR "RG1569"[Title/Abstract] OR "RHPM-1"[Title/Abstract] OR "RHPM1"[Title/Abstract] OR "RO-4877533"[Title/Abstract] "RO4877533"[Title/Abstract] OR "Secukinumab"[Title/Abstract] OR "Cosentyx"[Title/Abstract] OR "AIN-457"[Title/Abstract] OR "AIN457"[Title/Abstract] OR "AIN457A"[Title/Abstract] OR "Guselkumab"[Title/Abstract] OR "Tremfya"[Title/Abstract] OR "CNTO1959"[Title/Abstract] OR "CNTO-1959" OR "corticosteroid"[Title/Abstract] OR "corticosteroids"[Title/Abstract] OR "steroid"[Title/Abstract] OR "steroids"[Title/Abstract] OR "CS"[Title/Abstract] OR "prednisone"[Title/Abstract] OR "placebo"[Title/Abstract]	727,233
3	#1 AND #2	1,975
4	clinical trial[MeSH Terms] OR clinical trial as topic[MeSH Terms] OR clinical trials, randomized[MeSH Terms] OR controlled clinical trials, randomized[MeSH Terms] OR randomization[MeSH Terms] OR double blind method[MeSH Terms] OR double blind study[MeSH Terms] OR method, single blind[MeSH Terms] OR single blind studies[MeSH Terms] OR clinical trial overview[MeSH Terms]	697,486
5	"randomized controlled trial"[Title/Abstract] OR "randomised controlled trial"[Title/Abstract] OR "RCT"[Title/Abstract] OR "clinical trial"[Title/Abstract] OR "clinical study"[Title/Abstract] OR "clinical studies"[Title/Abstract] OR "trial"[Title/Abstract] OR "single-arm"[Title/Abstract] OR "non-random"[Title/Abstract] OR "non-randomized"[Title/Abstract] OR "non-randomised"[Title/Abstract] OR "quasi-random"[Title/Abstract] OR "nonrandom"[Title/Abstract] OR "nonrandomized"[Title/Abstract] OR "nonrandomised"[Title/Abstract] OR "quasirandom"[Title/Abstract] OR "pragmatic"[Title/Abstract] OR "equivalence"[Title/Abstract] OR "open-label"[Title/Abstract] OR "non-inferiority"[Title/Abstract] OR "allocation"[Title/Abstract]	1,230,832
6	retrospective study[MeSH Terms] OR retrospective studies[MeSH Terms] OR prospective study[MeSH Terms] OR prospective studies[MeSH Terms] OR analyses, cohort[MeSH Terms] OR analysis, cohort[MeSH Terms] OR cohort analyses[MeSH Terms] OR case control studies[MeSH Terms] OR case control study[MeSH Terms]	2,967,545
7	retrospective[Title/Abstract] OR prospective[Title/Abstract] OR observational[Title/Abstract] OR cohort[Title/Abstract] OR "case control"[Title/Abstract]	2,413,209
8	((review, systematic[MeSH Terms]) OR (meta analysis[MeSH Terms])) OR (meta analysis as topic[MeSH Terms])	40,920
9	systematic review[Title/Abstract] OR systematic literature review[Title/Abstract] OR SLR[Title/Abstract] OR meta-analysis[Title/Abstract] OR meta-analyses[Title/Abstract] OR network meta-analysis[Title/Abstract] OR network meta-analyses[Title/Abstract] OR NMA[Title/Abstract]	508,001
10	#4 OR #5	1,686,054
11	#6 OR #7	3,907,135
12	#8 OR #9	531,291
13	remission[Title/Abstract] OR steroid exposure[Title/Abstract] OR corticosteroid exposure[Title/Abstract] OR prednisone exposure[Title/Abstract] OR steroid dose[Title/Abstract] OR corticosteroid dose[Title/Abstract] OR prednisone dose[Title/Abstract] OR disease flare[Title/Abstract] OR SF 36[Title/Abstract] OR SF36[Title/Abstract] OR 36 item Short Form Quality of Life[Title/Abstract] OR Physical	2,633,663

Search String	Search Terms	Hits
	Component Score[Title/Abstract] OR PCS[Title/Abstract] OR Functional Assessment of Chronic Illness Therapy[Title/Abstract] OR FACIT[Title/Abstract] OR Treatment Satisfaction Questionnaire for Medication[Title/Abstract] OR TSQM[Title/Abstract] OR adverse event[Title/Abstract] OR adverse events[Title/Abstract] OR withdrawal[Title/Abstract] OR safety[Title/Abstract] OR efficacy[Title/Abstract] OR effectiveness[Title/Abstract]	
14	#3 AND #10 AND #13	83
15	#3 AND #11 AND #13	184
16	#3 AND #12 AND #13	18
17	#14 OR #15 OR #16	241

H.1.2 Systematic selection of studies

Study screening comprised multiple steps. Both title/abstract and full-text screening were performed based on PICOS criteria in Table 72. Screening was done independently by two researchers using the Covidence systematic review software. In title/abstract screening, researchers were able to select the options “yes/no/maybe” for article inclusion. Two votes of "yes" moved the record forward to full-text screening; two votes of "no" moved the record to irrelevant; votes consisting of "yes"/"no" and "maybe" were placed into a conflicts list. Records on the conflict list were discussed and consensus was reached on whether to move the reference forward to full-text or to the irrelevant category. No study was excluded at title/abstract screening due to insufficient information. Full-text reports in languages other than English were machine translated using Google and screened.

The full-text publications of citations that progressed through title/abstract screening were retrieved for further review. As with title/abstract screening, screening of full-text publications was conducted by two independent researchers using Covidence systematic review software. The same inclusion and exclusion criteria used in title/abstract screening were applied during full-text screening. Disagreements between researchers were resolved by discussion or by review with a third researcher. Studies were excluded if they did not meet PICOS inclusion criteria or were duplicate publications. Any study excluded during full-text screening was assigned a reason for exclusion based on the PICOS criteria

Table 72. Inclusion and exclusion criteria used for assessment of studies

Criterion	Inclusion criteria	Exclusion criteria	Local adaptation
Population	Adults (aged 18+ years) with GCA diagnosis • Overall • Subgroups if available: New onset disease, relapsing disease, by age	Non-human Non-GCA diagnosed patients Children (<18 years old)	
Interventions	Upadacitinib, tocilizumab, secukinumab, guselkumab, corticosteroids	Other non-biologics	Only trials including upadacitinib and tocilizumab are considered relevant for this application.

Criterion	Inclusion criteria	Exclusion criteria	Local adaptation
Comparators	Upadacitinib, tocilizumab, secukinumab, guselkumab, corticosteroids, placebo No comparator (single-arm trials)	Other non-biologics	
Outcomes	Examples of efficacy measures: • Proportion of subjects achieving sustained remission from w12 through w52 • Proportion of subjects achieving sustained complete remission from w12 through w52 • Proportion of subjects in complete remission at weeks 12, 24, 52, and other reported timepoints • CSD • Time to first disease flare • Proportion of subjects who experienced at least 1 disease flare through w52 • Number of disease flares per participant • Rate of CS-related AEs • Other efficacy related outcomes, e.g. proportion of participants with relapse-free survival, proportion of all-cause mortality, mean time to first relapse after induction of remission, proportion of participants who did not need escape therapy, vision changes or general quality of life changes PROs: • SF-36 PCS • FACIT-Fatigue • TSQM Patient Global Satisfaction Subscale Examples of safety measures: • Incidence of AEs • Incidence of SAEs • Treatment withdrawal (and reason for withdrawal, e.g., lack of efficacy, AEs, SAEs)	PK/PD outcomes Non-clinical outcomes	
Study type	RCTs with no restriction on phase or study design RCT sub-studies, if they report an additional outcome of interest or long-term follow-up data Registries Retrospective studies Non-randomized and single arm studies Observational studies Uncontrolled studies Case series Case reports SLRs and meta-analyses [4]	Non-human / pre-clinical studies Non-systematic reviews, editorials Notes, comments, letters Guidelines, consensus statements	
Other	No restrictions to publication language, publication date, or country/region		

AE, Adverse event; CS, Corticosteroid(s); CSD, Cumulative steroid dose; DMARD, Disease-modifying anti-rheumatic drug; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; GCA, Giant cell arteritis; GUS, Guselkumab; PBO, Placebo; PCS, Physical Component Summary; PRO, Patient-reported outcome; RCT, Randomized controlled trial; SAE, Serious adverse event; SECU, Secukinumab; SF-36, The Short Form (36) Health Survey; SLR, Systematic literature review; TCZ, Tocilizumab; THEIA, Study to Evaluate Guselkumab for

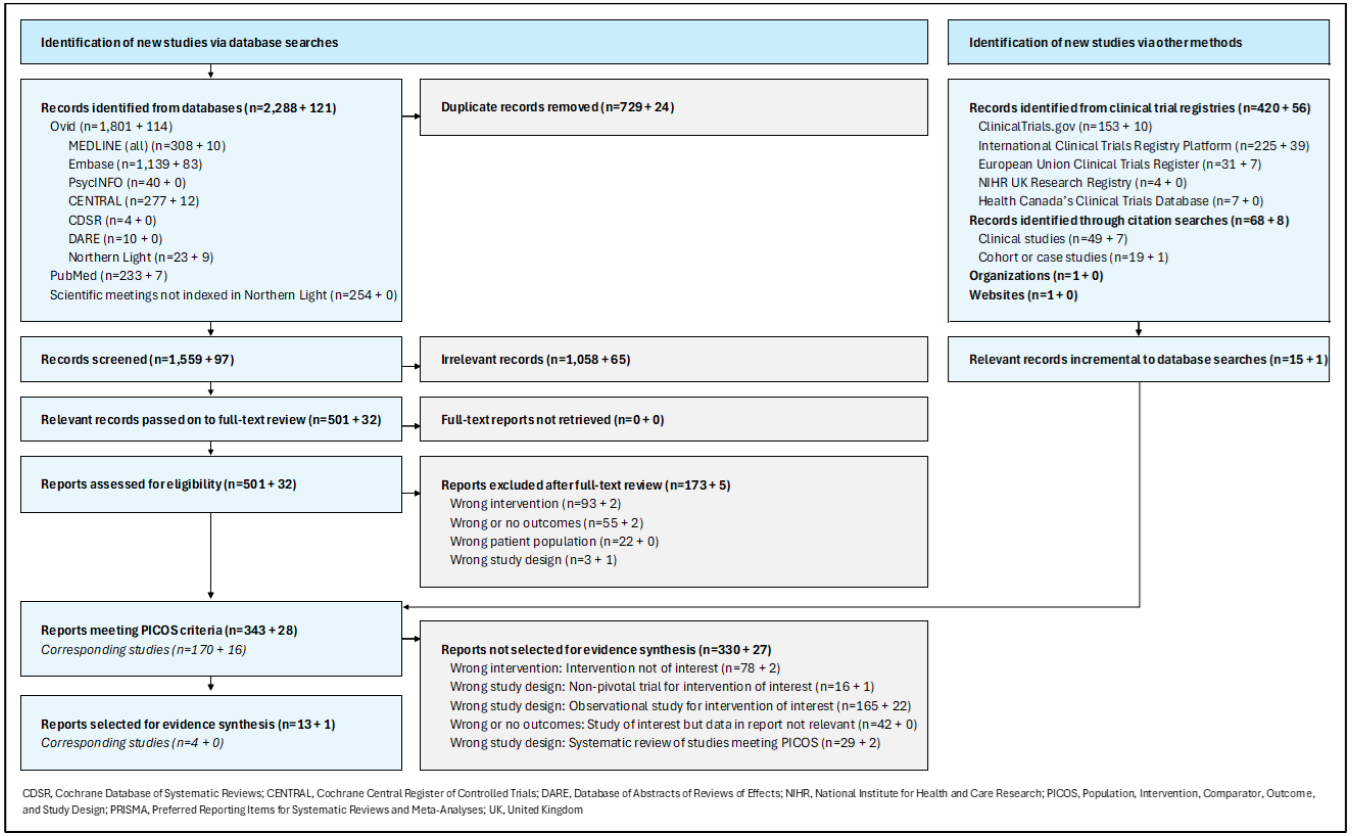
the Treatment of Participants with New-Onset or Relapsing Giant Cell Arteritis; TSQM, Treatment Satisfaction Questionnaire for Medication; UPA, Upadacitinib; w, Week

Following full-text screening, reports that met the broad PICOS eligibility criteria were further narrowed down to those suitable for quantitative synthesis via anchored ITC methods. For this purpose, only completed or ongoing pivotal Phase 3 RCTs (or, in the absence of Phase 3 data, Phase 2 RCTs) for available or potentially available treatments with published results were selected.

A schematic of the study selection process is summarized in Figure 21. Records identified through searches of bibliographic database and conference proceedings repositories are presented on the left side of the diagram, while records identified from supplemental searches of trial registries, citation searches, and other methods are presented in on the right side of the diagram.

The four studies selected for evidence synthesis before the local adaptation are presented in Table 73, including the final selection of studies for the comparison of upadacitinib and tocilizumab relevant for the Danish context

Figure 21. PRISMA diagram



Note: PRISMA values are formatted as (Number 1 + Number 2). Number 1 represents values from the initial SLR run conducted in April 2024. Number 2 represents values from the SLR re-run conducted in February 2025 that are *incremental* to the initial searches and screening activities conducted in

Table 73. Overview of study design for studies identified in the SLR, and final study selection for this application.

Study/ID	Aim	Study design	Patient population	Interven-tion and compara-tor (sample size (n))	Primary outcome and follow-up period	Secondary outcome and follow-up period	Local adaptation
SELECT-GCA, NCT03725202	Evaluate the safety and efficacy of upadacitinib in individuals with giant cell arteritis.	Randomized, parallel-group, double-blind, placebo-controlled, multicenter phase 3 study	• Patients aged ≥50 years with diagnosed GCA • Active disease within 8 weeks before BL • BL CS 20-60 mg/day	UPA 7.5mg QD/26w CS taper (n=107) UPA 15mg QD/26w CS taper (n=209) PBO QD/52w CS taper (n=112)	At week 52: Proportion of patients in sustained remission	At week 52: • Proportion of patients in sustained complete remission from week 12 • Cumulative CS dose • Time to first flare • Proportion of patients with ≥1 flare • Proportion of patients in complete remission • Number of flares per patient • Rate of CS-related AEs HRQoL: At week 52: • CFB in EQ-5D-5L VAS • CFB in SF-36: PCS • CFB in FACIT-Fatigue • TSQM patient global satisfaction subscale	Included

GiACTA, NCT01791153	To evaluate the efficacy and safety of tocilizumab in participants with GCA.	Randomized, parallel-group, double-blind, placebo-controlled, multicenter phase 3 study	• Patients aged ≥50 years with diagnosed GCA • Active disease within 6 weeks before BL • BL CS 20-60 mg/day	TCZ 162mg QW (SC)/26w CS taper (n=100) TCZ 162mg Q2W (SC)/26w CS taper (n=49) PBO/26w CS taper (n=50) PBO/52w CS taper (n=51)	At week 52: Proportion of patients in sustained remission (Experimental arm groups vs placebo comparator group C [26W taper])	Secondary: At week 52: • Proportion of patients in sustained remission (Experimental arm groups vs placebo comparator group D [52W taper]) • Time to first flare after clinical remission • Cumulative CS dose HRQoL: At week 52: • CFB in SF-36: PCS, MCS • CFB in PGA (VAS) • CFB in FACIT-Fatigue • CFB in EQ-5D	Included
TitAIN, **NCT03765788**	To evaluate the efficacy and safety of secukinumab compared to placebo to maintain disease remission up to 28 weeks including corticosteroid tapering, as well as up to 1 year (52 weeks) in patients with newly diagnosed or relapsing giant cell arteritis (GCA) who were naïve to biological therapy.	Randomized, parallel-group, double-blind, placebo-controlled, multicenter phase 2 study	• Patients aged ≥50 years with diagnosed GCA • Active disease within 6 weeks before BL • BL CS 25-60 mg/day	SECU 300 mg QW (BL to w4); 300 mg Q4W (after w4)/26w CS taper (n=27) PBO/26w CS taper (n=25)	Proportion of patients in sustained remission at week 28	Secondary: At week 52: •Proportion of patients in sustained remission • Time to first flare after remission • Cumulative CS dose • Proportion of patients on ≤5 mg/day of prednisolone • CFB in CRP • CFB in ESR HRQoL: At week 52: • CFB in PhGA (VAS)	Excluded, wrong comparator

						• CFB in PGA (VAS) • CFB in FACIT-Fatigue • CFB in SF-36: domains, PCS, MCS • CFB in EQ-5D-5L (VAS)	
Abatacept study, NCT00556439	Concurrent pilot studies in Giant Cell Arteritis and Takayasu's Arteritis to examine the safety, efficacy, and immunologic effects of Abatacept (CTLA4-Ig) in Large Vessel Vasculitis	Randomized, double-blind withdrawal multicenter phase 2 study	• Patients aged >50 years with diagnosed GCA • Active disease within 8 weeks before BL • BL CS 40-60 mg/day	Open-label phase: ABA 10mg/kg (BL to w12) Blinded randomized phase: ABA 10mg/kg Q4W (after w12)/28W Cs taper (n=20) PBO/28W CS taper (n=21)	Primary: At week 52: • Duration of remission (relapse-free survival) • Relapse-free survival rate	No secondary endpoints	Excluded, wrong comparator

H.1.3 Excluded fulltext references

The excluded full text references are presented in Table 74, Table 75, Table 76 and Table 77, for the initial SLR run and the SLR re-run respectively. The two studies excluded per Table 73 are not included in these tables.

Table 74. Excluded after full-text review per broad PICOS criteria (n=173) – Initial SLR run.

Reference	Reason for exclusion
Alammari Y, Abdalla A, Conway R, O'Neil LJ, Molloy E. 421. Giant Cell Arteritis during treatment with Tocilizumab. 2022:	Wrong or no outcomes
Alnaimat F, Alduradi H, Al-Qasem S, Ghazzal H, Alsarhan M. Giant cell arteritis: insights from a monocentric retrospective cohort study. Rheumatology international. 2024;doi:https://dx.doi.org/10.1007/s00296-024-05540-5	Wrong intervention
Alvarez CS, Bond M, Soowamber M, et al. A Systematic Literature Review to Generate Descriptors for the Development of New Response Criteria in Giant Cell Arteritis. Arthritis & rheumatology. 2022;74(suppl 9):970-972. doi:https://dx.doi.org/10.1002/art.42355	Wrong or no outcomes
Bahlas S, Ramos-Remus C, Davis P. Clinical outcome of 149 patients with polymyalgia rheumatica and giant cell arteritis. Journal of rheumatology. 1998;25(1):99-104.	Wrong patient population
Behn AR, Perera T, Myles AB. Polymyalgia rheumatica and corticosteroids: how much for how long? Annals of the Rheumatic Diseases. 1983;42(4):374-8. doi:10.1136/ard.42.4.374	Wrong patient population
Beketova T, Otteva E, Nasonov E. Interleukin-6 inhibition with tocilizumab for the treatment of giant cell arteritis and polymyalgia rheumatica in patients with serious comorbidities. Annals of the Rheumatic Diseases. 2020;79(suppl 1):1528-1529. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.2179	Wrong patient population
Bhurani M, Hall S, Ostor A, Gibson A. Time to flare in giant cell arteritis and polymyalgia rheumatica and review of the literature. Annals of the Rheumatic Diseases. 2020;79(suppl 1):683. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.2421	Wrong intervention
Boiardi L, Catanoso M, Restuccia G, Muratore F, Macchioni P, Salvarani C. Survival of large vessel giant cell arteritis in northern Italy during a 26-year period : No correlation with demographical, clinical, laboratory and imaging data. Arthritis & rheumatology. 2019;71(suppl 10):4694-4695. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Boiardi L, Galli E, Macchioni P, et al. Takayasu arteritis and large-vessel giant cell arteritis in Italian population. Comprehensive analysis from a single institutional cohort of 184 cases. Seminars in arthritis and rheumatism. 2023;59:152173. doi:10.1016/j.semarthrit.2023.152173	Wrong intervention
Boiardi L, Macchioni P, Galli E, et al. Takayasu Arteritis and Large-Vessel Giant Cell Arteritis in Italian Population. A Retrospective Cohort Study. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1567. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4496	Wrong or no outcomes
Boiardi L, MacChioni P, Muratore F, et al. Comparison between Clinical Features, Acute Phase Reactants, Imaging between Takayasu and LV-GCA Patients at Diagnosis and during Follow-up in Italian Patients in Monocentric Study. Arthritis & rheumatology. 2022;74(suppl 9):3080-3081. doi:https://dx.doi.org/10.1002/art.42355	Wrong intervention
Boiardi L, Marvisi C, Macchioni P, et al. Eosinophilic giant cell arteritis: A different subset of disease? Seminars in arthritis and rheumatism. 2024;65:152409. doi:10.1016/j.semarthrit.2024.152409	Wrong intervention
Boiardi L, Muratore F, Restuccia G, et al. Relapses and long-term remission in large vessel giant cell arteritis in northern ITALY: Characteristics and predictors in a long-term follow-up study. Annals of the Rheumatic Diseases. 2020;79(suppl 1):386. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.4729	Wrong intervention
Bourdin V, Deshayes S, Creveuil C, Becquemont L, Verstuyft C, Bienvenu B. Impact of GLCCI1 Genetic Polymorphism (rs37972) on response to Prednisone in giant cell arteritis (PREDICORT study). Fundamental & clinical pharmacology. 2021;35(suppl 1):41. doi:https://dx.doi.org/10.1111/fcp.12669	Wrong study design
Broder MS, Sarsour K, Chang E, et al. Corticosteroid-related adverse events in patients with giant cell arteritis: A claims-based analysis. Seminars in arthritis and rheumatism. 2016;46(2):246-252. doi:10.1016/j.semarthrit.2016.05.009	Wrong intervention

