Medicinrådet

Bilag til Medicinrådets vurdering af mirvetuximabsoravtansin til behandling af kræft i æggestokkene

Voksne patienter med folatreceptor-alfa (FRα)-positiv, platinresistent, høj-grads serøs (HGSC), epitelial ovarie-, æggeleder- eller primær peritonealcancer, der har modtaget et til tre tidligere systemiske behandlingsregimer

Vers. 1.0

Bilagsoversigt

1. Amgros' forhandlingsnotat vedr. mirvetuximabsoravtansin
2. Ansøgning vedr. mirvetuximabsoravtansin

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25/11/25

MBA/DBS

Forhandlingsnotat

Dato for behandling i Medicinrådet	17.12.2025
Leverandør	AbbVie
Lægemiddel	Elahere (mirvetuximab soravtansin)
Ansøgt indikation	Monoterapi til behandling af voksne patienter med folatreceptor-alfa (FRα)-positiv, platinresistent, høj-grads serøs, epitelial ovarie-, æggeleder- eller primær peritonealcancer, der har modtaget et til tre tidligere systemiske behandlingsregimer
Nyt lægemiddel / indikationsudvidelse	Nyt lægemiddel

Prisinformation

Amgros har forhandlet følgende pris på Elahere:

Tabel 1: Forhandlingsresultat

Lægemiddel	Styrke (pakningsstørrelse)	AIP (DKK)	Forhandlet SAIP (DKK)	Forhandlet rabat ift. AIP
Elahere	5 mg/ml (20 ml konc.t.inf.væsk.opl.)	22.370,71	[redacted]	[redacted]

Prisen er betinget af Medicinrådets anbefaling.

Det betyder, at hvis Medicinrådet ikke anbefaler Elahere, indkøbes lægemidlet til AIP.

Aftaleforhold

[redacted]

Informationer fra forhandlingen

[redacted]

Konkurrencesituationen

Jævnfør Medicinrådets vurderingsrapport er komparator "*investigators choice*", som er defineret som enten pegyleret liposomal doxorubicin (PLD), paclitaxel eller gemcitabin.

[redacted]

Tabel 2 viser lægemiddeludgifter for Elahere.

Tabel 2: Lægemiddeludgifter pr. patient

Lægemiddel	Styrke (pakningsstørrelse)	Dosering	Pris pr. pakning (SAIP, DKK)	Lægemiddeludgift per år (SAIP, DKK)
Elahere*	5 mg/ml (20 ml konc.t.inf.væsk.opl.)	6 mg/kg justeret idealvægt (AIBW) som i.v. infusion hver 3. uge (21 dages cyklus)	[redacted]	[redacted]

*Der antages en patient på 69 kg, 164,3 cm højde og BSA på 1,75, svarende til AIBW på 61,12 kg jævnfør Medicinrådets vurderingsrapport afsnit 3.4.1

Status fra andre lande

Tabel 3: Status fra andre lande

Land	Status	Link
Norge	Under vurdering	Link til vurdering
England	Under vurdering	Link til vurdering
Sverige	Under vurdering	Link til vurdering

Opsummering

[redacted]

Application for the assessment of mirvetuximab soravtansine (ELAHERE®) for the treatment of adult patients with folate receptor-alpha (FRα) positive, platinum-resistant high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens.

Color scheme for text highlighting	
Color of highlighted text	Definition of highlighted text
	Confidential information

Contact information

Contact information	
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Abbreviations

Abbreviation	Definition
1L	First-line
2L	Second-line
3L	Third-line
AE	Adverse event
AIBW	Adjusted ideal body weight
AIC	Akaike information criterion
ASCO	American Society for Clinical Oncology
BIC	Bayesian information criterion
BRCA	BReast CAncer gene
BRCA	BReast CAncer gene
BRCA1	BReast CAncer gene 1
BRCA2	BReast CAncer gene 2
BSA	Body surface area
CA-125	Cancer antigen 125
CI	Confidence interval
CR	Complete response
CSR	Clinical study report
DKK	Danish krona
DMC	Danish Medicines Council
DOR	Duration of response
DoT	Duration of treatment
DRG	Diagnosis-related group
ECOG	Eastern Cooperative Oncology Group
EMA	European Medicines Agency
EOC	Epithelial ovarian cancer
EORTC	European Organization for Research and Treatment of Cancer
EQ-5D-5L	EuroQol-5 Dimension 5-level
ESMO	European Society for Medical Oncology
FOLR1	Folate receptor 1 gene
FRα	Folate receptor alpha
G-CSF	Granulocyte-colony stimulating factor
GLOBOCAN	Global Cancer Observatory
HBV	Hepatitis B virus

HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HR	Hazard ratio
HRD	Homologous recombination deficiency
HRQoL	Health-related quality of life
IC	Investigator's choice
ICER	Incremental cost-effectiveness ratio
IgG1	Immunoglobulin G1
IHC	Immunohistochemistry
IMGN	Immunogen
ITT	Intent-to-treat
IV	Intravenous
MIRV	Mirvetuximab soravtansine
MMRM	Mixed model for repeated measures
mOS	Median overall survival
mPFS	Median progression-free survival
MRI	Magnetic resonance imaging
NICE TA	National institute for health and care excellence technology appraisal
NICE TSD	National institute for health and care excellence technical support document
OR	Odds ratio
ORR	Objective response rate
OS	Overall survival
PARPi	Poly-ADP ribose polymerase inhibitor
PET	Positron emission tomography
PFI	Platinum-free interval
PFS	Progression-free survival
PGIS	Patient Global Impression of Severity
PH	Proportional hazards
PLD	Pegylated liposomal doxorubicin
PR	Partial response
PRO	Patient-reported outcome
PROC	Platinum-resistant ovarian cancer
PS	Performance status
PSM	Partitioned survival modelling
Q3W	Every 3 weeks

Q4W	Every 4 weeks
QALY	Quality-adjusted life year
QLQ-C30	Quality of Life Questionnaire-Core 30
QLQ-OV28	Quality of Life Questionnaire-Ovarian Cancer Module
QoL	Quality of life
QW	Weekly
RECIST	Response Evaluation Criteria in Solid Tumors
SD	Standard deviation
SmPC	Summary of product characteristics
TEAE	Treatment-emergent adverse event
UK	United Kingdom

1. Regulatory information on the medicine

Overview of the medicine	
Proprietary name	ELAHERE®
Generic name	mirvetuximab soravtansine
Therapeutic indication as defined by EMA	Treatment of adult patients with folate receptor-alpha (FRα) positive, platinum-resistant, high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens.
Marketing authorization holder in Denmark	AbbVie
ATC code	L01FX26
Combination therapy and/or co-medication	No
(Expected) Date of EC approval	14 November 2024
Has the medicine received a conditional marketing authorization?	No
Accelerated assessment in the European Medicines Agency (EMA)	No
Orphan drug designation (include date)	Yes, initial EC decision: 19 March 2015; maintenance of designation – COMP positive opinion: 10 October 2024
Other therapeutic indications approved by EMA	No
Other indications that have been evaluated by the DMC (yes/no)	No
Joint Nordic assessment (JNHB)	Current treatment guidelines differ across Nordic countries. Therefore, AbbVie prefers national evaluations of ELAHERE®.
Dispensing group	BEGR
Packaging – types, sizes/number of units and concentrations	Each single-dose vial (volume: 20 mL) contains 100 mg of mirvetuximab soravtansine (strength: 5 mg/mL). Pack sizes available: 1 vial

2. Summary table

Summary	
Indication relevant for the assessment	Treatment of adult patients with FRα-positive, platinum-resistant, high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens. There are no deviations from the EMA indication.
Dosage regiment and administration	The recommended dose of mirvetuximab is 6 mg/kg adjusted ideal body weight (AIBW) administered as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.
Choice of comparator	Pooled chemotherapy, consisting of single agent paclitaxel, pegylated liposomal doxorubicin (PLD) and gemcitabine.
Prognosis with current treatment (comparator)	Patients with PROC have a very poor prognosis and response rates to additional rounds of chemotherapy are usually low. The median OS of PROC patients is less than 12 months but can vary between studies [1]. In MIRASOL, the median OS for the comparator arm was 13 months. [2]
Type of evidence for the clinical evaluation	Head-to-head study
Most important efficacy endpoints (Difference/gain compared to comparator)	Primary endpoint: median PFS of 5.59 months (95% CI: 4.34–5.88) for mirvetuximab vs. 3.98 months (95% CI: 2.86–4.47) for chemotherapy, reflecting a 37% reduction in risk of tumour progression or death (HR: 0.63; 95% CI: 0.51–0.79; <0.0001. Secondary endpoint: median OS of 16.85 months (95% CI: 14.36–19.78) for mirvetuximab and 13.34 months (95% CI: 11.37–15.15) for chemotherapy (HR: 0.68; 95% CI: 0.54–0.84; p=0.0004), representing a 32% reduction in risk of death with mirvetuximab. Both from latest data cut September 2024.
Most important serious adverse events for the intervention and comparator	35% and 11% of patients treated with mirvetuximab had TEAEs leading to dose reduction and drug discontinuation, respectively. In the chemotherapy group, 24% of patients had TEAEs leading to dose reduction and 15% leading to drug discontinuation. Death due to TEAE was reported in 4 patients receiving mirvetuximab and 5 patients receiving topotecan in the chemotherapy group. In the mirvetuximab arm, the most common Grade ≥3 ocular TEAEs were [redacted]. No Grade ≥3 ocular TEAEs occurred in the chemotherapy arm.

Summary	
	Grade ≥3 haematological TEAEs such as neutropenia, anaemia and thrombocytopenia occurred in less than 1% of patients in the mirvetuximab arm.
Impact on health-related quality of life	Clinical documentation: EQ-5D-5L data (MMRM including time-to-death, treatment type and AEs). The utility values predicted if > 24 weeks from death were 0.816 (95% CI: 0.791, 0.841) for mirvetuximab and 0.792 (95% CI: 0.764, 0.819) for chemotherapy. Health economic model: Better than the comparator
Type of economic analysis that is submitted	Cost-utility analysis using a partitioned survival model.
Data sources used to model the clinical effects	Mirasol (NCT04209855) – pivotal trial (final data cut) Moore KN, Angelergues A, Konecny GE, et al. Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer. N Engl J Med. 2023;389(23):2162-2174.
Data sources used to model the health-related quality of life	Post-hoc analysis was conducted on patient reported outcomes (PRO) data collected during the MIRASOL trial (data on file)
Life years gained	[redacted]
QALYs gained	0.420 QALYs
Incremental costs	[redacted]
ICER (DKK/QALY)	[redacted]
Uncertainty associated with the ICER estimate	The parameters with greatest impact on the ICER were [redacted]
Number of eligible patients in Denmark	We estimate that 76 patients per year are eligible for treatment with mirvetuximab
Budget impact (in year 5)	[redacted]

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

3.1 The medical condition

Ovarian cancer is the third most frequently diagnosed gynaecological cancer globally according to Global Cancer Observatory (GLOBOCAN) estimates [3]. Compared with common cancers that impact women, ovarian cancer has a low incidence yet high mortality rate [4, 5]. There are 3 main subtypes of ovarian cancer: epithelial, germ cell, and stromal ovarian cancers, which can be classified based on presentation and pathological examination [6, 7]. More than 90% of ovarian cancers are epithelial in origin, the majority of which are high-grade serous tumours [7, 8]. Epithelial ovarian cancer (EOC) arises from the epithelium covering of the fimbria of the fallopian tubes, the ovaries, or the peritoneal cavity [6].

Challenges in diagnosis have been attributed to the non-specific and vague symptoms considered suggestive of ovarian cancer including abdominal/pelvic pain, constipation, diarrhoea, urinary frequency, vaginal bleeding, abdominal distension, and fatigue [9]. The symptoms experienced by patients with ovarian cancer increase in severity as the disease progresses and in advanced stages, bowel obstructions due to compression of the tumour on the intestine or decreased peristalsis can occur, with an estimated incidence of bowel obstructions up to 50% of patients with ovarian cancer [10, 11].

Due to a lack of screening options and early diagnostic techniques, approximately two-thirds of patients with epithelial ovarian cancer are at an advanced stage at the time of initial diagnosis [12, 13]. Approx. 70-80% of patients with epithelial ovarian cancer have local spread or advanced disease (stage II-IV) at the time of diagnosis [14]. The ESMO-ESGO consensus conference recommendations on ovarian cancer outlines a number of accepted approaches to diagnosis [15]. For assessment of advanced-stage ovarian cancer, particularly in selection of patients for primary debulking surgery or neoadjuvant chemotherapy, the guideline recommends pre-operative diagnostic work-up using CT, PET-CT, or diffusion-weighted whole-body MRI. Ultrasound imaging can also be carried out. Diagnostic laparoscopy can also offer a definitive histopathological diagnosis and information on intra-abdominal disease burden. In the recurrent setting, CA-125, in addition to clinical examination and presence of symptoms, is considered a better approach than regular routine imaging for diagnosis. Radiographic imaging should only be carried out if clinically indicated, based on symptoms, clinical examination, or increasing CA-125 level. The guidelines published by the Danish gynaecological cancer group in 2023 follow closely the described ESMO-ESGO consensus conference recommendations for diagnosis [15, 16].

Although most patients with advanced ovarian cancer will initially respond to platinum-based chemotherapy, the majority (up to 70%) of patients will experience disease recurrence, with subsequent treatment determined by the duration of response following platinum therapy [17, 18]. Unfortunately, nearly all patients with recurrent disease will eventually develop platinum-resistance [1, 17]. Platinum-resistance has been defined as disease relapse or progression within 6 months of completing a platinum-based regimen [19]. Although there is no universally accepted definition of platinum-resistant ovarian cancer (PROC), European Society for Medical Oncology (ESMO) guidelines categorize platinum-resistance as either primary or secondary, a categorization based on the time frame in which patients develop platinum-resistance [15, 20]. The so-called "platinum-free interval" (PFI) – defined by the American Society of Clinical Oncology (ASCO) as the duration between the date of the last platinum dose and the date of relapse detection – has been widely used as a gauge to classify patients with recurrent ovarian cancer [21]. Finally, while there are no validated biomarkers for predicting primary platinum-refractory or platinum-resistant disease [15], multidrug resistance is considered one of the main causes of treatment failure [13].

No data are available on risk factors specific to PROC, however, reported risk factors of ovarian cancer include; age [22-24], genetic predispositions [13], personal history of breast cancer [22], family history ovarian cancer [22], hormonal replacement therapy after menopause (which has been associated with 4% of ovarian cancer cases the UK) [22], and increased mortality of ovarian cancer has been associated with medical conditions such as hypertension, diabetes, and lipid disorders [25].

Ovarian cancer accounts for the highest mortality rate among gynaecologic cancers [24]. The high mortality rate is attributable to diagnosis occurring at later stages due to non-specific signs and symptoms, as well as a high rate of disease recurrence due to chemotherapy (notably platinum-containing treatment) resistance [26]. In Denmark, the 5-year survival for patients with epithelial ovarian cancer between 2005-2014 varied according to stage (stage I: 86%; stage II: 68%; stage III: 36%; and stage IV: 25%) [14].

Additionally, a Danish observational study, including 142 women with ovarian cancer, concluded that the median overall survival (OS) from diagnosis was 48.5 months (95% confidence interval (CI): 36.6-57.9 months) [27]. Furthermore, median OS after first, second, third, fourth and fifth progression was 19.3 (95% CI: 13.9-27.3), 11.4 (95% CI: 7.7-18.8), 9.5 (95% CI: 6.3-12.7), 8.3 (95% CI: 7.6-11.5) and 5.6 (95% CI: 2.9-not assessed (NA)) months, respectively [27].

There is no cure for PROC. Treatment goals are to maximize or maintain health-related quality of life (HRQoL), while attempting to control disease or minimize further progression [15, 28]. Patients with PROC have a very poor prognosis and response rates to additional rounds of chemotherapy are usually low. The median OS of PROC patients is less than 12 months but can vary between studies [1]. PROC is an especially difficult to treat type of advanced cancer, characterized by low objective response rates (ORR: 10–15%) and, for those patients who do respond to anticancer therapy, typically only a short period of progression free survival (progression-free survival [PFS]: 3–4 months) [1, 21, 29-31]. Additionally, HRQoL is especially important in disease recurrence as patients with recurrent ovarian cancer, including PROC, experience poor HRQoL [32].

Patients with PROC are distinct from the broader ovarian cancer population in that they typically are heavily pretreated with a median of two prior lines of therapy [33-35]. Although data on the burden of disease among patients with PROC are limited, patients with ovarian cancer can experience substantial burden associated with disease symptoms, particularly in advanced disease stages. Patients with PROC frequently experience residual effects of prior therapy, including sensory and motor neurotoxicity following treatment with platinum-based chemotherapy and taxanes [36-41]. The burden of advanced ovarian cancer on caregivers is reported to be an important area of unmet need among the family and other caregivers of patients with ovarian cancer [42].

Folate receptor α (FRα) is a membrane protein that binds to and transports folate into cells [9, 43]. FRα has been shown to be elevated in tumors of epithelial origin, including ovarian, breast, brain, lung, and colorectal cancers, compared to normal tissue, and its overexpression is associated with increased disease progression and poor patient prognosis, making it a promising biomarker for cancer detection.[44-46] It is estimated to be overexpressed in a majority of OC tumors [47]and is maintained on metastatic foci and recurrent tumours [48]. In a publication from 2012 [49], focussing on serous OC, an increased FRα expression1 was linked to poorer responses to chemotherapy, and was "an independently poor prognostic factor for disease free interval (DFI)" and "had a negative impact on overall survival". Later correlative OC data evaluating FRα expression with clinical and disease characteristics suggests that higher FRα expression is associated with advanced disease at diagnosis, BRCA mutational status, and serous histology[50] .

In the MIRASOL and SORAYA trials, 32% versus 36% of patients screened for the trials were considered FRα-high which was an inclusion criteria. To be considered FRα-high ≥75% of cells must have ≥2+ staining intensity when using the PS2+ scoring method [51, 52].

3.2 Patient population

Denmark has the second highest incidence rate of ovarian cancer in the world (15 per 100,000 women) [14]. Furthermore, the median age of disease onset in Denmark is 63 years, and 80% of patients are postmenopausal [14]. According to Cancerregisteret data, there were 544 new patients diagnosed with ovarian cancer in 2023 in Denmark [53]. Regarding prevalence, there were 5,060 patients with ovarian, fallopian tube, or primary peritoneal cancer (C56, C570–4) alive in Denmark during that year (2023) [53]. Both the incident and prevalent populations have remained relatively constant over the past five years. Therefore, it is expected that they will also remain constant in Denmark in the next 5 years (2025-2029).

Table 1 provides an overview of the incidence and prevalence of ovarian cancer in Denmark for the past five years.

[1] Not to be confused with the more stringent FRα-high.

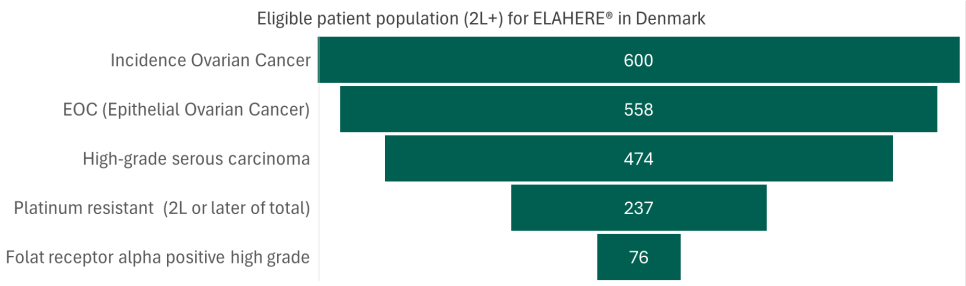
Table 1 Incidence and prevalence in the past 5 years

Year	2020	2021	2022	2023	2024*
Incidence in Denmark	580	526	535	544	544
Prevalence in Denmark	4,909	4,931	4,979	5,060	5,060

*Due to lack of published data, it was assumed the same numbers as for 2023. Source: [53]

Figure 1 shows an estimation of the patient population eligible for treatment with mirvetuximab in Denmark. The estimation is based on expert opinion on overall incidence and proportions of epithelial ovarian cancer (90-95%), high-grade serous carcinoma (85%), patients becoming platinum-resistant at some point (50%), as well as that 32% patients being screened for the MIRASOL trial were considered FRα-high [52].

Figure 1 Eligible patient population (2L) for mirvetuximab in Denmark



Sources: Danish expert input , FRα positive high grade: [52]

Hence, in Denmark, the estimated number of patients eligible for treatment with mirvetuximab is estimated to be 76 patients (Table 2).

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	76	76	76	76	76

3.3 Current treatment options

The Danish gynaecological cancer group (DGCG) published guidelines on the treatment of recurrent ovarian cancer in 2023 [16]. According to the guidelines, patients with platinum-sensitive ovarian cancer should first be treated with platinum-based single-agent or combined chemotherapy. Thereafter, the next step is to either treat patients with platinum-based chemotherapy in combination with bevacizumab or to administer a PARP inhibitor such as olaparib, niraparib or rucaparib. The second option is relevant for patients with BRCA mutation and/or homologous recombination deficiency (HRD) and

high-grade epithelial ovarian cancer who responds to platinum-based chemotherapy [16].

In case of PROC the guidelines recommend chemotherapy with liposomal doxorubicin, paclitaxel, topotecan, gemcitabine or trabectidine [16]. According to a Danish clinical expert, paclitaxel and PLD are used as first and second choice and gemcitabine as third. Topotecan is rarely used. The expert also mentions that bevacizumab is often administered as 1L treatment and patients with PROC are not re-treated with bevacizumab. PROC patients that did not previously receive bevacizumab may be treated with bevacizumab [54]. Additionally, PARP inhibitors can be considered for patients with a BRCA mutation [16].

3.4 The intervention

Table 3 provides information on ELAHERE® (mirvetuximab soravtansine, in this application referred to as mirvetuximab) is an antibody-drug conjugate. The antibody is an engineered IgG1 directed against folate receptor alpha (FRα). The function of the antibody portion is to bind to FRα expressed on the surface of ovarian cancer cells. DM4 is a microtubule inhibitor attached to the antibody via a cleavable linker. Upon binding to FRα, mirvetuximab soravtansine is internalised followed by intracellular release of DM4 via proteolytic cleavage. DM4 disrupts the microtubule network within the cell, resulting in cell cycle arrest and apoptotic cell death. Additionally, DM4 and its metabolites can enter neighbouring cells after release from target cells to induce bystander cytotoxicity, which is effective for heterogeneous and metastatic tumour cells [55].

Table 3 Summary information on ELAHERE®

Overview of intervention	
Indication relevant for the assessment	Indicated as monotherapy for the treatment of adult patients with FRα-positive, platinum-resistant high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens.
ATMP	Not applicable.
Method of administration	Intravenous infusion
Dosing	The recommended dose of mirvetuximab is 6 mg/kg AIBW administered once every 3 weeks (21-day cycle).
Dosing in the health economic model (including relative dose intensity)	The dosing recommended in the SmPC is used in the health economic model (6 mg/kg AIBW, Q3W) administered as an intravenous infusion. The relative dose intensity used in the model is 86.8% for mirvetuximab soravtansine and is informed by the MIRASOL trial.

Overview of intervention	
Should the medicine be administered with other medicines?	No concomitant administration is needed. Premedication with corticosteroid, antihistamine, antipyretic, antiemetic and lubricating eye drops is recommended. For patients found to have signs of grade 2 corneal adverse reactions (keratopathy) on slit lamp examination, secondary prophylaxis with ophthalmic topical steroids is recommended for subsequent cycles of mirvetuximab soravtansine.
Treatment duration / criteria for end of treatment	Treatment should be administered in 21-day cycles until disease progression or unacceptable toxicity.
Necessary monitoring, both during administration and during the treatment period	Patients should be monitored for signs of ocular disorders, pneumonitis, peripheral neuropathy and embryo-foetal toxicity. No other special remarks.
Need for diagnostics or other tests (e.g. companion diagnostics). How are these included in the model?	Yes, diagnostic testing for FRα is required. This is not established in Danish clinical practice yet but easily implemented and similar to other tests used; only requiring an additional IHC kit to Ventana panel (which is commonly used in Denmark). Patients receiving mirvetuximab soravtansine were assumed to incur FRα testing costs at the model entry. The proportion of screened patients with FRα positive expression was 32% in the MIRASOL trial [56]. Hence, the costs for 1/0,32≈3 tests are applied for a patient on mirvetuximab.
Package size(s)	Each single-dose vial (volume: 20 mL) contains 100 mg of mirvetuximab soravtansine (strength: 5 mg/mL). Pack sizes available: 1 vial

Abbreviations: AIBW, adjusted ideal body weight; SmPC, Summary of product characteristics. Source: [55]

The relative dose intensity (RDI) was calculated in the following manner: for each administration, the dose delivered (mg)/adjusted ideal body weight (kg) was calculated. This was then summed across all administrations and patients, and divided by the sum of the number of expected administrations which should have occurred per the MIRASOL protocol prior to discontinuation (summed across all patients).

In order to account for the administration schedule of MIRV, the number of expected administrations was defined as $1 + \lfloor t_{ONMIRV}/21 \rfloor$, where t_{ONMIRV} is the time on treatment in days, 21 represents the 3-weekly dosing schedule, and $\lfloor x \rfloor$ is the floor function (i.e. a function which rounds down to the nearest integer. For example, if a patient was on treatment for a total of 8 weeks from randomisation, we might expect them to have received $1 + \lfloor 56/21 \rfloor$ = 1 + $\lfloor 2.7 \rfloor$ = 1 + 2 = 3 administrations in total from randomisation over this time period).

