An addendum to this Public Summary Document has been included at the end of the document.

5.08 MIRVETUXIMAB SORAVTANSINE, solution for IV infusion 100 mg in 20 mL vial, Elahere®, Abbvie Pty Ltd

1 Purpose of submission

1.1 A Category 1 integrated codependent submission requesting Medicare Benefits Schedule (MBS) listing of folate receptor alpha (FRα) expression testing by immunohistochemistry (IHC) and Pharmaceutical Benefits Scheme (PBS) listing of mirvetuximab soravtansine (MIRV) for the targeted treatment of patients with platinum-resistant high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer (PROC), who have received at least one prior systemic treatment regimen, who have high FRα tumour cell expression (defined as ≥75% of viable tumour cells with moderate (2+) and/or strong (3+) membrane staining [≥75%, PS2+]) as determined by a validated test.

1.2 Listing was requested on the basis of a cost effectiveness analysis versus single agent non-platinum chemotherapy (as investigator's choice of chemotherapy; ICC).

1.3 The key PICO elements presented in the submission are presented in Table 1.

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Test: Patients with high-grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma cancer Drug: Patients with platinum-resistant high-grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma cancer. Patient must have high FRα expression, defined as ≥75% of viable tumour cells with moderate (2+) and/or strong (3+) membrane staining
Intervention	Test: Qualitative IHC assay for assessment of FRα protein expression in tumour tissue Drug: Mirvetuximab soravtansine
Comparator	Test: No testing for FRα expression levels Reference standard [a]: None Drug: • Non-platinum chemotherapy (paclitaxel, topotecan or pegylated liposomal doxorubicin) • Non-platinum chemotherapy plus bevacizumab
Outcomes	Test: Prognostic effect, diagnostic performance, clinical utility, safety Drug: OS, PFS, objective response rate, rates and nature of adverse events, and QoL measures
Clinical claim	Test: In patients with high grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma cancer, FRα testing is superior to no testing to identify patients suitable for MIRV treatment. Drug: In patients with platinum-resistant high-grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma cancer with high FRα expression, MIRV is: • Superior in terms of efficacy versus non-platinum chemotherapy on the basis of OS. • Superior in terms of efficacy versus non-platinum chemotherapy + bevacizumab on the basis of OS. • Non-inferior in terms of safety but with a different safety profile to non-platinum chemotherapy • Superior in terms of safety, with a different safety profile to non-platinum chemotherapy + bevacizumab • Superior in terms of QoL to non-platinum chemotherapy.

Source: Table 1.1 2 Key Components of the Clinical Issue Addressed by the Codependent Submission, pp5-6 of the submission.
FRα= folate-receptor alpha; IHC= immunohistochemistry; MIRV= mirvetuximab soravtansine; OS= overall survival; PFS= progression-free survival; QoL= quality of life.
[a] although not included in the source table, the lack of an applicable reference standard for this test is stated elsewhere in the submission.

2 Background

Registration status

2.1 A Therapeutic Goods Administration (TGA) application for MIRV was lodged on 19 December 2024 for treatment of adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer who have received one to three prior systemic treatment regimens. The application was made under the TGA comparable overseas regulator (COR) pathway, based on approval of MIRV in the European Union (EU). No TGA documents were available during the evaluation. The submission was made under the TGA/ PBAC Parallel Process. During the evaluation, the sponsor for MIRV advised that the TGA Delegate's request for ACM advice for the drug component would be available by 2 September 2025 and the outcome from the TGA Advisory Committee on Medicines (ACM) would be available by 24 October 2025. The Clinical Evaluation Report (CER) for the COR report-based process was provided with the Pre-PBAC response. The Pre-PBAC response noted that the CER proposed indication aligns with the EMA indication and includes 'high grade serous'.

The proposed indication based on the CER is: “ELAHERE as monotherapy is indicated 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."

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

3.1 Secretariat suggested additions to the proposed listing are in italics and deletions are in strikethrough.

MEDICINAL PRODUCT Form	Dispensed Price Max Amt	Max. Amount	№.of Rpts	Available brands
MIRVETUXIMAB SORAVTANSINE 100 mg/20 mL vial	Public $[redacted] (published) $[redacted] (effective) Private $[redacted] (published) $[redacted] (effective)	500 mg	~~8~~7	ELAHERE

Restriction Summary [new] / Treatment of Concept: [new]		
Concept ID (for internal Dept. use)		**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals
		Prescriber type: ☒Medical Practitioners
		Restriction type: ☒Authority Required – immediate assessment (telephone/online PBS Authorities system)
Prescribing rule level		~~**Administrative Advice:** Following 1 line of platinum therapy, platinum resistance is defined as having received at least four cycles of a platinum-containing regimen and then have experienced disease progression between 3 and 6 months after their last dose.~~
		~~**Administrative Advice:** Following 2 or more lines of platinum therapy, platinum resistance is defined as disease progression while receiving the therapy or within 6 months of the last dose.~~
		Administrative Advice: High FRα tumour cell expression is defined as having 75% or more tumour cells with FRα staining at moderate or high staining intensity (2+ staining) as determined by a validated test.
		Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*
		Administrative Advice: *No increase in the maximum number of repeats may be authorised.*
		Administrative Advice: *Special Pricing Arrangements apply.*
		Episodicity: [blank]
		Severity: High grade epithelial
		Condition: Ovarian, Fallopian Tube, or primary peritoneal cancer
		Indication: *High grade epithelial ovarian, fallopian tube or primary peritoneal cancer*
		~~**Treatment Phase:** Treatment of relapsed, platinum-resistant disease~~
		Clinical criteria:
		The condition must have relapsed after at least one prior therapy.
		AND
		The condition must be considered platinum-resistant.
		AND
		Clinical criteria:
		Patient must have high FRα tumour cell expression as determined by a validated test.
		AND
		~~**Clinical criteria:**~~
		~~Patient must not have received previous treatment with this drug for this condition.~~
		Clinical criteria:
		~~Patient must be undergoing treatment through this treatment phase listing for the first time (initial treatment)~~
		Patient must not have developed disease progression while ~~receiving treatment~~ *being treated with this drug* for this condition
		Prescribing Instructions: *Following 1 or more lines of platinum therapy, platinum resistance is defined as disease progression while receiving the therapy or within 6 months of the last dose.*
		Prescribing Instructions: *Evidence of FRα tumour expression must be derived through immunohistochemistry (IHC) testing and stored in the patients' medical records*
		Prescribing Instructions: *Confirm that the following information is documented/retained in the patient's medical records once only with the first PBS prescription (evidence obtained in relation to past PBS treatment is acceptable):* *1) Evidence of high FRα tumour cell expression*

3.2 The submission requested a special pricing arrangement (SPA) with proposed published and effective prices shown above (DPMQ for public and private hospitals). In the Pre-PBAC response the sponsor proposed a revised price reducing the AEMP from $ to $ per 100 mg/20 mL vial. Additionally, the Pre-PBAC response requested a revised published AEMP of $ per 100 mg/20 mL vial.

3.3 The submission proposed that patients should have received one or more prior lines of therapy, rather than one to three prior lines of therapy (as per the MIRASOL trial and proposed TGA indication), which would allow access for patients who have received additional lines of treatment.

3.4 The requested restriction omitted reference to serous tumour histology in the proposed target population to prevent inappropriate exclusion of patients with tumour histology difficult to identify, however the Pre-Sub-Committee Response (PSCR) proposed an update to the restriction to specify high grade serous epithelial ovarian cancer (EOC). The MIRV trials were all undertaken in patients with high grade serous EOC. Serous tumours are associated with more aggressive, poor prognosis disease (reviewed in Rendi, 2024) and the evaluation noted that they are reported to have higher FRα expression (Köbel et al, 2014; Previs et al, 2024). The ESCs noted the proportion of patients with non-serous ovarian cancers with high FRα expression is low, therefore excluding the term 'serous' in the population description would likely have minimal impact. The ESCs considered that the very small group of patients with non-serous ovarian cancer and high FRα expression is likely to benefit from treatment with MIRV and it may be reasonable for the PBAC to consider including them under the restrictions for MIRV.

3.5 The proposed target population of platinum resistant patients excluded those with a platinum-free interval of less than three months following one line of platinum therapy (these patients were defined in the submission as 'platinum refractory'). The evaluation noted that patients meeting the submission definition of 'platinum refractory' would be indicated for the same treatment as platinum resistant patients under current guideline recommendations (NCCN 2025). There was however no clinical evidence to support use of MIRV in these patients, who may represent a high risk of use outside the proposed restriction. The ESCs noted the additional details regarding platinum resistance provided in the PSCR (table 5) and considered the sponsor's proposed definition of platinum resistance to be reasonable and in line with the MIRV trials. The ESCs noted that patients classified as platinum refractory were not included, however the ESCs considered that patients classified as platinum refractory may also benefit from MIRV.

3.6 The proposed TGA indication specified treatment as monotherapy, and this criterion, not initially included in the proposed restriction, was proposed in the PSCR. The evaluation noted that MIRV in combination with other agents in PROC patients has been reported in at least five clinical trials and recommended in National Comprehensive Cancer Network (NCCN) Guidelines in some circumstances (NCCN, March 2025). The ESCs considered use in combination with BEVA is unlikely for patients with high FRα expression, however considered it would be appropriate for the restrictions to specify MIRV is used as monotherapy.

3.7 MIRV is administered via IV infusion at a dose of 6 mg/kg adjusted to ideal body weight (AIBW) once every 3 weeks (21-day cycle). The sponsor has requested a max amount sufficient to treat a patient with 83.3kg AIBW, which appears reasonable. The mean AIBW in MIRASOL was 59kg. The sponsor has proposed that an increase to maximum amounts be allowed for patients with an AIBW greater than 83.3kg, where a higher quantity of drug would be required as per the TGA dosing schedule (6mg/kg AIBW).

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 Epithelial ovarian, fallopian tube, and primary peritoneal cancer are collectively described as EOC. There are currently no recommended screening tests for EOC and the absence of definitive symptoms makes it difficult to diagnose in the early stages (Cancer Australia, 2019). Late-stage EOC is rarely curable despite optimal surgical resection and intensive adjuvant or neo-adjuvant chemotherapy. Due to the ambiguous nature of these disease symptoms, a lack of early detection tests, and because early-stage disease is typically asymptomatic, 70% of patients receive a late-stage diagnosis (stage III-IV) (Cancer Council, 2024).

4.2 At the time of diagnosis, women have a five-year survival rate of 48% (Australian Cancer Research Foundation [ACRF], 2022). Ovarian cancer was ranked 6th highest as a cause of cancer death in Australian women in 2022 (Cancer Australia, 2024; NCCI, 2022). For Australian patients with advanced or metastatic EOC with serous histology, a median overall survival (OS) of 5.2 years was reported for a cohort of 421 women, in an unpublished draft study commissioned for this submission (registry data collected by the not-for-profit Cancer Screening Program [CaSP]) (Quantium, 2025).

4.3 Ovarian cancer is managed according to tumour histology. The currently understood spectrum of tumour subtypes, differentiated according to histology, and their proportions, has been conceptualised during the evaluation, in Figure 1.

Figure 1: Diagram of ovarian cancer subtypes by histology

Epithelial ovarian cancer (EOC)	85-90%	Serous	70-75%	High grade	95-97%
				Low grade	3-5%
		Clear cell carcinoma (5-12%) Endometrioid (11-20%) Mucinous (3%) Others (mixed; undifferentiated <5%)	25-30%		
Non-epithelial OC (stromal or germ cell)	10-15%				

Source: Developed during the evaluation from Section 1.1.3.1. Disease Background (p5-7 of the submission); Redi et al, (2017); González-Martín et al, (2023); Bergstrom et al, (2017) (cited in the MIRASOL CSR); Fleury et al, (2015); Atallah et al, (2023) (cited in the 1787 PICO Confirmation).
EOC: epithelial ovarian cancer; OC: ovarian cancer (not including peritoneal or fallopian tube).

4.4 High grade serous tumours are the most common subtype of EOC. Clinical experts consulted for the submission noted that different EOC subtypes may not be readily distinguishable on examination.

4.5 In 2024, it was projected there would be 1,805 incident cases of ovarian cancer and serous carcinomas of the fallopian tube in Australia (AIHW, 2024), of which the

submission assumed 90% would be EOC. In 2020, the estimated 10-year prevalent population of Australian women with ovarian cancer, serous cancers of the fallopian tube, and peritoneal cancer was 8,950 (AIHW Cancer Data in Australia).

4.6 MIRV is an anti-body drug conjugate (ADC). The mirvetuximab antibody component binds with high affinity to the FRα cell surface protein, which in turn is over-expressed in a majority of ovarian cancers (Kelemen, 2006). The drug conjugate delivers the cytotoxic drug component (soravtansine) to cells expressing FRα proteins. Soravtansine is a maytansinoid – an anti-mitotic agent which inhibits tubulin function, causing cell cycle arrest and cell death, a mechanism similar to vinca alkaloids.

4.7 The submission proposed management of platinum resistant patients split between those with high FRα expression who would receive MIRV and those with low-medium FRα expression (i.e. who are in effect biomarker negative and who would receive non-platinum chemotherapy). Thresholds for FRα expression are discussed under Claim of codependence (paragraphs 6.61-6.65). The main proposed use of MIRV was as second line treatment on disease recurrence after platinum-based chemotherapy. The evaluation patients with malignant ascites may receive BEVA in preference to MIRV as it is known to be effective, or in patients with a history of ocular disorders who may be considered unsuitable for MIRV. MIRV was also proposed in later line treatment after non-platinum chemotherapy or other regimens.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The submission nominated non-platinum chemotherapy (paclitaxel, topotecan, or PEGylated doxorubicin [PLD]) either with or without concomitant BEVA as the main comparator. This was consistent with current clinical guidelines.

5.2 For the purpose of the clinical trials, non-platinum chemotherapy (as per paragraph 5.1) was defined as investigator's choice of chemotherapy (ICC). Direct evidence was available for the comparison of MIRV versus ICC. The comparison of MIRV versus BEVA+ICC relied on an indirect comparison with ICC as the common comparator.

5.3 The sponsor's registry study (Quantium 2025) showed the majority of patients defined as either platinum resistant or platinum refractory in the Australian CaSP cohort received PLD (33% or 35%, respectively) or PLD/non-platinum chemotherapy with BEVA (33% or 45%) as the first treatment after post-platinum relapse (second line). Notably, most patients in the CaSP cohort had already received paclitaxel in first line in combination with carboplatin (72%), precluding its use as single agent chemotherapy in subsequent lines. The proportion of topotecan use in treatment of these patients was very small (N=7 in platinum resistant patients across second and third line), suggesting a move away from use of this agent in Australian clinical practice. The distribution of therapies that comprised ICC in MIRASOL included paclitaxel (40.70%), PLD (35.80%) and topotecan (23.50%). Thus, the evaluation considered that with the exception of PLD, the distribution of therapies was not generally representative of that used in Australian clinical practice based on the CaSP registry data. The PSCR contended that that the small sample size of the Australian

CaSP cohort limits its applicability. The ESCs considered any efficacy and safety differences between the choice of non-platinum agents used in MIRASOL and those used in Australian clinical practice are unlikely to have a substantial impact on the trial outcomes.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician discussed the poor prognosis and current treatment options for platinum resistant ovarian cancer, how the drug would be used in practice, and addressed other matters in response to the Committee's questions. The clinician noted that despite good initial response rates to chemotherapy (80%), the majority of patients relapse within the first year, and ~20% of patients progress rapidly. For patients with platinum resistant EOC the median PFS is short (~3 months), and OS is approximately a year. The clinician had not personally used MIRV but cited real-world data consistent with MIRASOL trial outcomes. The clinician noted that toxicity and safety are very important in this condition and considered that MIRV has a superior safety profile to chemotherapy, except for ocular toxicity, which the clinician considered manageable. The clinician indicated that bevacizumab can be used in all lines of treatment and is used frequently but noted that it is contraindicated in many patients (e.g. those with bowl obstructions). The PBAC considered the hearing informative, providing a clinical perspective on the treatment of platinum-resistant ovarian cancer.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (1), health care professionals (1) and organisations (4) via the Consumer Comments facility on the PBS website. The comments described the impact and clinical outcomes for people living with ovarian cancer including burdensome symptoms, poor quality of life, and short life expectancy.

6.3 Individuals noted that there are few effective treatments for platinum resistant EOC and emphasized the need for effective new therapies. The PBAC noted the advice received from Rare Cancers Australia, Ovarian Cancer Australia, and Inherited Cancers Australia. Organisations described the experience of patients in terms of the morbidity of current treatments, which are associated with serious and bothersome side effects that impact quality of life (e.g. alopecia) and require travel to specialist settings for injections (often weekly). The comments described the benefit of having a targeted treatment with a demonstrated survival benefit, and considered side effects for MIRV to be manageable, particularly in comparison to chemotherapy. The PBAC noted that this advice was supportive of the evidence provided in the submission. The PBAC noted that based on the consumer input, the most important clinical need to address for this population is extending survival time.

6.4 The Medical Oncology Group of Australia (MOGA) also expressed its strong support for the MIRV submission, categorising it as one of the therapies of "high priority for PBS listing" on the basis of the MIRASOL trial. The PBAC noted that MOGA presented a European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) for MIRV, which was limited to 3 (out of a maximum of 5, where 5 and 4 represent the grades with substantial improvement)[1], based on an overall survival gain of approximately 3.7 months in a comparison with ICC, noting similar quality of life outcomes and improved grade 3 adverse events.

Overview of the evidence base

6.5 A linked evidence approach was presented to consider validity of the treatment effect of MIRV in FRα high expression patients. The MIRV clinical program was not designed to examine treatment of patients explicitly defined as FRα test negative. The included evidence is summarised in Table 2.

[1] Cherny NI, Dafni U, Bogaerts J, et al: ESMO-Magnitude of Clinical Benefit Scale version 1.1. Annals of Oncology 28:2340-2366, 2017]

Table 2: Summary of the linked evidence approach

	Type of evidence supplied	Extent of evidence supplied
Accuracy and performance of the test (cross-sectional accuracy)	James et al, (2024) Retrospective analysis of pathology samples from MIRV Phase II trial (SORAYA) used to establish concordance in use of the clinical utility standard in different settings Martin et al (2017) sub-study to the MIRV Phase I trial; testing of archived tissue vs fresh pre-treatment biopsy vs fresh post-treatment biopsy FDA (2022) evaluation report for Ventana FOLR1 assay; reports results of James et al, (2024); includes results of separate biomarker prevalence study (N=953)	☒ k=3 n=100+24+28+438 (based on multiple test performance analyses) n=27 n=953
Prognostic evidence (longitudinal accuracy)	Four non-comparative observational studies Lawson et al (2024) Köbel et al (2014) Crane et al (2012) Kalli et al (2008)	☒ k=4 n=251 n=2801 n=361 n=213
Change in patient management	No evidence presented	☐ k=0 n=0
Health outcomes (clinical utility)	No evidence presented	☐ k=0 n=0
Predictive effect (treatment effect variation)	Comparison of outcomes in the whole trial population (stratified according to FRα expression) vs FRα-high subgroup, both groups receive either MIRV or ICC. Exploratory analysis of FRα-high vs FRα-medium (latter is effectively test negative) according to previously used test scoring criteria. Post hoc analysis of re-scored patients in FRα-low, medium and high groups according to test scoring criteria proposed for the submission.	☒ k=2 n=366 n=148 FRα medium n=218 FRα high (based on 10X scoring)
Treatment effect (enriched)	Single RCT of MIRV vs ICC in patients that are FRα-high (test positive) in both arms	☒ k=1 n=453
Other	Single RCT of bevacizumab + ICC versus ICC as indirect evidence for the bevacizumab + ICC comparator	☒ k=1 n=361

Source: Compiled during the evaluation based on information presented in Section 2 of the submission
ICC: investigator's choice of chemotherapy; FDA= Food and Drug Administration; FRα: folate receptor alpha; k: number of studies, MIRV: mirvetuximab soravtansine; n: number of patients; RCT= randomised control trial.

