Medicinrådet

Bilag til Medicinrådets vurdering af tafasitamab (Minjuvi) i kombination med lenalidomid og rituximab (R²) til behandling af recidiverende eller refraktær follikulært lymfom

Vers. 1.0

Bilagsoversigt

1. Forhandlingsnotat fra Amgros vedr. tafasitamab
2. Ansøgers endelige ansøgning vedr. tafasitamab

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28.05.2026

LSC/DBS

Forhandlingsnotat

Dato for vurdering i Medicinrådet	24.06.2026
Leverandør	Incyte
Lægemiddel	Minjuvi (tafasitamab)
Ansøgt indikation	Minjuvi er indiceret i kombination med lenalidomide og rituximab til behandling af voksne patienter med relaps eller refraktær follikulært lymfom (FL) (Grad 1-3a) efter minimum én linje systemisk terapi
Nyt lægemiddel / indikationsudvidelse	Indikationsudvidelse

Prisinformation

Amgros har forhandlet følgende pris på Minjuvi:

Tabel 1: Forhandlingsresultat

Lægemiddel	Styrke (pakning)	AIP (DKK)	Nuværende SAIP (DKK)	Nuværende rabat ift. AIP	Forhandlet SAIP (DKK)	Forhandlet rabat ift. AIP
Minjuvi	200 mg (1 stk.)	5.120,28	[redacted]	[redacted]	[redacted]	[redacted]

Prisen er betinget af Medicinrådets anbefaling. Det betyder, at hvis Medicinrådet ikke anbefaler Minjuvi, indkøbes lægemidlet til nuværende SAIP.

Aftaleforhold

Amgros har en eksisterende aftale på Minjuvi. Aftalen gælder til den 30.09.2027 med mulighed for at forlænge i 12 måneder. Der er inkluderet mulighed for prisregulering i aftalen.

[redacted]

Informationer fra forhandlingen

[redacted]

Konkurrencesituationen

Patienter med relaps-refraktært follikulært lymfom kan behandles med flere forskellige behandlingsregimer, herunder rituximab i kombination med kemoterapi eller lenalidomid (R^2-regimet). Minjuvi gives i tillæg til R^2-regimet.

Minjuvi kan gives i op til 12 cyklusser á 28 dages varighed svarende til 48 uger. Tabel 2 viser lægemiddeludgifter ved behandling med Minjuvi.

Tabel 2: Lægemiddeludgifter pr. patient

Lægemiddel	Styrke (pakning)	Dosering*	Pris pr. pakning (SAIP, DKK)	Lægemiddeludgift pr. 48 uger (SAIP, DKK)
Minjuvi	200 mg (1 stk.)	Cyklus 1-3: 12 mg/kg** på dag 1, 8, 15 og 22, i.v. Cyklus 4-12: 12 mg/kg** på dag 1 og 15, i.v.	[redacted]	[redacted]

*Hver cyklus er 28 dage
** Kropsvægt er 76,93 kg jf. Medicinrådet.

Status fra andre lande

Tabel 3: Status fra andre lande

Land	Status	Link
Norge	Under vurdering	Link til status
Sverige	Under vurdering	Link ikke tilgængelig
England	Under vurdering	Link til status

Opsummering

Amgros har en eksisterende aftale på Minuvi der gælder indtil 30.09.2027.

[redacted]

Application for the assessment of tafasitamab (Minjuvi) + lenalidomide + rituximab (R^2)for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) (Grade 1-3a) after at least one line of systemic therapy

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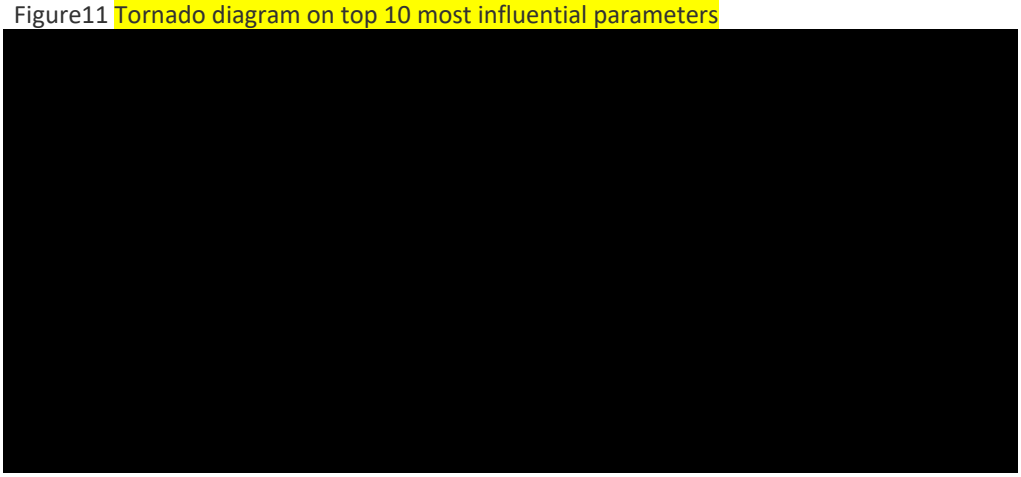

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Abbreviations

Abbreviation	Definition
1L	First-line
2L	Second-line
2L+	Second-line or later
3L	Third-line
3L+	Third-line or later
4L	Fourth-line
ADCC	Antibody-dependent cellular cytotoxicity
ADCP	Antibody-dependent cellular phagocytosis
AE	Adverse event
AIC	Akaike information criterion
ASCT	Autologous stem cell transplantation
Axi-cel	Axicabtagene ciloleucel
BEAM	Carmustine, etoposide, cytarabine + melphalan
BIC	Bayesian information criterion
CHOP	Cyclophosphamide, doxorubicin, vincristine, and predniso(lo)ne
CI	Confidence interval
CR	Complete response
CT	Computed tomography
CVP	Cyclophosphamide, vincristine, and predniso(lo)ne
DLBCL	Diffuse large B-cell lymphoma
DMC	Danish Medicines Council
EMA	European Medicines Agency
ECOG	Eastern Cooperative Oncology Group
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30
EOT	End of treatment
EQ-5D-5L	EuroQol 5-dimension 5-level
ESMO	European Society of Medical Oncology
FACT-Lym	Functional Assessment of Cancer Therapy-Lymphoma
FAS	Full Analysis Set
FDA	Food and Drug Administration
FL	Follicular lymphoma
HDC	High-dose chemotherapy
HES	Hospital episodes statistics
HR	Hazard ratio
HRQoL	Health-related quality of life
IA	Investigator assessment
ICER	Incremental cost-effectiveness ratio
IRC	Independent review committee

KM	Kaplan–Meier
LDH	Lactate dehydrogenase
LY	Life year
MedDRA	Medical Dictionary for Regulatory Activities
MRD	Minimal residual disease
MRI	Magnetic resonance imaging
MZL	Marginal zone lymphoma
NE	Not evaluable
NHL	Non-Hodgkin Lymphoma
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NK	Natural killer
OR	Odds ratio
ORR	Overall response rate/objective response rate
OS	Overall survival
PET	Positron emission tomography
PFS	Progression-free survival
POD24	Progression of disease within 24 months
PR	Partial response
PS	Performance status
PTSD	Posttraumatic stress disorder
QALY	Quality-adjusted life year
QD	Once a day
QoL	Quality of life
R^2	Lenalidomide + rituximab
R-CHOP	Rituximab, cyclophosphamide, doxorubicin, vincristine, + predniso(lo)ne
R-CVP	Rituximab, cyclophosphamide, vincristine, + predniso(lo)ne
RDI	Relative dose intensity
R/R	Relapsed or refractory
SAE	Serious adverse event
SCT	Stem cell transplantation
SLR	Systematic literature review
SmPC	Summary of product characteristics
SD	Standard deviation
TEAE	Treatment-emergent adverse event
TLV	Swedish Dental and Pharmaceutical Benefits Agency
TSD	Technical Support Document
TTD	Time to treatment discontinuation
TTNT	Time to next treatment
UK	United Kingdom

1. Regulatory information on the medicine

Overview of the medicine	
Proprietary name	Minjuvi®
Generic name	Tafasitamab
Therapeutic indication as defined by EMA	Minjuvi is indicated in combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) (Grade 1-3a) after at least one line of systemic therapy.[1]
Marketing authorization holder in Denmark	Incyte Biosciences Distribution B.V.
ATC code	L01XC41 [2]
Combination therapy and/or co-medication	Tafasitamab is administered in combination with rituximab and lenalidomide (R^2) [3]
(Expected) Date of EC approval	Expected January 2026
Has the medicine received a conditional marketing authorization?	Tafasitamab received a positive opinion (CHMP approval) for FL on 13th November 2025 [1] Tafasitamab received European Commission (EC) approval for FL indication on 15 December 2025.[4] Tafasitamab has been given a conditional marketing authorization for its currently approved indication, diffuse large B-cell lymphoma (DLBCL) (single arm trial) [2].
Accelerated assessment in the European Medicines Agency (EMA)	No
Orphan drug designation (include date)	Yes, for the relevant indication (FL) in February 2025 [5] EU/3/25/3027
Other therapeutic indications approved by EMA	Tafasitamab is currently indicated, in combination with lenalidomide followed by tafasitamab monotherapy, for the treatment of adult patients with relapsed or refractory DLBCL who are not eligible for autologous stem cell transplant (ASCT).[2]
Other indications that have been evaluated by the DMC (yes/no)	DLBCL in 2022 [6] (Danish Medicines Council (DMC) case number: 151299)
Joint Nordic assessment (JNHB)	No, rationale provided in request for assessment.

Overview of the medicine	
Dispensing group	BEGR [7]
Packaging – types, sizes/number of units and concentrations	1 x vial of powder contains 200 mg of tafasitamab (after reconstitution each mL of solution contains 40 mg of tafasitamab)

2. Summary table

Summary	
Indication relevant for the assessment	Tafasitamab in combination with lenalidomide and rituximab (R^2) for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) (Grade 1-3a) after at least one line of systemic therapy.[1] There are no deviations between the therapeutic indication relevant for assessment in Denmark and the EMA indication.
Dosage regiment and administration	**Tafasitamab**: 12 mg/kg IV on Days 1, 8, 15, and 22 of Cycles 1 to 3; and on Days 1 and 15 of Cycles 4 to 12. Each cycle is 28 days. **Lenalidomide**: 20 mg orally once daily (QD) on Days 1 to 21 of each 28-day cycle for Cycles 1–12. **Rituximab**: 375 mg/m² IV on Days 1, 8, 15, and 22 of Cycle 1; and Day 1 of Cycles 2 to 5.
Choice of comparator	R^2: Rituximab + Lenalidomide
Prognosis with current treatment (comparator)	The AUGMENT trial was conducted in relapsed or refractory (R/R) FL and investigated rituximab plus lenalidomide (R^2) versus rituximab alone. As of January 26, 2022, at a median follow-up of 65.9 months, median progression-free survival (PFS) as assessed by Investigator was 27.6 months for R^2 vs 14.3 months for control, with HR = 0.50 (95% CI, 0.38-0.66; p < 0.0001). Median overall survival (OS) was not reached for either group, while there was an improvement in OS for R^2 (HR = 0.59, 95% CI, 0.37-0.95, p = 0.0285).[8] These results establish R^2 as an effective chemotherapy-free option for patients with R/R FL.
Type of evidence for the clinical evaluation	Head-to-head study, InMIND (NCT04680052), pivotal trial [3, 9] An ongoing Phase 3, randomized, double-blind, placebo-controlled, multicentre study to evaluate the efficacy and safety of tafasitamab plus lenalidomide in addition to rituximab versus lenalidomide in addition to rituximab in patients with R/R FL Grade 1 to 3a or R/R Marginal zone lymphoma (MZL). The latest data cut is 23 February 2024.
Most important efficacy endpoints (Difference/gain compared to comparator)	The primary endpoint is PFS by investigator assessment (IA). The base case in the health economic model uses PFS by independent review committee (IRC) masked to study treatment to minimize any potential biases that may arise from investigators. Important efficacy endpoints in inMIND [10]: • PFS by IA. Median PFS of 22.4 months (95% CI, 19.2-not evaluable (NE)) for tafasitamab + R^2 arm vs. 13.9 months (95% CI, 11.5-16.4) for R^2. Results for PFS by IRC were consistent with PFS by IA, with an estimated HR of 0.41 (95% CI, 0.29-0.56) for the treatment effect between the tafasitamab + $R^2$and placebo + R^2 groups OS in the FL population. Median follow-up period: 15.8 and 14.6 months for tafasitamab + R^2 and placebo + R^2,

Summary	
	respectively. Median OS was not reached in either arm (HR of 0.59 [95% CI, 0.31-1.13]); however, OS rates were higher in the tafasitamab + R^2 arm at 12 months and 2 years, respectively (96.4% versus 93.7%, respectively and 92.5% versus 85.5%, respectively).
Most important serious adverse events for the intervention and comparator	• Any serious treatment-emergent adverse events (TEAE): 36.1% (tafasitamab + R^2) vs 31.6% (R^2). • Serious adverse events (SAEs) ≥5% in any arm (most important): ○ Pneumonia: 7.7% for tafasitamab + R^2 vs 4.8% for R^2; ○ COVID-19: 6.9% for tafasitamab + R^2 vs 2.6% for R^2; ○ COVID-19 pneumonia: 5.1% for tafasitamab + R^2 vs 1.8% for R^2
Impact on health-related quality of life	**Clinical documentation:** EuroQol 5-dimension 5-level (EQ-5D-5L) collected in inMIND; mapped to EQ-5D-3L using United Kingdom (UK) value set. Utility for the progression-free patient is XXXX (95% CI XXXX, XXXX). Utility for the progressed patient is XXXXX (95% CI XXXX, XXXX). **Health economic model:** Better health-related quality of life (HRQoL) with tafasitamab + R^2 vs the comparator group
Type of economic analysis that is submitted	Cost-utility analysis using a three-state partitioned survival model
Data sources used to model the clinical effects	InMIND patient-level data (PLD) for OS, PFS (IRC base case), time to treatment discontinuation (TTD)
Data sources used to model the health-related quality of life	EQ-5D-5L from inMIND, derived using Danish preference weights from Jensen et al. (2021) [11]; age-adjustment applied per standard practice.
Life years gained	XXXX years (discounted)
QALYs gained	XXXX QALY (discounted)
Incremental costs	XXXX DKK (discounted)
ICER (DKK/QALY)	XXXX DKK/QALY (discounted)
Uncertainty associated with the ICER estimate	The parameters with greatest impact are the utilities for health state and drug administration costs.
Number of eligible patients in Denmark	Prevalence: 2,623- Incidence: 103 (estimated annual patients treated with tafasitamab + R^2 is expected to be fewer than XX).
Budget impact (in year 5)	XXXX

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

3.1 The medical condition

Non-Hodgkin Lymphoma (NHL) is a cancer of the lymphatic system comprising a heterogeneous group of lymphoma subtypes, each with different epidemiologies, etiologies, immunophenotypic, genetic, and clinical features, and response to therapy.[12, 13] NHL can be divided into two groups, 'indolent' and 'aggressive,' based on the disease's prognosis. Indolent lymphomas grow and spread slowly and have few signs and symptoms initially.[12] Aggressive lymphomas grow and spread quickly and frequently have signs and symptoms such as weight loss, night sweats, and fever and can result in deaths within a few weeks if untreated.[12] DLBCL is the most common NHL overall and is a clinically aggressive lymphoma.[14] FL is the second most common NHL and the most common form of indolent NHL (iNHL) in Europe and the US, accounting for 13-26% of all NHL cases.[15-20]

Follicular lymphoma is a slow-dividing, slow-growing B-cell lymphoma that typically forms tumours in lymph nodes, although extra nodal disease in the bone marrow is also commonly reported.[21, 22] Temporary germinal centres form in lymph nodes as a normal response to an immune stressor such as infection or inflammation. However, when cells within germinal centres grow without proper regulation, this results in excessive amounts of abnormal B-cells grouping to form clusters (follicles) in the lymph nodes, causing FL.[21]

Most patients with FL present with asymptomatic generalized painless enlarged lymph nodes (lymphadenopathy), which may increase and decrease in size for several years.[22, 23] The lymph nodes in the armpit, neck, and groin are usually involved; rarely, FL may present with an asymptomatic large mass in the chest cavity.[23] Approximately 20% of patients with FL experience B symptoms (night sweats, fever, weight loss).[23] Increased serum lactate dehydrogenase (LDH) level is also seen in 20% of the patients.[23]

Transformation of FL to different aggressive forms of NHL, such as DLBCL, Burkitt and Burkitt-like lymphoma, high-grade B-cell lymphoma, and B-cell acute lymphoblastic leukaemia is associated with an unfavourable outcome. The 10-year cumulative incidence of transformation is reported to be 8.4% for Finland and 13–25% for Sweden.[24, 25] Predicting which patients are at greatest risk of transformation remains a challenge, and is likely a reflection of the heterogeneity of clinical, biological, and genetic factors that increase the risk of transformation.[26] Transformation of FL can be

suspected clinically when there are rapidly enlarging disproportionate masses, B symptoms, and abnormal laboratory tests (such as elevated serum LDH or calcium levels).[23]

Advanced FL produces a broad spectrum of symptoms. Fatigue is common, often severely debilitating, and affects activities of daily life, work capacity, caring for others, social life, libido, and overall enjoyment of life. Given the advanced age of many with FL, fatigue compounds problems of aging, frailty, and social isolation.[27]

Bone marrow involvement can reduce blood cell production and lead to cytopenias with clinical consequences [27]:

• Anaemia, which worsens fatigue.
• Thrombocytopenia, which increases bruising and bleeding risk.
• Neutropenia, which increases risk of bacterial infection.

Other lymphoma symptoms include drenching night sweats, fevers, and weight loss. Symptoms depend on disease sites, for example pleural effusion with chest pain and dyspnoea when the lungs are involved, or abdominal pain, bowel habit change, dyspepsia, or anorexia with abdominal or gastrointestinal involvement.[27]

Lenalidomide and rituximab is a chemotherapy-free approach to treating R/R FL that addresses treatment needs in patients who are unfit for further chemotherapy, have therapy-related toxicities from prior treatment, or are refractory to initial chemotherapy and would benefit from non–chemotherapy-based treatment.[28] Lenalidomide is an immunomodulatory drug with direct cytotoxicity to lymphoma cells as well as indirect antitumor effects mediated through changes in the tumour microenvironment.[29, 30] Rituximab is a human/murine, chimeric, monoclonal antibody with a specific affinity for CD20, which is expressed on normal B-cells (excluding stem cells, pro-B-cells, and plasma B-cells) and on most malignant B-cells.[31] The positive outcome of the AUGMENT Phase 3 study comparing R^2 versus rituximab plus placebo in patients with R/R FL who were considered appropriate for rituximab monotherapy led to regulatory approval in the US and EU.[32-35] Overall, compared with rituximab alone, the R^2 combination therapy demonstrated superior activity and showed greater efficacy than that of rituximab monotherapy in patients with R/R FL, as measured by PFS (HR, 0.47) and OS (HR, 0.61).[35, 36] The AUGMENT study also demonstrated PFS benefit in patients with prior chemotherapy resistance or prior rituximab resistance.[28]

In Denmark, the 10-year OS rate for FL is approximately 80%. The median OS for FL patients is presumed to be over 20 years.[37]

A diagnosis of an indolent NHL such as FL carries substantial short- and long-term psychological burden.[38] Within three months of diagnosis, 27.1 percent reported clinically significant anxiety and 14.6 percent reported posttraumatic stress disorder (PTSD) symptoms. Contributors included the incurable nature of disease, indefinite time course, prognostic uncertainty, and lack of personal control.[39] Distress can occur even without physical symptoms or active therapy, supporting the need for early screening, psychosocial support, and development of coping strategies. Improved emotional coping

is associated with lower anxiety, depression, and PTSD.[38] A watchful-waiting approach can conflict with patient expectations and contribute to distress.[38] A Danish registry study found higher 2-year cumulative risk of psychotropic drug use after NHL diagnosis versus matched comparators, with more persistent risk in indolent NHL than aggressive NHL.[40]

The financial and social economic burden associated with indolent NHL is high. Evidence from a systematic review indicated that 20–50% of patients with hematologic malignancies experience economic burden, including lost productivity, transport and food costs, and depletion of savings. Unlike many cancers treated with therapies of finite duration, indolent NHLs follow a chronic, relapsing disease course requiring long-term management, which can affect lifestyle, employment, and financial stability. Around retirement age, diagnosis or treatment initiation can trigger retirement, while younger patients may face disrupted workforce participation and threatened long-term finances. Together, these factors contribute to a meaningful long-term burden on patients and society.[38, 41]

Patient-reported quality of life is clearly affected in advanced FL. European organisation for research and treatment of cancer quality of life questionnaire core 30 (EORTC QLQ-C30) shows worsening global health and declines in functional scales with disease progression and with additional lines of therapy. Physical role, and social functioning decline the most, while symptoms such as fatigue, pain, and dyspnoea increase. Emotional functioning may remain relatively stable, possibly because being on therapy, regardless of line, helps patients feel more in control and reduces anxiety or depression.[42] Compared with an NHL reference population, patients with FL report lower global health state/quality of life (GHS/QoL) and higher symptom burden in several domains, including nausea and vomiting, pain, dyspnoea, appetite loss, and diarrhoea.[43] Across lines of therapy, GHS/QoL and especially physical role, and social functioning worsen from first-line (1L) to third-line and later (3L+). Fatigue, pain, and dyspnoea increase significantly across lines. The Jonckheere-Terpstra test confirms a significant trend across 1L, second-line (2L), and 3L+, without identifying the specific pairwise differences.[43]

3.2 Patient population

Follicular lymphoma accounts for a substantial share of NHL in Denmark and typically presents at advanced stage with median age around retirement.[44, 45] FL is characterized by an indolent, chronic, relapsing–remitting course.[46]

Target population for this assessment

The target population relevant for this assessment is adults with R/R FL Grade 1–3a who have received at least one prior anti-CD20–containing systemic therapy and are candidates for tafasitamab in combination with rituximab and lenalidomide (R^2), in line with the therapeutic indication relevant for Denmark.[37]

Typical characteristics include Eastern Cooperative Oncology Group (ECOG) performance status 0–2, documented CD20-positive disease, and patients should have received at

least one prior line of therapy including an anti-CD20 antibody (i.e rituximab). Factors guiding treatment choice in Denmark include age, frailty, comorbidities, tumour burden, response to prior therapy, and timing of relapse.[3, 47]

Relevance to Danish clinical practice

Danish guidelines list lenalidomide–rituximab–based therapy as a clinically equivalent option to rituximab-chemotherapy for symptomatic disease and as an option at relapse, with regimen selection individualized by tumour burden, frailty, and previous treatment exposure. The target population therefore aligns with current Danish practice patterns for R/R FL.[47]

Epidemiology and treatment patterns in Denmark

Between 2006 and 2023, the Danish Lymphoma Registry recorded 3,769 newly diagnosed FL patients, with a median follow-up of 6.4 years. Median age at diagnosis was 66 years with a balanced gender distribution. Most patients were diagnosed with advanced disease, with 69.9 percent in stage III–IV.[48]

In Europe, the incidence of FL is 2.2 cases per 100,000 persons (range in literature, 2.1-4.2); the prevalence is 44 per 100,000 persons.[49-52]

The incidence of FL patients from year 2020 to 2023 is taken from the Danish Lymphoma Database.[53] Since the incidence of 2024 is missing, we estimated the number by calculating the average yearly change in patients from 2020-2023 and adding this value to the 2023 count, resulting in an estimate of approximately 273 patients.

As no complete national FL prevalence is published in Danish registries, prevalence was estimated by applying the EU27 population-weighted complete prevalence of 4.66 per 10 000 individuals from the literature review (December 2023) to the Danish population. This yields approximately 2,560–2,620 living FL patients between 2020 and 2024. NORDCAN-based Nordic figures (4.06–4.76 per 10 000) provide consistent results and were used for cross-validation.

Table 1 Incidence and prevalence in the past 5 years

Year	2020	2021	2022	2023	2024
Incidence in Denmark	248	226	237	267	273*
Prevalence in Denmark	2,562	2,570	2,584	2,610	2,623
Global prevalence	≈ 3,520,000	≈ 3,570,000	≈ 3,620,000	≈ 3,670,000	≈ 3,720,000

Incidence [53]. Prevalence [49-52]: 44 / 100 000 × Danish population ≈ 2 560–2 620 living FL patients. Global prevalence: $8.1 \times 10^9 \times (44 / 100\,000) \approx 3.6$ million people worldwide living with FL.
*Estimated

In 2024, the total number of patients with FL was estimated at 273. Of these, 20% were managed with a watch-and-wait strategy only, 11% received radiotherapy without the need for subsequent systemic treatment, and 69% initiated first-line systemic therapy, corresponding to 188 patients. Among patients who started systemic treatment, 40% were estimated to proceed to second-line therapy, corresponding to 75 patients.[54] In addition, a limited number of patients are expected to be eligible for treatment in third or later lines. An additional 28 patients are therefore assumed to originate from later lines of therapy.

Table 2 Estimated number of patients eligible for treatment

Year	Year 1	Year 2	Year 3	Year 4	Year 5
Number of patients in Denmark who are eligible for treatment in the coming years	103	105	107	109	111

Overall, the number of patients expected to be treated with tafasitamab in combination with rituximab and lenalidomide is estimated to remain below [redacted] patients per year. This reflects the substantial heterogeneity in the management of relapsed or refractory follicular lymphoma, where treatment choice is highly individualized. As there is no single standard of care in the relapse setting, not all eligible patients will be considered for treatment with tafasitamab + R^2.

3.3 Current treatment options

The Danish guideline for FL [47] refers to the European Society of Medical Oncology (ESMO) guideline, and does not designate a single preferred regimen for patients with symptomatic relapse. Instead, it presents several first-choice options in parallel for symptomatic relapse, reflecting heterogeneity in patients and disease characteristics.