3.4.1 Description of ATMP

N/A.

3.4.2 The intervention in relation to Danish clinical practice

Mirvetuximab is not used in Denmark today. It is the first medicine to demonstrate increased OS for patients suffering from FRα-positive PROC and with fewer haematologic adverse events such as neutropenia, anaemia and thrombocytopenia. The anticipated place for mirvetuximab in the Danish treatment pathway is as a new standard treatment for patients suffering from FRα-positive, platinum-resistant high-grade serous epithelial ovarian cancer. These patients are today left with chemotherapy options only.

Diagnostic testing for FRα is required. This is not established in Danish clinical practice yet but easily implemented and similar to other tests used; only requiring an additional IHC kit to Ventana panel (which is commonly used in Denmark). This is the test used in clinical studies (Roche Diagnostics) and the Ventana panel is established and used in Denmark. When testing for FRα, a new slice from the already existing paraffin embedded tissue, that was prepared earlier during the patients' diagnosis, is taken. FRα expression does not change over time, so primary tissue sample can be used and no additional biopsy is needed for FRα testing [57].

3.5 Choice of comparator(s)

Based on the description above, the relevant comparator for mirvetuximab in Danish clinical practice is pooled chemotherapy, consisting mainly of single agent paclitaxel, PLD and gemcitabine. This is in line with the clinical guidelines published by DGCG [16] and has been confirmed by a Danish clinical expert [54]. All chemotherapies named above are administered intravenously.

In second-line chemotherapy of ovarian cancer in Denmark, paclitaxel can either be administered 175 mg/m^2 body surface every three weeks [58], or weekly paclitaxel between 80-90 mg/m^2 [16]. PLD is administered at a dose of 50 mg/m^2 once every 4 weeks [59]. For gemcitabine, the recommended dose at promedicin.dk is between 1,000-1,250 mg/m^2 2-3 times per week for a 3–4-week period but not stratified by different cancer types [60]. For PROC patients, the DGCG guidelines refers to a phase III trial where the dosing is 1,000 mg/m^2 on days 1 and 8 in a three week cycle [16]. The calculation of RDI for the comparator (pooled chemotherapy) corresponded to that described in Section 3.4 for the intervention (mirvetuximab).[2]

Danish clinical practice is relatively similar to the study design of the MIRASOL trial. The MIRASOL clinical trial compared treatment with mirvetuximab to pooled chemotherapy. In MIRASOL, pooled chemotherapy included paclitaxel, PLD or topotecan. Participants in

[2] In addition, 14 patients who received doses in excess of the amount expected as calculated under this approach, caused by receipt of doses a few days earlier than scheduled, were assumed to have an RDI of 100%

the chemotherapy group received paclitaxel (80 mg per square meter of body-surface area, administered intravenously on days 1, 8, 15, and 22 of a 4-week cycle), pegylated liposomal doxorubicin (40 mg per square meter, administered intravenously on day 1 of a 4-week cycle), or topotecan (4 mg per square meter, administered intravenously on days 1, 8, and 15 of a 4-week cycle, or 1.25 mg per square meter, administered intravenously on days 1 to 5 of a 3-week cycle) [52].

Although the comparator arm in MIRASOL consisted of paclitaxel, PLD and topotecan, and the Danish clinical expert describes that paclitaxel, PLD and gemcitabine are mainly used, the results from MIRASOL are still transferable to, and valid in, the Danish setting. Although there has been no randomised controlled trial that compared topotecan and gemcitabine, it can still be concluded that topotecan and gemcitabine are inseparable in effectiveness. This is since randomised controlled trials have not demonstrated any difference in efficacy in PROC between PLD and topotecan [61], or between PLD and gemcitabine [62, 63]. From this, it follows that topotecan results in MIRASOL can be transferred to gemcitabine.

Pooled chemotherapy in the Danish context is therefore composed of paclitaxel, PLD and gemcitabine with doses corresponding to Danish clinical practice. Table 4, Table 5 and Table 6 provide overviews over the chemotherapies included in the comparator.

Table 4 Overview of paclitaxel [58]

Overview of comparator	
Generic name	Paclitaxel
ATC code	L01CD01
Mechanism of action	Paclitaxel is an antimicrotubule agent that promotes the assembly of microtubules from tubulin dimers and stabilises microtubules by preventing depolymerisation. This stability results in the inhibition of the normal dynamic reorganisation of the microtubule network that is essential for vital interphase and mitotic cellular functions. In addition, paclitaxel induces abnormal arrays or “bundles” of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.
Method of administration	Intravenous infusion
Dosing	• **Monotherapy:** 175 mg/m^2 body surface over 3 hours. Repeat after 3 weeks, or: • 80-90 mg/m^2 per week [16] • **Combination treatment:** 135-175 mg/m ^{2} body surface over 3 hours.

Overview of comparator	
Dosing in the health economic model (including relative dose intensity)	80 mg/m^2 IV infusion on Days 1, 8, 15, and 22 of each treatment cycle (i.e., QW)
Should the medicine be administered with other medicines?	Dexamethasone and chlorphenamine, as per SmPC [64]
Treatment duration/ criteria for end of treatment	Set equal to the observed KM
Need for diagnostics or other tests (i.e. companion diagnostics)	No
Package size(s)	16.7 ml, 25 ml, 50 ml

Table 5 Overview of PLD [59]

Overview of comparator	
Generic name	Pegylated liposomal doxorubicin (PLD)
ATC code	L01DB01
Mechanism of action	The exact mechanism of the antitumour activity of doxorubicin is not known. It is generally believed that inhibition of DNA, RNA and protein synthesis is responsible for the majority of the cytotoxic effects. This is probably the result of intercalation of the anthracycline between adjacent base pairs of the DNA double helix thus preventing their unwinding for replication.
Method of administration	Intravenous infusion
Dosing	50 mg/m ^{2} body surface every 4 weeks
Dosing in the health economic model (including relative dose intensity)	50 mg/m^2 Q4W
Should the medicine be administered with other medicines?	N/A
Treatment duration/ criteria for end of treatment	Set equal to the observed KM

Overview of comparator	
Need for diagnostics or other tests (i.e. companion diagnostics)	No
Package size(s)	10 ml

Table 6 Overview of gemcitabine [60]

Overview of comparator	
Generic name	Gemcitabine
ATC code	L01BC05
Mechanism of action	Cellular metabolism and mechanism of action: Gemcitabine (dFdC), which is a pyrimidine antimetabolite, is metabolised intracellularly by nucleoside kinase to the active diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides. The cytotoxic effect of gemcitabine is due to inhibition of DNA synthesis by two mechanisms of action by dFdCDP and dFdCTP. First, dFdCDP inhibits ribonucleotide reductase, which is uniquely responsible for catalysing the reactions that produce deoxynucleoside triphosphates (dCTP) for DNA synthesis. Inhibition of this enzyme by dFdCDP reduces the concentration of deoxynucleosides in general and, in particular, dCTP. Second, dFdCTP competes with dCTP for incorporation into DNA (self-potentiation).
Method of administration	Intravenous infusion
Dosing	• 1,000-1,250 mg/m^2 body surface over 30 min. Once a week for 7 weeks, followed by 1 week break or 2-3 times in 3-4 weeks. *Not stratified by cancer type* • Can be used in combination with cisplatin or carboplatin. • 1,000 mg/m2 on days 1 and 8 in a three week cycle [16]
Dosing in the health economic model (including relative dose intensity)	1,000 mg/m^2 twice every three weeks (21-day cycle)
Should the medicine be administered with other medicines?	N/A

Overview of comparator	
Treatment duration/ criteria for end of treatment	Set equal to the observed KM
Need for diagnostics or other tests (i.e. companion diagnostics)	No
Package size(s)	25 ml, 50 ml, 120 ml, 140 ml, 160 ml, 180 ml, 200 ml, 220 ml

3.6 Cost-effectiveness of the comparator(s)

The chosen comparator, pooled chemotherapy composed of paclitaxel, PLD and gemcitabine has not been previously evaluated by the Danish Medicines Council (DMC). However, the comparator is considered standard of care in Danish clinical practice. Also, the chosen comparator has a documented effect on the patient population that is relevant for the assessment (according to the indication), and its costs are low.

3.7 Relevant efficacy outcomes

3.7.1 Definition of efficacy outcomes included in the application

The efficacy endpoints used in this application are summarized in Table 7. In MIRASOL, the pivotal trial for mirvetuximab, the primary endpoint was investigator-assessed PFS. Key secondary analytic endpoints included objective response, OS, and patient-reported outcomes [52]. These efficacy endpoints are considered important to establish a positive balance of benefits and harms in clinical trials of anticancer medicinal products [65].

Table 7 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) MIRASOL [52]	From randomization until PD or death, whichever occurred first (median follow-up was [redacted] months, reverse Kaplan-Meier method)	PFS is defined as the time from first dose of mirvetuximab to progressive disease as assessed by the investigator or patient death.	PFS was evaluated by the investigator at every study visit or patient death.

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
Overall survival (OS) MIRASOL [52]	Median follow-up was 30.49 months	OS is defined as the time from first dose of mirvetuximab until patient death.	OS was evaluated by the investigator at patient death.
Objective Response Rate (ORR) MIRASOL [52]		ORR is defined as percentage of participants with a confirmed best overall response (BOR) of complete response (CR) or partial response (PR).	ORR was evaluated by the investigator at every study visit or patient death.

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

Validity of outcomes

The efficacy outcomes relevant for this assessment (PFS and OS) are considered relevant endpoints in clinical trials of anticancer medicinal products according to the European Medicines Agency (EMA) [65]. Similarly, the patient-reported outcomes (PRO) instrument used in this application (EQ-5D-5L) is a validated tool to collect HRQoL data in cancer patients [66-69].

4. Health economic analysis

4.1 Model structure

The cost-utility model uses a three-state partitioned survival modelling (PSM) approach. The model structure is presented in Figure 2 and an illustrative example of the partitioned survival modelling approach is presented in Figure 3. The model is comprised of three mutually exclusive health states:

- **Pre-progression**: Patients are progression-free; health state membership is defined by the PFS curve.
- **Post-progression**: Patients have experienced disease progression, and health state membership is defined as the proportion of patients who are alive minus the proportion of patients who have not progressed (% overall survival [OS] - %PFS)
- **Death**: The absorbing state, the proportion of patients in the death state is defined as 1 minus the proportion of patients alive (1 - %OS).

Figure 2 Model structure

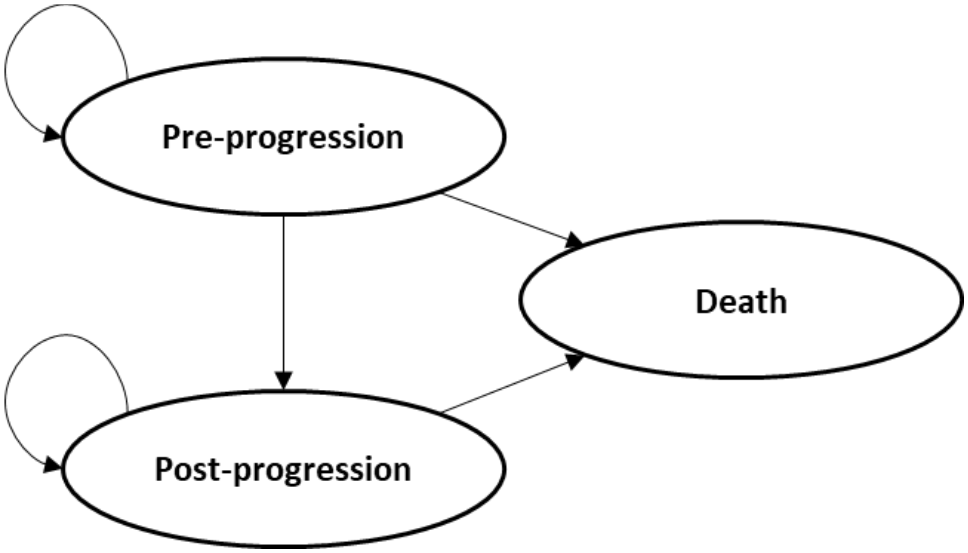
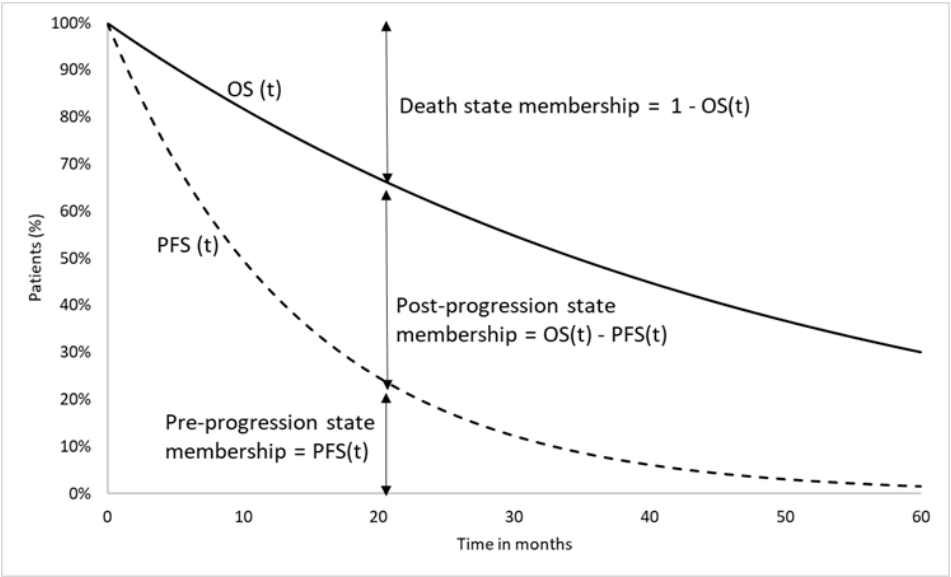


Figure 3 Schematic representation of partitioned survival approach



Abbreviations: PFS, progression-free survival; OS, overall survival.

The three-state PSM structure was considered appropriate to answer the current decision problem based on the following considerations:

- PSMs accurately reflect the progressive nature of the disease with separate pre- and post-progression states and reflect the clinical care pathway for PROC
- Progression-based models are common in economic analyses of oncology treatments as they align with trial endpoints and endpoints can be used directly to inform health state membership

    - PFS is the main endpoint used to assess efficacy outcomes within most oncology studies and has been used as the primary endpoint in clinical studies in the ovarian setting, including the MIRASOL trial [70-72]. OS is a key secondary endpoint of the MIRASOL trial and is used to capture survival benefit between treatments [56]
    - Where data requires extrapolation over the modelled time horizon, long-term estimations can be easily validated by clinical experts thus ensuring external validity of model outputs.
- The PSM approach is the most widely accepted method to model therapies for advanced oncology indications and has been used in previous HTA appraisals in ovarian cancer in Denmark [73, 74]

Patients enter the model in the pre-progression health state and are at risk of transitioning to the post-progression or death states in any model cycle.

Modelling of PFS, OS and duration of treatment (DoT) were informed by data from the pivotal trial of mirvetuximab, the MIRASOL study. The data-cut was September 2024, with a median follow-up time of 30.5 months. The analysis of PFS, OS and DoT data was carried out using the ITT population. The proportion of patients alive was defined using the OS curve and the proportion alive and progression-free was determined using the PFS curve. The proportion of patients on treatment was defined by the DoT curve. Given the different administration frequency of the components of the chemotherapy comparator arm in MIRASOL, DoT was considered independently for each of those treatments.

Furthermore, patients receive pre-progression treatments as directed by their respective dosing schedules. Patients may experience Grade 3+ AEs associated with pre-progression treatments. Once patients have progressed, they remain in the post-progression state until death (absorbing health state). During the post-progression state, a proportion of patients may receive post-progression treatments. The survival benefit of post-progression treatments was not explicitly modelled but was reflected in the OS of the treatment arms.

Patients accrue costs, life years (LYs) and quality-adjusted life years (QALYs) over the modelled time horizon. The model includes costs associated with pre-progression treatment, post-progression treatment, AEs, pre-progression disease management, post-progression disease management, testing, and terminal care. Pre-progression and post-progression health state utilities were adjusted for aging to capture HRQoL of patients over a lifetime.

4.2 Model features

The model features are summarized in Table 8.

Table 8 Features of the economic model

Model features	Description	Justification
Patient population	Adult patients with FRα-positive, platinum-resistant high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens	There are no deviations from Section 3.2.
Perspective	Limited societal perspective	According to DMC guidelines
Time horizon	Lifetime (37.2 years)	To capture all health benefits and costs in line with DMC guidelines. Based on mean age from the MIRASOL trial, which is in line with mean age at diagnosis in the Danish population (see Section 6.1.3).
Cycle length	7 days	To easily capture the different lengths of treatment cycle.
Half-cycle correction	Yes	
Discount rate	3.5 %	The DMC applies a discount rate of 3.5 % for all years.
Intervention	Mirvetuximab soravtansine (ELAHERE®)	
Comparator(s)	Pooled chemotherapy comprised of paclitaxel, PLD, and gemcitabine	According to national treatment guidelines. Validated by a Danish clinical expert [54]
Outcomes	OS, PFS	

Abbreviations: DMC, Danish Medicines Council; FR, Folate receptor; PFS, Progression-free survival; PLD, pegylated liposomal doxorubicin; OS, Overall survival.

5. Overview of literature

The clinical assessment and the clinical efficacy in the cost-utility analysis are exclusively informed by a head-to-head study with the most relevant comparator in Danish clinical practice. Hence, the literature search for efficacy and safety studies was omitted. 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. One additional input to the cost-utility model, median treatment duration to calculate post-progression costs for gemcitabine (included in relevant pooled chemotherapy constellation for the Danish setting, as described in previous sections), was informed by a literature value and thus described in section 5.3.

5.1 Literature used for the clinical assessment

A literature search was not conducted as the application is based on a head-to-head study with comparators relevant to Danish clinical practice.

Table 9 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*
Moore, K.N., et al., *Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer.* N Engl J Med, 2023. **389**(23): p. 2162-2174. [52]	MIRASOL	NCT04209855	Start: 31/12/19 Completion: 22/08/24 Data cut-off 06/03/23 Future data cut-offs 22/08/24	Mirvetuximab soravtansine vs. chemotherapy for platinum-resistant, high-grade serous ovarian cancer, previously received one to three lines of therapy and had high FRα tumour expression (≥75% of cells with ≥2+ staining intensity)
Data on file Unpublished data 2024.: ImmunoGen and AbbVie, Data on File. Final clinical study report. MIRASOL: A randomized, open-label, phase 3 study of mirvetuximab soravtansine vs. Investigator's choice of chemotherapy in platinum-resistant advanced highgrade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptoralpha expression. 2024. [75]	MIRASOL	NCT04209855	Start: 31/12/19 Completion: 22/08/24	Mirvetuximab soravtansine vs. chemotherapy for platinum-resistant, high-grade serous ovarian cancer, previously received one to three lines of therapy and had high FRα tumour expression (≥75% of cells with ≥2+ staining intensity)

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

Disutility values used in the model were derived from various published literature sources [76-78], which in turn were identified via a targeted search. Table 10 summarizes the literature sources used for the disutility values. Further information on the disutility values can be found in Section 10.3 in this dossier.

Table 10 Relevant literature included for documentation of health-related quality of life

Reference (Full citation incl. reference number)	Health state/Disutility	Reference to where in the application the data is described/applied
Sullivan, P.W. and V. Ghushchyan, *Preference-Based EQ-5D index scores for chronic conditions in the United States.* Med Decis Making, 2006. **26**(4): p. 410-20 [76]	Disutility value for: keratopathy and vision blurred	Section 10.3
Lloyd, A., et al., *Health state utilities for metastatic breast cancer.* Br J Cancer, 2006. **95**(6): p. 683-90 [77]	Disutility value for: fatigue	
Brown GC, B.M., Brown HC, Kindermann S, Sharma S. , *A value-based medicine comparison of interventions for subfoveal neovascular macular degeneration.* Ophthamology, 2007. **114**(6): p. 8 [79]	Disutility value for: cataract	
Shah, B.D., et al., *Cost-Effectiveness of KTE-X19 for Adults with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia in the United States.* Adv Ther, 2022. **39**(8): p. 3678-3695 [78]	Disutility value for: anaemia, neutropenia, and thrombocytopenia	

5.3 Literature used for inputs for the health economic model

Since pooled chemotherapy in MIRASOL consisted of paclitaxel, PLD and topotecan, and a Danish clinician confirms that gemcitabine is more commonly used, median treatment duration for the calculation of post-progression costs for gemcitabine was informed by a literature value. In a targeted search, the best sourced evidence in this setting consists of a randomized phase III trial of gemcitabine compared to PLD in PROC patients [62].

Table 11 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
Mutch, D.G., et al., Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. Journal of Clinical Oncology, 2007. 25(19): p. 2811-2818.	Median treatment duration (used for estimating post-progression costs): 12 weeks	Targeted search	Section 11.6 on subsequent treatment costs

6. Efficacy

6.1 Efficacy of mirvetuximab compared to pooled chemotherapy for adult patients with folate receptor-alpha (FRα) positive, platinum-resistant, high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens

6.1.1 Relevant studies

The relevant studies used in this application are summarised in Table 12.

Efficacy data were presented for the intention-to-treat (mITT) population of MIRASOL.

The data-cut for the results of the MIRASOL trial was September 2024 (median follow-up time: 30.5 months; this data-cut was predefined) which was the final one. The study is described in more detail in Appendix A.

Table 12 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
Mirasol, NCT04209855 (pivotal trial) [52]	Phase III, global, confirmatory, open-label, randomized, controlled trial	Median follow-up was 30.5 months	Participants who had platinum-resistant, high-grade serous ovarian cancer, previously received one to three lines of therapy and had high FRα tumor expression (≥75% of cells with ≥2+ staining intensity), 453 participants, who were stratified depending on the number of previous therapy and chemotherapy agent.	Mirvetuximab soravtansine (MIRV): 6 mg per kilogram of adjusted ideal body weight every 3 weeks until the occurrence of disease progression, an unacceptable toxic effect, withdrawal of consent, or death.	Investigator's choice of chemotherapy: Paclitaxel (80 mg/m2) administered QW within a 4-week cycle; PLD (40 mg/m2) administered Q4W; Topotecan (4 mg/m2) administered either on Days 1, 8, and 15 every 4 weeks or for 5 consecutive days (1.25 mg/m2 Days 1-5) Q3W until the occurrence of disease progression, an unacceptable toxic effect, withdrawal of consent, or death.	<u>Primary endpoint:</u> Progression-free survival; follow-up: from randomization until PD or death, whichever occurred first [redacted] <u>Secondary endpoints:</u> Number of participants with TEAEs; Objective Response Rate; Overall Survival; follow-up: median follow-up 31 months Number of Participants Achieving at Least 15 Point Absolute Improvement at Week 8 or 9 in the Abdominal/GI Scale of EORTC QLQ-OV28; follow-up: Baseline and Week 8 or 9 DOR; Percentage of Participants With CA-125 Confirmed Clinical Response Per GCIG Criteria; Time to PFS 2;

Abbreviations: DOR, Duration of Response; EORTC, European Organisation for Research and Treatment of Cancer; FRα, Folate receptor alpha; GCIG, Gynecologic Cancer Intergroup; GI, gastrointestinal; PD, (investigator-assessed) progressive disease; PFS 2, Second Progression-Free Survival; PLD, Pegylated liposomal doxorubicin, QLQ-OV28, Quality of Life Questionnaire - Ovarian Cancer Module 28; QW, once per week; Q3W, every 3 weeks; Q4W, every 4 weeks; TEAEs, Treatment-emergent Adverse Events (TEAEs)

6.1.2 Comparability of studies

Not applicable due to comparative evidence being based on head-to-head trial (the MIRASOL study).

6.1.2.1 Comparability of patients across studies

In MIRASOL, a total of 453 patients were enrolled, with 227 patients randomized to mirvetuximab and 226 randomized to chemotherapy [52]. Patient demographics and baseline characteristics are summarized in Table 13. Most patients had 2 (39%) or 3 (47%) prior lines of therapy and more than half had exposure to bevacizumab (62%) or PARPi (56%) [52].