6.6 Trials presented to inform comparisons for the relevant comparators and biomarker populations are summarised in Table 3.

Table 3: Data availability to inform comparisons

	MIRV	ICC; bevacizumab + ICC[a]
Biomarker test positive	MIRASOL	MIRASOL; AURELIA
Biomarker test negative	Partially applicable: FORWARD-I FRα-medium subgroup	Partially applicable: FORWARD-I FRα-medium subgroup

Source: Compiled during the evaluation based on information presented in Section 2 of the submission
ICC= investigator's choice of chemotherapy; FRα= folate receptor alpha; MIRV= mirvetuximab soravtansine.
[a] the comparator bevacizumab + ICC is only studied in the AURELIA trial.

6.7 The submission presented direct evidence of MIRV versus ICC in the target patient population of FRα-high expression (biomarker positive) EOC patients who have been diagnosed as platinum resistant, i.e. the key MIRASOL trial. The ESCs and the

evaluation considered that the MIRASOL trial was at high risk of bias due to the open label design, the choice of progression free survival (PFS) primary endpoint based on investigator assessment, and evidence of informative censoring leading to drop-outs at treatment allocation and prior to disease progression.

6.8 The MIRASOL trial was supported by the FORWARD-I trial which compared MIRV versus ICC in a broader population of FRα-medium and FRα-high expression patients. The FORWARD-I trial was at low risk of bias for the pre-specified analyses noting the primary outcome employed assessment by BICR.

6.9 Whereas the MIRASOL trial employed PS2+ staining and a ≥75% FRα expression cutoff for test positivity, FORWARD-I employed a previously used definition of FRα biomarker positivity (≥50% – 75% for medium; ≥75% expression for high) and a different scoring method (staining visible at 10X magnification).

6.10 The submission presented a post-hoc analysis of the FORWARD-I patients based on re-scoring of tissue samples according to the test criteria used for MIRASOL. The results for the patients re-scored as FRα-medium and FRα-low expression were considered representative of biomarker negative patients for the purpose of demonstrating the co-dependency between the proposed biomarker and treatment. The evaluation considered the results of the FORWARD-I post hoc analysis were at high risk of bias, however the ESCs considered that the difference in outcomes between FRα-medium and FRα-high expression patients still provides support for the FRα expression threshold and claim of codependence.

6.11 An indirect comparison of MIRASOL with a third trial (AURELIA) provided indirect evidence of MIRV versus BEVA + ICC based on the common comparator of ICC (noting the non-platinum agents were the same as in MIRASOL) in a biomarker agnostic population. The evaluation considered that this trial was at a high risk of bias due to the open label design, the choice of PFS primary endpoint based on investigator assessment and rules permitting cross-over in the ICC arm to single agent BEVA after disease progression (69/182 [35%] ICC patients).

Clinical trials on the safety/effectiveness of drug

6.12 The submission was based on two key head-to-head trials comparing MIRV to ICC, MIRASOL (n=453)[2] and FORWARD-I (n=366)[3]. The MIRASOL trial represented direct evidence for the treatment benefit of MIRV versus ICC in FRα-high expression patients. The FORWARD-I trial demonstrated the treatment benefit of MIRV versus ICC in FRα-high and FRα-medium expression patients (i.e., high expression as test positive and medium expression as proxy for test negative). The AURELIA trial provided evidence for the indirect comparison of MIRV and BEVA + ICC.

[2] MIRASOL patient disposition: MIRV, n=227 (50.1%); ICC, n=226 (49.9%) (Paclitaxel, n=92/226 [40.7%]; PLD, n=81/226 [35.8%]; topotecan, n=53/226 [23.5%]).
[3] FORWARD-I patient disposition: MIRV, n=248 (67.8%); ICC, n=118 (32.2%) (Paclitaxel, n=37/118 [31.4%]; PLD, n=54/118 [45.8%]; topotecan, n=27/118 [22.9%])

6.13 Details of the trials presented in the submission are provided in Table 4 (not including supplementary publications unless they were key to the evaluation).

Table 4: Listing of all direct randomised trials

Trial ID	Protocol title/ Publication title	Publication citation
Direct randomised trials: MIRV vs non-platinum chemotherapy		
MIRASOL IMGN853-0416 (NCT04296890)	Mirasol: A Randomized, Open-Label, Phase 3 Study Of Mirvetuximab Soravtansine Vs. Investigator's Choice Of Chemotherapy In Platinum-Resistant Advanced High Grade Epithelial Ovarian, Primary Peritoneal, Or Fallopian Tube Cancers With High Folate Receptor Alpha Expression.	CSR, primary analysis, dated 11 September 2023 (6 March 2023 data cutoff)
	MIRASOL: a randomized, open-label, phase 3 study of mirvetuximab soravtansine vs. Investigator's choice of chemotherapy in platinum-resistant advanced high grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptor alpha expression.	CSR, final analysis, dated 27 November 2024 (26 September 2024 data cutoff)
	Primary publication: Moore KN, Angelergues A, Konecny GE, García Y, Banerjee S, Lorusso D, Lee JY, Moroney JW, Colombo N, Roszak A, Tromp J. Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer.	New England Journal of Medicine. 2023 Dec 7;389(23):2162-74.
FORWARD-I IMGN853-0403 (NCT02631876)	FORWARD-I: A Randomized, Open-label Phase 3 Study to Evaluate the Safety and Efficacy of Mirvetuximab Soravtansine (IMGN853) Versus Investigator's Choice of Chemotherapy in Women with Folate Receptor α−positive Advanced Epithelial Ovarian Cancer, Primary Peritoneal Cancer or Fallopian Tube Cancer.	CSR (data cutoff 19 February 2019)
	Primary publication: Moore KN, Oza AM, Colombo N, et al. Phase III, randomized trial of mirvetuximab soravtansine versus chemotherapy in patients with platinum-resistant ovarian cancer: Primary analysis of FORWARD-I.	Annals of Oncology. 2021;32(6):757-765.
	Supplementary Publications: Moore K, Oza A, Colombo N, et al. FORWARD-I (GOG 3011): A phase III study of mirvetuximab soravtansine, a folate receptor alpha (FRa)-targeting antibody-drug conjugate (ADC), versus chemotherapy in patients (pts) with platinum-resistant ovarian cancer (PROC). [Conference Abstract]	Annals of Oncology. 2019;30:v403.
Supplementary randomised trial: Non-platinum chemotherapy with or without bevacizumab		
AURELIA (NCT00976911)	**Primary publication:** Pujade-Lauraine E, Hilpert F, Weber B, Reuss A, Poveda A, Kristensen G, Sorio R, Vergote I, Witteveen P, Bamias A, Pereira D. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: the AURELIA open-label randomized phase III trial.	Journal of clinical oncology. 2014 May 1;32(13):1302-8.

Source: Table 2.2 1 Trials (and Associated Reports) Presented in this Submission, pp24-26 of the submission; Attachment 2.1 Literature Search – ELAHERE.
CSR= Clinical Study Report.

6.14 The key features of the included evidence trials are summarised in Table 5 for the direct evidence (MIRASOL; FORWARD-I) and the trials used in the indirect comparison (MIRASOL; AURELIA) based on the ICC common comparator.

Table 5: Key features of the included evidence

Trial	N	Study design Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
MIRV vs ICC					
MIRASOL Moore et al, (2023) (NCT04296890)	453	R, OL, MC High	Women with PROC who had previously received 1-3 lines of systemic therapy, and who were positive for FRα-high expression (≥75%; PS2+ scoring)	PFS (INV); OS	PFS, OS
FORWARD-I Moore et al, (2021) (NCT02631876)	366	R (2:1), OL, MC Low (for pre-specified analysis) High (for post-hoc analysis)	Women with PROC; with no more than 3 prior systemic treatment regimens whose tumours had medium (≥50% to >75%) or high (≥75%) FRα expression levels (10X magnification scoring)	PFS (BICR); OS	Not used
BEVA+ICC vs ICC					
AURELIA Pujade-Lauraine et al, (2014) (NCT00976911)	361	R, OL, MC High	Women with EOC who had progressed within 6 months of completing 4 or more cycles of platinum-based therapy (biomarker agnostic population)	PFS (INV); OS	Not used

Source: complied during the evaluation from source trial publications.
BEVA= bevacizumab; BICR=blinded independent central review; DB=double blind; EOC=epithelial ovarian cancer; FRα=folate receptor alpha; ICC=investigator's choice of chemotherapy; INV=by investigator assessment; MC=multi-centre; MIRV=mirvetuximab soravtansine: OL=open label; OS=overall survival; PFS=progression-free survival; PROC=platinum-resistant ovarian cancer; R=randomised.

Comparative effectiveness

MIRASOL

6.15 The results from the MIRASOL trial for PFS by local investigator are summarised in Table 6 and the Kaplan-Meier plot for the September 2024 cutoff in Figure 2.

Table 6: Results of primary endpoint (ITT): PFS by local investigator

	MIRV (N=227)		ICC (N=226)				
Outcome	**n with event (%)**	**Median time to PFS event (mo) (95% CI)**	**n with event (%)**	**Median time to PFS event (mo) (95% CI)**	**Difference in median PFS**	**P-value (log rank test)**	**HR (95% CI)**
MIRASOL March 2023 data cutoff (median follow-up 11.20 mo [95% CI 9.99, 13.70])							
PFS	176 (77.5%)	5.62 (4.34, 5.95)	166 (73.5%)	3.98[b] (2.86, 4.47)	1.64	**<0.0001**	**0.65 (0.521, 0.808)**
PD[a]	163 (71.8%)	--	150 (66.4%)	--	--	--	--
Deaths	13 (5.7%)	--	16 (7.1%)	--	--	--	--
Censored	51 (22.5%)	--	60 (26.5%)	--	--	--	--
MIRASOL September 2024 data cutoff (median follow-up 28.35 mo [95% CI 24.97, --])							
PFS	204 (89.9%)	5.59 (4.34, 5.88)	174 (77.0%)	3.98[b] (2.86, 4.47)	1.61	**<0.0001**	**0.63 (0.513, 0.785)**
PD[a]	190 (83.7%)	--	158 (69.9%)	--	--	--	--
Deaths	14 (6.2%)	--	16 (7.1%)	--	--	--	--
Censored	23 (10.1%)	--	52 (23.0%)	--	--	--	--

Source: Table 2.5 1 Results of Primary Endpoint (ITT): PFS, p63 of the submission; Table 2.5 2 Results of Primary Endpoint (ITT): PFS (September 2024 data cut), p65 of the submission; Table 17, p104-5 MIRASOL CSR March 2023; Table 17, p105-6 MIRASOL CSR Sept 2024.

CI= confidence interval; CSR: clinical study report; HR= hazard ratio; ICC= investigator's choice of chemotherapy; ITT= intention to treat analysis; MIRV= mirvetuximab soravtansine; mo= months; PD= progressive disease; PFS= progression-free survival; RECIST= response evaluation criteria in solid tumours.

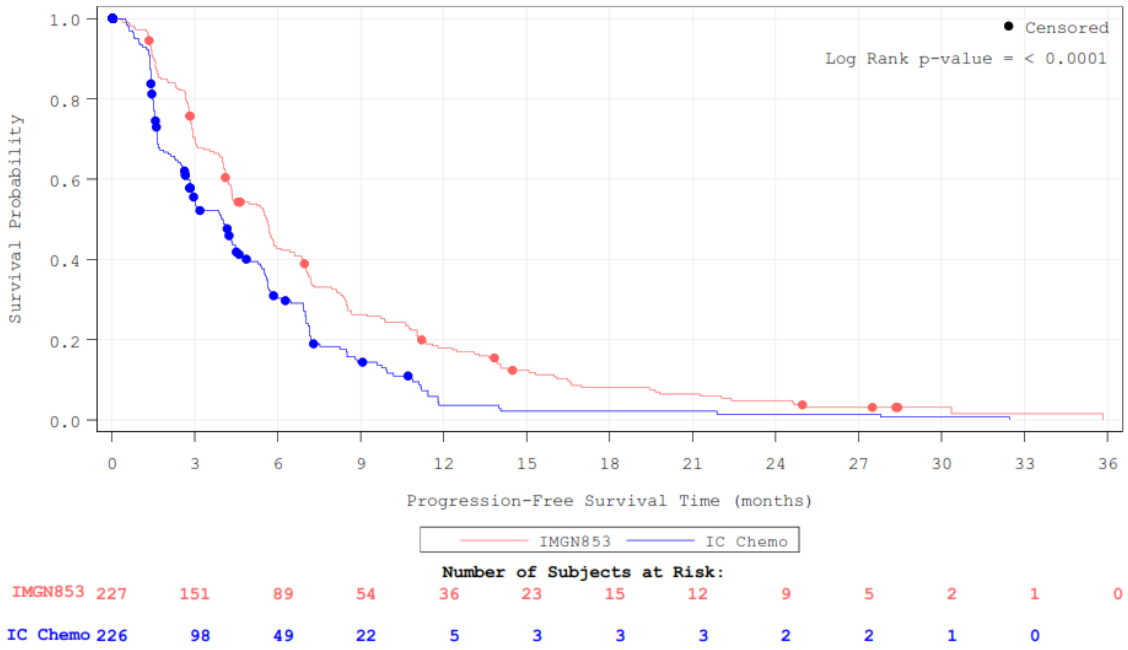
[a] Progressive disease was based on radiological progression assessed by RECIST (version 1.1) criteria.

[b] The ICC arm median PFS and CI values for each data cutoff were verified against the CSRs.

Values in **bold** were statistically significant.

6.16 The median time to a PFS event was longer in the MIRV arm (5.59 months) compared to the ICC arm (3.98 months). The HR favoured MIRV and was statistically significant (HR 0.63, 95% Confidence Interval [CI]: 0.513, 0.785).

Figure 2: Kaplan-Meier Plot of PFS by Investigator – ITT Population (September 2024 cutoff)



Source: Figure 2.5 1 Kaplan-Meier Plot for Progression-Free Survival by Investigator – ITT Population, p64 of the submission; Figure 2: Kaplan-Meier Plot for Progression-Free Survival by Investigator – ITT Population, p107 MIRASOL CSR Sept 2024.
CSR= clinical study report; IC chemo= investigator's choice of chemotherapy; IMGN853: mirvetuximab soravtansine development code; ITT= intention to treat analysis; PFS= progression-free survival.

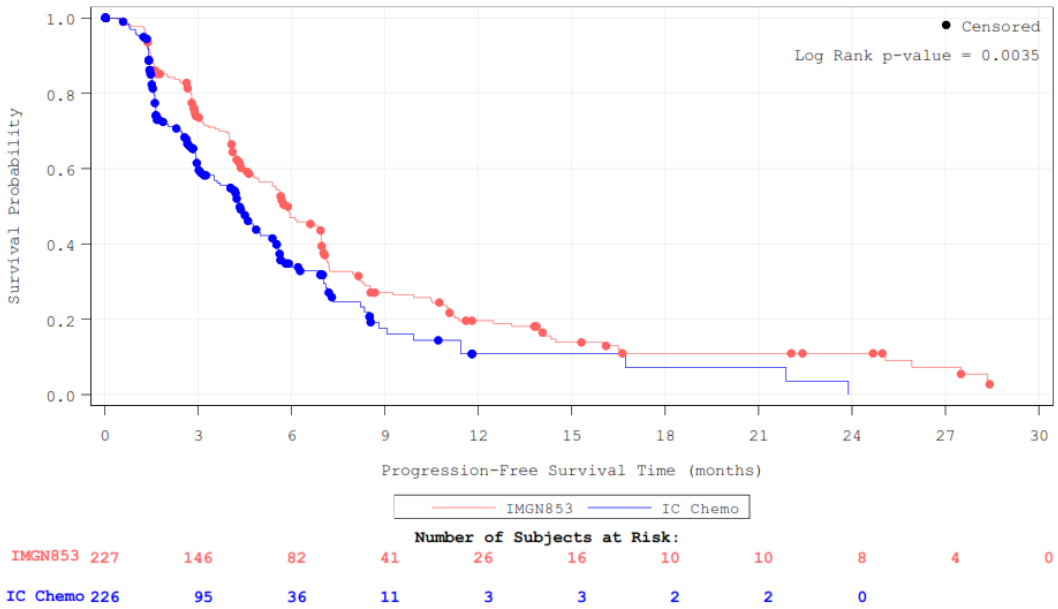
6.17 PFS by blinded independent central review (BICR) was not a pre-specified outcome for the trial but a conditional analysis to be undertaken only if the results for PFS by investigator were statistically significant. Results of the analysis for PFS by BICR are summarised in Table 7 and the Kaplan-Meier plot for the September 2024 cutoff in Figure 3.

Table 7: Results of PFS by BICR (ITT)

	MIRV (N=227)		ICC (N=226)				
Outcome	**n with event (%)**	**Median time to PFS event (mo) (95% CI)**	**n with event (%)**	**Median time to PFS event (mo) (95% CI)**	**Difference in median**	**P-value (log rank test)**	**HR (95% CI)**
MIRASOL March 2023 data cutoff (median follow-up 7.33 mo [95% CI 6.97, 8.48])							
PFS	146 (64.3%)	5.91 (4.93, 6.97)	123 (54.4%)	4.34[a] (3.52, 4.99)	1.57	**0.0082**	**0.72 (0.558, 0.920)**
MIRASOL September 2024 data cutoff (median follow-up 8.67 mo [95% CI 7.20, 11.79])							
PFS	164 (72.2%)	5.82 (4.93, 6.97)	127 (56.2%)	4.34[a] (3.52, 4.99)	1.48	**0.0035**	**0.70 (0.547, 0.890)**
PD[a]	143 (63.0%)	--	101 (44.7%)	--	--	--	--
Deaths	21 (9.3%)	--	26 (11.5%)	--	--	--	--
Censored	63 (27.8%)	--	99 (43.8%)	--	--	--	--

Source: Compiled during the evaluation using data sourced from Table 18, p108 MIRASOL CSR March 2023; Table 18, p109 MIRASOL CSR Sept 2024.
BICR= blinded independent central review; CI: confidence interval; CSR: clinical study report; HR: hazard ratio; ICC: investigator's choice of chemotherapy; ITT: intention to treat analysis; MIRV: mirvetuximab soravtansine; mo: months; PFS: progression-free survival.
a The ICC arm median PFS and CI values for each data cutoff were verified against the CSRs.

Figure 3: Kaplan-Meier Plot of PFS by BICR – ITT Population (September 2024 cutoff)



Source: Figure 4: Kaplan-Meier Plot for Progression-Free Survival by BICR – ITT Population, p110 MIRASOL CSR Sept 2024.
BICR= blinded independent central review; CSR= clinical study report; IC Chemo= investigator's choice of chemotherapy; IMGN853= mirvetuximab soravtansine development code; ITT= intention to treat analysis; PFS= progression-free survival.

6.18 The evaluation noted that the HR point estimates for PFS by BICR were less favourable than that assessed by investigator. At the second data cutoff (September 2024) the median duration of follow-up was substantially shorter for the participants included in the BICR analysis (8.67 months) compared with the corresponding investigator analysis (28.35 months). This appears to have been due to censoring of patients in the BICR analysis.