Reference	Reason for exclusion
Caceres VA, Pineiro ML, Ibanez-Beroiz B, Enguita-German M. Mass Switch from Intravenous to Subcutaneous Tocilizumab in Rheumatic Diseases during the SARS-COV-2 Pandemic. Journal of Clinical Rheumatology. 2022;28(7):346-348. doi:https://dx.doi.org/10.1097/RHU.0000000000001862	Wrong patient population
Cacoub P, Chemlal K, Khalifa P, et al. Deflazacort versus prednisone in patients with giant cell arteritis: effects on bone mass loss. Journal of rheumatology. 2001;28(11):2474-9.	Wrong or no outcomes
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Ischemic and systemic symptoms in giant cell arteritis patients, response to tocilizumab. Annals of the Rheumatic Diseases. 2019;78(suppl 2):819. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2230	Wrong or no outcomes
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Response to tocilizumab in patients with giant cell arteritis, according to ischemic vs systemic symptoms. Arthritis & rheumatology. 2019;71(suppl 10):4742-4744. doi:https://dx.doi.org/10.1002/art.41108	Wrong or no outcomes
Centre for Reviews and Dissemination. Effect of antiplatelet/anticoagulant therapy on severe ischemic complications in patients with giant cell arteritis: a cumulative meta-analysis (Provisional abstract). Database of Abstracts of Reviews of Effects. 2015;(2)	Wrong intervention
Chan CCK, Paine M, O'Day J. Predictors of recurrent ischemic optic neuropathy in giant cell arteritis. Journal of neuro-ophthalmology. 2005;25(1):14-17. doi:https://dx.doi.org/10.1097/00041327-200503000-00004	Wrong patient population
Chandran A, Udayakumar PD, Kermani TA, Warrington KJ, Crowson CS, Matteson EL. Glucocorticoid usage in giant cell arteritis over six decades (1950 to 2009). Clinical and experimental rheumatology. 2015;33(2 suppl 89):S-98.	Wrong intervention
Christ L, Gloor A, Kollert F, et al. Serum Proteomics in Giant Cell Arteritis: findings of the Giant Cell Arteritis Treatment with Ultra-short Glucocorticoids and Tocilizumab Trial (The GUSTO Trial). Arthritis & rheumatology. 2022;74:938-940. doi:https://doi.org/10.1002/art.42355	Wrong or no outcomes
Christ L, Gloor A, Kollert F, Reichenbach S, Villiger PM. SERUM PROTEOMICS in GIANT CELL ARTERITIS in RESPONSE to A THREE-DAY PULSE of GLUCOCORTICOID FOLLOWED by TOCILIZUMAB MONOTHERAPY (THE GUSTO TRIAL). Annals of the Rheumatic Diseases. 2022;81(suppl 1):374-375. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.434	Wrong or no outcomes
Chrysidis S, Hansen PR, Colic A, Diamantopoulos AP. Vascular complications in patients with active silent large vessel vasculitis. Nephron. 2015;129(suppl 2):231. doi:https://dx.doi.org/10.1159/000381120	Wrong intervention
Chu R, Ali M, Makhzoum JP. 19. Predictors of Relapse in Giant Cell Arteritis. 2022:	Wrong intervention
Ciechomska A, Melville AR. Follow up of Giant Cell Arteritis Patients with Ultrasound: Can Cranial Giant Cell Arteritis Phenotype Evolve Towards Large Vessel Vasculitis? Rheumatology. 2022;61(suppl 1):i159-i160. doi:https://dx.doi.org/10.1093/rheumatology/keac133.291	Wrong intervention
Clément J, Duffau P, Constans J, et al. Real-world Risk of Relapse of Giant Cell Arteritis Treated With Tocilizumab: A Retrospective Analysis of 43 Patients. Journal of rheumatology. 2021;48(9):1435-1441. doi:10.3899/jrheum.200952	Wrong patient population
ClinicalTrials.gov. A Study of the Safety and Effectiveness of Infliximab (Remicade) in Patients With Giant Cell Arteritis (NCT00076726). 2004;	Wrong or no outcomes
ClinicalTrials.gov. A Study to Evaluate Efficacy and Safety of Subcutaneous Abatacept With Steroid Treatment Compared to Steroid Treatment Alone in Adults With Giant Cell Arteritis (GCA) (NCT03192969). 2017;	Wrong or no outcomes
ClinicalTrials.gov. A Study to Evaluate Guselkumab for the Treatment of Participants With New-onset or Relapsing Giant Cell Arteritis (NCT04633447). 2020;	Wrong or no outcomes
ClinicalTrials.gov. A Study to Evaluate the Safety and Efficacy of Upadacitinib in Participants With Giant Cell Arteritis (NCT03725202). 2018;	Wrong or no outcomes
ClinicalTrials.gov. Abatacept for the Treatment of Giant Cell Arteritis (NCT04474847). 2020;	Wrong or no outcomes
ClinicalTrials.gov. Efficacy and Safety of Secukinumab in Patients With New Onset of Giant Cell Arteritis Who Are in Clinical Remission (NCT05380453). 2022;	Wrong or no outcomes
ClinicalTrials.gov. Efficacy of Tocilizumab for the Treatment of Acute AION Related to GCA (NCT04239196). 2019;	Wrong or no outcomes
ClinicalTrials.gov. Efficacy of Tocilizumab in Association to Steroids in Giant Cell Arteritis With Cerebro-vascular Involvement (NCT04888221). 2021;	Wrong or no outcomes

Reference	Reason for exclusion
ClinicalTrials.gov. Giant Cell Arteritis and Anakinra Trial (NCT02902731). 2016;	Wrong or no outcomes
ClinicalTrials.gov. Giant Cell Arteritis: comparison Between Two Standardized Corticosteroids Tapering (CORTODOSE) (NCT04012905). 2019;	Wrong or no outcomes
ClinicalTrials.gov. HECTHOR: humira to Spare Steroids in Giant Cell Arteritis (NCT00305539). 2006;	Wrong or no outcomes
ClinicalTrials.gov. Hydroxychloroquine in Giant Cell Arteritis (NCT00430807). 2007;	Wrong or no outcomes
ClinicalTrials.gov. MEthotrexate versus TOcilizumab for treatment of GIant cell Arteritis: a multicenter, randomized, controlled trial - METOGIA (NCT03892785). 2018;	Wrong or no outcomes
ClinicalTrials.gov. Phase II Randomized Study of Glucocorticoids With or Without Methotrexate for Treatment of Giant Cell Arteritis (NCT00004686). 2000;	Wrong or no outcomes
ClinicalTrials.gov. Phase III Study of Efficacy and Safety of Secukinumab Versus Placebo, in Combination With Glucocorticoid Taper Regimen, in Patients With Giant Cell Arteritis (GCA) (NCT04930094). 2021;	Wrong or no outcomes
ClinicalTrials.gov. TocilizuMab discontinuAtion in GIant Cell Arteritis (NCT06037460). 2023;	Wrong or no outcomes
ClinicalTrials.gov. Ustekinumab for the Treatment of Relapse of Refractory Giant Cell Arteritis (NCT03711448). 2018;	Wrong or no outcomes
Cochrane Central Register of Controlled Trials. A safety and efficacy study of ABT-494 in subjects with Giant Cell Arteritis (EUCTR2017 - 003978 - 13 - AT). 2019;	Wrong or no outcomes
Cochrane Central Register of Controlled Trials. GiAnT (Giant cell arteritis and Anakinra Trial) (EUCTR2015 - 005804 - 27 - FR). 2016;	Wrong or no outcomes
Cochrane Central Register of Controlled Trials. Study of efficacy and safety of secukinumab 300 mg in patients with giant cell arteritis (GCA) (EUCTR2020 - 004809 - 31 - DE). 2021;	Wrong or no outcomes
Concepcion L, Rosario Guzman E, Polanco Mora T, et al. Systemic vasculitis treatment, dominican republic. Journal of Clinical Rheumatology. 2020;20(3 suppl 1):S140.	Wrong or no outcomes
Craig G, Knapp K, Salim B, Mohan S, Michalska M. Treatment patterns, disease burden and outcomes in patients with giant cell arteritis and polymyalgia rheumatica. Arthritis & rheumatology. 2019;71(suppl 10):4770-4772. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Craig G, Knapp K, Salim B, Mohan SV, Michalska M. Treatment Patterns, Disease Burden, and Outcomes in Patients with Giant Cell Arteritis and Polymyalgia Rheumatica: A Real-World, Electronic Health Record-Based Study of Patients in Clinical Practice. Rheumatol Ther. 2021;8(1):529-539. doi:10.1007/s40744-021-00290-3	Wrong or no outcomes
Dammacco R, Alessio G, Giancipoli E, et al. Giant Cell Arteritis: The Experience of Two Collaborative Referral Centers and an Overview of Disease Pathogenesis and Therapeutic Advancements. Clinical ophthalmology. 2020;14:775-793. doi:10.2147/opth.S243203	Wrong intervention
David-Chausse J, Dehais J, Leman A. [Results of a regional survey on the treatment of rhizomelic pseudopolyarthritis and temporal arteritis. Apropos of 242 cases treated by various modalities with synthetic antimalarials, corticoids and non-steroidal anti-inflammatory agents]. Revue du Rhumatisme et des Maladies Osteo-Articulaires. 1983;50(8-9):563-71.	Wrong intervention
De Boysson H, Liozon E, Lambert M, et al. Giant-Cell Arteritis: Do We Treat Patients with Large-Vessel Involvement Differently? American Journal of Medicine. 2017;130(8):992-995. doi:https://dx.doi.org/10.1016/j.amjmed.2017.03.054	Wrong intervention
Do MP, Pugnet G, Moulis G, Guernec G, Lapeyre-Mestre M, Sailler L. Risks of non-cardiovascular corticosteroid related adverse events and cancer in giant cell arteritis: A french population-based cohort study. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong intervention
Emamifar A, Hess S, Ellingsen T, et al. Clinical presentation and treatment response in patients with polymyalgia rheumatica and giant cell arteritis during a 40-week follow-up. Rheumatology advances in practice. 2021;5(3) doi:https://dx.doi.org/10.1093/rap/rkab091	Wrong patient population
Eriksson P, Skoglund O, Hemgren C, Sjöwall C. Clinical experience and safety of Janus kinase inhibitors in giant cell arteritis: a retrospective case series from Sweden. Frontiers in immunology. 2023;14:1187584. doi:10.3389/fimmu.2023.1187584	Wrong intervention

Reference	Reason for exclusion
Espígol-Frigolé G, Corbera-Bellalta M, Planas-Rigol E, et al. Increased IL-17A expression in temporal artery lesions is a predictor of sustained response to glucocorticoid treatment in patients with giant-cell arteritis. Annals of the Rheumatic Diseases. 2013;72(9):1481-7. doi:10.1136/annrheumdis-2012-201836	Wrong or no outcomes
EU Clinical Trials Register. A study of the effectiveness and safety of delayed release prednisone in patients with newly diagnosed Giant Cell Arteritis (2011-005090-22). 2012;	Wrong or no outcomes
Fanlo P, Terry O, Arnáez R, et al. 241. CAUSES OF MORTALITY IN GIANT CELL ARTERITIS (GCA) IN A SERIES OF CASES IN THE NORTH OF SPAIN. Rheumatology. 2019;58(Supplement_2)doi:10.1093/rheumatology/kez062.015	Wrong intervention
Fardet L, Flahault A, Kettaneh A, et al. Corticosteroid-induced clinical adverse events: frequency, risk factors and patient's opinion. British journal of dermatology. 2007;157(1):142-8. doi:10.1111/j.1365-2133.2007.07950.x	Wrong patient population
Fardet L, Flahault A, Kettaneh A, Tiev KP, Toledano C, Cabane J. Natural history of corticosteroid-induced lipodystrophy: a prospective follow-up of 37 patients. [French]. Revue de medecine interne. 2007;28(12):825-831. doi:https://dx.doi.org/10.1016/j.revmed.2007.06.002	Wrong or no outcomes
Faurschou M, Ahlstrom M, Lindhardsen J, Obel N, Baslund B. Risk of diabetes mellitus among patients diagnosed with giant cell arteritis or granulomatosis with polyangiitis: A nationwide population-based cohort study. Rheumatology. 2017;56(suppl 3):iii55. doi:https://dx.doi.org/10.1093/rheumatology/kex108	Wrong intervention
Faurschou M, Ahlstrom MG, Lindhardsen J, Obel N, Baslund B. Risk of diabetes mellitus among patients diagnosed with giant cell arteritis or granulomatosis with polyangiitis: Comparison with the general population. Journal of rheumatology. 2017;44(1):78-83. doi:https://dx.doi.org/10.3899/jrheum.160797	Wrong intervention
Fuchs PS, Bigler MB, Kung C, et al. Prediction of relapses in autoimmune largevessel vasculitis-towards personalised immunosuppressive treatment stewardship. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1472. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.5474	Wrong intervention
Galli E, Muratore F, Boiardi L, et al. Comparison between transmural and isolated (PERI)adventitial inflammation at temporal artery biopsy: A single center cohort of biopsy-positive GCA with long term follow-up. Annals of the Rheumatic Diseases. 2020;79(suppl 1):685. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.2612	Wrong intervention
Galli E, Muratore F, Boiardi L, et al. Comparison between transmural and isolated periadventitial and/or adventitial inflammation at temporal artery biopsy: A single center cohort of biopsy-positive GCA with long term follow-up. Arthritis & rheumatology. 2019;71(suppl 10):4702-4703. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Galli E, Muratore F, Boiardi L, et al. Significance of inflammation restricted to adventitial/periadventitial tissue on temporal artery biopsy. Seminars in arthritis and rheumatism. 2020;50(5):1064-1072. doi:10.1016/j.semarthrit.2020.05.021	Wrong intervention
Gembitskii EV, Glazunov AV, Zhiliaev EV, Prekhorova EG. Etiology and treatment of temporal arteritis. [Russian]. Klinicheskaia meditsina. 1994;72(6):18-21.	Wrong intervention
Gibiansky L, Gibiansky E, Frey N, et al. Population pharmacokinetic and exposure-efficacy/safety analyses for selection of optimal dose regimen of tocilizumab in patients with giant cell arteritis (GCA). Journal of pharmacokinetics and pharmacodynamics. 2017;44(1):S131. doi:https://doi.org/10.1007/s10928-017-9536-y	Wrong or no outcomes
Gil W, Kodjikian L, Andre M, et al. Uveitis in Giant Cell Arteritis: A Retrospective Study of Seven Observational Cases and Literature Review. Ocul Immunol Inflamm. 2023:1-8. doi:10.1080/09273948.2023.2264383	Wrong or no outcomes
Gouet D, Maréchaud R, Le Berre D, et al. [Prognosis of treated temporal arteritis. Retrospective study of 87 cases]. Presse medicale. 1986;15(13):603-6.	Wrong intervention
Hayreh SS, Zimmerman B. Management of giant cell arteritis. Our 27-year clinical study: new light on old controversies. Ophthalmologica. 2003;217(4):239-59. doi:10.1159/000070631	Wrong or no outcomes
Herrero-Morant A, Loricera J, Ferraz-Amaro I, et al. Predictive Factors of Relapse in Giant Cell Arteritis Treated with Tocilizumab. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1557-1558. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4399	Wrong or no outcomes
Hetland H, Haugeberg G, Myklebust G, Diamantopoulos AP. Color doppler ultrasound as a monitoring tool of the response to treatment in large vessel giant cell arteritis. Nephron. 2015;129(suppl 2):181-182. doi:https://dx.doi.org/10.1159/000381120	Wrong or no outcomes
Hocevar A, Jese R, Rotar Z, Tomsic M. Does leflunomide have a role in giant cell arteritis? Arthritis & rheumatology. 2018;70(suppl 9):3198-3199. doi:https://dx.doi.org/10.1002/art.40700	Wrong intervention
Hysa E, Bond M, Ehlers L, et al. Treat-to-Target Strategies in Giant Cell Arteritis and Polymyalgia Rheumatica: A Systematic Literature Review Informing an International Taskforce. Annals of the Rheumatic Diseases. 2023;82(suppl 1):658. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.3193	Wrong or no outcomes

Reference	Reason for exclusion
Ince B, Artan S, Yalcinkaya Y, et al. Investigation of permanent organ damage in giant cell arteritis: Disease flares are associated with increased damage scores. Annals of the Rheumatic Diseases. 2020;79(suppl 1):1540. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.6379	Wrong intervention
Ince B, Artan S, Yalcinkaya Y, et al. Long-term follow-up of 89 patients with giant cell arteritis: a retrospective observational study on disease characteristics, flares and organ damage. Rheumatology international. 2021;41(2):439-448. doi:https://dx.doi.org/10.1007/s00296-020-04730-1	Wrong intervention
Jain, S., et al., P181 Clinical assessment of radiologically defined clinically isolated aortitis in a single centre study. Rheumatology, 2024. 63(Supplement_1).	Wrong or no outcomes
Jayatilleke C, Janagan S, Marshall R, et al. Tocilizumab for Refractory or Relapsing Giant Cell Arteritis: Audit Data from the Bristol and Bath Regional Multidisciplinary Meetings 2018-2021. Rheumatology. 2022;61(suppl 1):i160. doi:https://dx.doi.org/10.1093/rheumatology/keac133.292	Wrong or no outcomes
Jobard S, Magnant J, Blasco H, et al. Quality of life of patients treated for giant cell arteritis: a case-control study. Clinical rheumatology. 2017;36(9):2055-2062. doi:10.1007/s10067-017-3619-4	Wrong intervention
Kermani TA, Sreih A, Tomasson G, et al. 148. SHORT-FORM 36 AS A MEASURE OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH GIANT CELL ARTERITIS. Rheumatology. 2019;58(Supplement_2)doi:10.1093/rheumatology/kez059.025	Wrong intervention
Kermani TA, Warrington KJ, Cuthbertson D, et al. Disease Relapses among Patients with Giant Cell Arteritis: A Prospective, Longitudinal Cohort Study. Journal of rheumatology. 2015;42(7):1213-7. doi:10.3899/jrheum.141347	Wrong intervention
Kermani TA, Warrington KJ, Cuthbertson D, et al. Relapses among patients with giant cell arteritis. Arthritis & rheumatism. 2011;63(10 SUPPL. 1)	Wrong intervention
Kyle V, Hazleman BL. Treatment of polymyalgia rheumatica and giant cell arteritis. II. Relation between steroid dose and steroid associated side effects. Annals of the Rheumatic Diseases. 1989;48(8):662-6. doi:10.1136/ard.48.8.662	Wrong patient population
Larivière D, Sacre K, Klein I, et al. Extra- and intracranial cerebral vasculitis in giant cell arteritis: an observational study. Medicine. 2014;93(28):e265. doi:10.1097/md.0000000000000265	Wrong intervention
Larivière D, Sacre K, Klein I, et al. Extra-and intracranial cerebral vasculitis in giant cell arteritis: An observational study. Annals of the Rheumatic Diseases. 2015;2:299. doi:https://dx.doi.org/10.1136/annrheumdis-2015-eular.1081	Wrong intervention
Laskou F, Aung T, Gayford D, et al. Visual involvement in giant cell arteritis: A prospective multi center study. Arthritis & rheumatology. 2018;70(suppl 9):907-908. doi:https://dx.doi.org/10.1002/art.40700	Wrong intervention
Laverty UA, Banks E, McHenry M. E106 Case review of tocilizumab use in giant cell arteritis and large vessel vasculitis in Belfast Health and Social Care Trust. Rheumatology. 2019;58(Supplement_3)doi:10.1093/rheumatology/kez110.104	Wrong or no outcomes
Liozon F, Vidal E, Gaches F, et al. [Death in Horton disease. Prognostic factors]. Revue de medecine interne. 1992;13(3):187-91. doi:10.1016/s0248-8663(05)81324-4	Wrong intervention
Lyne S, Ruediger C, Lester SL, et al. 25. Prevalence, clinical phenotype and complications of large vessel giant cell arteritis: systematic review and meta-analysis. 2022:	Wrong intervention
Martinho J, Bandeira M, Barreira S, et al. 211. Differences in giant cell arteritis manifestations according to the ultrasound pattern of disease involvement. 2022:	Wrong intervention
Mohan S, Han J, Stone JH. Efficacy of adjunctive methotrexate in patients with giant cell arteritis treated with tocilizumab plus prednisone tapering: subanalysis of the giacta trial. Annals of the Rheumatic Diseases. 2020;79(SUPPL 1):693. doi:https://doi.org/10.1136/annrheumdis-2020-eular.2204	Wrong intervention
Mohan S, Neumann T, Han J, Stone JH. Efficacy of adjunctive methotrexate in patients with Giant Cell Arteritis treated with tocilizumab plus prednisone tapering: subanalysis of the GiACTA trial. Swiss medical weekly. 2020;150(SUPPL 245):5S-6S.	Wrong intervention
Muratore F, Boiardi L, Restuccia G, et al. Relapses and long-term remission in large vessel giant cell arteritis in northern Italy: Characteristics and predictors in a long-term follow-up study. Seminars in arthritis and rheumatism. 2020;50(4):549-558. doi:10.1016/j.semarthrit.2020.04.004	Wrong intervention
Muratore F, Crowson C, Boiardi L, et al. Comparison of biopsy proven giant cell arteritis in North America and South Europe: A population-based study. Arthritis & rheumatology. 2019;71(suppl 10):4697-4698. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Muratore F, Crowson CS, Boiardi L, et al. Comparison of biopsy proven giant cell arteritis in North America and southern Europe: A population-based study. Annals of the Rheumatic Diseases. 2017;76(suppl 2):609-610. doi:https://dx.doi.org/10.1136/annrheumdis-2017-eular.5156	Wrong intervention