Table 13 Baseline characteristics of patients in studies included for the comparative analysis of efficacy and safety

	MIRASOL	
	Mirvetuximab (n=227)	**Pooled chemotherapy (n=226)**
Age, median (range), years	64 (32–88)	62 (29–87)
Primary cancer diagnosis, n (%)		
Epithelial ovarian cancer	182 (80.2)	182 (80.5)
Fallopian tube cancer	27 (11.9)	23 (10.2)
Primary peritoneal cancer	16 (7.0)	20 (8.8)
Other	2 (0.9)	1 (0.4)
Stage at initial diagnosis, n (%)		
IA or IIA	7 (3.1)	1 (0.4)
IIB or IIC	2 (0.9)	8 (3.5)
IIIA	14 (6.2)	16 (7.1)
IIIB	16 (7.0)	11 (4.9)
IIIC	107 (47.1)	120 (53.1)
IV	76 (33.5)	65 (28.8)
Missing	5 (2.2)	5 (2.2)
ECOG performance status, n (%)		

	MIRASOL	
	Mirvetuximab (n=227)	Pooled chemotherapy (n=226)
0	130 (57.3)	120 (53.1)
1	97 (42.7)	101 (44.7)
2	0 (0)	3 (1.3)
Missing	0 (0)	2 (0.9)
BRCA mutations, n (%)		
BRCA1	24 (10.6)	29 (12.8)
BRCA2	9 (4.0)	7 (3.1)
Negative/Unknown	198 (87.2)	190 (84.1)
Prior systemic therapies, n (%)		
1	29 (12.8)	34 (15.0)
2	90 (39.6)	88 (38.9)
3	108 (47.6)	104 (46.0)
Prior exposure, n (%)		
Bevacizumab	138 (60.8)	143 (63.3)
PARPi	124 (54.6)	128 (56.6)
Taxanes	227 (100)	224 (99.1)
Doxorubicin/PLD	130 (57.3)	134 (59.3)
Topotecan	1 (0.4)	2 (0.9)
Primary platinum-free interval[a], n (%)		
≤ 12 months	145 (63.9)	142 (62.8)
> 12 months	81 (35.7)	84 (37.2)
Missing	1 (0.4)	0 (0)
Platinum-free interval[b], n (%)		

	MIRASOL	
	Mirvetuximab (n=227)	Pooled chemotherapy (n=226)
≤ 3 months	88 (38.8)	99 (43.8)
> 3 to ≤ 6 months	138 (60.8)	124 (54.9)
> 6 months	1 (0.4)	3 (1.3)

[a] Primary platinum-free interval was defined as time from last dose of first-line platinum therapy to date of disease progression and/or relapse following first-line therapy.
[b] Platinum-free interval was defined as time from last dose of latest-line platinum therapy to date of disease progression and/or relapse following that line of therapy.
Abbreviations: BRCA, BReast CAncer gene; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; PLD, pegylated liposomal doxorubicin.
Source: [52]

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

Table 14 summarises information of characteristics in the relevant population in Danish clinical practice and the values used in the health economic model. The average BSA and average AIBW[3] for the Danish population with PROC or ovarian cancer at any stage was not available. BSA and AIBW was calculated for each patient in MIRASOL and the average was used as input in the model. The average weight in MIRASOL was 69 kg and height was 161 cm [80].

Table 14 Characteristics in the relevant Danish population and in the health economic model

	Value in Danish population	Value used in health economic model [52]
Age in years	64 (median age at diagnosis) [81]	62.78 (SD: 9.58)
Gender	100% female	100% female
BSA (m^2)	-	1.73 (SD: 0.20)
AIBW (kg)	-	59.05 (SD: 8.28)

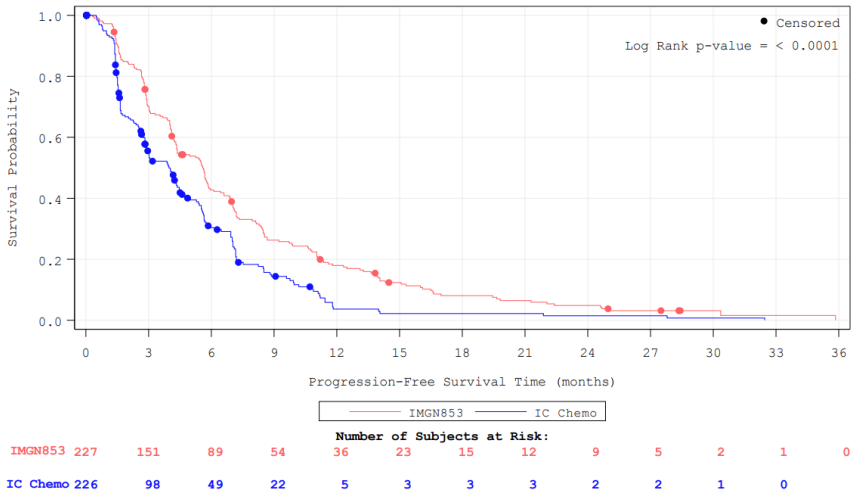
6.1.4 Efficacy – results per MIRASOL

Progression-free survival; data cut-off September 2024

[3] AIBW = Ideal Body Weight (IBW [kg]) + 0.4*(Actual weight [kg] – IBW where Female IBW [kg] = 0.9*height [cm] – 92

The primary endpoint was met, with mirvetuximab demonstrating statistically significant and clinically meaningful improvement in investigator-assessed PFS compared to chemotherapy, with a median PFS of 5.59 months (95% CI: 4.34–5.88) vs. 3.98 months (95% CI: 2.86–4.47), respectively, reflecting a 37% reduction in risk of tumour progression or death (HR: 0.63; 95% CI: 0.51–0.79; <0.0001 (Figure 4). There were 378 events of which 204 in the mirvetuximab arm and 174 in the chemotherapy arm.

Figure 4 Investigator-assessed PFS (MIRASOL final analysis: ITT population)



Abbreviations: IC Chemo, investigator's choice chemotherapy; IMGN, ImmunoGen; PFS, progression-free survival. Source: MIRASOL final data cut-off (September 2024) [80]

Subgroup analyses are presented in Figure 5.

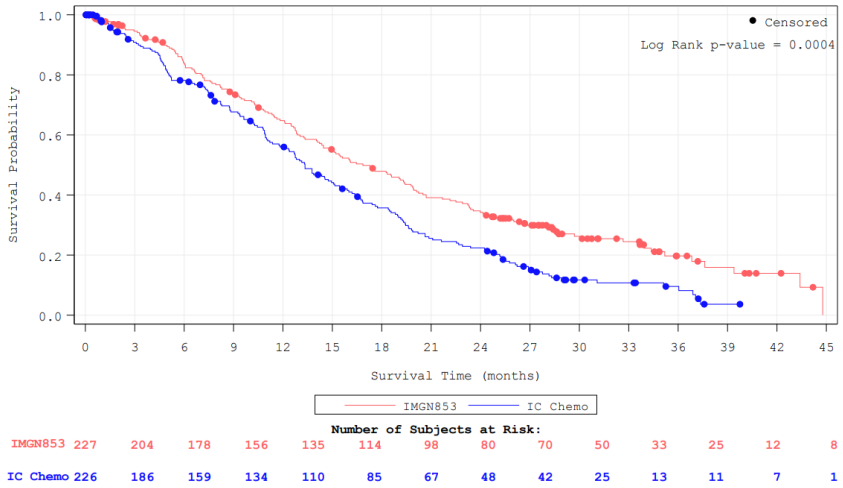
Figure 5: Subgroup analyses of investigator-assessed PFS (MIRASOL final analysis: ITT population)

Abbreviations: BRCA, BReast CAncer gene; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Score; IC Chemo, investigator's choice chemotherapy; ITT, intent-to-treat; kg, kilogram; PARPi, poly-ADP ribose polymerase inhibitor; PFS, progression-free survival; ROW, rest of world. Source: MIRASOL final data cut-off (September 2024) [80]

Overall survival; data cut-off September 2024

The median OS was 16.85 months (95% CI: 14.36–19.78) in the mirvetuximab arm and 13.34 months (95% CI: 11.37–15.15) in the chemotherapy arm (HR: 0.68; 95% CI: 0.54–0.84; p=0.0004), representing a 32% reduction in risk of death with mirvetuximab (Figure 6). There were 339 events of which there were 162 in the mirvetuximab arm and 177 in the chemotherapy arm.

Figure 6 OS (MIRASOL final analysis: ITT population)



Abbreviations: IC Chemo, investigator's choice chemotherapy; IMGN, ImmunoGen; ITT, intent-to-treat; OS, overall survival. Source: MIRASOL final data cut-off (September 2024) [80]

In the mirvetuximab arm, substantial censoring occurred after two years (month 24), likely due to patients reaching the end of the study follow-up period at the study cut-off in September 2024. This censoring significantly reduced the number of patients at risk towards the tail end of the survival curve, causing any subsequent events to have a pronounced impact on the curve's decline, particularly beyond month 40.

A similar phenomenon was observed in the chemotherapy arm, where a large number of censoring events occurred between month 24 and month 33. However, the impact of censoring in the chemotherapy arm was smaller compared to the mirvetuximab arm, as fewer patients remained at the end of the study due to the higher overall risk of death in the chemotherapy group.

While the small sample size at the tail end has little impact on the hazard ratio, it may influence the reliability of extrapolations beyond the observed data.

Subgroup analyses are presented in Figure 7.

Figure 7: Subgroup analyses OS (MIRASOL final analysis: ITT population)

Abbreviations: BRCA, BReast CAncer gene; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Score; IC Chemo, investigator's choice chemotherapy; ITT, intent-to-treat; kg, kilogram; OS, overall survival; PARPi, poly-ADP ribose polymerase inhibitor; ROW, rest of world. Source: MIRASOL final data cut-off (September 2024) [80]

7. Comparative analyses of efficacy

The clinical assessment and health economic analysis are exclusively informed by a head-to-head study with the most relevant comparator in Danish clinical practice. Hence, Section 7 (except for Table 15) was considered not 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 15 presents the results from the comparative analyses of mirvetuximab vs. pooled chemotherapy derived from the head-to-head trial (MIRASOL).

Table 15 Results from the comparative analysis of mirvetuximab vs. pooled chemotherapy (data cut: September 2024)

Outcome measure	Mirvetuximab (N=227)	Pooled chemotherapy (N=226)	Result
PFS	Median: 5.59 months (95 % CI: 4.34; 5.88)	Median: 3.98 months (95 % CI: 2.86; 4.47)	HR: 0.63 (95 % CI: 0.51; 0.79), p<0.0001
OS	Median: 16.85 months (95 % CI: 14.36; 19.78)	Median: 13.34 months (95 % CI: 11.37; 15.15)	HR: 0.68 (95 % CI: 0.54; 0.84), p=0.0004

Abbreviations: OS, overall survival; PFS, progression-free survival

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

Survival curves (OS, PFS and DoT) for mirvetuximab and pooled chemotherapy were extrapolated based on patient-level data from MIRASOL and followed the guidance from NICE Technical Support Document (TSD) 14 and TSD 21 on extrapolation of time to event data [82, 83]. The analysis presented here details the extrapolation of outcomes for the ITT population. Analyses in the cost-utility model were conducted using the September 2024 data cut from MIRASOL presented in sections above.

8.1.1 Extrapolation of efficacy data

Parametric functions considered for extrapolation included exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions. The suitability of parametric survival models was evaluated based on the following criteria:

- **Testing the proportional hazards (PH) assumption:** The PH assumption was examined to check whether the treatment effect is proportional over time between reference and comparator arms. The following were used to evaluate the PH assumption:
  - Examination of the log-cumulative hazard plots
  - Inspection of the Schoenfeld residuals.
- **Akaike's Information Criterion (AIC)/Bayesian Information Criterion (BIC) tests:** AIC and BIC provide useful statistical tests of the relative fit of different parametric survival models. These tests weight the improved fit of models with

the potentially inefficient use of additional parameters. Lower AIC and BIC values indicate better fit of the parametric survival model to the observed data.

- **Visual fit:** The parametric survival models with best goodness-of-fit statistics were also assessed for a good visual fit to the data.

8.1.1.1 Extrapolation of progression-free survival

Table 16 summarizes the assumptions associated with PFS data extrapolation.

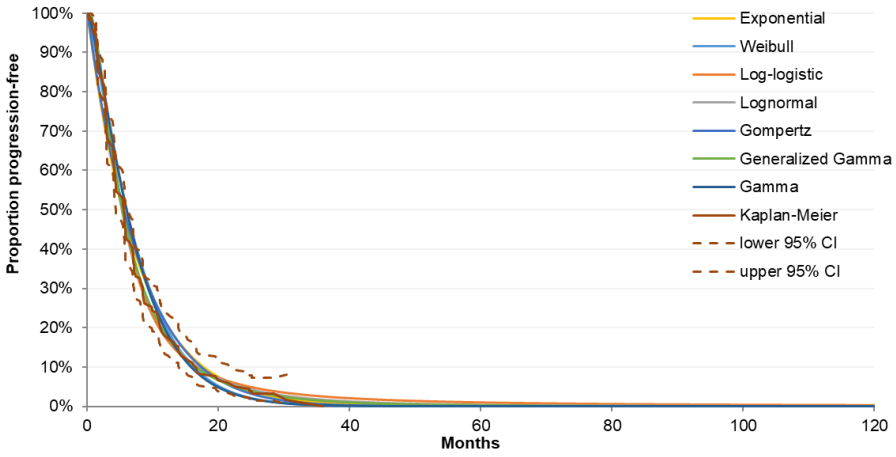
Table 16 Summary of assumptions associated with extrapolation of PFS

Method/approach	Description/assumption
Data input	MIRASOL, NCT04209855 (pivotal trial)
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	mirvetuximab: Lognormal function Pooled chemotherapy: Lognormal function
Function with best BIC fit	mirvetuximab: Lognormal function Pooled chemotherapy: Lognormal function
Function with best visual fit	All parametric survival functions produce relatively similar survival projections
Function with best fit according to evaluation of smoothed hazard assumptions	Not performed
Validation of selected extrapolated curves (external evidence)	Not performed (due to data maturity)
Function with the best fit according to external evidence	Not performed (due to data maturity)
Selected parametric function in base case analysis	mirvetuximab: Lognormal function Pooled chemotherapy: Lognormal function
Adjustment of background mortality with data from Statistics Denmark	Yes
Adjustment for treatment switching/cross-over	Not applicable

Method/approach	Description/assumption
Assumptions of waning effect	No
Assumptions of cure point	No

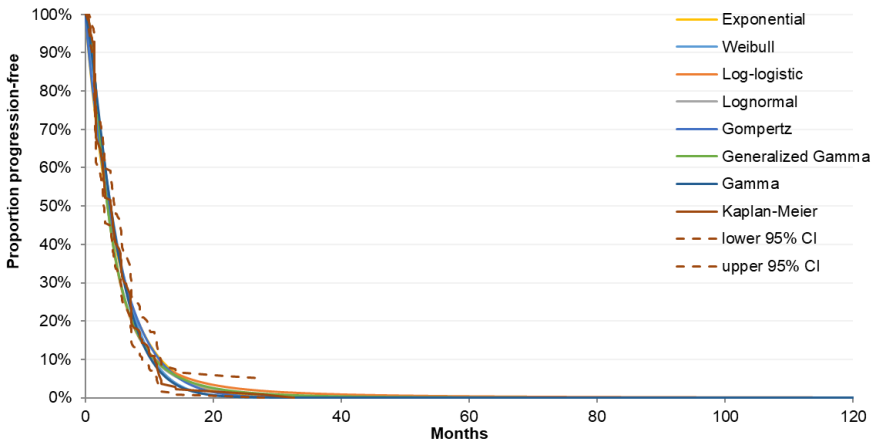
The predicted PFS curves associated with different parametric functions are shown in Figure 8 and Figure 9 for mirvetuximab and pooled chemotherapy, respectively. In the two figures, it is possible to observe that all parametric survival functions produce relatively similar survival projections. Rather than plotting all curves in one figure, we present it in two, as presenting all data in one figure hindered the evaluation of visual fit. The full method description and results for the OS extrapolation are presented in Appendix D.

Figure 8 Modelled survival functions for PFS – mirvetuximab



Abbreviations: CI, confidence interval; PFS, progression-free survival.

Figure 9 Modelled survival functions for PFS – pooled chemotherapy



Abbreviations: CI, confidence interval; PFS, progression-free survival.

8.1.1.2 Extrapolation of overall survival

Table 17 summarizes the assumptions associated with OS data extrapolation.

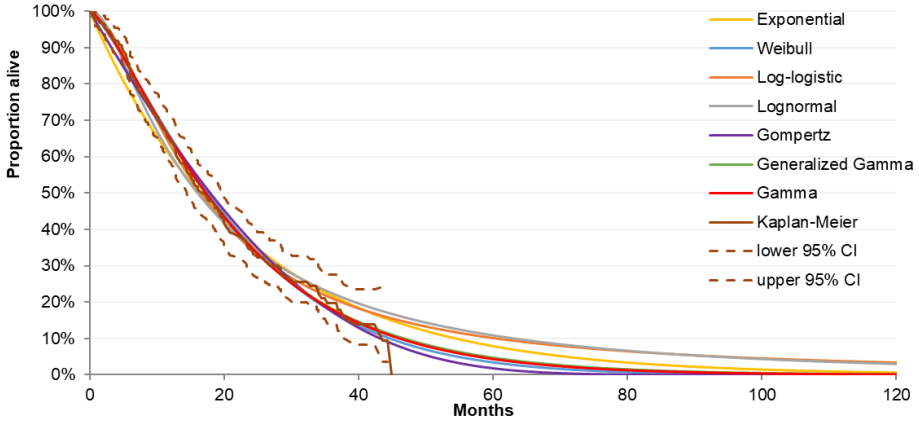
Table 17 Summary of assumptions associated with extrapolation of OS

Method/approach	Description/assumption
Data input	MIRASOL, NCT04209855 (pivotal trial)
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	mirvetuximab: Gamma function Pooled chemotherapy: Weibull function
Function with best BIC fit	mirvetuximab: Gamma function Pooled chemotherapy: Weibull function
Function with best visual fit	mirvetuximab: Gamma/generalized gamma functions Pooled chemotherapy: Weibull/gamma/generalized gamma functions
Function with best fit according to evaluation of smoothed hazard assumptions	Not performed
Validation of selected extrapolated curves (external evidence)	Not performed (due to data maturity)

Method/approach	Description/assumption
Function with the best fit according to external evidence	Not performed (due to data maturity)
Selected parametric function in base case analysis	mirvetuximab: Gamma function Pooled chemotherapy: Weibull function
Adjustment of background mortality with data from Statistics Denmark	Yes
Adjustment for treatment switching/cross-over	Not applicable
Assumptions of waning effect	No
Assumptions of cure point	No

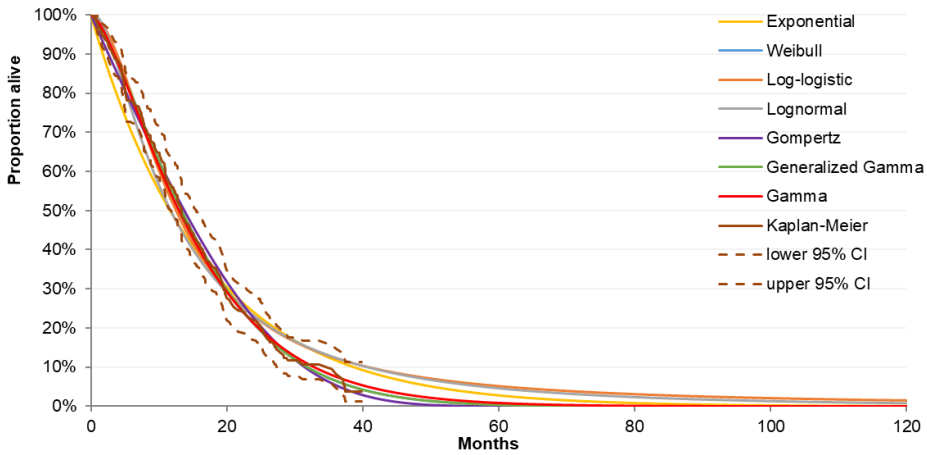
The predicted OS associated with different parametric functions are shown in Figure 10 and Figure 11 for mirvetuximab and chemotherapy, respectively. Rather than plotting all curves in one figure, we present it in two, as presenting all data in one figure hindered the evaluation of visual fit. The full method description and results for the OS extrapolation are presented in Appendix D.

Figure 10 Modelled survival functions for OS – mirvetuximab



Abbreviations: CI, confidence interval; OS, overall survival.

Figure 11 Modelled survival functions for OS – pooled chemotherapy



Abbreviations: CI, confidence interval; OS, overall survival.

Rationale for a scenario with log-logistic distribution for OS

The results of the hazard function estimated using kernel smoothing techniques (Figure 12), showed instability for both chemotherapy (starting around week 100) and mirvetuximab (starting around week 120 but very clear around week 150).

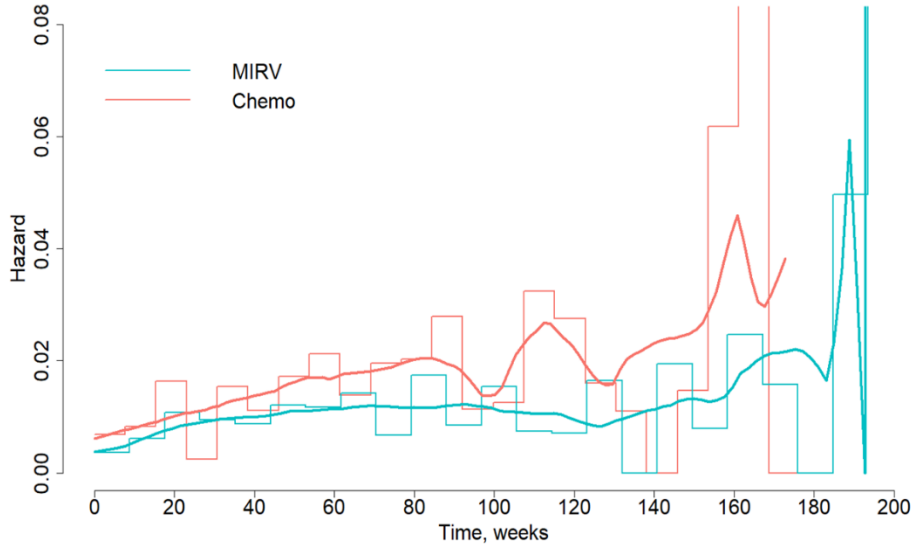
Additionally, in our study we observed a sharp decline in number of patients at risk after week 100, due not only to death but mainly (especially in the mirvetuximab arm) related to patients being censored at the last study visit. In the last three months before study termination (26 September 2024), 62 (44 patients from the mirvetuximab arm and 18 from chemotherapy arm) patients completed the last study visit. These 62 patients were censored at this time (from 22 July to 22nd August 2024) due to “study terminated by sponsor”. The 44 patients alive at the end of the study in the mirvetuximab soravtansine arm, including 3 patients still receiving treatment without progression, indicate that the September 2024 dataset includes observations potentially influenced by end-of-study artifacts.

All this has already been recognized as a potential issue in time-to-event analyses; hence it has been recommended to consider survival estimates from KM survival plots only to a point where the number of patients remaining at risk drops below a certain threshold. The definition of this threshold is open to debate and depends on the context. However, Pocock et al provided general guidance suggests that survival estimates should be considered reliable only until the proportion of patients remaining in follow-up drops to approximately 10–20% of the initial cohort [84].

Although the gamma distribution demonstrated a marginally superior statistical fit, its extrapolative predictions are heavily influenced by the unstable tail of the survival curve—particularly beyond week 100 (Chemotherapy) and week 120–150 (Mirvetuximab). The log-logistic distribution however relies less on the unstable tail and

is in that way more in line with the guidance by Pocock et al. The log-logistic distribution also provides a better visual fit than gamma until week 160.

Figure 12. Smoothed hazard function



8.1.1.3 Extrapolation of duration of treatment

Table 18 summarizes the assumptions associated with DoT data extrapolation. Kaplan-Meier data were complete for mirvetuximab, but parametric curves were used as these demonstrated a close visual fit to the Kaplan-Meier data.

DoT was modelled separately for each of the chemotherapies administered in the trial as each of these required differing dosing regimens and cycle lengths and so would be expected to demonstrate different DoT patterns over time. As gemcitabine was not part of the MIRASOL trial, the DoT for topotecan was used as an approximation for the DoT of gemcitabine. For pooled chemotherapy, observed Kaplan-Meier data were used for the DoT curves in the base case as Kaplan-Meier curves reach zero and parametric curves overestimated the proportion of patients remaining on treatment at the tail.

Table 18 Summary of assumptions associated with extrapolation of DoT

Method/approach	Description/assumption
Data input	MIRASOL, NCT04209855 (pivotal trial)
Model	Seven parametric models: exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions.
Assumption of proportional hazards between intervention and comparator	Not performed

Method/approach	Description/assumption
Function with best AIC fit	mirvetuximab: Exponential function Pooled chemotherapy: Not performed (DoT curves built directly from observed Kaplan-Meier data)
Function with best BIC fit	mirvetuximab: Exponential function Pooled chemotherapy: Not performed (DoT curves built directly from observed Kaplan-Meier data)
Function with best visual fit	mirvetuximab: all functions with the exception of lognormal and log-logistic Pooled chemotherapy: Not performed (DoT curves built directly from observed Kaplan-Meier data)
Function with best fit according to evaluation of smoothed hazard assumptions	Not performed
Validation of selected extrapolated curves (external evidence)	Not performed
Function with the best fit according to external evidence	Not performed
Selected parametric function in base case analysis	mirvetuximab: Exponential function Pooled chemotherapy: Not performed (DoT curves built directly from observed Kaplan-Meier data)
Adjustment of background mortality with data from Statistics Denmark	Yes
Adjustment for treatment switching/cross-over	Not applicable
Assumptions of waning effect	No
Assumptions of cure point	No

Figure 13 shows the visual fit of the exponential distribution to the KM data for DoT for mirvetuximab. The predicted and observed DoT associated with paclitaxel, PLD, and gemcitabine (pooled chemotherapy) are shown in Figure 14**,** Figure 15 and Figure 16.

Rather than plotting all curves in one figure, we present it in four, as presenting all data in one figure hindered the evaluation of visual fit. The full method description and results for the DoT extrapolation are presented in Appendix D.