Treatment Guidance for Relapsed or Refractory Follicular Lymphoma

In the relapse setting, both immunochemotherapy options (R-bendamustine, R-CVP, R-CHOP) and chemo-free regimens (rituximab monotherapy and R^2) are treatment alternatives, and treatment selection guided by presence of symptoms, time to relapse following prior therapy, prior treatments, comorbidities, and anticipated tolerability. The guideline's change log further noted that chemo-free regimens now stand as equivalent choices relative to R-chemotherapy in both the primary and relapse sections, as confirmed through discussions with Nordic lymphoma experts.

In the relapse section [47], treatment choice is individualized and the guideline highlight the need for tailoring rather than use of a single default regimen.

For asymptomatic relapse, observation ("watch and wait") remains recommended until the disease becomes symptomatic in the relapse setting. This reflects that not all relapses require immediate treatment, and that treatment initiation should be driven by clinical need.

For symptomatic, lower-risk relapses, several options are considered clinically appropriate and broadly equivalent. Immunochemotherapy with R- bendamustine, R-CVP, or R-CHOP are established choices. Chemo-free options are explicitly included as alternatives, including rituximab monotherapy and R^2, particularly when chemotherapy is less suitable.

If rituximab resistance is suspected, for example response duration < 6 months, rituximab can be substituted with obinutuzumab in the R-chemo regimens. If rituximab maintenance was not administered in first line, maintenance every 3 months for up to 2 years can be considered. Selection is individualized by prior therapy, remission duration, comorbidities, age, and preferences.

For higher-risk relapse – including progression of disease within 24 months (POD24), repeated relapses with high FLIPI, or suspected transformation – clinical trial enrolment is prioritized. Treatment options include R-CHOP or induction per the DLBCL guideline, followed by high-dose therapy and autologous stem cell transplant when appropriate, possibly followed by 2 years of rituximab maintenance. Allogeneic transplant may be considered in selected younger patients with repeated relapses, chemo-refractory disease, or relapse after autologous transplant.

For frail patients or those requiring palliative scenarios, lower-intensity approaches are appropriate. Chlorambucil can be considered, and low-dose radiotherapy (2 Gy × 2) is an option in localized disease or when lymphoma burden is concentrated to a single site.

The guideline also highlights rapid developments in immunotherapy, noting updated data for anti-CD19 therapy such as tafasitamab, bispecific antibodies, and CAR-T, and emphasizes protocol participation where possible.

Overall, the Danish guideline supports an individualized approach to relapsed/refractory follicular lymphoma, in which chemo-free regimens are considered equivalent choices relative to immunochemotherapy in selected patients, based on symptoms, time to relapse, and treatment tolerability, consistent with ESMO guidance and Nordic lymphoma expert consensus.

Table 3 Danish recommendations for R/R FL (grade 1-3a)

Clinical situation	Recommended approach	Notes
Asymptomatic relapse	Watch and wait until symptomatic disease	Treatment timing should be need-driven.
Symptomatic relapse, lower-risk	R-bendamustine, R-CVP, R-CHOP	Established immunochemotherapy options.

	R^2 (rituximab + lenalidomide)	Chemo-free option listed as equivalent.
	Rituximab monotherapy	Chemo-free option listed as equivalent. Suggested schedule: 4 weekly + 4 every 2 months.
If suspected rituximab resistance	Substitute obinutuzumab in R-chemo regimens	Use when response duration was less than 6 months.
If no R-maintenance in 1L	Consider rituximab maintenance	Every 3 months for up to 2 years.
Symptomatic relapse, high-risk (for example POD24, repeated relapses with high FLIPI, transformation)	Clinical trial enrolment	Priority pathway.
	R-CHOP or DLBCL-style induction	Followed as appropriate by high-dose therapy and ASCT.
	ASCT ± subsequent rituximab maintenance	Up to 2 years of maintenance may be used.
	Allogeneic transplant	Consider for younger patients with repeated relapses, chemo-refractory disease, or relapse post-ASCT.
Frail or palliative scenarios	Chlorambucil	Lower-intensity option.
	Low-dose radiotherapy (2 Gy × 2)	For localized burden or predominantly single-site disease.
Position of chemo-free regimens	R^2 and rituximab monotherapy are on par with R-chemo	Explicitly stated in the latest update to the guideline.

Clinical Evidence Context

For 1L patients, RELEVANCE[55] showed similar response rates and PFS between R^2 and immunochemotherapy, with comparable safety at 6-year follow-up. This underlines the positioning of R^2 as an equivalent alternative when chemotherapy is less suitable, according to ESMO and reflected in Danish guideline structure.

For R/R FL patients, AUGMENT [35] and ALLIANCE [56] show higher response and significantly longer PFS for R^2 compared with rituximab monotherapy or lenalidomide monotherapy, without an OS difference. The guideline notes that no head-to-head comparison exists between R^2 and R-chemo in the relapsed setting and therefore recommends using R^2 particularly for lower-risk or for patients unsuitable for chemotherapy.

Bispecific antibodies and CAR-T show high ORR and complete response (CR) in heavily pretreated R/R FL, with acceptable safety, but longer follow-up is awaited.[57-59]

3.4 The intervention

Table 4 provides an overview of the intervention relevant for this submission, tafasitamab + R^2.

Table 4 Overview of the intervention

Overview of intervention	
Indication relevant for the assessment	Tafasitamab in combination with lenalidomide and rituximab for the treatment of adult patients with R/R FL (Grade 1-3a) after at least one line of systemic therapy.[1] No deviations from the EMA indication are anticipated for the Danish assessment.
ATMP	Not applicable
Method of administration	Tafasitamab: IV infusion Rituximab: IV infusion Lenalidomide: oral
Dosing	28-day cycles Tafasitamab 12 mg/kg IV on Days 1, 8, 15, 22 of Cycles 1–3, and Days 1 & 15 of Cycles 4–12; Lenalidomide 20 mg PO daily on Days 1–21 of Cycles 1–12; Rituximab 375 mg/m² IV on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 2–5.
Dosing in the health economic model (including relative dose intensity)	Dosing in the health economic model is aligned with the dosing regimen described above. The relative dose intensity (RDI) is 97.47% for cycle 1-3 and 80.89% for cycle 4-12 for tafasitamab, 79.71% for lenalidomide and 100% for cycle 1 and 94.18% for cycle 2-5 for rituximab.
Should the medicine be administered with other medicines?	Yes. Tafasitamab is administered with rituximab and lenalidomide (R^2)
Treatment duration / criteria for end of treatment	Combination dosing is defined for 12 cycles as above
Necessary monitoring, both during administration and during the treatment period	Standard lymphoma care monitoring applies infusion observation during IV administrations and routine haematology and infection surveillance during therapy
Need for diagnostics or other tests (e.g. companion diagnostics). How are these included in the model?	No companion diagnostic. InMIND eligibility required documented CD19+ and CD20+ expression on lymphoma cells, which is part of routine pathology in Denmark; cost as

Overview of intervention	
	standard of care rather than a separate companion test in the model
Package size(s)	1 × vial of powder containing 200 mg tafasitamab; after reconstitution, each mL contains 40 mg tafasitamab

Mechanism of action

Tafasitamab is an Fc-enhanced monoclonal antibody that potently binds to the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes.[60-62] CD19 is broadly and homogeneously expressed across B-cell malignancies, including DLBCL and FL. Upon binding to CD19, tafasitamab mediates B-cell lysis through:[60, 61, 63]

- Engagement of immune effector cells like natural killer (NK) cells, γδ T cells, and phagocytes
- Direct induction of cell death (apoptosis)

The Fc modification results in enhanced antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).

The combination regimen R^2 is an established, chemotherapy-free treatment for FL that has shown activity in 1L and second-line and later (2L+) settings.[36, 64-67] Lenalidomide, an immunomodulatory agent, has been shown to enhance NK cell-mediated ADCC and macrophage-mediated ADCP when combined with tafasitamab in vitro.[30, 62, 68, 69] CD20 targeting with rituximab is an established strategy for treating B-cell malignancies.[70] The addition of tafasitamab to R^2 resulting in dual targeting of CD19 and CD20 is a rational approach to improve efficacy and outcomes in patients with lymphoma; compared with each monotherapy, the combination of tafasitamab and rituximab improved in vitro and in vivo efficacy in models of aggressive B-cell lymphoma.[60]

3.4.1 Description of ATMP

N/A

3.4.2 The intervention in relation to Danish clinical practice

Place in the Danish treatment algorithm

In Denmark, symptomatic relapse of FL grade 1–3a is treated with several listed options. R-chemotherapy regimens (R-bendamustine, R-CVP, R-CHOP) and chemo-free options (rituximab monotherapy and R^2) are all recommended, with selection individualized to patient and disease factors. Tafasitamab + R^2 is expected to be used in the same setting as guideline-listed R^2, that is, in adults with R/R FL after at least one prior anti-CD20–containing regimen. This aligns with the Danish guideline structure, which presents multiple options for symptomatic relapse without specifying a single preferred standard.[47]

How current clinical practice will be altered

Tafasitamab + R^2 introduces a chemo-free treatment option within the existing R^2 branch of the relapse pathway. In practice, clinicians could consider the use of tafasitamab + R^2 for patients who would otherwise receive R^2 or, in some cases, R-chemotherapy to avoid chemotherapy related toxicities. This is in alignment with feedback from Nordic lymphoma experts from the advisory board. The core algorithm remains unchanged:

- asymptomatic patients continue with watch-and-wait,
- symptomatic relapse continues to be managed with one of several guideline-listed first-choice options.

Relation to comparator and sequences

The pivotal study inMIND compares tafasitamab + R^2 with placebo + R^2, mirroring Danish practice where R^2 is an accepted relapse option.[47] Introducing tafasitamab + R^2 therefore constitutes as a substitution within an existing treatment choice rather than creating a new line or altering upstream decision points such as watch-and-wait. Subsequent treatment options following tafasitamab + R^2 remain those used today after R^2 or R-chemotherapy, including chemotherapy, immunotherapy, radiotherapy, or CAR T-cell therapy, selected as clinically appropriate.

Administration and operational considerations

Administration uses existing IV infusion infrastructure. Dosing follows 28-day cycles with tafasitamab on Days 1, 8, 15, 22 in Cycles 1–3 and on Days 1 and 15 in Cycles 4–12, together with the standard R^2 schedule (rituximab on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 2–5; lenalidomide orally on Days 1–21 in Cycles 1–12). Compared with R^2 alone, the main operational difference is the additional tafasitamab infusion on Day 15 in Cycles 4–12.

Diagnostics and patient selection

No companion diagnostic is required. Routine Danish lymphoma workup includes CD20 expression and commonly CD19 as part of standard immunophenotyping; therefore, no additional diagnostic procedures or pathways are introduced by tafasitamab + R^2.

Summary

Within the Danish relapse algorithm that presents multiple suitable options, tafasitamab + R^2 is expected to serve as an additional chemo-free choice in the same position as R^2. It is anticipated to substitute for a proportion of patients who might otherwise receive R^2 or R-chemotherapy, according to clinical judgement, without altering the overall treatment sequence or introducing new diagnostic steps.

3.5 Choice of comparator(s)

As presented above, in Danish clinical practice there is no single established standard at symptomatic relapse of FL grade 1–3a; the guideline lists several first-choice options side by side, including R-chemotherapy regimens (R-bendamustine, R-CVP, R-CHOP) and chemo-free options (rituximab monotherapy and R^2), with selection individualized to patient and disease factors.[47] R^2 is presented as one of several guideline-listed treatment options, on par with R-chemotherapy in this setting.

R^2 is also the backbone comparator in the pivotal inMIND trial that evaluates tafasitamab + R^2 versus placebo + R^2, providing direct head-to-head evidence for the incremental effect of adding tafasitamab to R^2 in the current Danish practice. Therefore, R^2 is considered the most relevant comparator as it mirrors the evidence base and the part of the Danish pathway in which tafasitamab + R^2 would be used. In discussions at a recent advisory board with Danish and Nordic lymphoma experts, there was a strong consensus that R^2 is the best suitable comparator.

Because the Danish guideline presents several alternatives without identifying a single preferred regimen at relapse, the appropriate comparator shall reflect the regimen to which tafasitamab is added in clinical practice. Tafasitamab is administered in combination with R^2. Accordingly, comparing tafasitamab + R^2 with R^2 alone provides the clinically and methodologically valid estimate of incremental effect. Consequently, R^2 is included as the relevant comparator.

No off-label use is proposed for the comparator; R^2 is a recognized option in Danish relapse practice. The choice of R^2 does not alter upstream or downstream sequencing: tafasitamab + R^2 constitutes a substitution within the existing R^2 branch and subsequent therapies after progression remain those already used after R^2 or R-chemotherapy (chemotherapy, immunotherapy, radiotherapy, cellular therapies) according to clinical judgement.

Table 5 provides an overview of R^2.

Table 5 Overview of comparator

Overview of comparator	
Generic name	Rituximab + lenalidomide (R^2)
ATC code	Rituximab: L01FA01, Lenalidomide: L04AX04
Mechanism of action	Rituximab targets CD20 on B cells (established strategy in B-cell malignancies). Lenalidomide is an immunomodulatory agent; in vitro it augments NK-cell–mediated ADCC and macrophage-mediated ADCP when combined with tafasitamab.
Method of administration	Rituximab intravenously, lenalidomide orally.

Overview of comparator	
Dosing	Lenalidomide 20 mg orally once daily on Days 1–21 of each 28-day cycle for Cycles 1–12. Rituximab 375 mg/m² IV on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 2–5.
Dosing in the health economic model (including relative dose intensity)	Model uses the same schedule. Base-case RDI assumptions from the CE model: lenalidomide RDI 84.16% (Cycles 1–12); rituximab RDI 100% in Cycle 1 and 94.18% in Cycles 2–5.
Should the medicine be administered with other medicines	The comparator is a two-drug combination (rituximab + lenalidomide). According to the Danish treatment guidelines and the Summary of Product Characteristics (SmPC) for lenalidomide Accord (which is approved in combination with rituximab for FL), no additional mandated co-medications are required as part of this regimen.[37, 71]
Treatment duration/ criteria for end of treatment	Rituximab completes at the end of Cycle 5 and lenalidomide completes at the end of Cycle 12 (no continuation beyond 12 cycles in the R^2 comparator arm).
Need for diagnostics or other tests (i.e. companion diagnostics)	No companion diagnostic is specified for R^2. Standard Danish pathology (including CD20 immunophenotyping) is routine.
Package size(s)	Lenalidomide (Tablet): 2.5 mg, 5 mg, 10mg, 20 mg Rituximab (10 mg/ml): 10 ml, 50 ml

In relapsed follicular lymphoma, treatment choice shall be considered not only in terms of short-term efficacy but also with regard to its impact on subsequent treatment options. Earlier disease progression following less effective therapy may necessitate earlier use of more resource-intensive or toxic treatments and may shorten the interval to later lines of therapy. In a disease characterized by long survival and multiple sequential treatments, postponement of disease progression and delay of the next treatment line represent clinically relevant benefits in themselves. By extending PFS and time to next treatment compared with R^2 alone, tafasitamab + R^2 has the potential to optimize treatment sequencing by preserving future options and reducing the cumulative burden associated with earlier relapse.

3.6 Cost-effectiveness of the comparator(s)

The comparator, R^2, has not been previously evaluated by DMC. However, R^2 is a recognized treatment option in Danish clinical practice and is listed in the national guideline for FL grade 1–3a, alongside R-chemotherapy and rituximab monotherapy in the relapsed setting.[37] According to the DMC methods guideline, when a comparator has not previously been assessed by the DMC, comparative evidence against placebo

should be made, including cost-effectiveness. In R/R FL, placebo or "watch and wait" is not a clinically relevant treatment option, as active treatment is required for patients with symptomatic relapse in Danish clinical practice. Nevertheless, the pivotal inMIND trial provided head-to-head comparison of tafasitamab + R^2 vs placebo + R^2 in R/R FL patients, allowing estimation of the relative efficacy between both treatments. Accordingly, placebo + R^2 data from inMIND trial are used to inform the comparator arm in the model, as this represents the available randomized evidence for R^2 in this patient population.

3.7 Relevant efficacy outcomes

3.7.1 Definition of efficacy outcomes included in the application

The efficacy outcomes used in this application are summarized in Table 6. In inMIND, the pivotal trial for tafasitamab + R^2, the primary, key secondary and additional secondary outcomes include:

- The primary outcome is PFS by IA in the FL Full Analysis Set (FAS) population
- Key secondary outcome is the OS in the FL FAS population
- Additional prespecified secondary outcome is PFS by IRC in the FL FAS population

These outcomes are considered both relevant and necessary to evaluate the effect of tafasitamab + R^2 vs placebo + R^2, reflecting international and Danish practice for R/R FL. For the base-case analysis in the health economic model , PFS by IRC is used, as the blinding in the assessment of PFS reduces the potential for assessment bias compared with PFS by IA.[72] Other outcomes from the inMIND trial are presented in Appendix B.

Table 6 Efficacy outcome measures relevant for the application

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
Progression-free survival (PFS) by IA, FL FAS inMIND [10]	From progression until PD, or death (whichever comes first). Median follow-up times are 14.3 and 14.1 months respectively for the intervention and comparator arm	Time from randomization to first documented disease progression (Lugano 2014) or death from any cause, whichever occurs first.	IA using computed tomography (CT), positron emission tomography (PET) or PET-CT (for FDG-avid disease), or magnetic resonance imaging (MRI) if CT contraindicated; analysed with stratified log-rank and Cox PH model.

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
Overall survival (OS), FL FAS inMIND [10]	Median follow-up time: 15.3 months	Time from randomization to death from any cause.	Vital status via study follow-up; analysed with Kaplan–Meier, stratified log-rank, and stratified Cox PH model.
Progression-free survival (PFS) by IRC, FL FAS inMIND [10]	From progression until PD, or death (whichever comes first). Median follow-up times are 14.3 and 14.1 months respectively for the intervention and comparator arm	Time from randomization to first documented disease progression (Lugano 2014) or death from any cause, whichever occurs first	Responses are reviewed by an IRC per charter

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

Validity of outcomes

The efficacy outcomes measured in the inMIND trial – PFS-IA, PFS-IRC, and OS – are internationally recognized and validated endpoints for indolent NHL, including FL. These endpoints have been accepted by the EMA and Food and Drug Administration (FDA) for prior FL approvals and have been used consistently in previous DMC assessments of treatments for lymphoma.

PFS has been accepted as a clinically relevant and appropriate efficacy measure in previous DMC assessments of lymphoma therapies, including obinutuzumab + bendamustine[73] and mosunetuzumab [74, 75]. The use of IRC-assessed PFS is aligned with the EMA guidance, which states that the standardized and objective assessment methods, including independent verification or central review of progression and response endpoints, support robust and consistent efficacy evaluation in oncology trials.[76]

OS is a universally recognized efficacy endpoint in oncology and is routinely included in clinical trials of FL. In indolent FL, OS is typically immature at interim analyses because patients have long natural survival and often receive multiple effective subsequent therapies. This pattern has been consistently observed in pivotal FL trials such as RELEVANCE [55] and AUGMENT [77] where substantial PFS improvements occurred while OS remained immature at primary read-outs. EMA regulatory assessments for FL therapies (including variation assessments for obinutuzumab [78]) similarly note that OS data are insufficiently mature for firm conclusions and that PFS constitutes the primary evidence of clinical benefit in indolent FL.

All efficacy endpoints included in the trial—PFS-IA, PFS-IRC, and OS—are validated, internationally accepted, and consistent with outcome measures previously endorsed by the DMC for decision-making in FL and other indolent lymphomas.

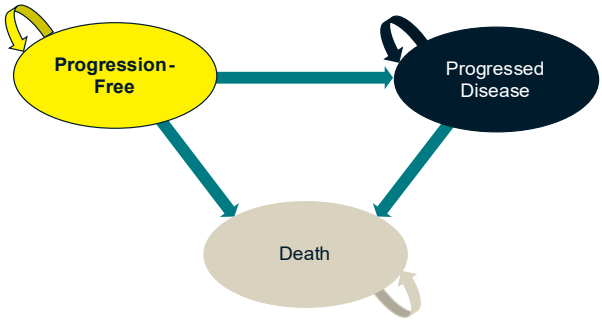
4. Health economic analysis

Submitted alongside this application is the cost-effectiveness model (CEM) assessing the cost-effectiveness of tafasitamab + R^2 as a treatment for R/R FL who had received at least one line of systemic therapy.

4.1 Model structure

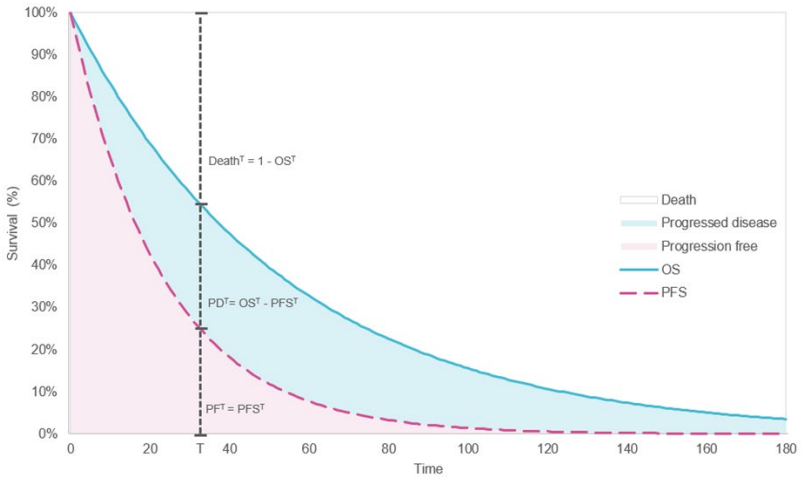
A three-state partitioned survival model was developed to estimate the economic value of tafasitamab + R^2 for the treatment of R/R FL in patients who had received at least one line of systemic therapy, compared to R^2 alone (Figure 1).

Figure1: Model diagram



All patients enter the model in the progression-free (PF) health state, where it is assumed that they receive tafasitamab + R^2 or R^2. During each cycle, patients may remain in the PF state, progress or die. Patients who have progressed may remain alive within the progressed disease (PD) state and receive subsequent treatment or die, with death being the absorbing state. In the PF and PD states, patients are either on or off treatment. All health states in the model are mutually exclusive. The partitioned survival analysis uses fitted PFS and OS curves to calculate a health state's occupancy at a given time using the area under the curve approach (Figure 2).

Figure 2: Health state occupancy at time T



Abbreviation: OS, overall survival; PD, progressed disease; PF(S), progression-free (survival).

To inform the cost-effectiveness analysis of tafasitamab + R² in R/R FL, the CEM utilized data from clinical trials, real-world evidence and relevant published literature. The model compares the costs and health outcomes of tafasitamab + R² with those of R². A targeted review of FL technology appraisals (TAs) submitted to the UK National Institute for Health and Care Excellence (NICE) was performed to inform model structure and key assumptions (TA604 [79], TA627 [80] TA629 (CDF review of TA472) [81], TA892 [82], TA894 [83]). For the Danish context, the national Danish clinical guidelines [47] were considered. Additionally, input from Danish clinical experts with experience in the management of R/R FL patients was obtained. These clinical experts agreed that R² presents a relevant comparator in the Danish setting. The clinical experts further indicated that tafasitamab + R² is considered as an improved treatment option compared with R² alone, and that the patient population enrolled in inMIND study [10] is more reflective of real-world Nordic clinical practice that that of the AUGMENT study.

In line with standard modelling practice and DMC methodological requirements, the following adjustments were applied:

- Mortality risk in each model cycle is capped at age-matched general population mortality, sourced from the latest available "Key figures including general mortality within the Danish population" in Medicinrådet.[84]
- Health state utility values (HSUV) were derived from EQ-5D-5L data collected in the inMIND trial, with utilities calculated using Danish EQ-5D-5L preference weights [11], in accordance with DMC stated methodological preference.

Consistent with best practice guidance on developing CEMs, including NICE Decision Support Unit (DSU) Technical Support Documents (TSD) [85-88], the partitioned survival modelling framework was selected after reviewing the literature and considering each of the following factors:

- Partitioned survival models are widely used in oncology modelling. Previous UK appraisals in FL [80-83] have also employed partitioned survival models to estimate clinical benefits in terms of delaying disease progression, delaying time to next treatment, and improvement in OS, as observed in inMIND
- Partitioned survival models allow the proportion of patients in each health state to be defined directly by the individual survival curves (OS, PFS, TTD) extrapolated from the trial data
- Partitioned survival models allow for considerable flexibility in incorporating long-term extrapolations of efficacy outcomes, and for performing scenario analysis to address uncertainty

The model was developed in Microsoft Excel for Office 365 in Microsoft Windows.

4.2 Model features

The model features are summarized in Table 7.

Table 7 Features of the economic model

Model features	Description	Justification
Patient population	Adult patients with R/R FL (Grade 1-3a) after at least one line of systemic therapy	In alignment with Section 3.2.
Perspective	Limited societal perspective	According to DMC guidelines [89]
Time horizon	Lifetime (40 years)	Sufficiently long to capture all health benefits and costs; in line with DMC guidelines. Based on a mean age of 64 years in inMIND.
Cycle length	7 days (1 week)	The cycle length is short enough to accurately capture key clinical outcomes, as well as to allow accurate estimation of drug acquisition and administration costs over time.
Half-cycle correction	No	Given the relatively short model cycle of 7 days, half-cycle correction is not necessary, as the timing bias is deemed negligible.
Discount rate	3.5 %	According to DMC guidelines [89]

Model features	Description	Justification
Intervention	Tafasitamab (Minjuvi) + R^2 (lenalidomide + rituximab)	
Comparator(s)	R^2 (lenalidomide + rituximab)	According to Danish treatment guideline [90] and in agreement with Danish clinical experts
Outcomes	OS, PFS, TTD	Relevant outcomes for R/R FL, commonly used and widely accepted for hematology and oncology modelling.

Abbreviations: DMC, Danish Medicines Council; FL, Folate receptor; PFS, Progression-free survival; OS, Overall survival; TTD, time to treatment discontinuation.

5. Overview of literature

Systematic literature reviews (SLRs) were conducted to identify and assess published evidence on clinical efficacy, safety, health-related quality of life (HRQoL), epidemiology, and economic outcomes in adult patients with R/R FL following prior anti-CD20 therapy.

