Mirvetuximab soravtansine for treating folate receptor-alpha-positive platinum-resistant advanced epithelial ovarian, fallopian tube or primary peritoneal cancer

Part 1: For screen – redacted

Technology appraisal committee A [10 March 2026]

Chair: Radha Todd

Presenter: Matt Walton (cost lead)

External assessment group: Peninsula Technology Assessment Group (PenTAG)

Technical team: Anna Willis, Albany Chandler, Lizzie Walker

Company: AbbVie

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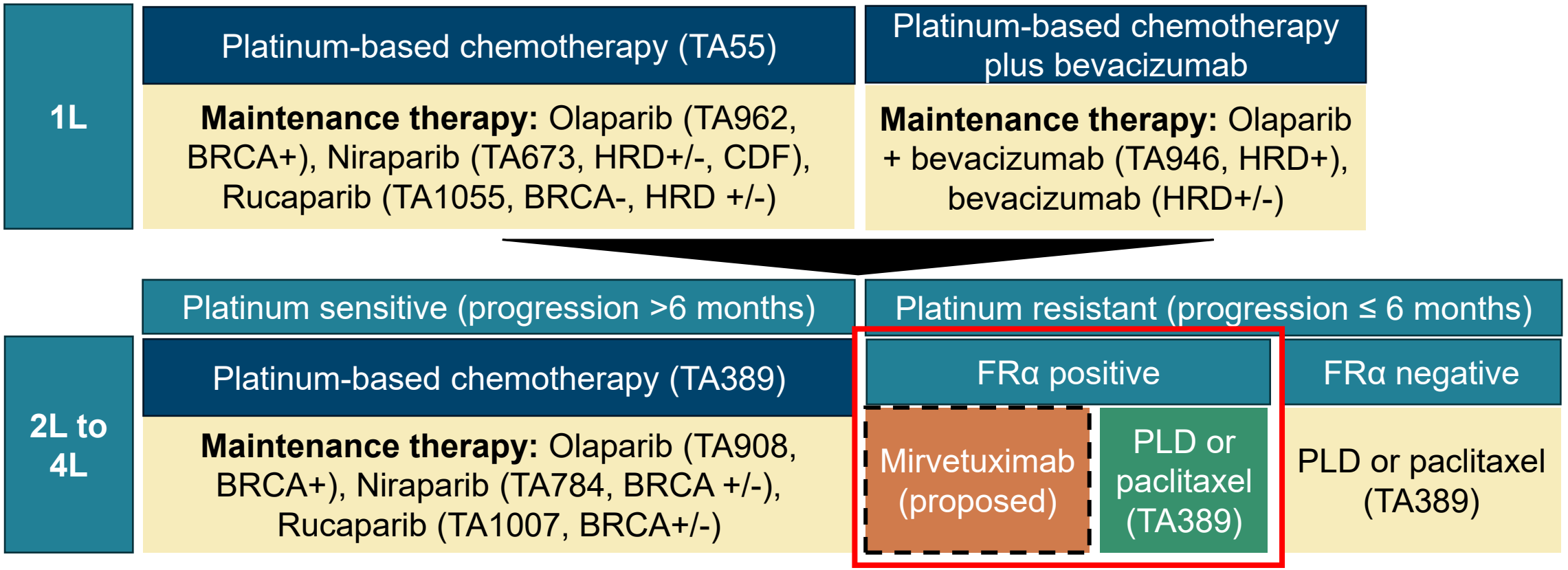
Mirvetuximab soravtansine (Elahere, AbbVie)

Marketing authorisation	• 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 1 to 3 prior systemic treatment regimens. • MHRA marketing authorisation granted in July 2025
Mechanism of action	• FRα-targeted antibody-drug conjugate comprising a monoclonal antibody that binds to the FRα protein and an anticancer medicine called DM4 • After mirvetuximab soravtansine attaches to the FRα protein, it enters the cancer cell and releases DM4
Administration	• Intravenous infusion administered every 21 days until disease progression or unacceptable toxicity
Price	• List price per 100mg vial: £4,950 • Average cost of a course of treatment (at list price): [redacted] • A patient access scheme has been agreed – **updated after first committee meeting**

Summary of Product Characteristics

Abbreviations: FRα, folate receptor alpha; MHRA, Medicines and Healthcare products Regulatory Agency

Treatment pathway and positioning of mirvetuximab



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Abbreviations: 1L, first line; 2L, second line; 4L, fourth line; BRCA, Breast Cancer gene; CDF, Cancer Drugs Fund; HRD, homologous recombination deficient; PLD, pegylated liposomal doxorubicin; TA, technology appraisal

Draft guidance recommendation

Mirvetuximab soravtansine (mirvetuximab) should not be used

- Trial evidence shows that mirvetuximab is more effective than chemotherapy
- But there are uncertainties in the economic model, including
    - how health-related quality of life differs for people having mirvetuximab and people having chemotherapy
    - how long people live after having mirvetuximab and after having chemotherapy
    - the average age of people starting treatment
- The most likely cost-effectiveness estimates are above the range that NICE considers an acceptable use of NHS resources. So, mirvetuximab should not be used.

Committee's preferred assumptions at ACM1 (1/2)

Draft guidance section	Issue	Committee's preferred assumption	Company base case aligned?
3.7	Subgroups	Mirvetuximab may be more clinically effective in people with a primary platinum-free interval of more than 6 months	No
3.9	Overall survival (OS) extrapolations	Gamma distribution for modelling mirvetuximab and chemotherapy OS	No
3.10	Health-state utility values	Treatment-dependent health-state utility values from MIRASOL for mirvetuximab and chemotherapy	No
3.11	Adverse event management	Anaemia and neutropenia are managed as day cases	No
3.12	Relative dose intensity (RDI)	Using the cycle-specific approach for modelling RDI	No
3.13	Vial sharing	No vial sharing for mirvetuximab, 50% vial sharing for chemotherapy	No

Abbreviations: ACM1, first appraisal committee meeting.

Committee's preferred assumptions at ACM1 (2/2)

Draft guidance section	Issue	Committee's preferred assumption	Company base case aligned?
3.15	Mirvetuximab duration of treatment	Observed Kaplan–Meier (KM) data up to 120 weeks, followed by exponential extrapolation	No
3.17	Severity modifier	Severity weight of 1.2 (based on QALY shortfall calculated from ACM1 assumptions)	No*
3.19	ICER threshold	Not stated – more information needed on the 3 key uncertainties (utilities, survival and age) to understand the extent of the uncertainty	N/A

*Company base case results in 1.2 modifier but company state that 1.7 modifier is appropriate

Company also aligned with many of the committee's preferred assumptions at ACM1 – see Appendix for full details of company base case updates

Abbreviations: ACM1, first appraisal committee meeting; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years.