Reference	Reason for exclusion
Muratore F, Kermani TA, Crowson CS, et al. Large-vessel giant cell arteritis: A cohort study. Rheumatology. 2015;54(3):463-470. doi:https://dx.doi.org/10.1093/rheumatology/keu329	Wrong intervention
Muratore F, Kermani TA, Crowson CS, Green AB, Matteson EL, Warrington KJ. Large vessel giant cell arteritis: A cohort study. Arthritis & rheumatism. 2012;10:S994. doi:https://dx.doi.org/10.1002/art.37735	Wrong intervention
Narvaez J, Estrada P, D LL, et al. Efficacy and safety of leflunomide in the management of large vessel vasculitis: A systematic review and metaanalysis of cohort studies. Seminars in arthritis and rheumatism. 2023;59doi:https://dx.doi.org/10.1016/j.semarthrit.2023.152166	Wrong intervention
O'Neill L, Conway R, Gallagher P, et al. Vasculitis damage assessment at 12 months in a cohort of patients with GCA. Nephron. 2015;129(suppl 2):228. doi:https://dx.doi.org/10.1159/000381120	Wrong intervention
Palmou-Fontana N, Loricera J, Blanco R, et al. Tocilizumab compared to anti-TNFalpha agents in refractory aortitis. Annals of the Rheumatic Diseases. 2015;2:522. doi:https://dx.doi.org/10.1136/annrheumdis-2015-eular.3849	Wrong patient population
Patel N, Fu X, Zhang Y, Stone JH. Baseline Glucocorticoid Toxicity in the Treatment of Giant Cell Arteritis: a Post Hoc Analysis of the GiACTA Trial. Arthritis & rheumatology. 2022;74:915-918. doi:https://doi.org/10.1002/art.42355	Wrong or no outcomes
Patel NJ, Fu X, Zhang Y, Stone JH. Baseline Glucocorticoid-Related Toxicity Scores in Giant Cell Arteritis: a Post Hoc Analysis of the GiACTA Trial. ACR open rheumatology. 2023;5(1):51-58. doi:https://doi.org/10.1002/acr2.11520	Wrong or no outcomes
Patel S, Ojak I, Atwal S, et al. Intracranial Giant Cell Arteritis: A Comprehensive Systematic Review. 21st International Vasculitis Workshop. 2024.	Wrong or no outcomes
Perrineau S, Ghesquiere T, Charles P, et al. A French cohort of patients with giant cell arteritis: Glucocorticoid treatment and its associated side effects. Clinical and experimental rheumatology. 2021;39(2):S155-S160.	Wrong intervention
Perrineau S, Paule R, Charles P, et al. Giant-cell arteritis: Is glucocorticoid-sparing treatment still relevant? a retrospective study. Arthritis & rheumatology. 2018;70(suppl 9):3084-3085. doi:https://dx.doi.org/10.1002/art.40700	Wrong intervention
Polachek A, Pauzner R, Levartovsky D, et al. The fine line between takayasu and giant cell arteritis: A retrospective study. Annals of the Rheumatic Diseases. 2013;72(SUPPL. 3)doi:https://dx.doi.org/10.1136/annrheumdis-2013-eular.2762	Wrong intervention
Polachek A, Pauzner R, Levartovsky D, et al. The fine line between Takayasu arteritis and giant cell arteritis. Clinical rheumatology. 2015;34(4):721-7. doi:10.1007/s10067-014-2813-x	Wrong intervention
Prieto-Peña D, Loricera J, Yuste SR, et al. JAKINIB in Refractory Giant Cell Arteritis. National Multicenter Study of 15 Cases and Literature Review. Arthritis & rheumatology. 2022;74(suppl 9):925-927. doi:https://dx.doi.org/10.1002/art.42355	Wrong intervention
Proven A, Gabriel SE, Orces C, O'Fallon WM, Hunder GG. Glucocorticoid therapy in giant cell arteritis: duration and adverse outcomes. Arthritis & rheumatism. 2003;49(5):703-8. doi:10.1002/art.11388	Wrong intervention
Prunte MKR, Naumann A, Christ M, Naumann M, Bayas A. Giant cell arteritis with vertebral artery involvement-baseline characteristics and follow-up of a monocentric patient cohort. Frontiers in Neurology. 2023;14doi:https://dx.doi.org/10.3389/fneur.2023.1188073	Wrong or no outcomes
Pugnet G, Sailler L, Bourrel R, Montastruc JL, Lapeyre-Mestre M. Is statin exposure associated with occurrence or better outcome in giant cell arteritis? results from a french population-based study. Journal of rheumatology. 2015;42(2):316-322. doi:https://dx.doi.org/10.3899/jrheum.140906	Wrong intervention
Pugnet G, Sailler L, Bourrel R, Montastruc JL, Lapeyre-Mestre M. Statins do not influence occurrence or prednisone requirement of giant cell arteritis. A french population-based cohort study. Arthritis & rheumatism. 2013;10:S710. doi:https://dx.doi.org/10.1002/art.38216	Wrong or no outcomes
Pupim L, Unizony S, Cid M, et al. A phase 2, randomized, double-blind placebo-controlled study to test the efficacy and safety of mavrilimumab in giant cell arteritis: study design and methodology. Rheumatology. 2019;58(suppl 2)doi:https://doi.org/10.1093/rheumatology/kez063.060	Wrong or no outcomes
Quartuccio L, Isola M, Bruno D, et al. Steroid sparing effect, lower incidence of disease relapse and diabetes in giant cell arteritis treated with immunosuppressors ab initio or very early: a multicenter retrospective case-control study. Annals of the Rheumatic Diseases. 2020;79(SUPPL 1):691-692. doi:https://doi.org/10.1136/annrheumdis-2020-eular.3085	Wrong intervention
Quartuccio L, Maset M, De Maglio G, et al. Role of oral cyclophosphamide in the treatment of giant cell arteritis. Rheumatology. 2012;51(9):1677-86. doi:10.1093/rheumatology/kes127	Wrong intervention
Rathore U, Thakare DR, Patro P, Agarwal V, Sharma A, Misra DP. A systematic review of clinical and preclinical evidences for Janus kinase inhibitors in large vessel vasculitis. Clinical rheumatology. 2022;41(1):33-44. doi:10.1007/s10067-021-05973-4	Wrong intervention

Reference	Reason for exclusion
Regola F, Bosio G, Cerudelli E, Tincani A, Toniati P. Long-term biological treatment in large vessels vasculitis: A retrospective single center study on 30 patients from 2011 to 2018. Annals of the Rheumatic Diseases. 2019;78(suppl 2):1764. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.4384	Wrong patient population
Regola F, Bosio G, Tincani A, Toniati P. Long-term biological treatment in 30 patients with large vessels vasculitis: 8 years' experience of a single italian center. Rheumatology. 2019;58(Supplement 2)doi:https://dx.doi.org/10.1093/rheumatology/kez063.063	Wrong patient population
Regola F, Mora J, Bosio G, Andreoli L, Franceschini F, Toniati P. Glucocorticoid-related Adverse Events in Giant Cell Arteritis: Application of the Glucocorticoid Toxicity Index in a Monocentric Cohort of 140 Patients. Arthritis & rheumatology. 2022;74(suppl 9):958-959. doi:https://dx.doi.org/10.1002/art.42355	Wrong intervention
Rhee RL, Dehghan N, Sreih AG, et al. Late-onset relapse in patients with systemic vasculitis. Arthritis & rheumatology. 2016;68(suppl 10):3954-3956. doi:https://dx.doi.org/10.1002/art.39977	Wrong intervention
Righetti G, Venerito V, Giannotta M, et al. Tocilizumab treatment for large vessels vasculitis: Real life preliminary experiences. Annals of the Rheumatic Diseases. 2019;78(suppl 2):1765. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2395	Wrong patient population
Righetti G, Venerito V, Giannotta M, et al. Tocilizumab treatment for large vessels vasculitis: Real life preliminary experiences. Rheumatology. 2019;58(Supplement 2)doi:https://dx.doi.org/10.1093/rheumatology/kez063.011	Wrong patient population
Rimland CA, Quinn KA, Rosenblum JS, et al. Outcome Measures in Large Vessel Vasculitis: Relationship Between Patient-, Physician-, Imaging-, and Laboratory-Based Assessments. Arthritis care & research. 2020;72(9):1296-1304. doi:https://dx.doi.org/10.1002/acr.24117	Wrong intervention
Rubbert-Roth A, Neumann T, Rein P, Koger N, Von Kempis J. Long-term outcome in real life patients with giant cell arteritis (GCA) and polymyalgia (PMR) treated with tocilizumab (TCZ). Swiss medical weekly. 2018;148(suppl 231):12S.	Wrong patient population
Rutherford P, Gotte D. Adverse events due to high dose glucocorticoids-lessons from anca-associated vasculitis and other inflammatory diseases. Annals of the Rheumatic Diseases. 2019;78(suppl 2):812. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2354	Wrong patient population
Saha P, Sandhu V, Robinson H, et al. P184 Developing a pathway for tocilizumab treatment in giant cell arteritis: a South London regional experience. Rheumatology. 2020;59(Supplement_2)doi:10.1093/rheumatology/keaa111.179	Wrong or no outcomes
Saito S, Okuyama A, Okada Y, et al. Tocilizumab monotherapy for large vessel vasculitis: Results of 104-week treatment of a prospective, single-center, open study. Arthritis & rheumatology. 2018;70(suppl 9):3087-3088. doi:https://dx.doi.org/10.1002/art.40700	Wrong patient population
Salvarani C, Boiardi L, Cavazza A, et al. Flares and long-term remission in large-vessel giant cell arteritis in northern Italy: Characteristics and predictors in a long-term follow-up study. Arthritis & rheumatology. 2019;71(suppl 10):4695-4696. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Salvarani C, Boiardi L, Macchioni P, et al. Role of peripheral CD8 lymphocytes and soluble IL-2 receptor in predicting the duration of corticosteroid treatment in polymyalgia rheumatica and giant cell arteritis. Annals of the Rheumatic Diseases. 1995;54(8):640-4. doi:10.1136/ard.54.8.640	Wrong patient population
Sammel A, Hsiao E, Schembri G, et al. PET/CT vascular findings at baseline and six months in patients with newly diagnosed giant cell arteritis. Arthritis & rheumatology. 2019;71(suppl 10):4731-4732. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Sanchez-Alvarez C, Bond M, Soowamber M, et al. Development of Response Criteria for Gca: An Slr Informing an International Task Force. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1565. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4165	Wrong or no outcomes
Sanchez-Alvarez C, Bond M, Soowamber M, et al. Measuring treatment outcomes and change in disease activity in giant cell arteritis: a systematic literature review informing the development of the EULAR-ACR response criteria on behalf of the EULAR-ACR response criteria in giant cell arteritis task force. RMD Open. 2023;9(2) doi:https://dx.doi.org/10.1136/rmdopen-2023-003233	Wrong or no outcomes
Sanchez-Alvarez C, Hawkins A, Koster M, Lehman VT, Crowson C, Warrington K. Giant cell arteritis with intracranial vasculitis: A case series. Arthritis & rheumatology. 2019;71(suppl 10):4730-4731. doi:https://dx.doi.org/10.1002/art.41108	Wrong intervention
Sanchez-Alvarez C, Hawkins AS, Koster MJ, Lehman VT, Crowson CS, Warrington KJ. Clinical and Radiographic Features of Giant Cell Arteritis With Intracranial Involvement. ACR open rheumatology. 2020;2(8):471-477. doi:https://dx.doi.org/10.1002/acr2.11161	Wrong intervention

Reference	Reason for exclusion
Sanchez-Costa JT, Hernandez I, Fernandez-Fernandez E, et al. TREATMENT, ADVERSE EVENTS and FOLLOW UP in PATIENTS with GIANT CELL ARTERITIS in the ARTESER MULTICENTER STUDY. Annals of the Rheumatic Diseases. 2022;81(suppl 1):686. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.1314	Wrong intervention
Sanchez-Costa JT, Hernandez-Rodriguez I, Fernandez-Fernandez E, et al. Treatment of giant cell arteritis in the arteser multicenter study of 1675 patients. Arthritis & rheumatology. 2021;73(suppl 9):2946-2948. doi:https://dx.doi.org/10.1002/art.41966	Wrong intervention
Sanchez-Martin J, Loricera J, Sanchez-Bilbao L, et al. ULTRASOUND ASSESSMENT of the EFFECTIVENESS of TOCILIZUMAB in GIANT CELL ARTERITIS. STUDY of 26 PATIENTS from CLINICAL PRACTICE. Annals of the Rheumatic Diseases. 2022;81(suppl 1):1788-1789. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.4098	Wrong or no outcomes
Schegk E, Berger CT, Imfeld S, et al. Vessel wall morphology in giant cell arteritis-a long-term sonographic follow-up study. Annals of the Rheumatic Diseases. 2018;77(suppl 2):785. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.5478	Wrong intervention
Schmalzing M, Gadeholt O, Gernert M, Tony HP, Schwaneck EC. Tocilizumab in Large Vessel Vasculitis - Different Routes of Administration. Open Rheumatology Journal. 2018;12:152-159. doi:10.2174/1874312901812010152	Wrong patient population
Schmitt C, Brockwell L, Giraudon M, et al. INTRAVENOUS TOCILIZUMAB for the TREATMENT of GIANT CELL ARTERITIS: A PHASE IB DOSERANGING PHARMACOKINETIC BRIDGING STUDY. Annals of the Rheumatic Diseases. 2022;81(suppl 1):376-377. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.898	Wrong study design
Schmitt C, Brockwell L, Giraudon M, et al. Intravenous tocilizumab for the treatment of giant cell arteritis: a phase Ib dose-ranging pharmacokinetic bridging study. Arthritis research & therapy. 2022;24(1):133. doi:https://dx.doi.org/10.1186/s13075-022-02815-9	Wrong study design
Schonau V, Corte G, Ott S, et al. CHARACTERIZATION of RELAPSES in PATIENTS with GIANT CELL ARTERITIS (GCA) PATIENTS-DATA from the REAL-LIFE TREATMENT and SAFETY (REATS)-GCA COHORT. Annals of the Rheumatic Diseases. 2022;81(suppl 1):694. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.3543	Wrong intervention
Sebastian A, Van der Geest K, Conticini E, et al. Southend Gca Probability Score (Gcaps) and Ultrasound Halo Score (Hs) as Markers for Diagnosis and Monitoring of Gca: Results from the Prospective, Multicenter Has-Gca Study. Annals of the Rheumatic Diseases. 2023;82(suppl 1):654. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.6159	Wrong intervention
Seitz L, Christ L, Lotscher F, et al. Quantitative ultrasound to monitor the vascular response to tocilizumab in giant cell arteritis. Rheumatology. 2021;60(11):5052-5059. doi:https://dx.doi.org/10.1093/rheumatology/keab484	Wrong or no outcomes
Seitz L, Lotscher F, Reichenbach S, Villiger P, Christ L. Ultrasound Shows Ongoing Vessel Wall Remodeling in Giant Cell Arteritis for Two Years after Discontinuation of Tocilizumab-Follow-up of the Gusto Trial. Annals of the Rheumatic Diseases. 2023;82(631)doi:https://doi.org/10.1136/annrheumdis-2023-eular.1198	Wrong or no outcomes
Seitz M, Reichenbach S, Bonel HM, Adler S, Wermelinger F, Villiger PM. Rapid induction of remission in large vessel vasculitis by IL-6 blockade. A case series. Swiss medical weekly. 2011;141:w13156. doi:10.4414/smw.2011.13156	Wrong patient population
Shankaranarayana S, Kubler P, Kevat S, Gunsberg M, Klestov A, Stockton K. Giant cell arteritis in a tertiary Queensland hospital: A 5-year retrospective study. Internal Medicine Journal. 2012;42(suppl1):24-25. doi:https://dx.doi.org/10.1111/j.1445-5994.2012.02761.x	Wrong intervention
Solans-Laque R, Fonseca E, Escalante B, et al. Giant cell arteritis (GCA) in octogenarian patients. Annals of the Rheumatic Diseases. 2017;76(Supplement 2):330. doi:https://doi.org/10.1136/annrheumdis-2017-eular.5247	Wrong intervention
Stollerman GH. Methotrexate for giant-cell arteritis. Hospital Practice. 2001;36(4):50.	Wrong intervention
Stone JH, Han J, Mohan SV. Efficacy of Adjunctive Methotrexate in Patients with Giant Cell Arteritis Treated with Tocilizumab Plus Prednisone Tapering: subanalysis of a Phase 3 Trial. Arthritis & rheumatology. 2020;72(SUPPL 10):3863-3865. doi:https://doi.org/10.1002/art.41538	Wrong intervention
Sugihara T, Uchida HA, Yoshifuji H, et al. Association between the patterns of large-vessel lesions and treatment outcomes in patients with large-vessel giant cell arteritis. Modern rheumatology. 2023;33(6):1145-1153. doi:https://dx.doi.org/10.1093/mr/roac122	Wrong intervention
Sugihara T, Uchida HA, Yoshifuji H, et al. Patterns of large-vessel lesions and poor treatment outcomes in patients with largevessel giant cell arteritis. Annals of the Rheumatic Diseases. 2021;80(suppl 1):395-396. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.824	Wrong intervention
Tedeschi S, Jin Y, Vine S, et al. Giant cell arteritis treatment patterns and rates of serious infections. Annals of the Rheumatic Diseases. 2021;80(suppl 1):651. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.561	Wrong intervention

Reference	Reason for exclusion
Tedeschi SK, Jin Y, Vine S, et al. Giant cell arteritis treatment patterns and rates of serious infections. Clinical and experimental rheumatology. 2022;40(4):826-833. doi:10.55563/clinexprheumatol/uonz1p	Wrong intervention
Tomelleri A, Campochiaro C, Sartorelli S, Farina N, Baldissera E, Dagna L. Cranial-limited and large-vessel giant cell arteritis: Presenting features and outcome. Annals of the Rheumatic Diseases. 2020;79(suppl 1):678-679. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.705	Wrong intervention
Tomelleri A, Campochiaro C, Sartorelli S, Farina N, Baldissera E, Dagna L. Presenting features and outcomes of cranial-limited and large-vessel giant cell arteritis: a retrospective cohort study. Scandinavian journal of rheumatology. 2022;51(1):59-66. doi:10.1080/03009742.2021.1889025	Wrong intervention
Trives-Folguera L, Molina-Collada J, López K, et al. Oral or pulse glucocorticoid use at the onset of giant cell arteritis and its influence on the risk of relapse: a retrospective study. Rheumatol Int. 2023;43(7):1333-1340. doi:10.1007/s00296-023-05321-6	Wrong intervention
Tsalapaki C, Lazarini A, Antonatou K, et al. Frequency of relapses and treatment discontinuation during long-term follow-up of patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2017;76(suppl 2):321. doi:https://dx.doi.org/10.1136/annrheumdis-2017-eular.6115	Wrong intervention
Tsalapaki C, Nikitopoulou E, Boki KA, et al. Five-year prospective multi-center cohort study of patients with giant cell arteritis in Greece. Mediterranean Journal of Rheumatology. 2018;29(2):103-105. doi:10.31138/mjr.29.2.103	Wrong or no outcomes
Twomlow EL, Prior JA, Mackie SL, et al. Characteristics of patients with prevalent giant cell arteritis in UK primary care. Rheumatology. 2019;58(suppl 3):iii130. doi:https://dx.doi.org/10.1093/rheumatology/kez107.032	Wrong intervention
Uechi E, Fushimi K. Epidemiological study of giant cell arteritis using a Japanese administrative database. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong intervention
Unizony S, Cid MC, Brouwer E, et al. Utility of crp and esr in the diagnosis of giant cell arteritis relapse in a phase 2 trial of mavrilimumab. Annals of the Rheumatic Diseases. 2021;80(SUPPL 1):1211-1212. doi:https://doi.org/10.1136/annrheumdis-2021-eular.2221	Wrong patient population
Urgelles JF, Rodriguez-Rodriguez L, Rosado ZR, et al. Treatment with methotrexate and risk of ischemic relapses in patients with giant cell arteritis in clinical practice. Arthritis & rheumatology. 2018;70(suppl 9):3120-3121. doi:https://dx.doi.org/10.1002/art.40700	Wrong intervention
Uyaguari Morocho MDC, Fernandez-Fernandez E, Monjo I, De Miguel E. Cranial, Extracranial and Mixed Involvement in Giant Cell Arteritis: Analysis of the Clinical Differences. Annals of the Rheumatic Diseases. 2023;82(suppl 1):650-651. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4167	Wrong intervention
Van Sleen Y, Arends S, Van Der Geest K, Sandovici M, Brouwer E. The Impact of Giant Cell Arteritis and Polymyalgia Rheumatica on Frailty, Daily Functioning and Quality of Life in a Prospective Longitudinal Standard-of-Care Cohort. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1577-1578. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.3626	Wrong intervention
Van Sleen Y, Geest KV, Boots A, Sandovici M, Brouwer E. 367. Patient reported outcomes on quality of life in Giant Cell Arteritis and Polymyalgia Rheumatica patients. 2022:	Wrong intervention
Vitiello G, Orsi Battaglini C, Carli G, et al. Tocilizumab in Giant Cell Arteritis: A Real-Life Retrospective Study. Angiology. 2018;69(9):763-769. doi:10.1177/0003319717753223	Wrong intervention
Wurmann P, Hernández C, Zamorano P, Sabugo F, Karsulovic C, Mac-Namara M. [Giant cell arteritis. Experience in 32 patients]. Rev Med Chil. 2022;150(6):720-726. doi:10.4067/s0034-98872022000600720	Wrong intervention
Yeruva K, Warrington KJ, Crowson CS, Koster MJ. Differences in presentation and outcome in patients with giant cell arteritis based on temporal artery biopsy positivity. Rheumatology. 2017;56(suppl 3):iii27-iii28. doi:https://dx.doi.org/10.1093/rheumatology/kex119	Wrong intervention
Yosra C, Moez J, Chifa D, et al. Adverse Events in Long-Term Corticosteroid Therapy in Elderly: A Case Series of 71 Patients. International Medical Journal. 2023;30(6):327-330.	Wrong patient population

Table 75 Excluded after full-text review per broad clinical PICOS criteria (n=5) – SLR re-run

Reference	Reason for exclusion
Dreyer AF, Borresen SW, Hansen SB, et al. Replace: a Randomized Controlled Trial On the Effect of Hydrocortisone Or Placebo In Patients With Reported Symptoms of Glucocorticoid-induced Adrenal Insufficiency After Terminating Prednisolone For Polymyalgia Rheumatic/Giant Cell Arteritis. Endocrine Abstracts 2024;99.	Wrong or no outcomes
Olugbode O, Garg K, Bharadwaj A, Nandagudi A. Adrenal insufficiency in rheumatic patients on long-term glucocorticoid therapy: A quality improvement project. Clinical Medicine 2024;24:10041.	Wrong or no outcomes
Read SL, Kim Y, Chihade DB, et al. Temporal Artery Biopsy Does Not Lead to Shorter Steroid Duration in Patients With Suspected Giant Cell Arteritis. Journal of Vascular Surgery. 2024;79(6):e292-e293.	Wrong intervention
Ricordi C, Marvisi C, Macchioni P, et al. Can Tocilizumab Turn Off Inflammation in Giant Cell Arteritis? Annals of the Rheumatic Diseases. 2024;83(Supplement 1):57.	Wrong intervention
Szarpak L, Cander B, Pruc M. Further clinical data on the more rapid achievement of remission without the use of steroids with tocilizumab compared to methotrexate in giant-cell arteritis. Internal and emergency medicine. 2024;04.	Wrong study design

Table 76. Met broad PICOS criteria but not suitable for anchored ITC/NMA (n=330) – Initial SLR run