The SLRs were undertaken according to PRISMA standards and NICE/Cochrane methodology, covering Embase, MEDLINE, and Cochrane databases, congress abstracts, HTA repositories, and relevant registries. These reviews confirmed that the Phase 3 inMIND study is the only available randomized, head-to-head trial comparing tafasitamab with R^2 with placebo + R^2, and that no additional head-to-head or indirect comparative data of sufficient quality are available.

Consequently, all comparative efficacy and HRQoL data included in this submission are derived from the inMIND trial, while the SLRs provide the broader contextual evidence base and verification that inMIND represents the most robust source of comparative data relevant to Danish clinical practice.

Therefore, although systematic literature searches were performed, the comparative analyses presented in this section are based exclusively on data from the inMIND randomized controlled trial. In the cost-utility model, health state utility values were also exclusively informed by the head-to-head study, but disutility values were stemming from the literature and are described in Section 5.2.

5.1 Literature used for the clinical assessment

The inMIND phase III trial constitutes the primary clinical evidence used in the assessment, underpinning the evaluation of relative efficacy and safety of tafasitamab plus R^2 compared with R^2 in the target population (Table 8 Relevant literature included in the assessment of efficacy and safety

).

Table 8 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
Sehn LH, Hübel K, Luminari S, Scholz CW, Salar A, Paneesha S, Wahlin BE, Panayiotidis P, Lee HP, Jiménez Ubieto A, Sancho JM, Kim TM, Domingo Domenech E, Kumode T, Poh C, Thieblemont C, Deeren D, de Wit E, Arbushites M, Casadebaig M, Trněný M, et al. Tafasitamab, lenalidomide, and rituximab in relapsed or refractory follicular lymphoma (inMIND): a global, phase 3, randomised controlled trial. Lancet. 2026 Jan 10;407(10524):133–146. doi:10.1016/S0140-6736(25)01778-7. [10]	InMIND	NCT04680052	Start date: 2021.04.15 Primary completion: 2024.02.23 Data cut-off: 2024.02.23 Estimated completion: 2028.08.09	Tafasitamab plus R^2 versus R^2 in patients with R/R FL Grade 1 to 3a

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

Health state utility values are derived from inMIND head-to-head data; therefore, no literature search was performed. Disutility values used in the health economic model were derived from various published literature sources, which are identified through a targeted literature search. Table 8 summarized the literature sources used for disutilities.

Table 9 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
Swinburn P, Lloyd A, Nathan P, et al. Elicitation of health state utilities in metastatic renal cell carcinoma. *Curr Med Res Opin*. 2010; 26(5):1091-6 [91]	Disutility for anaemia and leukopenia	Section 10.3
Sullivan PW, Slejko JF, Sculpher MJ and Ghushchyan V. Catalogue of EQ-5D scores for the United Kingdom. Med Decis Making. 2011; 31(6):800-4 [92]	Disutility for confusional state and headache	
Halpin S, O'Connor R and Sivan M. Long COVID and chronic COVID syndromes. J Med Virol 2020; 93(3):1242[93]	Disutility for COVID-19 and COVID-19 pneumonia	
Nafees B, Stafford M, Gavriel S, et al. Health state utilities for non small cell lung cancer. Health Qual Life Outcomes. 2008; 6:84 [94]	Disutility for diarrhoea, nausea, and neutropenia	
Doyle S, Lloyd A and Walker M. Health state utility scores in advanced non-small cell lung cancer. Lung Cancer. 2008; 62(3):374-80 [95]	Disutility for dyspnoea and hypoxia	
Nafees B, Stafford M, Gavriel S, et al. Health state utilities for non small cell lung cancer. Health Qual Life Outcomes. 2008; 6:84 [94]	Disutility for fatigue	
Lloyd A, Nafees B, Narewska J, et al. Health state utilities for metastatic breast cancer. Br J Cancer. 2006; 95(6):683-90 [96]	Disutility for febrile neutropenia	

Reference (Full citation incl. reference number)	Health state/Disutility	Reference to where in the application the data is described/applied
Hannouf MB, Sehgal C, Cao JQ, et al. Cost-effectiveness of adding cetuximab to platinum-based chemotherapy for first-line treatment of recurrent or metastatic head and neck cancer. *PLoS One*. 2012; 7(6):e38557 [97]	Disutility for hypertension and hypotension	
Tolley K, Goad C, Yi Y, et al. Utility elicitation study in the UK general public for late-stage chronic lymphocytic leukaemia. *Eur J Health Econ*. 2013; 14:749-59 [98]	Disutility for infection and infusion related reaction	
Stein EM, Yang M, Guerin A, et al. Assessing utility values for treatment-related health states of acute myeloid leukemia in the United States. *Health Qual Life Outcomes*. 2018; 16:193 [99]	Disutility for lymphopenia, neutrophil count decreased, and white blood cell count decreased	
Sullivan PW, Slejko JF, Sculpher MJ and Ghushchyan V. Catalogue of EQ-5D scores for the United Kingdom. Med Decis Making. 2011; 31(6):800-4 [92]	Disutility for neurological events	
Doyle S, Lloyd A and Walker M. Health state utility scores in advanced non-small cell lung cancer. *Lung Cancer*. 2008; 62(3):374-80 [95]	Disutility for pleural effusion and rash	
Hannouf MB, Xie B, Brackstone M and Zaric GS. Cost-effectiveness of a 21-gene recurrence score assay versus Canadian clinical practice in women with early-stage estrogen- or progesterone-receptor-positive, axillary lymph-node negative breast cancer. *BMC Cancer*. 2012; 12:1-15 [100]	Disutility for sepsis	

Reference (Full citation incl. reference number)	Health state/Disutility	Reference to where in the application the data is described/applied
Matza LS, Deger KA, Vo P, et al. Health state utilities associated with attributes of migraine preventive treatments based on patient and general population preferences. Qual Life Res. 2019; 28(9):2359-72 [101]	Disutility for syncope	
Armstrong N, Vale L, Deverill M, et al. Surgical treatments for men with benign prostatic enlargement: cost effectiveness study. *BMJ*. 2009; 338:b1288 [102]	Disutility for urinary tract infection	

5.3 Literature used for inputs for the health economic model

An economic SLR was conducted, however, there is currently a lack of published literature on the socio-economic burden of R/R FL that can inform the resource use inputs of the economic model, and therefore, a real-world study commissioned by Incyte included HCRU among R/R FL patients in England, was used in the health economic model. In addition, previous HTA assessments were evaluated and considered to bring relevant, previously HTA accepted inputs to the model. The data sources, targeted population, methods and study design of real-world study are further described in Appendix K.

Table 10 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
BILY RWE study	HCRU frequency	Real-world evidence study	Section 10.3.4

6. Efficacy

6.1 Efficacy of tafasitamab + R^2 compared to R^2 for R/R FL Grade 1–3a patients

6.1.1 Relevant studies

The comparative clinical evidence for tafasitamab + R^2 versus placebo + R^2 is based on the randomized, double-blind, placebo-controlled Phase 3 inMIND trial (INCMOR 0208-301; NCT04680052).[103]

The inMIND study enrolled adult patients (≥ 18 years) with R/R FL Grade 1–3a or R/R MZL who had received at least one prior systemic anti-CD20 therapy and had documented $CD19^+/CD20^+$ expression. The trial randomised patients 1:1 to receive tafasitamab 12 mg/kg IV or placebo on a 28-day schedule, both in combination with lenalidomide 20 mg orally (Days 1–21 of each cycle, up to 12 cycles) and rituximab 375 mg/m² IV (Days 1, 8, 15, 22 in Cycle 1, then Day 1 of Cycles 2–5).

In inMIND trial, the primary endpoint was PFS by IA in the FL population (Lugano 2014 criteria). Key secondary endpoints were PFS in the overall population (FL + MZL), PET-CR rate in FDG-avid FL, and OS in FL. Patient-reported outcomes (EQ-5D-5L, EORTC QLQ-C30, Functional Assessment of Cancer Therapy-Lymphoma [FACT-Lym]) were collected as exploratory endpoints. In this application, the relevant patient population are those with FL, and the relevant outcomes include PFS-IA, PFS-IRC and OS. All other endpoints are presented in Appendix B.

All data included in this application originate from the pre-defined data cut of 23 February 2024, representing the latest analysis submitted to EMA for regulatory review. The median duration follow-up for PFS was 14.3 months (95 % CI: 11.8–15.0). The data cut was pre-specified in the statistical analysis plan.

Table 11 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
INCMOR 0208-301 (inMIND), NCT04680052 (Clinical Study Report synopsis dated 03 Dec 2024; data cut 23 Feb 2024)	Randomized, double-blind, placebo-controlled, multicenter, Phase 3 trial comparing tafasitamab + lenalidomide + rituximab (R^2) versus placebo + R^2 in R/R FL Grade 1–3a and R/R MZL. Stratified by prior lines, POD24, and anti-CD20 refractoriness (FL); prior lines (MZL).	Study period: 16 Apr 2021 to 23 Feb 2024 (predefined data cut). Treatment period up to 12 cycles of 28 days, plus follow-up up to 5 years post-end of treatment (EOT). Total duration per participant up to ~6 years.	Adults ≥18 y with histologically confirmed R/R FL Grade 1–3a or R/R MZL after ≥1 prior systemic anti-CD20 therapy, with CD19+ and CD20+ tumor expression. The FL population is a predefined population in the protocol and is the primary analysis set for PFS. Randomized FL n=548 (273 tafasitamab + R^2; 275 placebo + R^2). Sites included Denmark and other countries.	Tafasitamab 12 mg/kg IV Days 1, 8, 15, 22 Cycles 1–3; Days 1, 15 Cycles 4–12 + lenalidomide 20 mg PO Days 1–21 Cycles 1–12 + rituximab 375 mg/m² IV Days 1, 8, 15, 22 Cycle 1; Day 1 Cycles 2–5.	Placebo IV on same schedule + lenalidomide 20 mg PO Days 1–21 Cycles 1–12 + rituximab 375 mg/m² IV Days 1, 8, 15, 22 Cycle 1; Day 1 Cycles 2–5.	Primary endpoint (FL): PFS by investigator per Lugano 2014. Key secondary: PFS (overall FL+MZL), PET-CR in FDG-avid FL, OS in FL. Additional secondary: PET-CR (overall), Minimal residual disease (MRD)-negativity at EOT, ORR, DoR, OS (overall), PFS/ORR/DoR by IRC, HRQoL (EORTC QLQ-C30, EQ-5D-5L, FACT-Lym), safety. Exploratory: Time to next treatment (TTNT), PFS2, subgroup analyses including POD24 and biomarker-defined groups. Median follow-up time: PFS (by IA and by IRC) is 14.3 and 14.1 months for the intervention and comparator arm. OS is 15.3 months.

6.1.2 Comparability of results

Not applicable; the comparison is based on a single randomized, double-blind, head-to-head study (inMIND). No cross-study comparison or evidence synthesis was therefore performed.

6.1.2.1 Comparability of patients across studies

In the inMIND trial, a total of 654 patients (548 with FL and 106 with MZL) were enrolled and randomized in the Overall Population, with the full sample analysed for efficacy, and 652 patients (546 with FL and 106 with MZL) analysed for safety.[103] Two patients randomized to the placebo + R^2 group were not included in the Safety Population because they did not receive study treatment due to confirmation of rituximab hypersensitivity, and withdrawal from the study.[103] The primary population of inMIND is the FL FAS population (n=548) and the primary endpoint of the trial is assessed exclusively in this population. Accordingly, this submission focuses on the FL FAS population, which is considered the relevant population for the assessment.[104, 105]

Table 12 describes the baseline characteristics of the patients included in the comparative analysis (FL FAS) as well as the overall population, to facilitate a comparison between the full population and FL FAS.

Table 12 Baseline characteristics of patients in studies included for the comparative analysis of efficacy and safety

	FL FAS (n=548)		Overall (n=654)	
	Tafasitamab + R^2 (N = 273)	**Placebo + R^2 (N = 275)**	**Tafasitamab + R^2 (N = 326)**	**Placebo + R^2 (N = 328)**
Region, n (%)				
North America	38 (13.9)	24 (8.7)	43 (13.2)	26 (7.9)
Europe	176 (64.5)	193 (70.2)	214 (65.6)	231 (70.4)
Rest of the world	59 (21.6)	58 (21.1)	69 (21.2)	71 (21.6)
Median age, years (range)	64.0 (36, 88)	64.0 (31, 85)	66.0 (30, 88)	66.0 (29, 87)
Male sex, n %	150 (54.9)	149 (54.2)	176 (54.0)	176 (53.7)
Race, n (%)				
White	219 (80.2)	219 (79.6)	262 (80.4)	260 (79.3)
Black or African American	1 (0.4)	0 (0.0)	1 (0.3)	1 (0.3)
Asian	40 (14.7)	42 (15.3)	47 (14.4)	48 (14.6)
Other	2 (0.7)	4 (1.5)	2 (0.6)	4 (1.2)
Not reported	11 (4.0)	10 (3.6)	14 (4.3)	14 (4.3)
ECOG score at screening visit, n (%)				

0	181 (66.3)	192 (69.8)	212 (65.0)	222 (67.7)
1	85 (31.1)	75 (27.3)	104 (31.9)	96 (29.3)
2	7 (2.6)	8 (2.9)	10 (3.1)	10 (3.0)
Time since initial diagnosis, years median (range)	5.2 (0, 34)	5.5 (1, 33)	-	-
FL grade at study entry, n (%)				
Grade 1	61 (22.3)	51 (18.5)	-	-
Grade 2	142 (52.0)	152 (55.3)	-	-
Grade 3a	67 (24.5)	71 (25.8)	-	-
Missing	3 (1.1)	1 (0.4)	-	-
Ann Arbor stage at study entry, n (%)				
Stage I	10 (3.7)	13 (14.7)	-	-
Stage II	42 (15.4)	37 (13.5)	-	-
Stage III	72 (26.4)	63 (22.9)	-	-
Stage IV	149 (54.6)	162 (58.9)	-	-
Bone marrow involvement at study entry, n (%)				
Bone marrow involvement, n (%)	66 (24.2)	65 (23.6)	-	-
POD24, n (%)	85 (31.1)	88 (32.0)	-	-
R/R status to the most recent prior therapya, n (%)				
Relapsed	148 (54.2)	164 (59.6)	-	-
Refractory	112 (41.0)	97 (35.3)	-	-
Indeterminate[b]	13 (4.8)	14 (5.1)	-	-
Refractory to prior anti-CD20 therapy, n (%)	118 (43.2)	115 (41.8)	-	-
FLIPI score at study entry, n (%)				
Low (0-1)	57 (20.9)	57 (20.7)	-	-
Intermediate (2)	79 (28.9)	67 (24.4)	-	-
High (≥ 3)	137 (50.2)	150 (54.5)	-	-
Missing	0 (0.0)	1 (0.4)	-	-

GELF criteria	222 (81.3)	232 (84.4)	-	-
B symptoms, n (%)	63 (23.1)	67 (24.4)	-	-

*Lugano Modification of Ann Arbor Staging System identifies the specific location and extent of lymphoma in the body. Abbreviations: **R²:** rituximab plus lenalidomide; **ECOG:** Eastern Cooperative Oncology Group; **PS:** performance status; **FL FAS:** Follicular Lymphoma Full Analysis Set; **FLIPI:** Follicular Lymphoma International Prognostic Index; **L:** line of therapy; **R/R:** Relapsed or Refractory; **POD24:** progression of disease within 24 months after initial diagnosis. References: Incyte. Data on file: Clinical Study Report (2024) [105]

6.1.3 Comparability of the study population(s) with Danish patients eligible for treatment

Table 12 summarizes information of characteristics in the relevant population in Danish clinical practice and the values used in the health economic model. Baseline patient characteristics applied in the model, including age, patient weight, body surface area (BSA), and sex applied in the model were derived from the inMIND trial.[105, 106] Based on clinical expert input, the inMIND study population is considered comparable to the Danish patients who are potentially eligible for treatment.

External validity to Denmark is supported by the conduct of inMIND at Nordic/Danish sites (Denmark n = 4; Sweden n = 6; Norway n = 5; Finland n = 11 among 548 FL patients), and by stratified randomization on key prognostic factors relevant in Danish practice (POD24; anti-CD20 refractoriness; number of prior lines). Baseline characteristics in the FL FAS population show median age in the mid-60s, ~55% males, ECOG 0–1 in ~68%, Ann Arbor stage III/IV in ~81%, and FLIPI high-risk in ~52%, which are consistent with observational Danish FL cohorts at diagnosis (median age ≈ 63 years; male ≈ 52%; FLIPI distribution reported) though Danish registry reporting for POD24 and anti-CD20 refractoriness at relapse is limited publicly.

Where Danish registry values were not identified, the model used the inMIND FL FAS distributions as the best available proxy. HRQoL inputs were sourced directly from the EQ-5D-5L data collected in the inMIND clinical trial [107] and derived using the Danish preference weights from Jensen et al (2011).[11]

Table 13 Characteristics in the relevant Danish population and in the health economic model

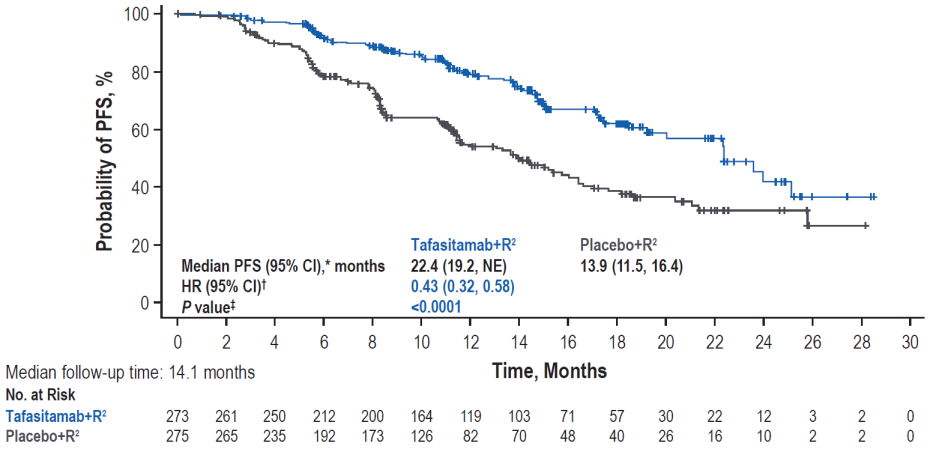
	Value in Danish population (reference)	Value used in health economic model (inMIND study [105, 106])
Age		XXXX (mean value)
Gender (male)		XXXX % male
Patient weight (mean, kg)		XXXX
Weight (SD)		XXXX
Mean BSA (mg/m2)		XXXX
BSA (SD)		XXXX

6.1.4 Efficacy – results per inMIND (INCMOR 0208-301)

Primary endpoint: PFS by IA

The primary endpoint of inMIND, PFS by IA in the FL FAS population, was met. At a median follow-up of 14.1 months there was a statistically significant difference in PFS between the treatment groups, with an estimated HR of 0.43 (95% CI, 0.32-0.58; p<0.0001). The estimated median PFS was 22.4 months (95% CI, 19.2-not evaluable [NE]) in the tafasitamab + R^2 group vs 13.9 months (95% CI, 11.5-16.4) in the placebo + R^2 group (Figure 3).[10] The estimated PFS rate at 18 months was [redacted] % (95% CI, [redacted]) in the tafasitamab + R^2 group and [redacted] % (95% CI [redacted], [redacted]) in the placebo + R^2 group.[103] At the time of analysis, 198 [72.5%] and 144 [52.4%] participants were censored in the tafasitamab + R^2 and placebo + R^2, respectively. In the tafasitamab + R^2 arm, censoring was due to ongoing follow-up (174 [63.7%]), initiation of new antilymphoma therapy (13 [4.8%]), no postbaseline assessment (6 [2.2%]), and study discontinuation (5 [1.8%]). In the placebo + R^2 arm, censoring was due to ongoing follow-up (121 [44.0%]), initiation of new antilymphoma therapy (13 [4.7%]), no postbaseline assessment (6 [2.2%]), study discontinuation (3 [1.1%]), and death or progression after ⩾2 missed assessments (1 [0.4%]).

Figure3 Kaplan–Meier Estimates of Progression-Free Survival by IA (FL FAS)



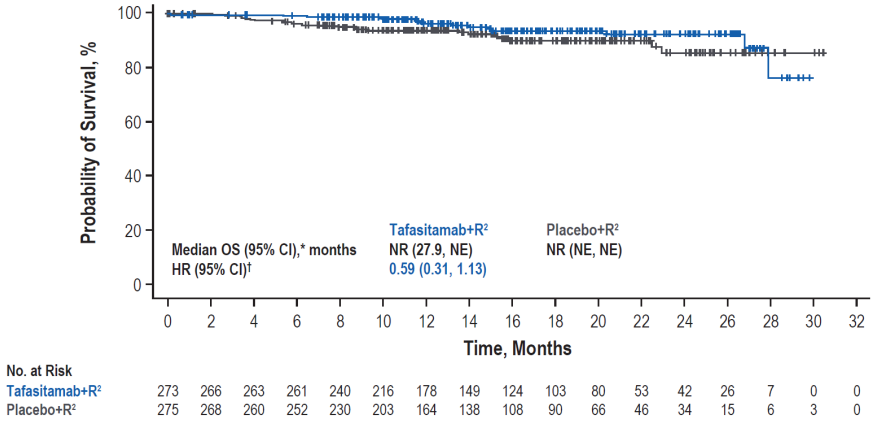
Source: Sehn et al. (2026).[10]

Abbreviations: CI, confidence interval; FAS, full analysis set; FL, follicular lymphoma; HR, hazard ratio; NE, not evaluable; PFS, progression-free survival; R^2, rituximab + lenalidomide.

Key secondary endpoint: OS

The predefined boundary for the nonbinding interim futility analysis for OS in the FL population (HR >1.24) was not reached, with an estimated HR of 0.59 (95% CI, 0.31-1.13).[10] These results suggest that there is no detriment to OS in the tafasitamab + R^2 group compared with the placebo + R^2 group. Moreover, preliminary OS data suggest a favorable trend toward improved survival in the tafasitamab + R^2 group compared with the placebo + R^2 group (Figure 4).[10] At the time of analysis, 258 (94.5%) and 252 (91.6%) participants were censored in the tafasitamab + R^2 and placebo + R^2, respectively. In the tafasitamab + R^2 arm, participants being last known alive (244 [89.4%]), with a smaller proportion due to study discontinuation (14 [5.1%]). In the placebo + R^2 arm, most censoring was likewise attributable to participants being last known alive (229 [83.3%]), while 23 [8.4%] were censored due to study discontinuation.

Figure4: Kaplan–Meier Estimates of OS (FL FAS)



Source: Sehn et al. (2024).[10]
Abbreviations: CI, confidence interval; FAS, full analysis set; FL, follicular lymphoma; HR, hazard ratio; NE, not evaluable; NR, not reported; OS, overall survival;. R^2, rituximab + lenalidomide.

OS data are still maturing, and the estimated median OS was not reached in the tafasitamab + R^2 group (95% CI, 27.9-NE) or in the placebo + R^2 group (95% CI, NE-NE). A low proportion of patients had died as of the data cutoff date, including 5.5% in the tafasitamab + R^2 group and 8.4% in the placebo + R^2 group. Most patients were censored as ongoing as of the data cutoff date (89.4% and 83.3%, respectively). At two years, the OS rate was [redacted] % (95% CI, [redacted]) vs [redacted] % (95% CI, [redacted]).[103]

As expected in an indolent lymphoma with long post-progression survival and multiple effective subsequent treatment options, overall survival data from the inMIND study are currently immature. This uncertainty does not reflect a lack of treatment effect but rather the underlying disease biology and study context. In follicular lymphoma, improvements in progression-free survival and durable response have repeatedly been accepted as clinically relevant indicators of benefit, as overall survival differences may only emerge after prolonged follow-up or may be confounded by effective post-progression therapies. The totality of evidence for tafasitamab + R^2 demonstrates consistent improvements across clinically meaningful endpoints, and overall survival will continue to be followed as planned in the ongoing study follow-up.

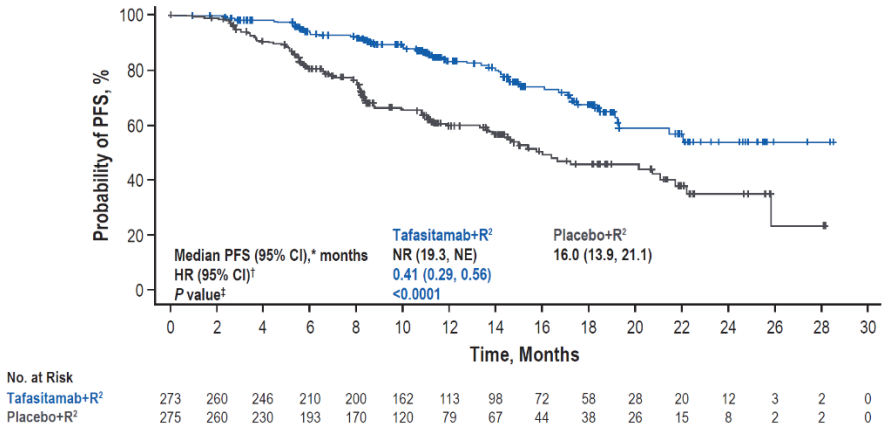
Hierarchical inferential statistical testing of OS will be performed at the time of final analysis after the end of the study, which is expected when the last patient has completed a minimum of 5 years of posttreatment follow-up.[10]

Additional secondary endpoint: PFS by IRC

Results for PFS by IRC review were consistent with PFS by IA, with an estimated HR of 0.41 (95% CI, 0.29-0.56) for the treatment effect between the tafasitamab + R^2 and placebo + R^2 groups (Figure 5). The estimated median PFS was not reached (95% CI, 19.3-NE) in the tafasitamab + R^2 group and was 16.0 months (95% CI, 13.9-21.1) in the placebo + R^2 group.[10]

The estimated PFS rate at 18 months was [redacted] % (95% CI, [redacted]) in the tafasitamab + R^2 group and [redacted] % (95% CI, [redacted]) in the placebo + R^2 group.[103] At the time of analysis, 214 [78.4%] and 164 [59.6%] participants were censored in the tafasitamab + R^2 and placebo + R^2, respectively.