Consultation overview

Comments received from:

- 1 clinical expert from the British Gynaecological Cancer Society (BGCS)
- 3 patient organisations: Ovacome, Ovarian Cancer Action and Target Ovarian Cancer – responses included extensive data collection from surveys on the impact of the condition, its treatment and availability of new treatment options
- 17 sets of comments received through the NICE website (web comments)
- AbbVie (company)
    - Updated base case to align with some of the committee preferred assumptions, and provided additional explanations or evidence for those not updated
    - Submitted an updated patient access scheme (PAS) discount

Report based on Systemic Anti-Cancer Therapy dataset (SACT report):

- To support committee discussions around average age and survival on chemotherapy

All responses have been provided to the committee in full as part of the committee papers

Patient organisation comments (1/2)

Quality of life for people having chemotherapy

- Side effects of chemotherapy are debilitating and impact heavily on all aspects of life
- They include extreme fatigue, peripheral neuropathy, weakness, breathlessness, nausea, pain, extreme anxiety and hair loss – some side effects can last long after chemotherapy treatment has finished
- People having chemotherapy describe having their life on hold, living in isolation, no longer seeing friends or doing hobbies, being unable to do housework, giving up jobs, and relying heavily on others for support

Unmet need for new treatment options for platinum-resistant ovarian cancer

- Very limited treatment options for platinum-resistant ovarian cancer, this has a huge impact on people's mental health
- There is an urgent need for innovation and alternatives to chemotherapy – hope and time are invaluable
- Ovarian cancer lags behind breast cancer in terms of the number of treatment options available – limited advances in treatment have occurred in recent years
- Mirvetuximab is now available over a lot of Europe and the US, we are significantly behind them

Patient organisation comments (2/2)

Impact of mirvetuximab

- For the few people who have had mirvetuximab, most reported a significantly improved quality of life, with fewer side effects
- People having mirvetuximab were more able to return to normal activities, contribute to their community and continue to work – this allows their support system to do the same
- Mirvetuximab would give people hope and allow more time with loved ones, family and grandchildren
- The wider value of mirvetuximab to family, friends, society and the community should be considered

"I have found my recovery time between treatments is so much quicker [with mirvetuximab], giving me 2 weeks out of 3 of feeling like myself and wanting to get out and do things vs the traditional chemo it was the reverse, 2 weeks of feeling not like yourself and maybe 1 week of 'normal'."

Web comments (1/2)

Theme	Comments
High unmet need	• People with platinum-resistant ovarian cancer benefit very little from current chemotherapy and have a poor prognosis (less than 12 months) • Response rates to chemotherapy are poor and there is a high symptom burden • Toxicity burden of standard chemotherapy options is also high, with many people experiencing neuropathy, fatigue, alopecia and neutropenia
Benefit of mirvetuximab	• Mirvetuximab is a biomarker-based, targeted treatment – a step-change in the management of this condition • First treatment to demonstrate a clinically significant survival advantage over standard-of-care in this condition • The 4-month improvement in median overall survival and the 3x higher response rates (42% mirvetuximab vs 16% chemotherapy) are extremely meaningful
Quality of life	• Higher response rates for mirvetuximab will translate to meaningful improvements in symptom burden and quality of life • Mirvetuximab also has a better safety profile than chemotherapy, with reduced rates of severe systemic toxicities • The ocular side effects of mirvetuximab are manageable

Web comments (2/2)

Theme	Comments
Overall survival	• Longer-term survival beyond 5 years is very difficult to predict • Limited discussion in draft guidance on survival after progression and PFS2 benefit – this should be considered by committee
Vial sharing	• As dosing is weight based, there are opportunities to vial share • Very rare to have only one patient on every [administration] occasion • 10-15% vial sharing is more than achievable
Management of adverse events	• [Neutropenia] can be managed as a day case for people who have easy transport and live close to hospital, but this is less likely for those who live further away
Severity modifier	• Platinum-resistant ovarian cancer should merit a rating of 1.7 given that people having NHS routine care will have a greater symptom burden than those enrolled in MIRASOL
Subgroups	• Committee's conclusion that mirvetuximab may be more clinically effective in people with a primary platinum-free interval of more than 6 months is a cause for concern – there is a danger of over-interpretation of subgroup analysis data

Abbreviations: PFS2, time to second disease progression.

Equality and health inequality considerations raised at consultation

- There are equality issues for people living in rural or deprived areas
- The treatment schedule and side effects of chemotherapy may disproportionately affect some patient groups over others
- People from ethnic minority backgrounds and those who have language barriers may be disproportionately affected by the side effects of chemotherapy
- Mirvetuximab requires fewer treatment visits than paclitaxel (when administered weekly), this would result in financial savings due to travel and time off work, which may particularly benefit people on low incomes
- People from Caribbean and African backgrounds and those who are older and from low-income groups may be more likely to be diagnosed with ovarian cancer at a later stage. A new treatment may therefore disproportionately benefit these groups
- Some groups of people (for example people with diabetes) are at higher risk of developing severe peripheral neuropathy making them ineligible for paclitaxel treatment – not recommending mirvetuximab could disproportionately disadvantage these groups

Equality issues at ACM1 presented in the Appendix

Are there any equality or health inequality issues?

Abbreviations: ACM1, first appraisal committee meeting.

Issues

Issue	Section in draft guidance	Title	ICER impact
Key issues			
1	3.9	Overall survival extrapolations	Large
2	3.10	Health-state utility values	Moderate
3	3.17	Severity modifier	Large
4	3.13	Vial sharing – mirvetuximab	Moderate
5	3.12	Relative dose intensity	Moderate
6	N/A	Caregiver disutility	Moderate
Other issues			
7	3.15	Mirvetuximab duration of treatment	Small
8	N/A	Cost updates in company's addendum	Small – presented in Appendix only
9a	3.11	Adverse events – management of anaemia and neutropenia	Small – presented in Appendix only
9b	3.10	Adverse events – disutility for alopecia	Small – presented in Appendix only

Abbreviations: ICER, incremental cost-effectiveness ratio; N/A, not applicable.