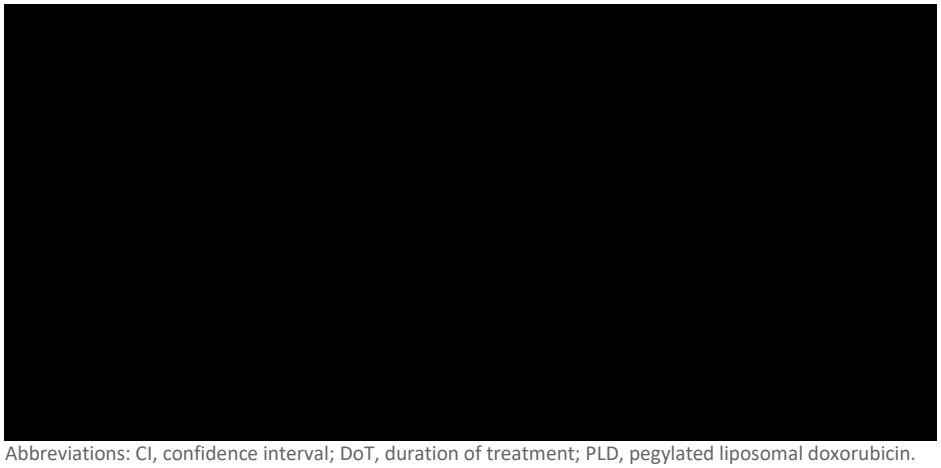
Figure 13 Chosen parametric function for DoT extrapolation (mirvetuximab arm)

Abbreviations: CI, confidence interval; DoT, duration of treatment.

Figure 14 Observed time-to-event data for DoT – paclitaxel

Abbreviations: CI, confidence interval; DoT, duration of treatment.

Figure 15 Observed time-to-event data for DoT – PLD



Abbreviations: CI, confidence interval; DoT, duration of treatment; PLD, pegylated liposomal doxorubicin.

Figure 16 Observed time-to-event data for DoT – gemcitabine (DoT data for topotecan from the MIRASOL trial are used as a proxy for DoT for gemcitabine)

Abbreviations: CI, confidence interval; DoT, duration of treatment.

8.1.2 Calculation of transition probabilities

N/A.

Table 19 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

Regarding subsequent treatment, a proportion of patients in the post-progression state were assumed to receive post-progression anti-cancer treatments and incur a one-off post-progression treatment cost at the point of progression.

In the health economic model, patients could receive single agent treatment with paclitaxel, gemcitabine, or PLD, based on subsequent treatments received by patients in Danish clinical practice. The frequencies and costs for subsequent (post-progression treatment) are presented in Section 11.6.

However, the survival benefit of post-progression treatments was not explicitly modelled and was assumed to be reflected in the OS of pre-progression treatments.

It should be noted that 10% of the patients in the control arm in MIRASOL received mirvetuximab after progression. This has not been adjusted for which, to some degree, is expected to overestimate the OS for the comparator arm.

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

Progression-free survival

Table 20 presents estimates for the modelled average and modelled median PFS and OS predicted by the extrapolation model.

Table 20 Estimates in the model (PFS)

	Modelled average PFS (reference in Excel)	Modelled median PFS (reference in Excel)	Observed median from relevant study
Mirvetuximab	8.06 months ("DMC – PSM" sheet, cell M26)	5.08 months ("DMC – PSM" sheet, cell M25)	5.59 months
Pooled chemotherapy	5.27 months ("DMC – PSM" sheet, cell M28)	3.46 months ("DMC – PSM" sheet, cell M27)	3.98 months

Abbreviations: PFS, Progression-free survival.

Overall survival

Table 21 presents estimates for the modelled average and modelled median OS predicted by the extrapolation model.

Table 21 Estimates in the model (OS)

	Modelled average OS (reference in Excel)	Modelled median OS (reference in Excel)	Observed median from relevant study
Mirvetuximab	22.21 months ("DMC – PSM" sheet, cell N26)	17.31 months ("DMC – PSM" sheet, cell N25)	16.85 months
Pooled chemotherapy	16.07 months ("DMC – PSM" sheet, cell N28)	13.38 months ("DMC – PSM" sheet, cell N27)	13.34 months

Abbreviations: OS, Overall survival.

Average treatment length

Table 22 presents the modelled average treatment length and time in model health state.

Table 22 Overview of modelled average treatment length and time in model health state, undiscounted and not adjusted for half cycle correction (adjust the table according to the model)

Treatment	Treatment length [months]	Progression-free state [months]	Post-progression state [months]
Mirvetuximab	[redacted]	[redacted]	[redacted]
Pooled chemotherapy	Paclitaxel: [redacted] PLD: [redacted] Gemcitabine: [redacted]	[redacted]	[redacted]

Abbreviations: OS, Overall survival; PFS, Progression-free survival; PLD, pegylated liposomal doxorubicin.

9. Safety

The presented safety results are from the MIRASOL trial and correspond to the results from the data cut-off of September, 2024 [80].

9.1 Safety data from the clinical documentation

The safety population in the MIRASOL final data cut-off comprised 425 patients who received ≥1 treatment dose (mirvetuximab: n=218; investigator's choice chemotherapy: n=207) [80]. Table 23 presents an overview of the safety events in MIRASOL. It is important to note that in MIRASOL CSR adverse events were reported as treatment-emergent adverse events (TEAEs). Adverse reactions were described as study drug-related TEAEs.

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

	Mirvetuximab (N=218) [80]	Pooled chemotherapy (N=207) [80]	Difference, % (95 % CI)
Number of adverse events, n	NR	NR	NR
Number and proportion of patients with ≥1 adverse events, n (%)	211 (97%)	194 (94%)	NR
Number of serious adverse events, n	NR	NR	NR
Number and proportion of	55 (25%)	69 (33%)	NR

	Mirvetuximab (N=218) [80]	Pooled chemotherapy (N=207) [80]	Difference, % (95 % CI)
patients with ≥ 1 serious adverse events, n (%)			
Number of CTCAE grade ≥ 3 events, n	NR	NR	NR
Number and proportion of patients with ≥ 1 CTCAE grade ≥ 3 events[§], n (%)	97 (44%)	113 (55%)	NR
Number of adverse reactions, n	NR	NR	NR
Number and proportion of patients with ≥ 1 adverse reactions, n (%)	[redacted]	[redacted]	[redacted]
Number and proportion of patients who had a dose reduction, n (%)	77 (35%)	50 (24%)	NR
Number and proportion of patients who discontinue treatment regardless of reason, n (%)	[redacted]	[redacted]	[redacted]
Number and proportion of patients who discontinue treatment due to adverse events, n (%)	[redacted]	[redacted]	[redacted]

§ AEs are evaluated based on NCI-CTCAE (version 5.0). Abbreviations: CI, Confidence interval; NR, Not reported.

In the table below, a summary of serious adverse events (AEs) occurring in more than >2 % of patients in either mirvetuximab arm or pooled chemotherapy arm in the MIRASOL study is presented. See Appendix E for more detailed information from CSR.

Table 24 Serious adverse events (final data cut)

Adverse events	mirvetuximab (N=218)		pooled chemotherapy (N=207)	
	Number of patients with adverse events	Number of adverse events	Number of patients with adverse events	Number of adverse events
Adverse event, n (%)				
Gastrointestinal disorders	[redacted]	[redacted]	[redacted]	[redacted]
Respiratory, thoracic and mediastinal disorders	[redacted]	[redacted]	[redacted]	[redacted]
Infections and infestations	[redacted]	[redacted]	[redacted]	[redacted]

* 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).

Modelled AEs include those that were grade ≥3, that occurred in ≥5% of patients in either arm of MIRASOL. The average number of AEs per patient is presented. It was assumed in the model that AE costs would be incurred as a one-time cost upon model entry. For more further information on how AEs costs were implemented in the model, refer to Section 11.5. The included AEs in the health economic model are presented Table 25.

Table 25 Adverse events (per patient) used in the health economic model

Adverse events	Intervention	Comparator		
	Frequency used in economic model for intervention	Frequency used in economic model for comparator	Source	Justification
Keratopathy	[redacted]	[redacted]	Patient-level analysis of MIRASOL	Grade ≥3 that occurred in ≥5% of patients in either arm of MIRASOL.
Vision blurred	[redacted]	[redacted]		
Fatigue	[redacted]	[redacted]		
Cataract	[redacted]	[redacted]		

Adverse events	Intervention	Comparator
Anaemia	[redacted]	[redacted]
Neutropenia	[redacted]	[redacted]
Thrombocytopenia	[redacted]	[redacted]

Additional monitoring and treatment of grade ≥2 ocular adverse reactions for the mirvetuximab arm were also included in the health economic analysis, in line with the mirvetuximab SmPC. [redacted]. Further details can be found in Section 11.5, as well as in the health economic model (sheet “Disease Management Costs”).

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

N/A.

Table 26 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 event, n	N/A							

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

A post-hoc analysis was conducted on patient reported outcomes (PRO) data collected during the MIRASOL trial using September 2024 data-cut to determine the effects of mirvetuximab compared with investigator's choice of chemotherapy on PRO/HRQoL endpoints in patients with platinum-resistant advanced high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high FRα expression. The planned analyses included examining longitudinal changes in PRO scores during the study and HRQoL deterioration. All PRO assessments followed the same assessment schedule and were completed together at the beginning of the clinical visit. For the MIRV arm, the median EQ-5D follow-up[4] was [redacted] months and for the chemo arm [redacted] months ([redacted] months for the study as a whole).

Patients were assessed by all domains of the EORTC QLQ-C30, EORTC QLQ-OV28, and Patient Global Impression of Severity (PGIS), and the EuroQol-5 Dimension 5-level (EQ-5D-5L). PRO results other than EQ-5D-5L data were not considered a priority for this application as these were not used in the health economic model (Table 27). For this reason, only a short summary is presented here. Across the PRO measures collected, [redacted]. Change from baseline in the EORTC QLQ-C30 and EORTC QLQ-OV28 scores were analysed using an MMRM methodology. The primary objective of this analysis was to examine treatment difference at Week 8/9. [redacted].

[redacted]

[4] The follow-up period was defined as the time from the randomization date to the date of the patient's last EQ-5D assessment.

Figure 17: MMRM: change from baseline in EORTC QLQ-C30

Table 27 Overview of included HRQoL instruments

Measuring instrument	Source	Utilization
EQ-5D-5L	MIRASOL (pivotal trial)	The instrument was used to calculate the utilities used in the health economic model

10.1 Presentation of the health-related quality of life

10.1.1 Study design and measuring instrument

The EQ-5D-5L is an international, standardized, generic instrument for describing and valuing HRQoL. It is also the preferred instrument by the DMC, according to the DMC methods guide [86].

The EQ-5D-5L was used to measure patients' HRQoL in the MIRASOL trial. The descriptive system comprises of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problem, slight problems, moderate problems, severe problems, and extreme problems [87].

10.1.2 Data collection

EQ-5D-5L in the MIRASOL trial was collected at the screening, day 1 of every treatment cycle (3 weeks for mirvetuximab and topotecan 1.25mg, and 4 weeks for other chemotherapies) through week 24, then every 12 weeks until documented progressive disease or start of a new anticancer therapy. After the assigned treatment ended, EQ-5D-5L data were collected once within a week of treatment discontinuation and then

approximately every three months during the follow-up period. Please see Table 28 for the assessment schedules based on clinical study protocol [88].

Table 28 EQ-5D-5L assessment schedule

Procedure	Screening	Cycle 1+ (Cycle = 3 or 4 weeks)[1]	End of treatment	Response/ Survival Follow-up
		Day 1	≤ 7 days from discontinuation	Every 3±1 month from end of treatment
EQ-5D-5L Assessment	×[2,3]	Day 1 of every cycle through Week 24, then every 12 weeks until documentation of progressed disease or start of a new anticancer therapy	×	×

Notes: 1. Cycle length is 3 weeks for MIRV and topotecan 1.25 mg, and 4 weeks for other chemotherapies (paclitaxel, pegylated liposomal doxorubicin, topotecan 4 mg). In the health economic model, topotecan was replaced by gemcitabine as these have similar effectiveness (see Section 3.5 for more information).
2. Must be within 14 days before day 1 of the first cycle.
3. EQ-5D-5L assessment may be performed predose at day 1 of the first cycle if not performed previously during screening.

Missing EQ-5D-5L data was assessed based on the observed number of visits divided by the expected number of visits. The utility analysis included only the observed visits with an assigned health state. Therefore, the percentage of missing data was further calculated based on the observed visits with health states divided by the expected number of visits.

The analysis was conducted separately by treatment arm and stratified by on- and off-treatment periods to account for variations in the EQ-5D-5L assessment schedule based on cycle lengths and treatment status (Table 28).

All patients in the ITT population (total=453 patients; mirvetuximab: n=227; pooled chemotherapy: n=226) were included in the missing data analyses except for those without a treatment start date (because the on/off treatment period could not be defined). Results for all patients are presented in Table 29.

Across all treatments, the percentage of EQ-5D-5L non-coverage/missingness during the on-treatment period reveals a variable pattern of data availability across scheduled visits. Missingness was [redacted]

[redacted]

Table 29 Pattern of missing data and completion

Time point	HRQoL population N	Missing N (%)	Expected to complete N	Completion N (%)
	Number of patients at randomization	Number of patients for whom data or health state is missing (% of patients at randomization)	Number of patients "at risk" at time point X	Number of patients who completed and could be assigned a health state (% of patients expected to complete)
On treatment				
Baseline	453	[redacted]	[redacted]	[redacted]
Week 3/4	453	[redacted]	[redacted]	[redacted]
Week 6	453	[redacted]	[redacted]	[redacted]
Week 8/9	453	[redacted]	[redacted]	[redacted]
Week 12	453	[redacted]	[redacted]	[redacted]
Week 15/16	453	[redacted]	[redacted]	[redacted]
Week 18	453	[redacted]	[redacted]	[redacted]
Week 20/21	453	[redacted]	[redacted]	[redacted]
Week 24	453	[redacted]	[redacted]	[redacted]
Week 36	453	[redacted]	[redacted]	[redacted]
Week 48	453	[redacted]	[redacted]	[redacted]
Off treatment				
Within 7 days of EoT	453	[redacted]	[redacted]	[redacted]
3-month post-EoT	453	[redacted]	[redacted]	[redacted]
6-month post-EoT	453	[redacted]	[redacted]	[redacted]
9-month post-EoT	453	[redacted]	[redacted]	[redacted]

Time point	HRQoL population N	Missing N (%)	Expected to complete N	Completion N (%)
12-month post-EoT	453	[redacted]	[redacted]	[redacted]
15-month post-EoT and after	453	[redacted]	[redacted]	[redacted]

Note: The number of expected visits was calculated based on the assessment schedule, and treatment end date (for on-treatment period). The number of observed visits ("Completion") refers to the number of patients who provided EQ-5D-5L response at each visit and who could be assigned a health state. On-treatment visits were captured based on the visit windows described in the Clinical Outcome Assessment Statistical Analysis Plan (COA SAP V1.0). Off-treatment visits (except for visits within 7 days) were captured based on a window of target month ± 1 month.

10.1.3 HRQoL results

Table 30 provide utility values at baseline and at on treatment data collection timepoints up to and including week 36. Utility values were generated by applying Danish-specific weights (published by Jensen et al. 2021 [89]) to the EQ-5D-5L profile data from the MIRASOL trial and that results inevitably are subject to survival bias if compared between arms.

The baseline utility values were [redacted]

Table 31 provides the corresponding results for EQ-5D-VAS.

Table 30 HRQoL [EQ-5D-5L] summary statistics

	Intervention		Comparator		Intervention vs. comparator
	N	Mean (SE)	N	Mean (SE)	Difference (95% CI) p-value
Baseline	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 8/9	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 12	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 15/16	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Intervention		Comparator		Intervention vs. comparator
Week 24	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 36	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: NR, Not reported.

Table 31 HRQoL [EQ-5D-VAS] summary statistics

	Intervention		Comparator		Intervention vs. comparator
	N	Mean (SE)	N	Mean (SE)	Difference (95% CI) p-value
Baseline	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 8/9	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 12	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 15/16	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 24	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Week 36	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: NR, Not reported.

Figure 18 display the mean utility change in EQ-5D-5L (with error bars showing the 95 % confidence intervals) from baseline through the different data collection time points for both mirvetuximab and pooled chemotherapy.

Figure 18 Mean utility change from baseline through the different data collection time points for both the mirvetuximab and pooled chemotherapy

Change from baseline in the EQ-5D-5L VAS score was analysed using an MMRM methodology, with examining treatment difference at Week 8/9 being the primary objective. The mirvetuximab group showed improvement or stability over time relative to baseline, while the IC Chemotherapy group experienced deterioration across timepoints (Figure 19). Positive differences in mean change from baseline were consistently observed between the groups, favouring MIRV at all timepoints. These differences were statistically significant, with mean differences [redacted].

Figure 19 Mixed model repeated measures: change from baseline in EQ-5D-5L VAS scores – ITT

Abbreviations: IC chemo, Investigator's Choice chemotherapy; ITT, Intent-To-Treat; VAS, Visual analogue scale

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

10.2.1 HSUV calculation

A descriptive analysis was conducted to summarize the Danish utility scores for each health state by arm (i.e., mirvetuximab vs. chemotherapy) and using the pooled data across arms. Number of patients (including completion rate), number of measurements, mean, standard error, and 95% CI were calculated. Results are presented in Appendix F.

A mixed model for repeated measures (MMRM) was used to estimate utility scores which can accommodate correlations within the repeated EQ-5D-5L measurements from the same individual over time. An identity link function was used for the continuous outcome, i.e., utility score. The model was specified with a random intercept which

accounts for individual baseline differences, and a random slope which accounts for individual variability in the fixed effect for health states.

A first order autoregressive covariance structure was used to account for correlations between repeated measurements (i.e. assuming measurements closer in time have a higher correlation than those that are further apart). The first order autoregressive correlation structure was selected based on Akaike's information criterion (AIC). The MMRM was conducted using the SAS PROC GLIMMIX procedure with the RANDOM statement.

A total of four models are available (

Table 32):

- Model 1: Progression status only ("pre-progression" and "post-progression" states)
- Model 2: Progression status and treatment type (mirvetuximab or chemotherapy)
- Model 3: Time-to-death only (≤ 4 weeks, > 4 and ≤ 12 weeks, > 12 and ≤ 24 weeks, and > 24 weeks)
- Model 4: Time-to-death and treatment type.

It is also important to note that in the time-to-death utilities, the time interval to death was defined as the duration between the EQ-5D-5L visit date and the date of death if the patient had a death event. The category was considered unknown if the patient did not die within the follow-up period (i.e., censored for OS) and the EQ-5D-5L was measured within the last 24 weeks before the end of follow-up.

Traditional cost-effectiveness models typically assume that health-state-specific utility values remain constant over time. However, previous research has shown that time to death significantly affects quality of life, independent of age [90]. Therefore, adjusting utilities only for age-related decrements is insufficient to fully capture the decline in health-related quality of life near the end of life. Moreover, data availability tends to decrease as patients approach death, leading to a higher prevalence of missing EQ-5D responses in the final stages of life. As a result, trial-collected EQ-5D data may be less representative of patients who are close to death, potentially introducing bias in utility estimates for this population. Therefore, the time-to-death utility estimates were chosen as the base case approach for the submitted health economic model as these better reflect the impact of proximity to death on patient-reported outcomes.

Furthermore, the base-case analysis model (model 4) was selected because the coefficients associated time-to-death were consistently statistically significant. The treatment effect and the effect of adverse events was not statistically significant in the HSUV analyses, but as all HRQoL analyses indicate that there are differences between the treatment arms when patients are on treatment, and when also both coefficients are in the expected direction, model 4 was judged to be the most relevant model.

Table 32 Model specifications for health state utility estimation

Models	Variables			
	Time-to-death	**Progression status**	**Treatment type**	**AE**
Model 1	x	✓	Not included (pooled)	✓
Model 2	x	✓	✓	✓
Model 3	✓	x	Not included (pooled)	✓
Model 4*	✓	**x**	✓	✓

*Base case model

Adjustment for AEs

Utility values were estimated while adjusting for the impact of AEs, which are expected to negatively affect quality of life. In the cost-utility analysis of mirvetuximab, AE-related utility decrements were considered separately from health states. Therefore, this analysis estimated the average utilities for health states unaffected by AEs by including AEs as a covariate (yes or no) in the model.

The following rules were applied to determine if a patient was being affected by AEs when the EQ-5D-5L data were collected:

- Only Grade 3+ treatment-emergent adverse events were considered
- Given the AE's impact on quality of life can remain after its resolution, an EQ-5D-5L measurement was determined to be affected by an AE if it was collected during an AE episode or within 7 days after the AE resolution. A 14-day interval between the AE resolution date and the EQ-5D-5L visit was also explored and the results can be obtained on request. The 7-day interval was selected as base case since it preserves more observations in the analysis, and is determined as sufficient for patients to return to a normal health state without the impact of AEs.
- Only AE records that have a non-missing start date were considered. For AE records with a missing end date, the average AE duration in the corresponding arm (mirvetuximab or chemotherapy) was used to impute the end date.

The regression estimates are presented in Table 33 and were used to derived values for HSUVs from model 4 (base case). Two examples of how utility values were calculated are described below and utilities for all health states are also described in Table 34.

- Pooled chemotherapy (treatment = "Chemo" [reference]) + <= 4 weeks (time_to_death_cat = "<= 4 weeks" [reference]): **Intercept = 0.3290**

- MIRV (treatment = “MIRV”) + >24 weeks (time_to_death_cat = “>24 weeks”): 0.3290 + 0.02439 + 0.4628 = **0.8162**

Table 33 Regression estimates for model 4 (base case)

Effect	AE_binary	treatment	time_to_death_cat	Estimate	SE	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Intercept				0.3290	0.04681	406	7.03	<.0001	0.05	0.2370	0.4211
AE_binary	Y			-0.00442	0.01447	98	-0.31	0.7608	0.05	-0.03314	0.02430
AE_binary	N			0	.	.	.	.	.	.	.
treatment		MIRV		0.02439	0.01807	406	1.35	0.1779	0.05	-0.01114	0.05992
treatment		Chemo		0	.	.	.	.	.	.	.
time_to_death_cat			> 12 and <= 24 weeks	0.4007	0.04689	116	8.54	<.0001	0.05	0.3078	0.4935
time_to_death_cat			> 24 weeks	0.4628	0.04626	116	10.00	<.0001	0.05	0.3712	0.5544
time_to_death_cat			> 4 and <= 12 weeks	0.2641	0.04663	116	5.66	<.0001	0.05	0.1718	0.3565
time_to_death_cat			Unknown	0.4655	0.05413	116	8.60	<.0001	0.05	0.3583	0.5727
time_to_death_cat			<= 4 weeks	0	.	.	.	.	.	.	

Age-adjustment of utilities

The health state utility values detailed in this section are assumed to apply at the start of the model; for every year after this, a multiplier was applied based on the ratio between the general population utility values for the current age and the starting age. General population utility values for Denmark were taken from DMC's Appendiks: Aldersjustering for sundhedsrelateret livskvalitet [91].

10.2.1.1 Mapping

N/A.

10.2.2 Disutility calculation

N/A. Disutilities used in the health economic model were based on external literature (see Section 10.3).

10.2.3 HSUV results

Traditional cost-effectiveness models typically assume that health-state-specific utility values remain constant over time. However, previous research has shown that time to death significantly affects quality of life, independent of age [90]. Therefore, adjusting utilities only for age-related decrements is insufficient to fully capture the decline in health-related quality of life near the end of life. Moreover, data availability tends to decrease as patients approach death, leading to a higher prevalence of missing EQ-5D responses in the final stages of life. As a result, trial-collected EQ-5D data may be less representative of patients who are close to death, potentially introducing bias in utility estimates for this population. Therefore, the time-to-death utility estimates were chosen as the base case approach for the submitted health economic model as these better reflect the impact of proximity to death on patient-reported outcomes.

The utility estimates for model including time-to-death and treatment type (base case, model 4) based on an MMRM adjusting for AEs are presented in Table 34. In addition to the reasons just presented, this was selected because the coefficients associated time-to-death were consistently statistically significant. The effect of adverse events was not statistically significant, however the coefficient associated with adverse events was in the correct direction and the analysis may have been underpowered to detect these effects.

The utility values predicted if > 24 weeks from death were 0.816 (95% CI: 0.791, 0.841) for mirvetuximab and 0.792 (95% CI: 0.764, 0.819) for chemotherapy. As expected, utility values decreased as patients approached to death both in the mirvetuximab and chemotherapy arms. Specifically, utility values remained relatively stable with slow deterioration until the last month of life and then declined considerably until death. It is worth noting that the sample size was small for the group with less than 4 weeks of time to death (n=18 in total) and thus the utility estimates in this group may have a higher risk of bias.

Results for the remaining utility models are shown in Appendix F.

Table 34 Overview of health state utility values

	Sample size	Results [95% CI]	Instrument	Tariff (value set) used	Comments
HSUVs					
Mirvetuximab: <= 4 weeks	9	0.353 (0.261, 0.446)	EQ-5D-5L	DK	HSUVs were derived from a MMRM including time-to-death, treatment type and adverse events.
Mirvetuximab: > 4 and <= 12 weeks	51	0.618 (0.569, 0.666)			
Mirvetuximab: > 12 and <= 24 weeks	97	0.754 (0.715, 0.793)			
Mirvetuximab: > 24 weeks	1193	0.816 (0.791, 0.841)			
Pooled chemotherapy: <= 4 weeks	9	0.329 (0.236, 0.422)			
Pooled chemotherapy: > 4 and <= 12 weeks	36	0.593 (0.544, 0.642)			
Pooled chemotherapy: > 12 and <= 24 weeks	67	0.73 (0.690, 0.769)			
Pooled chemotherapy: > 24 weeks	684	0.792 (0.764, 0.819)			

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

N/A. Only used for disutilities.

10.3.1 Study design

N/A. Only used for disutilities.

10.3.2 Data collection

N/A. Only used for disutilities.

10.3.3 HRQoL Results

N/A. Only used for disutilities.