Reference	Reason for exclusion
Addario A, Reynaud Q, Samson M, et al. Prevalence of relapses of giant cell arteritis in patients treated with corticosteroids: A meta-analysis. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong study design – Systematic review
Adler S, Reichenbach S, Gloor A, Yerly D, Cullmann JL, Villiger PM. Risk of relapse after discontinuation of tocilizumab therapy in giant cell arteritis. Rheumatology. 2019;58(9):1639-1643. doi:https://doi.org/10.1093/rheumatology/kez091	Wrong study design – Non-pivotal trial for intervention of interest
Adler S, Reichenbach S, Kuchen S, et al. Termination of tocilizumab-treatment in giant cell arteritis: Follow-up of patients after the rct (clinicaltrials.gov registration number: NCT01450137). Arthritis & rheumatology. 2016;68(suppl 10):1151-1152. doi:https://dx.doi.org/10.1002/art.39977	Wrong study design – Non-pivotal trial for intervention of interest
Adler S, Reichenbach S, Kuchen S, et al. Tocilizumab for the treatment of giant cell arteritis-a randomized placebo-controlled trial. Arthritis & rheumatology. 2015;67doi:https://doi.org/10.1002/art.39448	Wrong study design – Non-pivotal trial for intervention of interest
Ahmed S, Heaney J, Smith A, et al. Outcome for Patients with Giant Cell Arteritis (Gca) Treated with Tocilizumab According to Nice Guidance in a Single Tertiary Uk Centre. Annals of the Rheumatic Diseases. 2023;82(suppl 1):633-634. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.714	Wrong study design – Observational study for intervention of interest
Alba MA, Ana GM, Itziar TB, et al. Relapses in patients with giant-cell arteritis: Prevalence, characteristics and associated clinical findings in a prospectively followed cohort of 106 patients. Arthritis & rheumatism. 2012;10:S994. doi:https://dx.doi.org/10.1002/art.37735	Wrong intervention – Intervention not of interest
Alba MA, García-Martínez A, Prieto-González S, et al. Relapses in patients with giant cell arteritis: prevalence, characteristics, and associated clinical findings in a longitudinally followed cohort of 106 patients. Medicine. 2014;93(5):194-201. doi:10.1097/md.0000000000000033	Wrong intervention – Intervention not of interest
Alibaz-Oner F, Balci MA, Pamuk ON, et al. Is relapse rate of giant cell arteritis in real-life experience lower than in the controlled trials? results of a retrospective, multi-centre cohort study. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1118-1119. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.3983	Wrong study design – Observational study for intervention of interest
Alibaz-Oner F, Kelesoglu B, Balci MA, et al. Low relapse rate in patients with giant cell arteritis in a multi-centre retrospective Turkish Registry. Clinical and experimental rheumatology. 2023;15:816-821. doi:https://dx.doi.org/10.55563/clinexprheumatol/zr7s0g	Wrong study design – Observational study for intervention of interest
Alibaz-Oner F. Is relapse rate of giant cell arteritis in real-life experience lower than in the controlled trials? results of a retrospective, multi-center cohort study. Rheumatology. 2019;58(Supplement 2)doi:https://dx.doi.org/10.1093/rheumatology/kez062.003	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Alvarez-Reguera C, Calderon-Goercke M, Loricera J, et al. Optimization of tocilizumab therapy in giant cell arteritis - a multicenter real-life study of 471 patients. Annals of the Rheumatic Diseases. 2022;81:692-693. doi:https://doi.org/10.1136/annrheumdis-2022-eular.3279	Wrong study design – Observational study for intervention of interest
Alvarez-Reguera C, Loricera J, Tofade T, et al. Effectiveness of Janus Kinase Inhibitors in Giant Cell Arteritis in Clinical Practice. Real-World Clinical Practice Study and Literature Review. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1559-1560. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4939	Wrong study design – Observational study for intervention of interest
Antonio AA, Santos RN, Abariga SA. Tocilizumab for giant cell arteritis. Cochrane Database of Systematic Reviews. 2021;8(8):Cd013484. doi:10.1002/14651858.CD013484.pub2	Wrong study design – Systematic review
Antonio AA, Santos RN, Abariga SA. Tocilizumab for giant cell arteritis. Cochrane Database of Systematic Reviews. 2022;5(5):Cd013484. doi:10.1002/14651858.CD013484.pub3	Wrong study design – Systematic review
Antonio-Santos A, Santos RN. Tocilizumab for giant cell arteritis. Cochrane Database of Systematic Reviews. 2019;2019(11) doi:https://dx.doi.org/10.1002/14651858.CD013484	Wrong study design – Systematic review
Baldissera E, Tomelleri A, Campochiaro C, Sartorelli S, Dagna L. Efficacy and safety of tocilizumab in giant cell arteritis: A monocentric real-life experience. Arthritis & rheumatology. 2019;71(suppl 10):4724-4726. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Bandeira M, Raimundo D, Martins-Martinho J, et al. Does age at diagnosis of giant cell arteritis influence the clinical phenotype and outcomes? 21st International Vasculitis Workshop 2024.	Wrong study design – Observational study for intervention of interest
Barreira S, Cruz-Machado AR, Dourado E, et al. Efficacy and Safety of Methotrexate in Giant Cell Arteritis: Results from a Bicentric Portuguese Cohort Study. Arthritis & rheumatology. 2020;72(suppl 10):3848-3850. doi:https://dx.doi.org/10.1002/art.41538	Wrong study design – Observational study for intervention of interest
Bender TTA, Leyens J, Sellin J, et al. Therapeutic options for patients with rare rheumatic diseases: a systematic review and meta-analysis. Orphanet Journal of Rare Diseases. 2020;15(1):308. doi:10.1186/s13023-020-01576-5	Wrong study design – Systematic review
Bengtsson BA, Malmvall BE. Prognosis of giant cell arteritis including temporal arteritis and polymyalgia rheumatica. A follow-up study on ninety patients treated with corticosteroids. Acta Med Scand. 1981;209(5):337-45. doi:10.1111/j.0954-6820.1981.tb11604.x	Wrong study design – Observational study for intervention of interest
Best J, Kong A, Tran O, Michalska M. Risk of potential glucocorticoid-related adverse events in patients with giant cell arteritis: Results from a us-based electronic health records database. Rheumatology. 2019;58(Supplement 2)doi:https://dx.doi.org/10.1093/rheumatology/kez063.010	Wrong study design – Observational study for intervention of interest
Best J, Kong AM, Tran O, Michalska M. Risk of potential glucocorticoid-related adverse events in patients with giant cell arteritis: Results from a us-based electronic health records database. Arthritis & rheumatology. 2019;71(suppl 10):4738-4740. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Best JH, Kong AM, Tran O, Michalska M. Risk of potential glucocorticoid-related adverse events in patients with giant cell arteritis: Results from a us-based electronic health records database. Annals of the Rheumatic Diseases. 2019;78(suppl 2):816-817. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.1657	Wrong study design – Observational study for intervention of interest
Best JH, Kong AM, Unizony S, Tran O, Michalska M. Risk of Potential Glucocorticoid-Related Adverse Events in Patients with Giant Cell Arteritis: Results from a USA-Based Electronic Health Records Database. Rheumatology and therapy. 2019;6(4):599-610. doi:https://dx.doi.org/10.1007/s40744-019-00180-9	Wrong study design – Observational study for intervention of interest
Boiardi L, Macchioni P, Muratore F, et al. Influence of histological tempol artery biopsy findings on outcomes of biopsy-proven giant cell arteritis in Italian patients : a long single center follow-up study. 21st International Vasculitis Workshop. 2024.	Wrong intervention – Intervention not of interest
Broner J, Arnaud E. [Efficacy and tolerance of tocilizumab for corticosteroid sparing in giant cell arteritis and aortitis: Experience of Nimes University Hospital about eleven patients]. Revue de medecine interne. 2018;39(2):78-83. doi:10.1016/j.revmed.2017.11.001	Wrong study design – Observational study for intervention of interest
Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. JAMA. 2016;315(22):2442-58. doi:10.1001/jama.2016.5444	Wrong study design – Systematic review
Caceres VA, Mateos JM, Perez SG, et al. Giant cell arteritis. treatment with tocilizumab. Journal of Clinical Rheumatology. 2019;25(3 suppl):S12. doi:https://dx.doi.org/10.1097/RHU.0000000000001070	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Calderon-Goercke M, Castaneda S, Aldasoro V, et al. Tocilizumab in giant cell arteritis: differences between the GiACTA trial and a multicentre series of patients from the clinical practice. Clinical and experimental rheumatology. 2020;38(2 suppl 124):112-119.	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Castaneda S, Aldasoro V, et al. Tocilizumab in refractory giant cell arteritis. Monotherapy versus combined therapy with conventional immunosuppressive drugs. Observational multicenter study of 134 patients. Seminars in arthritis and rheumatism. 2021;51(2):387-394. doi:https://dx.doi.org/10.1016/j.semarthrit.2021.01.006	Wrong study design – Observational study for intervention of interest
Calderón-Goercke M, Loricera J, Aldasoro V, et al. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Seminars in arthritis and rheumatism. 2019;49(1):126-135. doi:10.1016/j.semarthrit.2019.01.003	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Moriano C, et al. Optimisation of tocilizumab therapy in giant cell arteritis. A multicentre real-life study of 471 patients. Clinical and experimental rheumatology. 2023;41(4):829-836. doi:https://dx.doi.org/10.55563/clinexprheumatol/oqs8u9	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. A multicenter series of giant cell arteritis patients from clinical practice in treatment with tocilizumab compared with giacta trial. Arthritis & rheumatology. 2018;70(suppl 9):3102-3104. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Efficacy and safety of tocilizumab in giant cell arteritis independently of the inicial prednisone dose. Annals of the Rheumatic Diseases. 2019;78(suppl 2):1185. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2209	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Efficacy of tocilizumab in giant cell arteritis, independent of the time of disease evolution. Arthritis & rheumatology. 2019;71(suppl 10):4751-4753. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Time of disease evolution and efficacy of tocilizumab in giant cell arteritis. Annals of the Rheumatic Diseases. 2019;78(suppl 2):818-819. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2222	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Tocilizumab in giant cell arteritis. Monotherapy versus combined with conventional immunosuppressive drugs. Annals of the Rheumatic Diseases. 2019;78(suppl 2):252-253. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2198	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Tocilizumab in giant cell arteritis. national multicenter study of 134 patients of clinical practice. Arthritis & rheumatology. 2018;70(suppl 9):3096-3097. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Tocilizumab in giant cell arteritis. Route of administracion: Intravenous or subcutaneous. Annals of the Rheumatic Diseases. 2019;78(suppl 2):1750. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2226	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Tocilizumab in giant cell arteritis: Route of administration: Intravenous or subcutaneous. Arthritis & rheumatology. 2019;71(suppl 10):4744-4746. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Tocilizumab in giant cell arteritis: The safest and most effective initial dose of prednisone. Arthritis & rheumatology. 2019;71(suppl 10):4748-4751. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Loricera J, Prieto-Peña D, et al. Utility of tocilizumab in visual affection of patients with giant cell arteritis. Arthritis & rheumatology. 2018;70(suppl 9):3101-3102. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Prieto-Peña D, Castaneda S, et al. Serious infections in 134 patients with giant cell arteritis with tocilizumab in clinical practice. frequency, type and clinical associations. Annals of the Rheumatic Diseases. 2020;79(SUPPL 1):376-377. doi:https://doi.org/10.1136/annrheumdis-2020-eular.2583	Wrong study design – Observational study for intervention of interest
Calderon-Goercke M, Prieto-Peña D, Loricera J, et al. Comparison between tocilizumab prescribed as monotherapy versus combined with conventional immunosuppressant agents in giant cell arteritis patients. Arthritis & rheumatology. 2018;70(suppl 9):3099-3101. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Campbell AM, Martin JR, Erstad BL. Corticosteroid Tapering Regimens in Rheumatic Disease: A Systematic Review. Journal of Clinical Rheumatology. 2020;26(2):41-47. doi:10.1097/rhu.0000000000000917	Wrong study design – Systematic review

Reference	Reason for exclusion
Carbonella A, Berardi G, Petricca L, et al. Immunosuppressive Therapy (Methotrexate or Cyclophosphamide) in Combination with Corticosteroids in the Treatment of Giant Cell Arteritis: Comparison with Corticosteroids Alone. J Am Geriatr Soc. Mar 2016;64(3):672-374. doi:10.1111/jgs.14004	Wrong intervention – Intervention not of interest
Castan P, Dumont A, Deshayes S, et al. Impact of Glucocorticoid Cumulative Doses in a Real-Life Cohort of Patients Affected by Giant Cell Arteritis. Journal of Clinical Medicine. 2022;11(4) 1034. doi:https://dx.doi.org/10.3390/jcm11041034	Wrong study design – Observational study for intervention of interest
Castano I, Monjo I, Balsa A, Peiteado D, Garcia-Carazo S, De Miguel E. Metotrexate in the treatment of giant cell arteritis: To be or not to be. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong intervention – Intervention not of interest
Chevalet P, Barrier JH, Glemarec J, et al. [Horton's disease in elderly patients aged over 75: clinical course, complications of corticotherapy. Comparative study of 164 patients. Towards a reduced initial dose]. Revue de medecine interne. 2001;22(7):624-630. doi:https://dx.doi.org/10.1016/s0248-8663(01)00399-x	Wrong study design – Observational study for intervention of interest
Chevalet P, Barrier JH, Pottier P, et al. A randomized, multicenter, controlled trial using intravenous pulses of methylprednisolone in the initial treatment of simple forms of giant cell arteritis: a one year followup study of 164 patients. Journal of rheumatology. 2000;27(6):1484-1491.	Wrong intervention – Intervention not of interest
Chmelewski WL, McKnight KM, Agudelo CA, Wise CM. Presenting features and outcomes in patients undergoing temporal artery biopsy. A review of 98 patients. Archives of Internal Medicine. 1992;152(8):1690-5.	Wrong study design – Observational study for intervention of interest
Christ L, Seitz L, Scholz G, et al. A proof-of-concept study to assess the efficacy of tocilizumab monotherapy after ultra-short glucocorticoid administration to treat giant cell arteritis -The gusto trial. Annals of the Rheumatic Diseases. 2021;80(suppl 1):33. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.522	Wrong study design – Non-pivotal trial for intervention of interest
Christ L, Seitz L, Scholz G, et al. Long-term effect of tocilizumab monotherapy after ultrashort glucocorticoid administration to treat giant cell arteritis - one year-follow up of the GUSTO Trial. Swiss medical weekly. 2022;152	Wrong study design – Non-pivotal trial for intervention of interest
Christ L, Seitz L, Scholz G, et al. Long-term Efficacy of Tocilizumab Monotherapy after Ultra-short Glucocorticoid Administration to Treat Giant Cell Arteritis-One Year Follow-up of the GUSTO Trial. Arthritis & rheumatology. 2022;74:936-938. doi:https://doi.org/10.1002/art.42355	Wrong study design – Non-pivotal trial for intervention of interest
Christ L, Seitz L, Scholz G, et al. Long-Term Efficacy of Tocilizumab Monotherapy after Ultra-Short Glucocorticoid Administration to Treat Giant Cell Arteritis-Two Year Follow-up of the Gusto Trial. Annals of the Rheumatic Diseases. 2023;82:636. doi:https://doi.org/10.1136/annrheumdis-2023-eular.2249	Wrong study design – Non-pivotal trial for intervention of interest
Christ L, Seitz L, Scholz G, et al. Tocilizumab monotherapy after ultra-short glucocorticoid administration in giant cell arteritis: a single-arm, open-label, proof-of-concept study. The lancet rheumatology. 2021;3(9):e619-e626. doi:https://dx.doi.org/10.1016/S2665-9913%2821%2900152-1	Wrong study design – Non-pivotal trial for intervention of interest
Cid MC, Unizony S, Blockmans D, et al. Efficacy and safety of mavrilimumab in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Annals of the Rheumatic Diseases. 2022;81(5):653-661. doi:https://doi.org/10.1136/annrheumdis-2021-221865	Wrong intervention – Intervention not of interest
Cid MC, Unizony S, Pupim L, et al. Mavrilimumab (anti gm-csf receptor alpha monoclonal antibody) reduces risk of flare and increases sustained remission in a phase 2 trial of patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2021;80(suppl 1):31-32. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.1915	Wrong intervention – Intervention not of interest
ClinicalTrials.gov. Efficacy and Safety Study of Sirukumab in Patients With Giant Cell Arteritis (NCT02531633). 2015;	Wrong intervention – Intervention not of interest
ClinicalTrials.gov. Evaluation of Efficacy and Safety of Sarilumab in Patients with GCA (NCT03600805). 2018;	Wrong intervention – Intervention not of interest
ClinicalTrials.gov. KPL-301 for Subjects With Giant Cell Arteritis (NCT03827018). 2019;	Wrong intervention – Intervention not of interest
ClinicalTrials.gov. Tocilizumab for Patients With Giant Cell Arteritis (NCT01450137). 2011;	Wrong study design – Non-pivotal trial for intervention of interest
Cochrane Central Register of Controlled Trials. A clinical study to test treatment of KPL-301 compared to placebo in giant cell arteritis (EUCTR2018-001003-36-SI). 2018;	Wrong intervention – Intervention not of interest
Cochrane Central Register of Controlled Trials. A study to assess the efficacy and safety of Sirukumab in the treatment of patients with Giant Cell Arteritis, using multiple sites, and an untreated patient group (EUCTR2015-001758-14-ES). 2015;	Wrong intervention – Intervention not of interest

Reference	Reason for exclusion
Cochrane Central Register of Controlled Trials. Study in patients with giant cell arteritis to assess efficacy of secukinumab compared to placebo (EUCTR2018-002610-12-DE). 2018;	Wrong or no outcomes – Study of interest but data in report not relevant
Conticini E, Sota J, Falsetti P, et al. The Role of Multimodality Imaging in Monitoring Disease Activity and Therapeutic Response to Tocilizumab in Giant Cell Arteritis. Mediators Inflamm. 2020;2020:3203241. doi:10.1155/2020/3203241	Wrong study design – Observational study for intervention of interest
Cowley S, Kirby C, Harkins P, et al. Clinical Outcomes With Dose Spacing Of Tocilizumab In Giant Cell Arteritis. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Czihal M, Piller A, Schroettle A, et al. Impact of cranial and axillary/subclavian artery involvement by color duplex sonography on response to treatment in giant cell arteritis. J Vasc Surg. May 2015;61(5):1285-91. doi:10.1016/j.jvs.2014.12.045	Wrong intervention – Intervention not of interest
Danesh-Meyer H, Savino PJ, Gamble GG. Poor prognosis of visual outcome after visual loss from giant cell arteritis. Ophthalmology. 2005;112(6):1098-1103. doi:https://dx.doi.org/10.1016/j.ophtha.2005.01.036	Wrong study design – Observational study for intervention of interest
Daumas A, Bichon A, Rioland C, et al. Characteristics of giant cell arteritis patients under and over 75-years-old: A comparative study on 164 patients. Revue de medecine interne. 2019;40(5):278-285. doi:https://dx.doi.org/10.1016/j.revmed.2018.11.004	Wrong study design – Observational study for intervention of interest
Davanzo F, Iorio L, Codirenzi M, Padoan R, Doria A. Differences between Glucocorticoids, Conventional Dmards and Tocilizumab in Achieving Disease Remission and in Preventing the Progression of Damage in Giant Cell Arteritis Patients. Annals of the Rheumatic Diseases. 2023;82(suppl 1):652-653. doi:https://ard.bmj.com/content/82/Suppl_1/652.2	Wrong study design – Observational study for intervention of interest
Davanzo F, Iorio L, Campochiaro C, et al. Differences between glucocorticoids, conventional DMARDs and tocilizumab in achieving disease remission and in preventing the progression of damage in giant cell arteritis patients. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
De Boysson H, Le Besnerais M, Blaison F, et al. Assessment of the efficacy and safety of tocilizumab in patients over 80 years old with giant cell arteritis. Arthritis research & therapy. 2021;23(1) doi:https://dx.doi.org/10.1186/s13075-021-02529-4	Wrong study design – Observational study for intervention of interest
Dominguez-Casas LC, Loricera J, Hernandez JL, et al. Efficacy of tocilizumab in 31 patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2017;76(suppl 2):614. doi:https://dx.doi.org/10.1136/annrheumdis-2017-eular.3262	Wrong study design – Observational study for intervention of interest
Dominguez-Casas LC, Loricera J, Hernandez JL, et al. Short and long-term follow-up with tocilizumab in giant cell arteritis. National multicenter study of 49 patients of clinical practice. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong study design – Observational study for intervention of interest
Dua AB, Husainat NM, Kalot MA, et al. Giant Cell Arteritis: A Systematic Review and Meta-Analysis of Test Accuracy and Benefits and Harms of Common Treatments. ACR open rheumatology. 2021;3(7):429-441. doi:https://dx.doi.org/10.1002/acr2.11226	Wrong study design – Systematic review
Ducker G, Mills K, Yong C, Jones C, Mukhtyar C. Improved relapse-free survival with the Norwich prednisolone regimen for giant cell arteritis. Annals of the Rheumatic Diseases. 2022;81(suppl 1):683-684. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.847	Wrong study design – Observational study for intervention of interest
Ducker G, Mills K, Yong C, Jones C, Mukhtyar C. P294 Improved relapse-free survival with the Norwich prednisolone regimen for giant cell arteritis. Rheumatology. 2022;61(Supplement_1)doi:10.1093/rheumatology/keac133.293	Wrong study design – Observational study for intervention of interest
Ducker G, Mukhtyar C. Incidence of adrenal insufficiency in patients with giant cell arteritis tapering glucocorticoids with the Norwich Prednisolone Regimen. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Ducker G, Mukhtyar C. E076 Incidence of adrenal insufficiency in patients with giant cell arteritis tapering glucocorticoids with the Norwich prednisolone regimen. Rheumatology 2022;63(Supplement 1). doi: https://doi.org/10.1093/rheumatology/keae163.303	Wrong study design – Observational study for intervention of interest
Edel Y, Avni T, Shepshelovich D, et al. The safety of pulse corticosteroid therapy- Systematic review and meta-analysis. Seminars in arthritis and rheumatism. 2020;50(3):534-545. doi:https://dx.doi.org/10.1016/j.semarthrit.2019.11.006	Wrong study design – Systematic review