Key issue 1: OS extrapolations (1/11)

Large ICER impact

Committee conclusion at ACM1 (draft guidance section 3.9)

- Preferred the EAG's approach to modelling OS (gamma distribution for both arms) over the company's (log-logistic for mirvetuximab and Weibull for chemotherapy), because:
  - There is no strong justification for selecting different distributions for each arm
  - The company's log-logistic model had a poor visual fit towards end of the mirvetuximab KM curve
  - The hazard implied by the company's log-logistic model (initially increasing then decreasing) was not consistent with the observed hazard for mirvetuximab, which increased again after having initially increased then decreased
- Acknowledged uncertainty in both the company and EAG approaches
- Agreed that later part of KM curve (after 24 months) should be interpreted with caution because of heavy censoring
- Would be useful to see a more recent data cut from MIRASOL if available, as well as alternative data sources for chemotherapy

Clinical expert comments

- *"Length of life after platinum resistance, is between 9 to 12 months for people having chemotherapy compared with 18 to 24 months for people having mirvetuximab"*

Abbreviations: ACM1, first appraisal committee meeting; EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; KM, Kaplan–Meier; OS, overall survival.

Key issue 1: OS extrapolations (2/11) – overview

Large ICER impact

Table: Company, EAG and committee preferred base cases at different stages of appraisal process

Stage	Company	EAG
ACM1	MIRASOL Chemotherapy – Weibull Mirvetuximab – log-logistic	MIRASOL Chemotherapy – Gamma Mirvetuximab – Gamma **(Committee preferred at ACM1)**
Draft guidance response	**As per ACM1 base case:** MIRASOL Chemotherapy – Weibull Mirvetuximab – log-logistic	**Updated base case informed by SACT:** MIRASOL Chemotherapy – log-logistic Mirvetuximab – log-logistic **EAG scenario 1:** Chemotherapy – SACT data, log-logistic Mirvetuximab – MIRASOL hazard ratio **EAG scenario 2:** Chemotherapy – SACT data, log-logistic Mirvetuximab – MIRASOL gamma
Company addendum	**As per ACM1 base case:** MIRASOL Chemotherapy – Weibull Mirvetuximab – log-logistic **Preferred SACT scenario, EAG scenario 1:** Chemotherapy – SACT data, log-logistic Mirvetuximab – MIRASOL hazard ratio	**Maintained draft guidance response base case:** MIRASOL Chemotherapy – log-logistic Mirvetuximab – log-logistic SACT scenarios presented

Abbreviations: ACM1, first appraisal committee meeting; EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; SACT, Systemic Anti-Cancer Therapy.

Key issue 1: OS extrapolations (3/11) – MIRASOL

Large ICER impact

Company: appropriate to use different extrapolations for each arm
EAG: prefers to use same extrapolation

Company

- Mirv and chemo have substantially different mechanisms of action – noted by ACM1 clinical experts
- Mirv significantly extends duration of response
- Observed hazard for mirv mostly stable, final increase occurs when low numbers at risk and data should be interpreted with caution
- In contrast, the observed hazard for chemo increases over time (**Figure 1 vs 2**)

EAG comments

- Clinical expert opinion to EAG that mechanism of action not different enough to justify a different long-term survival profile
- An increase in the hazard at the end of the dataset for mirv cannot be ruled out – this starts at week 120 when 46 patients remain at risk, which is sufficient to be interpretable

Figure 1: Hazard plots for mirvetuximab

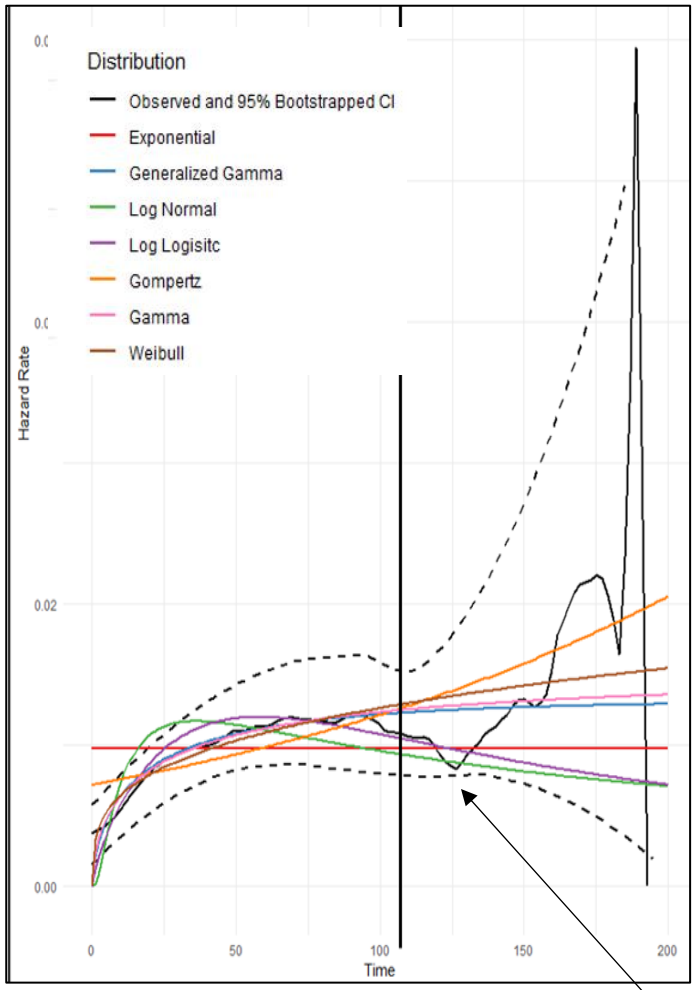
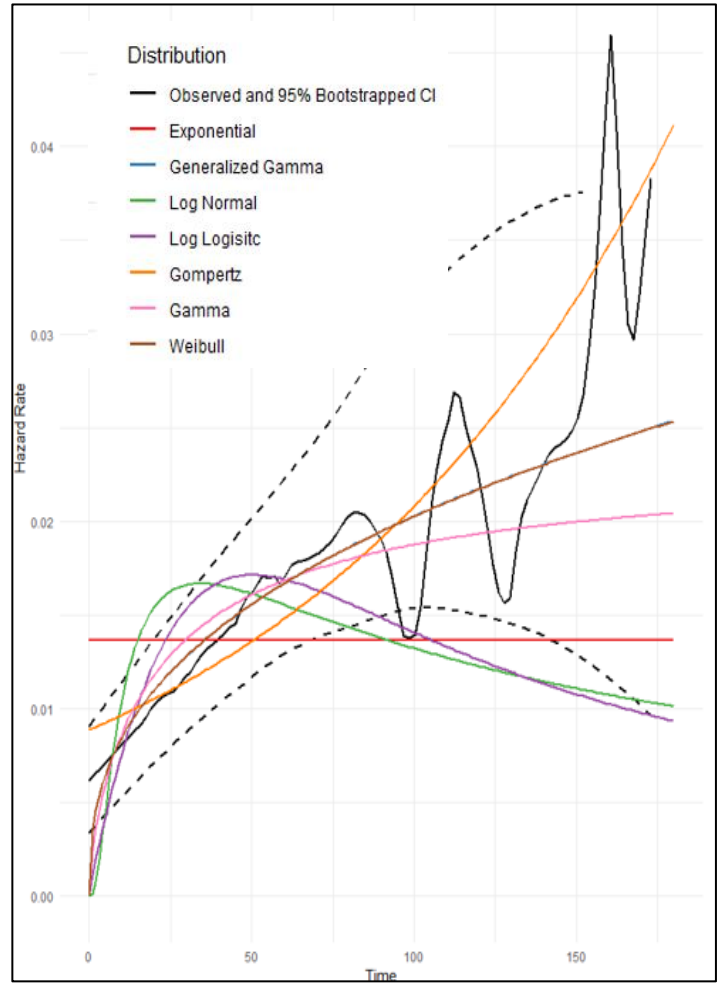