6.19 Differences between the PFS by investigator and PFS by BICR were evident in the proportions of patients included in the analysis for each treatment arm, and the median duration of follow-up. The censoring of patients for PFS is summarised in Table 8.

Table 8: Censoring of patients for PFS by investigator versus PFS by BICR (ITT population) (September 2024)

Patient events	Investigator		BICR	
	MIRV (N=227)	ICC (N=226)	MIRV (N=227)	ICC (N=226)
Number of patients with events, n (%)	**204 (89.9)**	**174 (77.0)**	**164 (72.2)**	**127 (56.2)**
Radiological progression	190 (83.7)	158 (69.9)	143 (63.0)	101 (44.7)
Death	14 (6.2)	16 (7.1)	21 (9.3)	26 (11.5)
Number of patients censored, n (%)	**23 (10.1)**	**52 (23.0)**	**63 (27.8)**	**99 (43.8)**
PD or death after missing ≥ 2 consecutive radiological assessments	3 (1.3)	5 (2.2)	3 (1.3)	7 (3.1)
New anti-cancer therapy prior to PD or death	7 (3.1)	22 (9.7)	45 (19.8)	61 (27.0)
No baseline or post-baseline assessment and patient did not die within 105 days of randomization	8 (3.5)	22 (9.7)	9 (4.0)	27 (11.9)
Database cut	5 (2.2)	3 (1.3)	6 (2.6)	4 (1.8)

Source: Table 14.2.1.1 Progression Free Survival Per Investigator Intent-to-Treat Population and Table 14.2.1.2 Progression Free Survival per BICR Intent-to-Treat Population, p439 and p445, MIRASOL CSR September 2024.
BICR=blinded independent central review; ITT= intention to treat; MIRV=mirvetuximab soravtansine; PD= progressed disease; PFS=progression-free survival.
Shading added during the evaluation. Cells in light shading indicate events censored at a higher rate than the MIRV arm which appear to be due to study drop-outs in the ICC arm on treatment allocation; dark shading indicates censored events across both arms, in patients who discontinued prior to disease progression (likely considered to have clinically progressive disease).

6.20 PFS analyses were affected heavily by inclusion of patients who should have been censored, and the investigator assessed outcomes were likely to be biased in favour of MIRV. Censoring of patients was higher in the ICC arm for both local and investigator and BICR analyses. In particular, censoring due to new anti-cancer treatment prior to disease progression was pronounced in the BICR analysis (both arms) but low in the MIRV arm investigator analysis. The evaluation considered that the pronounced difference in numbers of patients judged by the BICR (compared to investigator assessment) to have switched to new treatment prior to disease progression in both arms suggested the investigator assessment of disease progression was subject to bias. The PSCR contended that imaging assessments conducted by someone familiar with the patient's disease history are often more reliable and investigator-assessed PFS is more reflective of clinical practice, and that increased withdrawals in the ICC arm would have biased against MIRV due to exclusion of sicker patients. However, the ESCs considered the PFS results to be associated with a high degree of uncertainty.

6.21 The results of the analysis for overall survival (OS) in the MIRASOL trial are summarised in Table 9 and Figure 4.

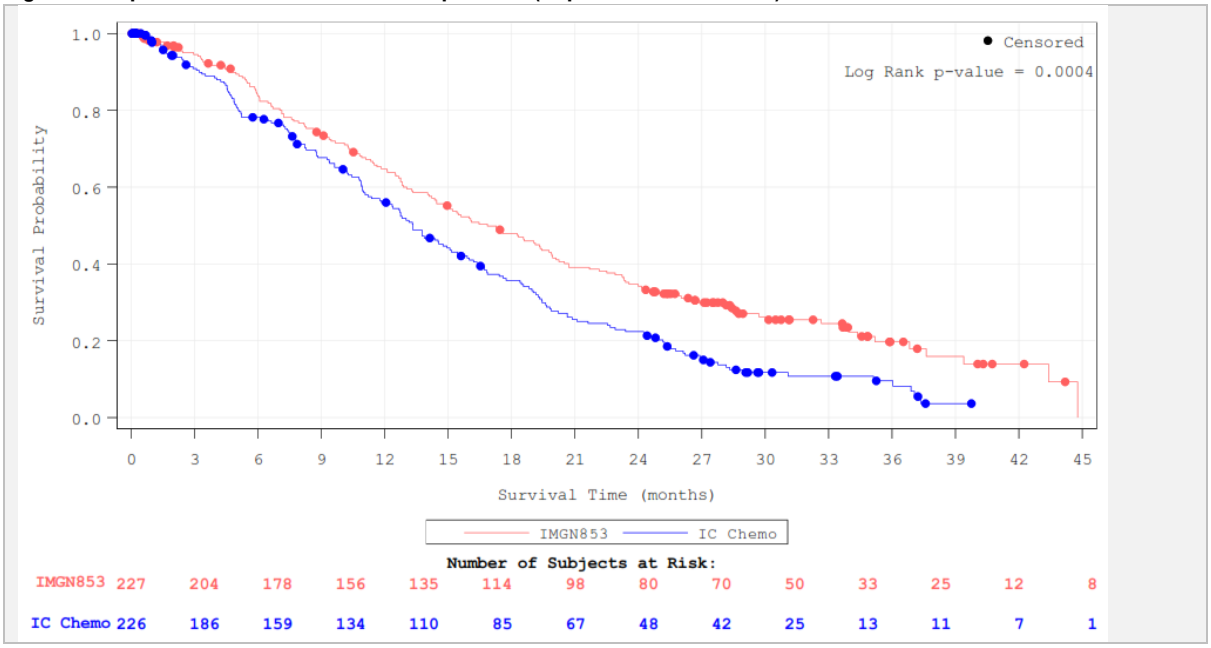
Table 9: Results of Secondary Endpoint (ITT): OS

		MIRV (N=227)		ICC (N=226)			
Outcome	**n with event (%)**	**Median time to event (mo) (95% CI)**	**n/N with PD (%)**	**Median time to event (mo) (95% CI)**	**Difference in median**	**P-value (log rank test)**	**HR (95% CI)**
MIRASOL March 2023 data cutoff (median follow-up 13.11 mo [95% CI12.09, 14.13])							
OS	90 (39.6)	16.46 (14.46, 24.57)	114 (50.4)	12.75 (10.91, 14.36)	3.74	**0.0046**	**0.67 (0.504, 0.885)**
Censored	137 (60.4%)	--	112 (49.6%)	--	--	--	--
MIRASOL September 2024 data cutoff (median follow-up 30.49 mo [95% 28.75, 33.68])							
OS	162 (71.4)	16.85 (14.36, 19.78)	177 (78.3)	13.34 (11.37, 15.15)	3.51	**0.0004**	**0.68 (0.543, 0.840)**
Censored	65 (28.6%)	--	49 (21.7%)	--	--	--	--

Source: Table 2.5 5 Results of Secondary Outcomes (ITT): OS, p68 of the submission; Table 2.5 6 Results of Secondary Outcomes (ITT): OS (September 2024 data cut), p70 of the submission; Table 23, p115-16 MIRASOL CSR March 2023; Table 23, p117 MIRASOL CSR Sept 2024.

CI= confidence interval; CSR: clinical study report; HR= hazard ratio; ICC= investigator's choice of chemotherapy; ITT: intention to treat analysis; MIRV: mirvetuximab soravtansine; mo: months; PD: progressive disease; PFS= progression free survival; OS: overall survival. Values in **bold** were statistically significant.

Figure 4: Kaplan-Meier Plot of OS – ITT Population (September 2024 cutoff)



Source: Figure 2.5 3 Kaplan-Meier Plot for Overall Survival – ITT Population, p68 of the submission; Figure 6: Kaplan-Meier Plot for Overall Survival – ITT Population, p118 MIRASOL CSR Sept 2024.
CSR= clinical study report; IC= investigator's choice; ITT= intention to treat analysis; OS= overall survival.

6.22 MIRASOL patients treated with MIRV achieved a statistically significant improvement in OS compared with ICC (HR 0.67, 95% CI: 0.504, 0.885). Although the trial focused on PFS (as the primary outcome), the MIRASOL result for OS was a more objective outcome than the PFS surrogate, particularly for an open label study and noting the issues discussed above regarding the PFS analyses.

6.23 Based on data from the March 2023 data cutoff, 96 (42.3%) patients achieved an objective (complete or partial) response (ORR) in the MIRV arm compared to 36 (15.9%) patients in the ICC arm, an absolute difference of 26.4% (95% CI: 18.4, 34.4). Complete response was achieved by 12 (5.3%) patients in the MIRV arm and no patients in the ICC arm. In the MIRV arm, 84 (37.0%) patients achieved partial response compared to 36 (15.9%) patients in the ICC arm. Overall, the key secondary efficacy endpoint of ORR was met (p<0.0001). The ORR results from the September 2024 data cutoff aligned with the results from the March 2023 data-cut.

6.24 Subgroup analyses reported in MIRASOL indicated that PFS results from BEVA-pretreated and BEVA-naïve subgroups showed a consistent benefit with MIRV in patients with PROC with HRs of 0.64 (p=0.021) and 0.67 (p=0.0184), respectively. For other subgroup analyses, including prior exposure to BEVA, PARP inhibitors and number of prior lines (1, 2, or 3 lines) of therapy, benefits were observed for MIRV versus ICC. For OS, there was a consistent trend for benefit of MIRV over ICC across subpopulation analyses, including prior exposure to BEV, PARP inhibitors, and the number of prior lines of therapy. However, patients in the primary progression-free interval (PFI) > 6 months subgroup appear to achieve better OS outcomes (HR 0.54; 95% CI 0.415, 0.707) compared to those with primary PFI ≤6 months (HR 1.07; 95% CI 0.735, 1.562).

6.25 The submission reported MIRASOL quality of life (QoL) outcomes for European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Ovarian Cancer Module (EORTC QLQ-OV28) (abdominal/gastrointestinal [GI] scores), four subscales of the EORTC QLQ-C30 instrument: Global Health Status/Quality of Life [GHS/QoL], Physical Functioning [PF], Role Functioning [RF], and Fatigue Symptoms [FA]); and EuroQol 5 Dimensions, 5 Levels (EQ-5D-5L) visual analogue scale (VAS) scores. Completion rates at baseline were between 78% and 85% of participants and had decreased to approximately 28% in the MIRV arm and 17% in the ICC arm at week 24.

6.26 The primary responder analysis for EORTC QLQ-OV28 (abdominal/GI scores) at Week 8/9 showed that more MIRV patients (21%) met the improvement threshold (change from baseline of at least 16.67 points compared with ICC patients (15%). Three of the four EORTC QLQ-C30 subscales showed statistically differences for the percentage of improved patients for MIRV versus ICC participants at Week 8/9 (GHS/QoL 22.9% vs 10.4% [p=0.0023]; FA 14.3% vs 4.6% [p=0.0386]; RF 10.1% vs 3.9% [p=0.0038], respectively). Results for the PF subscale showed no difference. For EQ-5D-5L VAS score at Week 8/9, results favoured MIRV, showing a statistically significant difference in mean change from baseline of 6.9 (95% CI: [3.6, 10.1]; p<0.0001). Although the QoL results tended to favour MIRV, some of the results were only evident in the analysis of only patients completing the week 8/9 survey, who may not be representative of the whole trial population based on the reducing, low completion rates throughout the trial. For EORTC QLQ-OV28 (abdominal/GI scores), completion rates at Week 8/9 were 68.7% in the MIRV arm and 58.8% for ICC.

FORWARD-I

6.27 The FORWARD-I trial employed a different definition of FRα expression test positivity than used for MIRASOL (and proposed for the PBS restriction) however, the trial supports clinical utility of the biomarker, in that it shows the rationale behind the choice of cutoff for the eligible patient population and offers a subgroup that represents a biomarker negative population.

6.28 The sponsor explored the FORWARD-I data by re-scoring the tissue samples used to determine FRα expression status in the trial using the PS2+ method and compared them to the simplified 10X method used as the basis for the trial (Table 10).

Table 10: Results of re-scoring FORWARD-I patients FRα expression levels (N=332) [a]

FRα expression Level	Cutoff	10X, N	%	PS2+, N	%	Outcome of re-scoring
FRα-low (<50%)	**0<50%**	**0**	**--**	**114**	**34%**	**Below intended expression cutoff for the FORWARD-I trial**
FRα-medium	50<75%	134	40%	20[a] 82[a]	31%	Intended expression level FRα-medium
FRα-high	≥75%	198	60%	116	35%	Intended expression level FRα-high

Source: slide 11 FORWARD I 10X SCORING COMPARED WITH EXPLORATORY PS2+ SCORING, Moore et al, (2019).
FRα=folate receptor alpha; PS2+= FRα membrane staining at moderate (2) or high (3) intensity.
[a] Analysis population for whom samples were available; percentages indicated are of the total N=332.
[b] Values for the re-scored medium group (20+82=102) were derived during the evaluation from the numbers presented in the source document which gave a value of n=103. Investigation of these discrepancies was considered unlikely to change the resulting proportions. Shading was added to indicate the origin of the values in the re-scored groups. Light green shading indicated patients originally classified as FRα-medium and dark green shading indicated patients originally scored as FRα-high. Hatched indicated a mix of both.

6.29 Of the group originally scored as FRα-high, 82 (41%) were rescored as medium and 116 (59%) remained as FRα-high. Therefore, according to definition of FRα test positivity requested in the submission, all the patients in the FORWARD-I FRα-medium group would have been defined as test negative and just over half (59%) of the patients in the FRα-high group would have been defined as test positive. The re-scored groups formed the basis of the post-hoc analyses.

6.30 The results from the analysis of PFS by BICR in the FORWARD-I trial are summarised in Table 11, including the re-analysed FRα expression groups based on the post-hoc analysis (low, medium and high by PS2+ scoring as per Table 10).

Table 11: FORWARD-I: analysis of PFS by BICR (February 2019 data cutoff)

Analysis	n/N with event (%)	Median time to PFS event (mo) (95% CI)	n/N with event (%)	Median time to PFS event (mo) (95% CI)	Difference in median	P-value (log rank test)	HR (95% CI)
PFS – Whole trial population							
	MIRV (N=248)		**ICC (N=118)**				
ITT	174/248 (70%)	4.14 (3.75, 4.53)	70/118 (59%)	4.44 (2.83, 5.59)	-0.3	0.897	0.981 (0.734, 1.310)
PFS – FRα-high (≥75%, using 10X scoring) (pre-specified)							
	MIRV (N=147)		**ICC (N=71)**				
FRα-high	93/147 (63%)	4.76 (4.11, 5.68)	45/71 (63%)	3.25 (1.97, 5.59)	1.51	0.049	0.693 (0.480, 1.000)
PFS – FRα-medium (<75%, using 10X scoring) (pre-specified)							
	MIRV (N=101)		**ICC (N=46)**				
FRα-medium	81/101 (80)	2.92 (2.76, 4.14)	25/46 (54)	5.55 (2.73, 8.34)	-2.63	0.061	1.560 (0.976, 2.492)
PFS – FRα expression groups (≥75%, using PS2+ scoring) (post-hoc)							
	MIRV		**ICC**				
FRα-high	50/82 (61%)	5.62 (4.04, 7.06)	25/34 (74%)	3.22 (1.51, 5.49)	2.4	0.0151	0.549 (0.336, 0.897)
FRα-medium	53/69 (77%)	4.30 (4.11, 5.59)	22/34 (65%)	5.55 (1.61, 9.10)	-1.25	0.9543	1.015 (0.611, 1.687)
FRα-low	57/76 (75%)	3.75 (2.83, 4.14)	21/38 (55%)	5.49 (1.97, 6.97)	-1.74	0.1425	1.458 (0.878, 2.420)

Source: compiled during the evaluation from:
Table 9 Primary and secondary endpoint results for the ITT population and the FRα- high population, p18 of submission Appendix A;
Table 21: Progression-free Survival per BIRC – ITT Population, pp97-99, FORWARD-I CSR February 2019 data cutoff;
Table 22: Progression-free Survival per BIRC – FRα-high Population, pp100-102, FORWARD-I CSR February 2019 data cutoff;
Table 10 Post hoc analysis of FORWARD I: primary and secondary endpoints results for the FRα- high, FRα- medium and FRα- low population, p19 of submission Appendix A.
Table 14.2.1.1.3: Progression Free Survival BIRC - FR A Medium Level ITT Population, p662, FORWARD-I CSR.
Slides 12; 14, FORWARD I 10X SCORING COMPARED WITH EXPLORATORY PS2+ SCORING, Moore et al, (2019).
Table 65, Table 66 and Table 67, pp1-6 of Corrected Attachment 2.7 to the submission.
BICR= blinded independent central review; CI= confidence interval; CSR= clinical study report; FRα= folate receptor alpha; HR= hazard ratio; ICC= investigator's choice of chemotherapy; ITT= intention to treat analysis; MIRV= mirvetuximab soravtansine; mo= months; n= number of events; N= number of patients; PFS= progression-free survival.

6.31 The primary endpoint of PFS by BICR did not meet statistical significance in either the intention to treat (ITT) (whole trial) population or FRα-high expression (≥75%, using 10X scoring) subgroup. The median PFS for the FRα-medium population showed a pronounced lack of benefit, in which MIRV patients did worse than the ICC patients (a difference of -2.63 months median time to progression or death). The HR point estimate was above 1.0 with wide confidence intervals (1.560 [95% CI 0.976, 2.492] p=0.061). The re-scored subgroups showed a benefit only for the FRα-high expression group (HR 0.549 [95% CI 0.336, 0.897] p=0.0151) – this formed the basis for the hypothesis tested in the MIRASOL trial.

6.32 The results for OS in the FORWARD-I trial are summarised in Table 12. The submission presented OS results for the pre-specified subgroups from three analyses (February 2019; August 2019; March 2020). The post hoc analysis of the re-scored low, medium and high FRα expression groups was based on February 2019 data.