Reference	Reason for exclusion
EU Clinical Trials Register. A clinical study in which neither staff at the site nor the patient nor the sponsor's team know if the patient received drug with an active ingredient or drug without an active ingredient. The aim of this study is to find out if tocilizumab is an effective and safe treatment in patients with Giant Cell Arteritis, an inflammatory disease of the blood vessels (2011-006022-25). 2013;	Wrong or no outcomes – Study of interest but data in report not relevant
Font Urgelles J, Rosales Rosado Z, Freites Nunez DD, et al. Treatment with methotrexate and risk of ischaemic relapses in patients with giant cell arteritis in clinical practice. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1121. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.2690	Wrong intervention – Intervention not of interest
Fore R, Liozon E, Dumonteil S, et al. BOB-ACG study: Pulse methylprednisolone to prevent bilateral ophthalmologic damage in giant cell arteritis. A multicentre retrospective study with propensity score analysis. Joint Bone Spine. 2024;91(1) doi:https://dx.doi.org/10.1016/j.jbspin.2023.105641	Wrong intervention – Intervention not of interest
Gale S, Dimonaco S, Trinh H, et al. Safety events in giant cell arteritis and rheumatoid arthritis patient populations. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong intervention – Intervention not of interest
Gale S, Trinh H, Tuckwell K, et al. Adverse Events in Giant Cell Arteritis and Rheumatoid Arthritis Patient Populations: Analyses of Tocilizumab Clinical Trials and Claims Data. Rheumatology and therapy. 2019;6(1):77-88. doi:https://dx.doi.org/10.1007/s40744-019-0139-5	Wrong intervention – Intervention not of interest
Gale S, Wilson JC, Chia J, et al. Risk Associated with Cumulative Oral Glucocorticoid Use in Patients with Giant Cell Arteritis in Real-World Databases from the USA and UK. Rheumatology and therapy. 2018;5(2):327-340. doi:https://dx.doi.org/10.1007/s40744-018-0112-8	Wrong intervention – Intervention not of interest
García-Martínez A, Hernández-Rodríguez J, Espígol-Frigolé G, et al. Clinical relevance of persistently elevated circulating cytokines (tumor necrosis factor alpha and interleukin-6) in the long-term followup of patients with giant cell arteritis. Arthritis care & research. 2010;62(6):835-41. doi:10.1002/acr.20043	Wrong intervention – Intervention not of interest
Garcia-Martinez A, Hernandez-Rodriguez J, Grau JM, Cid MC. Treatment with statins does not exhibit a clinically relevant corticosteroid-sparing effect in patients with giant cell arteritis. Arthritis Rheum. Aug 15 2004;51(4):674-8. doi:10.1002/art.20541	Wrong intervention – Intervention not of interest
Gérard AL, Simon-Tillaux N, Yordanov Y, et al. Efficacy and safety of steroid-sparing treatments in giant cell arteritis according to the glucocorticoids tapering regimen: A systematic review and meta-analysis. European journal of internal medicine. 2021;88:96-103. doi:10.1016/j.ejim.2021.03.040	Wrong study design – Systematic review
Grazzini S, Conticini E, Falsetti P, et al. Tocilizumab Vs Methotrexate in a Cohort of Patients Affected by Active GCA: A Comparative Clinical and Ultrasonographic Study. Biologics: Targets and Therapy. 2023;17:151-160. doi:https://dx.doi.org/10.2147/BTT.S431818	Wrong study design – Observational study for intervention of interest
Guarda M, Hanson A, Langenfeld H, et al. Concordance of relapse symptoms with initial baseline presentation features among patients with giant cell arteritis. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Hachulla E, Boivin V, Pasturel-Michon U, et al. Prognostic factors and long-term evolution in a cohort of 133 patients with giant cell arteritis. Clinical & Experimental Rheumatology. 2001;19(2):171-6.	Wrong study design – Observational study for intervention of interest
Harigai M, Miyamae T, Hashimoto H, Umetsu K, Yamashita K, Nakaoka Y. A multicentre, large-scale, observational study of tocilizumab in patients with giant cell arteritis in Japan. Modern rheumatology. 2023;31:775–783. doi:https://dx.doi.org/10.1093/mr/road074	Wrong study design – Observational study for intervention of interest
Haskova Z, Strand V, Dimonaco S, et al. Health-related quality of life in patients with giant cell arteritis treated with tocilizumab in a phase 3 randomized controlled trial. Investigative ophthalmology & visual science. 2018;59(9):2174.	Wrong or no outcomes – Study of interest but data in report not relevant
Haskova Z, Tuckwell K, Collinson N, Klearman M, Dimonaco S, Stone JH. Baseline data on patients enrolled in a randomized, double-masked trial of tocilizumab in giant cell arteritis. Investigative ophthalmology & visual science. 2016;57(12):5409.	Wrong or no outcomes – Study of interest but data in report not relevant
Hayreh SS, Zimmerman B, Kardon RH. Visual improvement with corticosteroid therapy in giant cell arteritis. Report of a large study and review of literature. Acta Ophthalmol Scand. 2002;80(4):355-67. doi:10.1034/j.1600-0420.2002.800403.x	Wrong study design – Observational study for intervention of interest
Hayreh SS, Zimmerman B. Visual deterioration in giant cell arteritis patients while on high doses of corticosteroid therapy. Ophthalmology. Jun 2003;110(6):1204-15. doi:10.1016/S0161-6420(03)00228-8	Wrong intervention – Intervention not of interest
Health Canada's Clinical Trials Database. A placebo-controlled, proof-of concept study of the efficacy and safety of gevokizumab in the treatment of patients with giant cell arteritis. 2013;	Wrong intervention – Intervention not of interest

Reference	Reason for exclusion
Henningson H, Hammar B, Turesson C, Mohammad A. The Use of Intravenous Methylprednisolone in Patients with Giant Cell Arteritis: A Population-Based Study. Arthritis & rheumatology. 2022;74(suppl 9):913-915. doi:https://dx.doi.org/10.1002/art.42355	Wrong study design – Observational study for intervention of interest
Hočevar A, Ješe R, Rotar Ž, Tomšič M. Does leflunomide have a role in giant cell arteritis? An open-label study. Clinical rheumatology. 2019;38(2):291-296. doi:10.1007/s10067-018-4232-x	Wrong intervention – Intervention not of interest
Hocevar A, Jese R, Rotar Z, Tomsic M. The role of leflunomide in the treatment of giant cell arteritis. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1114-1115. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.2751	Wrong intervention – Intervention not of interest
Hocevar A, Rotar Z, Jese R, et al. Do Early Diagnosis and Glucocorticoid Treatment Decrease the Risk of Permanent Visual Loss and Early Relapses in Giant Cell Arteritis: A Prospective Longitudinal Study. Medicine (Baltimore). Apr 2016;95(14):e3210. doi:10.1097/MD.0000000000003210	Wrong intervention – Intervention not of interest
Hoffman GS, Cid MC, Hellmann DB, et al. A multicenter, randomized, double-blind, placebo-controlled trial of adjuvant methotrexate treatment for giant cell arteritis. Arthritis & rheumatism. 2002;46(5):1309-1318. doi:https://dx.doi.org/10.1002/art.10262	Wrong intervention – Intervention not of interest
Hoffman GS, Cid MC, Rendt-Zagar KE, et al. Infliximab for maintenance of glucocorticosteroid-induced remission of giant cell arteritis: a randomized trial. Annals of internal medicine. 2007;146(9):621-630. doi:https://doi.org/10.7326/0003-4819-146-9-200705010-00004	Wrong intervention – Intervention not of interest
Hunder GG, Sheps SG, Allen GL, Joyce JW. Daily and alternate-day corticosteroid regimens in treatment of giant cell arteritis: comparison in a prospective study. Annals of internal medicine. 1975;82(5):613-618. doi:https://doi.org/10.7326/0003-4819-82-5-613	Wrong intervention – Intervention not of interest
Hutton LMM. Real Life Experience of Tocilizumab Treatment for Giant Cell Arteritis. Rheumatology. 2023;62(suppl 2):ii17. doi:https://dx.doi.org/10.1093/rheumatology/kead104.031	Wrong study design – Observational study for intervention of interest
Hysa E, Bond M, Ehlers L, et al. Evidence on treat to target strategies in polymyalgia rheumatica and giant cell arteritis: a systematic literature review. Rheumatology. 2024;63(2):285-297. doi:https://dx.doi.org/10.1093/rheumatology/kead471	Wrong study design – Systematic review
International Clinical Trials Registry Platform. A study to determine how safe and effective Tocilizumab is when given by subcutaneous route in patients with GCA. https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2020/11/028814	Wrong study design – Non-pivotal trial for intervention of interest
Iorio L, Campaniello D, Zucchetta P, et al. GLUCOCORTICOIDS, CONVENTIONAL DMARDS and TOCILIZUMAB DIFFERENTLY AFFECT 18F-FDG PET METABOLIC ACTIVITY in GIANT CELL ARTERITIS PATIENTS. Annals of the Rheumatic Diseases. 2022;81(suppl 1):696. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.3781	Wrong study design – Observational study for intervention of interest
Jover JA, Hernández-García C, Morado IC, Vargas E, Bañares A, Fernández-Gutiérrez B. Combined treatment of giant-cell arteritis with methotrexate and prednisone. a randomized, double-blind, placebo-controlled trial. Annals of internal medicine. 2001;134(2):106-14. doi:10.7326/0003-4819-134-2-200101160-00010	Wrong intervention – Intervention not of interest
Juchet H, Arlet P, Ollier S, Montane de la Roque P, Le Tallec Y. [Bolus of methylprednisolone and Horton's disease/rhizomelic pseudo-polyarthritis. Preliminary results of a pilot study of treating the bolus with low doses of corticoids]. Annales de Medecine Interne. 1992;143(2):85-8.	Wrong intervention – Intervention not of interest
Karabayas M, Dospinescu P, Locherty M, et al. Stratified glucocorticoid monotherapy is safe and effective for most cases of giant cell arteritis. Rheumatol Adv Pract. 2020;4(2):rkaa024. doi:10.1093/rap/rkaa024	Wrong study design – Observational study for intervention of interest
Karabayas M, Dospinescu P, Moulindu P, et al. Stratified glucocorticoid monotherapy is effective for most cases of giant cell arteritis. Rheumatology. 2019;58(Supplement 2)doi:https://dx.doi.org/10.1093/rheumatology/kez063.040	Wrong study design – Observational study for intervention of interest
Kastrati K, Aletaha D, Burmester GR, et al. A systematic literature review informing the consensus statement on efficacy and safety of pharmacological treatment with interleukin-6 pathway inhibition with biological DMARDs in immune-mediated inflammatory diseases. RMD Open. 2022;8(2) e002359. doi:https://dx.doi.org/10.1136/rmdopen-2022-002359	Wrong study design – Systematic review
Khalid S, Davidson B, Hopkinson N, et al. P024 Real-world experience of Tocilizumab withdrawal in GCA. Rheumatology. 2022;61(Supplement_1)doi:10.1093/rheumatology/keac133.023	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Khalid S, Smith R, Cole Z. TOCILIZUMAB: is out of sight really out of mind? Rheumatology advances in practice. 2019;3:i13-i14. doi:https://doi.org/10.1093/rap/rkz024.004	Wrong study design – Observational study for intervention of interest
Khanna RK, Hage R, Lecler A, Sene T, Vignal-Clermont C, Clavel-Refregiers G. Giant cell arteritis with ocular involvement successfully treated with tocilizumab and very short-course glucocorticoids: A case report. Journal francais d'ophtalmologie. 2021;44(4):481-484. doi:https://dx.doi.org/10.1016/j.jfo.2020.08.028	Wrong study design – Observational study for intervention of interest
Kieffer P, Hinschberger O, Ciobanu E, et al. [Clinical and biological efficacy of tocilizumab in giant cell arteritis: report of three patients and literature review]. Revue de medecine interne. 2014;35(1):56-9. doi:https://dx.doi.org/10.1016/j.revmed.2012.12.012	Wrong study design – Observational study for intervention of interest
Koster M, Labarca C, Crowson CS, Makol A, Matteson E, Warrington K. Glucocorticoid use and associated complications in a cohort of patients with biopsy-proven giant cell arteritis. Nephron. 2015;129(suppl 2):77. doi:https://dx.doi.org/10.1159/000381120	Wrong study design – Observational study for intervention of interest
Koster M, Warrington KJ, Han J, Mohan S. The efficacy and safety of tocilizumab in patients with giant cell arteritis: A systematic review and meta-analysis. Annals of the Rheumatic Diseases. 2021;80(suppl 1):651-652. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.600	Wrong study design – Systematic review
Koster MJ, Crowson C, Labarca CS, Muratore F, Warrington KJ. Efficacy of methotrexate in giant cell arteritis. Annals of the Rheumatic Diseases. 2016;75(suppl 2):796. doi:https://dx.doi.org/10.1136/annrheumdis-2016-eular.5001	Wrong intervention – Intervention not of interest
Koster MJ, Crowson CS, Labarca C, Muratore F, Warrington KJ. Efficacy of methotrexate in giant cell arteritis. Arthritis & rheumatology. 2016;68(suppl 10):1142-1143. doi:https://dx.doi.org/10.1002/art.39977	Wrong intervention – Intervention not of interest
Koster MJ, Labarca C, Crowson CS, et al. Glucocorticoid use and associated adverse events based on initial daily oral prednisone dose in biopsy-proven giant cell arteritis. Annals of the Rheumatic Diseases. 2015;2:515-516. doi:https://dx.doi.org/10.1136/annrheumdis-2015-eular.2439	Wrong study design – Observational study for intervention of interest
Koster MJ, Labarca C, Crowson CS, et al. Relapse characteristics and glucocorticoid use in patients with biopsy-proven giant cell arteritis. Arthritis & rheumatology. 2015;67(SUPPL. 10)doi:https://dx.doi.org/10.1002/art.39448	Wrong study design – Observational study for intervention of interest
Koster MJ, Warrington K, Han J, Mohan SV. The Efficacy and Safety of Tocilizumab in Patients with Giant Cell Arteritis: A Systematic Review and Meta-Analysis. Arthritis & rheumatology. 2020;72(suppl 10):2890-2893. doi:https://dx.doi.org/10.1002/art.41538	Wrong study design – Systematic review
Koster MJ, Yeruva K, Crowson CS, Muratore F, Labarca C, Warrington KJ. Efficacy of Methotrexate in Real-world Management of Giant Cell Arteritis: A Case-control Study. Journal of rheumatology. 2019;46(5):501-508. doi:10.3899/jrheum.180429	Wrong intervention – Intervention not of interest
Kramarič J, Rotar Ž, Tomšič M, Hočevar A. Performance of leflunomide as a steroid-sparing agent in giant cell arteritis: A single-center, open-label study. Frontiers in Medicine. 2022;9:1069013. doi:10.3389/fmed.2022.1069013	Wrong intervention – Intervention not of interest
Kulkarni S, Durham H, Glover L, et al. Metabolic adverse events associated with systemic corticosteroid therapy - A systematic review and meta-analysis. BMJ Open. 2022;12(12) e061476. doi:https://dx.doi.org/10.1136/bmjopen-2022-061476	Wrong study design – Systematic review
Kupersmith MJ, Langer R, Mitnick H, et al. Visual performance in giant cell arteritis (temporal arteritis) after 1 year of therapy. British journal of ophthalmology. 1999;83(7):796-801. doi:10.1136/bjo.83.7.796	Wrong intervention – Intervention not of interest
Kupersmith MJ, Langer R, Paget S, Mitnick H, Speira H. Visual outcome in patients with giant cell arteritis after 1 year of therapy. Investigative Ophthalmology & Visual Science. 1997;38	Wrong intervention – Intervention not of interest
Kupersmith MJ, Langer R, Paget S, Mitnick H, Speira R, Speira H. Outcome in Patients with Giant Cell Arteritis After One Year of Therapy. American academy of ophthalmology. 1997;83(7):163.	Wrong intervention – Intervention not of interest
Kupersmith MJ, Speira R, Langer R, et al. Visual function and quality of life among patients with giant cell (temporal) arteritis. Journal of neuro-ophthalmology. 2001;21(4):266-73. doi:10.1097/00041327-200112000-00008	Wrong intervention – Intervention not of interest
Kupersmith MJ, Speira R, Mitnick H, Paget S, Richmond M, Peterson M. Visual outcome and complications of steroid therapy after one year of steroids in temporal arteritis. Neurology. 1998;50(4 Suppl 4):A252.	Wrong intervention – Intervention not of interest
Kupersmith MT, Langer R, Paget S, Mitnick H, Speira R, Speira H. Visual performance and quality of life measures in patients with giant cell arteritis. Investigative Ophthalmology & Visual Science. 1998;39	Wrong intervention – Intervention not of interest

Reference	Reason for exclusion
Kyle V, Hazleman BL. The clinical and laboratory course of polymyalgia rheumatica/giant cell arteritis after the first two months of treatment. Annals of the Rheumatic Diseases. 1993;52(12):847-850. doi:https://doi.org/10.1136/ard.52.12.847	Wrong intervention – Intervention not of interest
Kyle V, Hazleman BL. Treatment of polymyalgia rheumatica and giant cell arteritis. I. Steroid regimens in the first two months. Annals of the Rheumatic Diseases. 1989;48(8):658-661.	Wrong intervention – Intervention not of interest
Labarca C, Koster MJ, Crowson CS, et al. Predictors of relapse and treatment outcomes in biopsy-proven giant cell arteritis: a retrospective cohort study. Rheumatology. 2016;55(2):347-56. doi:10.1093/rheumatology/kev348	Wrong study design – Observational study for intervention of interest
Les I, Martinez Berriotxoa A, Rodriguez R, Egurbide MV, Ruiz-Irastorza G. Medium doses of glucocorticoids are as effective as and safer than high doses of glucocorticoids in patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2013;72(SUPPL. 3)doi:https://dx.doi.org/10.1136/annrheumdis-2013-eular.1463	Wrong study design – Observational study for intervention of interest
Les I, Pijoán JI, Rodríguez-Álvarez R, Ruiz-Irastorza G, Martínez-Berriotxoa A. Effectiveness and safety of medium-dose prednisone in giant cell arteritis: a retrospective cohort study of 103 patients. Clinical and experimental rheumatology. 2015;33(2 Suppl 89):S-90.	Wrong study design – Observational study for intervention of interest
Liozon F, Vidal E, Barrier J. Does dapsone have a role in the treatment of temporal arteritis with regard to efficacy and toxicity? Clinical and experimental rheumatology. Nov-Dec 1993;11(6):694-5.	Wrong intervention – Intervention not of interest
Lo Giudice LF, Scolnik M, Martinez Perez J, et al. Systemic vasculitis: Incidence of glucocorticoidrelated adverse events. Journal of Clinical Rheumatology. 2018;24(3 suppl 1):S18-S19.	Wrong study design – Observational study for intervention of interest
Lo Giudice LF, Scolnik M, Martinez Perez J, Luissi A, Scaglioni V, Soriano ER. Systemic vasculitis: Incidence of glucocorticoid related adverse events. Arthritis & rheumatology. 2018;70(suppl 9):3078-3079. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Loricera J, Blanco R, Hernández JL, et al. Tocilizumab in giant cell arteritis: Multicenter open-label study of 22 patients. Seminars in arthritis and rheumatism. 2015;44(6):717-23. doi:10.1016/j.semarthrit.2014.12.005	Wrong study design – Observational study for intervention of interest
Loricera J, Castaneda S, Moriano C, et al. Tocilizumab in visual involvement of giant cell arteritis: a multicenter study of 471 patients. Therapeutic Advances in Musculoskeletal Disease. 2022;14doi:https://dx.doi.org/10.1177/1759720X221113747	Wrong study design – Observational study for intervention of interest
Loricera J, Tofade T, Prieto-Pena D, et al. Effectiveness of janus kinase inhibitors in relapsing giant cell arteritis in real-world clinical practice and review of the literature. Arthritis Res Ther. Jun 5 2024;26(1):116. doi:10.1186/s13075-024-03314-9	Wrong study design – Observational study for intervention of interest
Luo J, Su QY, Li Q, et al. Efficacy and Safety of Tocilizumab in Patients with Vasculitis. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1583. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4347	Wrong study design – Systematic review
Mahr AD, Jover JA, Spiera RF, et al. Adjunctive methotrexate for treatment of giant cell arteritis: an individual patient data meta-analysis. Arthritis & rheumatism. 2007;56(8):2789-97. doi:10.1002/art.22754	Wrong intervention – Intervention not of interest
Mainboug S, Addario A, Durieu I, Lega JC. Corticosteroid exposure in trials testing immunosuppressive drugs for giant cell arteritis: The effect of undertreatment. Fundamental & clinical pharmacology. 2019;33(suppl 1):21. doi:https://dx.doi.org/10.1111/fcp.12468	Wrong study design – Systematic review
Mainbourg S, Tabary A, Cucherat M, et al. Indirect Comparison of Glucocorticoid-Sparing Agents for Remission Maintenance in Giant Cell Arteritis: A Network Meta-analysis. Mayo Clinic Proceedings. 2022;97(10):1824-1835. doi:https://dx.doi.org/10.1016/j.mayocp.2022.03.010	Wrong study design – Systematic review
Mariette X, Baron G, Hachulla E, et al. Results of a randomized controlled study of adalimumab for steroid sparing in patients with giant-cell arteritis. Arthritis & rheumatism. 2011;63(10)	Wrong intervention – Intervention not of interest
Martinez-Berriotxoa A, Les I, Rodriguez R. Combined therapy with pulse intravenous methylprednisolone, prednisone and methotrexate in giant cell arteritis. Annals of the Rheumatic Diseases. 2013;72(SUPPL. 3)doi:https://dx.doi.org/10.1136/annrheumdis-2013-eular.1462	Wrong intervention – Intervention not of interest
Martinez-Lado L, Calviño-Díaz C, Piñeiro A, et al. Relapses and recurrences in giant cell arteritis: a population-based study of patients with biopsy-proven disease from northwestern Spain. Medicine. 2011;90(3):186-193. doi:10.1097/MD.0b013e31821c4fad	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Martinez-Taboada VM, Rodriguez-Valverde V, Carreno L, et al. A double-blind placebo controlled trial of etanercept in patients with giant cell arteritis and corticosteroid side effects. Annals of the Rheumatic Diseases. 2008;67(5):625-630. doi:https://doi.org/10.1136/ard.2007.082115	Wrong intervention – Intervention not of interest
Marvisi C, Muratore F, Ricordi C, et al. Treatment of Giant Cell Arteritis with Ultra-short Glucocorticoids and Tocilizumab: results from the extension to 76 weeks. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Matza M, Dagincourt N, Mohan S, et al. Outcomes during and after long-term tocilizumab treatment in patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2022;81(suppl 1):376. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.1108	Wrong study design – Observational study for intervention of interest
Matza M, Jarvie A, Fernandes A, Stone JH, Unizony S. Tocilizumab in combination with 8 weeks of prednisone for giant cell arteritis. Arthritis & rheumatology. 2021;73(SUPPL 9):2958-2960. doi:https://doi.org/10.1002/art.41966	Wrong intervention – Intervention not of interest
Matza MA, Dagincourt N, Mohan SV, et al. Outcomes during and after long-term tocilizumab treatment in patients with giant cell arteritis. RMD Open. 2023;9(2):e002923. doi:10.1136/rmdopen-2022-002923	Wrong study design – Observational study for intervention of interest
Mazlumzadeh M, Hunder GG, Easley KA, et al. Treatment of giant cell arteritis using induction therapy with high-dose glucocorticoids: a double-blind, placebo-controlled, randomized prospective clinical trial. Arthritis & rheumatism. 2006;54(10):3310-8. doi:10.1002/art.22163	Wrong intervention – Intervention not of interest
Mensch N, Hemmig AK, Aschwanden M, et al. Rapid glucocorticoid tapering regimen in patients with giant cell arteritis: a single centre cohort study. RMD Open. 2023;9(3) e003301. doi:https://dx.doi.org/10.1136/rmdopen-2023-003301	Wrong study design – Observational study for intervention of interest
Mollan SP, Tuckwell K, Dimonaco S, Klearman M, Collinson N, Stone JH. Tocilizumab in patients with giant cell arteritis: results from a Phase 3 randomized controlled trial. Journal of headache and pain. 2018;19(suppl 1)doi:https://doi.org/10.1186/s10194-018-0900-0	Wrong or no outcomes – Study of interest but data in report not relevant
Mollan SP, Tuckwell K, Dimonaco S, Klearman M, Collinson N, Stone JH. Tocilizumab in patients with giant cell arteritis: results from a phase 3 randomized controlled trial. Neuro ophthalmology. 2017;41:S86-S87. doi:https://doi.org/10.1080/01658107.2017.1353798	Wrong or no outcomes – Study of interest but data in report not relevant
Monti S, Agueda AF, Luqmani R, et al. Results of a systematic literature review informing the 2018 update of the eular recommendations for the management of large vessel vasculitis: Evidence to guide the management of giant cell arteritis. Annals of the Rheumatic Diseases. 2019;78(suppl 2):823. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.5873	Wrong study design – Systematic review
Monti S, Agueda AF, Luqmani RA, et al. Systematic literature review informing the 2018 update of the EULAR recommendation for the management of large vessel vasculitis: Focus on giant cell arteritis. RMD Open. 2019;5(2) e001003. doi:https://dx.doi.org/10.1136/rmdopen-2019-001003	Wrong study design – Systematic review
Moreel L, Betrains A, Boeckxstaens L, et al. Polymyalgia rheumatica is a risk factor for more recalcitrant disease in giant cell arteritis: a retrospective cohort study. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Moreel L, Boeckxstaens L, Betrains A, et al. Association between total vascular score and clinical presentation and outcome in giant cell arteritis: a retrospective cohort study. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Moreel L, Boeckxstaens L, Betrains A, et al. Presentation and outcome of silent giant cell arteritis: a retrospective cohort study. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Mukhtyar C, Ducker G, Jones C. 316. Improved relapse-free survival with the Norwich Prednisolone Regimen for Giant Cell Arteritis. 2022:	Wrong study design – Observational study for intervention of interest
Muller G, Devilliers H, Besancenot JF, Manckoundia P. Giant cell arteritis (Horton's disease) in very elderly patients aged 80 years and older: A study of 25 cases. Geriatrics and Gerontology International. 2016;16(6):679-685. doi:https://dx.doi.org/10.1111/ggi.12536	Wrong study design – Observational study for intervention of interest
Muratore F, Cassone G, Marvisi C, et al. Treatment of Giant Cell Arteritis Patients with Ultra-Short Glucocorticoids and Tocilizumab: Role of Imaging in a Prospective Study. Annals of the Rheumatic Diseases. 2023;82(suppl 1):633. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.5776	Wrong intervention – Intervention not of interest