Figure 2: Hazard plots for chemotherapy



Number at risk 120 weeks (27.6 months) = 46

Large ICER impact

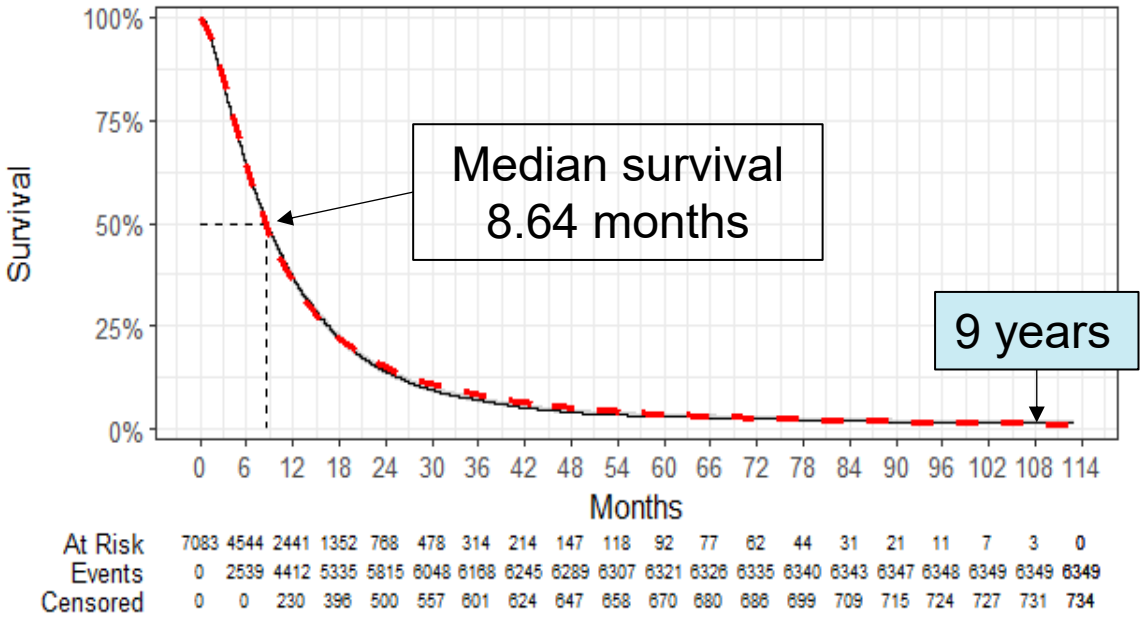
Key issue 1: OS extrapolations (4/11) – MIRASOL

EAG: align with company preference to use log-logistic for mirvetuximab arm, but also prefer to use log-logistic of chemotherapy arm

EAG comments

- SACT data for chemotherapy showed a steep initial hazard followed by a slowing in the long-term hazard with some people alive at 9 years (**Figure**)
- A log-logistic curve provided the best fit (**Figure)**
- EAG updated base case uses log-logistic (fit to MIRASOL data) for both arms
- Using the same extrapolation for both arms maintains principle of assuming same long-term survival profile
- EAG's preference would have been to use the SACT data to model outcomes for chemotherapy, but EAG unable to this implement because:
  - EAG did not have access to MIRASOL data to estimate time-dependent hazard ratios
  - SACT data not available for PFS
- Provided alternative scenarios – see overview slide

Figure: SACT report, KM data (**black**) and best fitting log-logistic curve (**red**)



Abbreviations: EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; KM, Kaplan–Meier; OS, overall survival; PFS, progression-free survival; SACT, Systemic Anti-Cancer Therapy.

Please note SACT data were updated after the appraisal meeting - please see the committee papers and Final Draft Guidance for more information and the updated SACT data.

Key issue 1: OS extrapolations (5/11) – MIRASOL

Large ICER impact

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Company: Weibull is the most appropriate extrapolation for chemotherapy

Company

- Weibull provides the best fit to the smoothed hazard plot
- Weibull predicts 0.3% alive at 5 years, allowing for a very small possibility of people in the chemotherapy arm being alive at 5 years and beyond

EAG comments

- Company's Weibull curve underestimates observed survival in SACT in the long-term (**Figure 1**)
- EAG's log-logistic curve applied to the MIRASOL data provides the best fit to long-term trends in SACT data (**Figure 2**)
- BGCS's clinical expert expects a survival advantage for mirvetuximab of around 6 months over current treatments
  - this compares to the modelled mean undiscounted incremental life years of [redacted] months in the company base case and [redacted] in the revised EAG base case

Please note SACT data were updated after the appraisal meeting - please see the committee papers and Final Draft Guidance for more information and the updated SACT data.