Figure5 Kaplan–Meier estimates of PFS by IRC (FL FAS)



Source: Sehn et al. (2024).[10]
Abbreviations: CI, confidence interval; FAS, full analysis set; FL, follicular lymphoma; HR, hazard ratio; NE, not evaluable; NR, not reported, PFS, progression-free survival; R^2, rituximab + lenalidomide.

The higher rate of PET-confirmed complete responses (PET-CR) observed with tafasitamab + R^2 reflects deeper disease control, which is clinically meaningful in an indolent lymphoma characterised by repeated relapses and cumulative treatment burden. In this setting, depth of response, durability of disease control and postponement of subsequent therapy represent interrelated aspects of treatment benefit rather than isolated outcomes. The consistent improvement across PFS, PET-CR and time to next treatment supports that the addition of tafasitamab to R^2 results in more sustained disease control, translating into longer periods without progression and without need for further systemic therapy.

7. Comparative analyses of efficacy

The clinical assessment and health economic analysis were exclusively informed by the head-to-head inMIND trial, which includes the most relevant comparator in Danish clinical practice, as supported by national clinical guidelines and clinical expert opinion. Accordingly, Section 7 (except for Table 13) is not considered applicable.

7.1.1 Differences in definitions of outcomes between studies

N/A

7.1.2 Method of synthesis

N/A

7.1.3 Results from the comparative analysis

Table 14 presents the results from the comparative analysis of tafasitamab + R^2 vs placebo + R^2 from the head-to-head trial (inMIND).

Table 14 Results from the comparative analysis of tafasitamab + R^2 vs. R^2 for R/R FL patients (1-3a)

Outcome measure	Tafasitamab + R^2 (N=273)	R^2 (N=275)	Result
PFS by IA	Median: 22.4 months (19.2, NE)	Median: 13.9 months (11.5, 16.4)	HR: 0.43 (95% CI, 0.32-0.58; p<0.0001)
OS	Median: NR (27.9, NE)	Median: NR (NE, NE)	HR: 0.59 (95% CI, 0.31-1.13)
PFS by IRC	Median: NR (19.3, NE)	Median: 16 months (13.9, 21.1)	HR: 0.41 (95% CI, 0.29-0.56, p<0.0001)

Abbreviations: CI, confidence interval; FL, follicular lymphoma; HR, hazard ratio; IA, investigator assessment; NE, not evaluable; NR, not reported; OS, overall survival; PFS, progression-free survival; R^2, rituximab + lenalidomide.

7.1.4 Efficacy – results per [outcome measure]

N/A, all relevant results are summarized in Section 6.1.4.

8. Modelling of efficacy in the health economic analysis

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

Efficacy outcomes (OS and PFS) for tafasitamab + R^2 and R^2 were based on patient-level data (PLD) for the FAS FL population. Both PFS-IA and PFS-IRC were available from inMIND; PFS-IRC was used for the base-case analysis as the blinding in the assessment of PFS minimizes any

potential biases that may arise from investigators.[72] This approach is also aligned with guidance from the EMA and from prior Norwegian and Swedish HTAs in FL, which used PFS-IRC (Nye metoder ID2022_040 [108] and Swedish Dental and Pharmaceutical Benefits Agency (TLV) 2129/2022 [109]). Use of PFS-IA was assessed in a scenario analysis.

Extrapolation of outcomes beyond the trial period was required to assess the cost-effectiveness of tafasitamab + R^2 over a lifetime horizon due to the relatively short trial follow-up period of inMIND and the indolent nature of FL.

The proportional hazards assumption was assessed for OS and PFS to determine if separately fitted models would be appropriate. This assessment used visual inspection of the observed Kaplan–Meier (KM) curves, Schoenfeld residuals and log-cumulative hazard plots.

The analysis presented in this submission (and used in the cost-utility model) details the extrapolation of outcomes for the FAS FL population, which was conducted using the latest data cut of February 23, 2024, from inMIND.

8.1.1 Extrapolation of efficacy data

Parametric survival curves were fitted to OS and PFS outcomes from inMIND (both separately and jointly) to inform efficacy in the tafasitamab + R^2 and R^2 arms of the economic model. Standard parametric survival curves (exponential, Weibull, log-normal, log-logistic, Gompertz, gamma and generalized gamma) were considered, based on guidance from NICE DSU TSD 14.[110]

For the model base case, curve selection was informed by several considerations, including:

- Visual fit to the observed KM data within the inMIND trial period
- Whether or not the proportional hazards assumption was violated
- Within-trial goodness-of-fit statistics per the Akaike information criterion (AIC) and Bayesian information criterion (BIC)
- Clinical plausibility of long-term extrapolations
- Consistency with clinical validation from previous NICE appraisals where appropriate (e.g. TA627)
- Consistency of extrapolations across correlated modelled endpoints, where plausible

The most appropriate and plausible models for OS and PFS were then used to inform the model base case, with alternative plausible models tested in scenario analyses.

In the base case analysis, the gamma curve was selected for OS, and the log-logistic curve was chosen for PFS, as these curves had the best statistical fit among the plausible curves, see more information in Sections 8.1.1.1 and 8.1.1.2.

8.1.1.1 Extrapolation of PFS

Table 15 summarizes the assumptions associated with PFS data extrapolation. PFS-IRC was assessed and extrapolated in the base case and are presented in this section.

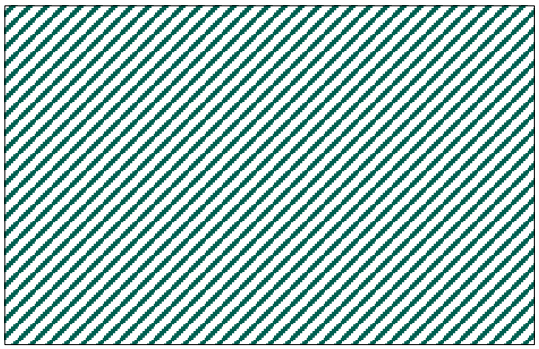
Table 15 Summary of assumptions associated with extrapolation of PFS

Method/approach	Description/assumption
Data input	inMIND, NCT04680052 (pivotal trial) [104]

Method/approach	Description/assumption
Model	Seven parametric models: exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions.
Assumption of proportional hazards between intervention and comparator	Proportional hazard assumption is violated
Function with best AIC fit	Tafasitamab + R^2: Log-logistic R^2: Log-logistic
Function with best BIC fit	Tafasitamab + ^{R2}: Log-logistic R^2: Log-logistic
Function with best visual fit	Tafasitamab + R^2: Generalized gamma and log-logistic curve R^2: Generalized gamma and log-logistic curve
Function with best fit according to evaluation of smoothed hazard assumptions	Not performed
Validation of selected extrapolated curves (external evidence)	UK real-world study [111]
Function with the best fit according to external evidence	Not performed
Selected parametric function in base case analysis	Tafasitamab + R^2: Log-logistic R^2: Log-logistic
Adjustment of background mortality with data from Statistics Denmark	Yes
Adjustment for treatment switching/cross-over	No
Assumptions of waning effect	No waning effect applied; PFS is modelled directly using parametric survival functions fitted to observed trial data.
Assumptions of cure point	No

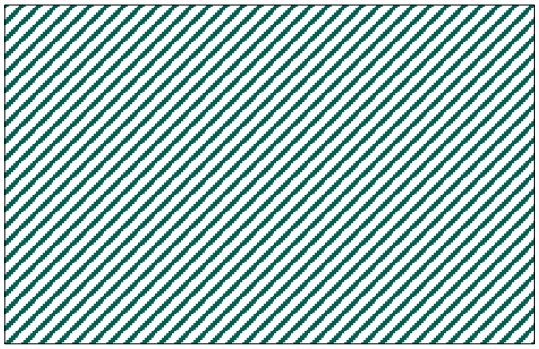
The predicted PFS curves associated with different parametric functions are shown in Figure 6 and Figure 7 for tafasitamab + R^2 and R^2, respectively. Due to the fact that several models were fitted to the observed KM data, we provide two separate figures for the intervention and the comparator for the fits to be better visualized (a joint figure is presented in Figure 18 in Appendix D).

Figure6. Parametric fitting and extrapolation of PFS-IRC – tafasitamab + R^2



Abbreviations: KM, Kaplan-Meier; PFS, progression-free survival; R^2, rituximab + lenalidomide

Figure7. Parametric fitting and extrapolation of PFS-IRC - R^2



Abbreviations: KM, Kaplan-Meier; PFS, progression-free survival; R^2, rituximab + lenalidomide

8.1.1.2 Extrapolation of OS

Table 16 summarizes the assumptions associated with the extrapolation of OS. The gamma curve was chosen for the base-case analysis, since the log-logistic curve, while having the best statistical fit, produced high long-term estimates that may not be clinically plausible. The assumption of constant hazards used by the exponential distribution may not be plausible given the likely long-term increase in hazards due to ageing. Hence, of the remaining plausible curves, the gamma had the best fit based on both AIC and BIC. The full method description and results for the OS extrapolation are presented in Appendix D.

Table 16 Summary of assumptions associated with extrapolation of OS

Method/approach	Description/assumption
Data input	inMIND, NCT04680052 (pivotal trial) [104]
Model	Seven parametric models: exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions.
Assumption of proportional hazards between intervention and comparator	Proportional hazard assumption holds
Function with best AIC fit	Tafasitamab + R^2: Log-logistic R^2: Log-logistic

Method/approach	Description/assumption
Function with best BIC fit	Tafasitamab + R^2: Exponential R^2: Exponential
Function with best visual fit	Tafasitamab + R^2: Weibull, log-logistic, and gamma R^2: Weibull, log-logistic, and gamma
Function with best fit according to evaluation of smoothed hazard assumptions	Not performed
Validation of selected extrapolated curves (external evidence)	UK real-world study [111]
Function with the best fit according to external evidence	XXXX
Selected parametric function in base case analysis	Tafasitamab + R^2: Gamma R^2: Gamma
Adjustment of background mortality with data from Statistics Denmark	Yes
Adjustment for treatment switching/cross-over	No
Assumptions of waning effect	No waning effect applied in the base case, supported by clinical expert opinion; uncertainty in long-term durability explored in scenario analyses.
Assumptions of cure point	No

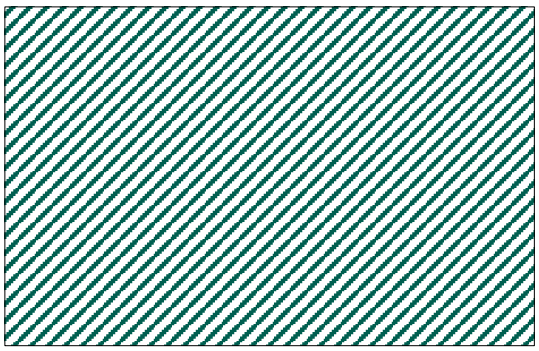
The predicted OS curves associated with different parametric functions are shown in Figure 8 and Figure 9 for tafasitamab + R^2 and R^2, respectively. As multiple parametric functions were fitted to the observed KM data, intervention and the comparator are presented in separate figures to facilitate visual interpretation (a joint figure is presented in Figure 24 in Appendix D).

The apparent step change in the KM curve at approximately year 2 reflects sparse follow-up beyond this timepoint, with a limited number of patients remaining at risk. Under these conditions, individual events have a larger visual impact on the KM estimate. OS data are therefore immature, and the median OS has not yet been reached.

Due to the immaturity of the OS KM data and the indolent nature of FL, there is insufficient evidence to draw conclusions regarding treatment effect over time. In the base case analysis, no treatment-effect waning was applied. This approach is informed by input from a Nordic lymphoma clinical expert advisory board and local clinical expert opinion. Based on clinical experience and available evidence in FL, clinical experts consider it reasonable that the treatment advantage observed with tafasitamab + R^2 compared with R^2 alone may continue over time, while acknowledging uncertainty beyond the observed follow-up. To explore the impact of

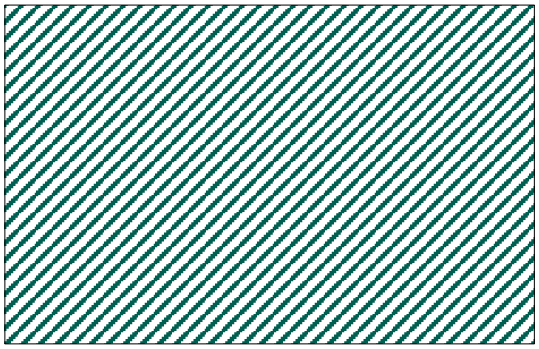
alternative long-term assumptions, a scenario analysis was conducted in which treatment waning was introduced, assuming waning to start at 10 years and over a 5-year period.

Figure8: Parametric fitting and extrapolation of OS – tafasitamab + R^2



Abbreviations: KM, Kaplan-Meier; OS, overall survival; R^2, rituximab + lenalidomide

Figure9: Parametric fitting and extrapolation of OS – R^2



Abbreviations: KM, Kaplan-Meier; OS, overall survival; R^2, rituximab + lenalidomide

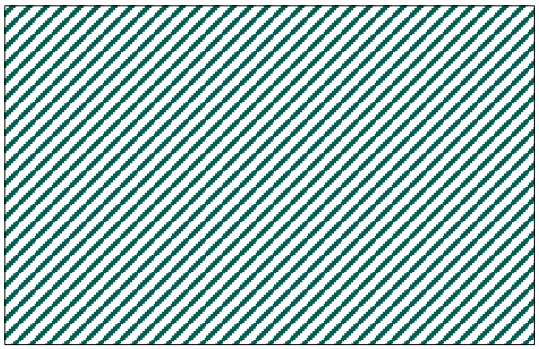
8.1.2 Extrapolation of time-to-treatment discontinuation (TTD)

Given the maturity of the Kaplan-Meier data for TTD, extrapolation was not required, and this section focuses on the modelling of TTD within the health economic model.

In the model, TTD is used to estimate the proportion of patients who are on or off treatment in each model cycle. TTD is defined as the time from the date of the first dose to the date of the last treatment exposure. The KM curves for both treatment arms (tafasitamab + R^2 and R^2) are presented in Figure 10. Both KM curves show a notable decline reflecting treatment-stopping rules. This pattern is consistent with the treatment-stopping rules applied in inMIND and implemented in the model. As described in Sections 3.4 and 3.5, tafasitamab and lenalidomide are administered for a maximum of 12 cycles; accordingly, all patients in both arms were assumed to discontinue treatment from Month 12 onwards.

As KM data are available through the full treatment period for both arms, the trial KM estimates were used directly to inform the treatment duration in the model.

Figure10. Observed Kaplan–Meier curve of TTD, 2L+ – tafasitamab + R^2 versus R^2



8.1.3 Calculation of transition probabilities

N/A

Table 17 Transitions in the health economic model

Health state (from)	Health state (to)	Description of method	Reference
N/A			

8.2 Presentation of efficacy data from [additional documentation]

N/A

8.3 Modelling effects of subsequent treatments

The health economic model includes subsequent lines of FL treatments, and treatments are assumed to affect costs only and they do not factor in any adjustments to efficacy, as this impact is assumed to be implicitly included in the extrapolated OS estimates.

For information on which subsequent treatments that are included in the model and the proportion of patients receiving each line of treatment are described in Section 11.6.

8.4 Other assumptions regarding efficacy in the model

N/A

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

Table 18 and Table 19 present the modelled average and median PFS and OS estimates predicted by the extrapolation model, respectively. The modelled estimates are undiscounted and adjusted for background mortality using Danish population life tables, in line with DMC guidance. Observed inMIND results for the FL FAS are presented for reference [104].

Progression-free survival

Although median PFS was not reached in the tafasitamab + R^2 arm, PFS was longer in the tafasitamab + R^2 arm compared with the R^2 arm with an estimated HR of 0.407 (95% CI: 0.294, 0.563). PFS rates were higher in the tafasitamab + R^2 arm than the R^2 arm at 6 months (XXXX% versus XXXX % for each arm, respectively), 12 months (XXXX % versus XXXX %) and 2 years (XXXX % versus XXXX %).

Table 18 Estimates in the model (PFS)

	Modelled average PFS (reference in Excel)	Modelled median PFS (reference in Excel)	Observed median from relevant study
Tafasitamab + R^2	XXXX	XXXX	Not reached
R^2	XXXX	XXXX	16 months

Abbreviations: PFS, progression-free survival; R^2, tafasitamab + lenalidomide

Overall survival

The median OS was not reached in either treatment arm; however, OS rates were higher with tafasitamab + R^2 than with R^2 alone at 12 months (XXXX % vs XXXX %) and 2 years (XXXX % vs XXXX %).

Table 19 Estimates in the model (OS)

	Modelled average OS (reference in Excel)	Modelled median OS (reference in Excel)	Observed median from relevant study
Tafasitamab + R^2	XXXX	XXXX	Not reached
R^2	XXXX	XXXX	Not reached

Abbreviations: OS, overall survival; R^2, tafasitamab + lenalidomide

Average treatment length

Table 20 presents the modelled average treatment length and time in the model health states, PFS and OS, respectively.

Table 20 Overview of modelled average treatment length and time in model health state, undiscounted and not adjusted for half cycle correction

Treatment	Treatment length [years]	Progression-free survival [years]	Overall survival [years]
Tafasitamab + R^2	XXXX	XXXX	XXXX
R^2	XXXX	XXXX	XXXX

Abbreviations: OS, overall survival; PFS, Progression-free survival; R^2, tafasitamab + lenalidomide

9. Safety

The safety results are from the inMIND trial, and with a data cut-off 23 Feb 2024.

9.1 Safety data from the clinical documentation

The Safety Analysis Set included all randomized participants who received at least one dose of tafasitamab or placebo, lenalidomide, or rituximab, and was used for all safety analyses. The safety population comprised the FL FAS population (n=548). The safety population (n=546) is two patients smaller than the FL FAS population because two patients randomized to the placebo + R^2 group did not receive any study treatment due to confirmed rituximab hypersensitivity and subsequent withdrawal from the study.[103]

The median duration of treatment with tafasitamab was XXXX days in the tafasitamab + R^2 group and the median duration of treatment with placebo was XXXX days in the placebo + R^2 group.

Overall safety outcomes were similar between treatment groups, with a high incidence of TEAEs and comparable rates of serious and fatal adverse events (Table 21).

No clinically meaningful imbalance in serious or fatal adverse events was observed between tafasitamab + R^2 and R^2.

Table 21 Overview of safety events (data cut: 23 Feb 2024)

	Intervention (N=274) (inMIND CSR [112])	Comparator (N=272) (inMIND CSR [112])	Difference, % (95 % CI)†
TEAE	272 (99.3%)	270 (99.3%)	0.0 (−2.4 to 2.4)
Serious TEAE	99 (36.1%)	86 (31.6%)	4.5 (−6.7 to 15.6)
Fatal TEAE	6 (2.2%)	6 (2.2%)	0.0 (−3.7 to 3.7)

† Calculated values
‡ In FL FAS population (n = 548): n = 273 for tafasitamab + R^2, and n = 275 for placebo + R^2 (Table 8 in CSR).
* 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). § CTCAE v. 5.0 must be used if available. All safety data are summarised descriptively; no formal statistical testing was planned or performed (SAP v3 § 8.2) *Difference represents tafasitamab + R^2 minus placebo + R^2; 95 % confidence interval calculated post hoc using Newcombe method for risk difference. Safety analyses were descriptive per SAP v3 § 8.2.

Table 21 presents selected treatment-emergent adverse events (TEAEs) occurring in ≥5% of patients in either treatment group from the inMIND trial.[103]

Overall, the safety profile of tafasitamab + R2 was consistent with the known safety profiles of the individual components. The most frequently reported TEAEs were predominantly hematological and infectious events, including neutropenia, diarrhoea and COVID-19-related events, with comparable patterns observed between the treatment groups. [103]

No new or unexpected safety signals were identified. A complete overview of TEAEs occurring in ≥5% of patients in any group is provided in Appendix E.

Table 22 reports the TEAEs that occurred in ≥5% of patients in any group.

Table 22 Most common treatment-emergent serious adverse events in ≥ 5% of Patients in Any Group by MedDRA Preferred Term (FL safety population)

MedDRA PT, n (%)	Tafasitamab + R^2 (N=274)		R^2 (N=272)	
	Number (%) of patients with adverse events	Number of adverse events	Number (%) of patients with adverse events	Number of adverse events
Participants with any TEAE	272 (99.3)	NR	270 (99.3)	NR
Neutropenia	133 (48.5)	NR	123 (45.2)	NR
Diarrhoea	103 (37.6)	NR	77 (28.3)	NR
COVID(19	86 (31.4)	NR	64 (23.5)	NR
Constipation	80 (29.2)	NR	67 (24.6)	NR
Rash	60 (21.9)	NR	58 (21.3)	NR
Fatigue	58 (21.2)	NR	43 (15.8)	NR

Abbreviation: TEAE, treatment-emergent adverse event

Note: Participants were counted once under each MedDRA PT. Preferred terms are listed in decreasing order of frequency by the tafasitamab + R^2 group. 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 impact of adverse events (AEs) on health-related quality of life is accounted for in the model by using incidences of treatment-related AEs reported from inMIND for both arms.[107] AEs (Grade 3+) that occurred in at least 2.0% of patients in each arm of inMIND were included in the model for tafasitamab + R^2 and R^2, in accordance with other oncology appraisals. The frequencies of AEs included in the model is presented in Table 23.

As inMIND was conducted during the COVID-19 pandemic, incidences of COVID-19 infections and COVID-19 pneumonia were recorded. The overall incidence of COVID-19 AEs was similar between tafasitamab + R^2 and R^2.

In the health economic model, AE costs are applied based on the reported AE rate (proportion of patients experiencing the AE) and applied to the first cycle as one-off costs (see more information on AE costs in Section 11.5). Therefore, Table 23 does not present frequencies of AEs but rather the number/proportion (%) of patients experiencing each AE.

Table 23 Adverse events used in the health economic model

Adverse events	Tafasitamab + R^2 (n=274)	R^2 (n=272)	Source: inMIND [104]	Justification
	Number of patients (%) in economic model for intervention	Number of patients (%) in economic model for comparator		
Acute kidney injury**, n (%)**	8 (2.9%)	6 (2.2%)	[104]	N/A
Anaemia, **n (%)**	12 (4.4%)	16 (5.9%)	[104]	N/A
COVID-19, **n (%)**	16 (5.8%)	6 (2.2%)	[104]	N/A
COVID-19 pneumonia, **n (%)**	13 (4.7%)	3 (1.1%)	[104]	N/A
Febrile neutropenia, **n (%)**	12 (4.4%)	6 (2.2%)	[104]	N/A
Neutropenia, **n (%)**	109 (39.8%)	102 (37.5%)	[104]	N/A
Neutrophil count decreased, **n (%)**	16 (5.8%)	18 (6.6%)	[104]	N/A
Pneumonia, **n (%)**	23 (8.4%)	14 (5.1%)	[104]	N/A
Pyrexia, **n (%)**	4 (1.5%)	6 (2.2%)	[104]	N/A
Thrombocytopenia, **n (%)**	17 (6.2%)	20 (7.4%)	[104]	N/A

Abbreviations: AE, adverse event; R^2, rituximab + lenalidomide.

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

N/A

Table 24 Adverse events that appear in more than X % of patients

Adverse events	Intervention (N=x)			Comparator (N=x)			Difference, % (95 % CI)	
	Number of patients with adverse events	Number of adverse events	Frequency used in economic model for intervention	Number of patients with adverse events	Number of adverse events	Frequency used in economic model for comparator	Number of patients with adverse events	Number of adverse events

Adverse events	Intervention (N=x)	Comparator (N=x)	Difference, % (95 % CI)
Adverse event, n			

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

The model uses HRQoL data from inMIND trial with EQ-5D-5L Danish preference weights [11] to inform health state utility values (HSUVs).

Table 25 Overview of included HRQoL instruments

Measuring instrument	Source	Utilization
EQ-5D-5L	inMIND study	To inform health state utilities

10.1 Presentation of the health-related quality of life

10.1.1 Study design and measuring instrument

The primary evidence source for the statistical analysis is the inMIND study. HRQoL in the FL FAS population (n=548) was assessed using three different patient reported outcome (PRO) measures; EQ-5D-5L, EORTC QLQ-C30 and FACT-Lym. In this application, only EQ-5D-5L data were used, as this instrument was applied in the health economic model. The analysis aimed to estimate the HRQoL values associated with each model health state, while accounting for prognostic factors and multiple observations per patient, for use in the cost-effectiveness model. Additionally, descriptive EORTC QLQ-C30 outcomes are presented in Appendix F to provide complementary evidence on HRQoL.

The EQ-5D-5L is a standardized, generic instrument for describing and valuing HRQoL, developed by the EuroQol Group, and is the preferred HRQoL instrument according to the DMC methods guide [113].

Estimated utility values derived from EQ-5D-5L (Danish) and EORTC QLQ-C30 (UK) are presented in Table 28 Overview of health state utility values [and disutilities].

10.1.2 Data collection

The questionnaires was administered to patients at the following time points:

- Baseline: Day 1 of Cycle 1
- During treatment: Day 1 of each cycle, ± 2 days
- Post-treatment: at the end of the treatment ± 2 days, and at efficacy follow-up for patients who discontinue study treatment for reasons other than disease progression, initiation of new anticancer therapy, lost to follow-up, withdrawal of consent or death.

The analysis considered health state utilities to be independent of treatments, and EQ-5D questionnaire values were therefore pooled across both arms for the analysis. Only patients with a baseline and at least one post-baseline EQ-5D questionnaire observation were included in the final analysis. To align with the structure of the cost-effectiveness

model, all post-baseline EQ-5D questionnaire observations were further categorized to the following:

- Progression-free (PF): observations before the date of progression of disease
- Progressed (PD): observations on and after the date of progression of disease

The number of patients and observations included in the utility analysis by progression status is shown in Table 26.

Table 26 Number of patients and observations included in the utility analysis

Source	Progression-free		Progressed	
	Number of patients	Number of observations	Number of patients	Number of observations
inMIND	XXXX	XXXX	XXXX	XXXX

Completion of the EQ-5D-5L questionnaire was high at baseline (96.5%) and remained above 75% through Cycle 6. A gradual decline in completion was observed over later cycles, consistent with treatment discontinuation and disease progression. Detailed information on missing data and questionnaire completion over time is provided in Appendix F.