Reference	Reason for exclusion
Muratore F, Cassone G, Marvisi C, et al. Treatment of Giant Cell Arteritis Patients with Ultra-short Glucocorticoids and Tocilizumab: Role of Imaging in a Prospective Study. Arthritis & rheumatology. 2022;74(suppl 9):956-958. doi:https://dx.doi.org/10.1002/art.42355	Wrong intervention – Intervention not of interest
Muratore F, Crowson CS, Boiardi L, et al. Comparison of biopsy-proven giant cell arteritis in North America and Southern Europe: a population-based study. Clinical and experimental rheumatology. 2020;38(suppl 124)(2):79-83.	Wrong study design – Observational study for intervention of interest
Muratore F, Marvisi C, Cassone G, et al. Treatment of giant cell arteritis with ultra-short glucocorticoids and tocilizumab: the role of imaging in a prospective observational study. Rheumatology. 2024;63(1):64-71. doi:https://dx.doi.org/10.1093/rheumatology/kead215	Wrong intervention – Intervention not of interest
Muratore F, Marvisi C, Castrignano P, et al. Effectiveness and safety of a 26-week taper regimen of glucocorticoid in GCA patients: Results from a prospective cohort study. Seminars in arthritis and rheumatism. 2024;64doi:https://dx.doi.org/10.1016/j.semarthrit.2023.152351	Wrong study design – Observational study for intervention of interest
Nannini C, Niccoli L, Sestini S, Laghai I, Coppola A, Cantini F. Remission maintenance after tocilizumab dose-tapering and interruption in patients with giant cell arteritis: an open-label, 18-month, prospective, pilot study. Annals of the Rheumatic Diseases. Oct 2019;78(10):1444-1446. doi:10.1136/annrheumdis-2019-215585	Wrong study design – Non-pivotal trial for intervention of interest
Narváez J, Bernad B, Nolla JM, Valverde J. Statin therapy does not seem to benefit giant cell arteritis. Seminars in arthritis and rheumatism. 2007;36(5):322-7. doi:10.1016/j.semarthrit.2006.10.001	Wrong study design – Observational study for intervention of interest
Nepal D, Sattui S, Wallace Z, et al. Risk of major adverse cardiac events among patients with giant cell arteritis who received tocilizumab. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Nesher G, Berkun Y, Mates M, Baras M, Rubinow A, Sonnenblick M. Low-dose aspirin and prevention of cranial ischemic complications in giant cell arteritis. Arthritis Rheum. Apr 2004;50(4):1332-7. doi:10.1002/art.20171	Wrong intervention – Intervention not of interest
Nesher G, Rubinow A, Sonnenblick M. Efficacy and adverse effects of different corticosteroid dose regimens in temporal arteritis: a retrospective study. Clinical and experimental rheumatology. 1997;15(3):303-6.	Wrong study design – Observational study for intervention of interest
Neumann T, Stone JH, Bao M, et al. Long-term outcome of tocilizumab for patients with giant cell arteritis: results from part 2 of the GiACTA trial. Swiss medical weekly. 2019;149	Wrong or no outcomes – Study of interest but data in report not relevant
Nordborg E, Schaufelberger C, Andersson R, Bosaeus I, Bengtsson BA. The ineffectiveness of cyclical oral clodronate on bone mineral density in glucocorticoid-treated patients with giant-cell arteritis. Journal of Internal Medicine. Nov 1997;242(5):367-71. doi:10.1046/j.1365-2796.1997.00210.x	Wrong intervention – Intervention not of interest
Okuyama A, Kondo T, Takei H, et al. Tocilizumab monotherapy for large vessel vasculitis. a prospective, single-center, open-label study. Rheumatology. 2017;56(suppl 3):iii59. doi:https://dx.doi.org/10.1093/rheumatology/kex108	Wrong intervention – Intervention not of interest
Oliveira F, Butendieck RR, Ginsburg WW, Parikh K, Abril A. Tocilizumab, an effective treatment for relapsing giant cell arteritis. Clinical and experimental rheumatology. 2014;32(suppl 82):S76-S78.	Wrong study design – Observational study for intervention of interest
Osman M, Pagnoux C, Dryden D, Storie D, Homik J, Yacyshyn E. The role of biological agents in the management of large vessel vasculitis (LVV): A systematic review and meta-analysis. Journal of rheumatology. 2014;41(7):1527. doi:https://dx.doi.org/10.3899/jrheum.140420	Wrong study design – Systematic review
Osman M, Pagnoux C, Dryden DM, Storie D, Yacyshyn E. The role of biological agents in the management of large vessel vasculitis (LVV): a systematic review and meta-analysis. PLoS One. 2014;9(12):e115026. doi:10.1371/journal.pone.0115026	Wrong study design – Systematic review
Osman M, Pagnoux C, Homik J, Dryden D, Storie D, Yacyshyn E. The role of biological agents in the management of large vessel vasculitis (LVV): A systematic review. Annals of the Rheumatic Diseases. 2013;72(SUPPL. 3)doi:https://dx.doi.org/10.1136/annrheumdis-2013-eular.1887	Wrong study design – Systematic review
Patel N, Tozzo V, Higgins J, Stone JH. The Effects of Daily Prednisone and Tocilizumab on Hemoglobin A1c during the Treatment of Giant Cell Arteritis. Arthritis & rheumatology. 2022;74:919-921. doi:https://doi.org/10.1002/art.42355	Wrong or no outcomes – Study of interest but data in report not relevant

Reference	Reason for exclusion
Patel NJ, Fu X, Zhang Y, et al. The Effects of Treatment on Body Mass Index in Giant Cell Arteritis: A Post Hoc Analysis of the GiACTA Trial. Rheumatol Ther. 2022;9(2):497-508. doi:10.1007/s40744-021-00411-y	Wrong or no outcomes – Study of interest but data in report not relevant
Patel NJ, Tozzo V, Higgins JM, Stone JH. The effects of daily prednisone and tocilizumab on hemoglobin A1c during the treatment of giant cell arteritis. Arthritis & rheumatology. 2023;75(4):586-594. doi:https://doi.org/10.1002/art.42405	Wrong or no outcomes – Study of interest but data in report not relevant
Pokroy-Shapira E, Dortort-Lazar A, Molad Y. Comorbidity accrual and mortality in an inception cohort of patients with giant cell arteritis and polymyalgia rheumatica: A single-center, observational long-term study. Arthritis & rheumatology. 2018;70(suppl 9):3115-3116. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Preston H, Cronin O, Kuske B, McKay ND, Hauser B. Tocilizumab versus prednisolone onlytreatment for giant cell arteritis: An observational study. Rheumatology. 2021;60(suppl 1):i114. doi:https://dx.doi.org/10.1093/rheumatology/keab247.205	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Calderon-Goercke M, Loricera J, et al. Comparative study of clinical, analytical and vascular 18F-FDG uptake evolution in patients with giant cell arteritis treated with methotrexate vs tocilizumab. Annals of the Rheumatic Diseases. 2019;78:435-436. doi:https://doi.org/10.1136/annrheumdis-2019-eular.3623	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Calderon-Goercke M, Loricera J, et al. Real-world comparative study of methotrexate vs tocilizumab in patients with giant cell arteritis with large vessel involvement. Arthritis & rheumatology. 2019;71(suppl 10):4755-4758. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Loricera J, Castaneda S, et al. Tocilizumab in large-vessel giant cell arteritis and Takayasu arteritis: multicentric observational comparative study. Annals of the Rheumatic Diseases. 2022;81(suppl 1):691-692. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.2330	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Loricera J, Castaneda S, et al. Tocilizumab in Large-Vessel Giant Cell Arteritis and Takayasu Arteritis: Multicentric Observational Comparative Study. Arthritis & rheumatology. 2022;74(suppl 9):928-930. doi:https://dx.doi.org/10.1002/art.42355	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Loricera J, Moriano C, et al. Evolution of visual affection in patients with giant cell arteritis treated with tocilizumab. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1117. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.4908	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Martinez-Rodriguez I, Atienza-Mateo B, et al. Clinical, laboratory and imaging outcomes in tocilizumab-treated patients with large vessel-giant cell arteritis according to early onset therapy. Annals of the Rheumatic Diseases. 2021;80(suppl 1):1208. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.1733	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Martinez-Rodriguez I, Atienza-Mateo B, et al. Clinical, laboratory and imaging outcomes in tocilizumab-treated patients with large vessel-giant cell arteritis according to early onset therapy. Arthritis & rheumatology. 2021;73(suppl 9):2933-2935. doi:https://dx.doi.org/10.1002/art.41966	Wrong study design – Observational study for intervention of interest
Prieto-Peña D, Martinez-Rodriguez I, Atienza-Mateo B, et al. Evidence for uncoupling of clinical and 18-FDG activity of PET/CT scan improvement in tocilizumab-treated patients with large-vessel giant cell arteritis. Clinical and experimental rheumatology. 2021;39(2 suppl 129):69-75.	Wrong study design – Observational study for intervention of interest
Punekar R, Lafontaine P, Stone JH. Real-world clinical burden and glucocorticoid use in patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2020;79(suppl 1):171-172. doi:https://dx.doi.org/10.1136/annrheumdis-2020-eular.4263	Wrong study design – Observational study for intervention of interest
Quartuccio L, Isola M, Bruno D, et al. Treatment strategy introducing immunosuppressive drugs with glucocorticoids ab initio or very early in giant cell arteritis: A multicenter retrospective controlled study. Journal of Translational Autoimmunity. 2020;3:100072. doi:10.1016/j.jtauto.2020.100072	Wrong study design – Observational study for intervention of interest
Quick V, Abusalameh M, Ahmed S, et al. Relapse after cessation of weekly tocilizumab for giant cell arteritis: a multicentre service evaluation in England. Rheumatology. 2023;11doi:https://dx.doi.org/10.1093/rheumatology/kead604	Wrong study design – Observational study for intervention of interest
Quinn K, Ahlman M, Grayson P. Use of FDG-PET to Monitor Disease Activity in Patients with Giant Cell Arteritis on Tocilizumab. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Raine C, Stapleton PP, Merinopoulos D, et al. A 26-week feasibility study comparing the efficacy and safety of modified-release prednisone with immediate-release prednisolone in newly diagnosed cases of giant cell arteritis. International journal of rheumatic diseases. 2018;21(1):285-291. doi:10.1111/1756-185x.13149	Wrong intervention – Intervention not of interest