10.3.4 HSUV and disutility results

Treatment-related grade 3+ AEs occurring in ≥5% of any arm of the MIRASOL trial were included in the model (Section 9.1). Patients were assumed to incur a one-off QALY loss associated with AEs by taking the product of the disutility, the average number of events per patient, and the AE duration. Disutility values for AEs were independent of treatment and applied to all treatment options. Disutility inputs were derived from various published literature sources [76-78], which in turn were identified via a targeted search. It was assumed in the model that the AE duration would be 4 weeks for each AE. Table 36 presents the disutilities in the published literature that were used to estimate the QALY decrement due to each AE.

Table 35 Overview of health state utility values [and disutilities]

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

Table 36 Overview of literature-based health state utility values

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
Disutilities				
Keratopathy	-0.008	EQ-5D -3L	NA	Disutility was directly retrieved from Sullivan et al. 2006 [76]
Vision blurred	-0.005			
Fatigue	-0.115	EQ-5D	NA	Disutility was directly retrieved from Lloyd et al. 2006 [77]
Cataract	-0.140	Patient-elicited TTO	NA	Disutility was directly retrieved from Brown et al. 2007 [79]
Anaemia	-0.120	NR	NA	Disutility was directly retrieved from Shah et al. 2022 [78]
Neutropenia	-0.090			
Thrombocytopenia	-0.110			

Note: Confidence intervals are not available for the disutilities used. Abbreviations: NA, Not available; NR, Not reported; TTO, time trade-off.

11. Resource use and associated costs

The model considered several categories of cost inputs, including pre-progression treatment costs, post-progression treatment costs, safety-related costs (including AE costs), disease management costs associated with health states, testing costs, terminal care costs, and patient costs. The analysis was conducted from a limited societal perspective. Cost data were taken from the latest available sources at the time of model adaption in 2025. Detailed inputs and assumptions are described below.

11.1 Medicines - intervention and comparator

Pre-progression treatment costs were calculated based on the drug acquisition cost per administration, drug administration cost per administration, pre-medication costs per administration, number of administrations per week, and proportion of patients remaining on treatment at each week according to the DoT curves.

Details of the estimated DoT curves are presented in Section 8.1.1.3 and Appendix D. Due to the differing dosing regimens of each of the chemotherapies and their separately calculated DoT curves, each regimen's costs were calculated separately. A weighted average value was then calculated to represent the overall chemotherapy pre-progression drug cost for each cycle based on the proportions of patients receiving each chemotherapy in the MIRASOL trial: 40.7% of patients in the chemotherapy arm of MIRASOL received paclitaxel, 35.8% received pegylated liposomal doxorubicin, and 23.5% received topotecan (in the model represented by gemcitabine, validated as a relevant comparator in Danish clinical practice) [80].

The drug acquisition cost per administration was calculated as a function of dosage, unit drug cost, and relative dose intensity (RDI). To calculate the RDI, for each administration, the dose delivered (mg)/adjusted ideal body weight (kg) was calculated. This was then summed across all administrations and patients, and divided by the sum of the number of expected administrations which should have occurred per the MIRASOL protocol prior to discontinuation (summed across all patients). In order to account for the administration schedule of mirvetuximab, the number of expected administrations was defined as $1 + \lfloor t_{ONMIRV}/21 \rfloor$, where t_{ONMIRV} is the time on treatment in days, 21 represents the 3-weekly dosing schedule, and $\lfloor x \rfloor$ is the floor function (i.e. a function which rounds down to the nearest integer). For example, if a patient was on treatment for a total of 8 weeks from randomisation, they would be expected to have received $1 + \lfloor 56/21 \rfloor$ = 1 +$\lfloor 2.7 \rfloor$ = 1 + 2 = 3 administrations in total from randomisation over this time period). Corresponding calculations were performed for all chemotherapy agents.[1] The

[1] In addition, 14 patients who received doses in excess of the amount expected as calculated under this approach, caused by receipt of doses a few days earlier than scheduled, were assumed to have an RDI of 100%

dosing schedules and respective RDIs of all treatments are presented in Section 3.4 for mirvetuximab and Section 3.5 for the comparator (pooled chemotherapy).

The cost per pack (Apotekernes indkøbspris, AIP)) used in the model for mirvetuximab was provided by AbbVie and was 22,370.71 DKK (strength: 5 mg/ml; pack size: 1). The costs per pack for the pooled chemotherapy were retrieved from the Danish Medicines Agency's Medicinpriser [92] and were the following: paclitaxel was DKK 201.50 (strength: 6 mg/ml; pack size: 1), PLD was DKK 9,250.00 (strength: 2 mg/ml; pack size: 1); and gemcitabine was DKK 325.00 (strength: 38 mg/ml; pack size: 1). As multiple strengths and pack sizes were available for the comparators, the prices sourced in the model correspond to the cheapest price per mg (among all available strengths and pack sizes).

Modelled costs were calculated using the method of moments, assuming a normal distribution around the mean BSA or AIBW from MIRASOL, to incorporate wastage (i.e. in the absence of vial sharing). In the base-case analysis, it was assumed that treatment vials could be shared between patients, i.e., it was assumed no wastage. The inclusion of wastage was tested in scenario analysis. The "no wastage"/vial sharing option uses a cost per mg approach (final acquisition costs is calculated using the respective dosing type, e.g., mg/m^2 etc.). The "wastage" option uses a cost per pack calculation, in which the distribution of BSA or AIBW (given as the proportion of patients requiring a certain dose) is matched to a number of entire packages that have to be opened to deliver that dose (and then applying a weighted average of these to the cost per pack).

Table 37 Medicines used in the model

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Intervention: mirvetuximab	6 mg/kg AIBW	86.8%	Day 1 of each treatment cycle Q3W 21-day cycle	Yes
Comparator: Pooled chemotherapy, composed of:				
Paclitaxel	80 mg/m^2	84.3%	Days 1, 8, 15, and 22 of each treatment cycle (i.e., QW) 28-day cycle	Yes
Pegylated liposomal doxorubicin	40 mg/m^2	94.6%	Day 1 of each treatment cycle Q4W 28-day cycle	Yes
Gemcitabine	800 mg/m^2	90.8%	Days 1 and 8 of each treatment cycle Q3W 21-day cycle	Yes

Abbreviations: AIBW, adjusted ideal body weight; QW, every week; Q3W, every 3 weeks; Q4W, every 4 weeks.

11.2 Medicines– co-administration

The chosen pre-medications were validated with or informed by a Danish clinical expert [54]. Pre-medication dosing schedules were obtained from the clinical trial protocol for MIRASOL [93] and relevant SmPCs [64, 94], whereas the respective costs were taken from the Danish Medicines Agency's Medicinpriser [92] (Table 38). Pre-medications were assumed to not incur any administration costs, as it was assumed that these would be accounted for in the administration costs already incurred each cycle. As previously described, the medicine with the cheapest cost per mg for the chosen strength was sourced.

Total pre-medication costs were calculated as DKK 612.71 per drug administration for mirvetuximab, DKK 582.50 per drug administration for the paclitaxel regimen, and DKK 565.00 per drug administration for the PLD and gemcitabine regimens.

Table 38 Pre-medication dose per administration of mirvetuximab or chemotherapy

Regimen	Pre-medication recommended in SmPC	Dose as recommended in SmPC (mg)	Expected use in clinical practice (mg)	Dose per drug administration (mg) – value used in the model	Reference
Mirvetuximab	Paracetamol	325 mg to 650 mg	500 mg	500 mg	MIRASOL Trial Protocol [93], mirvetuximab SmPC [94] and discussions with a Danish clinical expert [54]
	Diphenhydramine	25 - 50 mg	Desloratadine 10 mg	Not included due to low cost	
	Dexamethasone	10 mg (IV)	20 mg (oral)	20 mg (oral)	
	Antiemetics	Not stated	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	
	Ophthalmic topical steroids	Not stated	Prednisolone eye drops 4.2 mg (full dose for treatment cycle)	Prednisolone eye drops 4.2 mg (full dose for the treatment cycle)	
	Lubricating eye drops	1-2 drops 3 times a day or as needed	Hypromellose eye drops 16.8 mg (full dose for the treatment cycle)	Hypromellose eye drops 16.8 mg (full dose for the treatment cycle)	

Paclitaxel	Dexamethasone	20 mg (oral or IV)	20 mg (oral)	20 mg (oral)	Paclitaxel SmPC [64] and discussions with a Danish clinical expert [54]
	Difenhydramine or equivalent antihistamine such as chlorphenamine	50 mg IV	None	None	
	Cimetidine or ranitidine	300 mg IV 50 mg IV	None	None	
	Antiemetics	Not stated	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	
PLD	Antiemetics	Not stated	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	PLD SmPC [95] and discussions with a Danish clinical expert [54]
Gemcitabine	Antiemetics	Not stated	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	Gemcitabine SmPC [96] and discussions with a Danish clinical expert [54]

Abbreviations: IV, intravenous; SmPC, Summary of Product Characteristics.

Table 39 Pre-medication drug acquisition unit costs

Drug	Product number	Strength	Pack size	AIP per pack (DKK)	Reference
Prednisolone eye drops (Softacort®)	583775	3.35 mg/ml	30 x 0.4 ml	90	Danish Medicines Agency's Medicinpriser [92]
Hypromellose eye drops (Artelac®)	418896	3.2 mg/ml	60 x 0.5 ml	107 (assumed same as AUP price)	
Paracetamol (Paracetamol Zentiva)	459274	500 mg	100	9	

Desloratadine (Desloratadine Actavis)	116009	5 mg	100	98
Dexamethasone (Dexametasone Krka)	80431	4 mg	20	70
Akynzeo® (300 mg netupitant/0.5 mg palonosetron)	376235	300mg/0.5mg	1	656

Note: Lowest cost per mg was chosen if multiple strengths are available.

11.3 Administration costs

IV administration cost was sourced from the Sundhedsdatastyrelsen's Interactive DRG dashboard [97] and is presented in Table 40. Administration costs were applied on the first day of each cycle regardless of the number of components administered. It was assumed that all administrations would occur in an outpatient setting.

Table 40 Administration costs used in the model

Administration type	Frequency	Unit cost [DKK]	DRG code	Reference
IV infusion	First day of each cycle	1,411	13MA98	Interactive DRG: Selected Diagnosis: (DC569) Æggestokkræft. Selected Procedures: (BWAA60)Medicingivning ved intravenøs injection [97]

Abbreviations: IV, intravenous

11.4 Disease management costs

The disease management cost associated with each health state included costs of visits to healthcare professionals and computed tomography (CT) scans. Unit costs of resource use were obtained from the Sundhedsdatastyrelsen's Interactive DRG dashboard [97], and are summarised in Table 41.

Frequencies for pre- and post-progression resource use are based on discussions with a Danish clinical expert [54]. From this, we expect the regular visit to the oncologists typically occur every 3 weeks. Computer tomography is used for response evaluation, approximately every 3 months. The frequency of blood tests is the same as the visit to the oncologist (every 3 weeks). Please note that the blood test cost is considered to be included in the DRG for the oncologist visit.

Table 41 Disease management costs used in the model

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
Gynaecological oncology consultation	PFS and PPS: once every 3 weeks	1,411	13MA98	Interactive DRG: Selected Diagnosis: (DC569) Æggestokkræft Selected Procedures: (AAF21) Førstegangsbesøg [97]
CT scan	PFS and PPS: once every 3 months	2,701	30PR06	Interactive DRG: Selected Diagnosis: (DC569) Æggestokkræft Selected Procedures: (UXCD15) CT-skanning af nedre abdomen, inkl. Bækken [97]

Abbreviations: CT, computed tomography; DRG, Diagnosis-related group; NA, Not applicable; PFS; Progression-free state; PPS, post-progression state

11.5 Costs associated with management of adverse events

AE costs were calculated based on the unit cost per AE (Table 42) and the average number of AEs per patient. These number was calculated based on treatment-related grade 3+ AEs reported with incidence ≥5% of patients in either arm in MIRASOL (described in Section 9.1) [80]. The unit cost of each AE was derived from the Sundhedsdatastyrelsen's Interactive DRG dashboard [97]. Furthermore, it was assumed in the model that AE costs would be incurred as a one-time cost upon model entry.

Table 42 Cost associated with management of adverse events

	DRG code	Unit cost/DRG tariff
Keratopathy	Interactive DRG: Selected Diagnosis: (DH161J)Neurotrofisk keratopati. DRG identified: 02MA01	1,085.00
Vision blurred	Interactive DRG: Selected Diagnosis: (DH538)Anden synsforstyrrelse. DRG identified: 02MA01	1,085.00
Fatigue	Assumed same as anaemia	2,208.00
Cataract	Interactive DRG: Selected Diagnosis: (DH263) Grå stær forårsaget af lægemiddel. DRG identified: 02MA01	1,085.00

	DRG code	Unit cost/DRG tariff
Anaemia	Interactive DRG: Selected Diagnosis: (DD508A)Jernmangelanæmi forårsaget af insufficient indtag af jern. DRG identified: 16MA98	2,208.00
Neutropenia	Interactive DRG: Selected Diagnosis: (DD709A)Neutropeni og agranulocytose forårsaget af lægemiddel. DRG identified: 16MA03	37,482.00
Thrombocytopenia	Interactive DRG: Selected Diagnosis: (DD696)Trombocytopeni UNS. DRG identified: 16MA03	37,482.00

Abbreviations: DRG, Diagnosis-related group. Source: [97]

In addition, costs for hospitalisation, blood transfusion and granulocyte colony-stimulating factor (G-CSF) from a patient-level analysis of MIRASOL data were also included in the base case (Table 43). Costs are described below, whereas frequencies are described in detail in the health economic model (sheet "Safety"). It was assumed in the model that these costs would be incurred as a one-time cost upon model entry. Additionally, it was assumed in the model that patients would receive a 300 µg dose of filgrastim, the most commonly used G-CSF in the MIRASOL trial [80]. It was assumed that there was no administration cost associated with the subcutaneous administration of filgrastim.

Table 43 Additional costs to manage or prevent adverse events

	Unit cost (DKK)	Comment/Reference
Hospitalisation (cost per day)	1,411	Takstsystem 2025 Vejledning. Specifikation 13 - Sygdomme i kvindelige kønsorganer. MDC13 1-dagsgruppe, pat. mindst 7 år - 13MA98 [98]
Transfusion	6,876	Takstsystem 2025 Vejledning. Specifikation 16 - Sygdomme i blod og bloddannende organer. Transfusion af plasma og/eller behandlet blod - 16PR01 [98]
G-CSF	Total costs mirvetuximab: DKK 219.82 Total costs pooled chemotherapy: DKK 742.10	Danish Medicines Agency's Medicinpriser [92]

Abbreviations: G-CSF, Granulocyte colony-stimulating factor.

Additional monitoring and treatment for ocular adverse events was also included in line with the mirvetuximab SmPC. The SmPC states that:

- An ophthalmic exam including visual acuity and slit lamp exam should be conducted before the initiation of mirvetuximab, and if a patient develops any new or worsening ocular symptoms prior to the next dose.
- In patients with Grade ≥2 ocular adverse reactions, additional ophthalmic exams should be conducted at a minimum of every other cycle and as clinically indicated until resolution or return to baseline.
- For patients with Grade ≥2 keratopathy, secondary prophylaxis with ophthalmic topical steroids is recommended for subsequent cycles of mirvetuximab, unless the patient's eye care professional determines that the risks outweigh the benefits of such therapy.
- Patients should be instructed to use steroid eye drops on the day of infusion and through the next 7 days of each subsequent cycle of mirvetuximab.
- During treatment with ophthalmic topical steroids, the measurement of intraocular pressure and an examination with slit lamp should be carried out regularly.

Parameters used to derive the total cost of additional monitoring and treatment for ocular AEs in the mirvetuximab arm are described in detail in the health economic model (sheet “Disease Management Costs”). Almost all of the cost stems from the unit cost of ophthalmologist visit (Table 44).

Table 44 Monitoring and treatment for ocular adverse events in the mirvetuximab arm

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
Ophthalmologist visit	Every other treatment cycle	1,501	Øjenundersøgelse, mindre - 02PR02	Takstsystem 2025 Vejledning. Specifikation 02 - Øjensygdomme [98]

11.6 Subsequent treatment costs

As in the final datacut of MIRASOL [redacted] had received next line of treatment, this was also used as input in the model. The proportion of patients in each treatment arm receiving each post-progression treatment were obtained from the MIRASOL trial [80]. Taking this into consideration, as well as investigators’ choice of chemotherapy before randomization in MIRASOL and the Danish guidelines and clinical practice, assumptions were made regarding what treatments would be used after progression in the model. The composition of subsequent treatment is presented in Table 45.

The one-off post-progression treatment cost per patient was calculated as the product of the proportion of patients receiving post-progression treatments, the distribution of

post-progression treatments, the weekly cost of each treatment, and the calculated average treatment duration based on median duration of each treatment. The median duration for all mirvetuximab, paclitaxel and PLD was informed by MIRASOL values, whereas the median duration for gemcitabine reported as 12 weeks was informed by Mutch et al [62]. The unit drug acquisition cost, dose, RDI, frequency and assumptions on wastage are the same as described in Section 11.1, and the administration costs are the same as described in Section 11.3, respectively.

Table 45 Medicines of subsequent treatments

Medicine	Dose	Relative dose intensity	Frequency	Calculated average treatment length	Vial sharing
Paclitaxel	80 mg/m^2	[redacted]	Days 1, 8, 15, and 22 of each treatment cycle (i.e., QW) 28-day cycle	22.6 weeks	Yes
PLD	40 mg/m^2	[redacted]	Day 1 of each treatment cycle Q4W 28-day cycle	11.7 weeks	Yes
Gemcitabine	800 mg/m^2	[redacted]	Days 1 and 8 of each treatment cycle Q3W 21-day cycle	17.3 weeks	Yes

Furthermore, some patients in the chemotherapy arm crossed over to mirvetuximab in the MIRASOL trial, patients in the chemotherapy arm were also able to receive mirvetuximab as a post-progression treatment in the model [80]. However, this was not allowed in the base-case scenario, and mirvetuximab as a post-progression treatment was set to 0% of the patients.

The distributions of the different post-progression treatments among patients receiving post-progression treatment are presented in Table 46.

Table 46 Distribution of treatments among patients receiving post-progression treatment

	Pre-progression treatment	
	Model: mirvetuximab	Model: Pooled chemotherapy
Percentage of patients receiving post-progression treatment	[redacted]	[redacted]

Taxanes	50%	40%
PLD	40%	50%
Gemcitabine	10%	10%
Mirvetuximab	0%	0%
Pembrolizumab	0%	0%

Abbreviations: PLD, pegylated liposomal doxorubicin. Source: Assumption

11.7 Patient costs

The unit costs from DMC's Værdisætning af enhedsomkostninger were applied in the model [99]: with patient time being costed as 188 DKK/h, and travel expenses (round trip) being costed as DKK 140. Patient costs were calculated in line with the patient resource use in connection with treatment and in a similar way described in Sections 11.1, and 11.4 - 11.6.

Table 47 presents the patient costs incurred as a consequence of the medicine treatment (and respective time estimations). In general, these costs were then multiplied by the proportion of patients using each of the disease management activities included to calculate the total patient costs.

Table 47 Patient costs used in the model

Activity	Time spent [minutes, hours, days]
Pre-progression treatment[a]	Per activity:
Post-progression treatment	mirvetuximab: 4 hours (188 DKK/h * 4h + DKK 140 = DKK 892)
Management of adverse events (transfusion, G-CSF use)	Pooled chemotherapy: 4 hours (DKK 892)
Additional treatment-specific monitoring for mirvetuximab	
Management of adverse events (hospitalization)	mirvetuximab: 8 hours (DKK 1,644) Pooled chemotherapy: 8 hours (DKK 1,644)

[a]Patient costs for the pre-progression state were calculated in a similar way to the pre-progression acquisition costs (based on the duration of treatment and dosing schedule) for each treatment. In the comparator arm, a weighted average value was then calculated to represent the overall patient costs in the chemotherapy arm for each cycle based on the proportions of patients receiving each chemotherapy in the MIRASOL trial: 40.7% of patients received paclitaxel, 35.8% received pegylated liposomal doxorubicin, and 23.5% received topotecan (in the model represented by gemcitabine).

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

Testing costs

Patients receiving mirvetuximab were assumed to incur FRα testing costs at model entry. The proportion of screened patients with FRα positive expression was 32% in the MIRASOL trial; therefore, approximately three tests were required to identify one patient with FRα positive expression [52]. It was assumed that each test was associated with 30-45 minutes of a consultant pathologist's time (DKK 318) and the cost of consumables (DKK 787.88). Therefore, the estimated cost to detect one patient with FRα positive expression was DKK 3,455.88 (Table 48).

Table 48 Testing costs

		Value	Reference
% PROC patients that test positive for FR-alpha		32%	MIRASOL [52]
Cost per FR-alpha test (DKK)	Pathologist time (30-45 minutes)	318	"Bioanalytikere" (Timeløn, DKK: 424) [99]
	Cost of consumables	787.88	Communication with Roche Diagnostics
Market share of testing options		100%	Assumption
Total cost to detect one patient with mutation (DKK)		3,455.88	Calculation

Abbreviations: FR, Folate receptor; PROC, patients with recurrent ovarian cancer.

Terminal care costs

In the model, patients were assumed to incur one-time terminal care costs before death. The terminal care cost per death was estimated as DKK 89,879 from the Sundhedsdatastyrelsen's DRG list for 2025 [98]. In the cost-utility model, 51.28% of patients were assumed to incur terminal care costs, which was based on the NICE TA693 submission for olaparib for the treatment of ovarian, fallopian tube or primary peritoneal cancer [100]. This resulted in an average cost per patient of DKK 46,089.95 (Table 49). The cost was intended to reflect the intensive palliative and hospice related care which is necessary at the end of life.

Table 49 Terminal care costs

	Value	Reference
% patients receiving end-of-life care	51%	NICE TA693 [100]
Terminal care cost (DKK)	89,879	Takstsystem 2025 Vejledning. Specifikation 26 - Uden for MDC-grupper. Specialiseret

		Palliativ indsats, Øvrig - 26MP47 [98]
Weighted cost	46,089.95	Calculation

Abbreviations: NICE, National Institute for Health and Care Excellence.

12. Results

12.1 Base case overview

Table 50 provides an overview of the health economic base case.

Table 50 Base case overview

Feature	Description
Comparator	Pooled chemotherapy (composed of paclitaxel, PLD and gemcitabine)
Type of model	Partitioned survival model
Time horizon	Life-time (37.2 years)
Treatment line	Patients in the health economic model could have received one to three prior systemic treatment regimens (in line with indication). Subsequent treatment lines are included.
Measurement and valuation of health effects	Health-related quality of life measured with EQ-5D-5L in MIRASOL [85]. Danish population weights were used to estimate health-state utility values
Costs included	Medicine costs Administration costs Disease management costs Costs of adverse events Subsequent treatment costs Patient costs Other costs (testing and terminal care costs)
Dosage of medicine	Mirvetuximab: Based on adjusted ideal body weight Pooled chemotherapy: Based on body surface area
Average time on treatment	Mirvetuximab: [redacted] Comparator (pooled chemotherapy): *Paclitaxel:* [redacted] *PLD:* [redacted]

Feature	Description
	Gemcitabine: [redacted]
Parametric function for PFS	Mirvetuximab: Lognormal Pooled chemotherapy: Lognormal
Parametric function for OS	Mirvetuximab: Gamma Pooled chemotherapy: Weibull
Inclusion of waste	No
Average time in model health state	
PF	Mirvetuximab: [redacted] / Pooled chemotherapy: [redacted]
PP	Mirvetuximab [redacted] / Pooled chemotherapy: [redacted]

12.1.1 Base case results

The base case results are presented Table 51. The results of the base case show that the incremental cost-effectiveness ratio (ICER; i.e., the cost of an additional QALY gained) for mirvetuximab, compared to pooled chemotherapy, is predicted to be [redacted]. Treatment with mirvetuximab is predicted to lead to 0.420 additional QALYs and [redacted] additional life-years, compared to pooled chemotherapy. Treatment with mirvetuximab is predicted to lead to additional costs of [redacted], compared to pooled chemotherapy.

Table 51 Base case results, discounted estimates

	Mirvetuximab	Pooled chemotherapy	Difference
Medicine costs (pre-progression, includes administration)	[redacted]	[redacted]	[redacted]
Medicine costs (post-progression, includes administration)	[redacted]	[redacted]	[redacted]
Disease management – Pre-progression	[redacted]	[redacted]	[redacted]
Disease management – Post-progression	[redacted]	[redacted]	[redacted]

	Mirvetuximab	Pooled chemotherapy	Difference
Costs associated with management of adverse events	[redacted]	[redacted]	[redacted]
Patient costs	[redacted]	[redacted]	[redacted]
Palliative care costs	[redacted]	[redacted]	[redacted]
Total costs	[redacted]	[redacted]	[redacted]
Life years gained (health state A)	[redacted]	[redacted]	[redacted]
Life years gained (health state B)	[redacted]	[redacted]	[redacted]
Total life years	[redacted]	[redacted]	[redacted]
QALYs (state A)	[redacted]	[redacted]	[redacted]
QALYs (state B)	[redacted]	[redacted]	[redacted]
QALYs (adverse reactions)	[redacted]	[redacted]	[redacted]
Total QALYs	**1.368**	**0.948**	**0.420**
Incremental costs per life year gained		[redacted]	
Incremental cost per QALY gained (ICER)		[redacted]	

12.2 Sensitivity analyses

12.2.1 Deterministic sensitivity analyses

The impact of individual parameters on the ICER was tested in one-way deterministic sensitivity analyses. Key model settings, cost inputs and utility inputs were systematically and independently varied over a plausible range. Where possible, confidence intervals were used, otherwise an arbitary interval of +/- 20% was used. The ICER was recorded at the upper and lower values to produce a tornado diagram.