Table 12: FORWARD-I: analysis of OS (February 2019 and March 2020 data cutoffs)

	MIRV (N=248)		ICC (N=118)				
Outcome	**n/N with event (%)**	**Median time to event (mo) (95% CI)**	**n/N with event (%)**	**Median time to event (mo) (95% CI)**	**Difference in median**	**P-value (log rank test)**	**HR (95% CI)**
OS – Whole trial population							
	MIRV (N=248)		**ICC (N=118)**				
ITT February 2019	96/248 (39%)	16.4 (12.81, NC)	50/118 (42%)	14.0 (11.01, NC)	2.4	0.248	0.815 (0.575, 1.154)
ITT August 2019 exploratory analysis	96/248 (39%)	15.6 (NR)	50/118 (42%)	13.9 (NR)	1.7	0.278	0.846 (0.625, 1.145)
ITT March 2020	152/248 (61%)	15.57 (12.85, 18.04)	75/118 (64%)	13.93 (11.40, 18.50)	1.64	0.276	0.855 (0.644, 1.134)
OS – FRα-high (≥75%, using 10X scoring) (pre-specified)							
	MIRV (N=147)		**ICC (N=71)**				
FRα-high February 2019	50/147 (34%)	NC (12.58, NC)	33/71 (46%)	11.76 (9.20, NC)	NC	0.033	0.618 (0.395, 0.966)
ITT August 2019 exploratory analysis	50/147 (34%)	16.4 (NR)	33/71 (46%)	12.0 (NR)	4.4	0.048	0.678 (0.460, 0.999)
FRα-high March 2020	82/147 (56%)	17.31 (12.81, 20.50)	45/71 (63%)	12.02 (9.20, 18.07)	5.29	0.063	0.706 (0.489, 1.020)
OS – FRα-medium (<75%, using 10X scoring) (pre-specified)							
	MIRV (N=101)		**ICC (N=46)**				
FRα-medium February 2019	46/101 (46)	14.36 (12.06, 20.50)	17/46 (37)	15.18 (11.43, ---)	-0.82	0.521	1.203 (0.683, 2.120)
FRα-medium March 2020	NR	NR	NR	NR	NR	NR	NR
OS – FRα- expression groups (≥75%, using PS2+ scoring) (post-hoc)							
FRα-high	34/82 (41%)	16.43 (11.27, -)	17/34 (50%)	13.47 (6.11, -)	3.0	0.187	0.675 (0.375, 1.214)
FRα-medium	27/69 (39%)	14.23 (12.16, -)	13/34 (38%)	NC (11.76, -)	NC	0.7637	1.108 (0.569, 2.156)
FRα-low	30/76 (39%)	16.99 (12.25, -)	18/38 (47%)	11.43 (8.28, -)	5.6	0.2357	0.702 (0.390, 1.263)

Source: compiled during the evaluation from:
Table 9 Primary and secondary endpoint results for the ITT population and the FRα- high population, p18 of submission Appendix A;
Table 10 Post hoc analysis of FORWARD I: primary and secondary endpoints results for the FRα- high, FRα- medium and FRα- low population, p19 of submission Appendix A;
Table 25: Overall Survival – ITT Population, pp106-107, FORWARD-I CSR,
Table 26: Overall Survival – FRα-high Population, pp109-110, FORWARD-I CSR.
Table 1: Overall Survival – ITT Population, pp2917-2919, FORWARD-I CSR addendum;
Table 2: Overall Survival – FRα-high Population, pp2920-2921, FORWARD-I CSR addendum.
Table 14.2.3.3: Overall Survival - FR A Medium Level ITT Population, p712, FORWARD-I CSR
Slide 9, 12 FORWARD I 10X SCORING COMPARED WITH EXPLORATORY PS2+ SCORING, Moore et al, (2019).
Table 65, Table 66 and Table 67, pp1-6 of Corrected Attachment 2.7 to the submission.
BICR= blinded independent central review; CI= confidence interval; CSR= clinical study report; FRα= folate receptor alpha; HR= hazard ratio; ICC= investigator's choice of chemotherapy; ITT= intention to treat analysis; MIRV= mirvetuximab soravtansine; mo= months; NC= not calculated; n= number of events; N= number of patients; NR= not reported; OS= overall survival.
Note: the conference presentation (Moore 2019) (slides 13-14) which presented the FORWARD-I post hoc analysis did not match the submission OS values for the HRs or the K-M plot and appeared to have been results from a different data cutoff.

6.33 The difference in OS for MIRV versus ICC for the pre-specified FRα-high expression group was not statistically significant for the three analyses presented. For the re-scored FRα-high expression group, the median OS was 16.4 months in the MIRV arm versus 13.5 months in the ICC arm, but the results were not statistically significant

(HR=0.675, p=0.187). The ESCs noted that the median is the widest point between the curves, raising questions around the reliability of the difference, but noted that approximately 3 months improvement in median PFS is consistent with the MIRASOL trial.

6.34 The predictive value of FRα level on the primary endpoint of PFS from FORWARD-I was examined by comparing outcomes for the pre-specified FRα-high and FRα-medium subgroups (Table 13).

Table 13: Predictive value of FRα level on PFS per BICR – ITT Population (December 2019 data)

		MIRV		ICC			
Type of Analysis FRα Level	**N**	**Events (%)**	**Median (95% CI) (Months)**	**N**	**Events (%)**	**Median (95% CI) (Months)**	**HR (95% CI)**
FRα-high[a]	147	93 (63)	4.8 (4.11, 5.68)	71	45 (63)	3.3 (1.97, 5.59)	0.7 (0.48, 0.98)
FRα-medium[a]	101	81 (80)	2.9 (2.76, 4.14)	46	25 (54)	5.6 (2.73, 8.34)	1.6 (0.99, 2.45)
Interaction[b]							**0.4 (0.24, 0.76) p=0.004**

Source: Table 32: Predictive Value of FRα Level on Progression-free Survival per BIRC – ITT Population, p117, FORWARD-I CSR.
BICR= blinded independent central review; CI= confidence interval; FRα= folate receptor alpha; HR= hazard ratio; ICC= investigator's choice of chemotherapy; ITT= intent to treat; MIRV= mirvetuximab soravtansine; N= number of patients; PFS= progression-free survival.
[a] Hazard ratio is MIRV to ICC within each subgroup (high or medium). A hazard ratio < 1 indicates a reduction in hazard rate in favour of MIRV.
[b] Hazard ratio is for interaction between treatment group and FRα subgroup.

6.35 The comparison of PFS from the pre-specified analysis of FRα-high and FRα-medium groups (Table 13) indicates an interaction between treatment with MIRV and FRα expression level (nominal p-value for interaction = 0.004). The evaluation considered that since the FRα-high group as defined in the trial included a subset of patients who would be considered biomarker negative for this outcome, a more compelling approach would have been to conduct this analysis with the re-scored FRα-high versus FRα-medium + FRα-low groups to focus on the groups being proposed as test positive and test negative for this biomarker. The Pre-PBAC response provided analysis of re-scored (post-hoc) FRα high expression subgroup versus the complement of the trial population (Table 14). The Pre-PBAC response noted that "Patients not in this [FRα high] subgroup showed no significant benefit from MIRV, with PFS (0.91) and OS (0.95) hazard ratios near 1.0, and 95% confidence intervals crossing 1.0."

Table 14: PFS and OS by FRα expression: Requested analysis of FORWARD-1 and primary analysis of MIRASOL

Analysis	**Hazard ratio (95% CI)**	**Data source**
Progression free survival		
MIRV vs ICC: FRα-high (≥75% with ≥2+ staining)	0.65 (0.52, 0.81)	MIRASOL, ITT population
MIRV vs ICC: FRα-high (≥75% with ≥2+ staining)	0.63 (0.41, 0.97)	FORWARD-1 requested post-hoc analysis
MIRV vs ICC: FRα-Low/Medium (complement of FRα-high)	0.91 (0.67, 1.24)	
Overall survival		
MIRV vs ICC: FRα-high (≥75% with ≥2+ staining)	0.67 (0.50, 0.89)	MIRASOL, ITT population
MIRV vs ICC: FRα-high (≥75% with ≥2+ staining)	0.65 (0.40, 1.05)	FORWARD-1 requested post-hoc analysis
MIRV vs ICC: FRα-Low/Medium (complement of FRα-high)	0.95 (0.67, 1.35)	

Source: Pre-PBAC response, table 2

INDIRECT COMPARISON (MIRASOL vs AURELIA)

6.36 The submission conducted an anchor-based MAIC using individual-level patient data from MIRASOL and published aggregate data from AURELIA using the common

comparator ICC to support the claim of superior safety and efficacy of MIRV versus BEVA + ICC. The results of the MAIC are summarised in Table 15.

Table 15: Summary of the adjusted outcomes for the MAIC (MIRV vs BEV+ICC)

Outcome	Parameter	Before matching (MIRV vs BEV+ICC)	After matching (MIRV vs BEV+ICC)
PFS	HR [95% CI] p-value	1.38 [1.01, 1.90] P=0.0444	1.11 [0.64, 1.91] 0.7179
OS	HR [95% CI] p-value	0.78 [0.54, 1.12] 0.1787	0.59 [0.32, 1.07] 0.0819

Source: Table 2.6 2 Summary of the HR for PFS, OS, and Comparison for ORR, Grade 3+ TEAEs, and Discontinuation due to any TEAE (MIRV vs ICC+ BEV), p101 of the submission.
BEV= bevacizumab; CI= confidence interval; HR= hazard ratio; ICC= investigator's choice of chemotherapy; MAIC= matching adjusted indirect comparison; MIRV= mirvetuximab soravtansine; PFS= progression-free survival; OR= odds ratio; OS= overall survival; TEAE= treatment-emergent adverse event.
*Statistically significant

6.37 The evaluation and the ESCs considered that transitivity issues that may have limited the exchangeability of the two trials included: differences in exposure to prior treatments (Poly (ADP-ribose) polymerase [PARP] inhibitors and BEVA in MIRASOL; data absent in AURELIA), stage of disease and number of lines of prior treatment (both greater in MIRASOL), as well as the time elapsed between the two trials (the AURELIA trial commenced in October 2009 whereas MIRASOL commenced in December 2019).

6.38 For PFS, the unadjusted (before matching) HRs for MIRV versus BEVA+ICC gave a non-statistically significant point estimate and interval that favoured BEVA+ICC. For OS, the unadjusted point estimate favoured MIRV, but with wide confidence intervals. The evaluation did not consider the size of the matching adjusted median OS for the MIRASOL MIRV arm (adjusted from 16.46 months to 24.57 months) plausible. With the pronounced increase in the median OS for MIRV after adjustment, the point estimate for the non-significant HR favoured MIRV compared with BEVA + ICC.

6.39 The effective sample size after matching was 58 from MIRASOL ICC and 48 from MIRV. This represents a reduction in sample size of 79.0% and 73.9%, respectively. The evaluation and the ESCs considered that these relatively small sample sizes/large reductions may indicate that the weights were highly variable due to a lack of population overlap, and that the resulting estimate may be unstable (Phillippo et al, 2016). A plot of the distribution of weights provided in the submission indicated that the analysis relied on a small number of individuals (i.e. the individuals with larger weights), reflecting poor overlap between the underlying trial populations.

6.40 The submission concluded there were limitations in the MAIC as the adjusted sample size after matching was small due to the differences in disease characteristics between trials. This result had little statistical power to detect differences between treatments and estimates of relative treatment effect may become uncertain due to the dependence on a small number of patients. Despite these conclusions, the submission and the PSCR maintained their claim of superior safety and efficacy of MIRV versus BEVA + ICC. The pre-PBAC response also noted that AURELIA did not show a statistically significant difference in OS, whereas the MIRASOL trial achieved a statistically significant OS benefit compared to non-platinum chemotherapy. The

evaluation and the ESCs considered that the MAIC offered limited support for the claim of superior efficacy and safety for MIRV compared to BEVA + ICC. The ESCs considered that the results indicate that MIRV is likely to be no worse in effectiveness compared to BEVA + ICC. The evaluation and the ESCs considered that overall, these results should be interpreted with caution given the transitivity issues described above, and the concerns relating to the stability of the estimates given the small sample size used to inform the analysis after matching.

Comparative harms

6.41 A summary of the treatment emergent adverse events (TEAEs) for MIRV versus ICC in the MIRASOL trial is presented in Table 16.

Table 16: Overview of TEAEs – Safety Population (MIRASOL September 2024)

Number of subjects (%)	MIRV (N=218)	ICC (N=207)	RR (95% CI)	RD (95% CI)
TEAEs, all grades	211 (97)	194 (94)	1.033 (0.99, 1.078)	0.031 (-0.010, 0.075)
TEAEs, Grade 3+	97 (44)	113 (55)	0.815 (0.672, 0.989)	-0.101 (-0.195, -0.006)
Drug-related TEAEs, all grades	191 (88)	167 (81)	1.086 (0.999, 1.18)	0.070 (0.000, 0.140)
Drug-related TEAEs, grade 3+	59 (27)	77 (37)	0.728 (0.549, 0.963)	-0.101 (-0.189, -0.013)
Serious TEAEs, all grades	55 (25)	69 (33)	0.757 (0.561, 1.021)	-0.081 (-0.167, 0.006)
Serious TEAEs, grade 3+	47 (22)	60 (29)	0.744 (0.534, 1.036)	-0.074 (-0.157, 0.009)
Drug-related Serious TEAEs, all grades	21 (10)	16 (8)	1.246 (0.669, 2.321)	0.019 (-0.036, 0.074)
Drug-related Serious TEAEs, grade 3+	17 (8)	16 (8)	1.009 (0.524, 1.944)	0.001 (-0.052, 0.053)
TEAEs Leading to Study Drug Discontinuation, all grades	25 (11)	31 (15)	0.766 (0.469, 1.252)	-0.035 (-0.101, 0.030)
TEAEs Leading to Study Drug Discontinuation, Grade 3+	12 (6)	22 (11)	0.518 (0.263, 1.019)	-0.051 (-0.106, 0.001)
Drug-related TEAEs Leading to Study Drug Discontinuation, all grades	19 (9)	17 (8)	1.061 (0.567, 1.985)	0.005 (-0.050, 0.059)
Drug-related TEAEs Leading to Study Drug Discontinuation, Grade 3+	7 (3)	11 (5)	0.604 (0.239, 1.529)	-0.021 (-0.063, 0.018)
Patients with any TEAE Leading to Death	4 (2)	5 (2)	0.76 (0.207, 2.79)	-0.006 (-0.038, 0.024)
Drug–Related TEAE Leading to Death	0	1 (<1)	0 (0, 0)	-0.006 (-0.023, 0.010)

Source: Table 2.5 19. Overview of TEAEs – Safety Population; September 2024, pp83-84 of the submission; Table 33: Overview of Treatment Emergent Adverse Events – Safety Population, p142-143, MIRASOL CSR, September 2024.
CI= confidence interval; ICC= investigator choice chemotherapy; MIRV= mirvetuximab soravtansine; RD= risk difference; RR= risk ratio; TEAE= treatment emergent adverse event.
A positive RD indicates higher TEAE frequency in MIRV. A RR > 1 indicates that MIRV was associated with higher rate of TEAE.

6.42 In the MIRASOL trial, the incidence of study drug-related TEAEs was similar across the two treatment arms (88% vs 81% for MIRV and ICC, respectively), except the following events:

- Eye disorders, which occurred more frequently in those treated with MIRV (52% vs 2%). These were consistent with the known Adverse Event (AE) profile of MIRV. There were also small numbers of events of pneumonitis 7 (3%) which led to MIRV discontinuation.

- Blood and lymphatic system disorders, which occurred more frequently in ICC–treated patients (44% vs 19%). These were consistent with the known AE profiles of the ICC agents, paclitaxel and topotecan.

6.43 Fewer MIRASOL patients treated with MIRV experienced TEAEs leading to discontinuation compared to those treated with ICC (11% vs 15%). The most common TEAEs leading to treatment discontinuation were pneumonitis (3%) and blurred vision (2%). At the September 2024 cutoff, 5 (2%) patients were permanently discontinued from MIRV due to ocular TEAEs. Among patients treated with ICC, the most common events that led to treatment discontinuation were gastrointestinal disorders (4%), peripheral neuropathy (2%) and thrombocytopenia (2%).

6.44 The ESCs noted the increased corneal keratopathy adverse events in patients treated with MIRV (52%, compared with 2% for ICC), and considered that the toxicity profile may significantly affect quality of life, as vision changes can be quite distressing for patients. While the ESCs noted the higher discontinuation rate in the ICC arm compared to MIRV, the sub-committees considered that this was likely due to increased motivation for patients to continue with the experimental drug in the open label trials. The Pre-PBAC response claimed that keratopathy symptoms (e.g. blurred vision, dryness, and irritation) "typically resolve as the corneal epithelium regenerates every 1–2 weeks", and "[I]n the MIRV pooled safety analysis, Grade 3 and 4 ocular adverse events occurred in only 5% of patients, with no instances of corneal ulcer or perforation, only temporary changes in visual acuity', and that of the 52% of patients with ocular AEs reported for MIRV in the MIRASOL study, most (96%) improved to Grade 1 or better.

6.45 Gastrointestinal disorders including serious adverse events (SAEs) and Grade 3+ events were similar between the arms. There were no study drug-related deaths due to MIRV in the trial and one death reported in the ICC arm. Grade 3+ ocular events occurred in 34 (16%) MIRV patients but were absent from ICC patients. MIRV patients experienced Grade 3+ gastrointestinal disorders at a similar rate to ICC patients (30 (14%) patients versus 31 (15%), respectively). Conversely, Grade 3+ blood and lymphatic system disorders were experienced in 51 (25%) ICC patients compared to 6 (3%) in the MIRV arm, consistent with the known toxicity profile of the ICC agents.

6.46 In the MIRV arm, 4 (2%) patients experienced TEAEs leading to death compared to 5 (2%) patients in the ICC arms. For deaths where TEAEs were the primary cause of death, 3 (1.4%) occurred in each trial arm. In the MIRV arm, these events were respiratory failure, intestinal obstruction and cardiopulmonary failure, in the ICC arm these were from Clostridioides difficile colitis, septic shock (also drug-related due to topotecan) and intestinal occlusive syndrome.

6.47 Looking at individual ICC agents, TEAEs for paclitaxel were generally higher than MIRV (Grade 3+ TEAEs 63% vs 44%; discontinuations 18% vs 11%). The evaluation noted that patients who received PLD (the dominant agent used in PROC reported in CaSP registry data, see paragraph 5.3), experienced slightly fewer TEAEs compared to MIRV (TEAEs 91% vs 97%; Grade 3+ TEAEs 42% vs 44%; discontinuations due to study drug-related TEAEs 0 vs 9%, respectively). The evaluation and the ESCs considered that real world adverse events may be milder for patients receiving non-platinum chemotherapy

compared to MIRV. For some events, rates for PLD were lower than either MIRV or ICC overall (fatigue, diarrhoea, neuropathy, thrombocytopenia).

Benefits/ harms

6.48 A summary of the comparative benefits and harms for MIRV versus ICC for patients classified as biomarker positive is presented in Table 17.

Table 17: Summary of comparative benefits and harms for MIRV and ICC (MIRASOL)

Outcome	MIRV (N=227)	ICC (N=226)	Absolute Difference	HR (95% CI)
BENEFITS				
PFS by investigator – September 2024 data cutoff (median follow-up 28.35 mo; 95% CI 24.97, --)				
Median PFS, months (95% CI)	5.59 (4.34, 5.88)	3.98 (2.86, 4.47)	1.61 mo	**0.63 (0.513, 0.785) p<0.0001**
% not experienced PFS event[a]				--
at 3 mo	67%	43%	23%	
at 6 mo	39%	22%	18%	
at 9 mo	24%	10%	14%	
at 12 mo	16%	2%	14%	
OS – September 2024 data cutoff (median follow-up 30.49 mo; 95% 28.75, 33.68)				
Deaths, n/N (%)	162/227 (71.4)	177/226 (78.3)	--	**0.68 (0.543, 0.840) p=0.0004**
Median OS, months (95% CI)	16.85 (14.36, 19.78)	13.34 (11.37, 15.15)	3.51 mo	
% survival[a]:				--
at 3 mo	90%	82%	8%	
at 6 mo	78%	70%	8%	
at 9 mo	69%	59%	9%	
at 12 mo	59%	49%	11%	

HARMS

Outcome	MIRV (N=218)	ICC (N=207)	RR (95% CI)	Event rate/100 patients		RD (95% CI)
				MIRV	ICC	
TEAEs, Grade 3+	97 (44)	113 (55)	0.82 (0.67, 0.99)	44.5	54.6	-0.101 (-0.195, -0.006)
TEAEs leading to study drug discontinuation, Grade 3+	12 (6)	22 (11)	0.52 (0.26, 1.02)	5.5	10.6	-0.051 (-0.106, 0.001)
Patients with any TEAE leading to death	4 (2)	5 (2)	0.76 (0.207, 2.79)	1.8	2.4	-0.006 (-0.038, 0.024)
Ocular TEAEs[b], any grade	125 (57)	18 (9)	6.59 (4.18, 10.40)	57.3	8.7	0.487 (0.382, 0.600)
Ocular TEAEs[b], Grade 3+	34 (16)	0	--	15.6	0.0	0.157 (0.112, 0.209)
Blood and lymphatic system disorders[c], any grade	49 (22)	105 (51)	0.44 (0.33, 0.59)	22.5	50.7	-0.282 (-0.369, -0.193)
Blood and lymphatic system disorders[c], Grade 3+	6 (3)	51 (25)	0.11 (0.05, 0.25)	2.8	24.6	-0.219 (-0.284, -0.158)

Source: Table 2.5 1 Results of Primary Endpoint (ITT): PFS, p63 of the submission; Table 2.5 2 Results of Primary Endpoint (ITT): PFS (Sept 2024 data cut), p65 of the submission; Table 17, p104-5 MIRASOL CSR March 2023; Table 17, p105-6 MIRASOL CSR Sept 2024; Table 18, p108 MIRASOL CSR March 2023; Table 18, p109 MIRASOL CSR Sept 2024.; Table 2.5 5 Results of Secondary Outcomes (ITT): OS, p68 of the submission; Table 2.5 6 Results of Secondary Outcomes (ITT): OS (September 2024 data cut), p70 of the submission; Table 23, p115-16 MIRASOL CSR March 2023; Table 23, p117 MIRASOL CSR Sept 2024.; Table 2.5 19. Overview of TEAEs – Safety Population; September 2024, pp83-84 of the submission; Table 33: Overview of Treatment Emergent Adverse Events – Safety Population, p142-143, MIRASOL CSR, September 2024. ; Table 14.3.1.2.1, p574 & p744 MIRASOL CSR (September 2024).