Reference	Reason for exclusion
Rakholiya J, Koster M, Langenfeld H, et al. Treatment of giant cell arteritis with tocilizumab: A retrospective cohort study of 119 patients. Annals of the Rheumatic Diseases. 2021;80(suppl 1):655. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.1674	Wrong study design – Observational study for intervention of interest
Rakholiya J, Koster M, Langenfeld H, et al. Treatment of giant cell arteritis with tocilizumab: A retrospective cohort study of 119 patients. Arthritis & rheumatology. 2021;73(suppl 9):2923-2925. doi:https://dx.doi.org/10.1002/art.41966	Wrong study design – Observational study for intervention of interest
Regent A, Redeker S, Deroux A, et al. Tocilizumab in giant cell arteritis: A multicenter retrospective study of 34 patients. Journal of rheumatology. 2016;43(8):1547-1552. doi:https://dx.doi.org/10.3899/jrheum.151252	Wrong study design – Observational study for intervention of interest
Regent A, Redeker S, Deroux A, et al. Tocilizumab in giant cell arteritis: A multicentre open-label study in france. Arthritis & rheumatology. 2015;67(SUPPL. 10)doi:https://dx.doi.org/10.1002/art.39448	Wrong study design – Observational study for intervention of interest
Regent A, Redeker S, Deroux A, et al. Tocilizumab in giant cell arteritis: A multicentre open-label study of 34 patients. Annals of the Rheumatic Diseases. 2016;75(suppl 2):794. doi:https://dx.doi.org/10.1136/annrheumdis-2016-eular.4722	Wrong study design – Observational study for intervention of interest
Regola F, Cerudelli E, Bosio G, et al. Long-term treatment with tocilizumab in giant cell arteritis: efficacy and safety in a monocentric cohort of patients. Rheumatol Adv Pract. 2020;4(2):rkaa017. doi:10.1093/rap/rkaa017	Wrong study design – Observational study for intervention of interest
Reichenbach S, Adler S, Bonel H, et al. Magnetic resonance angiography in giant cell arteritis: results of a randomized controlled trial of tocilizumab in giant cell arteritis. Rheumatology. 2018;57(6):982-986. doi:https://doi.org/10.1093/rheumatology/key015	Wrong study design – Non-pivotal trial for intervention of interest
Reichenbach S, Adler S, Cullmann J, et al. Tocilizumab for the treatment of giant cell arteritis-MR-angiography results from the first randomized placebo-controlled trial. Arthritis & rheumatology. 2016;68:4255-4256. doi:https://doi.org/10.1002/art.39977	Wrong study design – Non-pivotal trial for intervention of interest
Restuccia G, Boiardi L, Cavazza A, et al. Flares in Biopsy-Proven Giant Cell Arteritis in Northern Italy: Characteristics and Predictors in a Long-Term Follow-Up Study. Medicine. 2016;95(19):e3524. doi:10.1097/md.0000000000003524	Wrong study design – Observational study for intervention of interest
Restuccia G, Boiardi L, Cavazza A, et al. Long-term remission in biopsy proven giant cell arteritis: A retrospective cohort study. Journal of Autoimmunity. 2017;77:39-44. doi:10.1016/j.jaut.2016.10.002	Wrong study design – Observational study for intervention of interest
Reynolds G, Griffiths B, Houghton K, Thompson B, Lorenzi AR, Heaney J. Tocilizumab for giant cell arteritis: Real world experience in a single UK centre. Rheumatology. 2020;59(suppl 2):ii87. doi:https://dx.doi.org/10.1093/rheumatology/keaa111.183	Wrong study design – Observational study for intervention of interest
Rossi D, Cecchi I, Rubini E, Radin M, Sciascia S, Roccatello D. Clinical and serological outcomes of patients with giant cell arteritis treated with tocilizumab or abatacept as steroidsparing agents. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1477. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.6691	Wrong study design – Observational study for intervention of interest
Rossi D, Cecchi I, Rubini E, Radin M, Sciascia S, Roccatello D. Clinical and serological outcomes of patients with giant cell arteritis treated with tocilizumab or abatacept as steroid-sparing agents. Arthritis & rheumatology. 2018;70(suppl 9):3085-3087. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Rossi D, Cecchi I, Rubini E, Radin M, Sciascia S, Roccatello D. Outcomes of patients treated with tocilizumab or abatacept as steroid-sparing agents with giant cell arteritis. Annals of the Rheumatic Diseases. 2019;78(suppl 2):436. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.4807	Wrong study design – Observational study for intervention of interest
Rossi D, Cecchi I, Sciascia S, Naretto C, Alpa M, Roccatello D. An agent-to-agent real life comparison study of tocilizumab versus abatacept in giant cell arteritis. Clinical and experimental rheumatology. 2021;39(2):S125-S128.	Wrong study design – Observational study for intervention of interest
Rubbert-Roth A, Tschuppert S, Neumann T, Benecke U, Pirker I, Von Kempis J. Efficacy and safety of tocilizumab in patients with giant cell arteritis and visual disturbances. Annals of the Rheumatic Diseases. 2019;78(suppl 2):825. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.1748	Wrong study design – Observational study for intervention of interest
Rubbert-Roth A, Tschuppert S, Neumann T, Benecke U, Pirker I, Von Kempis J. Efficacy and safety of tocilizumab in patients with giant cell arteritis and visual disturbances. Swiss medical weekly. 2019;149(suppl 238):14S.	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Rubbert-Roth A, Tschuppert S, Neumann T, Benecke U, Pirker I, Von Kempis J. Efficacy and Safety of Tocilizumab in Patients with Giant Cell Arteritis and Visual Impairment. Arthritis & rheumatology. 2020;72(suppl 10):3851-3852. doi:https://dx.doi.org/10.1002/art.41538	Wrong study design – Observational study for intervention of interest
Ruediger C, Dyer K, Lyne S, et al. Clinical characteristics of biopsy-proven Giant Cell Arteritis (GCA) in Australia: Results from the South Australian Giant Cell Arteritis (GCA) Registry. 21st International Vasculitis Workshop. 2024	Wrong study design – Observational study for intervention of interest
Sailler L, Carreiro M, Ollier S, et al. Initial treatment of non-complicated giant-cell arteritis: 15 patients treated by pulse methylprednisolone 500 mg/d for three days followed by 20 mg/day oral prednisone. [French]. Revue de medecine interne. 2001;22(11):1032-1038. doi:https://dx.doi.org/10.1016/S0248-8663%2801%2900468-4	Wrong intervention – Intervention not of interest
Sailler L, Lapeyre-Mestre M, Geffray L, et al. Adding hydroxychloroquine to prednisone does not improve the outcome in giant cell arteritis: a double blind randomized controlled trial. Arthritis & rheumatism. 1972;60doi:https://doi.org/10.1002/art.27045	Wrong intervention – Intervention not of interest
Saito S, Okuyama A, Okada Y, et al. Tocilizumab monotherapy for large vessel vasculitis: results of 104-week treatment of a prospective, single-centre, open study. Rheumatology. 2020;59(7):1617-1621. doi:10.1093/rheumatology/kez511	Wrong intervention – Intervention not of interest
Salvarani C, Magnani L, Catanoso M, et al. Tocilizumab: a novel therapy for patients with large-vessel vasculitis. Rheumatology. 2012;51(1):151-6. doi:https://dx.doi.org/10.1093/rheumatology/ker296	Wrong study design – Observational study for intervention of interest
Samec MJ, Rakholiya J, Langenfeld H, et al. Relapse Risk and Safety of Long-Term Tocilizumab Use Among Patients With Giant Cell Arteritis: A Single-Enterprise Cohort Study. Journal of rheumatology. 2023;50(10):1310-1317. doi:https://dx.doi.org/10.3899/jrheum.2022-1214	Wrong study design – Observational study for intervention of interest
Samson M, Devilliers H, Ly KH, et al. Tocilizumab as an add-on therapy to glucocorticoids during the first 3 months of treatment of Giant cell arteritis: A prospective study. European journal of internal medicine. 2018;57:96-104. doi:https://dx.doi.org/10.1016/j.ejim.2018.06.008	Wrong intervention – Intervention not of interest
Samson M, Devilliers H, Ly KH, et al. Tocilizumab as an add-on therapy to glucocorticoids during the first 3 months of treatment of giant cell arteritis: Results of a french multicenter prospective open-label study. Arthritis & rheumatology. 2016;68(suppl 10):1295-1296. doi:https://dx.doi.org/10.1002/art.39977	Wrong intervention – Intervention not of interest
Sanchez-Bilbao L, Loricera J, Acha JPV, et al. Effectiveness of tocilizumab in the visual involvement of giant cell arteritis: Multicenter study of 471 patients of clinical practice. Arthritis & rheumatology. 2021;73(suppl 9):2956-2958. doi:https://dx.doi.org/10.1002/art.41966	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Loricera J, Aldasoro V, et al. Tocilizumab in cranial and extracranial refractory giant cell arteritis: A multicenter study of 312 cases. Annals of the Rheumatic Diseases. 2021;80(suppl 1):34-35. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.2139	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Loricera J, Aldasoro V, et al. Tocilizumab in visual involvement of giant cell arteritis. multicenter study of 312 patients of clinical practice. Annals of the Rheumatic Diseases. 2021;80(suppl 1):35-36. doi:https://dx.doi.org/10.1136/annrheumdis-2021-eular.2169	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Loricera J, Castaneda S, et al. Effectiveness of tocilizumab in cranial and extracranial phenotypes of giant cell arteritis: Multicenter study of 471 cases. Arthritis & rheumatology. 2021;73(suppl 9):2940-2942. doi:https://dx.doi.org/10.1002/art.41966	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Loricera J, Castaneda S, et al. Intravenous versus subcutaneous tocilizumab in a series of 471 patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2022;81(suppl 1):379-380. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.3260	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Loricera J, Castaneda S, et al. Intravenous versus Subcutaneous Tocilizumab in a Series of 471 Patients with Giant Cell Arteritis. Arthritis & rheumatology. 2022;74(suppl 9):272-274. doi:https://dx.doi.org/10.1002/art.42355	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Loricera J, Melero R, et al. Involvement of the aorta and/or its main branches in giant cell arteritis: Treatment with tocilizumab. Annals of the Rheumatic Diseases. 2022;81(suppl 1):689-690. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.2157	Wrong study design – Observational study for intervention of interest
Sanchez-Bilbao L, Prieto-Peña D, Gonzalez-Mazon I, et al. Ongoing Vascular 18F-FDG Uptake Despite Clinical Remission in Patients Receiving Tocilizumab for Large Vessel Vasculitis-Giant Cell Arteritis: Single Universitary Center Experience of 30 Patients. Arthritis & rheumatology. 2020;72(suppl 10):3852-3854. doi:https://dx.doi.org/10.1002/art.41538	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Sanchez-Martin J, Loricera J, Moriano C, et al. Assessing the Effectiveness of Tocilizumab in Newly Diagnosed Giant Cell Arteritis versus Refractory/recurrent Giant Cell Arteritis in Clinical Practice. Arthritis & rheumatology. 2022;74(suppl 9):966-968. doi:https://dx.doi.org/10.1002/art.42355	Wrong study design – Observational study for intervention of interest
Sanchez-Martin J, Loricera J, Moriano C, et al. Tocilizumab in newly diagnosed giant cell arteritis versus refractory/recurrent giant cell arteritis: Multicenter study of 471 patients of clinical practice. Annals of the Rheumatic Diseases. 2022;81(suppl 1):698-699. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.4027	Wrong study design – Observational study for intervention of interest
Santos-Gomez M, Loricera J, Blanco R, et al. Tocilizumab in giant cell arteritis: Multicenter open-label study of 22 patients. Arthritis & rheumatology. 2014;10:S357. doi:https://dx.doi.org/10.1002/art.38914	Wrong study design – Observational study for intervention of interest
Sarnes E, Crofford L, Watson M, Dennis G, Kan H, Bass D. Incidence and US Costs of Corticosteroid-Associated Adverse Events: A Systematic Literature Review. Clinical Therapeutics. 2011;33(10):1413-1432. doi:https://dx.doi.org/10.1016/j.clinthera.2011.09.009	Wrong study design – Systematic review
Schaufelberger C, Andersson R, Nordborg E. No additive effect of cyclosporin A compared with glucocorticoid treatment alone in giant cell arteritis: results of an open, controlled, randomized study. British journal of rheumatology. Apr 1998;37(4):464-5. doi:10.1093/rheumatology/37.4.464	Wrong intervention – Intervention not of interest
Schaufelberger C, Mollby H, Uddhammar A, Bratt J, Nordborg E. No additional steroid-sparing effect of cyclosporine A in giant cell arteritis. Scandinavian journal of rheumatology. 2006;35(4):327-329. doi:https://doi.org/10.1080/03009740500474537	Wrong intervention – Intervention not of interest
Schmidt W, Dasgupta B, Luqmani R, et al. A Multi-Center, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of sirukumab in the treatment of patients with giant cell arteritis. Annals of the Rheumatic Diseases. 2019;78:827. doi:https://doi.org/10.1136/annrheumdis-2019-eular.5846	Wrong intervention – Intervention not of interest
Schmidt WA, Dasgupta B, Luqmani R, et al. A Multicentre, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Sirukumab in the Treatment of Giant Cell Arteritis. Rheumatol Ther. 2020;7(4):793-810. doi:10.1007/s40744-020-00227-2	Wrong intervention – Intervention not of interest
Schmidt WA, Dasgupta B, Sloane J, et al. A phase 3 randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of sarilumab in patients with giant cell arteritis. Arthritis research & therapy. 2023;25(1):199. doi:10.1186/s13075-023-03177-6	Wrong intervention – Intervention not of interest
Schonau V, Roth J, Tascilar K, et al. Resolution of vascular inflammation in patients with new-onset giant cell arteritis: data from the RIGA study. Rheumatology. 2021;60(8):3851-3861. doi:https://dx.doi.org/10.1093/rheumatology/keab332	Wrong study design – Observational study for intervention of interest
Sebastian A, Kayani A, Prieto-Peña D, et al. Efficacy and safety of tocilizumab in giant cell arteritis: A single centre NHS experience using imaging (ultrasound and PET-CT) as a diagnostic and monitoring tool. RMD Open. 2020;6(3) e001417. doi:https://dx.doi.org/10.1136/rmdopen-2020-001417	Wrong study design – Observational study for intervention of interest
Sebastian A, Kayani A, Ranasinghe C, et al. Efficacy & safety of tocilizumab in GCA: A multi-centre experience of NHS clinical practice. Rheumatology. 2020;59(suppl 2):ii16. doi:https://dx.doi.org/10.1093/rheumatology/keaa110.034	Wrong study design – Observational study for intervention of interest
Seneviratne AC, Graham C, Mills K, Mukhtyar C. A planned prednisolone regimen to improve compliance and lower relapse rates in patients with giant cell arteritis. Rheumatology. 2017;56(suppl 2):ii183. doi:https://dx.doi.org/10.1093/rheumatology/kex062.002	Wrong study design – Observational study for intervention of interest
Serling-Boyd N, Fu X, Zhang Y, et al. Effect of Cumulative Glucocorticoid Dose and Inflammation on Weight Change during Treatment of Giant Cell Arteritis. Arthritis & rheumatology. 2020;72(SUPPL 10):3874-3875. doi:https://doi.org/10.1002/art.41538	Wrong or no outcomes – Study of interest but data in report not relevant
Seror R, Baron G, Hachulla E, et al. Adalimumab for steroid sparing in patients with giant-cell arteritis: results of a multicentre randomised controlled trial. Annals of the Rheumatic Diseases. 2014;73(12):2074-81. doi:10.1136/annrheumdis-2013-203586	Wrong intervention – Intervention not of interest
Silva L, Blanco R, Martinez-Taboada V, et al. Biological therapy for large vessel vasculitis: A systematic review. Annals of the Rheumatic Diseases. 2012;71(supp 3):682. doi:https://dx.doi.org/10.1136/annrheumdis-2012-eular.762	Wrong study design – Systematic review
Singh M, Scott N, Hauser B. Efficacy of tocilizumab use in giant cell arteritis (GCA) and takayasu arteritis (TA) patients allowing glucocorticoid dose reduction. Rheumatology. 2019;58(suppl 3):iii84. doi:https://dx.doi.org/10.1093/rheumatology/kez108.009	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Skaug HK, Fevang BTS, Assmus J, et al. Giant Cell Arteritis - Glucocorticoid treatment and disease phenotypes. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Song GG, Lee YH. Efficacy and safety of biological agents in patients with giant cell arteritis: A meta-analysis of randomized trials. International journal of clinical pharmacology and therapeutics. 2020;58(9):504-510. doi:10.5414/cp203738	Wrong study design – Systematic review
Sousa A, Martinez-Vidal A, Soto-Peleteiro A, et al. Comparison of two initial prednisone dose regimens in giant cell arteritis. Annals of the Rheumatic Diseases. 2016;75(suppl 2):1085. doi:https://dx.doi.org/10.1136/annrheumdis-2016-eular.6001	Wrong intervention – Intervention not of interest
Spiera R, Unizony S, Bao M, et al. Clinical outcomes of patients with giant cell arteritis with polymyalgia symptoms only vs cranial symptoms only treated with tocilizumab or Placebo in a Randomized Clinical Trial. Arthritis & rheumatology. 2019;71(suppl 10):3274-3276. doi:https://dx.doi.org/10.1002/art.41108	Wrong or no outcomes – Study of interest but data in report not relevant
Spiera R, Unizony S, Bao M, et al. Clinical outcomes of patients with giant cell arteritis with polymyalgia symptoms only vs cranial symptoms only treated with tocilizumab or placebo in the giacta trial. Annals of the Rheumatic Diseases. 2019;78:811. doi:https://doi.org/10.1136/annrheumdis-2019-eular.1379	Wrong or no outcomes – Study of interest but data in report not relevant
Spiera R, Unizony S, Bao M, et al. Tocilizumab vs placebo for the treatment of giant cell arteritis with polymyalgia rheumatica symptoms, cranial symptoms or both in a randomized trial. Seminars in arthritis and rheumatism. 2021;51(2):469-476. doi:10.1016/j.semarthrit.2021.03.006	Wrong or no outcomes – Study of interest but data in report not relevant
Spiera RF, Mitnick HJ, Kupersmith M, et al. A prospective, double-blind, randomized, placebo controlled trial of methotrexate in the treatment of giant cell arteritis (GCA). Clinical and experimental rheumatology. 2001;19(5):495-501.	Wrong intervention – Intervention not of interest
Stoilov I, McCulley TJ, Pei J, et al. Visual impairment in patients with giant cell arteritis treated with tocilizumab in realworld clinical practice. Investigative Ophthalmology & Visual Science. 2019;60(9)	Wrong study design – Observational study for intervention of interest
Stone JH, Bao M, Han J, et al. Long-term outcome of tocilizumab for patients with giant cell arteritis: Results from part 2 of a randomized controlled phase 3 trial. Arthritis & rheumatology. 2019;71(suppl 10):1389-1390. doi:https://dx.doi.org/10.1002/art.41108	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Bao M, Han J, et al. Long-term outcome of tocilizumab for patients with giant cell arteritis: results from part 2 of the GiACTA trial. Annals of the Rheumatic Diseases. 2019;78:145-146. doi:https://doi.org/10.1136/annrheumdis-2019-eular.2099	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Han J, Aringer M, et al. Long-term effect of tocilizumab in patients with giant cell arteritis: open-label extension phase of the Giant Cell Arteritis Actemra (GiACTA) trial. The lancet rheumatology. 2021;3(5):e328-e336. doi:10.1016/s2665-9913(21)00038-2	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Han J, Unizony S, et al. Maintained benefit in health-related quality of life of patients with giant cell arteritis treated with tocilizumab plus prednisone tapering: results from the open-label, long-term extension of a phase 3 randomized controlled trial. Annals of the Rheumatic Diseases. 2020;79(SUPPL 1):1081-1082. doi:https://doi.org/10.1136/annrheumdis-2020-eular.1541	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Neumann T, Spotswood H, et al. Time to flare in patients with new-onset versus relapsing giant cell arteritis treated with tocilizumab or placebo plus predni-sone tapering: 3-year results from a randomized controlled phase 3 trial. Swiss medical weekly. 2020;150(SUPPL 245):5S.	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Spotswood H, Unizony S, et al. Time to flare and glucocorticoid exposure in patients with new-onset versus relapsing giant cell arteritis treated with tocilizumab or placebo plus prednisone tapering: 3-year results from a randomized controlled phase 3 trial. Annals of the Rheumatic Diseases. 2020;79(SUPPL 1):20. doi:https://doi.org/10.1136/annrheumdis-2020-eular.1538	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Spotswood H, Unizony S, et al. Time to flare in patients with new-onset versus relapsing giant cell arteritis treated with tocilizumab or placebo plus prednisone Tapering: 3-Year Results from a Randomized Controlled Phase 3 Trial. Arthritis & rheumatology. 2019;71(suppl 10):3278-3280. doi:https://dx.doi.org/10.1002/art.41108	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Tuckwell K, Dimonaco S, et al. Acute phase reactant levels and prednisone doses at disease flare in patients with giant cell arteritis: Prospective data from the giacta trial. Annals of the Rheumatic Diseases. 2018;77(suppl 2):1120-1121. doi:https://dx.doi.org/10.1136/annrheumdis-2018-eular.2719	Wrong or no outcomes – Study of interest but data in report not relevant

Reference	Reason for exclusion
Stone JH, Tuckwell K, Dimonaco S, et al. Acute phase reactant levels and prednisone doses at disease flare in patients with giant cell arteritis: Prospective data from the giacta trial. Rheumatology. 2019;58(suppl 3):iii159. doi:https://dx.doi.org/10.1093/rheumatology/kez107.088	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Tuckwell K, Dimonaco S, et al. Effects of baseline prednisone dose on remission and disease flare in patients with giant cell arteritis treated with tocilizumab in a phase 3 randomized controlled trial. Arthritis & rheumatology. 2018;70(suppl 9):3094-3095. doi:https://dx.doi.org/10.1002/art.40700	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Tuckwell K, Dimonaco S, et al. Effects of baseline prednisone dose on remission and disease flare in patients with giant cell arteritis treated with tocilizumab in the giacta trial. Rheumatology. 2019;58(suppl 3)doi:https://doi.org/10.1093/rheumatology/kez105.025	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Tuckwell K, Dimonaco S, et al. Efficacy and safety of tocilizumab in patient subgroups with new-onset and relapsing giant cell arteritis from a randomized, doubleblind, placebo-controlled, phase 3 trial. Rheumatology. 2017;56:iii10–iii12. doi:https://doi.org/10.1093/rheumatology/kex112	Wrong or no outcomes – Study of interest but data in report not relevant
Stone JH, Tuckwell K, Dimonaco S, et al. Efficacy and safety of tocilizumab in patients with giant cell arteritis: Primary and secondary outcomes from a phase 3, randomized, double-blind, placebo-controlled trial. Arthritis & rheumatology. 2016;68(suppl 10):1204-1206. doi:https://dx.doi.org/10.1002/art.39977	Wrong or no outcomes – Study of interest but data in report not relevant
Strand V, Dimonaco S, Tuckwell K, Klearman M, Collinson N, Stone JH. Health-related quality of life in patients with giant cell arteritis treated with tocilizumab in a randomized controlled phase 3 trial. Arthritis & rheumatology. 2017;69	Wrong or no outcomes – Study of interest but data in report not relevant
Sugihara T, Hasegawa H, Uchida H, et al. Characteristics and treatment outcomes of giant cell arteritis with large-vessel lesions in a nationwide, retrospective cohort study in Japan. Arthritis & rheumatology. 2017;69(Supplement 10)	Wrong study design – Observational study for intervention of interest
Sugihara T, Hasegawa H, Uchida HA, et al. Associated factors of poor treatment outcomes in patients with giant cell arteritis: Clinical implication of large vessel lesions. Arthritis research & therapy. 2020;22(1) doi:https://dx.doi.org/10.1186/s13075-020-02171-6	Wrong study design – Observational study for intervention of interest
Sun GH, Sarsour K, Chang E, et al. Corticosteroid-related adverse events in patients with giant cell arteritis: A claims-based analysis. Arthritis & rheumatology. 2014;10:S351-S352. doi:https://dx.doi.org/10.1002/art.38914	Wrong intervention – Intervention not of interest
Terribili R, Grazzini S, Conticini E, et al. Safety and efficacy of long-term treatment with Tocilizumab in a cohort of patients affected by Giant Cell Arteritis: an Italian monocentric retrospective study. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Tomelleri A, Campochiaro C, Farina N, et al. Effectiveness of a two-year tapered course of tocilizumab in patients with giant cell arteritis: A single-centre prospective study. Seminars in arthritis and rheumatism. 2023;59:152174. doi:10.1016/j.semarthrit.2023.152174	Wrong study design – Observational study for intervention of interest
Tomelleri A, Campochiaro C, Sartorelli S, Baldissera E, Dagna L. Efficacy and safety of tocilizumab in giant cell arteritis: A monocentric real-life experience. Rheumatology. 2019;58(Supplement 2)doi:https://dx.doi.org/10.1093/rheumatology/kez063.081	Wrong study design – Observational study for intervention of interest
Tomelleri A, Campochiaro C, Sartorelli S, Cariddi A, Baldissera E, Dagna L. Efficacy and safety of tocilizumab in giant cell arteritis: A monocentric real-life experience. Annals of the Rheumatic Diseases. 2019;78(suppl 2):1770-1771. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.3081	Wrong study design – Observational study for intervention of interest
Tomelleri A, Campochiaro C, Sartorelli S, et al. 315. Effectiveness of every-other-week tocilizumab maintenance therapy in giant cell arteritis: a prospective single-centre study. 2022:	Wrong study design – Observational study for intervention of interest
Tomelleri A, Campochiaro C, Sartorelli S, et al. Effectiveness of a spacing-up strategy after one-year course of weekly tocilizumab in patients with giant cell arteritis: A single-centre prospective study. Annals of the Rheumatic Diseases. 2022;81(suppl 1):375-376. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.784	Wrong study design – Observational study for intervention of interest
Treppo E, Isola M, De Martino M, et al. Greater steroid-sparing effect of tocilizumab than methotrexate: A real-life monocentric experience. Annals of the Rheumatic Diseases. 2022;81(suppl 1):1421. doi:https://dx.doi.org/10.1136/annrheumdis-2022-eular.2879	Wrong study design – Observational study for intervention of interest
Tuckwell K, Collinson N, Dimonaco S, et al. Newly diagnosed vs. relapsing giant cell arteritis: baseline data from the GiACTA trial. Seminars in arthritis and rheumatism. 2017;46(5):657-664. doi:https://doi.org/10.1016/j.semarthrit.2016.11.002	Wrong or no outcomes – Study of interest but data in report not relevant

Reference	Reason for exclusion
Tuckwell K, Collinson N, Klearman M, Dimonaco S, Stone JH. Baseline data on patients enrolled in a randomized, double-blind trial of tocilizumab in giant cell arteritis. Arthritis & rheumatology. 2015;67doi:https://doi.org/10.1002/art.39448	Wrong or no outcomes – Study of interest but data in report not relevant
Tuckwell K, Collinson N, Klearman M, Dimonaco S, Stone JH. Baseline data on patients in GiACTA (tocilizumab in giant cell arteritis). Nephron. 2015;129(175):1–44. doi:https://doi.org/10.1159/000381120	Wrong or no outcomes – Study of interest but data in report not relevant
Tuckwell K, Collinson N, Klearman M, Dimonaco S, Stone JH. FRI0248 Baseline Data on Patients in Giacta (Tocilizumab in Giant Cell Arteritis). Annals of the Rheumatic Diseases. 2015;74(Suppl 2):514.2-514. doi:10.1136/annrheumdis-2015-eular.2417	Wrong or no outcomes – Study of interest but data in report not relevant
Tuckwell K, Dimonaco S, Klearman M, Collinson N, Stone JH. Tocilizumab for the treatment of giant cell arteritis: efficacy and safety analysis from the giacta trial. Annals of neurology. 2017;82:S1-S233. doi:https://doi.org/10.1002/ana.25024	Wrong or no outcomes – Study of interest but data in report not relevant
Turbin R, Kupersmith M, Langer R, et al. Systemic corticosteroids do not adversely affect vision in the elderly. Investigative Ophthalmology & Visual Science. 1996;37	Wrong intervention – Intervention not of interest
Unizony S, Arias-Urdaneta L, Miloslavsky E, et al. Tocilizumab for the treatment of large-vessel vasculitis (giant cell arteritis, Takayasu arteritis) and polymyalgia rheumatica. Arthritis care & research. 2012;64(11):1720-9. doi:10.1002/acr.21750	Wrong study design – Observational study for intervention of interest
Unizony S, Bao M, Han J, et al. Risk factors for treatment failure in patients with giant cell arteritis treated with tocilizumab plus prednisone versus prednisone alone. Annals of the Rheumatic Diseases. 2019;78:810. doi:https://doi.org/10.1136/annrheumdis-2019-eular.2698	Wrong or no outcomes – Study of interest but data in report not relevant
Unizony S, Bao M, Han J, et al. Risk factors for treatment failure in patients with giant cell arteritis treated with tocilizumab plus prednisone versus prednisone Alone. Arthritis & rheumatology. 2019;71(suppl 10):3282-3284. doi:https://dx.doi.org/10.1002/art.41108	Wrong or no outcomes – Study of interest but data in report not relevant
Unizony S, Bao M, Han J, Luder Y, Pavlov A, Stone JH. Treatment failure in giant cell arteritis. Annals of the Rheumatic Diseases. 2021;80(11):1467-1474. doi:10.1136/annrheumdis-2021-220347	Wrong or no outcomes – Study of interest but data in report not relevant
Unizony S, Bao M, Luder Y, Sidiropoulos P, Pei J, Stone JH. Risk factors for treatment failure in patients with giant cell arteritis treated with tocilizumab plus prednisone versus prednisone alone. Rheumatology. 2019;58(suppl 2)doi:https://doi.org/10.1093/rheumatology/kez063.082	Wrong or no outcomes – Study of interest but data in report not relevant
Unizony S, Cid MC, Blockmans D, et al. Utility of CRP and ESR in the assessment of giant cell arteritis relapse in a phase 2 trial of mavrilimumab. Arthritis & rheumatology. 2021;73(SUPPL 9):2931-2933. doi:https://doi.org/10.1002/art.41966	Wrong intervention – Intervention not of interest
Unizony S, Dasgupta B, Fisheleva E, et al. Design of the tocilizumab in giant cell arteritis trial. International journal of rheumatology. 2013;2013:912562. doi:10.1155/2013/912562	Wrong or no outcomes – Study of interest but data in report not relevant
Unizony S, Keroack B, Stone JH. Tocilizumab for the treatment of giant cell arteritis: Extended follow-up. Presse medicale. 2013;42(4 PART 2):727. doi:https://dx.doi.org/10.1016/j.lpm.2013.02.178	Wrong study design – Observational study for intervention of interest
Unizony S, Matza M, Jarvie A, Fernandes A, Stone JH. Tocilizumab in combination with 8 weeks of prednisone for giant cell arteritis. Annals of the Rheumatic Diseases. 2022;81:123. doi:https://doi.org/10.1136/annrheumdis-2022-eular.2096	Wrong intervention – Intervention not of interest
Unizony S, Matza MA, Jarvie A, O'Dea D, Fernandes AD, Stone JH. Treatment for giant cell arteritis with 8 weeks of prednisone in combination with tocilizumab: a single-arm, open-label, proof-of-concept study. The lancet rheumatology. 2023;5(12):e736-e742. doi:10.1016/s2665-9913(23)00265-5	Wrong intervention – Intervention not of interest
Unizony S, McCulley TJ, Spiera R, et al. Clinical outcomes of patients with giant cell arteritis treated with tocilizumab in real-world clinical practice: decreased incidence of new visual manifestations. Arthritis research & therapy. 2021;23(1):8. doi:10.1186/s13075-020-02377-8	Wrong study design – Observational study for intervention of interest
Unizony S, Mohan S, Han J, Stone JH. Characteristics of giant cell arteritis flares after successful treatment with tocilizumab: results from the long-term extension of a randomized controlled phase 3 trial. Annals of the Rheumatic Diseases. 2021;80(SUPPL 1):656-657. doi:https://doi.org/10.1136/annrheumdis-2021-eular.2602	Wrong or no outcomes – Study of interest but data in report not relevant