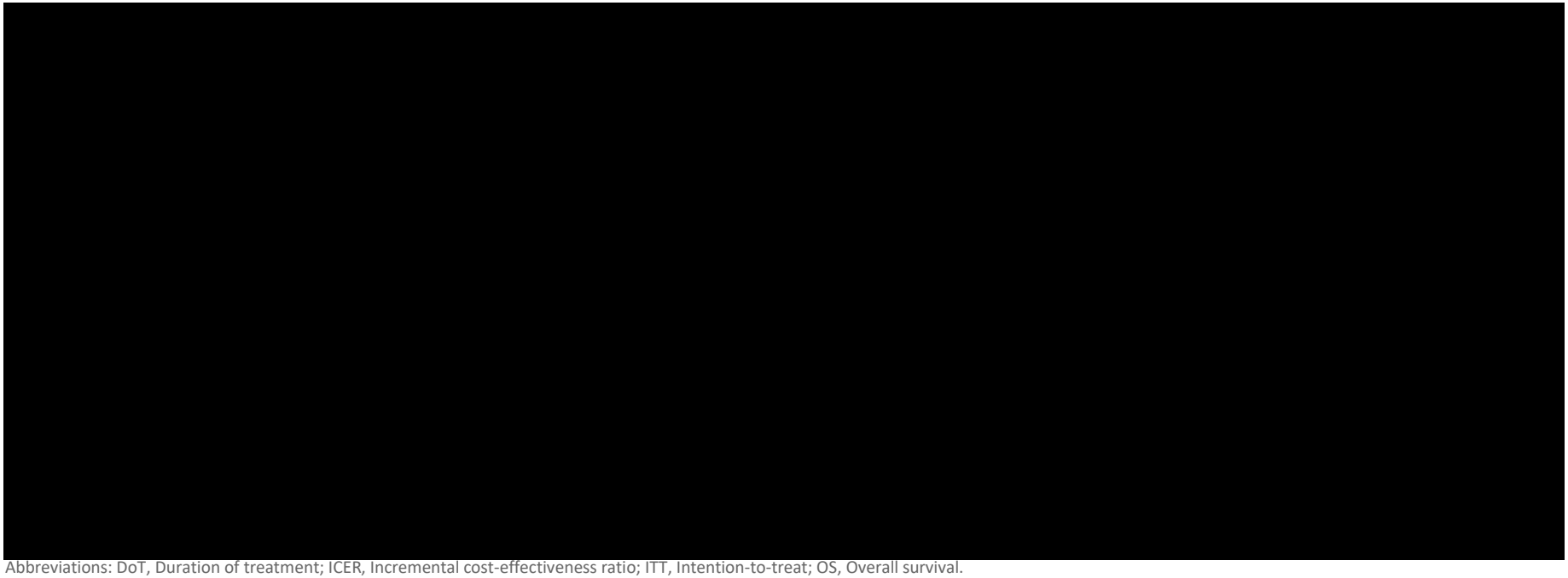
The results of the deterministic sensitivity analyses are presented in Table 52 and Figure 20. The tornado diagram and table present the ten parameters that have the greatest impact on the ICER for mirvetuximab compared to pooled chemotherapy. The parameters with greatest impact on the ICER were the rate and shape of the Gamma

distribution used to extrapolate OS in the mirvetuximab arm, as well as the scale of the Weibull distribution used to extrapolate OS in the pooled chemotherapy arm

Table 52 One-way sensitivity analyses results

	Lower bound ICER	% change from base-case ICER	Upper bound ICER	% change from base-case ICER
OS - Mirvetuximab - ITT - Gamma - rate	[redacted]	[redacted]	[redacted]	[redacted]
OS - Mirvetuximab - ITT - Gamma - shape	[redacted]	[redacted]	[redacted]	[redacted]
OS - Pooled chemotherapy - ITT - Weibull - scale	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Exponential - Parameter rate - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
Utility model - Time to death and treatment type - Mirvetuximab - > 24 weeks	[redacted]	[redacted]	[redacted]	[redacted]
Utility model - Time to death and treatment type - Pooled chemotherapy - > 24 weeks	[redacted]	[redacted]	[redacted]	[redacted]
OS - Pooled chemotherapy - ITT - Weibull - shape	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Adjusted ideal body weight (AIBW) - mean - ITT	[redacted]	[redacted]	[redacted]	[redacted]
Utility model - Time to death and treatment type - Pooled chemotherapy - > 12 and <= 24 weeks	[redacted]	[redacted]	[redacted]	[redacted]

Figure 20 Tornado diagram



Abbreviations: DoT, Duration of treatment; ICER, Incremental cost-effectiveness ratio; ITT, Intention-to-treat; OS, Overall survival.

Scenario analyses

Table 53 shows the results for the different scenario analyses. The scenario analyses indicated that the base case results were relatively stable to changes in key parameters (choice of utility model and distribution to extrapolate OS data), with the exception of the choice of log-logistic distribution to extrapolate OS in the mirvetuximab arm.

Table 53 Scenario analyses

Scenario	Deterministic				
	Change	Reason / Rational / Source	Incremental cost (DKK)	Incremental benefit (QALYs)	ICER (DKK/QALY)
Base case	[redacted]		[redacted]	[redacted]	[redacted]
Include vial sharing? No (i.e. include wastage)	[redacted]		[redacted]	[redacted]	[redacted]
Utility model - progression status only	[redacted]	Test the impact of different utility selections	[redacted]	[redacted]	[redacted]
Utility model approach - Progression status and treatment type	[redacted]	Test the impact of different utility selections	[redacted]	[redacted]	[redacted]
Utility model approach - Time to death only	[redacted]	Test the impact of different utility selections	[redacted]	[redacted]	[redacted]
Utility model approach - Time to death and treatment type	[redacted]	Test the impact of different utility selections	[redacted]	[redacted]	[redacted]
Optimistic scenario: OS - distribution for the Parametric Curve - Independent Models - Mirvetuximab (Log-Logistic)	[redacted]	Optimistic scenario, please	[redacted]	[redacted]	[redacted]

		see 8.1.1.2	
OS - distribution for the Parametric Curve - Independent Models - Mirvetuximab (Weibull)	[redacted]	Second best statistical fit	[redacted]
OS - distribution for the Parametric Curve - Independent Models - Pooled chemotherapy (Gamma)	[redacted]	Second best statistical fit	[redacted]
Discount rate 0 % for effects and costs	[redacted]	Present undiscounted results	[redacted]

Abbreviations: ICER, Incremental cost-effectiveness ratio; OS, Overall survival; QALYs, Quality-adjusted life-years.

12.2.2 Probabilistic sensitivity analyses

The results of the probabilistic sensitivity analyses are presented graphically in Figure 21 and Figure 22. The incremental cost-effectiveness scatterplot presents the variation in incremental costs and QALYs over 700 simulations (the dots are all situated in quadrant I, i.e., mirvetuximab is more costly but also more effective than pooled chemotherapy; Figure 21). The cost-effectiveness acceptability curve indicates that mirvetuximab had a 50% probability of being cost-effective at a willingness-to-pay of approximately [redacted] (Figure 22).

Figure 21 Cost-effectiveness plane

Abbreviations: QALYs, Quality-adjusted life-years.

Figure 22 Cost-effectiveness acceptability curve

13. Budget impact analysis

This budget impact analysis described how budgets will be affected over a five-year period if mirvetuximab 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 the mentioned Section, this budget impact analysis included an estimated 76 patients who are eligible for treatment with mirvetuximab.

Market shares were assumed to be 60% in year 1, 70% in year 2, and 80% onwards (years 3-5). The number of new patients expected to be treated (adjusted for market share) is presented in Table 54.

Table 54 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		
Mirvetuximab	46	53	61	61	61
Pooled chemotherapy	30	23	15	15	15
			Non-recommendation		
Mirvetuximab	-	-	-	-	-
Pooled chemotherapy	76	76	76	76	76

Budget impact

As per guidelines, the results from this budget impact analysis are based on undiscounted costs from the Markov traces and have excluded patient costs. The obtained budget impact is presented in Table 55. In 2030 (year 5), the introduction of mirvetuximab is expected to have a budget impact of approximately [redacted].

Table 55 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	[redacted]				
The medicine under consideration is NOT recommended	[redacted]				
Budget impact of the recommendation	[redacted]				

14. List of experts

Mansoor Raza Mirza, Chief Oncologist at the Department of Oncology, Rigshopitalet [54]

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Appendix A. Main characteristics of studies included

Table 56 Main characteristic of studies included

Trial name: MIRASOL	NCT number: NCT04209855
Objective	The objective of the MIRASOL trial was to compare the efficacy and safety of ELAHERE versus investigator's choice of chemotherapy (paclitaxel, PLD, or topotecan) in patients with platinum-resistant high-grade EOC, primary peritoneal, or fallopian tube cancer, whose tumours express a high level of FRα [52].
Publications – title, author, journal, year	Moore KN, Angelergues A, Konecny GE, et al. Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer. N Engl J Med. 2023;389(23):2162-2174.
Study type and design	MIRASOL is a global (253 sites in 21 countries), open label, randomized, Phase 3 trial. Eligible patients must have received 1 to 3 prior systemic anticancer therapies and experienced progression on or after immediate prior therapy, FRα-positive tumours as assessed by the Ventana FOLR1 assay, and platinum-resistant disease (PFI 3–6 months) [52]. The study excluded patients with primary platinum refractory disease (primary PFI <3 months). FRα positivity was defined as ≥75% of tumour cells exhibiting 2+/3+ IHC staining intensity. Randomization was stratified by number of prior therapy lines (1 versus 2 versus 3) and chemotherapy agent (paclitaxel versus PLD versus topotecan).
Sample size (n)	A total of 453 patients were enrolled, with 227 patients randomized to mirvetuximab and 226 randomized to chemotherapy [52].
Main inclusion criteria	• Female patients ≥18 years of age • Platinum-resistant disease • ECOG PS 0 or 1 • Advanced platinum-resistant high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers • Prior therapy of 1-3 lines of systemic anticancer therapy • Progressed on or after most recent line of therapy • At least 1 lesion that meets the definition of measurable disease by RECIST v1.1 criteria Tumour positive for FRα expression as defined by the Ventana FOLR1 Assay (≥75% of viable tumour cells exhibiting 2+ IHC staining intensity)
Main exclusion criteria	• Primary platinum-refractory disease • Patients with serious concurrent illness or clinically relevant active infection, including, but not limited to HBV, HCV, HIV, active cytomegalovirus infection, or any other concurrent infectious disease requiring IV antibiotics within 2 weeks before starting study drug • Patients demonstrated pre-existing Grade > 1 peripheral neuropathy per Common Terminology Criteria for Adverse Events v5.0

Trial name: MIRASOL	NCT number: NCT04209855
	• Patients had a chronic corneal disorder, a history of corneal transplantation, or an active ocular condition that required ongoing treatment/monitoring Women who are pregnant or lactating
Intervention	227 patients were randomized to receive 6 mg/kg AIBW mirvetuximab every 3 weeks (Q3W) via IV infusion Patients receiving mirvetuximab were premedicated with acetaminophen/paracetamol, dexamethasone, and diphenhydramine for infusion-related reactions; prophylactic corticosteroid eye drops were required, and preservative-free lubricating artificial tears were recommended. All participants received ocular examinations at screening. Patients receiving mirvetuximab underwent additional ocular examinations at ocular symptom emergence and at every other cycle thereafter.
Comparator(s)	226 patients were randomized to receive chemotherapy (paclitaxel, PLD, or topotecan). Patients receiving paclitaxel were administered 80 mg/m2 weekly (QW). Patients receiving PLD received 40 mg/m2 every 4 weeks (Q4W). Patients receiving topotecan were administered 4 mg/m2 on Days 1, 8, and 15 (Q4W) or 1.25 mg/m2 on Days 1–5 (Q3W). Patients receiving chemotherapy were premedicated at the investigator's discretion.
Follow-up time	September 2024 data-cut: follow-up of 30.5 months
Is the study used in the health economic model?	Yes.
Primary, secondary and exploratory endpoints	Primary: • Investigator assessed progression-free survival (PFS)[a] Secondary: • Investigator assessed objective response rate (ORR)[b] • Overall survival (OS)[c] • Primary patient reported outcome[d] Other secondary endpoints: • Duration of response (DOR)[e] • Safety and tolerability (TEAEs, laboratory test results, PE findings, and vital signs) • Cancer antigen-125 (CA-125) response rate by GCIG criteria • PFS2[f]
Method of analysis	All efficacy analyses presented in this application were intention-to-treat analyses. The primary endpoint in MIRASOL was PFS per investigator assessment, estimated using the Kaplan-Meier method, with comparison between treatment groups conducted using Cox proportional hazard regression and log rank test.

Trial name: MIRASOL	NCT number: NCT04209855
Subgroup analyses	Not applicable for this submission.
Other relevant information	Not applicable.

[a] PFS defined as time from date of randomization until investigator assessed progressive disease or death.
[b] Confirmed complete plus partial response per RECIST v1.1.
[c] Time from date of randomization until date of death.
[d] Defined as the umber of patients achieving at least a 15-point absolute improvement at Week 8 or Week 9 in the Abdominal/GI subscale of EORTC QLQ-OV28.
[e] DOR defined as time from initial response until investigator-assessed progressive disease or death for all who achieved a confirmed objective response.
[f] PFS2 defined as time from randomization until second disease progression
Abbreviations: CA-125, cancer antigen 125; DOR, duration of response; GCIG, Gynecologic Cancer InterGroup; ORR, objective response rate; OS, overall survival; PE, physical examination; PFS, progression-free survival; TEAE, treatment-emergent adverse event.
Source: Moore et al (2023) [52]

Appendix B. Efficacy results per study

Results per study

Table 57 Results per study

Results of MIRASOL (NCT04209855)											
				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**		
Datacut: September, 2024											
mPFS	mirvetuximab	227	5.59 months (4.34–5.88)	NR	NR	NR	HR: 0.63	2.86–4.47	<0.0001	Comparison between treatment groups conducted using Cox proportional hazard regression and log rank test	[80]
	Chemotherapy	226	3.98 months (2.86–4.47),								[80]
mOS	mirvetuximab	227	16.85 months (14.36–19.78)	NR	NR	NR	HR: 0.68	0.54–0.84	p=0.0004	Comparison between treatment groups conducted using Cox proportional hazard regression and log rank test	[80]
	Chemotherapy	226	13.34 months (11.37–15.15)								[80]
ORR	mirvetuximab	227	41.9% (35.4–48.6)	NR	NR	NR	OR: 3.75	2.01-5.02	p<0.0001	Comparison between treatment groups conducted	[80]

Results of MIRASOL (NCT04209855)											
				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**		
	Chemotherapy	226	15.9% (11.4–21.4)							using Cox proportional hazard regression and log rank test	[80]
Datacut: March 6, 2023 (published in Moore et al. 2023) [52]											
mPFS	mirvetuximab	227	5.62 months (4.34–5.95)	NR	NR	NR	NR	NR	NR	Comparison between treatment groups conducted using Cox proportional hazard regression and log rank test	[52]
	Chemotherapy	226	3.98 months (2.86–4.47),								[52]
mOS	mirvetuximab	227	16.46 months (14.46–24.57)	NR	NR	NR	HR: 0.67	0.50–0.89	p=0.005	Comparison between treatment groups conducted using Cox proportional hazard regression and log rank test	[52]
	Chemotherapy	226	12.75 months (10.91–14.36)								[52]
ORR	mirvetuximab	227	42.3% (35.8–49.0)	NR	NR	NR	OR: 3.81	2.44–5.94	p<0.001	Comparison between treatment groups conducted using Cox proportional hazard regression and log rank test	[52]
	Chemotherapy	226	15.9% (11.4–21.4)								[52]

Abbreviations: NR, Not reported

Appendix C. Comparative analysis of efficacy

N/A.

Table 58 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		
N/A									

Appendix D. Extrapolation

D.1 Extrapolation of PFS

D.1.1 Data input

As mentioned in Section 8.1.1.1, PFS extrapolation was informed by the September 2024 data cut from MIRASOL [80].

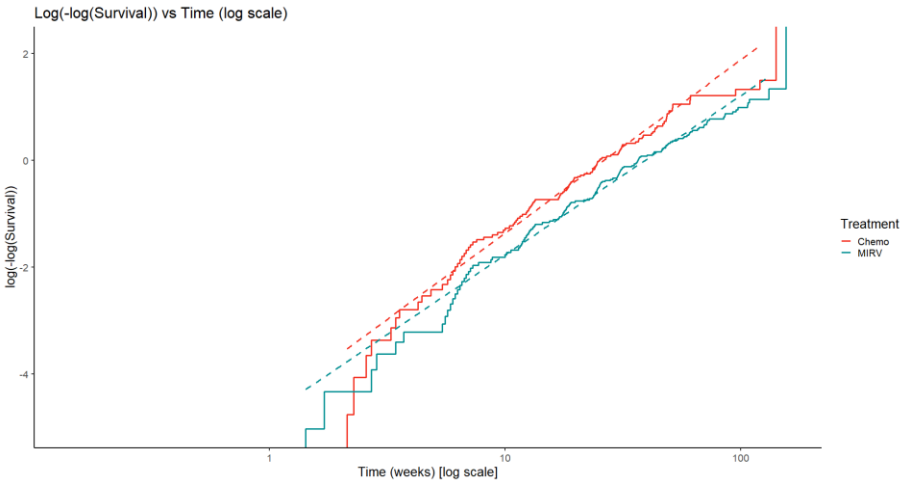
D.1.2 Model

As mentioned in Section 8.1.1.1, the parametric functions considered for extrapolation included exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions.

D.1.3 Proportional hazards

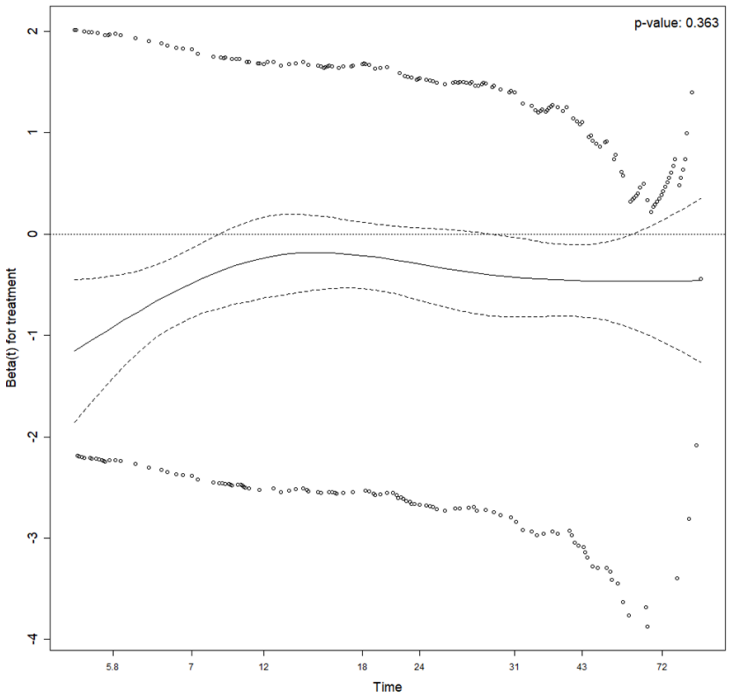
The proportional hazards assumption was evaluated using a log-cumulative hazard plot (Figure 23), and the Schoenfeld residuals plot (Figure 24). The log-cumulative hazard plots showed that the lines are non-parallel. The Schoenfeld residuals plot showed a slight pattern, but this was not statistically significant (p=0.363).

Figure 23 Log cumulative hazard plot for PFS – mirvetuximab vs. pooled chemotherapy



Abbreviations: MIRV, mirvetuximab; PFS, progression-free survival.

Figure 24 Schoenfeld residuals plot for PFS – mirvetuximab vs. pooled chemotherapy



Abbreviations: PFS, progression-free survival.

Based on guidance from NICE TSD 14, i.e., provided the log cumulative hazard plots were not parallel, fitting individual models (independent fitting) was considered the most appropriate to extrapolate observed PFS data [82].

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

The goodness-of-fit (AIC and BIC) associated with the different parametric functions are summarised in Table 59 and Table 60. Based on goodness of fit statistics, the independent lognormal distribution was the best parametric survival model extrapolate both mirvetuximab and pooled chemotherapy PFS data.

Table 59 Statistical goodness of fit for PFS – mirvetuximab

Parametric function	AIC†	BIC†
Exponential	1832.650	1836.075
Weibull	1823.642	1830.491
Log-logistic	1805.801	1812.651
Lognormal	**1802.668**	**1809.518**
Gompertz	1833.948	1840.798

Gamma	1816.810	1823.660
Generalised Gamma	1804.343	1814.618

†Lowest AIC and BIC values are highlighted in bold. Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; PFS, progression-free survival.

Table 60 Statistical goodness of fit for PFS – pooled chemotherapy

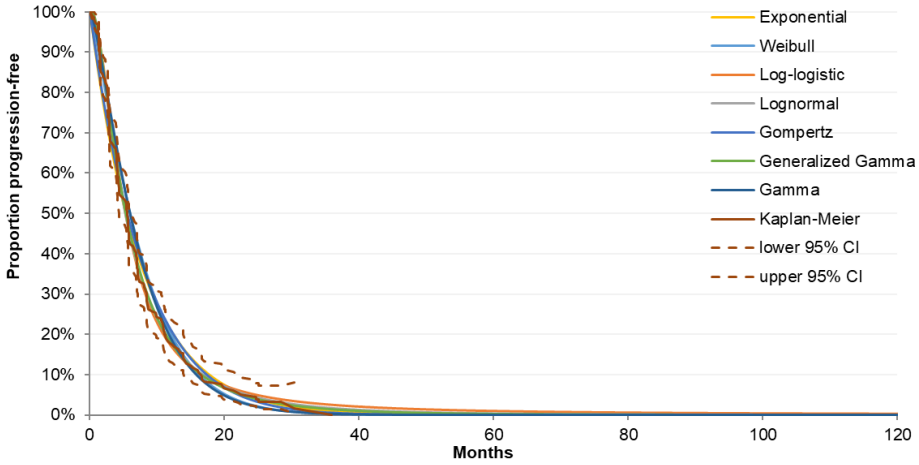
Parametric function	AIC†	BIC†
Exponential	1429.801	1433.222
Weibull	1419.539	1426.380
Log-Logistic	1408.009	1414.850
Lognormal	**1397.088**	**1403.929**
Gompertz	1431.005	1437.846
Gamma	1412.367	1419.208
Generalised Gamma	1398.982	1409.244

†Lowest AIC and BIC values are highlighted in bold. Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; PFS, progression-free survival.

D.1.5 Evaluation of visual fit

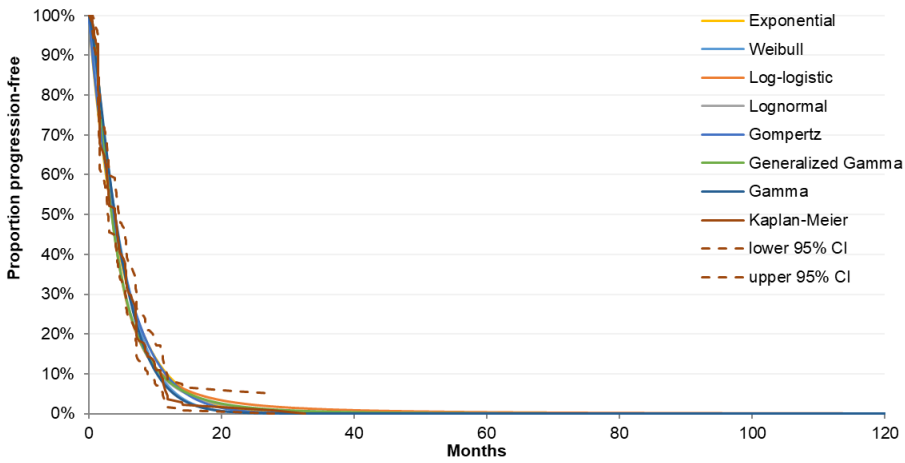
The predicted PFS curves associated with different parametric functions are shown in Figure 25 and Figure 26 for mirvetuximab and pooled chemotherapy, respectively. In the two figures, it is possible to observe that all parametric survival functions produce relatively similar survival projections.

Figure 25 Modelled survival functions for PFS – mirvetuximab



Abbreviations: CI, confidence interval; PFS, progression-free survival.

Figure 26 Modelled survival functions for PFS – pooled chemotherapy



Abbreviations: CI, confidence interval; PFS, progression-free survival.

D.1.6 Evaluation of hazard functions

Not performed.

D.1.7 Validation and discussion of extrapolated curves

The independent lognormal distribution was selected in the base case for both mirvetuximab and pooled chemotherapy based on statistical goodness of fit alone (Figure 27 and Figure 28). This was considered appropriate given that PFS data were complete for both mirvetuximab and pooled chemotherapy, and because all parametric survival models predicted relatively similar extrapolations for the PFS curve.

No further validation was pursued.