BICR=blinded independent central review; CI= confidence interval; ICC= investigator choice chemotherapy; MIRV= mirvetuximab soravtansine; mo= months; n= number of events; N= number of patients; OS= overall survival; PFS=progression-free survival; RD= risk difference; RR= risk ratio; TEAE= treatment emergent adverse event.

a Percentage of patients not progressed (PFS) or surviving (OS) at each timepoint was not presented in the submission therefore this was inferred based on the Kaplan-Maier plot (Figure PBAC.2). No 95% CI were reported.

b Ocular disorders were most commonly vision blurred, keratopathy, dry eye, photophobia and visual acuity reduced.

c Blood and lymphatic system disorders were most commonly anaemia, neutropenia and thrombocytopenia.

A positive RD indicates higher TEAE frequency in MIRV. A RR > 1 indicates that MIRV was associated with higher rate of TEAE.

6.49 On the basis of direct evidence presented by the submission, for every 100 patients treated with MIRV compared to ICC:

- Approximately 23 additional patients would remain progression free at 3 months.

- Approximately 14 additional patients would remain progression free at 12 months.
- Approximately 8 additional patients will remain alive at 3 months.
- Approximately 11 additional patients will remain alive at 12 months.

6.50 Based on direct evidence presented by the submission, for every 100 patients treated with MIRV instead of ICC for a median duration of 30.49 months follow-up:

- Approximately 49 additional patients will have ocular, drug-related AE.
- Approximately 16 additional patients will have a grade 3 or 4 ocular drug-related AE.
- Approximately 22 fewer patients will have a grade 3 or 4 blood and lymphatic system related AE.

6.51 The MAIC presented in the submission did not allow for a quantitative comparison of the benefits and harms of MIRV and BEVA+ICC. Accordingly, a benefits/harms table has not been presented.

Clinical claim

6.52 The submission claimed MIRV was superior in terms of effectiveness compared to ICC. The evaluation considered that this claim appears to be adequately supported for OS (HR 0.68 [95% CI 0.543, 0.840] p=0.0004), noting the outcome was at risk of bias due to informative censoring which may have confounded trial results (paragraph 6.7). There was less certainty with the evidence for PFS due to issues with the investigator assessed outcome (para 6.16) and also given the censoring issues, as noted for OS (paragraph 6.20). The ESCs considered that the claim of superior effectiveness compared to ICC was reasonable for patients with high FRα expression, noting the modest benefit in the FRα-high population, and risk of bias associated with the key trial.

6.53 The submission claimed MIRV was non-inferior in terms of safety but with a different safety profile to non-platinum chemotherapy. The evaluation considered that this claim was adequately supported for safety in comparison with ICC overall. However, the evaluation considered proportions of ICC single agent use were likely to be different in Australian clinical practice compared to MIRASOL, with the majority of patients receiving PLD, a small proportion receiving paclitaxel and very few receiving topotecan. While the ESCs considered that MIRV may be non-inferior in terms of safety compared to chemotherapy, the ESCs noted the significant impacts on QoL of the ocular adverse events associated with MIRV.

6.54 The submission claimed MIRV was superior in terms of quality of life (QoL) to non-platinum chemotherapy. The ESCs agreed with the evaluation that this claim was not adequately supported – while the patient reported outcomes (PROs) generally favoured MIRV, the analyses were based on declining, low overall completion rates which may have had the effect that responder groups were enriched for better performing patients. Although MIRASOL collected EQ-5D-5L patient utility values, no

results or analyses were reported in the submission, nor in the CSRs or trial publications to support this outcome. Additionally, the ESCs considered that the high incidence of ocular adverse events associated with MIRV would have a significant impact on QoL.

6.55 The submission claimed MIRV was superior in terms of efficacy versus BEVA + non-platinum chemotherapy on the basis of OS. The ESCs agreed with the evaluation that this claim was not adequately supported, as the outcome of the MAIC for OS was not statistically significant and given the limitations of the MAIC (as per para 6.42). Overall, the evaluation and the ESCs considered that the MAIC did not offer a robust comparison of MIRV versus BEVA+ICC. The ESCs considered that the effectiveness of MIRV compared to ICC + BEVA was uncertain, but likely no worse.

6.56 The submission claimed that MIRV was superior in terms of safety, with a different safety profile to BEVA+ICC. The evaluation and the ESCs considered that similar concerns relating to the MAIC and exchangeability of the trials apply. The available data limited the comparison to two safety outcomes, only one of which was statistically significant (discontinuations due to any TEAE; HR 0.10 [95% CI 0.03, 0.36] p=0.0004). Overall, the evaluation and the ESCs considered that the MAIC did not offer a robust comparison of MIRV versus BEVA+ICC and the claim was not adequately supported. The ESCs considered that the safety of MIRV compared to ICC + BEVA was uncertain.

6.57 The PBAC considered that the claim of superior comparative effectiveness was supported by the data versus chemotherapy (noting modest benefit and high risk of bias so benefit likely overestimated) but not supported versus chemotherapy with bevacizumab.

6.58 The PBAC considered that the claim of non-inferior but different comparative safety was reasonable versus chemotherapy, but uncertain versus chemotherapy with bevacizumab.

Claim of codependence

6.59 The evaluation noted that the FORWARD-I trial results showed a difference in outcomes between the whole trial population and the FRα-high (≥75% using the PS2+ scoring method i.e., ≥75% of viable tumour cells with moderate [2+] or strong [3+] staining) subgroup, however the clearest difference was observed on comparison of the FRα-high and FRα-medium (from 50% to <75%, using the PS2+ method) subgroups. For PFS, the prespecified analyses gave HRs for FRα-high of 0.693 (95% CI 0.480, 1.000) (p=0.049) versus 1.560 (95% CI 0.976, 2.492) (p=0.061) for FRα-medium ([redacted]). There was a clear trend to improved HR for the FRα-high group, though not statistically significant. In the FRα-medium group, in comparison, patients on MIRV did worse than those receiving ICC. Values for OS were similar (Table 12).

6.60 A test for interaction based on a comparison of the PFS results was statistically significant (p-value = 0.004) ([redacted], see also paragraph 6.35). Given the lack of treatment response to MIRV in the FRα-medium subgroup (and the absence of data from patients either unselected for or lacking FRα tumour expression) the evaluation

considered this group as a test negative population. This supported the predictive validity of FRα expression as a biomarker as long as the expression level is high using the PS2+ scoring criteria.

6.61 The ESCs considered FRα expression is critical to identifying patients likely to benefit from MIRV, given the potential for patients without high FRα expression to have worse survival outcomes when treated with MIRV compared to ICC, and in the context of specific safety concerns for MIRV. Noting that the cut-off threshold for high FRα expression was selected based on trial data, the ESCs considered that the binary threshold has a high risk of bias due to the retrospective nature of the analysis, the inherent subjectivity of IHC interpretation, and lack of blinding in the trial.

6.62 The evaluation noted that the selection of the ≥75%, PS2+ FRα expression threshold was based on an assumption that FRα levels remained constant over the EOC disease course which the ESCs considered may be reasonable, based on data from a recent conference presentation, suggesting that further research was needed to determine the reliability of archival tissue versus fresh biopsies for FRα IHC testing. However, the ESCs considered that retesting of FRα expression following development of platinum resistance should remain an option.

Economic analysis

6.63 The submission presented a modelled cost-utility analysis (CUA) comparing MIRV to a mixed comparator (weighted 50:50) of ICC (based on direct evidence from MIRASOL) and BEVA + ICC (based on the indirect treatment comparison using evidence from MIRASOL and AURELIA) in a population of patients with PROC who have received at least one prior systemic treatment regimen and have high FRα expression (≥ 75% of tumour cells).

6.64 A summary of the model structure and key inputs for the economic evaluation is presented in Table 18.

Table 18: Summary of model structure, key inputs and rationale

Component	Summary
Comparison modelled	MIRV vs mixed comparator ICC (50%) and BEVA + ICC (50%) in patients with high FRα expression (≥ 75% of tumour cells). The submission did not include any test outcomes in the economic model; this was not consistent with PBAC guidelines which state that, for a co-dependent technology, the model structure should capture patients at the point of testing such that the incremental benefits and costs are included for those who are both positive and negative for the test.
Time horizon	10 years in the model base case vs 13.1 months in the MIRASOL trial and 13.0 months in the BEVA + ICC arm in the AURELIA trial (median follow-up). This was consistent with previous PBAC considerations for treatments for ovarian cancer. However, patients with PROC have a worse-prognosis than those who are platinum-sensitive – as such, a 5-year time horizon (explored in a sensitivity analysis) may be more appropriate.
Outcomes	LYG, QALYs. This was appropriate
Methods used to generate results	Partition survival analysis. Results reported on the basis of average expected costs and consequences per patient. This was consistent with economic evaluations in the literature for similar patient populations.
Health states	Pre-progression, Post-progression and Death. This was consistent with economic evaluations in the literature for similar patient populations.
Cycle length	1 week. A half-cycle correction was applied to account for any transitions or events that occurred midcycle. This was appropriate.
Test parameters	The submission stated that as there is no reference standard for FRα expression testing, outcomes of sensitivity and specificity and the flow-on outcomes of positive and negative predictive values are not applicable for inclusion in the model.
Allocation to health states	MIRV and ICC: The transitioning of patients is based on independent parametric survival models fitted to PFS and OS data reported in the MIRV and chemotherapy arms of MIRASOL. This was appropriate. BEVA + ICC: The transitioning of patients is based on hazard ratios (derived from the MAIC for MIRV vs BEVA + ICC) applied to the PFS and OS parametric survival models for MIRV (derived from the MIRASOL trial as described above). There are concerns regarding the validity of the MAIC due to issues with the exchangeability of the trials used in the comparison to support the proposed clinical claim of superiority.
Extrapolation method	MIRV and ICC: independent parametric models fitted to each treatment arm with Log-logistic selected in base case for OS (and Log-normal for PFS) for MIRV and Weibull selected in base case for OS (and Log-normal for PFS) for ICC, based on goodness of fit (AIC/BIC) and visual inspection. BEVA + ICC: OS and PFS curves are based on the application of HRs derived from the MAIC of MIRV vs BEVA + ICC For OS and PFS, convergence was not assumed to occur within the modelled time horizon. 88% of QALYs, 93% of LYG and 18% of incremental costs (vs ICC) and 85% of QALYs, 88% of LYG and 14% of incremental costs (vs BEVA + ICC) occur in the extrapolated period. The choice of parametric survival models for the base case were reasonable, except for the Log-logistic model for OS for MIRV, which ranked second best fit per AIC/BIC statistics but was deemed by the submission to be a better fit over the observed period (based on visual assessment) than the gamma survival model (best fit based on AIC/BIC statistics). Use of the Log-logistic model resulted in an estimated 4% of patients in the MIRV arm remaining alive at the end of the model time-horizon (10 years), while use of the gamma model results in no patients remaining alive after approximately 7.8 years; given the poor prognosis of patients with PROC, the use of the gamma model would be a more appropriate (conservative) choice.
Health related quality of life	Treatment-dependent utility values for the pre-progression (MIRV = 0.753, ICC = 0.736) and post-progression (MIRV = 0.681, ICC = 0.629) health states, derived from EQ-5D-5L data (UK value set) from the MIRASOL trial. Utility values for the BEVA + ICC arm assumed to be the same as ICC from MIRASOL. Pooled utility values for the pre-progression (0.747) and post-progression (0.657) health states were explored in a sensitivity analysis. Given there was declining EQ-5D-5L completion rates through the MIRASOL trial (67%/58% at week 8/9 and 27.8%/16.8% at week 24 for MIRV and ICC respectively), and likely significant QoL impacts of ocular AEs associated with MIRV, the use of a pooled utility value for the post-progression health state would be more appropriate.

Source: Table 3.1-1, pp162-163 and Table 3.5-2, p186 of the submission.

AIC= Akaike Information Criterion; BEVA= bevacizumab; BIC=Bayesian Information Criterion; EQ-5D-5L= EuroQoL 5-Dimension 5-Level; FRα= Folate receptor alpha; HR= hazard ratio; ICC= investigators choice of chemotherapy; LYG= life years gained; MAIC= matching-adjusted indirect comparison; MIRV= mirvetuximab soravtansine; OS= overall survival; PBAC= Pharmaceutical Benefit Advisory Committee; PASC=PICO Confirmation Advisory Sub-Committee; PFS= progression-free survival; PROC= platinum-resistant ovarian cancer; QALY= quality-adjusted life years.

6.65 The model structure did not incorporate any FRα expression testing variables. The submission justified the exclusion of test variables by stating that there is no reference standard for FRα expression testing, therefore outcomes of sensitivity and specificity and the flow-on outcomes of positive and negative predictive values are not applicable (see also paragraph 6.64). The submission stated that this was consistent with the ratified PICO which outlined that "PASC agreed with the nominated outcomes for the test, with the exception of 'sensitivity and specificity' (and by extension, the positive and negative predictive values and likelihood ratios) on the basis there is no reference standard to compare the specified test against" (p. 22, 1787 Ratified PICO Confirmation, December 2024 PASC meeting). However, this was not consistent with PBAC guidelines which state that, for a co-dependent technology, the model structure should capture patients at the point of testing such that the incremental benefits and costs are included for those who are both positive and negative for the test.

6.66 The use of the model input population from the MIRASOL trial (which consisted of patients with high FRα expression only) restricted the feasibility of conducting a scenario analysis excluding the biomarker test (assessing the net clinical benefit of providing MIRV to PROC patients both with and without the biomarker). However, the submission could have used sub-group data from the FORWARD-I trial (presented as supportive evidence) to address this.

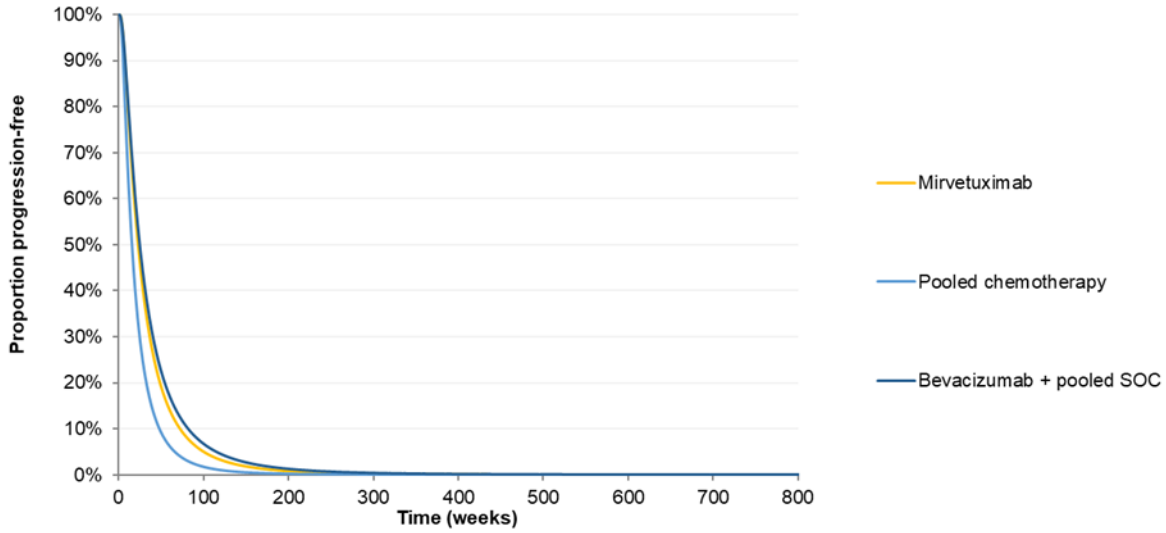
6.67 The model included costs related to two scenarios for FRα expression testing: at primary diagnosis of high grade ovarian, fallopian tube or primary peritoneal cancer (base case) and at platinum resistance (sensitivity analysis). Testing costs were based on the number of tests required to identify 1 patient with high FRα expression and a proposed testing fee of $125. Additionally, for the testing scenario at platinum resistance, the costs of archival block retrieval ($85, MBS item 72860) and re-biopsy (average cost of $50.51, based on an estimated 10% of patients receiving a re-biopsy) were applied per patient. Whether FRα testing occurs at primary diagnosis or at platinum resistance made a negligible impact on the incremental cost effectiveness ratio (ICER).

6.68 The choice of a 10-year time-horizon in the model base case was justified by the submission from survival outcomes from a cohort of 261 patients from the Netherlands diagnosed with ovarian cancer between January 2000 and December 2010 (approximately 20% of patients remain alive 10 years from the end of first-line therapy). However, Australian registry data report the 5-year survival rate of PROC patients is less than half compared to those who have remained platinum-sensitive, at 21% and 76%, respectively (Quantium, 2025). Further, clinical practice and published evidence indicate that once patients are deemed platinum-resistant, they are in the last 6 to 12 months of life (Sponsor Oncology Advisory Board, 2024; Davis et al, 2014). The evaluation considered that given the population is platinum-resistant a 10-year time-horizon is likely optimistic. The PSCR contended that it is foreseeable that 5-year survival rates for PROC patients will increase, given that MIRASOL reports

a significant survival advantage in favour of MIRV over current SOC. However, the ESCs considered that the survival advantage associated with MIRV is modest, with median survival in MIRASOL only 16 months, and a 5-year time horizon would be more reasonable for the platinum resistant population. The time-horizon was a key driver of the Incremental Cost Effectiveness Ratio (ICER), favouring MIRV. The Pre-PBAC response contended that a 5-year horizon is overly conservative, and noting the previous PBAC acceptance of a 7.5-year horizon for olaparib in a later line of therapy, proposed 'a 6-year time horizon to minimise uncertainty and fairly reflect MIRV's value and impact for this high-need population', which it included in an updated Pre-PBAC base case (see paragraph 6.83).