Reference	Reason for exclusion
Unizony S, Mohan S, Han J, Stone JH. Characteristics of Giant Cell Arteritis Flares After Successful Treatment With Tocilizumab: Results From the Long-Term Extension of a Randomized Controlled Phase 3 Trial. Arthritis & rheumatology. 2020;72(suppl 10)	Wrong or no outcomes – Study of interest but data in report not relevant
Unizony S, Pei J, Sidiropoulos P, Best J, Birchwood C, Stone JH. 274. Clinical outcomes of patients with giant cell arteritis treated with tocilizumab in real-world clinical practice. Rheumatology. 2019;58(Supplement_2)doi:10.1093/rheumatology/kez062.048	Wrong study design – Observational study for intervention of interest
Unizony S, Pei J, Sidiropoulos P, Best JH, Birchwood C, Stone JH. Clinical outcomes of patients with giant cell arteritis treated with tocilizumab in real-world clinical practice. Annals of the Rheumatic Diseases. 2019;78(suppl 2):1200-1201. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.1239	Wrong study design – Observational study for intervention of interest
Unizony S, Pei J, Sidiropoulos PN, Best JH, Birchwood C, Stone JH. Clinical outcomes of patients with giant cell arteritis treated with tocilizumab in real-world clinical practice. Arthritis & rheumatology. 2018;70(suppl 9):3108-3109. doi:https://dx.doi.org/10.1002/art.40700	Wrong study design – Observational study for intervention of interest
Unizony S, Spiera R, Pei J, Sidiropoulos P, Best J, Stone JH. Clinical outcomes of patients with giant cell arteritis and polymyalgia rheumatica symptoms treated with tocilizumab in routine clinical practice. Arthritis & rheumatology. 2019;71(suppl 10):4721-4723. doi:https://dx.doi.org/10.1002/art.41108	Wrong study design – Observational study for intervention of interest
Unizony S, Spiera R, Pei J, Sidiropoulos P, Best JH, Stone JH. Clinical outcomes of patients with giant cell arteritis and polymyalgia rheumatica symptoms treated with tocilizumab in routine clinical practice. Annals of the Rheumatic Diseases. 2019;78(suppl 2):440. doi:https://dx.doi.org/10.1136/annrheumdis-2019-eular.2676	Wrong study design – Observational study for intervention of interest
Unizony S, Stone JH, Keroack B. Long-term use of tocilizumab for the treatment of giant cell arteritis. Arthritis & rheumatism. 2013;65:S1-S1331. doi:https://doi.org/10.1002/art.38216	Wrong study design – Observational study for intervention of interest
Van Sleen Y, Arends S, Van Der Geest K, et al. Five-year analysis of patient reported outcomes in a longitudinal cohort of giant cell arteritis and polymyalgia rheumatica patients. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Vegas-Revenga N, Loricera J, Mera A, et al. Comparison between giacta trial and a multicenter series of giant cell arteritis patients from clinical practice with tocilizumab. Arthritis & rheumatology. 2017;69	Wrong study design – Observational study for intervention of interest
Vela Casasempere P, Tudela L, Cano-Alameda R, Gomez-Sabater S. Evolution of Patients with Giant Cell Arteritis: Before and after the Biological Era. Annals of the Rheumatic Diseases. 2023;82(suppl 1):1586. doi:https://dx.doi.org/10.1136/annrheumdis-2023-eular.4492	Wrong study design – Observational study for intervention of interest
Venhoff N, Schmidt W, Bergner R, et al. Secukinumab in giant cell arteritis: a randomized, parallel-group, double-blind, placebo-controlled, multicenter phase 2 trial. Arthritis & rheumatology. 2021;73(SUPPL 9):4130-4133. doi:https://doi.org/10.1002/art.41966	Wrong or no outcomes – Study of interest but data in report not relevant
Venhoff N, Schmidt WA, Bergner R, et al. Secukinumab in giant cell arteritis: The randomised, parallel-group, double-blind, placebo-controlled, multicentre phase 2 TITAIN trial. Annals of the Rheumatic Diseases. 2022;81:121-122. doi:https://doi.org/10.1136/annrheumdis-2022-eular.806	Wrong or no outcomes – Study of interest but data in report not relevant
Villanueva FB, Corrales C, Loricera J, et al. Utility of Optimization of Tocilizumab Therapy in Giant Cell Arteritis: A Multicenter Study of 471 Patients. Arthritis & rheumatology. 2022;74(suppl 9):944-946. doi:https://dx.doi.org/10.1002/art.42355	Wrong study design – Observational study for intervention of interest
Villiger PM, Adler S, Kuchen S, et al. Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. The lancet. 2016;387(10031):1921-7. doi:10.1016/s0140-6736(16)00560-2	Wrong study design – Non-pivotal trial for intervention of interest
Villiger PM, Adler S, Kuchen S, et al. Tocilizumab for induction and maintenance of remission in giant cell arteritis-first randomized placebo-controlled trial. Swiss medical weekly. 2016;146	Wrong study design – Non-pivotal trial for intervention of interest
Vinicki JP, Garcia-Vicuna R, Arredondo M, et al. Sustained remission after long-term biological therapy in patients with large vessel vasculitis: an analysis of ten cases. Reumatologia clinica. 2017;13(4):210-213. doi:https://dx.doi.org/10.1016/j.reuma.2016.06.003	Wrong study design – Observational study for intervention of interest
Vionnet J, Buss G, Mayer C, Sokolov AA, Borruat FX, Spertini F. Tocilizumab for giant cell arteritis with corticosteroid-resistant progressive anterior ischemic optic neuropathy. Joint Bone Spine. 2017;84(5):615-619. doi:10.1016/j.jbspin.2017.04.009	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Weyand CM, Fulbright JW, Hunder GG, Evans JM, Goronzy JJ. Treatment of giant cell arteritis: Interleukin-6 as a biologic marker of disease activity. Arthritis & rheumatism. 2000;43(5):1041-1048. doi:https://dx.doi.org/10.1002/1529-0131%28200005%2943:5%3C1041::AID-ANR12%3E3.0.CO;2-7	Wrong study design – Non-pivotal trial for intervention of interest
Wilson JC, Sarsour K, Collinson N, et al. Incidence of outcomes potentially associated with corticosteroid therapy in patients with giant cell arteritis. Seminars in arthritis and rheumatism. 2017;46(5):650-656. doi:10.1016/j.semarthrit.2016.10.001	Wrong intervention – Intervention not of interest
Wilson JC, Sarsour K, Collinson N, et al. Risk for serious adverse events associated with corticosteroid therapy in patients with giant cell arteritis: A UK population-based study. Nephron. 2015;129(suppl 2):188. doi:https://dx.doi.org/10.1159/000381120	Wrong intervention – Intervention not of interest
Wilson JC, Sarsour K, Collinson N, et al. Serious adverse effects associated with glucocorticoid therapy in patients with giant cell arteritis (GCA): A nested case-control analysis. Seminars in arthritis and rheumatism. 2017;46(6):819-827. doi:https://dx.doi.org/10.1016/j.semarthrit.2016.11.006	Wrong intervention – Intervention not of interest
Yamaguchi T, Fukui S, Oda N, et al. Multi-Center Study on the Safety of Tocilizumab Use for Giant Cell Arteritis in Japan. 21st International Vasculitis Workshop. 2024.	Wrong study design – Observational study for intervention of interest
Yates M, Loke Y, Watts R, MacGregor A. Systematic review of drug trials in the treatment of giant cell arteritis. Annals of the Rheumatic Diseases. 2013;72(SUPPL. 3)doi:https://dx.doi.org/10.1136/annrheumdis-2013-eular.1466	Wrong study design – Systematic review
Yates M, Loke Y, Watts R, MacGregor A. Systematic review of steroid trials in giant cell arteritis. Rheumatology. 2012;3):iii183. doi:https://dx.doi.org/10.1093/rheumatology/kes108	Wrong study design – Systematic review
Yates M, Loke YK, Watts RA, MacGregor AJ. Prednisolone combined with adjunctive immunosuppression is not superior to prednisolone alone in terms of efficacy and safety in giant cell arteritis: Meta-analysis. Clinical rheumatology. 2014;33(2):227-236. doi:https://dx.doi.org/10.1007/s10067-013-2384-2	Wrong study design – Systematic review

Table 77. Met broad PICOS criteria but not suitable for anchored ITC/NMA (n=27) – SLR re-run

Reference	Reason for exclusion
Blanco R, Aldasoro V, Maiz O, et al. Tocilizumab in cranial and extracranial giant cell arteritis: a national multicenter study of 471 cases. Rheumatology. 2024;10doi:https://dx.doi.org/10.1093/rheumatology/keae666	Wrong study design – Systematic review
Christ L, Seitz L, Scholz G, Kollert F, Reichenbach S, Villiger P. Long-Term Efficacy of Tocilizumab Monotherapy after Ultra-Short Glucocorticoid Administration to Treat Giant Cell Arteritis: Three Year Follow-up of the Gusto Trial. Annals of the Rheumatic Diseases. 2024;83(60):2024-06. doi:https://doi.org/10.1136/annrheumdis-2024-eular.2167	Wrong study design – Non-pivotal trial for intervention of interest
Conticini E, Terribili R, Grazzini S, et al. Safety and Efficacy of Long-Term Tocilizumab in a Cohort of Patients with Giant Cell Arteritis: An Italian Monocentric Retrospective Study. Annals of the Rheumatic Diseases. 2024;83(Supplement 1):2005. doi:https://dx.doi.org/10.1136/annrheumdis-2024-eular.794	Wrong study design – Observational study for intervention of interest
Davanzo F, Iorio L, Delvino P, et al. Comparative Efficacy and Safety of Glucocorticoids, Methotrexate and Tocilizumab in the Treatment of New-Onset Large Vessel Giant Cell Arteritis. Annals of the Rheumatic Diseases. 2024;83(Supplement 1):2014. doi:https://dx.doi.org/10.1136/annrheumdis-2024-eular.6269	Wrong study design – Observational study for intervention of interest
de Boysson H, Ly K, Geffray L, et al. Anakinra in Giant Cell Arteritis: A Multicenter, Randomized, Double-blind, Placebo-controlled Trial [abstract]. Arthritis Rheumatol. 2024; 76 (suppl 9).	Wrong intervention – Intervention not of interest
Gil W, Kodjikian L, Andre M, et al. Uveitis in Giant Cell Arteritis: A Retrospective Study of Seven Observational Cases and Literature Review. Ocul Immunol Inflamm. 2024;32(8):1844-1851. doi:https://dx.doi.org/10.1080/09273948.2023.2264383	Wrong study design – Observational study for intervention of interest
Kang MK, Hong Y, Kim YH, et al. Diagnosis, Treatment, and Follow-Up of Giant-Cell Arteritis: A Retrospective Multicenter Study. Journal of Clinical Neurology (Korea). 2024;20(3):306-314. doi:https://dx.doi.org/10.3988/jcn.2023.0169	Wrong study design – Observational study for intervention of interest
Lee YH, Song GG. Comparative Efficacy and Safety of Biologic Treatments in Giant Cell Arteritis: A Network Meta-Analysis of Randomized Controlled Trials. Pharmaceutical Sciences. 2024;30(2):143-152. doi:https://dx.doi.org/10.34172/PS.2023.26	Wrong study design – Systematic review

Reference	Reason for exclusion
Lopez-Gutierrez F, Loricera J, Tofade T, et al. Effectiveness of Janus Kinase Inhibitors in Relapsing Giant Cell Arteritis in Realworld Clinical Practice and Review of the Literature. Annals of the Rheumatic Diseases. 2024;83(Supplement 1):443-444. doi:https://dx.doi.org/10.1136/annrheumdis-2024-eular.4089	Wrong study design – Observational study for intervention of interest
Loricera J, Tofade T, Prieto-Pena D, et al. Effectiveness of janus kinase inhibitors in relapsing giant cell arteritis in real-world clinical practice and review of the literature. Arthritis Research and Therapy. 2024;26(1) (no pagination)doi:https://dx.doi.org/10.1186/s13075-024-03314-9	Wrong study design – Observational study for intervention of interest
Martin-Gutierrez A, Loricera J, Aldasoro V, et al. Relapses in giant cell arteritis treated with tocilizumab. Retrospective multicenter study of 407 patients in clinical practice. Seminars in arthritis and rheumatism. 2025;71(no pagination)doi:https://dx.doi.org/10.1016/j.semarthrit.2025.152640	Wrong study design – Observational study for intervention of interest
Martin-Gutierrez A, Loricera J, Narvaez J, et al. Effectiveness Of Tocilizumab In Aortitis And Aneurysms Associated With Giant Cell Arteritis. European journal of internal medicine. 2024;129:78-86. doi:https://dx.doi.org/10.1016/j.ejim.2024.06.013	Wrong study design – Observational study for intervention of interest
Martín-Gutiérrez A, Loricera J, Secada Gómez C, et al. Effectiveness of Tocilizumab in Aortitis and Aneurysms Associated with Giant Cell Arteritis. Multicenter Open-label Study [abstract]. Arthritis Rheumatol. 2024; 76 (suppl 9).	Wrong study design – Observational study for intervention of interest
Martín-Gutiérrez A, Loricera J, Secada Gómez C, et al. Factors Associated with Relapse in Giant Cell Arteritis Treated with Tocilizumab. Multicenter Open-label Study of 407 Patients [abstract]. Arthritis Rheumatol. 2024; 76 (suppl 9).	Wrong study design – Observational study for intervention of interest
Martín-Gutiérrez A, Loricera J, Secada Gómez C, et al. Tocilizumab in Monotherapy vs. Combined in Aortitis Associated with Giant Cell Arteritis. Multicenter Open-label Study of 196 Patients [abstract]. Arthritis Rheumatol. 2024; 76 (suppl 9).	Wrong study design – Observational study for intervention of interest
Marvisi C, Muratore F, Ricordi C, et al. Treatment of Giant Cell Arteritis with Ultra-Short Glucocorticoids and Tocilizumab: Results from the Extension to 76 Weeks. Annals of the Rheumatic Diseases. 2024;83(Supplement 1):59-60. doi:https://dx.doi.org/10.1136/annrheumdis-2024-eular.4250	Wrong study design – Observational study for intervention of interest
Muratore F, Marvisi C, Cassone G, et al. Treatment of giant cell arteritis with ultra-short glucocorticoids and tocilizumab: results from the extension of the TOPAZIO study. Rheumatology. 2024;16doi:https://dx.doi.org/10.1093/rheumatology/keae400	Wrong intervention – Intervention not of interest
Nagase FN, Fukui S, Takizawa N, et al. Tocilizumab for Giant Cell Arteritis: Clinical Outcomes Following Relapses and Tocilizumab Discontinuation Due to Adverse Events. The Journal of rheumatology. 2024;15doi:https://dx.doi.org/10.3899/jrheum.2024-0612	Wrong study design – Observational study for intervention of interest
Peyrac G, Mageau A, Gaudemer A, et al. Limb arteries involvement assessed by FDG/PET CT at diagnosis of giant cell arteritis and risk of relapse: An observational study. Joint Bone Spine. 2024;91(5) (no pagination)doi:https://dx.doi.org/10.1016/j.jbspin.2024.105734	Wrong study design – Observational study for intervention of interest
Quartuccio L, Treppo E, De Martino M, et al. Faster steroid-free remission with tocilizumab compared to methotrexate in giant cell arteritis: a real-life experience in two reference centres. Internal and emergency medicine. 2024;19(8):2177-2184. doi:https://dx.doi.org/10.1007/s11739-024-03722-4	Wrong study design – Observational study for intervention of interest
Ricordi C, Marvisi C, Macchioni P, et al. Does tocilizumab eliminate inflammation in GCA? A cohort study on repeated temporal artery biopsies. RMD Open. 2024;10(4) (no pagination)doi:https://dx.doi.org/10.1136/rmdopen-2024-005132	Wrong study design – Observational study for intervention of interest
Rossi GM, Mannoni A, Di Scala G, et al. Low-dose tocilizumab for relapsing giant cell arteritis in the elderly, fragile patient: beyond the GiACTA trial. Autoimmunity reviews. 2018;Vol.17(12):1265-1267p. doi:https://doi.org/10.1016/j.autrev.2018.07.004	Wrong study design – Observational study for intervention of interest
Rubortone P, Lazzaro FG, Leone F, et al. Methotrexate Versus Tocilizumab in Maintaining Remission: A Retrospective Monocentric Cohort Study in Patients with Giant Cell Arteritis. Annals of the Rheumatic Diseases. 2024;83(Supplement 1):2012. doi:https://dx.doi.org/10.1136/annrheumdis-2024-eular.5477	Wrong study design – Observational study for intervention of interest
Sacre K, Peyrac G, Mageau A, et al. Limb Arteries Involvement Assessed by Fdg/ Pet Ct at Diagnosis of Giant Cell Arteritis and Risk of Relapse: An Observational Study. Annals of the Rheumatic Diseases. 2024;83(Supplement 1):1995-1996. doi:https://dx.doi.org/10.1136/annrheumdis-2024-eular.1289	Wrong study design – Observational study for intervention of interest
Sanada A, Abe N, Bohgaki M, Kasahara H. Therapeutic effectiveness of upadacitinib combined with glucocorticoid on remission induction and maintenance in giant cell arteritis. Rheumatology (Oxford). 2022 Aug 30;61(9):e274-e276. doi: 10.1093/rheumatology/keac203.	Wrong study design – Observational study for intervention of interest

Reference	Reason for exclusion
Terribili R, Grazzini S, Conticini E, et al. Safety and Efficacy of Long-Term Tocilizumab in a Cohort of Patients with Giant Cell Arteritis: An Italian Monocentric Retrospective Study. Biologics: Targets and Therapy. 2024;18:297-305. doi:https://dx.doi.org/10.2147/BTT.S470107	Wrong study design – Observational study for intervention of interest
Wallmeier P, Arnold S, Tais A, et al. The Joint Vasculitis Registry in German-speaking countries (GeVas): subgroup analysis of 195 GCA patients. Clinical and experimental rheumatology. 2024;42(4):895-904. doi:https://dx.doi.org/10.55563/clinexprheumatol/d3o0gu	Wrong study design – Observational study for intervention of interest

H.1.4 Quality assessment

The SLR were conducted in accordance with guidance from the Cochrane Handbook for Systematic Reviews of Interventions, the National Institute for Health and Care Excellence (NICE), and the Centre for Reviews and Dissemination (CRD).

Studies suitable for inclusion were critically appraised for quality independently by two researchers; any disagreements were resolved by discussion or by a third researcher. Quality assessment was conducted using the Revised Cochrane risk-of-bias tool for randomized trials.This tool uses five distinct domains of potential bias: randomization, deviations from intended interventions, incomplete outcome data, measurement of outcome and selective reporting of outcomes. The response options are “yes,” “probably yes,” “probably no,” “no,” and “no information.” Within each domain responses to set questions lead to judgements of “low risk of bias”, “some concerns” or “high risk of bias”. Domain level judgements are aggregated into an overall risk of bias judgement for the study results assessed.

H.1.5 Unpublished data

Unpublished data from the SELECT-GCA trial is included in this application.

Appendix I. Literature searches for health-related quality of life

I.1 Health-related quality-of-life search

A targeted literature search was conducted to identify previous HTA evaluations of tocilizumab in GCA from relevant HTA agencies, see Table 78. The purpose of the search was to identify any outcomes for change from baseline for EQ-5D for tocilizumab.

Table 78 Sources included in the literature search

Source name	Location/source	Search strategy	Date of search
Medicinrådet	https://medicinraadet.dk/	Tocilizumab/RoActemra	26.08.2024
TLV	https://www.tlv.se/	Tocilizumab/RoActemra	26.08.2024
Nye Metoder	https://www.nyemetoder.no/	Tocilizumab/RoActemra	26.08.2024
NICE	www.nice.org.uk	Tocilizumab/RoActemra	26.08.2024
CADTH	https://www.cda-amc.ca/find-reports	Tocilizumab	26.08.2024

I.1.1 Search strategies

NA

I.1.2 Quality assessment and generalizability of estimates

NA

I.1.3 Unpublished data

NA

Appendix J. Literature searches for input to the health economic model

J.1 External literature for input to the health economic model

J.1.1 Targeted literature search for resource use estimates and costs

A targeted literature search for was conducted to identify resource use and costs associated with treatment of GCA.

Table 79. Sources included in the targeted literature search.

Source name/ database	Location/source	Search strategy	Date of search
Medicinrådet	https://medicinraadet.dk/	Tocilizumab/RoActemra	26.08.2024
TLV	https://www.tlv.se/	Tocilizumab/RoActemra	26.08.2024
Nye Metoder	https://www.nyemetoder.no/	Tocilizumab/RoActemra	26.08.2024
NICE	www.nice.org.uk	Tocilizumab/RoActemra	26.08.2024
CADTH	https://www.cda-amc.ca/find-reports	Tocilizumab	26.08.2024

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