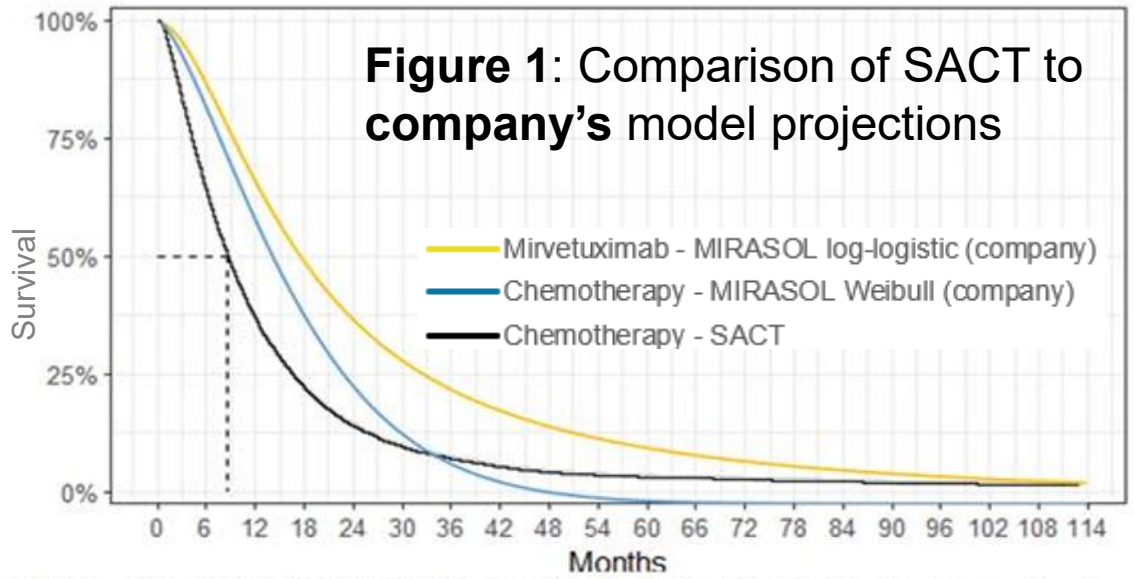

Figure 1: Comparison of SACT to **company's** model projections

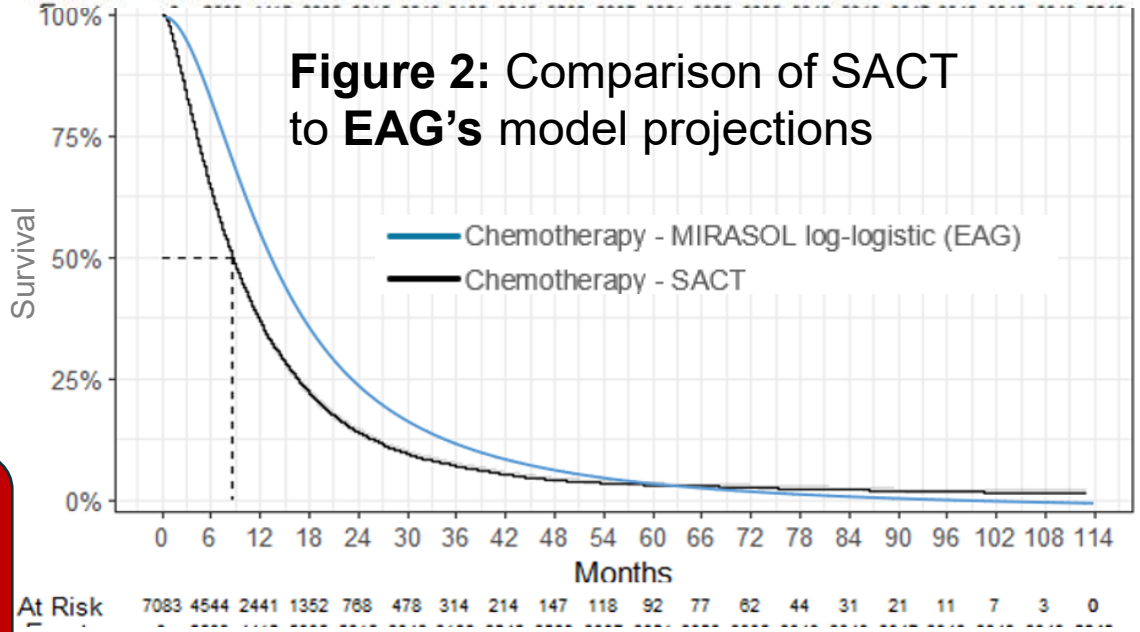

Figure 2: Comparison of SACT to **EAG's** model projections

Key issue 1: OS extrapolations (6/11) – MIRASOL

Large ICER impact

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Figure 1: MIRVETUXIMAB – company and EAG base case extrapolation based on MIRASOL data

Figure 2: CHEMOTHERAPY – company and EAG base case extrapolations based on MIRASOL data, alongside SACT data for comparison

Table: Landmark and median OS for company's and EAG's base case using MIRASOL

Scenario	Treatment arm	Median OS (months)	1-year OS (%)	2-year OS (%)	3-year OS (%)	5-year OS (%)	10-year OS (%)
EAG base case - MIRASOL	Mirvetuximab (MIRASOL log-logistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Chemotherapy (MIRASOL log-logistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Company base case - MIRASOL	Mirvetuximab (MIRASOL log-logistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Chemotherapy (MIRASOL Weibull)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Large ICER impact

Key issue 1: OS extrapolations (7/11) – MIRASOL

EAG: Still concerned around plausibility of long-term treatment effect and implausible post-progression survival gains

EAG comments

- Company's base case assumes a continued improvement in the hazard ratio favouring mirvetuximab over time (**Figure**) – EAG considers this implausible
- There may be some post-progression benefit from prior treatment with mirvetuximab, but EAG not convinced by extent of benefit modelled by company:
  - That is, [redacted] the benefit in post-progression survival compared to progression-free survival ([redacted] vs [redacted])

Figure: Treatment effect over time: company base case

Abbreviations: EAG, External Assessment Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; OS, overall survival.

Key issue 1: OS extrapolations (8/11) – SACT + HR

Company: if real-world evidence is used, company prefers to use EAG scenario 1: log-logistic curve fit to SACT data, with the hazard ratio (HR) of 0.68 from MIRASOL applied to estimate outcomes for mirvetuximab

Company

- SACT has a large sample size (n=7,083) and long-follow up (113 months vs 45 months in MIRASOL)
- Median survival in SACT of 8.64 months aligns with other sources
- Presents analysis using EAG scenario 1, applying HR from MIRASOL to SACT data

Please note SACT data were updated after the appraisal meeting - please see the committee papers and Final Draft Guidance for more information and the updated SACT data.

Abbreviations: HR, hazard ratio; ICER, incremental cost-effectiveness ratio; OS, overall survival; SACT, Systemic Anti-Cancer Therapy.