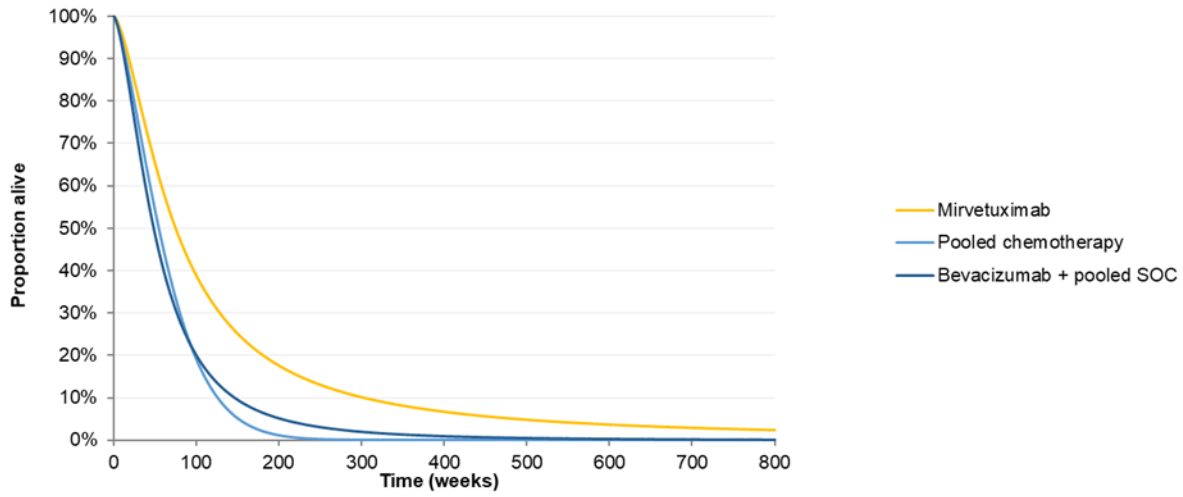
6.69 Plots of PFS and OS for MIRV, ICC and BEVA + ICC based on the extrapolated survival data used in the base case are provided in Figure 5 and Figure 6, respectively. In line with hazard ratios derived from the MAIC for MIRV vs BEVA + ICC (PFS=1.11, OS=0.59), patients in the BEVA + ICC arm demonstrate superior PFS (but inferior OS) over the extrapolated time-horizon. The ESCs noted concerns regarding the validity of the MAIC due to small sample sizes small after matching and issues with exchangeability of the trials used in the comparison (paragraphs 6.41-6.42) result in uncertainty associated with the outcomes included in the model. However, the ESCs considered it was not unreasonable to include ICC + BEVA as a comparator in the economic evaluation as this reflects clinical practice, and varying the proportion of patients receiving BEVA did not have a substantial impact on the ICER.

Figure 5: Survival Data used in Base Case: PFS



Source: Figure 3.4.6, p184 of the submission.
PFS = Progression-free survival; SOC = standard of care (investigators choice of chemotherapy)

Figure 6: Survival data used in the Base Case: OS

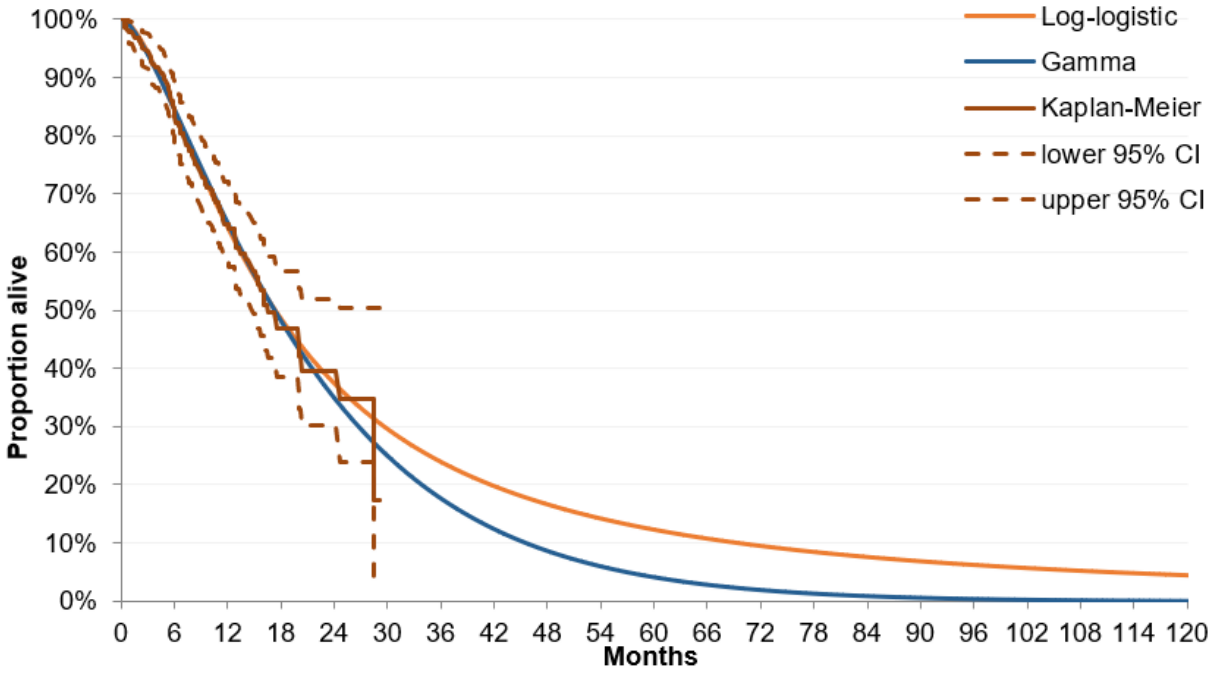


Source: Figure 3.4.7, p184 of the submission.
OS = Overall survival; SOC = standard of care (investigators choice of chemotherapy)

6.70 The evaluation considered that the chosen parametric survival models in the base case for ICC (PFS and OS) and MIRV (PFS) were reasonable. The Log-logistic model for OS for MIRV, ranked second best fit per AIC/BIC statistics but was deemed by the submission to be a better fit over the observed period (based on visual assessment) than the gamma survival model (best fit based on Akaike Information Criterion [AIC]/ Bayesian Information Criterion [BIC]). The evaluation considered the choice of the Log-logistic model for MIRV OS was not well justified and noted the gamma survival model provides a more conservative estimate consistent with the poor prognosis of patients with PROC. The use of the Log-logistic model results in an estimated 4% of patients in the MIRV arm remaining alive at the end of the model time-horizon (10 years), while use of the gamma model results in no patients remaining alive after approximately 7.8 years – see Figure 7. The choice of the log-logistic survival model for extrapolation of OS data for MIRV was a key driver of the ICER, favouring MIRV. The PSCR contended that from approximately 18 months onward, the Gamma model begins to underestimate the observed OS benefit reported for MIRV, while the Log-logistic model continues to align closely with the observed data. The ESCs considered that the Gamma function provides more clinically plausible estimates of OS for patients with PROC. The ESCs noted that the observed data at 18 months also likely to be unreliable due to the small number of patients remaining event-free (based on the March 2023 data cut used in the economic model). Further, the ESCs noted that for OS and PFS, convergence was not assumed to occur within the modelled time horizon, which demonstrates the uncertainty associated with extrapolation functions chosen and their application over a 10-year time frame. The ESCs considered that it was unclear why the more mature KM data from the September 2024 data cut (as per Figure 4) were not applied in the model, as this would provide greater confidence in the modelled OS. The ESCs considered that given the gamma extrapolation provided more clinically plausible estimates of survival, the more conservative function was more appropriate. The Pre-PBAC response maintained that 'the application of the gamma distribution for MIRV OS as suggested in the ESC advice is not supported by 5-year survival rates for patients with PROC reported in Australian

registry data: 21% (from start of first systemic treatment) and 7% (from date of platinum resistance)'.

Figure 7: Extrapolation of OS Data Reported in MIRASOL: MIRV



Source: Sheet 'Parametric Curves' from the economic workbook.
MIRV = mirvetuximab soravtansine; OS = overall survival.

6.71 For the base case, the submission used treatment-dependent utility values derived from EQ-5D-5L data (applying the UK value set) from the MIRASOL trial for both pre-progression and post-progression health states. The submission stated that this approach was reasonable given the difference in patient reported outcomes reported in MIRASOL (in favour of MIRV), as well as the differing adverse event (AE) profile reported for patients treated with MIRV and ICC, however the ESCs considered that the ocular AEs associated with MIRV likely to significantly impact QoL. The submission assumed that utility values for patients treated with BEVA + ICC were equal to utility values for patients treated with ICC in MIRASOL, stating that this is a conservative approach as it assumes there is no disutility from AEs associated with BEVA.

6.72 The approach used by the submission assumes that AEs are captured within the between group differences for the EQ-5D-5L; however, the evaluation considered it unknown whether patients who experienced Grade 3+ AEs in MIRASOL trial were adequately captured by the EQ-5D-5L throughout the trial. The PSCR and pre-PBAC response contended that there are notable differences in QoL between patients treated with MIRV and ICC in the MIRASOL trial, however the evaluation and the ESCs considered that there is a high risk of selection bias based on the response rate for PROs. Given the above, the evaluation and the ESCs considered that the use of pooled utility values for the pre-progression and post-progression health states would be a more conservative choice and more consistent with approaches taken in economic evaluations in the literature and previously seen by the PBAC for similar patient populations. Health state utility values were a key driver of the ICER, favouring MIRV. The PBAC noted that QoL outcomes in MIRASOL generally favoured MIRV, though

there was some uncertainty due to potential selection bias. The PBAC considered that there was no basis for assuming a difference in post-progression utilities, but that it may be reasonable to apply the trial-based treatment-specific utility values for the pre-progression health state in order to capture possible differences in AE profiles and QoL for MIRV and chemotherapies.

6.73 A disaggregated summary of quality adjusted life years (QALYs) included in the economic evaluation is presented in Table 19.

Table 19: Disaggregated summary of QALYs included in the economic evaluation

Outcome	MIRV	ICC	Increment	% of total increment	BEVA + ICC	Increment	% of total increment
QALYs							
Pre-progression	0.47	0.31	0.16	24%	0.51	-0.04	-7%
Post-progression	0.99	0.47	0.52	76%	0.35	0.64	107%
Total	1.46	0.79	0.68	100%	0.87	0.60	100%

Source: Table 3.8-4, p197 of the submission.
BEVA = bevacizumab; ICC = investigators choice of chemotherapy; MIRV = mirvetuximab soravtansine; QALYs= quality-adjusted life years

6.74 Incremental life years and QALYs gained were predominantly accrued in the post-progression health state for MIRV. In the pre-progression health state, life years and QALYs gained were greater in the BEVA + ICC arm than in the MIRV arm; this was consistent with the PFS HR of 1.11 for MIRV vs BEVA + ICC derived from the MAIC.

6.75 Overall, the evaluation considered that the health care resource items and unit costs applied in the economic model were appropriate.

6.76 A summary of the key drivers of the model is presented in Table 20.

Table 20: Key drivers of the model

Description	Method/Value	Impact **Base case ICER: $[redacted][1]/QALY gained**
Time Horizon	10 years in the base case	Moderate, favours MIRV Use of a 7.5-year time horizon increased the ICER to $[redacted][2]/QALY gained (+[redacted]%)
Extrapolation	Choice of parametric survival model to extrapolate OS in MIRV arm (base case = Log-logistic)	High, favours MIRV Use of the gamma distribution (best fit based on AIC/BIC statistics and considered more clinically plausible), increased the ICER to $[redacted][3]/QALY gained (+[redacted]%)
Utilities	Base case = treatment dependent utility values for pre-progression and post-progression health states	Moderate, favours MIRV Use of pooled utility values (sourced from MIRASOL) for the pre-progression and post-progression health states increased the ICER to $[redacted][2]/QALY gained.(+[redacted]%).

Source: Developed during the evaluation.
AIC= Akaike Information Criterion; BIC=Bayesian Information Criterion; ICER = incremental cost-effectiveness ratio; MIRV = mirvetuximab soravtansine; OS = overall survival; QALY = quality-adjusted life year.
The redacted values correspond to the following ranges:.
[1] *$75,000 to < $95,000*
[2] *$95,000 to < $115,000*
[3] *$135,000 to < $155,000*

6.77 The results of the stepped economic evaluation are presented in Table 21.

Table 21: Results of the stepped economic evaluation

Step and component	MIRV	ICC	Increment	BEVA + ICC	Increment
Step 1: Trial-based costs and outcomes (last reliable observation of clinical data = 21 months)					
Costs	$	$29,850	$	$40,763	$
LYG	1.23	1.06	0.17	1.00	0.23
ICER ($/LYG)	-	-	$ [1]/LYG	-	$ [2]/LYG
Weighted ICER ($/LYG)					**$ [1]/LYG**
QALYs	0.88	0.71	0.17	0.70	0.18
ICER ($/QALY)	-	-	$ [1]/QALY	-	$ [1]/QALY
Weighted ICER ($/QALY)					**$ [1]/QALY**
Step 2: Time horizon extended to 10 years					
Costs	$	$31,067	$	$44,042	$
LYG	2.34	1.23	1.11	1.35	0.99
ICER ($/LYG)	-	-	$ [3]/LYG	-	$ [4]/LYG
Weighted ICER ($/LYG)					**$ [3]/LYG**
QALYs	1.64	0.82	0.745	0.93	0.71
ICER ($/QALY)	-	-	$ [5]/QALY	-	$ [3]/QALY
Weighted ICER ($/QALY)					**$ [5]/QALY**
Step 3: Discounting (%) included					
Costs	$	$30,578	$	$42,854	$
LYG	2.08	1.18	0.91	1.26	0.82
ICER ($/LYG)	-	-	$ [3]/LYG	-	$ [3]/LYG
Weighted ICER ($/LYG)					**$ [3]/LYG**
QALYs	1.46	0.79	0.68	0.87	0.60
ICER ($/QALY)	**-**	**-**	**$ [5]/QALY**	**-**	**$ [5]/QALY**
Weighted ICER ($/QALY)					**$ [5]/QALY**

Source: Table 3.8-5, p197 and Table 3.8-6, p198 of the submission.
BEVA = bevacizumab; ICC = investigators choice of chemotherapy; ICER = incremental cost-effectiveness ratio; LYG = life years gained; MIRV = mirvetuximab soravtansine; QALY = quality-adjusted life years.
The redacted values correspond to the following ranges:
[1] *$255,000 to < $355,000*
[2] *$155,000 to < $255,000*
[3] *$55,000 to < $75,000*
[4] *$45,000 to < $55,000*
[5] *$75,000 to < $95,000*

6.78 The results of the economic evaluation were most sensitive to the step taken to extrapolate data over the 10-year time horizon. This is due to the choice of parametric survival model applied to extrapolate OS for MIRV and the time horizon used in the base case (10 years), both of which were key drivers of the ICER, favouring MIRV.

6.79 The results of key univariate and multivariate sensitivity analyses are summarised below in Table 22.

Table 22: Sensitivity analyses

Analyses	MIRV vs ICC			MIRV vs BEVA + ICC			Weighted ICER
	Incremental cost ($)	Incremental QALY	ICER	Incremental cost ($)	Incremental QALY	ICER	
Base case	[redacted]	**0.68**	[redacted]	[redacted]	**0.60**	[redacted]	[redacted]
Univariate analyses							
Pre-PBAC price reduction [a]	[redacted]	0.68	[redacted]	[redacted]	0.60	[redacted]	[redacted]
Time horizon (base case 10 years)							
• 5 years	[redacted]	0.50	[redacted]	[redacted]	0.45		[redacted]
• 7.5 years	[redacted]	0.62	[redacted]	[redacted]	0.54	[redacted]	[redacted]
FRα testing population (base case = at primary diagnosis)							
• At platinum resistance	[redacted]	0.68	[redacted]	[redacted]	0.60	[redacted]	[redacted]
Extrapolation OS for MIRV (base case = Log-logistic)							
• Gamma	[redacted]	0.41	[redacted]	[redacted]	0.41	[redacted]	[redacted]
Health state utility values for pre-progression and post-progression health states (base case = treatment dependent utility values)							
• Pooled utility values pre-progression and post-progression	[redacted]	0.61	[redacted]	[redacted]	0.53	[redacted]	[redacted]
• Pooled utility value for post-progression only	[redacted]	0.62	[redacted]	[redacted]	0.55	[redacted]	[redacted]
Weighting mixed comparator (base 50:50 ICC: ICC+BEVA)							
• 25:75	[redacted]	0.68	[redacted]	[redacted]	0.60	[redacted]	[redacted]
• 75:25	[redacted]	0.68	[redacted]	[redacted]	0.60	[redacted]	[redacted]
• 100:0	[redacted]	0.68	[redacted]	[redacted]	0.60	[redacted]	[redacted]
Multivariate analysis							
• Time horizon 5 years • Pooled utility value for pre- and post-progression health states • OS extrapolation for MIRV = Gamma	[redacted]	0.33	[redacted]	[redacted]	0.33	[redacted]	[redacted]
• Time horizon 5 years • Pooled utility value for post-progression health state only • OS extrapolation for MIRV = Gamma	[redacted]	0.34	[redacted]	[redacted]	0.35	[redacted]	[redacted]
• Time horizon 5 years • Pooled utility value for post-progression health state only • OS extrapolation for MIRV = Gamma • Pre-PBAC Price reduction[a]	[redacted]	0.34	[redacted]	[redacted]	0.35	[redacted]	[redacted]
Pre-PBAC updated base case • Time horizon 6 years • Pre-PBAC Price reduction[a]	[redacted]	0.56	[redacted]	[redacted]	0.49	[redacted]	[redacted]

Source: Table 3.9-1, p200 and Table 3.9-2, p201 of the submission.

BEVA = bevacizumab; FRα = folate receptor alpha; ICC = investigators choice of chemotherapy; ICER = incremental cost effectiveness ratio; MIRV = mirvetuximab soravtansine; OS = overall survival; PFS = progression-free survival; QALY = quality adjusted life year.
Note: see Table 3.9.2 in Attachment 3 of the Commentary for details on how sensitivity analyses were undertaken
[a] The Pre-PBAC response offered a [redacted]% price reduction from the proposed effective AEMP of $[redacted] to $[redacted] per 100 mg/20 mL vial.
The redacted values correspond to the following ranges:
[1] $75,000 to < $95,000
[2] $55,000 to < $75,000
[3] $115,000 to < $135,000
[4] $95,000 to < $115,000
[5] $135,000 to < $155,000
[6] $155,000 to < $255,000

6.80 The univariate sensitivity analyses most impacting the ICER included use of the gamma parametric distribution to extrapolate OS for MIRV (best model of fit based on AIC/BIC and results in more conservative estimates for survival, +|%), reducing the time horizon to 7.5 years (+|%) and use of a pooled utility value for the pre-progression and post-progression health states (+|%). The PSCR contended that simultaneous application of an abbreviated time horizon and more conservative parametric model to extrapolate OS for MIRV effectively 'double counts' uncertainty in the long-term survival benefit of MIRV. However, the ESCs considered that the truncated time horizon and choice of gamma extrapolation address different issues (ie survival duration, and data fit, respectively), and therefore do not result in double counting. The ESCs considered that a 5-year time horizon may be more appropriate, and should be used in a respecified base case, along with pooled utility values and gamma OS extrapolation; this increased the ICER to $155,000 to < $255,000/QALY gained (+|%).

6.81 The PBAC agreed with the ESC that the respecified base should include a 5-year time horizon, gamma OS extrapolation, and pooled post-progression utilities only, which resulted in an ICER $115,000 to < $135,000per QALY gained, using the reduced price (effective AEMP reduced by |%) proposed in the pre-PBAC response.