10.1.3 HRQoL results

Mean EQ-5D-5L index values, derived using the Danish EQ-5D-5L value set [11], were similar between treatment arms across all assessment time points, with no consistent or clinically meaningful differences observed. Given the absence of systematic differences over time, health state utilities applied in the economic model were estimated by progression status and pooled across treatment arms. Detailed descriptive HRQoL results over time are provided in Appendix F.

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

As presented above, the inMIND trial collected data using EQ-5D-5L, HSUVs could be derived using Danish 5L preference weights [11] in line with DMC guidance.[114]

10.2.1 HSUV calculation

A regression model was selected to estimate a utility value for each health state, after adjusting for prognostic factors and multiple observations from a given patient for use within the cost-effectiveness model. The ‘emmeans’ r package was used to calculate the marginal mean utility value estimates and SE from the respective fitted linear mixed model. Stepwise covariate selection was used to pragmatically identify covariates to be included in the final model. Conditional AIC values were used to compare the fits of

various models, where a lower conditional AIC score indicates better model fit. Model section was done using the following variables:

- Baseline_utility = baseline utility
- Prog_status = progression status
- TRT = Treatment
- AGE = Age
- SEX = Sex
- RACE = Race
- BMI = Body mass index
- REGION1 = Region
- ECOGSC = ECOG at screening
- PRTPYCAT = Number of prior anti-lymphoma treatment
- PRCDCAT = Number of prior anti-CD20 treatment
- REGDUCAT = Time from last prior chemotherapy
- BBSYMPT = B-symptoms at study entry
- BAAS = Ann Arbor staging at study entry

Five models were considered (AIC score):

1. utility ~ prog_status + baseline_utility (-7523.835753)

2. utility ~ prog_status + baseline_utility + TRT + AGE + SEX + RACE + BMI + REGION1 + ECOGSC + PRTPYCAT + PRCDCAT + REGDUCAT + BBSYMPT + BAAS (-7534.16648)

3. utility ~ prog_status + baseline_utility + TRT (-7523.344137)

4. utility ~ prog_status + baseline_utility + PRTPYCAT + PRCDCAT + BAAS + AGE + REGDUCAT + BBSYMPT + REGION1 (-7538.13245)

5. utility ~ prog_status + baseline_utility + PRTPYCAT + PRCDCAT + BAAS + AGE + REGDUCAT + BBSYMPT + REGION1 + TRT (-7537.704253)

The final chosen model (model 4) included the following covariates: progression status, baseline utility, number of prior anti-lymphoma and prior anti-CD20 treatments, time from last prior chemotherapy, B-symptoms at study entry, age and Ann Arbor staging at study entry. Note that the model includes a random effect for the patient, to adjust for the correlation between multiple observations from the same patient – not explicitly written in the formula.

Age adjustments

Age-related utility decrements are included in the model base case to account for the natural decline in quality of life associated with age, as recommended by the DMC. General population utility values for Denmark were taken from Appendiks: Aldersjustering for sundhedsrelateret livskvalitet [115].

10.2.1.1 Mapping

Not applicable; EQ-5D-5L assessed in the inMIND trial.

10.2.2 Disutility calculation

Not applicable (not collected in inMIND)

10.2.3 HSUV results

Table 27 Overview of health state utility values [and disutilities]

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
HSUVs				
Progression-free	XXXX	EQ-5D-5L	DK	The analysis considered health state utilities to be independent of treatments, and values were therefore pooled across both arms for the analysis.
Progressed	XXXX	EQ-5D-5L	DK	The analysis considered health state utilities to be independent of treatments, and values were therefore pooled across both arms for the analysis.
Progression-free	XXXX	EORTC QLQ-C30	UK	*Complementary (not in health-economic model)*
Progressed	XXXX	EORTC QLQ-C30	UK	*Complementary (not in health-economic model)*

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

Disutilities for AEs were derived from different literature sources (as presented in section 5.2), using a targeted search approach.

10.3.1 Study design

Not applicable as only used for disutilities.

10.3.2 Data collection

Not applicable as only used for disutilities.

10.3.3 HRQoL Results

Not applicable as only used for disutilities.

10.3.4 HSUV and disutility results

The disutility values for each AE are presented in Table 29. For each AE, a quality-adjusted life-year (QALY) decrement was calculated by multiplying the incidence rate, disutility and duration (the median durations and sources of median duration of disutilities are presented in Appendix F). The QALY decrements were then summed across all AEs and then applied as a one-off decrement in the first cycle, based on the assumption that AEs occur immediately after the treatment and would only require acute care to resolve them.

Table 28 Overview of health state utility values [and disutilities]

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
N/A				

Table 29 Overview of literature-based health state utility values

	Results Disutility	Instrument	Tariff (value set) used	Comments
Disutilities for AEs				
Acute kidney injury	XXXX			XXXX
Anaemia	XXXX			XXXX
Febrile neutropenia	XXXX			XXXX
Neutropenia	XXXX			XXXX
Neutrophil count decreased	XXXX			XXXX
Pneumonia	XXXX			XXXX
Pyrexia	XXXX			XXXX
Thrombocytopenia	XXXX			XXXX

11. Resource use and associated costs

The model considered several categories of cost inputs, including treatment costs, AE costs, disease management costs (including administration) by health state, terminal care costs, and patient time and transportation costs. The analysis was conducted from a limited societal perspective (and therefore the inclusion of patient costs). All costs are expressed in 2025 prices. Cost inputs were sourced from the most recent publicly available Danish sources, including Legemiddelstyrelsen (medicinpriser.dk) [121], DMC's Værdisætning af enhedsomkostninger [122], and DRG tariffs from the Danish Health Data Authority [123]. Detailed inputs and assumptions are described below.

11.1 Medicines - intervention and comparator

Drug acquisition costs for the intervention tafasitamab + R^2 and the comparator R^2 were calculated for patients who were on treatment in each arm of the model. These costs were calculated per component, based on the TTD observed in inMIND, the planned dosing and administration regimen, and acquisition cost. The dosing schedules implemented for each treatment are outlined in Table 31. In the base case, the relative dose intensity (RDI) was sourced from inMIND.

All unit costs were sourced from medicinpriser.dk and were based on the pharmacy purchase price (AIP) excluding VAT.[121] The drug acquisition cost per administration was calculated as a function of dosage, unit drug cost, and RDI. The dosing schedules and respective RDIs of all treatments are presented in Section 3.4 for tafasitamab + R^2 and Section 3.5 for R^2.

In the base case analysis, the confidential net price agreed between Incyte and Amgros is used. This reflects the actual acquisition cost to the Danish regions and is therefore considered the most relevant price assumption for decision-making. For transparency, an additional analysis was conducted using the publicly available list price for tafasitamab.

In the base case, drug wastage was assumed for all intravenously administered treatments, meaning that a full vial would be used when opened, without considering vial sharing. This assumption was applied to all injection-based treatments in the model. For drugs with either body surface area- (BSA-) or weight-based dosing, the method of moments technique was used to estimate the average number of vials required per dose. For lenalidomide, the 20 mg pack was used and considered the most efficient based on dose schedule. This allowed for the cost of a full pack of lenalidomide (21 tablets) to be incurred per cycle, thereby eliminating any potential wastage. For rituximab, where multiple strengths and pack sizes were available, unit cost were based on the lowest available price per mg.

As stated in Section 8.1.2, TTD estimates were used to inform the duration of treatment in the model. TTD is available up to the end of the treatment period for both arms. The

dosing regimens of the intervention and comparator are presented in Table 30, whereas the medicine costs are reported in the Excel sheet *'Medicine',* embedded in the CEM.

Table 30 Medicines used in the model

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Intervention - Tafasitamab + R²				
Tafasitamab	12 mg/kg	Cycle 1-3: XXXX % Cycle 4-12: XXXX %	Cycle 1-3: Days 1, 8, 15 and 22 Cycle 4-12: Days 1 and 15 of Cycles 4 to 12	No
Lenalidomide	20 mg	XXXX %	Cycle 1-12: Daily on Days 1 to 21	No
Rituximab	375 mg/m²	XXXX %	Cycle 1: Days 1, 8, 15 and 22 Cycle 2-5: Day 1	No
Comparator - R²				
Lenalidomide	20 mg	XXXX %	Cycle 1-12: Daily on Days 1 to 21	No
Rituximab	375 mg/m²	XXXX %	Cycle 1: Days 1, 8, 15 and 22 Cycle 2-5: Day 1	No

Abbreviations: R², rituximab + lenalidomide

11.2 Medicines– co-administration

In the model, all patients were assumed to receive allopurinol 100 mg once daily as prophylaxis for tumour lysis syndrome during the first week of the cycle, in accordance with the SmPC for lenalidomide.[124] The medicine cost of allopurinol is reported in the Excel sheet *'Medicine',* embedded in the CEM, and sourced from medicinpriser.dk [121].

11.3 Administration costs

Administration costs were applied dependent on whether the drug is administered intravenously, as a simple or complex procedure, or orally. All IV administrations were assumed to be performed in an outpatient setting. All unit costs were sourced from the Danish Health Data Authority DRG 2025.[123]

The drug administration costs per treatment component and model cycle are presented in Table 31. When multiple drugs are administered on the same day, it is assumed that only a single administration cost is incurred. Co-administrations are implemented in the model by multiplying the unadjusted administration cost per cycle by the percentage of administrations that are co-administered. For example, during Cycles 1 to 3, tafasitamab is co-administered on six occasions with rituximab on Days 1, 8, 15 and 22 of Cycle 1 and Day 1 of Cycles 2 and 3. Given that the total number of administrations required for tafasitamab for Cycles 1 to 3 is 12, tafasitamab is co-administered 50% of the time with rituximab. Therefore, adjusting the total costs of tafasitamab by this proportion avoids double-counting of administration costs that already accounted for in the administration of rituximab. The total administration cost for each component was then divided by the corresponding number of weeks per dosing period to obtain the average administration cost per model cycle by component (Table 31). The administration frequencies presented in Table 31are only presented for the intervention (tafasitamab + R^2) and comparator (R^2).

The average administration cost per component of each regimen is then aggregated across its constituents.

Table 31 Administration costs used in the model

Administration type	Frequency	Unit cost [DKK]	DRG code	Reference
Oral	N/A	0	N/A	Assumption
IV Simple (First)	Tafasitamab & R^2: Once every cycle for cycle 1 to 5; Every cycle is 28 days	2,136	17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]
IV Complex (First)	Tafasitamab & R^2: Once every cycle for cycle 1 to 12; Every cycle is 28 days	2,136	17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]
IV Complex/Simple (Subsequent)	Tafasitamab: Three times per cycle for cycles 1 to 3; Once per cycle for cycle 4 to 12 Rituximab: Three times per cycle for cycle 1; No subsequent	2,136	17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]

Administration type	Frequency	Unit cost [DKK]	DRG code	Reference
	administration for cycles 2 to 5			
Inpatient administration		2,136 DKK	Used for CAR-T conditional chemotherapy. Danish Health Data Authority, DRG taktser 2025; DRG-code: 17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år	DRG 2025 [123]

Abbreviations: ICU, intensive care unit; IV, intravenous; N/A, not applicable

11.4 Disease management costs

Costs associated with disease management and monitoring were included in the model. Health care resource use (HCRU) was assumed to be different between the PF and PD states and to be independent of the treatment received. As there is currently a lack of published literature on the socio-economic burden of R/R FL to inform the resource use inputs for the economic model, including Danish-specific studies, a real-world study commissioned by Incyte that collected HCRU among patients with R/R FL patients in England was used. This UK real-world study was therefore used in the base case to inform resource use items and frequencies in the CEM.[111] Additionally, Nordic clinical experts indicated that the HCRU from the UK real-world study are also plausible in Nordic clinical practice, with the patterns being broadly comparable, even if the exact numerical cannot be directly validated.

In addition, HCRU frequencies from a cost-utility assessment by TLV of another medicine (Lunsumio, dnr 2129/2022 [109]) in the R/R FL population were used in a scenario analysis. This approach was applied solely for the purpose of scenario analysis, as Lunsumio is indicated for 3L+ patients.

The UK real-world study provided HCRU estimates that are specific and precise for the patient population but did not distinguish HCRU between induction and maintenance phases [111]. Frequencies of HCRU by progression status and line of therapy were collected. In addition, the study included interventions and procedures recorded and classified based on UK Classification of Interventions and Procedures (OPCS-4), including those for disease diagnosis and monitoring, disease management, blood transfusions and others (including stem cell transplant [SCT]).

Local clinical expert opinions were sought to validate the HCRU inputs informed by the UK real-world study. Based on feedback from a Danish clinical expert, the types of HCRU included were considered generally reflective of clinical practice in Denmark; however,

MRI and ultrasound are not routinely used. Accordingly, MRI and ultrasound were excluded from the CEM.

The frequencies of HCRU from the UK real-world study for the 2L+ population are summarized in Table 32. The frequencies from TLV Lunsumio assessment are presented in Table 33 [109]. Note that the frequencies from TLV Lunsumio were reported as the percentage of patients per month in the original assessment report. These patient frequencies were converted into visit frequencies by assuming that each patient with at least one contact contributes exactly one visit per month. The disease management costs in the model were based on DRG codes sourced from the Danish Health Data Authority [123] and costs from Takstkort 1 from Laeger.dk [121] (see Table 32)

Table 32 Disease management costs used in the model – UK real world study [111]

Activity	Frequency (per patient year)		Unit cost [DKK]	DRG code	Reference
	Progression-free	Progressed			
Inpatient admissions: inpatient/overnight stays	XXXX	XXXX	4,700	17MA01 Malign hæmatologisk sygdom uden specifik behandling, pat. mindst 18 år with trimpoint 11 days (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123, 125]
Inpatient admissions: day cases	XXXX	XXXX	2, 136	17MA98 MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]
Inpatient admissions: emergency admissions	XXXX	XXXX	11,660	21MP04 Traumemodtagelse (trauma reception)	DRG 2025 [123]
Inpatient admissions: intensive care admissions	XXXX	XXXX	11,660	21MP04 Traumemodtagelse (trauma reception)	DRG 2025 [123]
Outpatient visits: Haematology or oncology	XXXX	XXXX	2,136	17MA98 MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]

Activity	Frequency (per patient year)		Unit cost [DKK]	DRG code	Reference
	Progression-free	Progressed			
Outpatient visits: Non-specialist	XXXX	XXXX	2,136	17MA98 MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]
Accident and emergency visits	XXXX	XXXX	2,136	17MA98 MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]
Disease diagnosis and monitoring: PET or CT scans	XXXX	XXXX	3,331	30PR05 CT-scanning af hjertet med angiografi (Radiologiske procedurer)	DRG 2025 [123]
Disease diagnosis and monitoring: X-rays	XXXX	XXXX	1,731	30PR18, Røntgenundersøgelse (alm), ukompliceret (Radiologiske procedurer)	DRG 2025 [123]
Disease diagnosis and monitoring: Blood test	XXXX	XXXX	0	Assumed to be included in the hematologist led or outpatient visit	
Disease diagnosis and monitoring: Tissue sampling/biopsy	XXXX	XXXX	6,027	05PR02, Nålebiopsi på kar el. Lymfesystem (Sygdomme i kredsløbsorganerne)	DRG 2025 [123]
Disease diagnosis and monitoring: Unspecified radiology	XXXX	XXXX	1,731	30PR18, Røntgenundersøgelse (alm), ukompliceret (Radiologiske procedurer)	DRG 2025 [123]

Activity	Frequency (per patient year)		Unit cost [DKK]	DRG code	Reference
	Progression-free	Progressed			
Disease management: Radiotherapy	XXXX	XXXX	1,731	30PR18, Røntgenundersøgelse (alm), ukompliceret (Radiologiske procedurer)	DRG 2025 [123]
Blood transfusions: Blood product transfusion/unspecified blood transfusion	XXXX	XXXX	6,876	16PR01, Transfusion af plasma og/eller behandlet blod (Sygdomme i blod og bloddannende organer)	DRG 2025 [123]
Blood transfusions: Platelet infusion	XXXX	XXXX	6,876	16PR01, Transfusion af plasma og/eller behandlet blod (Sygdomme i blod og bloddannende organer)	DRG 2025 [123]

Abbreviations: CT, computed tomography; PET, positron emission tomography.

Table 33 Disease management costs used in the model – TLV Lunsumio dnr 2129/2022 [109]

Activity	Frequency (every 4 weeks)				Unit cost [DKK]	DRG code	Reference
	Progression-free			Progressed			
	Induction	Maintenance	Follow-up				
Outpatient visit: haematologist led	XXXX	XXXX	XXXX	XXXX	2,136	17MA98 MDC17 1-dagsgruppe, pat. mindst 7 år (Svulster i lymfatisk og bloddannende væv)	DRG 2025 [123]
FBC (diagnostic test)	XXXX	XXXX	XXXX	XXXX	Assumed to be included in the hematologist visit		

Patient history/physical exam (Diagnostic test)	XXXX	XXXX	XXXX	XXXX			
Full profile (U&E, LFT, calcium) (Diagnostic tests)	XXXX	XXXX	XXXX	XXXX			
Serum IgG, IgA, IgM and electrophoresis (Diagnostic tests)	XXXX	XXXX	XXXX	XXXX			
LDH test (Diagnostic test)	XXXX	XXXX	XXXX	XXXX			
CT scans	XXXX	XXXX	XXXX	XXXX	3,331	30PR05 CT-scanning af hjertet med angiografi (Radiologiske procedurer)	DRG 2025 [123]

11.5 Costs associated with management of adverse events

Grade 3+ drug-related AEs that occurred in at least 2% of patients in each treatment arm of inMIND were included. The impact on incremental costs of less severe AEs and AEs occurring in fewer than 2% of patients on cost-effectiveness results is expected to be negligible.

AE unit costs are presented in Table 34, and these were applied to the reported AE rate and incurred in the first cycle of the model as one-off costs. AE costs were informed by the 2025 DRG tariffs published by the Danish Health Data Authority.[123]

Table 34 Cost associated with management of adverse events

	DRG code	Unit cost/DRG tariff (DKK)
Acute kidney injury	11MA01, Akutte medicinske nyresygdomme uden dialyse og uden plasmaferese	51,134

	DRG code	Unit cost/DRG tariff (DKK)
Anaemia	17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år (assumed to be 2 hematologist visit)	4,272
Febrile neutropenia	16MA10, Øvrige sygdomme i blod og bloddannende organer	28,342
Neuropenia	16MA10, Øvrige sygdomme i blod og bloddannende organer	283,42
Neutropenia count decreased	17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år	28,342
Pneumonia	04MA26, Observation for sygdom i åndedrætsorganerne	29,561
Pyrexia	17MA98, MDC17 1-dagsgruppe, pat. mindst 7 år	2,136
Thrombocytopenia	16MA03, Granulo- og trombocytopeni	34,842

Abbreviations: AE, adverse event

11.6 Subsequent treatment costs

Subsequent lines of FL treatment are assumed to affect costs only and do not factor in any adjustments to efficacy, as this impact is assumed to be implicitly captured in the extrapolated OS estimates (Table 35). Given that patients may be at different lines of therapy at baseline, and consequently the line at which they receive subsequent treatment may be different, the 2L+ population are sub-divided to reflect this.

Table 35 Proportion of patients receiving each line of therapy

Population	Proportion receiving each line of therapy, at baseline				Source
	2L	3L	4L	Total	
R/R FL (2L+)	XXXX %	XXXX %	XXXX %	100.00%	inMIND [104] Assume all 3L+ baseline treated patients received 3L treatment at baseline, given that no further breakdown was reported

Abbreviations: 2L, second-line; 3L, third-line; 3L+, third-line or later; 4L, fourth-line

In the base case, costs associated with subsequent treatments were applied as a one-off cost at the start of the model, based on the proportion of patients who received subsequent therapy in inMIND (XXXX % and XXXX % for tafasitamab + R^2 and R^2 respectively). As a scenario analysis, subsequent treatment costs based on the proportion of newly progressed patients at each cycle. For this, costs are applied to the

proportion of patients who have progressed weighted by the proportion of patients who had progressed and received subsequent treatment from inMIND (XXXX % and XXXX % for tafasitamab + R^2 and R^2 respectively).

A list of possible anti-lymphoma subsequent treatments was compiled based on those used in inMIND and treatment guidelines for FL. Nordic clinical experts verified that the subsequent treatments align with Nordic clinical practice. This list included chemotherapy, immunotherapy and radiotherapy (Table 36).

In the model, values from the UK real-world study were used in the base case to inform the distribution of subsequent therapies and were assumed to be the same irrespective of initial treatment. The mean duration of each subsequent treatment was approximated from the median PFS of patients receiving the treatment from either the UK real-world study (where available) or the respective pivotal trial, if available Table 37).

Table 36 Distribution of subsequent treatments in base case analysis

Subsequent treatment	Initial treatment	
	2L (%)	3L (%)
O-Benda	XXXX %	XXXX %
R-Benda	XXXX %	XXXX %
R-CHOP	XXXX %	XXXX %
ASCT	XXXX %	XXXX %
Radiotherapy	XXXX %	XXXX %
R^2	XXXX %	XXXX %

Abbreviations: 2L, second-line; ASCT, autologous stem cell transplantation; O-Benda, Obinutuzumab + Bendamustine; R^2, rituximab + lenalidomide; R-benda, rituximab + bendamustine; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride and vincristine sulfate; SE, standard error.

Table 37 Mean duration of subsequent treatment, by population

Subsequent treatment	Mean duration (weeks)			
	2L	Source	3L	Source
O-Benda	110.0	GADOLIN	111.0	GADOLIN
R-Benda	77.2	BRB	77.2	BRB
R-CHOP	XXXX	UK real-world study	XXXX	UK real-world study
ASCT	NA	NA	NA	NA
Radiotherapy	NA	NA	NA	NA
R^2	63.1	inMIND	63.1	inMIND

Abbreviations: 2L, second-line; ASCT, autologous stem cell transplantation; NA; not applicable; O-Benda, Obinutuzumab + Bendamustine; PFS, progression-free survival; R^2, rituximab + lenalidomide; R-benda, rituximab + bendamustine; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride and vincristine sulfate; TTNT, time to next treatment.

All drug unit costs were sourced from the Danish Medicines Agency (medicinpriser.dk) [121]. Drug costs applied in the model are reported in the *'Medicine'* sheet of the CEM. The doses and dosing frequency for each regimen were obtained from relevant SmPCs

(Table 38). For drugs with either BSA- or weight-based dosing, the method of moments technique was used to estimate the average number of vials required per dose. XXXX. Due to the lack of available data, an RDI of 100% was assumed for all subsequent treatments, consistent with a conservative modelling approach. Where multiple strengths and pack sizes were available for several of the treatments within a regimen, unit costs were based on the lowest available price per mg, consistent with Danish procurement practice, except for lenalidomide, where the 20 mg package was applied, as this pack size was considered the most appropriate based on the dosing schedule, as described in Section 11.1.

Table 38 Medicines of subsequent treatments

Medicine		Dose	Relative dose intensity	Frequency	Vial sharing
R²	Lenalidomide	20 mg	XXXX %	Daily days 1-21	No
	Rituximab	375 mg/m²	Induction Cycle 1 (28 days): XXXX **%** Induction Cycle 2-5 (28 days): XXXX **%**	Cycle 1: once weekly Cycle 2-5: Day 1	No
O-Benda	Obinutuzumab	1,000 mg	XXXX %	Induction Cycle 1 (28 days): Day 1, 8 & 15 Induction Cycle 2-6 (28 days): Day 1 Maintenance (28 days): Day 1 for 2 years after induction cycles	No
	Bendamustine	120 mg/m²	XXXX %	Induction Cycle 1 (28 days): Days 1 & 2 Induction Cycle 2-6 (28	No

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
			days): Days 1 & 2	
R-Benda	Rituximab	375 mg/m^2	XXXX %	Induction Cycle 1-6 (28 days): Day 1 Maintenance (28 days): Day 1 for 2 years after induction cycles	No
	Bendamustine	90 mg/m^2	XXXX %	Induction Cycle 1-6 (28 days): Day 1 & 2	No
R-CHOP	Rituximab	375 mg/m^2 on Day 1	XXXX %	Induction Cycle 1-8 (21 days): Day 1 Maintenance (21 days): Day 1 for 2 years after induction cycles	No
	Doxorubicin	50 mg/m^2 on Day 1	XXXX %	Induction Cycle 1-8 (21 days): Day 1	No
	Vincristine	1 mg/m^2 on Day 1	XXXX %		No
	Cyclophosphamide (IV)	750 mg/m^2 on Day 1	XXXX %		No
	Prednisolone	40 mg/m^2 on Day 1 to 5	XXXX %	Induction Cycle 1-8 (21 days): Day 1-5	No
BEAM *	Carmustine	300 mg/m^2	XXXX %	Day 1	No
	Etoposide	200 mg/m^2	XXXX %	Day 2 to 5	No
	Cytarabine	200 mg/m^2	XXXX %	Day 2 to 5	No
	Melphalan	140 mg/m^2	XXXX %	Day 6	No

* Assumed to be covered by ASCT procedure, in line with TA1048[126] and TA895[127]

Apart from chemotherapy and immunotherapy, patients may also receive a stem cell transplantation (SCT) or radiotherapy as subsequent treatments. For SCTs, patients may receive either autologous stem cell transplantation (ASCT) or allogeneic stem cell transplant (allo-SCT). Unit costs for ASCT, allo-SCT and radiotherapy were obtained from the Danish Health Data Authority [123], and are presented in the table below.