Key issue 1: OS extrapolations – (9/11) SACT + HR

EAG: SACT + HR approach is valid, but appropriateness depends on proportional hazards (PH) assumption holding

EAG comments

- Log cumulative hazards plot (**figure**) shows cumulative hazards cross in several places, and the distance between the curves changes over time – suggests that PH assumption may be inappropriate
- However, the gap between the two treatments remains relatively constant after initial crossing and there is no evidence of the hazards trending towards each other – indicates that applying a constant HR to longer term estimates is unlikely to bias towards mirvetuximab

Please note SACT data were updated after the appraisal meeting - please see the committee papers and Final Draft Guidance for more information and the updated SACT data.

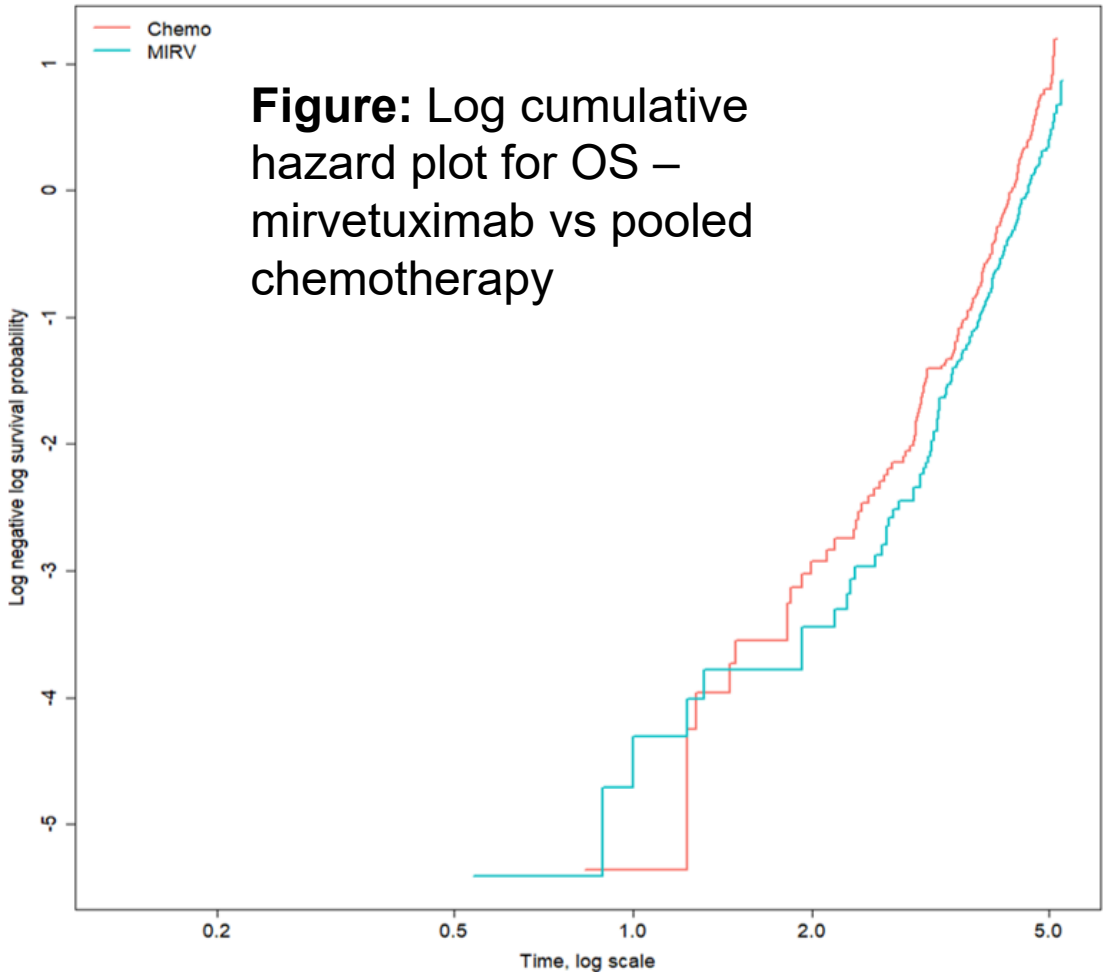

Figure: Log cumulative hazard plot for OS – mirvetuximab vs pooled chemotherapy

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Abbreviations: EAG, External Assessment Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; OS, overall survival; SACT, Systemic Anti-Cancer Therapy.

Large ICER impact

Key issue 1: OS extrapolations (10/11) – SACT + HR

EAG: Still has concerns around plausibility of survival gain using SACT + HR approach

EAG comments

- BGCS's clinical expert expects a survival advantage for mirvetuximab of around 6 months over current treatments
- See **table** for comparison
- EAG does not consider the magnitude of the post-progression gain in either the company base case or the scenario applying the HR to SACT data to hold face validity given that this is [redacted] times the gain observed pre-progression

Please note SACT data were updated after the appraisal meeting - please see the committee papers and Final Draft Guidance for more information and the updated SACT data.

Table: OS and PPS gain for mirvetuximab

	OS gain (months)	PPS gain (months)
Company base case: MIRASOL; chemo – Weibull, mirv – log-log	[redacted]	[redacted]
EAG base case: MIRASOL; chemo – log-log, mirv – log-log	[redacted]	[redacted]
EAG scenario 1: Chemo – SACT log-log, mirv – MIRASOL HR	[redacted]	[redacted]
EAG scenario 2: Chemo – SACT log-log; mirv – MIRASOL gamma	[redacted]	[redacted]

Abbreviations: BGCS, British Gynaecological Cancer Society; EAG, External Assessment Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; OS, overall survival; SACT, Systemic Anti-Cancer Therapy.

Large ICER impact

Key issue 1: OS extrapolations (11/11) – SACT + HR

Figure: Extrapolations for company's and EAG's scenario using SACT data + HR for OS (PFS extrapolations also presented)

Table: Landmark and median OS for company's and EAG's scenario using SACT data + HR for OS

Treatment arm	Median OS (months)	1-yr OS (%)	2-yr OS (%)	3-yr OS (%)	5-yr OS (%)	10-yr OS (%)
Mirv (HR from MIRASOL applied to SACT)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Chemo (SACT loglogistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

What is the most appropriate approach for modelling overall survival for mirvetuximab and chemotherapy?

Please note SACT data were updated after the appraisal meeting - please see the committee papers and Final Draft Guidance for more information and the updated SACT data.

Abbreviations: EAG, External Assessment Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival; SACT, Systemic Anti-Cancer Therapy.