Drug cost/patient/course

6.82 The drug cost/patient/treatment course for MIRV (effective price) and comparators (ICC and BEVA + ICC) is presented in Table 23.

Table 23: Drug cost per patient for proposed and comparator drugs (undiscounted)

	MIRV			ICC [a]			BEVA + ICC [a,b]		
	Trial	**Model**	**Financial estimates**	**Trial**	**Model**	**Financial estimates**	**Trial**	**Model**	**Financial estimates**
Mean dose	Day 1 of a 3-week cycle, 6mg/kg AIBW			Paclitaxel: Days 1, 8, 15, and 22 of a 4-week cycle, 80 mg/m^2 PLD: Day 1 of a 4-week cycle, 40 mg/m2 Topotecan: Days 1, 8, and 15 of a 4-week cycle, 4mg/m^2 or Days 1 to 5 of a 3-week cycle, 1.25 mg/m^2			Paclitaxel: Days 1, 8, 15, and 22 of a 4-week cycle, 80 mg/m^2 PLD: Day 1 of a 4-week cycle, 40 mg/m2 Topotecan: Days 1, 8, and 15 of a 4-week cycle, 4mg/m2 Days 1 to 5 of a 3-week cycle, 1.25 mg/m^2 BEVA: 10 mg/kg IV every 2 weeks or 15 mg/kg every 3 weeks if used in combination with topotecan 1.25 mg/m^2 on Days 1-5 of a 3-week cycle		
Mean duration (weeks)	26.6	31.68	26.6	Paclitaxel: 20.6 PLD: 21.2 Topotecan: 19.3	Paclitaxel: 17.30 PLD: 16.60 Topotecan: 15.38	Paclitaxel: 20.6 PLD: 21.2 Topotecan: 19.3	Paclitaxel: 20.6 PLD: 21.2 Topotecan: 19.3 BEVA: 22.9	35.22[c]	Paclitaxel: 20.6 PLD: 21.2 Topotecan: 19.3 BEVA: 22.9
Mean number of admin	8.87	10.56	8.87	Paclitaxel: 20.6 PLD: 5.3 Topotecan: 17.7	Paclitaxel: 17.31 PLD: 4.67 Topotecan: 14.69	Paclitaxel: 20.6 PLD: 5.3 Topotecan: 17.7	Paclitaxel: 20.6 PLD: 5.3 Topotecan: 17.7 BEVA: 10.8	Paclitaxel: 35.21 PLD: 9.18 Topotecan: 32.84 BEVA: 17.61	Paclitaxel: 20.6 PLD: 5.3 Topotecan: 17.7 BEVA: 10.8
Cost/patient/ admin	$[redacted][d]	$[redacted][e]	$[redacted][d]	Paclitaxel: $157.72 [d] PLD: $593.05 [d] Topotecan: $185.36 [d]	Paclitaxel: $132.92 [e] PLD: $639.40 [e] Topotecan: $144.37 [e]	Paclitaxel: $157.72 [d] PLD: $593.05 [d] Topotecan: $185.36 [d]	Paclitaxel: $157.72 [d] PLD: $593.05 [d] Topotecan: $185.36 [d] BEVA: $500.93 [d]	Paclitaxel: $132.92 [e] PLD: $639.40 [e] Topotecan: $144.37 [e] BEVA: $467.60 [e]	Paclitaxel: $157.72 [d] PLD: $593.05 [d] Topotecan: $185.36 [d] BEVA: $500.93 [d]
Cost/patient/ course	$[redacted]	$[redacted]	$[redacted]	Weighted [f]: $3,218.63	Weighted [f]: $2,465.75	Weighted [f]: $3,218.63	Weighted [f]: $5,923.63	Weighted [f]: $13,357.88	Weighted [f]: $5,923.63
Pre-PBAC price	$[redacted]	$[redacted]	$[redacted]						

Source: Table 3.8-2, p195 of the submission and sheet 'DoT_Calc' of the economic workbook.
AIBW = adjusted ideal body weight; BEVA = bevacizumab; ICC = investigators choice of chemotherapy; kg= kilogram; mg= milligram; MIRV= mirvetuximab soravtansine; PLD = pegylated liposomal doxorubicin; RDI= relative dose intensity.
[a] Distribution of ICC based on safety population of MIRASOL trial: Paclitaxel 40.70%/PLD 35.80%/Topotecan 23.50% (Topotecan patients on Q4W dosing [vs. Q3W dosing] = 82%)
[b] Bevacizumab patients on Q3W dosing (vs. Q2W dosing) = 4.23%
[c] Reported in economic workbook as mean duration for all treatments in BEVA + ICC
[d] Weighted DPMA/DPMQ price, based on public: private split of 32%/68% based on PBS data for BEVA and ICC items from calendar year 2023.
[e] Costs adjusted for RDI, informed by MIRASOL and AURELIA trials
[f] Refers to average cost per patient based on distribution of therapies as described in [a] and [b] above

6.83 The mean cost/patient/course applied in the economic model for MIRV and BEVA + ICC was higher (and that for ICC was lower) compared to that applied in the financial estimates. This was due to the mean treatment duration (and subsequent mean number of administrations) for MIRV and BEVA + ICC being higher (and that for ICC

was lower) compared to that applied in the financial estimates. Treatment duration in the economic model for each arm was informed by extrapolated DoT estimates, whereas the financial estimates were informed by the mean treatment duration from the MIRASOL and AURELIA trials.

Estimated PBS usage & financial implications

6.84 This submission was considered by the Drug Utilisation Sub Committee (DUSC).

6.85 The submission used an epidemiological approach for the financial estimates, assuming the use of MIRV will substitute the use of ICC and BEVA + ICC in patients with PROC and high FRα expression.

6.86 Consistent with the economic evaluation, the estimates considered two contexts for FRα expression testing: at primary diagnosis (base case) and at development of platinum-resistance (scenario analysis). In both scenarios, testing was a one-off event (no re-testing is considered). However, the ESCs considered that retesting of FRα expression following development of platinum resistance should remain an option (see paragraph 6.63).

6.87 A summary of the key inputs used by the submission to estimate the use and financial impact of the proposed codependent technologies is presented in Table 24.

[redacted]**Table 24: Estimation of number of treated patients and prescriptions**

Data	Value and (Year 1[a])	Source and comment
Eligible population		
Total incident cases epithelial ovarian, fallopian tube or primary peritoneal cancer	Yr 1: [redacted][1] Yr 2: [redacted][1] Yr 3: [redacted][1] Yr 4: [redacted][1] Yr 5: [redacted][1] Yr 6: [redacted][1]	Linear growth trend of incidence reported 2020 thorough 2024 by AIHW. The evaluation considered this was reasonable.
% incident cases that are high grade epithelial	90% (Yr 1: [redacted][1])	Sourced from Reid et al (2017). This source reports that 90% of ovarian cancer patients are epithelial origin (all grades);it is unclear whether it is reasonable to assume 100% of epithelial ovarian cancer incident patients are high-grade cases. DUSC considered 90% to be an overestimate. DUSC considered that the proportion of these cases which are high grade serous should also be applied. According to Reid et al (2017) this would be 70% of the total 90% of cases making this input 63% and more in line with the MIRASOL trial which excluded other histopathology types.
% of incident cases with FRα testing requested (test uptake rate) – at primary diagnosis	[redacted]% (Yr 1: [redacted][1])	Assumption. The Commentary and DUSC considered this was reasonable given that FRα expression testing is required to determine eligibility for treatment with MIRV, which has demonstrated superior efficacy compared to current SOC.
% incident cases initiating 2nd/3rd/4th line treatment	2nd line: 64.1% 3rd line: 44.6% 4th line: 29.9% (Yr 1: [redacted][1])	Sourced from Beachler et al (2020). This was a cohort study of 12,569 patients with advanced stage ovarian cancer in the US between 2010 to 2018. DUSC considered this to be uncertain but reasonable, noting the study includes all ovarian cancers not delineated by epithelial histopathology.
% 2nd/3rd/4th line treated with non-platinum treatment (platinum-resistant)	2nd line: 37% 3rd line: 49% 4th line: 57% (Yr 1: [redacted][1])	Houben et al (2017). This was a cohort study of 261 patients from the Netherlands diagnosed with ovarian cancer and reports the proportion of patients at each line treated with non-platinum chemotherapy (used by the submission as a proxy for platinum resistance). Subsequent treatment lines were defined based on the administration of a different type of agent or different combination of agents than was initially started with, OR an interval of more than 42 days between the start date of a treatment cycle and the start date of the following cycle. The study includes patients defined by the submission as 'platinum-refractory' (platinum-free interval of less than 3 months). The median time between treatment lines was 3 months for both the 1st-2nd line and 2nd-3rd line intervals and 1 month between the 3rd-4th lines. DUSC considered this to be an overestimate, noting the study includes all ovarian carcinomas.
% of cases with FRα testing requested (test uptake rate) – at platinum resistance	[redacted]% (Yr 1: [redacted][1])	Assumption. The evaluation and DUSC considered this was reasonable given that FRa expression testing is required to determine eligibility for treatment with MIRV, which has demonstrated superior efficacy compared to current SOC.
% cases FRα-high tumour cell expression (≥75% tumour cells with ≥ staining intensity) (Prevalence of biomarker)	36% (Yr 1: [redacted][2])	Matulonis et al (2023). This was the prevalence of high FRα expression reported across the MIRV clinical development program. The evaluation and DUSC considered this was reasonable.

Total eligible patients	Yr 1: [redacted][2] Yr 2: [redacted][2] Yr 3: [redacted][2] Yr 4: [redacted][2] Yr 5: [redacted][2] Yr 6: [redacted][2]	Calculation: Total patients with platinum-resistant high grade epithelial ovarian, fallopian tube, or primary peritoneal cancer x % of cases with FRα testing requested x % cases FRα-high tumour cell expression. DUSC considered this to be an overestimate due to the inputs being overestimated.
Treatment utilisation		
Treatment uptake rate	Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%	The submission assumed [redacted]% of eligible patients would elect for treatment with MIRV, increasing to [redacted]% in Years 2+. The evaluation and DUSC considered this was reasonable given that MIRV is a novel treatment that is claimed to have an improvement in PFS and OS over SOC in patients with PROC, and a favourable adverse event profile compared to SOC chemotherapy.
Total patients treated	Yr 1: [redacted][2] Yr 2: [redacted][2] Yr 3: [redacted][2] Yr 4: [redacted][2] Yr 5: [redacted][2] Yr 6: [redacted][2]	Calculations include [redacted][2] grandfathered patients assumed to receive a full course of treatment funded through the PBS/RPBS. The evaluation considered this assumption seems unreasonable.
Scripts/patient/ treatment course	8.87	The average number of scripts dispensed to deliver a course of MIRV was based on the dosing (Q3W) and mean duration of treatment (26.6 weeks) of MIRV reported in the MIRASOL trial. Assumes 100% compliance.
Total Scripts Dispensed	Yr 1: [redacted][1] Yr 2: [redacted][1] Yr 3: [redacted][1] Yr 4: [redacted][1] Yr 5: [redacted][1] Yr 6: [redacted][1]	Calculation: Number treated x scripts/patient/treatment course.

Source: Developed during the evaluation using data from Tables 4.2-1 – 4.2-6, pp207-210 of the submission
AIHW= Australian Institute Health and Welfare; BIA = budget impact analysis; DUSC = Drug Utilisation sub-committee; FRα=folate receptor alpha; MIRV = mirvetuximab soravtansine; OS = overall survival; PBS= Pharmaceutical Benefits Scheme; PFS = progression-free survival; PROC = platinum resistant ovarian cancer; RPBS= Repatriation Pharmaceutical Benefits Scheme; Q3W = every 3 weeks; SOC = standard of care
[a] Number of treated patients estimated at each step in Year 1 of the financial estimates.
The redacted values correspond to the following ranges:
[1] 500 to < 5,000
[2] <500

6.88 The estimates considered additional costs to the PBS/Repatriation Pharmaceutical Benefits Scheme (RPBS) from the use of prophylactic treatments for ocular events (for patients treated with MIRV) and cost offsets flowing from a reduction in comparator treatments (ICC and BEVA + ICC). Consistent with the economic evaluation, the estimates assumed a 50:50 split between patients treated with ICC or BEVA + ICC. The selection of substituted treatments, scripts per treatment and population split is based on that used in the comparator arm of the MIRASOL (ICC- PLD, paclitaxel, topotecan) and AURELIA trials (BEVA). However, the chemotherapy regimens used in MIRASOL were not consistent with non-platinum chemotherapy regimens used in Australia (based on CaSP registry data) which demonstrate greater use of PLD and BEVA and little to no use of paclitaxel and topotecan. Given the greater unit costs of PLD and BEVA, cost offsets to the PBS/RPBS related to listing of MIRV may be underestimated.

6.89 The financial estimates also considered additional costs to the MBS associated with ophthalmic examinations for monitoring of ocular events for patients treated with MIRV (1 pre-treatment examination and 7 on-treatment examinations, as per

prescribing instructions for the first 8 cycles), as well as cost offsets resulting from changes in MBS items used for the administration of antineoplastic agents (flowing from the reduction in the number of administrations required to complete a course of treatment with MIRV [8.87] compared with ICC or BEVA + ICC [14.41]). This was appropriate.

6.90 The estimated use and financial implications of listing the proposed co-dependent technologies to the health budget is presented in Table 25.

Table 25: Estimated use and financial implications

	Year 1 2025	Year 2 2026	Year 3 2027	Year 4 2028	Year 5 2029	Year 6 2030
Estimated extent of use of FRα expression testing						
Number of patients tested (at primary diagnosis)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of patients tested (at platinum resistance)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Predicted number of patients with FRα-high tumour cell expression and platinum-resistance (eligible for treatment with MIRV)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated extent of use of MIRV						
Number of patients likely to be treated with proposed drug	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Number of scripts dispensed[b]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated financial implications of the FRα expression testing to the MBS						
Cost to the MBS less copayments – testing at primary diagnosis (base case)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Cost to the MBS less copayments – testing at platinum resistance (scenario)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Estimated financial implications of MIRV to the PBS/RPBS						
Cost to PBS/RPBS less copayments	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Estimated financial implications of changes to other services to the MBS						
Cost to MBS less copayments	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Estimated financial implications of changes to affected medicines to the PBS/RPBS						
Cost to PBS/RPBS less copayments	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Net financial implications						
Net cost to PBS/RPBS	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net cost to MBS (testing at primary diagnosis)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to MBS (testing at platinum resistance)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to health budget (testing at primary diagnosis)	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net cost to health budget (testing at platinum resistance)	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]

Source: Developed during the evaluation using data from Table 4.2-8, p211,Table 4.3-3, p215, Table 4.4-1, p217, Tables 4.5-3 – 4.5-5, pp223-225 of the submission and sheet '7.Net changes – MBS' from the financial workbook.
FRα=folate receptor alpha; MBS= Medicare Benefits Schedule; MIRV= mirvetuximab soravtansine; PBS=Pharmaceutical Benefits Scheme; RPBS= Repatriation Pharmaceutical Benefits Schedule.
[a] Includes <500 Grandfathered patients estimated to access MIRV through a pre-reimbursement program prior to PBS listing
[b] Assuming 8.87 scripts/patient/course of treatment as estimated by the submission
Note: Values in italics represent those corrected during the evaluation
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *<500*
[3] *$0 to < $10 million*
[4] *$20 million to < $30 million*
[5] *net cost saving*

6.91 The net cost to the PBS/RPBS of listing MIRV was estimated to be $20 million to < $30 million in Year 6, and a total of $100 million to < $200 million in the first 6 years of listing (based on the submission proposed effective price). With the reduced price proposed in the Pre-PBAC response this was reduced to a net cost to the PBS/RPBS of

$10 million to < $20 million in year 6, and a total of $100 million to < $200 million in the first 6 years of listing.

6.92 The evaluation considered that the approach used by the submission to estimate the number of patients eligible for treatment with MIRV may have double counted incident patients or underestimated prevalent patients. The evaluation also considered it unreasonable that the submission assumed that all < 500 grandfathered patients will receive a full course of treatment funded through the PBS/RPBS, but did not include cost-offsets to the PBS/RPBS (from changes to affected medicines) from the grandfathered patients.

6.93 The submission noted that platinum resistant ovarian cancer prevalent patients were not included in the financial estimates due to poor survival outcomes and few patients expected to remain alive after one year. DUSC noted data provided by Quantium (included in the submission) suggests that 54% (<500/<500) of patients were alive twelve months after diagnosis of platinum resistance. DUSC considered that this prevalent population should be included in the potential eligible population for the first year of listing. Additionally, the DUSC considered that there is an overestimation of the incident population with high grade serous ovarian cancer and an overestimation in the proportion of patients who progress to later line therapies.

6.94 The DUSC considered that the MBS cost inputs used in the submission's financial estimates to be reasonable, with the exception of anaesthesia-associated costs ('Professional attendance for Anaesthesia'; and 'Intrathecal, combined spinal-epidural or epidural infusion'), for which the DUSC noted some biopsies may be possible under local anaesthetic and may not require general anaesthesia.

6.95 When tested during the evaluation, the financial estimates were not sensitive to the timing of FRα testing, i.e. whether FRα testing was undertaken at primary diagnosis or at platinum resistance made a negligible impact on financial estimates.

6.96 DUSC presented a sensitivity analysis that indicates that the financial estimates are overestimated in the first five years of listing with the addition of the prevalent pool and reduction in the proportion of incident patients. The sensitivity analysis showed a decrease in overall costs over 6 years from $100 million to < $200 million to $100 million to < $200 million. DUSC advised that minor changes to the methods used to derive the utilisation and financial estimates and structure of the estimates model should be considered with the addition of a prevalent population and reduction in the proportion of incident patients to only include high grade serous cases.

Table 26: Sensitivity Analysis - Estimated use and financial implications including DUSC advice on incident and prevalent cases

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total Incident cases	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
% cases high-grade epithelial and serous[a]	63%	63%	63%	63%	63%	63%
Predicted number of patients with FRα-high tumour cell expression and platinum-resistance (eligible for treatment with MIRV)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Prevalent population from 2024[b]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated extent of use of MIRV						
Number of patients likely to be treated with proposed drug	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Number of scripts dispensed	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated financial implications of MIRV to the PBS/RPBS						
Cost to PBS/RPBS less copayments	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Estimated financial implications of changes to affected medicines to the PBS/RPBS						
Cost to PBS/RPBS less copayments	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Net financial implications						
Net cost to PBS/RPBS	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]

Source: Table 3, DUSC Advice (derived from Section 4 workbook).

[a] Proportion of high-grade epithelial ovarian cancers that are serous according to Reid et al 2017 which states 70% of the total 90% of high-grade epithelial cancers are serous.

[b] Prevalent population derived based on extrapolation of survival data from Quantium (Submission Attachment 1.1 p35) where 2-year survival was 33.7% and 5-year survival was 7.3%. Prevalent population includes < 500 grandfathered patients with a 6-month duration of treatment and [redacted]% of patients electing treatment. The remaining prevalent population have an [redacted]% electing treatment rate applied, which may be an overestimate, noting that some will be at advanced stages of disease.