Table 39 Breakdown of costs from stem cell transplant and radiotherapy

Therapy	Components	Cost (DKK)	Source
ASCT	Stem cell collection	16,156	Danish Health Data Authority (2025). DRG-taktser, 017PR01 Udtagning af knoglemarv til diagnostisk undersøgelse [123]
	ASCT	103,174	Danish Health Data Authority (2025). DRG-taktser, Sum of 26MP24, Kemoterapi, højdosis, m. autolog stamcellestøtte [123]
Allo-SCT	Allo-SCT	1,035,036	Danish Health Data Authority (2025). DRG-taktser, 26MP22, Allogen stamcelletransplantation [123]
Radiotherapy	Radiotherapy	2,643	Danish Health Data Authority (2025). DRG-taktser, 27MP43, Strålebehandling, kompleks, 1 fraktion [123]

Abbreviations: Allo-SCT, allogeneic stem cell transplant; ASCT, autologous stem cell transplant; HRG, healthcare resource group; NHL, Non-Hodgkin's lymphoma

In addition, prior to ASCT, patients will also require conditioning with high-dose chemotherapy (HDCT). In the model, it is assumed that the BEAM regimen (carmustine, etoposide, cytarabine, and melphalan) was used. Unit costs for BEAM components were sourced from the Danish Medicines Agency (medicinpriser.dk) [121], and administration costs were assumed to be included within the ASCT procedure, in line with TA895 and TA1048. Details on the dosing regimen are provided in the *'Medicine'* sheet embedded in the CEM.[126, 127] In the base case, it was assumed that all patients undergoing ASCT will require HDCT.

11.7 Patient costs

In accordance with DMC method guidance [114], costs incurred by patients and their families as a consequence of the medicine treatment, including transportation costs and time costs, were included in the health economic model. The value of time for patients and their families was applied uniformly, regardless of employment situation, and was valued as leisure time. In the model, the value of leisure time was retrieved from DMC's Værdisætning af enhedsomkostninger [122], based on the average wage for an employee in Denmark after tax, based on Statistics Denmarks database (LONS20), and inflated to 2025 prices, corresponding to 190.92 DKK per hour [128]. The cost of transportation for a round trip were sourced from the same reference [122] and, after inflation to 2025 prices, amounted to 142.8 DKK.

Patient time and transportation costs were applied as a cost per model cycle for both the intervention, tafasitamab + R^2 and the comparator, R^2, and were assumed to accrue only while patients were receiving treatment. For tafasitamab + R^2, patient time and transportation costs were calculated using visit frequencies informed by two data sources. When using the UK real-world study [111], an inpatient admission with an overnight stay was assumed to last 24 hours, and an outpatient haematology visit was assumed to last 3 hours. When using TLV Lunsumio data for the frequencies, a haematology admission with an overnight stay was likewise assumed to last 24 hours, and an outpatient visit for diagnostic tests was assumed to last 3 hours. A round trip transportation cost was added to each visit. Regarding treatment-related time assumptions used in the model, the first infusion of rituximab was assumed to require 5 hours, with subsequent infusions taking 3.25 hours, as reported on the official product website [129]. For tafasitamab, the first infusion was assumed to require 2.5 hours, and subsequent infusions 1.5 hours [130].

Table 40 presents the estimated patient time and transportation costs associated with medicine treatment, including the corresponding time assumptions. These costs were multiplied by the proportion of patients using each disease management activity to estimate total patient costs, based on frequency inputs from the UK real-world study and the TLV Lunsumio assessment, presented in Table 32 and Table 33.

Table 40 Patient costs used in the model

Activity	Time spent [minutes, hours, days]
Drug administration – first infusion (progression-free state)	**Intervention:** Tafasitamab: 2.50 hours (assumed same infusion time as for the DLBCL indication) [130] Rituximab: 5 hours [129] (190.92 DKK/h * (2.50h + 5h) + 142.8 DKK = 1,574.7 DKK) **Comparator:** Rituximab: 5 hours [129] (190.92 DKK/h * 5h + 142.8 DKK = 1,097.4 DKK
Drug administration – subsequent infusions (progression-free state)	**Intervention:** Tafasitamab: 1.5 hours (assumed same infusion time as for the DLBCL indication) [130] (190.92 DKK/h * 1.50h + 142.8 DKK = 429.18 DKK) **Comparator:** Rituximab: 3.25 hours [129] (190.92 DKK/h * 3.25h + 142.8 DKK = 763.29 DKK)
Outpatient monitoring	3 hours (assumption) (190.92 DKK/h * 3 + 142.8 DKK = 715.56 DKK)
Inpatient monitoring (inpatient admission)	24 hours (assumption) (190.92 DKK/h * 24 + 142.8 DKK = 4,652 DKK)

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

A one-off end-of-life cost was applied to patients at the point of dying to reflect the cost of terminal care. The end-of-life cost was sourced from the 2025 DRG published by the Danish Health Data Authority, amounting to 89,879 DKK. The DRG code applied was 26MP47 (Specialiseret Palliativ indsats, Øvrig).[123]

12. Results

12.1 Base case overview

The overview of base case is presented in Table 41.

Table 41 Base case overview

Feature	Description
Comparator	Tafasitamab + R^2
Type of model	Partitioned survival model
Time horizon	40 years
Treatment line	2+ line
Measurement and valuation of health effects	HRQoL was measured using the EQ-5D-5L in the inMIND trial [10], and utility values were derived by applying the Danish-specific EQ-5D-5L value set [131]
Costs included	Medicine costs Administration costs Disease management costs Costs of AEs Subsequent treatment costs Patient costs
Dosage of medicine	28-day cycles **Tafasitamab + R^2:** Tafasitamab 12 mg/kg IV on Days 1, 8, 15, 22 of Cycles 1–3, and Days 1 & 15 of Cycles 4–12; Lenalidomide 20 mg PO daily on Days 1–21 of Cycles 1–12; Rituximab 375 mg/m² IV on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 2–5. **R^2:** Lenalidomide 20 mg orally once daily on Days 1–21 of each 28-day cycle for Cycles 1–12; Rituximab 375 mg/m² IV on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 2–5.

Feature	Description
Average time on treatment	Tafasitamab + R^2: [redacted] years R^2: [redacted] years
Parametric function for PFS	Tafasitamab + R^2: Log-logistic R^2: Log-logistic
Parametric function for OS	Tafasitamab + R^2: Gamma R^2: Gamma
Inclusion of waste	Yes
Average time in model health state	Progression-free Tafasitamab + R^2: [redacted] years R^2: [redacted] years Progressed Tafasitamab + R^2: [redacted] years R^2: [redacted] years

12.1.1 Base case results

The base case results are presented in Table 42. Treatment with tafasitamab + R^2, compared to R^2 alone, resulted in an incremental cost of DKK [redacted] and incremental gains of [redacted] LYs and [redacted] QALYs. The resulting ICER was estimated to be DKK [redacted] per QALY gained.

In the base case analysis, the incremental cost-effectiveness ratio (ICER) is calculated using the confidential net price agreed between Incyte and Amgros. This reflects the actual acquisition cost to the Danish regions and is therefore considered the most relevant price assumption for decision-making. For transparency, an additional analysis was conducted using the publicly available list price for tafasitamab. The result is presented in the scenario analysis section.

Table 42 Base case results

	Tafasitamab + R^2	R^2	Difference
Medicine costs	[redacted]	[redacted]	[redacted]
Administration	[redacted]	[redacted]	[redacted]
Costs associated with management of adverse events	[redacted]	[redacted]	[redacted]

	Tafasitamab + R^2	R^2	Difference
Disease management costs	XXXX	XXXX	XXXX
Subsequent treatment costs	XXXX	XXXX	XXXX
Palliative care costs	XXXX	XXXX	XXXX
Patient costs	XXXX	XXXX	XXXX
Total costs	XXXX	XXXX	XXXX
Life years gained (Progression-free)	XXXX	XXXX	XXXX
Life years gained (Progressed)	XXXX	XXXX	XXXX
Total life years	XXXX	XXXX	XXXX
QALYs (Progression-free)	XXXX	XXXX	XXXX
QALYs (Progressed)	XXXX	XXXX	XXXX
QALYs (adverse reactions)	XXXX	XXXX	XXXX
Total QALYs	XXXX	XXXX	XXXX
Incremental costs per life year gained		XXXX	
Incremental cost per QALY gained (ICER)		XXXX	

12.2 Sensitivity analyses

12.2.1 Deterministic sensitivity analyses

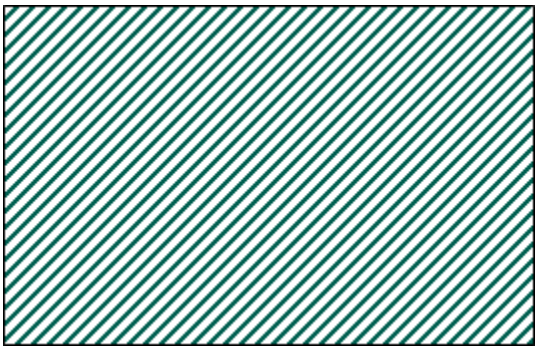
Deterministic sensitivity analyses (DSAs) were conducted by varying the input for each parameter in the model, whilst keeping all other inputs the same. For parameters where SEs of the mean were available, the lower and upper limits were defined by the 95% CI around the mean. In the absence of 95% CI, the inputs were arbitrarily varied by ±10%. Results are depicted in the form of a table (Table 43) and a tornado diagram (Figure 11) which shows the top 10 most influential parameters on the ICER. The parameters with the greatest influence is the mean starting age used in the model. At the upper bound (77 years), the shorter remaining life expectancy leads to substantially lower accumulated health benefits and fewer QALYs gained, resulting in a higher ICER.

Table 43 One-way sensitivity analysis results

	Lower bound ICER	% change from base-case ICER	Upper bound ICER	% change from base-case ICER
Age at model start	[redacted]	[redacted]	[redacted]	[redacted]
Utility: Progression-free (off-treatment)	[redacted]	[redacted]	[redacted]	[redacted]
Utility: Progressed (off-treatment)	[redacted]	[redacted]	[redacted]	[redacted]
Cost per administration: IV Complex/Simple (Subsequent)	[redacted]	[redacted]	[redacted]	[redacted]
Cost per resource: Inpatient admission	[redacted]	[redacted]	[redacted]	[redacted]
Cost per administration: IV Complex (First)	[redacted]	[redacted]	[redacted]	[redacted]
Cost per resource: Inpatient admission - overnight stay	[redacted]	[redacted]	[redacted]	[redacted]
Cost per resource: Outpatient - haematology or oncology	[redacted]	[redacted]	[redacted]	[redacted]
Cost per resource: Inpatient admission - emergency case	[redacted]	[redacted]	[redacted]	[redacted]
Adverse event incidence (Tafasitamab+R^2): Neutropenia (%)	[redacted]	[redacted]	[redacted]	[redacted]

Figure11 Tornado diagram on top 10 most influential parameters

Abbreviations: ICER, incremental cost-effectiveness ratio; IV, intravenous; R^2, rituximab + lenalidomide



Scenario analysis

Table 44 presents scenario analyses. The results indicate that the base case results were relatively stable to changes in key parameters, such as the PFS extrapolation method, use of PFS-IA. OS extrapolation and OS waning scenarios showed a moderate impact on the ICER, reflecting uncertainty in long-term survival projections, although results remained broadly consistent with the base case.

Table 44 Scenario analysis

	Change	Reason / Rational / Source	Incremental cost (DKK)	Incremental benefit (QALYs)	ICER (DKK/QALY)
Base case	-		XXXX	XXXX	XXXX
Extrapolation for OS: Joint, Log-logistic	XXXX	Best fit based on AIC and second-best fit based on BIC	XXXX	XXXX	XXXX
Extrapolation for PFS: Joint, generalized gamma	XXXX	Second-best fit based on AIC	XXXX	XXXX	XXXX
PFS-IA	XXXX	Alternative censoring criteria for PFS and to test the primary endpoint	XXXX	XXXX	XXXX
Transportation and patient time turned off	XXXX	Test the impact of removing limited societal perspective	XXXX	XXXX	XXXX
Discount rate 0% for all costs and effects	XXXX	Present undiscounted results	XXXX	XXXX	XXXX
Discounting 5% for all costs and effects	XXXX	Present results with higher discount rate	XXXX	XXXX	XXXX

	Change	Reason / Rational / Source	Incremental cost (DKK)	Incremental benefit (QALYs)	ICER (DKK/QALY)
HRCU frequency: Lunsumio	XXXX	Alternative HRCU source	XXXX	XXXX	XXXX
Subsequent treatment cost: proportion of newly progressed patients per cycle	XXXX	Alternative subsequent treatment cost approach	XXXX	XXXX	XXXX
OS waning effect: after 10 years and over 5 years	XXXX	OS waning effect scenario	XXXX	XXXX	XXXX

For transparency, an additional analysis was conducted using the publicly available list price for tafasitamab. When the list price is applied instead of the agreed net price, the resulting ICER is DKK XXXX per QALY gained. This scenario is presented for illustrative purposes only and does not represent the expected cost to the Danish healthcare system under the existing agreement.

12.2.2 Probabilistic sensitivity analyses

To assess the uncertainty surrounding the parameters included in the cost-effectiveness analysis, a probabilistic sensitivity analysis (PSA) was conducted by performing a Monte-Carlo simulation with 1,000 iterations. Multiple input parameters were varied simultaneously by sampling their values from uncertainty distributions. The ICER convergence plot demonstrated that the ICER stabilized after approximately 600 iterations (Figure 12).

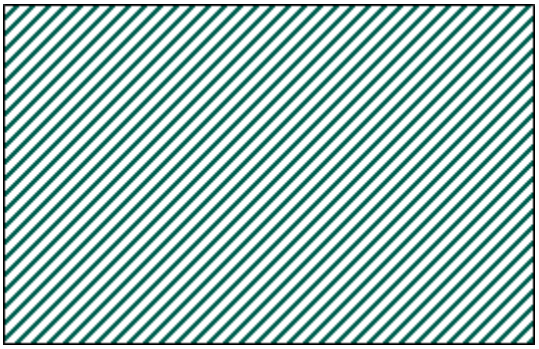


Figure12 PSA convergence plot

The ICER results obtained from the PSA are presented in Table 46, where the results are robust and similar compared to the base-case discounted results. The corresponding scatterplot is presented in Figure 13, where all the iterations fall in the northeast

quadrant, demonstrating that tafasitamab + R^2 is associated with higher costs and QALYs gained and most iterations are south of the WTP threshold of 1,000,000 DKK, which implies that a high probability of cost-effectiveness at this threshold. This is similarly observed in the cost-effectiveness acceptability curve (CEAC), where tafasitamab + R^2 had a 50% probability of being cost effective at a WTP threshold of approximately XXXX DKK at the current price (Figure 14).

Table 45 Results based on probabilistic sensitivity analysis

Treatment	Total costs (DKK)	Total QALYs	Incremental costs	Incremental QALYs	ICER (DKK/QALY)
Tafasitamab + R^2	XXXX	XXXX	XXXX	XXXX	XXXX
R^2	XXXX	XXXX	XXXX	XXXX	XXXX

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; R2, rituximab + lenalidomide.

Figure 13 Scatterplot of 1,000 PSA iterations

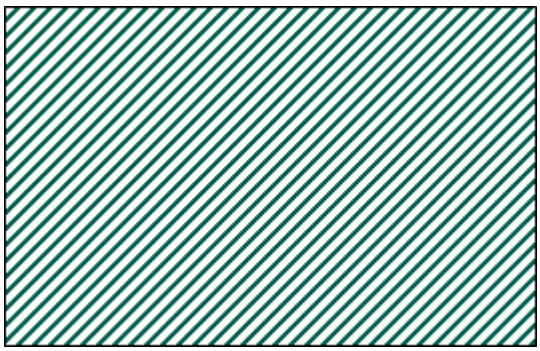
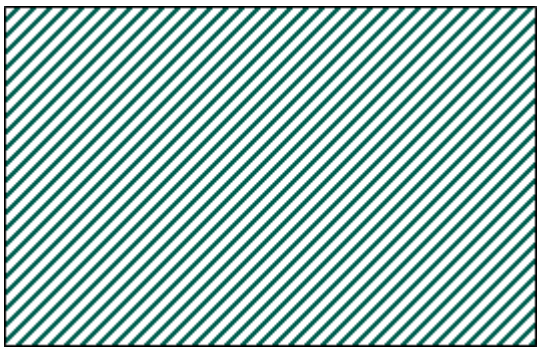


Figure14 Cost-effectiveness acceptability curve



13. Budget impact analysis

This budget impact analysis described how budgets will be affected over a five-year period if tafasitamab + R^2 is introduced in Denmark.

Number of patients (including assumptions of market share)

The number of eligible patients is described in detail in Section 3.2. In line with Section 3.2, this budget impact analysis estimated 103 patients who will be eligible for treatment with tafasitamab + R^2.

Market shares were assumed to be XXXX % in year 1, XXXX % in year 2, and XXXX % in year 3, XXXX % in year 4 and 5. The number of new patients expected to be treated (adjusted for market share) is presented in Table 47.

Table 46 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		
Tafasitamab + R^2	XXXX	XXXX	XXXX	XXXX	XXXX
R^2	XXXX	XXXX	XXXX	XXXX	XXXX
			Non-recommendation		
Tafasitamab + R^2	-	-	-	-	-
R^2	XXXX	XXXX	XXXX	XXXX	XXXX

Budget impact

An overview of the results of the budget impact analysis is presented in Table 47, which shows the total costs of treatment per year when tafasitamab + R^2 is recommended and when tafasitamab + R^2 is not recommend. The budget impact of recommending tafasitamab + R^2 increases from XXXX DKK at year 1 to XXXX DKK at year 3 and decreases to XXXX DKK at year 5.

Table 47 Expected budget impact of recommending the medicine for the indication

	Year 1	Year 2	Year 3	Year 4	Year 5
The medicine under consideration is recommended	XXXX	XXXX	XXXX	XXXX	XXXX
The medicine under consideration is NOT recommended	XXXX	XXXX	XXXX	XXXX	XXXX
Budget impact of the recommendation	XXXX	XXXX	XXXX	XXXX	XXXX

14. List of experts

Peter de Nully Brown, Consultant at Rigshospitalet.

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Appendix A. Main characteristics of studies included

Table 48 Main characteristics of studies included

Trial name: inMIND study	NCT number: NCT04680052
Objective	To investigate whether tafasitamab and lenalidomide as an add-on to rituximab provides improved clinical benefit compared with lenalidomide as an add-on to rituximab in patients with R/R FL Grade 1 to 3a or R/R MZL.
Publications – title, author, journal, year	Sehn LH, Hübel K, Luminari S, Scholz CW, Salar A, Paneesha S, et al; inMIND Study Team. Tafasitamab, lenalidomide, and rituximab in relapsed or refractory follicular lymphoma (inMIND): a global, phase 3, randomised controlled trial. Lancet. 2026;407:133–146. doi:10.1016/S0140-6736(25)01778-7.[10]
Study type and design	Phase 3, randomized, double-blind, placebo-controlled, multicenter study. Patients were randomized 1:1 to receive tafasitamab + R^2 vs placebo + R^2. No crossover was allowed.
Sample size (n)	*654 patients (548 with FL and 106 with MZL)*
Main inclusion criteria	• Aged 18 years or older • Histologically confirmed Grade 1, 2, or 3a R/R FL or histologically confirmed R/R nodal MZL, splenic MZL, or extranodal MZL as assessed locally, with documented CD19+ and CD20+ expression on lymphoma cells • Received at least one prior systemic anti-CD20 therapy immunotherapy or chemoimmunotherapy including rituximab monotherapy or chemotherapy plus immunotherapy with rituximab or obinutuzumab, with or without maintenance • ECOG PS of 0 to 2 No prior R^2 therapy.
Main exclusion criteria	• Women who are pregnant or breastfeeding. • Any histology other than FL and MZL or clinical evidence of transformed lymphoma • Prior non-hematologic malignancy • Congestive heart failure • HCV positivity, chronic HBV infection or history of HIV infection

Trial name: inMIND study	NCT number: NCT04680052
	• Active systemic infection • CNS lymphoma involvement • Any systemic anti-lymphoma and/or investigational therapy within 28 days prior to the start of Cycle 1 Prior use of lenalidomide in combination with rituximab
Intervention	Tafasitamab at 12 mg/kg intravenously on Days 1, 8, 15, 22 of Cycles 1-3, then Day 1 and Day 15 of Cycles 4-12 (28-day cycles) + R^2 - lenalidomide orally 20 mg of every day on Days 1 to 21 of Cycles 1 to 12 + rituximab 375 mg/m2 intravenously on Days 1, 8, 15 and 22 of Cycle 1, and Day 1 of Cycles 2 to 5. The overall population of inMIND study consisted of participants with FL and MZL (n=654). For this submission, the in-focus population is the primary population of inMIND, the FL FAS population (n=548), of which 273 patients were part of the experimental arm receiving tafasitamab +R^2.
Comparator(s)	Placebo + R^2 with same dosing schedule as above. For FL FAS population, 275 patients were part of the comparator arm receiving placebo + R^2.
Follow-up time	Median duration of follow-up of 14.1 months (0.9-19.4 months).
Is the study used in the health economic model?	Yes, this is the pivotal trial.
Primary, secondary and exploratory endpoints	Primary: • PFS by IA in the FL Population, using the Lugano 2014 criteria.[132] PFS is defined as the time from randomization to first documented disease progression, or death from any cause, whichever occurs first. Secondary: • PFS by IA in the Overall Population (FL and MZL). • PET-CR rate by IA in the FDG-avid FL Population, defined as a complete metabolic response at any time after start of treatment. • OS in the FL Population. Additional secondary endpoints: • PET-CR rate by IA in the FDG-avid Overall Population. • MRD-negativity rate (at thresholds of 10−4 and 10−5) at EOT in the FL and the Overall Populations. • ORR by IA in the FL and Overall Populations.

- DoR by IA in the FL and Overall Populations.
- OS in the Overall Population.
- PFS by IRC assessment in the FL and Overall Populations.
- ORR by IRC assessment in the FL and Overall Populations.
- DoR by IRC assessment in the FL and Overall Populations.
- QoL as measured by the EORTC QLQ-C30, the EQ-5D-5L, and FACT-Lym tools in the FL and Overall Populations.
- Safety based on the incidence and severity of TEAEs in the FL and Overall Populations.

Exploratory:

- TTNT by investigator in the FL and Overall Populations.
- PFS by baseline NKCC in the FL and Overall Populations.
- PFS2 by investigator in the FL and Overall Populations.
- PFS by POD24 state in the FL Population.
- Rate of HT of FL into more aggressive histology (DLBCL).
- Time to HT of FL into more aggressive histology (DLBCL).
- PK (C_{max} and C_{min}) of tafasitamab in the FL and Overall Populations.
- Number and percentage of patients who develop anti–tafasitamab antibodies and determination of anti–tafasitamab antibody titer and neutralizing activity for confirmed positive samples.
- Analysis of the dynamic composition of immune cell populations and sub-populations in the peripheral blood by flow cytometry.
- Analysis of the tumor microenvironment using RNA expression signatures (screening and EOT).
- Analysis of RNA splicing patterns and DNA insertion/deletion single nucleotide polymorphism (screening, EOT, and relapse).
- Analysis of expression levels of CD19 and CD20 in tumor tissue using immunohistochemistry (screening, EOT, and relapse).
- PFS and PET-CR by subgroups defined by molecular or cellular markers in the FL and Overall Populations, for example:
    - NKCC in peripheral blood,
    - NK cell gene signature in tumor tissue, and
    - Macrophage gene expression.

Endpoints included in this application:

Trial name: inMIND study	NCT number: NCT04680052
	The study included several endpoints. However, only results of the key study endpoints are presented in this submission (Section 6). The key endpoints of interest for this application and used to inform the model are PFS by IRC assessment in the FL Population, OS in the FL Population and TTD. **Other endpoints:** The results for the other endpoints are therefore not presented, as these are not considered relevant to this submission.
Method of analysis	The full FL analysis set (FL FAS) included all randomized patients and was used for the summary of demographics, baseline characteristics, patient disposition, and analyses of all efficacy data.[103, 106] The Safety Analysis Set included all randomized patients who received at least one dose of tafasitamab/placebo, lenalidomide, or rituximab and was used for safety analyses.[103, 106] For the primary analysis of PFS, the primary endpoint and the first two key secondary endpoints were tested by inferential statistical testing.[103, 106] For the third key secondary endpoint OS, an interim futility test was performed, and the final analysis with inferential statistical testing will be performed once the last patient completes 5 years of follow-up.[103, 106] The median PFS and OS with 95% CIs were estimated using the Kaplan–Meier (KM) method and compared between treatment groups using a stratified log-rank test, with estimation of a HR with 95% CIs using a stratified Cox proportional hazard model.[103, 106] The QoL questionnaires (EQ-5D-5L, EORTC QLQ-C30, and FACT-Lym) were analyzed by descriptive statistics. Safety data were summarized descriptively; no formal statistical testing was performed for safety.
Subgroup analyses	Pre-specified subgroup analyses included several high-risk groups (POD24 and refractory to prior anti-CD20 therapy) and number of prior lines of therapy (<2 vs ≥2).
Other relevant information	*N/A.*

Appendix B. Efficacy results per study

Results per study

Table 49 Results per study

Results of inMIND (NCT04680052)											
				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		
PFS by IA	Tafasitamab + R^2	273	22.4 (95% CI, 19.2-not evaluable [NE]) months	NR	NR	NR	HR: 0.43	0.32-0.58	0.0001	The median PFS with 95% CIs was estimated using the KM method and compared between treatment groups using a stratified log-rank test, with estimation of an HR with 95% CIs using a stratified Cox proportional hazard model.	[133, 134]
	Placebo + R^2	275	13.9 (95% CI, 11.5-16.4) months								
PET-CR rate by IA (14.1 months)	Tafasitamab + R^2	201	49.4% (95% CI, 43.1-55.8)	NR	NR	NR	OR: 1.5	1.04-2.13	0.0286	Calculated based on patients with a positive PET scan at baseline, defined as having a Deauville score of 4 or 5 at baseline. The PET-CR rates and 95% CIs were calculated using the Clopper-Pearson method and were compared between the treatment groups using a	[133, 134]
	Placebo + R^2	205	39.8% (95% CI, 33.7-46.1)								

Results of inMIND (NCT04680052)											
				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		
										stratified CMH test, with estimation of an OR with 95% CIs.	
Overall survival	Tafasitamab + R^2	273	Not reached (95% CI, 27.9-NE) months	NR	NR	NR	HR: 0.59	0.31-1.13	NR	Analysis of OS and comparison between treatment groups was performed as described for PFS.	[103, 134]
	Placebo + R^2	275	Not reached (95% CI, NE-NE) months								
MRD negativity rate at EOT	Tafasitamab + R^2	29	XXXX % (95% CI, XXXX)	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	The MRD-negativity rate is defined as the proportion of participants who achieved a negative MRD result at EOT and was analyzed the same as the PET-CR rate.	[103]
	Placebo + R^2	33	XXXX % (95% CI, XXXX)								
ORR (14.1 months)	Tafasitamab + R^2	273	83.5% (95% CI, 78.57-87.72)	NR	NR	NR	OR: 2.0	1.30-3.02	0.0014	The ORR is defined as the proportion of participants who achieved a CR or PR as determined per Lugano classification at any time during the study but before	Sehn et al. (2024).[133]
	Placebo + R^2	275	72.4% (95% CI, 66.67-77.56)								

Results of inMIND (NCT04680052)											
				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		
										the first PD and before/at the start of a new antilymphoma treatment. The ORR was analyzed the same as the PET-CR rate.	
Median duration of response by IA	Tafasitamab + R^2	228	21.2 (95% CI, 19.5-NE) months	NR	NR	NR	HR:0.47	0.33-0.68	<0.0001	Duration of response is defined as the time from first tumor response (CR or PR) until the time of first documented disease progression, or death from any cause, among participants who achieve an objective response. The DoR was estimated using the KM method with 95% CIs.	Sehn et al. (2024).[133]
	Placebo + R^2	199	13.6 (95% CI, 12.4-18.6) months								
PFS by IRC	Tafasitamab + R^2	273	not reached (95% CI, 19.3-NE)	NR	NR	NR	HR:0.41	0.29-0.56	<0.0001	The median PFS with 95% CIs was estimated using the KM method and compared between treatment groups using a stratified log-rank test, with estimation of an HR with 95% CIs using a stratified Cox proportional hazard model.	Sehn et al. (2024).[133]
	Placebo + R^2	275	16.0 (95% CI, 13.9-21.1) months								

Results of inMIND (NCT04680052)											
				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 next treatment	Tafasitamab + R^2	273	XXXX	XXXX	XXXX	XXXX	HR: XXXX	XXXX	XXXX	Median survival time was estimated using the Kaplan–Meier method. The 2-sided 95% CIs were calculated using the method of Brookmeyer and Crowley (1982) with log-log transformation. The HR between the tafasitamab + R^2 group and the placebo + R^2 group was estimated using a stratified Cox proportional hazards model.	Source: Incyte. DOF InMIND CSR[103], Sehn et al. (2024).[134]
	Placebo + R^2	275	28.8 (20.7, NE)								

Abbreviations: CI, confidence interval; CMH, Cochran-Mantel-Haenszel; CR, complete response; EOT, end of treatment; FAS, full analysis set; FL, follicular lymphoma; HR, hazard ratio; IRT, interactive response technology; KM, Kaplan Meier; MRD, minimal residual disease; NE, not estimable; NR, not reported; OR, odds ratio; ORR, overall response rate; PET-CT, positron emission tomography computed tomography; PR, partial response; R^2, lenalidomide + rituximab; TTNT, time to next therapy.