Moderate ICER impact

Key issue 2: Health-state utility values (1/2)

Committee conclusion at ACM1 (draft guidance section 3.10)

- Preferred EAG approach of using MIRASOL health-state utility values for both arms, rather than company approach of using MIRASOL utilities for mirvetuximab and Havrilesky et al. utilities for chemotherapy
- It is possible that the MIRASOL utilities did not fully capture the improvement in HRQoL with mirvetuximab

Company

- Utility difference between mirvetuximab and chemotherapy in MIRASOL is not clinically plausible:
  - MIRASOL utility values as used by the EAG suggest only a small (0.03) difference in HRQoL between mirvetuximab and chemotherapy, in both the pre- and post-progression states
- Company's updated base case uses MIRASOL utilities, with an interaction term between treatment and progression – this better reflects post-progression benefits of mirvetuximab
- Also presented a scenario which assumes the utility between first and second progression for mirvetuximab is equivalent to pre-progression utility for chemotherapy, as people would have the same treatments

Clinical expert, patient group and web comments:

- People having standard treatment for platinum-resistant ovarian cancer have a high symptom burden as well as substantial toxicity from chemotherapy treatments
- Mirvetuximab improves response rates, symptom burden and toxicity allowing people to people to live more fulfilled better-quality lives than with chemotherapy.
- **Clinical expert:** *"The benefit in terms of response rate and quality of life for women with platinum resistant ovarian cancer has been underestimated"*

Moderate ICER impact

Key issue 2: Health-state utility values (2/2)

EAG comments

- Maintains original base case – MIRASOL utilities without interaction term
- Company's updated base case results in a smaller difference of 0.02 pre-progression and a much larger difference of 0.08 post progression, than original approach – this lacks face validity
- Company's scenario is logical, but company could have used trial data for this analysis rather than relying on assumptions
- EAG note that adverse event disutilities are included separately
- EAG presents scenarios assuming greater utility differences of 0.05 and 0.1 in pre-progression utility

Table: Alternative approaches to modelling utility

	EAG base case – MIRASOL without interaction term	Company base case – MIRASOL with interaction term	Company scenario – MIRASOL with mirv. post prog assumption
Mirvetuximab pre-prog	0.737	0.732	0.737
Mirvetuximab post-prog	0.655	0.675	Before 2nd prog: 0.706 After 2nd prog: 0.655
Chemotherapy pre-prog	0.706	0.712	0.706
Chemotherapy post-prog	0.625	0.596	0.625

What is the preferred approach to modelling utility?

Abbreviations: EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio.

Key issue 3: Severity modifier (1/3)

Large ICER impact

The calculated severity modifier in the company and EAG base cases and scenarios using SACT + HR approach is 1.2 (based on proportional shortfall between 85 and 95%)

Table: Company and EAG absolute and proportional QALY shortfall analyses	QALYs of people without condition	QALYs with condition on current treatment	Abs. shortfall (years)	Prop. shortfall (%)	Calculated QALY weighting
Company base case • 62.8 as starting age (MIRASOL) • Utilities MIRASOL with interaction term • Chemotherapy OS: MIRASOL Weibull	11.64	0.78	10.86	93.3%	x1.2
EAG base case • 62.8 as starting age (MIRASOL) • Utilities MIRASOL without interaction term • Chemotherapy OS: MIRASOL log-logistic	11.64	0.98	10.67	91.6%	x1.2
Company scenario (SACT + HR) • 67 as starting age (SACT) • Utilities MIRASOL with interaction term • Chemotherapy OS: SACT log-logistic	10.18	0.75	9.42	92.6%	x1.2
EAG scenario (SACT + HR) • 67 as starting age (SACT) • Utilities MIRASOL without interaction term • Chemotherapy OS: SACT log-logistic	10.18	0.77	9.40	92.4%	x1.2

See Appendix for shortfalls and corresponding QALY weights

Large ICER impact

Key issue 3: Severity modifier (2/3)

Company welcomes committee consideration of broader factors when determining severity weighting – company also presented a scenario analysis exploring how different combinations of median OS and age affect the severity modifier

Company

- May be some combinations of median OS and age, in which severity modifier of 1.7 applies (see appendix)
- Proportional QALY shortfall assumptions are close to the threshold for applying a 1.7 severity modifier
- RWE (Nicola Murray Centre for Ovarian Cancer Research) shows a median survival of 9 months for standard care, which aligns closely with estimates from SACT
- AbbVie would welcome the committee's consideration of broader factors, such as:
  - the high unmet need and the lack of new treatment options in over 20 years
  - patient survey results reflecting the highly severe nature of the disease in terms of the impact on health-related quality of life

Patient group and web comments:

- People having standard treatment for platinum-resistant ovarian cancer have a high symptom burden as well as substantial toxicity from chemotherapy treatments
- People with platinum-resistant ovarian cancer have a very poor prognosis – survival is less than 12 months

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Abbreviations: ICER, incremental cost-effectiveness ratio; OS, overall survival; QALY, quality-adjusted life year; RWE, real-world evidence; SACT, Systemic Anti-Cancer Therapy.

Large ICER impact

Key issue 3: Severity modifier (3/3)

EAG: Modifier of 1.2 remains appropriate

EAG comments

- Regarding the company's analysis of the severity modifier based on combinations of median OS and age:
  - Previous NICE end-of-life appeals have determined that economic analyses should consider mean survival rather than median survival in line with general health economics principles
  - The same principle applies to the calculation of proportional QALY shortfall
  - EAG therefore considers that analyses based on median OS are not appropriate
- Mean OS is much higher than median OS
- EAG also notes that the 62.8 years mean age from MIRASOL, 66 years mean age at diagnosis reported in the National Ovarian Cancer Audit report and 69 years as the mean age of people starting first-line maintenance PARP inhibitor treatment in England, all fall within the upper part of the range considered by the company's analysis
- Based on this the EAG considers that the company's scenario analysis does not provide sufficient numeric justification for applying the 1.7 severity modifier, and the 1.2 modifier remains appropriate

Should the starting age in the model be based on MIRASOL or SACT?
Should a severity modifier of 1.2 or 1.7 be used?

NICE

Abbreviations: EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; OS, overall survival; PARP; Poly (ADP-ribose) polymerase; RWE, real-world evidence; SACT, Systemic Anti-Cancer Therapy.