The redacted values correspond to the following ranges:

[1] *500 to < 5,000*

[2] *<500*

[3] *$30 million to < $40 million*

[4] *$10 million to < $20 million*

[5] *$0 to < $10 million*

6.97 The pre-PBAC response considered the methods applied by DUSC in conducting the sensitivity analysis to be a reasonable alternative estimate of the number of patients treated with MIRV each year (including reducing the annual number of incident patients and increasing the number of prevalent patients), and provided updated estimates incorporating DUSC advice, noting some minor amendments to the estimated prevalent population to account for FRα prevalence and the expected shorter duration of treatment with MIRV for the prevalent and grandfathered populations. The Pre-PBAC response indicated that proposed new vial price for MIRV of $[redacted] results in a further decrease in overall costs over 6 years from $100 million to < $200 million in the DUSC sensitivity analysis to $80 million to < $90 million.

Quality use of medicines

6.98 The submission stated that the introduction of MIRV will require some management of a patient's ocular health due to the occurrence of adverse events, with the draft TGA Product Information including guidance on performing an ocular examination prior to treatment initiation and the ongoing use of prophylactic eye drops. The submission stated that the sponsor intends to work closely with the clinical and

patient community as appropriate to ensure adequate education and support is provided so that this aspect of MIRV treatment is optimally managed. The sponsor outlined a risk minimisation strategy for managing ocular side effects associated with MIRV supported by insights from advisory boards and international experience. Efforts are also underway to strengthen referral pathways between oncologists and eye specialists to support optimal patient care.

Financial management – risk sharing arrangements

6.99 The submission did not propose a Risk Sharing Arrangement (RSA), however stated they would be open to working with the PBAC and the Department of Health and Aged Care on an appropriate arrangement if required as part of the Deed behind MIRV listing on the PBS.

6.100 DUSC considered it unlikely that there would be use beyond the requested restriction or beyond expectations.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC deferred its consideration of mirvetuximab soravtansine (MIRV) for the treatment of patients with platinum-resistant high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, (EOC) who have received at least one prior systemic treatment regimen and have high folate receptor alpha (FRα) tumour cell expression. The PBAC was of a mind to recommend MIRV, but noted that as an integrated codependent submission, MBS listing of FRα expression testing by immunohistochemistry would be considered at the August 2025 MSAC meeting, and that the TGA delegate's overview is expected by September 2025. The PBAC considered that there is a clinical need for additional treatments for this population, acknowledging the severe impact of disease. The PBAC considered that MIRV provides a moderate clinical benefit in the small group of patients with high FRα tumour cell expression, noting the potential for inferior outcomes for those patients without high FRα tumour cell expression. The PBAC considered that MIRV would be cost-effective with a substantial reduction in the price, to reflect the moderate benefit, and uncertainties in the economic model.

7.2 The PBAC considered that there is a moderate clinical need for new therapies for platinum resistant EOC, noting the severity of symptoms and impact on patient quality of life. The PBAC also noted that currently available chemotherapy options are associated with significant side effects and are only modestly effective, with approximately 21% of patients alive at 5 years.

7.3 The PBAC considered that a Telephone/online authority listing for MIRV is appropriate, and that the restriction should include the following:

- The submission proposed that patients should have received one or more prior lines of therapy, rather than one to three prior lines of therapy (as per the MIRASOL trial and proposed TGA indication), which would allow access for the

small number of patients who may have received additional lines of treatment. The PBAC considered this to be appropriate (paragraph 3.2).

- The requested restriction omitted reference to serous tumour histology in the proposed target population to prevent inappropriate exclusion of patients with tumour histology difficult to identify. The PBAC agreed with the ESCs that the very small group of patients with non-serous ovarian cancer and high FRα expression is likely to benefit from treatment with MIRV and it is reasonable for the restrictions to be silent regarding tumour histology (paragraph 3.3).
- The PBAC considered it was reasonable for the restriction to be silent on whether MIRV should be used as monotherapy or combination therapy, to allow for potential future use in combination use with bevacizumab (paragraph 3.5).
- The proposed target population (as defined in the submission) of platinum resistant patients excluded those with a platinum-free interval of less than three months following one line of platinum therapy (these patients were defined in the submission as 'platinum refractory'). The PBAC agreed with the ESCs that patients classified in the submission as 'platinum refractory' may also benefit from MIRV, and that platinum resistance should be defined in prescribing instructions as progression during or within 6 months of the last dose (not 3-6 months) (paragraph 3.4).

7.4 The PBAC accepted the submission's clinical place for MIRV, noting it is recommended in relevant international clinical guidelines. The PBAC accepted the claim of codependence for the test (IHC testing of solid tumour tissue to determine FRα expression status) and treatment (MIRV). The PBAC noted that the FORWARD-I trial results showed a clear difference in outcomes between the FRα-high population and the FRα-medium population and the test for interaction was statistically significant. The PBAC agreed with the ESCs that FRα expression is critical to identifying patients likely to benefit from MIRV, given the potential for patients without high FRα expression to have worse survival outcomes when treated with MIRV compared to chemotherapy, and in the context of specific safety concerns for MIRV (see paragraph 7.9).

7.5 The PBAC considered the place in therapy for MIRV may change in the future as more evidence becomes available for a broader population including those with platinum-sensitive ovarian cancer or for use in combination therapy including bevacizumab. The PBAC noted that MIRV treatment is administered intravenously and requires screening and monitoring for corneal keratopathy, which the Committee considered may reduce access for rural and regional patients.

7.6 The PBAC accepted the submission's proposed comparator of non-platinum chemotherapy (+/- bevacizumab) including comparators of paclitaxel, topotecan, liposomal doxorubicin, which the Committee considered reflects current standard of care for platinum-resistant ovarian cancer in Australia.

7.7 The PBAC considered that the submission's key trial, MIRASOL RCT (n=453, vs investigator's choice of chemotherapy (ICC, including paclitaxel, topotecan, or liposomal doxorubicin)) had a high risk of bias due to its open-label design due to

dropouts at treatment allocation and prior to disease progression, however the impact of these biases was unclear. The PBAC also noted that there was poor concordance between the primary endpoint of PFS based on investigator assessment and secondary outcome of PFS based on BICR due to differences in censoring and the assessment of these outcomes, however the secondary outcome of OS was supportive of a treatment effect. The PBAC considered that the MIRASOL trial population and standard care arm were representative of the Australian population and clinical practice, except that bevacizumab is also commonly used with chemotherapy in Australia.

7.8 The PBAC noted for patients with FRα-high expression MIRV was associated with a small benefit in median investigator assessed PFS (1.6 months) in MIRASOL, which it considered was likely to be overestimated due to the trial's high risk of bias (see paragraph). The PBAC also noted that MIRV treatment resulted in a modest increase in median OS of 3.5 months in MIRASOL. The PBAC considered that the claim of superior comparative effectiveness compared with chemotherapy was supported by the data. The PBAC noted that while the patient reported outcomes (PROs) generally favoured MIRV, the analyses were not statistically significant and were likely to be affected by low completion rates.

7.9 The PBAC considered that the indirect comparison of MIRV versus chemotherapy + bevacizumab using the MIRASOL and AURELIA trials was also at high risk of bias due to limitations of the MAIC, particularly due to the small sample size after matching, resulting from the limited exchangeability of the trials. The PBAC considered that the claim of superior comparative effectiveness versus chemotherapy with bevacizumab was not supported by the evidence, as the outcome of the MAIC for OS was not statistically significant (HR for OS of 0.78 and 0.59 with wide 95% CI), though noting the limitations of the MAIC.

7.10 The PBAC noted that in the MIRASOL trial, the incidence of study drug-related TEAEs was similar across the two treatment arms. Although blood and lymphatic system disorders occurred more frequently in patients treated with chemotherapy, there was a higher risk of distressing eye disorders associated with MIRV (52% vs 2% of MIRASOL patients). The PBAC noted the claim in the Pre-PBAC response that corneal keratopathy typically resolve and result in only temporary changes in visual acuity but did not accept the claim that these AEs would not have a meaningful impact on quality of life. The PBAC considered that the claim of non-inferior but different comparative safety was reasonable versus chemotherapy, supported by the similar number of adverse events in MIRASOL. The PBAC considered the claim of non-inferior safety versus chemotherapy + bevacizumab was uncertain due to the limited exchangeability of the MIRASOL and AURELIA trials.

7.11 The submission presented a modelled cost-utility analysis comparing MIRV to a mixed comparator (weighted 50:50) of ICC (based on direct evidence from MIRASOL) and BEVA + ICC (based on the MAIC using evidence from MIRASOL and AURELIA). The PBAC noted that the proportion of patients receiving bevacizumab in combination with chemotherapy was uncertain, but considered the submission's estimate was

reasonable. The PBAC agreed with the ESC that the model structure and model inputs were reliable for decision-making, with inputs updated in a re-specified base case:

- A 5-year time horizon, given the poor prognosis of the platinum resistant high grade EOC population.
- Gamma function for extrapolation of OS in the MIRV arm as it was a better fit based on AIC/BIC, provides more clinically plausible estimates of OS for patients with platinum resistant high grade EOC and is more consistent with the later data cut from MIRASOL (see paragraph 6.83).
- Pooled post-progression utilities as there was no basis for assuming a difference in post-progression utilities, but trial-based treatment-specific utility values for the pre-progression health state were reasonable in order to capture possible differences in AE profiles and QoL for MIRV and chemotherapies (see paragraph).

The PBAC noted that this resulted in an ICER of $115,000 to < $135,000per QALY gained, using the reduced price proposed in the pre-PBAC response. The PBAC considered MIRV would be acceptably cost-effective at an ICER below $35,000 to < $45,000/QALY using the respecified base case and noted that a substantial price reduction would be required to achieve this ICER.

7.12 The PBAC noted that DUSC provided advice regarding amendments to the financial estimates (inclusion of a prevalent population, reduction of the eligible population with high grade serous EOC as per the proposed TGA indication, and reduction in the length of treatment for prevalent and grandfathered patients, see Table 26). These changes were accepted as reasonable in the Pre-PBAC response. The PBAC considered these changes to the financial estimates were reasonable and also noted that the total cost of listing MIRV would be further reduced when incorporating the MIRV price considered acceptably cost effective (as per paragraph 7.11).

7.13 The PBAC considered that a risk sharing agreement would not be required as it agreed with the DUSC it is unlikely that there would be use beyond the requested restriction.

Outcome:
Deferred

8 Recommended listing

Add new item:

MEDICINAL PRODUCT Form	PBS item code	Max. Amount	№.of Rpts
MIRVETUXIMAB SORAVTANSINE	NEW (Public) NEW (Private)	500mg	7
Available brands			
Elahere (Mirvetuximab soravtansine 100 mg/20 mL injection, 20 mL vial)			
Restriction Summary [new] / Treatment of Concept: [new]			
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
	Prescriber type: ☒Medical Practitioners		
	Restriction type: ☒Authority Required – immediate assessment (telephone/online PBS Authorities system)		
Prescribing rule level	**Administrative Advice:** High FRα tumour cell expression is defined as having 75% or more tumour cells with FRα staining at moderate or high staining intensity (2+ staining) as determined by a validated test.		
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.		
	Administrative Advice: No increase in the maximum number of repeats may be authorised.		
	Administrative Advice: Special Pricing Arrangements apply.		
	Episodicity: [blank]		
	Severity: High grade		
	Condition: Ovarian, Fallopian Tube, or primary peritoneal cancer		
	Indication: High grade ovarian, fallopian tube or primary peritoneal cancer		
	Clinical criteria:		
	The condition must have relapsed after at least one prior therapy,		
	AND		
	The condition must be considered platinum-resistant.		
	AND		
	Clinical criteria:		
	Patient must have high FRα tumour cell expression as determined by a validated test.		
	AND		
	Clinical criteria: Patient must not have developed disease progression while being treated with this drug for this condition		
	Prescribing Instructions: Following 1 or more lines of platinum therapy, platinum resistance is defined as disease progression while receiving the therapy or within 6 months of the last dose.		
	Prescribing Instructions: Evidence of FRα tumour expression must be derived through immunohistochemistry (IHC) testing and stored in the patients' medical records		
	Prescribing Instructions: Confirm that the following information is documented/retained in the patient's medical records once only with the first PBS prescription (evidence obtained in relation to past PBS treatment is acceptable): 1) Evidence of high FRα tumour cell expression		

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about

other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

AbbVie thanks the PBAC for its clear acknowledgement of the unmet need for patients in Australia living with platinum-resistant ovarian cancer. As highlighted in the PBAC's feedback, there is strong support for this submission from the community, given the significant lack of progress in outcomes and new treatment options over the past decades. As a priority, AbbVie is considering the implications of this minded recommendation, alongside feedback provided by the PBAC. Our intention is to work with the PBAC towards a mutually acceptable path to listing mirvetuximab soravtansine, enabling equitable access for Australian patients. AbbVie will continue to collaborate with the PBAC and Department regarding next steps, recognising the considerable advocacy and support from the wider community for women living with ovarian cancer to access additional treatment options.

Addendum to the July 2025 PBAC Public Summary Document:

11 Background

11.1 At its July 2025 meeting the PBAC deferred its consideration of MIRV for the treatment of patients with platinum-resistant high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, (EOC) who have received at least one prior systemic treatment regimen and have high FRα tumour cell expression. The PBAC was of a mind to recommend MIRV, but noted that as an integrated codependent submission, MBS listing of FRα expression testing would be considered at the August 2025 MSAC meeting, and that the TGA delegate's overview is expected by September 2025.

MSAC consideration – July 2025

11.2 At its July 2025 meeting MSAC deferred its advice on the public funding of immunohistochemistry (IHC) testing of solid tumour tissue to determine folate receptor alpha (FRα) expression status in adults with platinum-resistant ovarian cancer, to determine eligibility for PBS-subsidised mirvetuximab soravtansine. MSAC noted that the PBAC at its July 2025 meeting deferred its consideration of MIRV noting the TGA delegate's overview is expected by September 2025. Additionally, MSAC noted that the PBAC was of a mind to recommend MIRV pending updates.

11.3 MSAC acknowledged there was a high clinical need for treatments for this condition. MSAC considered FRα testing would identify patients expected to benefit from MIRV and testing would have no additional safety concerns. MSAC was inclined to support the test if the PBAC recommended MIRV and the TGA approves MIRV and the companion diagnostic test for FRα testing. MSAC considered the financial impact of testing to the MBS would be relatively low.

Table 27 MBS item descriptor (MSAC inclined to support)

Category 6 – Pathology Services
MBS item XXXX A test of tumour tissue using immunohistochemistry for the detection of membrane folate receptor alpha (FRα) tumour expression status, requested by a specialist or consultant physician, if the test is: in a patient with high-grade serous epithelial ovarian, fallopian tube or primary peritoneal, high-grade endometrioid, or undifferentiated epithelial ovarian cancer; and to determine eligibility for a relevant treatment under the Pharmaceutical Benefits Scheme. (See PN.1.2 of explanatory notes to this Category)
Fee: $112.00 Benefit: 75% = $84.00; 85% = $95.20

TGA Delegate's Overview

11.4 The TGA Delegate's Overview was received on 9 October 2025. The Delegate was supportive of the application to register the product on the ARTG, for the following indication:

"ELAHERE as monotherapy is indicated 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"

Outstanding issues

11.5 In July 2025 the PBAC agreed with the ESCs that the very small group of patients with non-serous ovarian cancer and high FRα expression is likely to benefit from treatment with MIRV and it is reasonable for the restrictions to be silent regarding tumour histology (paragraph 7.33.4). However the proposed MBS item descriptor includes "serous".

12 PBAC Outcome

12.1 The PBAC recommended listing of mirvetuximab soravtansine (MIRV) for the treatment of patients with platinum-resistant high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received at least one prior systemic treatment regimen, who have high FRα tumour cell expression. The PBAC recalled that at its July 2025 meeting it was of a mind to recommend MIRV, but noted that as an integrated codependent submission, MBS listing of folate receptor alpha (FRα) expression testing by immunohistochemistry would be considered at the August 2025 MSAC meeting, and that the TGA Delegate's Overview was expected by September 2025. The PBAC noted that MSAC had now indicated it was of a mind to recommend FRα expression testing and that a positive TGA Delegate's Overview was available for MIRV.

12.2 The PBAC recalled that it had previously considered that MIRV provides a moderate clinical benefit in the small group of patients with high FRα tumour cell expression, noting the potential for inferior outcomes for those patients without high FRα tumour cell expression.

12.3 The PBAC noted that it had previously considered that it would be reasonable for the restrictions to be silent regarding tumour histology (paragraph 7.3). However, the PBAC noted that the MBS item descriptor proposed to MSAC and TGA indication included "serous" histology. The PBAC considered it would be reasonable for the restriction to include "serous" histology consistent with the proposed MBS item descriptor for testing and with the TGA indication, noting that it would be expected to impact few, if any, patients.

12.4 The PBAC maintained that MIRV would be cost-effective with a substantial reduction in the price, to reflect the moderate benefit, and uncertainties in the economic model. The PBAC noted that the parameters for MIRV to be considered cost-effective remained as outlined in paragraph 7.11 above and appropriate amendments to the financial estimates remained as per 7.12 above.

12.5 The PBAC recommended that MIRV should not be treated as interchangeable on an individual patient basis with any other drugs.

12.6 The PBAC advised that MIRV is not suitable for prescribing by nurse practitioners.

12.7 The PBAC advised that MIRV is suitable for prescribing by medical practitioners only.

12.8 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically the PBAC found that in the circumstances of its recommendation for MIRV:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over alternative therapies, as it provides only a moderate clinical benefit in the small group of patients with high FRα tumour cell expression;

b) The treatment is not expected to address a high and urgent unmet clinical need as other treatments for ovarian cancer are available;

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

12.9 The PBAC noted that this submission is not eligible for an Independent Review as it is a positive recommendation.

Outcome:
Recommended

13 Recommended listing

Add new item:

MEDICINAL PRODUCT **Form**		**PBS item code**	**Max. Amount**	**№.of Rpts**
MIRVETUXIMAB SORAVTANSINE Injection		NEW (Public) NEW (Private)	500mg	7
Available brands				
Elahere (Mirvetuximab soravtansine 100 mg/20 mL injection, 20 mL vial)				
Restriction Summary [new] / Treatment of Concept: [new]				
Concept ID (for internal Dept. use)		**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
		Prescriber type: ☒Medical Practitioners		
		Restriction type: ☒Authority Required – immediate assessment (telephone/online PBS Authorities system)		
Prescribing rule level		**Administrative Advice:** High FRα tumour cell expression is defined as having 75% or more tumour cells with FRα staining at moderate or high staining intensity (2+ staining) as determined by a validated test.		
		Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.		
		Administrative Advice: No increase in the maximum number of repeats may be authorised.		
		Administrative Advice: Special Pricing Arrangements apply.		
		Episodicity: [blank]		
		Severity: High grade		
		Condition: Serous epithelial ovarian, Fallopian Tube, or primary peritoneal cancer		
		Indication: High grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer		
		Clinical criteria:		
		The condition must have relapsed after at least one prior therapy,		
		AND		
		Clinical criteria:		
		The condition must be considered platinum-resistant.		
		AND		
		Clinical criteria:		
		Patient must have high FRα tumour cell expression as determined by a validated test.		
		AND		
		Clinical criteria: Patient must not have developed disease progression while being treated with this drug for this condition		
		Prescribing Instructions: Following 1 or more lines of platinum therapy, platinum resistance is defined as disease progression while receiving the therapy or within 6 months of the last dose.		
		Prescribing Instructions: Evidence of FRα tumour expression must be derived through immunohistochemistry (IHC) testing and stored in the patients' medical records		
		Prescribing Instructions: Confirm that the following information is documented/retained in the patient's medical records once only with the first PBS prescription (evidence obtained in relation to past PBS treatment is acceptable): 1) Evidence of high FRα tumour cell expression		

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

14 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

15 Sponsor's Comment

The sponsor had no comment.