Appendix C. Comparative analysis of efficacy

Not applicable

Table 50 Comparative analysis of studies comparing [intervention] to [comparator] for patients with [indication]

Outcome		Absolute difference in effect			Relative difference in effect			Method used for quantitative synthesis	Result used in the health economic analysis?
	Studies included in the analysis	Difference	CI	P value	Difference	CI	P value		
Not applicable.									

Appendix D. Extrapolation

Following sections describe how extrapolations are performed for OS and PFS.

D.1 Extrapolation of Progression-free survival (PFS)

D.1.1 Data input

As mentioned in Section 8.1, PFS extrapolation was informed by the February 23, 2024 data cut from inMIND. [104]

D.1.2 Model

As mentioned in Section 8.1, standard parametric survival curves (exponential, Weibull, log-normal, log-logistic, Gompertz, gamma and generalized gamma) were considered.

D.1.3 Proportional hazards

The Schoenfeld residual test, observed Kaplan-Meier curve and the log-cumulative hazard plot are shown in Figure 15, Figure 16 and Figure 17, respectively. While the Schoenfeld residual plot indicated that the proportional hazards assumption does not hold, the observed KM curve and log-cumulative hazard plot was relatively parallel between arms across the entire follow-up period. Therefore, consistent with the approach taken for OS, jointly fitted curves were explored to estimate long-term projections of PFS.

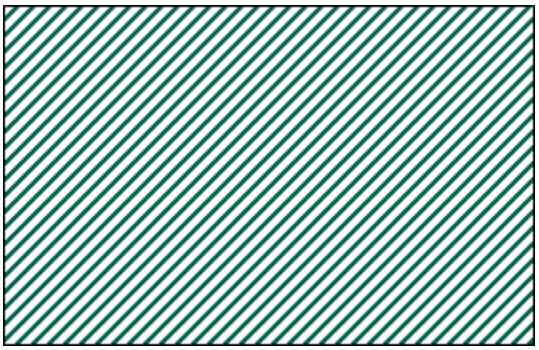


Figure15: Schoenf eld residual plot (PFS, 2L+, IRC) – tafasitamab + R^2 versus R^2

Abbreviations: 2L+, second-line or later; IRC, Independent Review Committee; PFS, progression-free survival; R^2, rituximab + lenalidomide.

Figure16. Kaplan–Meier curve (OS, 2L+) – tafasitamab + R^2 versus R^2

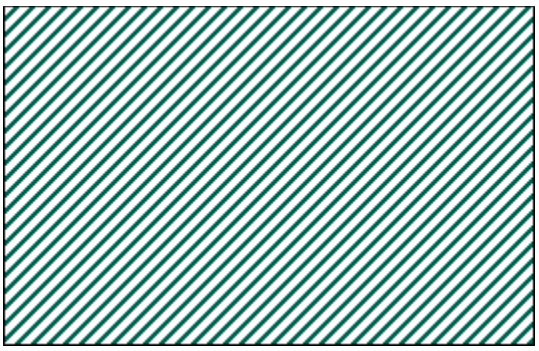
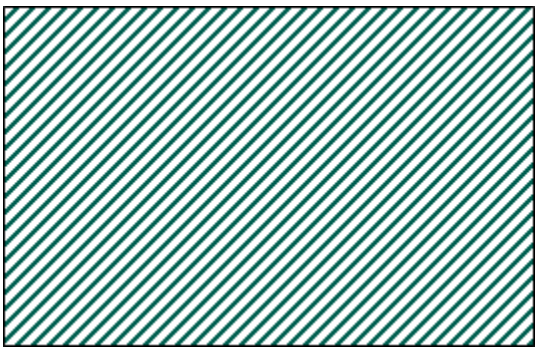


Figure17: Log-cumulative hazard plot (PFS, 2L+, IRC) – tafasitamab + R^2 versus R^2



Abbreviations: 2L+, second-line or later; IRC, Independent Review Committee; PFS, progression-free survival; R^2, rituximab + lenalidomide.

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

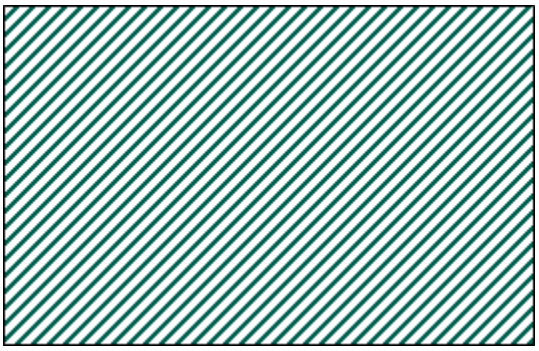
Table 52 summarizes the goodness-of-fit statistics of the parametric models. The log-logistic curve had the best statistical fit based on AIC and BIC. Only the gamma model was within 5 points of the log-logistic model based on both AIC and BIC, while the generalized gamma model was within 5 points based on AIC. The long-term (up to 15 years) fit for the parametric models and observed PFS-IRC KM data from inMIND are presented in Figure 18.

Table 51 Fit statistics of PFS extrapolation (PFS-IRC), 2L+

Distribution	AIC	AIC rank	BIC	BIC rank
Exponential	XXXX	XXXX	XXXX	XXXX
Gamma	XXXX	XXXX	XXXX	XXXX
Generalized gamma	XXXX	XXXX	XXXX	XXXX
Gompertz	XXXX	XXXX	XXXX	XXXX
Log-logistic	XXXX	XXXX	XXXX	XXXX
Log-normal	XXXX	XXXX	XXXX	XXXX
Weibull	XXXX	XXXX	XXXX	XXXX

Abbreviations: 2L+, second-line or later; AIC, Akaike information criterion; BIC, Bayesian information criterion; PFS, progression-free survival; PFS-IRC, progression-free survival by Independent Review Committee. Note: Green shade represents the model with the best statistical fit; orange shade represents the models within 5 points of the model with the best fit.

Figure18. Parametric fitting and extrapolation of PFS-IRC (long-term, 2L+), tafasitamab + R^2 & R^2, respectively



Abbreviations: 2L+, second-line or later; Gen, generalized; PFS-IRC, progression-free survival by Independent Review Committee; R^2, rituximab + lenalidomide.

D.1.5 Evaluation of visual fit

The best distribution for standard parametric models according to AIC and BIC were the log-logistic curve (Table 52). The proportions of patients expected to survive at various landmarks are presented in Table 53 and Table 53 for tafasitamab + R^2 and R^2, respectively. Based on these:

- The gamma curve deviated from the observed PFS KM curve of R^2 at approximately XXXX years, and therefore had overall poorer fit compared with generalized gamma and log-logistic curves
- There was good visual fit to the observed KM curve for both the generalized gamma and log-logistic curves (Figure 19)
- Both the exponential and log-normal functions yielded optimistic values for both arms
- The log-logistic curve was chosen for the base-case analysis as it had the best statistical fit among these plausible curves
- As detailed in D.1.7, validation of the model choice is performed.

Table 52 : Estimated landmark PFS (PFS-IRC), 2L+ – tafasitamab + R²

Extrapolations	Years					
	1	2	5	10	20	30
Exponential	[redacted]					
Gamma	[redacted]					
Generalized gamma	[redacted]					
Gompertz	[redacted]					
Log-logistic	[redacted]					
Log-normal	[redacted]					
Weibull	[redacted]					
Kaplan–Meier estimates	[redacted]					

Abbreviations: 2L+, second-line or later; PFS, progression-free survival; PFS-IRC, progression-free survival by Independent Review Committee; R², rituximab + lenalidomide.

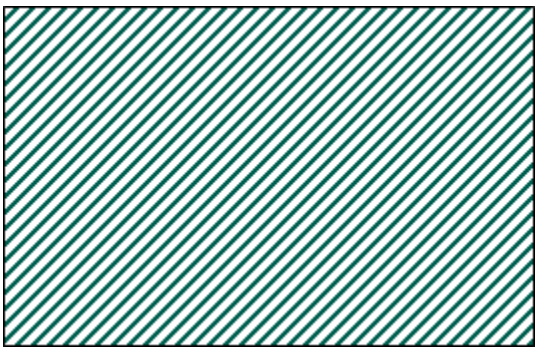
Table 53 Estimated landmark PFS (PFS-IRC), 2L+ – R²

Extrapolations	Years					
	1	2	5	10	20	30
Exponential	[redacted]					
Gamma	[redacted]					
Generalized gamma	[redacted]					
Gompertz	[redacted]					
Log-logistic	[redacted]					
Log-normal	[redacted]					
Weibull	[redacted]					
Kaplan–Meier estimates	[redacted]					

Abbreviations: 2L+, second-line or later; PFS, progression-free survival; PFS-IRC, progression-free survival by Independent Review Committee; R², rituximab + lenalidomide.

The long-term (up to 15 years) fit for the parametric models and observed PFS-IRC KM data from inMIND are presented in Figure 19.

Figure19: Parametric fitting and extrapolation of PFS-IRC (long-term, 2L+)



Abbreviations: 2L+, second-line or later; Gen, generalized; PFS-IRC, progression-free survival by Independent Review Committee; R², rituximab + lenalidomide.

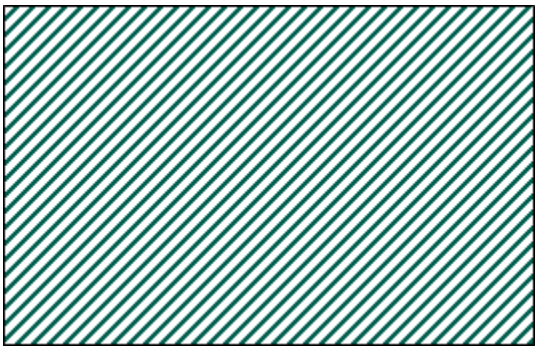
D.1.6 Evaluation of hazard functions

Not performed.

D.1.7 Validation and discussion of extrapolated curves

The log-logistic extrapolation of the R^2 arm yielded a decreasing hazards profile that mirrored the trend observed in UK real-world R/R FL patients who had 1 prior line of therapy (Figure 20) [104, 111]. No further validation has been pursued.

Figure20: PFS hazards plot, 2L+ – inMIND (PFS-IRC) versus UK real-world study



Abbreviations: 2L+, second-line or later; PFS, progression-free survival; PFS-IRC, progression-free survival by Independent Review Committee.

D.1.8 Adjustment of background mortality

Adjustment of background mortality is the same as for OS, see Section D.2.8.

D.1.9 Adjustment for treatment switching/cross-over

Not applicable.

D.1.10 Waning effect

No explicit waning effect was applied. Progression-free survival was modelled directly using parametric survival functions fitted to observed trial data.

D.1.11 Cure-point

Not applicable.

D.2 Extrapolation of Overall Survival (OS)

D.2.1 Data input

As mentioned in Section 8.1, OS extrapolation was informed by the February 23, 2024 data cut from inMIND. [104]

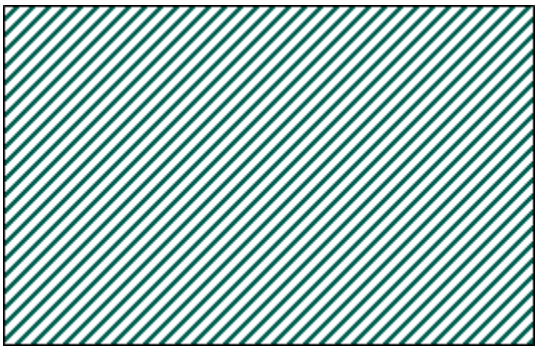
D.2.2 Model

As mentioned in Section 8.1, standard parametric survival curves (exponential, Weibull, log-normal, log-logistic, Gompertz, gamma and generalized gamma) were considered.

D.2.3 Proportional hazards

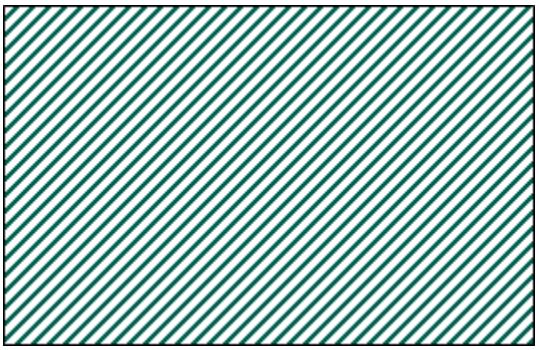
The Schoenfeld residual test and the log-cumulative hazard plot are shown in Figure 21 and Figure 22, respectively. Results of the Schoenfeld residual test suggest that the proportional hazards assumption holds, with a p-value of 0.116 and a relatively flat residual curve. While the observed KM curve and the log-cumulative hazard plot crossed at approximately 28 months, the low number of deaths observed during the entire trial follow-up period (XXXX for tafasitamab + R^2, XXXX for R^2), as well as the heavy censoring towards the tail end of the curve, might have contributed to this crossing (the number of patients at risk was fewer than 10 in both arms at the time of crossing). Therefore, proportional hazards were assumed to hold in the base case, and jointly fitted curves were explored to extrapolate long-term OS.

Figure21: Schoenfeld residual plot (OS, 2L+) – tafasitamab + R^2 versus R^2



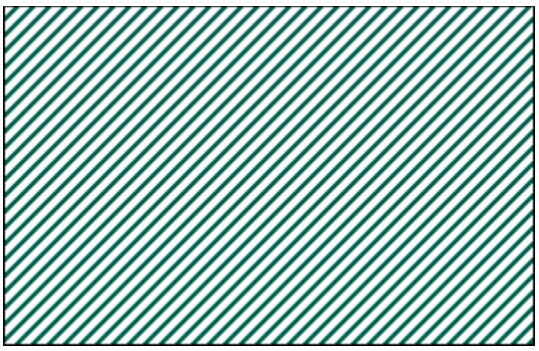
Abbreviations: 2L+, second-line or later; OS, overall survival; R^2, rituximab + lenalidomide.

Figure22: Kaplan–Meier curve (OS, 2L+) – tafasitamab + R^2 versus R^2



Abbreviations: 2L+, second-line or later; OS, overall survival; R^2, rituximab + lenalidomide.

Figure23: Log-cumulative hazard plot (OS, 2L+) – tafasitamab + R^2 versus R^2



Abbreviations: 2L+, second-line or later; OS, overall survival; R^2, rituximab + lenalidomide.

D.2.4 Evaluation of statistical fit (AIC and BIC)

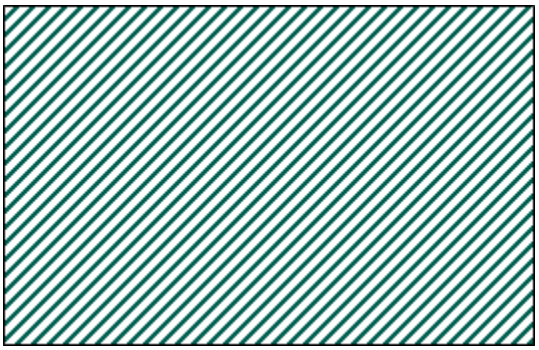
Table 55 summarizes the goodness-of-fit statistics of the jointly fitted parametric models. The log-logistic and exponential curves had the best statistical fit based on AIC and BIC, respectively. All curves were within 5 points of the log-logistic model based on AIC, and all except generalized gamma and log-normal were within 5 points of the exponential model based on BIC, indicating that these curves had relatively good statistical fit without meaningful differences between them.[135] The long-term (up to 15 years) fit for the parametric models and observed OS KM data from inMIND are presented in Figure 24.

Table 54 Fit statistics of OS extrapolation, 2L+

Distribution	AIC	AIC rank	BIC	BIC rank
Exponential	[redacted]	[redacted]	[redacted]	[redacted]
Gamma	[redacted]	[redacted]	[redacted]	[redacted]
Generalized gamma	[redacted]	[redacted]	[redacted]	[redacted]
Gompertz	[redacted]	[redacted]	[redacted]	[redacted]
Log-logistic	[redacted]	[redacted]	[redacted]	[redacted]
Log-normal	[redacted]	[redacted]	[redacted]	[redacted]
Weibull	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: 2L+, second-line or later; AIC, Akaike information criterion; BIC, Bayesian information criterion; OS, overall survival. Notes: Green shade represents the model with the best statistical fit; orange shade represents the models within 5 points of the model with the best fit.

Figure24. Parametric fitting and extrapolation of OS (long-term, 2L+), tafasitamab + R^2 & R^2, respectively



Abbreviations: 2L+, second-line or later; Gen, generalized; OS, overall survival; R^2, rituximab + lenalidomide.

D.2.5 Evaluation of visual fit

The two best distributions for standard parametric models according to AIC and BIC were the log-logistic and exponential curves, respectively (Table 55). However, of the curves with satisfactory statistical fit, the following conclusions were drawn:

- The Gompertz curve was deemed to be too pessimistic for both arms as it predicted that no patients would survive by Year 10. Survival at Year 10 ranged from XXXX % to XXXX % for the other curves for tafasitamab + R^2 and from XXXX % to XXXX % for R^2 (see Table 56 and Table 57)
- The exponential and log-normal functions yielded the most optimistic extrapolations – for example, 10-year survival was 65.8% and XXXX %, respectively, for tafasitamab + R^2, whilst the next largest estimate was XXXX % (see Table 56 and Table 57)
- The remaining gamma, Weibull and log-logistic curves all had relatively good visual and statistical fits to the observed KM curve
- The gamma curve was chosen for the base-case analysis since the log-logistic curve, while having the best statistical fit, produced high long-term estimates that may not be clinically plausible. The assumption of constant hazards used by the exponential distribution may not be plausible given the likely long-term increase in hazards due to ageing. Hence, of the remaining plausible curves, the gamma had the best fit based on both AIC and BIC.

The long-term (up to 15 years) fit for the parametric models and observed OS Kaplan–Meier data from inMIND are presented in Figure 25.

Table 55 Estimated proportion of patients expected to survive at landmark time points, 2L+ for tafasitamab + R^2

Extrapolations	Years					
Exponential	[redacted]					
Gamma	[redacted]					
Generalized gamma	[redacted]					
Gompertz	[redacted]					
Log-logistic	[redacted]					
Log-normal	[redacted]					
Weibull	[redacted]					
Kaplan–Meier estimates	[redacted]					

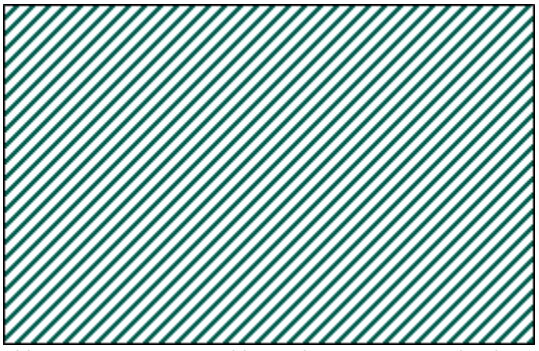
Abbreviations: 2L+, second-line or later; R^2, rituximab + lenalidomide.

Table 56 Estimated proportion of patients expected to survive at landmark time points, 2L+ for R^2

Extrapolations	Years					
Exponential	[redacted]					
Gamma	[redacted]					
Generalized gamma	[redacted]					
Gompertz	[redacted]					
Log-logistic	[redacted]					
Log-normal	[redacted]					
Weibull	[redacted]					
Kaplan–Meier estimates	[redacted]					

Abbreviations: 2L+, second-line or later; R^2, rituximab + lenalidomide.

Figure25: Parametric fitting and extrapolation of OS (long-term, 2L+)



Abbreviations: 2L+, second-line or later; Gen, generalized; OS, overall survival; R^2, rituximab + lenalidomide.

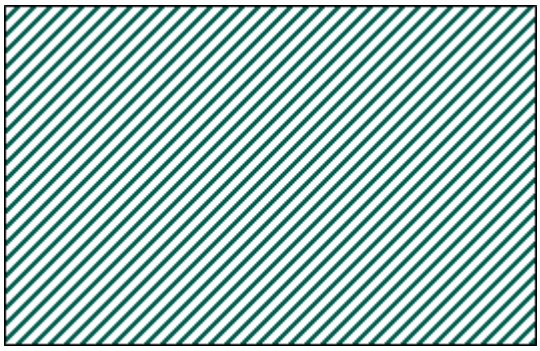
D.2.6 Evaluation of hazard functions

Not performed.

D.2.7 Validation and discussion of extrapolated curves

To validate the curve choice, hazards of the R^2 arm were compared to the hazards estimated from the UK real-world study. [redacted] (Figure 26). No further validation was pursued.

Figure 26 OS hazards plot (2L+) – inMIND versus UK real-world study



Abbreviations: 2L+, second-line or later; OS, overall survival.

D.2.8 Adjustment of background mortality

The general population mortality of the Danish population was retrieved from the DMC's Excel sheet *'Medicine',* embedded in the CEM [136]. As described in Section 4.1, in order to maintain logical consistency in the patient flow, the mortality risk at each model cycle is capped by age-matched general population mortality.

D.2.9 Adjustment for treatment switching/cross-over

Not applicable.

D.2.10 Waning effect

A treatment-waning effect for OS is included in the model to allow exploration of alternative long-term assumptions. When treatment waning is applied, the cycle-specific hazard for that treatment is assumed to be equal to that for R^2 beyond a pre-specified time point. Treatment waning may be implemented over a defined period, in which case linear interpolation is used to calculate the change in hazard between the start point (no waning) and end point (full treatment waning applied), or as immediate waning (the start and end date of waning are the same).

In the base-case analysis, no treatment-effect waning is applied to overall survival. This approach is informed by input from a Nordic lymphoma clinical expert advisory board and local clinical expert opinion. Based on clinical experience and available evidence in FL, clinical experts consider it reasonable that the treatment advantage observed with tafasitamab + R^2 compared with R^2 alone may continue over time, while acknowledging uncertainty beyond the observed follow-up. Given the uncertainty in long-term OS extrapolation, a scenario analysis was conducted in which treatment waning is assumed to start at 10 years and wane over a 5-year period.

D.2.11 Cure-point

Not applicable.

Appendix E. Serious adverse events

A total of 185 patients (33.9%) in the FL Safety Population had at least one serious TEAE (see Table 58).[103] Serious TEAEs were reported for 36.1% of patients in the tafasitamab + R^2 group and 31.6% of patients in the placebo + R^2 group.[103]

Serious TEAEs that occurred more frequently (≥ 2% difference) in the tafasitamab + R^2 group versus the placebo + R^2 group, respectively, included pneumonia (7.7% vs 4.8%), COVID-19 (6.9% vs 2.6%), and COVID-19 pneumonia (5.1% vs 1.8%).[103]

Table 57 Summary of Serious Treatment-Emergent Adverse Events in ≥ 1% of Patients in Any Group by MedDRA Preferred Term (FL Safety Population)

MedDRA PT, n (%)	Tafasitamab + R^2 (N=274)	Placebo + R^2 (N=272)	Total (N=546)
Patients with any serious TEAE	99 (36.1)	86 (31.6)	185 (33.9)
Pneumonia	21 (7.7)	13 (4.8)	34 (6.2)
COVID-19	19 (6.9)	7 (2.6)	26 (4.8)
COVID-19 pneumonia	14 (5.1)	5 (1.8)	19 (3.5)
Acute kidney injury	8 (2.9)	4 (1.5)	12 (2.2)
Febrile neutropenia	7 (2.6)	6 (2.2)	13 (2.4)
Pyrexia	4 (1.5)	7 (2.6)	11 (2.0)
Sepsis	3 (1.1)	3 (1.1)	6 (1.1)
Neutropenia	2 (0.7)	3 (1.1)	5 (0.9)
Abdominal pain	0 (0.0)	5 (1.8)	5 (0.9)
Diarrhea	0 (0.0)	3 (1.1)	3 (0.5)

Source: Incyte. DOF InMIND CSR.