Figure 27 KM data and projected survival (PFS) with a lognormal model for mirvetuximab

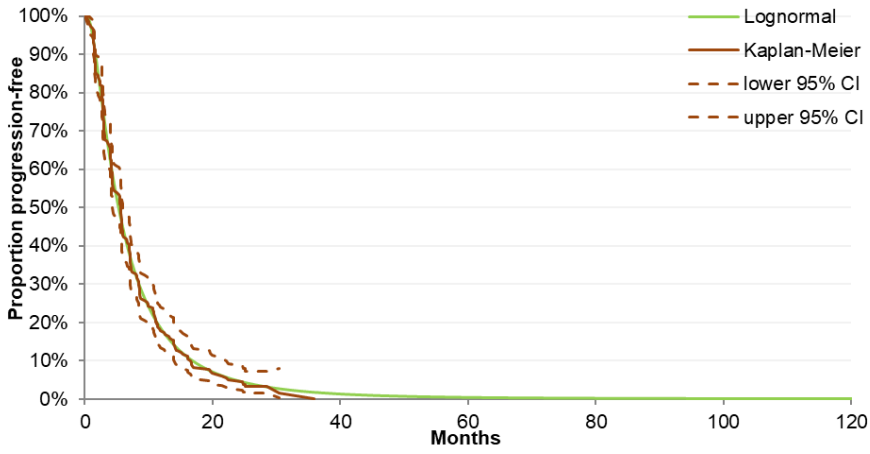
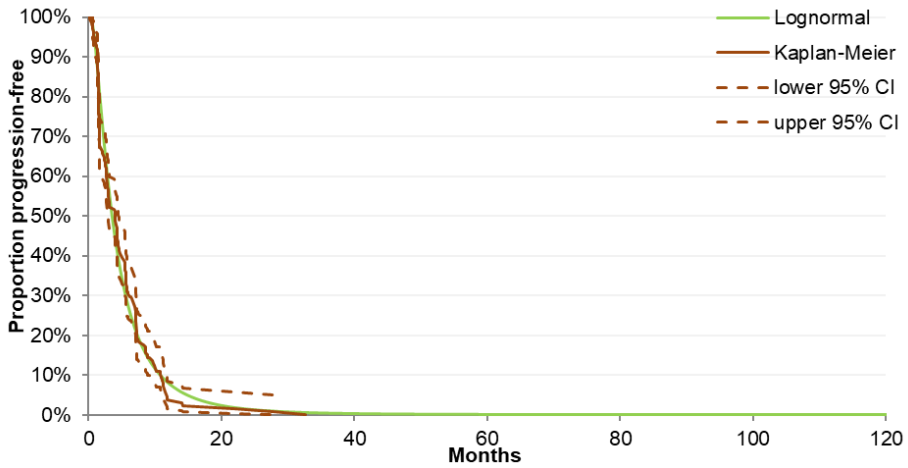


Figure 28 KM data and projected survival (PFS) with a lognormal model for pooled chemotherapy



D.1.8 Adjustment of background mortality

The general mortality of the Danish population was retrieved from DMC Excel template 'Key figures including general mortality' [101]. General population mortality values were included to constrain the minimum mortality rate based on age and gender matched rates of the cohort in each model cycle, i.e., the risk of progression or death of the patients in the cost-utility model was not allowed to be lower than the risk of death for the general population.

D.1.9 Adjustment for treatment switching/cross-over

N/A.

D.1.10 Waning effect

N/A.

D.1.11 Cure-point

N/A.

D.2 Extrapolation of OS

D.2.1 Data input

As mentioned in Section 8.1.1.2, OS extrapolation was informed by the September 2024 data cut from MIRASOL [80].

D.2.2 Model

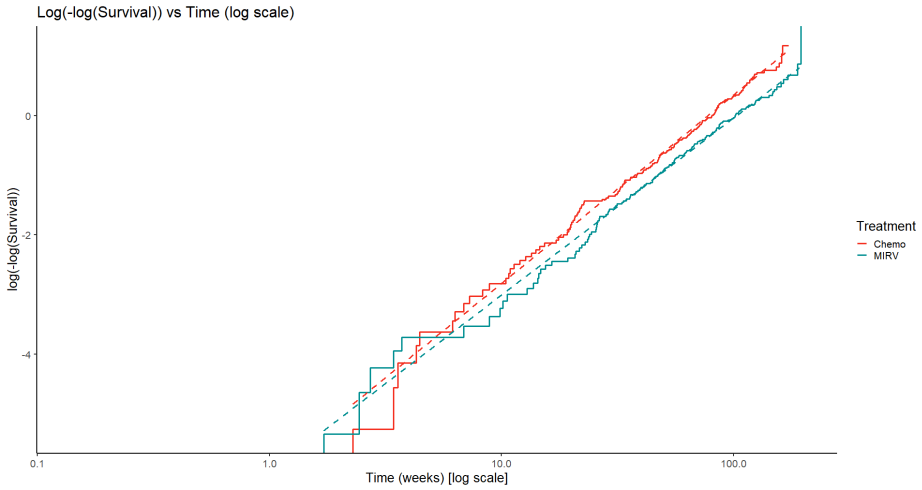
As mentioned in Section 8.1.1.2, the parametric functions considered for extrapolation included exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions.

D.2.3 Proportional hazards

The proportional hazards assumption was evaluated using a log-cumulative hazard plot (Figure 29), and the Schoenfeld residuals plot (Figure 30). The log-cumulative hazard plots showed the lines are non-parallel. Please note that the x-axis is on log scale. At early times (before 7 weeks, x=2.0), the two lines are close together, indicating similar risks for both groups. This is expected, given the treatment is unlikely to have impact on OS in the early stages when it was just initiated.

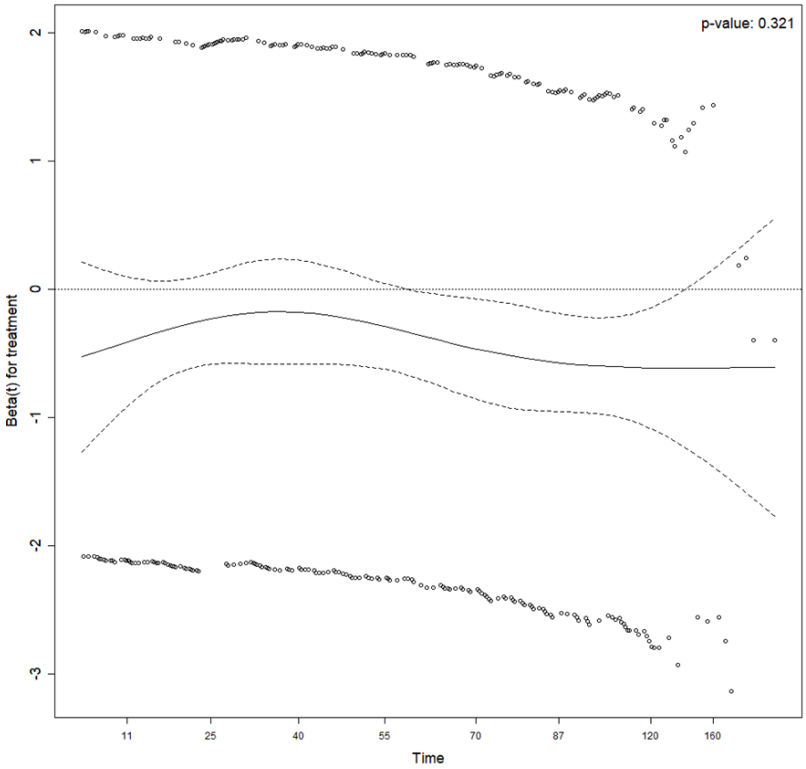
The Schoenfeld residuals plot showed a slight pattern, with the confidence bands becoming considerably broader beyond 120 weeks, indicating increased uncertainty towards the tail end. The p-value of the Schoenfeld tests was however not statistically significant (p=0.321).

Figure 29 Log cumulative hazard plot for OS – mirvetuximab vs. chemotherapy



Abbreviations: MIRV, mirvetuximab; OS, overall survival.

Figure 30 Schoenfeld residuals plot for OS – mirvetuximab vs. chemotherapy



Abbreviations: OS, overall survival.

Based on guidance from NICE TSD 14, i.e., provided the log cumulative hazard plots were not parallel, fitting individual models (independent fitting) was considered the most appropriate method to extrapolate observed OS data [82].

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

The goodness-of-fit (AIC and BIC) associated with the different parametric functions are summarised in Table 61 and Table 62. Based on goodness of fit statistics, the independent gamma and the independent Weibull distributions were the best parametric survival models to extrapolate mirvetuximab and pooled chemotherapy OS data, respectively.

Table 61 Statistical goodness of fit for OS – mirvetuximab

Parametric function	AIC†	BIC†
Exponential	1826.850	1830.274
Weibull	1815.392	1822.242
Log-Logistic	1817.525	1824.375

Lognormal	1825.857	1832.707
Gompertz	1820.862	1827.711
Gamma	**1814.625**	**1821.475**
Generalised Gamma	1816.571	1826.846

†Lowest AIC and BIC values are highlighted in bold

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion OS, overall survival.

Table 62 Statistical goodness of fit for OS – pooled chemotherapy

Parametric function	AIC†	BIC†
Exponential	1875.726	1879.146
Weibull	**1853.477**	**1860.318**
Log-logistic	1867.257	1874.098
Lognormal	1873.860	1880.701
Gompertz	1858.912	1865.753
Gamma	1854.381	1861.222
Generalised Gamma	1855.477	1865.738

†Lowest AIC and BIC values are highlighted in bold

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion OS, overall survival.

D.2.5 Evaluation of visual fit

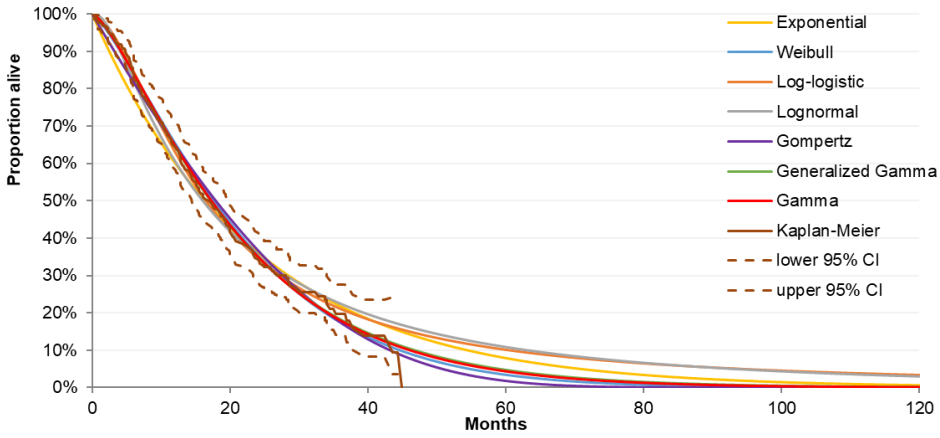
The predicted OS associated with different parametric functions are shown in Figure 31 and Figure 32 for mirvetuximab and chemotherapy, respectively.

For the pooled chemotherapy arm, the plot shows that the Weibull, generalized gamma, and gamma generally provide a better fit to the OS curve of the pooled chemotherapy arm, because these captured better the sharp decline of OS. Note that the Weibull curve (blue line) is largely overlapped with generalized gamma curve (green line) in the below plot.

For the mirvetuximab arm, the generalized gamma and gamma provided an overall good fit to the OS curve. The exponential and log-normal curves provided the worst fit compared to the other curves. These underestimated the survival before month 23 and then overestimated the survival thereafter. The other curves captured the OS reasonably well up to around month 28, after which they diverged into two groups. The 'higher' group (i.e., log-logistic distribution) continued to predict a good fit to the observed data

until month 35. In contrast, the 'lower' group underestimated the survival between months 30 and 37, before capturing the drops in the curve at the tail end. The 'lower' group included the generalized gamma, gamma, Weibull and Gompertz. It is important to note that only 18 patients remained at risk at month 35, indicating substantial uncertainty in the KM curve beyond this point.

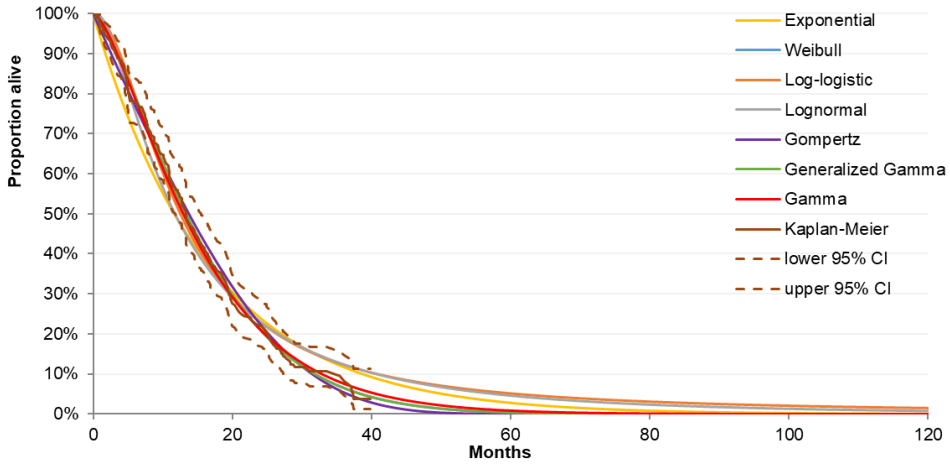
Figure 31 Modelled survival functions for OS – mirvetuximab



Abbreviations: CI, confidence interval; OS, overall survival.

For the pooled chemotherapy arm, the plot shows that the Weibull, generalized gamma, and gamma generally provide a better fit to the OS curve of the pooled chemotherapy arm, because these captured better the sharp decline of OS. Note that the Weibull curve (blue line) is largely overlapped with generalized gamma curve (green line) in the below plot.

Figure 32 Modelled survival functions for OS – pooled chemotherapy



Abbreviations: CI, confidence interval; OS, overall survival.

D.2.6 Evaluation of hazard functions

Not performed.

D.2.7 Validation and discussion of extrapolated curves

In the base case, the independent gamma distribution was selected to extrapolate the OS data for mirvetuximab, and the independent Weibull distribution was selected to extrapolate the OS data for pooled chemotherapy (Figure 33 and Figure 34, respectively). This choice was based on statistical goodness of fit statistics and visual fit. Approximately 80% and 92% of patients in the mirvetuximab and pooled chemotherapy arms, respectively, had experienced the event of interest (death) by final study visit. It is worth noting that a third of the censored 8% of patients from the pooled chemotherapy arm had shifted to mirvetuximab treatment. Other standard parametric distributions were tested in scenario analyses and are presented in Section 12.2.1.

No further validation was pursued.

Figure 33 KM data and projected survival (OS) with a gamma model for mirvetuximab

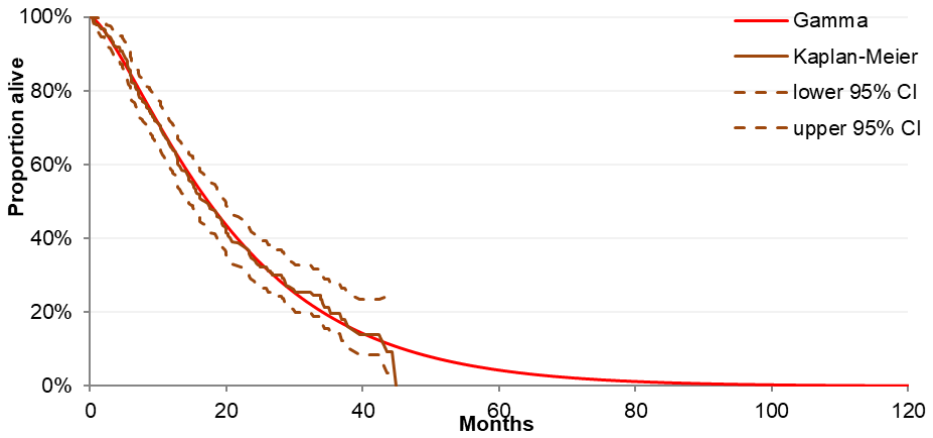
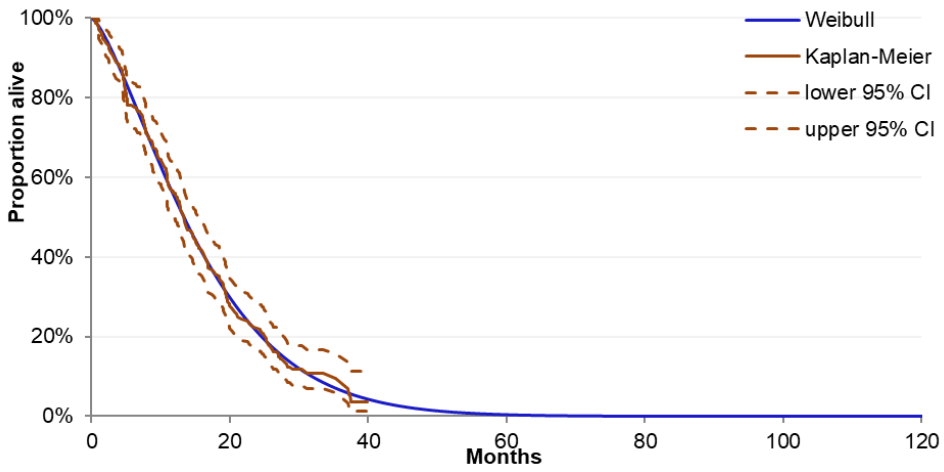


Figure 34 KM data and projected survival (OS) with a Weibull model for pooled chemotherapy



D.2.8 Adjustment of background mortality

Similarly to PFS, the risk of the death of the patients in the cost-utility model was not allowed to be lower than the risk of death for the Danish general population [101].

D.2.9 Adjustment for treatment switching/cross-over

It should be noted that 10% of the patients in the control arm in MIRASOL received mirvetuximab soravtansine after progression. This has not been adjusted for which, to some degree, is expected to overestimate the OS for the comparator arm.

D.2.10 Waning effect

N/A.

D.2.11 Cure-point

N/A.

D.3 Extrapolation of DoT

DoT was capped by PFS to reflect the fact that treatment beyond progression was not permitted in the MIRASOL trial.

D.3.1 Data input

As mentioned in Section 8.1.1.3, DoT extrapolation for mirvetuximab was informed by the September 2024 data cut from MIRASOL [80].

D.3.2 Model

Kaplan-Meier data were complete for mirvetuximab, but parametric curves were used as these demonstrated a close visual fit to the Kaplan-Meier data. The seven parametric functions fitted were the exponential, Weibull, lognormal, log-logistic, Gompertz, gamma and generalised gamma distributions. The predicted and observed DoT associated with mirvetuximab are shown in Figure 35.

Figure 35 Modelled time-to-event curves for DoT – mirvetuximab

Abbreviations: CI, confidence interval; DoT, duration of treatment.

D.3.3 Proportional hazards

Not performed.

D.3.4 Evaluation of statistical fit (AIC and BIC)

The goodness-of-fit (AIC and BIC) associated with the different parametric functions for mirvetuximab is summarised in Table 63.

Table 63 Statistical goodness of fit for DoT – mirvetuximab

Parametric function	AIC[†]	BIC[†]
Exponential	**1882.164**	**1885.548**
Weibull	1883.061	1889.830
Log-logistic	1904.797	1911.566
Lognormal	1925.107	1931.876
Gompertz	1883.854	1890.623
Gamma	1882.889	1889.658
Generalised Gamma	1884.862	1895.016

[†]Lowest AIC and BIC values are highlighted in bold

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; DoT, duration of treatment.

D.3.5 Evaluation of visual fit

Not performed.

D.3.6 Evaluation of hazard functions

Not performed.

D.3.7 Validation and discussion of extrapolated curves

In the base case, the exponential distribution was selected for mirvetuximab based on statistical goodness of fit. Figure 36 shows the visual fit of the exponential distribution to the KM data for DoT for mirvetuximab.

No further validation was pursued.

Figure 36 Chosen parametric function for DoT extrapolation (mirvetuximab arm)

D.3.8 Adjustment of background mortality

N/A.

D.3.9 Adjustment for treatment switching/cross-over

N/A.

D.3.10 Waning effect

N/A.

D.3.11 Cure-point

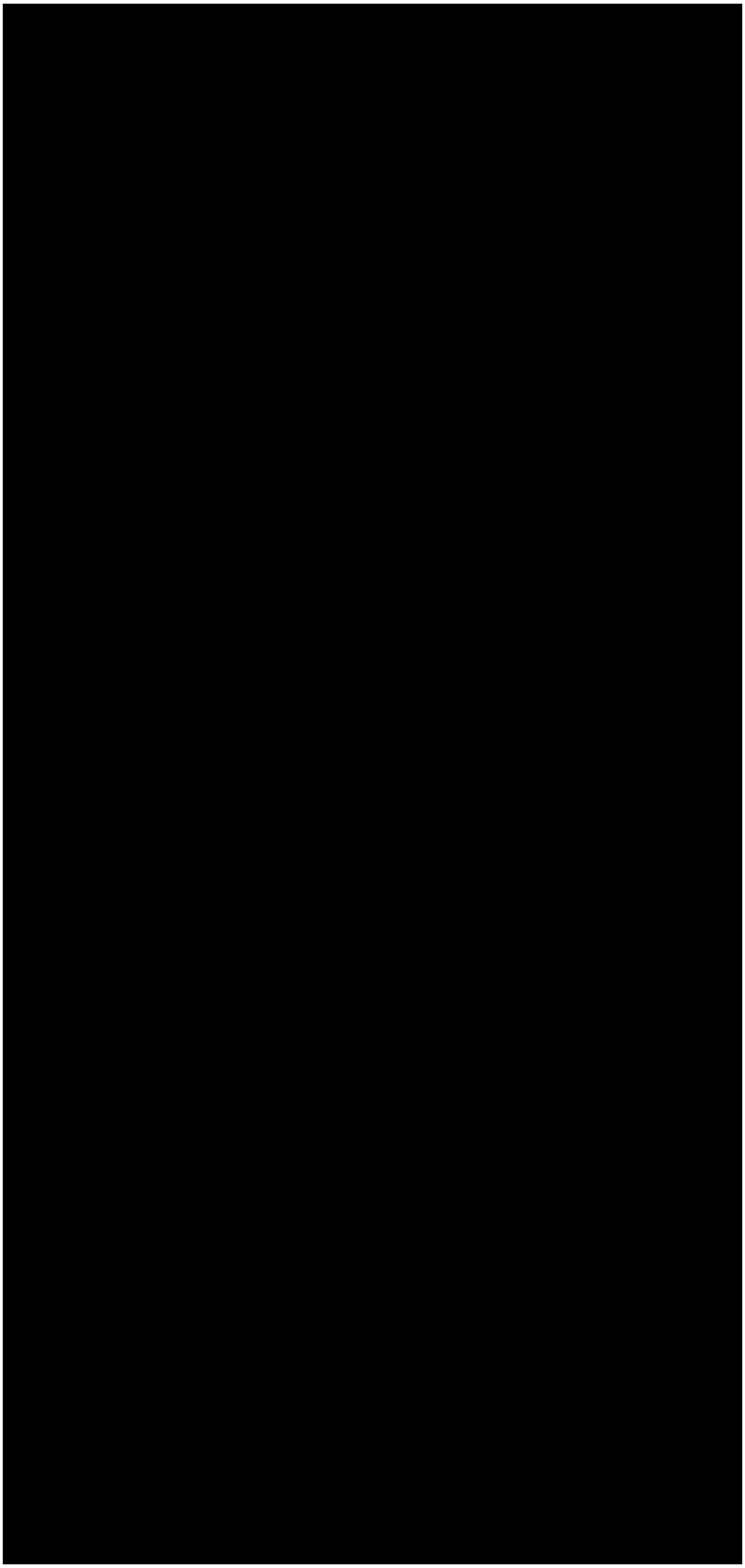
N/A.

Appendix E. Serious adverse events

Tables reporting the serious TEAEs occurring in >2% of patients and serious study drug-related TEAEs are presented below.

Table 64 Serious TEAEs in MIRASOL

Table 65 Serious study drug-related TEAEs in MIRASOL



Appendix F. Health-related quality of life

Descriptive analysis results

The descriptive analysis results are presented in Table 66 and Table 67.

Table 66 Descriptive analysis: pooled utility values by progression status

Utility values	Pre-progression	Post-progression
N of measurements	[redacted]	[redacted]
Mean	[redacted]	[redacted]
Standard error	[redacted]	[redacted]
95% CI	[redacted]	[redacted]

Abbreviations: CI, confidence interval

Table 67 Descriptive analysis: utility values by progression status and treatment type

	Mirvetuximab (N of patients = 227)		Chemotherapy (N of patients = 226)	
Utility values	Pre-progression	Post-progression	Pre-progression	Post-progression
N of measurements	[redacted]	[redacted]	[redacted]	[redacted]
Mean	[redacted]	[redacted]	[redacted]	[redacted]
Standard error	[redacted]	[redacted]	[redacted]	[redacted]
95% CI	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: CI, confidence interval

MMRM analysis results

The MMRM analysis results are presented in Table 68 for the model including progression status only, and Table 69 for the model including progression status and treatment type. These utility values are based on an MMRM adjusting for AEs.

As expected [redacted].

Table 68 MMRM: model based on progression status only (model 1)

Utility values	Pre-progression	Post-progression
N of measurements	[redacted]	[redacted]
Mean	[redacted]	[redacted]
Standard error	[redacted]	[redacted]
95% CI	[redacted]	[redacted]

Abbreviations: CI, confidence interval; MMRM, mixed model for repeated measures

Table 69 MMRM: model based on progression status and treatment type (model 2)

	Mirvetuximab (N of patients = 227)		Chemotherapy (N of patients = 226)	
Utility values	Pre-progression	Post-progression	Pre-progression	Post-progression
N of measurements	[redacted]	[redacted]	[redacted]	[redacted]
Mean	[redacted]	[redacted]	[redacted]	[redacted]
Standard error	[redacted]	[redacted]	[redacted]	[redacted]
95% CI	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: CI, confidence interval; MMRM, mixed model for repeated measures

Utility estimates for the model including time to death only based on an MMRM adjusting for AEs are presented in Table 70 for pooled arms. As expected, utility values decreased as patients approached to death. Specifically, utility values remained relatively stable with slow deterioration until the last month of life and then declined considerably until death. This was observed for both mirvetuximab and chemotherapy arms, and for both scenarios (i.e., within each health state, and regardless of health state). The pooled mean utility was highest in the category of patients with more than 24 weeks from death at [redacted] and decreased to [redacted] for patients between 12 and 24 weeks from death, then further decreased to [redacted] for patients between 4 and 12 weeks from death, and lastly fell steeply to [redacted] for patients with less than 4 weeks of life. It is worth noting that the sample size was small for the group with less than 4 weeks of time to death ([redacted] observations in total) and thus the utility estimates in this group may have a higher risk of bias.