Note 1: Patients were counted once under each MedDRA PT.
Note 2: PTs are listed in decreasing order of frequency in the tafasitamab + R^2 group.
Abbreviations: COVID-19, Coronavirus disease; FL, follicular lymphoma; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; R^2, rituximab + lenalidomide; TEAE, treatment-emergent adverse event.

Table 58 Overview of safety events (data cut: 23 Feb 2024)

	Intervention (N=274) (inMIND CSR [112])	Comparator (N=272) (inMIND CSR [112])	Difference, % (95 % CI)†
TEAE	272 (99.3%)	270 (99.3%)	XXXX
Serious TEAE	99 (36.1%)	86 (31.6%)	XXXX
Fatal TEAE	6 (2.2%)	6 (2.2%)	XXXX
Number of adverse events, n	NR	NR	XXXX
Number and proportion of patients with ≥1 adverse events, n (%)	XXXX	XXXX	XXXX
Number of serious adverse events*, n	NR	NR	NR
Number and proportion of patients with ≥ 1 serious adverse events*, n (%)	XXXX	XXXX	XXXX
Number of CTCAE grade ≥ 3 events, n	XXXX	XXXX	XXXX
Number and proportion of patients with ≥ 1 CTCAE grade ≥ 3 events§, n (%)	NR	NR	NR
Number of adverse reactions, n	NR	NR	NR
Number and proportion of patients with ≥ 1 adverse reactions, n (%)	NR	NR	NR
Number and proportion of patients who had a dose reduction, n (%)	NR	NR	NR
Number and proportion of	XXXX	XXXX	XXXX

	Intervention (N=274) (inMIND CSR [112])	Comparator (N=272) (inMIND CSR [112])	Difference, % (95 % CI)†
patients who discontinue treatment regardless of reason‡, n (%)			
Number and proportion of patients who discontinue treatment due to adverse events, n (%)	XXXX	XXXX	XXXX

† Calculated values
‡ In FL FAS population (n = 548): n = 273 for tafasitamab + R^2, and n = 275 for placebo + R^2 (Table 8 in CSR).
* 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). § CTCAE v. 5.0 must be used if available. All safety data are summarised descriptively; no formal statistical testing was planned or performed (SAP v3 § 8.2) *Difference represents tafasitamab + R^2 minus placebo + R^2; 95 % confidence interval calculated post hoc using Newcombe method for risk difference. Safety analyses were descriptive per SAP v3 § 8.2.

Table 59 Treatment-emergent serious adverse events in ≥ 5% of Patients in Any Group by MedDRA Preferred Term (FL safety population)

MedDRA PT, n (%)	Tafasitamab + R^2 (N=274)		R^2 (N=272)	
	Number (%) of patients with adverse events	Number of adverse events	Number (%) of patients with adverse events	Number of adverse events
Participants with any TEAE	272 (99.3)	NR	270 (99.3)	NR
Neutropenia	133 (48.5)	NR	123 (45.2)	NR
Diarrhoea	103 (37.6)	NR	77 (28.3)	NR
COVID(19	86 (31.4)	NR	64 (23.5)	NR
Constipation	80 (29.2)	NR	67 (24.6)	NR
Rash	60 (21.9)	NR	58 (21.3)	NR
Fatigue	58 (21.2)	NR	43 (15.8)	NR
Cough	52 (19)	NR	47 (17.3)	NR

MedDRA PT, n (%)	Tafasitamab + R^2 (N=274)		R^2 (N=272)	
Pyrexia	52 (19)	NR	44 (16.2)	NR
Muscle spasms	49 (17.9)	NR	49 (18)	NR
Nausea	49 (17.9)	NR	38 (14)	NR
Pruritus	44 (16.1)	NR	28 (10.3)	NR
Infusion related reaction	43 (15.7)	NR	41 (15.1)	NR
Anaemia	39 (14.2)	NR	36 (13.2)	NR
Thrombocytopenia	37 (13.5)	NR	42 (15.4)	NR
Asthenia	36 (13.1)	NR	28 (10.3)	NR
Pneumonia	32 (11.7)	NR	24 (8.8)	NR
Back pain	31 (11.3)	NR	15 (5.5)	NR
Decreased appetite	27 (9.9)	NR	24 (8.8)	NR
Headache	27 (9.9)	NR	18 (6.6)	NR
Oropharyngeal pain	25 (9.1)	NR	10 (3.7)	NR
Upper respiratory tract infection	25 (9.1)	NR	29 (10.7)	NR
Neutrophil count decreased	23 (8.4)	NR	19 (7)	NR
Hypokalaemia	22 (8)	NR	32 (11.8)	NR
Dizziness	21 (7.7)	NR	19 (7)	NR
Insomnia	21 (7.7)	NR	17 (6.3)	NR
Pain in extremity	21 (7.7)	NR	7 (2.6)	NR
Abdominal pain	20 (7.3)	NR	29 (10.7)	NR
Oedema peripheral	20 (7.3)	NR	35 (12.9)	NR

MedDRA PT, n (%)	Tafasitamab + R^2 (N=274)		R^2 (N=272)	
Urinary tract infection	20 (7.3)	NR	17 (6.3)	NR
Arthralgia	19 (6.9)	NR	21 (7.7)	NR
Vomiting	19 (6.9)	NR	14 (5.1)	NR
Alanine aminotransferase increased	18 (6.6)	NR	20 (7.4)	NR
Dyspnoea	18 (6.6)	NR	25 (9.2)	NR
Rash maculo-papular	18 (6.6)	NR	14 (5.1)	NR
Respiratory tract infection	18 (6.6)	NR	24 (8.8)	NR
Nasopharyngitis	17 (6.2)	NR	20 (7.4)	NR
COVID-19 pneumonia	15 (5.5)	NR	5 (1.8)	NR
Influenza	15 (5.5)	NR	9 (3.3)	NR
Myalgia	15 (5.5)	NR	13 (4.8)	NR
Dyspepsia	14 (5.1)	NR	12 (4.4)	NR
Hypotension	14 (5.1)	NR	13 (4.8)	NR
Rhinorrhoea	14 (5.1)	NR	10 (3.7)	NR
White blood cell decreased	14 (5.1)	NR	14 (5.1)	NR
Weight decreased	13 (4.7)	NR	14 (5.1)	NR

Abbreviation: TEAE, treatment-emergent adverse event

Note: Participants were counted once under each MedDRA PT. Preferred terms are listed in decreasing order of frequency by the tafasitamab + R^2 group. 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).

Appendix F. Health-related quality of life

In the table below, patterns of EQ-5D-5L questionnaire completion (complete forms) are presented. The data show the number of complete EQ-5D-5L assessments from which utility values could be derived. EQ-5D-5L completion rates were high and broadly comparable between treatment arms during the on-treatment period, with completion declining during later follow-up as expected due to disease progression and attrition.

Table 60 Pattern of missing data and completion, EQ-5D-5L

Study visit	Tafasitamab + R^2			Placebo + R^2		
	Observations, n (% of FAS)	Missing, n (%)	Observation not scheduled, n	Observations, n (% of FAS)	Missing, n (%)	Observation not scheduled, n
BASELINE	253 (92)	22 (8)	0	250 (92)	22 (8)	0
CYCLE 2 DAY 1	226 (82)	40 (15)	9	229 (84)	41 (15)	2
CYCLE 3 DAY 1	222 (81)	42 (16)	11	229 (84)	34 (13)	9
CYCLE 4 DAY 1	214 (78)	46 (18)	15	207 (76)	49 (19)	16
CYCLE 5 DAY 1	210 (76)	41 (16)	24	204 (75)	39 (16)	29
CYCLE 6 DAY 1	205 (75)	44 (18)	26	198 (73)	35 (15)	39
CYCLE 7 DAY 1	201 (73)	44 (18)	30	177 (65)	41 (19)	54
CYCLE 8 DAY 1	183 (67)	50 (21)	42	174 (64)	33 (16)	65
CYCLE 9 DAY 1	181 (66)	45 (20)	49	156 (57)	42 (21)	74
CYCLE 10 DAY 1	165 (60)	56 (25)	54	141 (52)	46 (25)	85

Study visit	Tafasitamab + R²			Placebo + R²		
	Observations, n (% of FAS)	Missing, n (%)	Observation not scheduled, n	Observations, n (% of FAS)	Missing, n (%)	Observation not scheduled, n
CYCLE 11 DAY 1	145 (53)	71 (33)	59	132 (49)	45 (25)	95
CYCLE 12 DAY 1	135 (49)	72 (35)	68	127 (47)	45 (26)	100
END OF TREATMENT	176 (64)	90 (34)	9	177 (65)	84 (32)	11
FOLLOW-UP (MONTH 16)	43 (16)	159 (79)	73	25 (9)	138 (85)	109
FOLLOW-UP (MONTH 18)	39 (14)	161 (80)	75	34 (12)	131 (79)	107
FOLLOW-UP (MONTH 20)	23 (8)	177 (88)	75	19 (7)	142 (88)	111
FOLLOW-UP (MONTH 24)	15 (5)	183 (92)	77	14 (5)	147 (91)	111
FOLLOW-UP (MONTH 28)	2 (1)	196 (99)	77	3 (1)	158 (98)	111
All Scheduled Visits	2638 (63)	1539 (37)	-	2496 (66)	1272 (34)	-

Abbreviations: FAS, full analysis set; R2, lenalidomide with rituximab.

Table 61 HRQoL [EQ-5D-5L] summary statistics presents the mean values and standard error (SE) for Danish EQ-5D-5L index scores (derived using Jensen et al 2021 [11]) as well as EQ-5D visual analogue scale (VAS) scores, at baseline and at all data collection time points.

Table 61 HRQoL [EQ-5D-5L] summary statistics

	Intervention		Comparator		Intervention vs. comparator
	N	Mean (SE)	N	Mean (SE)	Difference (95% CI) p-value
EQ-5D-5L index					
Baseline	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 2 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 3 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 4 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 5 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 6 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 7 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 8 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 9 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 10 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 11 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
Cycle 12 Day 1	XXXX	XXXX	XXXX	XXXX	XXXX
End of treatment/Safety follow-up	XXXX	XXXX	XXXX	XXXX	XXXX
Follow-up (month 16)	XXXX	XXXX	XXXX	XXXX	XXXX
Follow-up (month 18)	XXXX	XXXX	XXXX	XXXX	XXXX

	Intervention		Comparator		Intervention vs. comparator
Follow-up (month 20)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 24)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 28)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
EQ-5D-VAS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Baseline	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 2 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 3 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 4 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 5 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 6 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 7 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 8 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 9 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 10 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 11 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 12 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
End of treatment/Safety follow-up	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 16)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 18)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 20)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Intervention		Comparator		Intervention vs. comparator
Follow-up (month 24)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 28)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviation: NR, not reported.

Table 62 HRQoL [EORTC QLQ-C30] summary statistics provides the mean values and standard errors for UK EORTC QLQ-C30 index scores.

Table 62 HRQoL [EORTC QLQ-C30] summary statistics

	Intervention		Comparator		Intervention vs. comparator
	N	Mean (SE)	N	Mean (SE)	Difference (95% CI) p-value
EORTC QLQ-C30					
Baseline	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 2 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 3 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 4 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 5 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 6 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 7 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 8 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 9 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 10 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 11 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 12 Day 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Intervention		Comparator		Intervention vs. comparator
End of treatment/Safety follow-up	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 16)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 18)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 20)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 24)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Follow-up (month 28)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Note: SE and 95% CI calculated using observed means and SD assuming independent samples.

Table 63 presents the duration of AEs and the source of the durations.

Table 63 Duration of AEs

	Median duration (days)	Data source (Duration)
Acute kidney injury	[redacted]	[redacted]
Anaemia	[redacted]	[redacted]
Febrile neutropenia	[redacted]	[redacted]
Neutropenia	[redacted]	[redacted]
Neutrophil count decreased	[redacted]	[redacted]
Pneumonia	[redacted]	[redacted]

Pyrexia	XXXX	XXXX
Thrombocytopenia	XXXX	XXXX

Appendix G. Probabilistic sensitivity analyses

Table 64 presents an overview of all the parameters included in the PSA in the health economic model. All parameters relevant for the analysis are included in the PSA. The assumptions and data for the PSA can be found in the model on the 'Parameter' sheet.

Table 64 Overview of parameters in the PSA

Input parameter	Point estimate	Lower bound	Upper bound	Probability distribution
Age	XXXX	XXXX	XXXX	XXXX
Weight	XXXX	XXXX	XXXX	XXXX
Cost per administration: Oral	XXXX	XXXX	XXXX	XXXX
Cost per administration: IV Complex/Simple (Subsequent)	XXXX	XXXX	XXXX	XXXX
Cost per administration: Inpatient administration	XXXX	XXXX	XXXX	XXXX
Cost per administration: IV Simple (First)	XXXX	XXXX	XXXX	XXXX
Cost per administration: IV Simple (First)	XXXX	XXXX	XXXX	XXXX
Cost per administration: ICU	XXXX	XXXX	XXXX	XXXX
Overall % PFS events that are death	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - O-Benda	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - R-Benda	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - R-CHOP	XXXX	XXXX	XXXX	XXXX

Subs treatment duration (months) - R-GemOx	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - R-GDP	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Zanu-obi	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Mosunetuzumab	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Idelalisib	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Odronextamab	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Epcoritamab	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Tisa-cel	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Axi-cel	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Allo-SCT	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Auto-SCT	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - Radiotherapy	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - R-CVP	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - R2	XXXX	XXXX	XXXX	XXXX
Subs treatment duration (months) - R-BMD	XXXX	XXXX	XXXX	XXXX
Leucopheresis	XXXX	XXXX	XXXX	XXXX
CAT T-cell tariff	XXXX	XXXX	XXXX	XXXX

Cost per adverse event: Abdominal pain	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Acute kidney injury	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Allergic reaction	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Alopecia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Arthralgia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Anaemia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Asthenia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Back pain	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: COVID-19 pneumonia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Decreased appetite	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Diarrhoea	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Dyspepsia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Dyspnoea	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Fatigue	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Febrile neutropenia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Hypokalaemia	XXXX	XXXX	XXXX	XXXX

Cost per adverse event: Hypotension	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Infection	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Infusion related reaction	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Leukopenia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Lymphocyte count decreased	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Lymphopenia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Muscle spasms	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Myalgia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Nasopharyngitis	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Nausea	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Neutropenia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Neutrophil count decreased	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Oedema peripheral	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Oropharyngeal pain	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Pain in extremity	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Pneumonia	XXXX	XXXX	XXXX	XXXX

Cost per adverse event: Pruritus	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Pulmonary embolism	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Pyrexia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Rash	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Rash maculo-papular	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Respiratory tract infection	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Rhinorrhoea	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Sepsis	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Thrombocytopenia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Upper respiratory tract infection	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Urinary tract infection	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Vomiting	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Weight decreased	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: White blood cell count decreased	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Cytokine release syndrome	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Confusional state	XXXX	XXXX	XXXX	XXXX

Cost per adverse event: Hypoxia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Hypophosphataemia	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Neurological events	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Renal failure	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Syncope	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Hypertension	XXXX	XXXX	XXXX	XXXX
Cost per adverse event: Pleural effusion	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Acute kidney injury (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Anaemia (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): COVID-19 (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): COVID-19 pneumonia (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Febrile neutropenia (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Neutropenia (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Neutrophil count decreased (%)	XXXX	XXXX	XXXX	XXXX

Adverse event incidence (Tafasitamab + R^2): Pneumonia (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Pyrexia (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (Tafasitamab + R^2): Rash (%)	XXXX	XXXX	XXXX	XXXX
Adverse event incidence (R^2): Thrombocytopenia (%)	XXXX	XXXX	XXXX	XXXX
EOL Cost: Danish Health Data Authority	XXXX	XXXX	XXXX	XXXX
Cost per resource: Haematologist led	XXXX	XXXX	XXXX	XXXX
Cost per resource: CT scans	XXXX	XXXX	XXXX	XXXX
Cost per resource: Inpatient admission - overnight stay	XXXX	XXXX	XXXX	XXXX
Cost per resource: Inpatient admission - day case	XXXX	XXXX	XXXX	XXXX
Cost per resource: Inpatient admission - emergency case	XXXX	XXXX	XXXX	XXXX
Cost per resource: Inpatient admission - ICU	XXXX	XXXX	XXXX	XXXX
Cost per resource: Outpatient - haematology or oncology	XXXX	XXXX	XXXX	XXXX
Cost per resource: Outpatient - non-specialist	XXXX	XXXX	XXXX	XXXX
Cost per resource: A&E visits	XXXX	XXXX	XXXX	XXXX
Cost per resource: PET or CT scans	XXXX	XXXX	XXXX	XXXX
Cost per resource: MRI	XXXX	XXXX	XXXX	XXXX
Cost per resource: Ultrasound	XXXX	XXXX	XXXX	XXXX

Cost per resource: X-ray	XXXX	XXXX	XXXX	XXXX
Cost per resource: Biopsy	XXXX	XXXX	XXXX	XXXX
Cost per resource: Unspecified radiology	XXXX	XXXX	XXXX	XXXX
Cost per resource: Radiotherapy	XXXX	XXXX	XXXX	XXXX
Cost per resource: Blood product transfusion/unspecified blood transfusion	XXXX	XXXX	XXXX	XXXX
Cost per resource: Platelet infusion	XXXX	XXXX	XXXX	XXXX
Stem cell collection	XXXX	XXXX	XXXX	XXXX
Auto-SCT	XXXX	XXXX	XXXX	XXXX
Allo-SCT	XXXX	XXXX	XXXX	XXXX
Radiotherapy	XXXX	XXXX	XXXX	XXXX
Utility: Progression-free (on-treatment)	XXXX	XXXX	XXXX	XXXX
Utility: Progression-free (off-treatment)	XXXX	XXXX	XXXX	XXXX
Utility: Progressed (on-treatment)	XXXX	XXXX	XXXX	XXXX
Utility: Progressed (off-treatment)	XXXX	XXXX	XXXX	XXXX

Appendix H. Literature searches for the clinical assessment

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

Not applicable.

Table 65 Bibliographic databases included in the literature search

Database	Platform/source	Relevant period for the search	Date of search completion
Embase	e.g. Embase.com	E.g. 1970 until today	dd.mm.yyyy
Medline			dd.mm.yyyy
CENTRAL	Wiley platform		dd.mm.yyyy

Abbreviations:

Table 66 Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
e.g. NICE	www.nice.org.uk		dd.mm.yyyy
e.g. EMA website			dd.mm.yyyy

Abbreviations:

Table 67 Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
Conference name	e.g. conference website	Manual search	List individual terms used to search in the conference material:	dd.mm.yyyy
	Journal supplement [insert reference]	Skimming through abstract collection		dd.mm.yyyy

H.1.1 Search strategies

Table 68 of search strategy table for [name of database]

No.	Query	Results
#1		88244
#2		85778
#3		115048
#4		7011
#5		10053
#6		12332
#7		206348
#8		211070
#9	#7 OR #8	272517
#10	#3 AND #6 AND #9	37

H.1.2 Systematic selection of studies

Table 69 Inclusion and exclusion criteria used for assessment of studies

Clinical effectiveness	Inclusion criteria	Exclusion criteria	Changes, local adaption
Population			
Intervention			
Comparators			
Outcomes			
Study design/publication type			
Language restrictions			

Figure 27 Overview of study design for studies included in the analyses

Study/ID	Aim	Study design	Patient population	Intervention and comparator (sample size (n))	Primary outcome and follow-up period	Secondary outcome and follow-up period
Study 1						
Study 2						

H.1.3 Excluded fulltext references

H.1.4 Quality assessment

H.1.5 Unpublished data

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

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

Not applicable.

Table 70 Bibliographic databases included in the literature search

Database	Platform	Relevant period for the search	Date of search completion
Embase	Embase.com		dd.mm.yyyy
Medline	Ovid		dd.mm.yyyy
Specific health economics databases [1]			dd.mm.yyyy

Abbreviations:

Table 71 Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
e.g. NICE	www.nice.org.uk		dd.mm.yyyy
CEA Registry	Tufts CEA - Tufts CEA		dd.mm.yyyy

Table 72 Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
Conference name	e.g. conference website	Electronic search	List individual terms used to search in the congress material:	dd.mm.yyyy
	Journal supplement [insert reference]	Skimming through abstract collection		dd.mm.yyyy

[1] Papaioannou D, Brazier J, Paisley S. Systematic searching and selection of health state utility values from the literature. Value Health. 2013;16(4):686-95.

I.1.1 Search strategies

Table 73 Search strategy for [name of database]

No.	Query	Results
#1		88244
#2		85778
#3		115048
#4		7011
#5		10053
#6		12332
#7		206348
#8		211070
#9	#7 OR #8	272517
#10	#3 AND #6 AND #9	37

Literature search results included in the model/analysis:

[Insert results in a table]

I.1.2 Quality assessment and generalizability of estimates

I.1.3 Unpublished data

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

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

Not applicable.

J.1.1 Example: Systematic search for […]

[Objective of the literature search: What questions is the literature search expected to answer?]

Table 74 Sources included in the search

Database	Platform/source	Relevant period for the search	Date of search completion
Embase	e.g. Embase.com	e.g. 1970 until today	dd.mm.yyyy
Medline			dd.mm. yyyy
CENTRAL	Wiley platform		dd.mm. yyyy

Abbreviations:

[Describe the selection process and criteria for inclusion or exclusion. For systematic searches, the requirements from the literature search for clinical evidence apply, see Appendix H].

J.1.2 Example: Targeted literature search for [estimates]

[Objective of the literature search: What questions is the literature search expected to answer?]

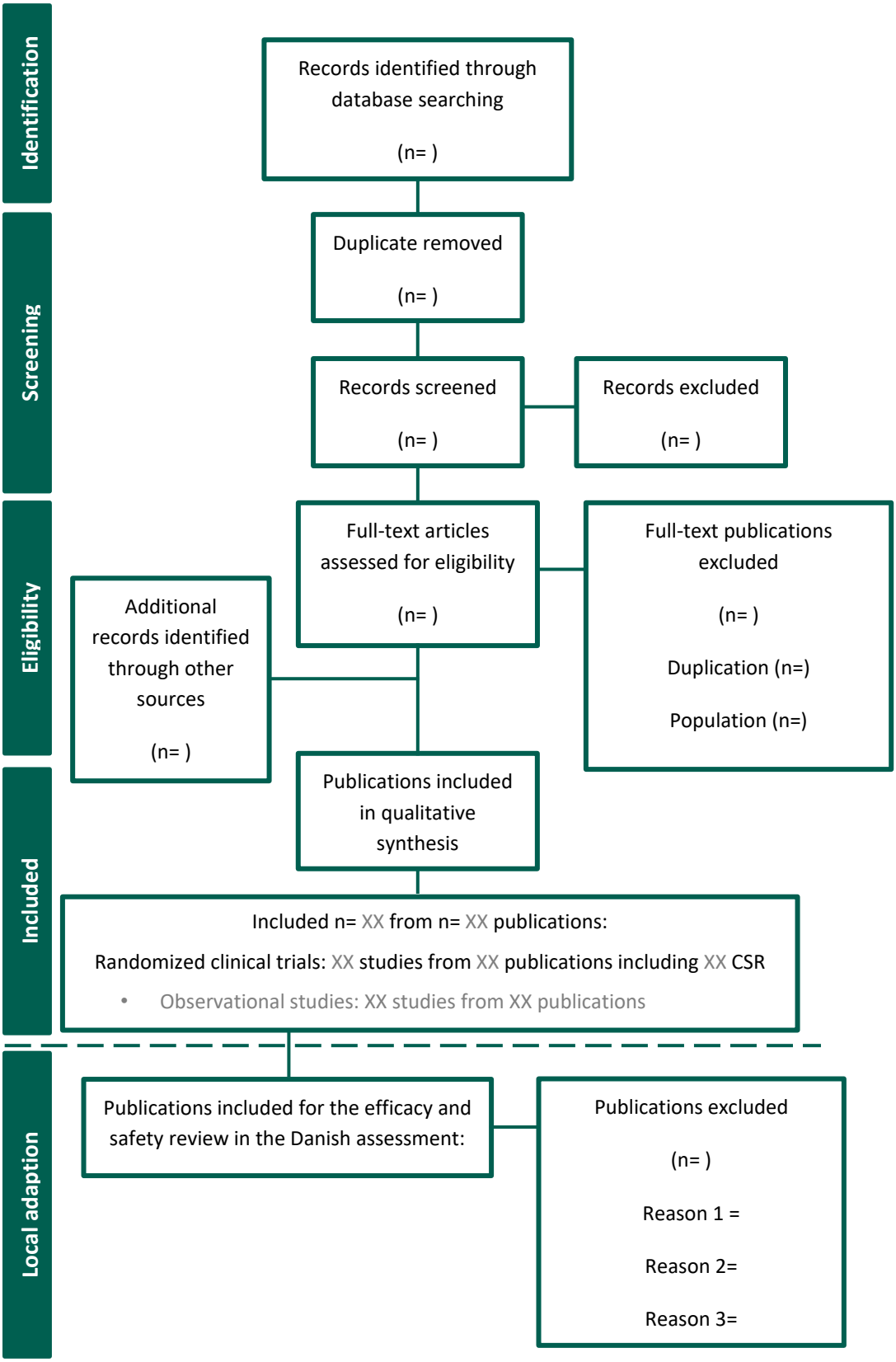
Table 75 Sources included in the targeted literature search

Source name/ database	Location/source	Search strategy	Date of search
e.g. NICE	www.nice.org.uk		dd.mm.yyyy
			dd.mm.yyyy

Abbreviations:

[Describe the selection process and criteria for inclusion or exclusion.]

Example of PRISMA diagram. The diagram is editable and may be used for recording the records flow for the literature searches and for the adaptation of existing SLRs.



Appendix K. UK BILY RWE Study