Table 70 MMRM: model based on time-to-death only (model 3)

Time to death	Mean	Standard error	95% CI
<= 4 weeks	[redacted]	[redacted]	[redacted]
> 4 and <= 12 weeks	[redacted]	[redacted]	[redacted]

Time to death	Mean	Standard error	95% CI
> 12 and <= 24 weeks	[redacted]	[redacted]	[redacted]
> 24 weeks	[redacted]	[redacted]	[redacted]

Abbreviations: CI, confidence interval; MMRM, mixed model for repeated measures

Appendix G. Probabilistic sensitivity analyses

Table 71 summarises the parameters included in the PSA.

Table 71. Overview of parameters in the PSA

Input parameter	Point estimate	Lower bound	Upper bound	Probability distribution
Body surface area (BSA) - mean - ITT	1.73	1.34	2.13	Normal
Adjusted ideal body weight (AIBW) - mean - ITT	59.05	57.95	60.15	Normal
Weight - mean - ITT	68.84	67.35	70.34	Normal
Median DoT (weeks) - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Median DoT (weeks) - Paclitaxel (pooled chemotherapy)	[redacted]	[redacted]	[redacted]	[redacted]
Median DoT (weeks) - PLD (pooled chemotherapy)	[redacted]	[redacted]	[redacted]	[redacted]
Median DoT (weeks) - Gemcitabine (pooled chemotherapy)	[redacted]	[redacted]	[redacted]	[redacted]
Chemotherapy patients receiving paclitaxel	0.41	0.33	0.49	Beta
Chemotherapy patients receiving pegylated liposomal doxorubicin	0.36	0.29	0.43	Beta
Chemotherapy patients receiving Gemcitabine	0.24	0.19	0.28	Beta
Administration Costs (by component) - Unit Cost (2025 DKK) - IV	1411.00	1128.80	1693.20	Gamma
Relative Dose Intensity - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Paclitaxel (first day)	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Paclitaxel (subsequent days)	[redacted]	[redacted]	[redacted]	[redacted]

Relative Dose Intensity - Pegylated liposomal doxorubicin	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Gemcitabine (first day)	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Gemcitabine (subsequent days)	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Gemcitabine (first day)	[redacted]	[redacted]	[redacted]	[redacted]
Relative Dose Intensity - Gemcitabine (subsequent days)	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - Median Treatment Duration (weeks)1 - Mirvetuximab	21.64	17.31	25.97	Gamma
Post-Prog Trt Cost - Median Treatment Duration (weeks)1 - Taxanes	15.64	12.51	18.77	Gamma
Post-Prog Trt Cost - Median Treatment Duration (weeks)1 - Gemcitabine	12.00	9.60	14.40	Gamma
Post-Prog Trt Cost - Median Treatment Duration (weeks)1 - Pembrolizumab	9.13	7.30	10.95	Gamma
Post-Prog Trt Cost - Median Treatment Duration (weeks)1 - Olaparib	8.14	6.51	9.77	Gamma
Post-Prog Trt Cost - % of progressed patients receiving post-progression treatment - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - % of progressed patients receiving post-progression treatment - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - Distribution among patients who receive post-progression treatment - Taxanes - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - Distribution among patients who receive post-progression treatment - Taxanes - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - Distribution among patients who receive post-progression	[redacted]	[redacted]	[redacted]	[redacted]

treatment - Gemcitabine - Mirvetuximab				
Post-Prog Trt Cost - Distribution among patients who receive post-progression treatment - Gemcitabine - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - Distribution among patients who receive post-progression treatment - Olaparib - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Post-Prog Trt Cost - Distribution among patients who receive post-progression treatment - Olaparib - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Keratopathy	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Vision blurred	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Fatigue	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Cataract	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Anaemia	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Neutropenia	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Mirvetuximab - Thrombocytopenia	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Pooled chemotherapy - Fatigue	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Pooled chemotherapy - Anaemia	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Pooled chemotherapy - Neutropenia	[redacted]	[redacted]	[redacted]	[redacted]
Grade 3+ AEs - Pooled chemotherapy - Thrombocytopenia	[redacted]	[redacted]	[redacted]	[redacted]

Grade 3+ AEs - AE Cost (2025 DKK) - Keratopathy	1085.00	868.00	1302.00	Gamma
Grade 3+ AEs - AE Cost (2025 DKK) - Vision blurred	1085.00	868.00	1302.00	Gamma
Grade 3+ AEs - AE Cost (2025 DKK) - Fatigue	2208.00	1766.40	2649.60	Gamma
Grade 3+ AEs - AE Cost (2025 DKK) - Cataract	1085.00	868.00	1302.00	Gamma
Grade 3+ AEs - AE Cost (2025 DKK) - Anaemia	2208.00	1766.40	2649.60	Gamma
Grade 3+ AEs - AE Cost (2025 DKK) - Neutropenia	37482.00	29985.60	44978.40	Gamma
Grade 3+ AEs - AE Cost (2025 DKK) - Thrombocytopenia	37482.00	29985.60	44978.40	Gamma
Grade 3+ AEs - Disutility - Keratopathy	0.01	0.006	0.010	Beta
Grade 3+ AEs - Disutility - Vision blurred	0.00	0.004	0.006	Beta
Grade 3+ AEs - Disutility - Fatigue	0.12	0.092	0.138	Beta
Grade 3+ AEs - Disutility - Cataract	0.14	0.112	0.168	Beta
Grade 3+ AEs - Disutility - Anaemia	0.12	0.096	0.144	Beta
Grade 3+ AEs - Disutility - Neutropenia	0.09	0.072	0.108	Beta
Grade 3+ AEs - Disutility - Thrombocytopenia	0.11	0.088	0.132	Beta
Grade 3+ AEs - AE duration (weeks) - Keratopathy	4.00	3.20	4.80	Gamma
Grade 3+ AEs - AE duration (weeks) - Vision blurred	4.00	3.20	4.80	Gamma
Grade 3+ AEs - AE duration (weeks) - Fatigue	4.00	3.20	4.80	Gamma

Grade 3+ AEs - AE duration (weeks) - Cataract	4.00	3.20	4.80	Gamma
Grade 3+ AEs - AE duration (weeks) - Anaemia	4.00	3.20	4.80	Gamma
Grade 3+ AEs - AE duration (weeks) - Neutropenia	4.00	3.20	4.80	Gamma
Grade 3+ AEs - AE duration (weeks) - Thrombocytopenia	4.00	3.20	4.80	Gamma
Proportion of patients requiring hospitalization - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of patients requiring hospitalization - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Average hospitalizations per hospitalized patient - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Average hospitalizations per hospitalized patient - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Average length of hospitalization (days) - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Average length of hospitalization (days) - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of patients requiring transfusions - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of patients requiring transfusions - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Average transfusions per transfused patient - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Average transfusions per transfused patient - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of patients requiring G-CSF - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of patients requiring G-CSF - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]

Mean number of doses per patient receiving G-CSF - Mirvetuximab	[redacted]	[redacted]	[redacted]	[redacted]
Mean number of doses per patient receiving G-CSF - Pooled chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
% biosimilar usage - Mirvetuximab	0.50	0.40	0.60	Beta
% biosimilar usage - Pooled chemotherapy	0.50	0.40	0.60	Beta
Utility model - Progression status only - Pre-progression	0.79	0.77	0.81	Beta
Utility model - Progression status only - Post-progression	0.70	0.67	0.73	Beta
Utility model - Progression status and treatment type - Mirvetuximab - Pre-progression	0.80	0.78	0.83	Beta
Utility model - Progression status and treatment type - Mirvetuximab - Post-progression	0.71	0.68	0.75	Beta
Utility model - Progression status and treatment type - Pooled chemotherapy - Pre-progression	0.78	0.75	0.81	Beta
Utility model - Progression status and treatment type - Pooled chemotherapy - Post-progression	0.69	0.65	0.72	Beta
Utility model - Time to death only - <= 4 weeks	0.34	0.25	0.43	Beta
Utility model - Time to death only - > 4 and <= 12 weeks	0.61	0.56	0.65	Beta
Utility model - Time to death only - > 12 and <= 24 weeks	0.74	0.71	0.78	Beta
Utility model - Time to death only - > 24 weeks	0.81	0.79	0.82	Beta
Utility model - Time to death and treatment type - Mirvetuximab - <= 4 weeks	0.35	0.26	0.45	Beta

Utility model - Time to death and treatment type - Mirvetuximab - > 4 and <= 12 weeks	0.62	0.57	0.67	Beta
Utility model - Time to death and treatment type - Mirvetuximab - > 12 and <= 24 weeks	0.75	0.72	0.79	Beta
Utility model - Time to death and treatment type - Mirvetuximab - > 24 weeks	0.82	0.79	0.84	Beta
Utility model - Time to death and treatment type - Pooled chemotherapy - <= 4 weeks	0.33	0.24	0.42	Beta
Utility model - Time to death and treatment type - Pooled chemotherapy - > 4 and <= 12 weeks	0.59	0.54	0.64	Beta
Utility model - Time to death and treatment type - Pooled chemotherapy - > 12 and <= 24 weeks	0.73	0.69	0.77	Beta
Utility model - Time to death and treatment type - Pooled chemotherapy - > 24 weeks	0.79	0.76	0.82	Beta
Pre-Progression Disease Management Costs - Outpatient visit, gynaecological oncology - Mirvetuximab	17.33	13.87	20.80	Gamma
Pre-Progression Disease Management Costs - Outpatient visit, gynaecological oncology - Pooled chemotherapy	17.33	13.87	20.80	Gamma
Pre-Progression Disease Management Costs - CT scan - Mirvetuximab	4.33	3.47	5.20	Gamma
Pre-Progression Disease Management Costs - CT scan - Pooled chemotherapy	4.33	3.47	5.20	Gamma
Post-Progression Disease Management Costs - Outpatient visit, gynaecological oncology - Mirvetuximab	4.00	3.20	4.80	Gamma
Post-Progression Disease Management Costs - Outpatient visit, gynaecological oncology - Pooled chemotherapy	4.00	3.20	4.80	Gamma

Mean number of Grade ≥2 ocular AEs in mirvetuximab patients	[redacted]	[redacted]	[redacted]	[redacted]
Frequency of ophthalmologist visits per week	0.17	0.13	0.20	Gamma
Duration of Grade ≥2 ocular AEs (weeks)	4.00	3.20	4.80	Gamma
% of patients with Grade ≥2 keratopathy	[redacted]	[redacted]	[redacted]	[redacted]
Frequency of ophthalmologist visits per treatment cycle	0.17	0.13	0.20	Gamma
Mean duration of treatment (weeks)	[redacted]	[redacted]	[redacted]	[redacted]
% PROC patients that test positive for FR-alpha	0.32	0.26	0.38	Beta
FR-alpha test - Pathologist time - Unit Cost (2025 DKK)	318.00	254.40	381.60	Gamma
FR-alpha test - cost of consumables - Unit Cost (2025 DKK)	787.88	630.30	945.46	Gamma
% patients receiving end-of-life care	0.51	0.41	0.62	Beta
OS - Mirvetuximab - ITT - Exponential - rate	0.01	0.01	0.01	Log-normal
OS - Mirvetuximab - ITT - Weibull - shape	1.29	1.13	1.47	Multivariate normal
OS - Mirvetuximab - ITT - Weibull - scale	101.64	90.20	114.52	Multivariate normal
OS - Mirvetuximab - ITT - Lognormal - meanlog	4.25	4.09	4.40	Multivariate normal
OS - Mirvetuximab - ITT - Lognormal - sdlog	1.07	0.95	1.20	Multivariate normal
OS - Mirvetuximab - ITT - Log-Logistic - shape	1.69	1.49	1.92	Multivariate normal
OS - Mirvetuximab - ITT - Log-Logistic - scale	71.74	62.44	82.42	Multivariate normal

OS - Mirvetuximab - ITT - Gompertz - shape	0.01	0.00	0.01	Multivariate normal
OS - Mirvetuximab - ITT - Gompertz - rate	0.01	0.01	0.01	Multivariate normal
OS - Mirvetuximab - ITT - Gamma - shape	1.48	1.22	1.79	Multivariate normal
OS - Mirvetuximab - ITT - Gamma - rate	0.02	0.01	0.02	Multivariate normal
OS - Mirvetuximab - ITT - Generalized Gamma - mu	4.54	4.33	4.75	Multivariate normal
OS - Mirvetuximab - ITT - Generalized Gamma - sigma	0.84	0.68	1.03	Multivariate normal
OS - Mirvetuximab - ITT - Generalized Gamma - Q	0.77	0.29	1.24	Multivariate normal
OS - Pooled chemotherapy - ITT - Exponential - rate	0.01	0.01	0.02	Log-normal
OS - Pooled chemotherapy - ITT - Weibull - shape	1.38	1.22	1.55	Multivariate normal
OS - Pooled chemotherapy - ITT - Weibull - scale	75.68	67.92	84.33	Multivariate normal
OS - Pooled chemotherapy - ITT - Lognormal - meanlog	3.94	3.80	4.07	Multivariate normal
OS - Pooled chemotherapy - ITT - Lognormal - sdlog	0.97	0.87	1.08	Multivariate normal
OS - Pooled chemotherapy - ITT - Log-Logistic - shape	1.86	1.65	2.11	Multivariate normal
OS - Pooled chemotherapy - ITT - Log-Logistic - scale	54.49	47.95	61.93	Multivariate normal
OS - Pooled chemotherapy - ITT - Gompertz - shape	0.01	0.00	0.01	Multivariate normal
OS - Pooled chemotherapy - ITT - Gompertz - rate	0.01	0.01	0.01	Multivariate normal

OS - Pooled chemotherapy - ITT - Gamma - shape	1.63	1.35	1.96	Multivariate normal
OS - Pooled chemotherapy - ITT - Gamma - rate	0.02	0.02	0.03	Multivariate normal
OS - Pooled chemotherapy - ITT - Generalized Gamma - mu	4.33	4.13	4.52	Multivariate normal
OS - Pooled chemotherapy - ITT - Generalized Gamma - sigma	0.72	0.60	0.88	Multivariate normal
OS - Pooled chemotherapy - ITT - Generalized Gamma - Q	1.00	0.53	1.47	Multivariate normal
PFS - Exponential - Parameter rate - Mirvetuximab - ITT	0.03	0.03	0.03	Log-normal
PFS - Weibull - Parameter shape - Mirvetuximab - ITT	1.20	1.08	1.33	Multivariate normal
PFS - Weibull - Parameter scale - Mirvetuximab - ITT	35.17	31.23	39.62	Multivariate normal
PFS - Lognormal - Parameter meanlog - Mirvetuximab - ITT	3.13	3.01	3.25	Multivariate normal
PFS - Lognormal - Parameter sdlog - Mirvetuximab - ITT	0.91	0.82	1.00	Multivariate normal
PFS - Log-Logistic - Parameter shape - Mirvetuximab - ITT	1.91	1.71	2.14	Multivariate normal
PFS - Log-Logistic - Parameter scale - Mirvetuximab - ITT	22.93	20.30	25.90	Multivariate normal
PFS - Gompertz - Parameter shape - Mirvetuximab - ITT	0.00	0.00	0.01	Multivariate normal
PFS - Gompertz - Parameter rate - Mirvetuximab - ITT	0.03	0.02	0.03	Multivariate normal
PFS - Gamma - Parameter shape - Mirvetuximab - ITT	1.49	1.25	1.77	Multivariate normal
PFS - Gamma - Parameter rate - Mirvetuximab - ITT	0.05	0.04	0.06	Multivariate normal

PFS - Generalized Gamma - Parameter mu - Mirvetuximab - ITT	3.17	2.97	3.37	Multivariate normal
PFS - Generalized Gamma - Parameter sigma - Mirvetuximab - ITT	0.90	0.82	1.00	Multivariate normal
PFS - Generalized Gamma - Parameter Q - Mirvetuximab - ITT	0.11	-0.26	0.47	Multivariate normal
DoT - Exponential - Parameter rate - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Weibull - Parameter shape - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Weibull - Parameter scale - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Lognormal - Parameter meanlog - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Lognormal - Parameter sdlog - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Log-Logistic - Parameter shape - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Log-Logistic - Parameter scale - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gompertz - Parameter shape - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gompertz - Parameter rate - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gamma - Parameter shape - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gamma - Parameter rate - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Generalized Gamma - Parameter mu - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Generalized Gamma - Parameter sigma - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]

DoT - Generalized Gamma - Parameter Q - Mirvetuximab - ITT	[redacted]	[redacted]	[redacted]	[redacted]
PFS - Exponential - Parameter rate - Pooled chemotherapy - ITT	0.04	0.04	0.05	Log-normal
PFS - Weibull - Parameter shape - Pooled chemotherapy - ITT	1.22	1.10	1.36	Multivariate normal
PFS - Weibull - Parameter scale - Pooled chemotherapy - ITT	23.40	20.64	26.52	Multivariate normal
PFS - Lognormal - Parameter meanlog - Pooled chemotherapy - ITT	2.73	2.60	2.85	Multivariate normal
PFS - Lognormal - Parameter sdlog - Pooled chemotherapy - ITT	0.87	0.79	0.97	Multivariate normal
PFS - Log-Logistic - Parameter shape - Pooled chemotherapy - ITT	1.92	1.70	2.16	Multivariate normal
PFS - Log-Logistic - Parameter scale - Pooled chemotherapy - ITT	15.28	13.39	17.43	Multivariate normal
PFS - Gompertz - Parameter shape - Pooled chemotherapy - ITT	0.00	0.00	0.01	Multivariate normal
PFS - Gompertz - Parameter rate - Pooled chemotherapy - ITT	0.04	0.03	0.05	Multivariate normal
PFS - Gamma - Parameter shape - Pooled chemotherapy - ITT	1.56	1.29	1.88	Multivariate normal
PFS - Gamma - Parameter rate - Pooled chemotherapy - ITT	0.07	0.06	0.09	Multivariate normal
PFS - Generalized Gamma - Parameter mu - Pooled chemotherapy - ITT	2.69	2.46	2.92	Multivariate normal
PFS - Generalized Gamma - Parameter sigma - Pooled chemotherapy - ITT	0.87	0.79	0.97	Multivariate normal
PFS - Generalized Gamma - Parameter Q - Pooled chemotherapy - ITT	-0.08	-0.54	0.38	Multivariate normal
DoT - Exponential - Parameter rate - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]

DoT - Weibull - Parameter shape - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Weibull - Parameter scale - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Lognormal - Parameter meanlog - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Lognormal - Parameter sdlog - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Log-Logistic - Parameter shape - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Log-Logistic - Parameter scale - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gompertz - Parameter shape - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gompertz - Parameter rate - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gamma - Parameter shape - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Gamma - Parameter rate - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Generalized Gamma - Parameter mu - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Generalized Gamma - Parameter sigma - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]
DoT - Generalized Gamma - Parameter Q - Paclitaxel (pooled chemotherapy) - ITT	[redacted]	[redacted]	[redacted]	[redacted]

Appendix H. Literature searches for the clinical assessment

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

N/A.

Table 72 Bibliographic databases included in the literature search

Database	Platform/source	Relevant period for the search	Date of search completion
N/A			

Abbreviations:

Table 73 Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
N/A			

Abbreviations:

Table 74 Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
N/A				

H.1.1 Search strategies

N/A.

Table 75 of search strategy table for [name of database]

No.	Query	Results
N/A		88244

H.1.2 Systematic selection of studies

N/A.

Table 76 Inclusion and exclusion criteria used for assessment of studies

Clinical effectiveness	Inclusion criteria	Exclusion criteria	Changes, local adaption
N/A			

N/A.

Table 77 Overview of study design for studies included in the analyses

Study/ID	Aim	Study design	Patient population	Interven-tion and compara-tor (sample size (n))	Primary outcome and follow-up period	Secondary outcome and follow-up period
N/A						

H.1.3 Excluded fulltext references

N/A.

H.1.4 Quality assessment

N/A.

H.1.5 Unpublished data

N/A.

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

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

N/A.

Table 78 Bibliographic databases included in the literature search

Database	Platform	Relevant period for the search	Date of search completion
N/A			

Abbreviations:

Table 79 Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
N/A			

Table 80 Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
N/A				

I.1.1 Search strategies

N/A.

Table 81 Search strategy for [name of database]

No.	Query	Results
N/A		

Literature search results included in the model/analysis: N/A.

I.1.2 Quality assessment and generalizability of estimates

N/A.

I.1.3 Unpublished data

N/A.

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

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

N/A.

J.1.1 Example: Systematic search for […]

N/A.

Table 51 Sources included in the search

Database	Platform/source	Relevant period for the search	Date of search completion
N/A			

Abbreviations:

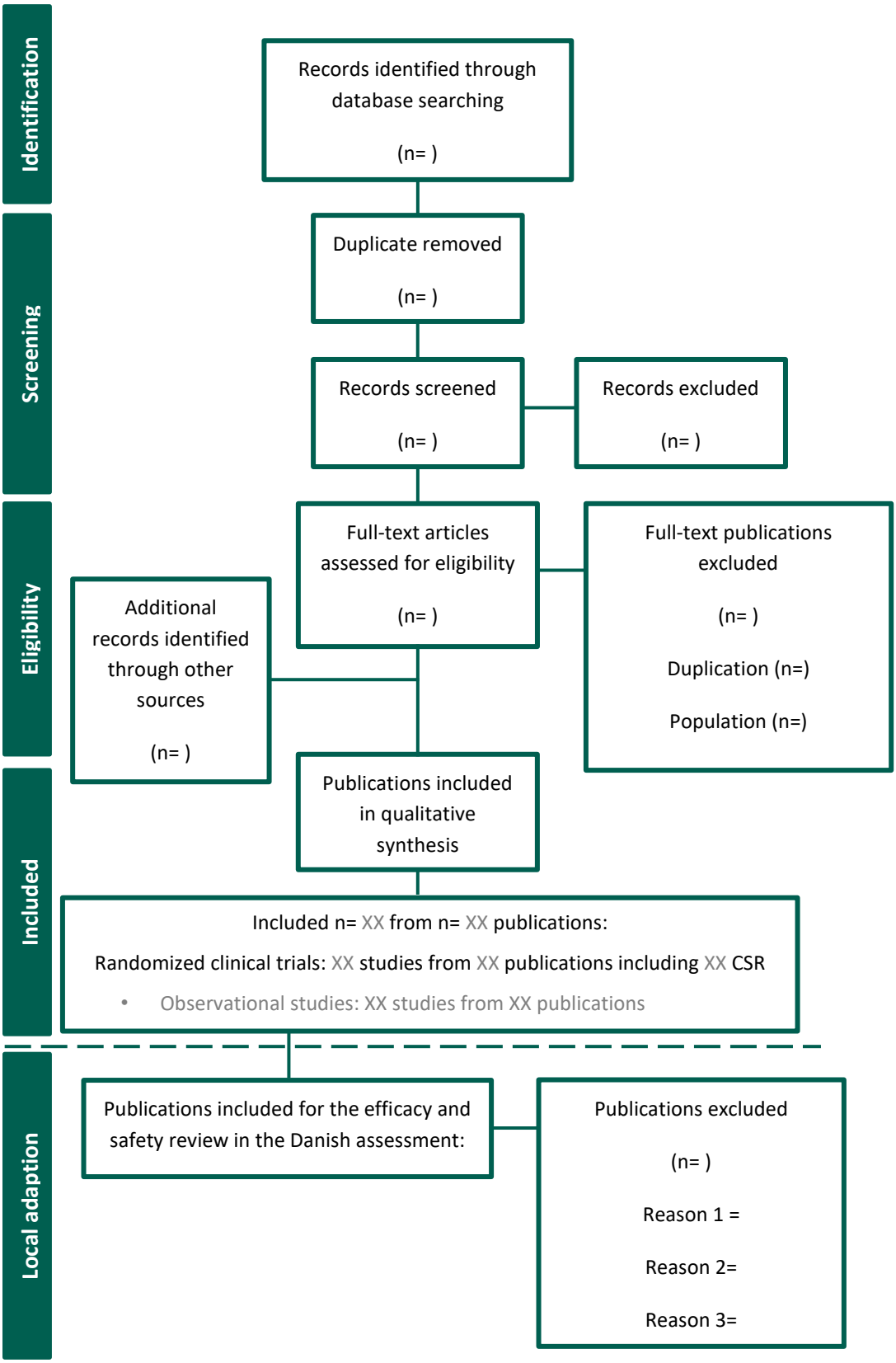
J.1.2 Targeted literature search for disutilities for adverse events

Table 52 Sources included in the targeted literature search

Source name/ database	Location/source	Search strategy	Date of search
Google Scholar	Google Scholar	disutility AND adverse event AND (keratopathy OR vision OR eye) disutility AND adverse event AND fatigue disutility AND adverse event AND (“bowel obstruction” OR gastrointestinal OR bowel) disutility AND adverse event AND (hematological OR neutropenia OR thrombocytopenia OR anemia OR leukopenia)	October 12, 2023
NICE technology appraisal guidance: eye conditions (link)	TA409 committee-papers Table 77	Reviewed prior NICE technology appraisals in eye conditions to identify an appropriate source for cataracts	January 5, 2025

Abbreviations:

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.



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