Moderate ICER impact

Key issue 4: Vial sharing – mirvetuximab

Committee conclusion at ACM1 (draft guidance section 3.13)

- Vial sharing for mirvetuximab unlikely to be achievable based on input from NHSE Cancer Drugs Fund lead – the model should include **not** include vial sharing for mirvetuximab

Company

- Maintains 50% vial sharing is reasonable for mirvetuximab
- Similar numbers of people having mirvetuximab as having trastuzumab deruxtecan in TA862 – where 50% vial sharing assumption was accepted by committee
- Feedback from NHS pharmacists is that people are frequently scheduled for treatment on specific days of the week, so the opportunity for vial sharing is enhanced

EAG comments

- ~600 people across both trastuzumab breast cancer indications (TA704 and TA862)
- In the company's budget impact analysis for mirvetuximab, there are lower patient numbers than this in Y1; and lower but comparable numbers by Y5
- However, EAG's clinical expert advice is that trastuzumab is also used in other indications
- Time on treatment for trastuzumab longer than mirvetuximab – this leads to considerably more people ([redacted]) expected to be treated with trastuzumab than mirvetuximab
- EAG's clinical expert did not consider in-house vial sharing feasible as typically only 1 to 2 people are having mirvetuximab at any time, but this may be more feasible for hospitals using outsourcing companies
- EAG retains base case assumption of 0% vial sharing for mirvetuxumab but tests scenarios of 25% and 50%

Is vial sharing anticipated in NHS practice? If so, what % should be assumed?

Moderate ICER impact

Key issue 5: Relative dose intensity (RDI)

Committee conclusion at ACM1 (draft guidance section 3.12)

- EAG's cycle-specific RDI approach more accurately reflects drug use and wastage

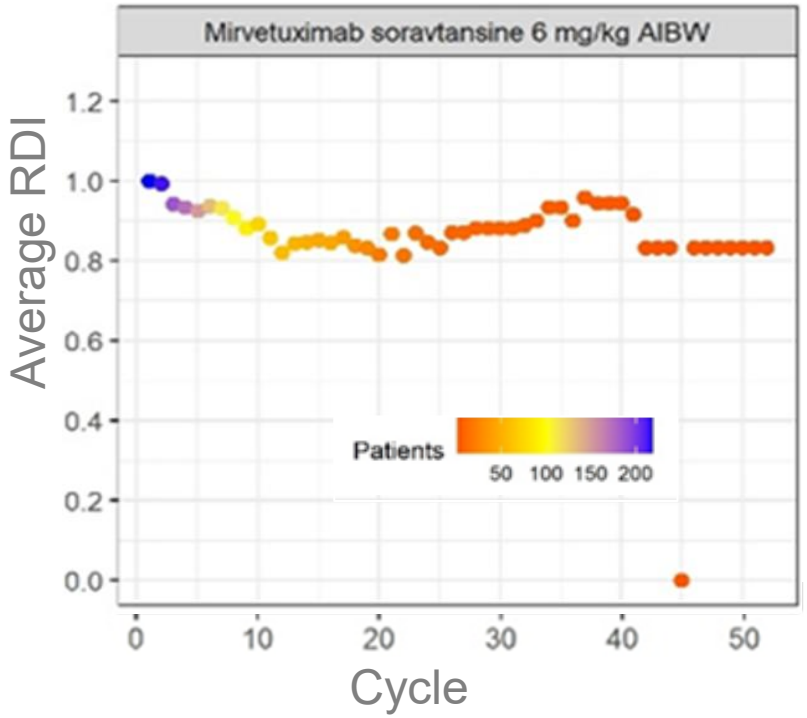
Company

- Maintains that using a mean value for RDI across all timepoints is most appropriate
- RDI is broadly consistent over time, and the EAG's cycle-specific RDI is determined by low patient numbers at later timepoints so would not necessarily be more accurate

EAG comments

- The mean RDI used in the company model is [redacted] - this is actually higher than the long-term RDI used for mirvetuximab in the cycle-specific analysis ([redacted] after 28 weeks)
- The driver of cost-effectiveness is that in the earliest cycles, where patient numbers are highest, the trial observed RDI values are greater than the mean
- EAG therefore maintains that cycle-specific RDI values are more appropriate

Figure: Per-cycle RDI for mirvetuximab (company response, Figure 7)



What is the more appropriate approach to modelling RDI? The EAG's cycle-specific approach or the company's mean value approach?

Abbreviations: AIBW, adjusted ideal body weight; ICER, incremental cost-effectiveness ratio; RDI, relative dose intensity.

Moderate ICER impact

Key issue 6: Caregiver disutility

EAG comments

- Provides scenarios to demonstrate model sensitivity to the inclusion of caregiver burden
  - Including carer disutility for 39% of patients – based on estimate from Adelphi Real World Evidence survey suggesting 50% of people have some additional support or care, but 11% of this group had a professional caregiver (50%-11% = 39%)
  - Including carer disutility for 100% of patients

Company

- Both the treatment and management of platinum-resistant ovarian cancer has a significant detrimental effect on both patients and their caregivers
- As mirvetuximab has a more favourable safety profile than chemotherapy, it is reasonable to assume that caregiver burden would be lower
- Agrees with EAG scenarios incorporating carer disutility – these should be reflected in the analysis
- Company's updated base case (in addendum) assumes carer disutility for 70% patients, with 39% and 100% tested as scenarios

EAG comments

- Does not accept company's base case assumption that 70% have an informal carer – this is not supported by evidence and contradicts Adelphi survey results

Should a caregiver disutility apply? If so, what proportion of patients should this apply to?

Small ICER impact

Other issues 7: Mirvetuximab duration of treatment

Committee conclusion at ACM1 (draft guidance section 3.15)

- Company's approach of using an exponential distribution may have slightly underestimated mirvetuximab duration of treatment
- Preferred EAG's approach of using the observed Kaplan–Meier (KM) data up to 120 weeks followed by an exponential distribution

Company

- Maintains preference to use exponential distribution
- Using KM data directly risks overinterpreting small variations in the trial data

EAG comments

- Maintains that company's exponential approach underestimates the proportion on treatment early in time horizon (**Figure**)
- Data for duration of treatment are complete, so the EAG revised base case uses the KM data directly for both arms

Figure: Company and EAG approaches to modelling mirvetuximab duration of treatment

[redacted]

Abbreviations: EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; KM, Kaplan–Meier.

What is the committee's preferred approach to modelling duration of treatment for mirv and chemo?

Summary of company and EAG base case assumptions

Assumption	Committee preference at ACM1	Company base case	EAG base case
OS extrapolations	Gamma (both arms)	MIRASOL Log-logistic (mirv), Weibull (chemo) SACT + HR scenarios	MIRASOL log-logistic (both arms) SACT + HR scenarios
Health-state utility values	MIRASOL	MIRASOL (**with** treatment interaction effect)	MIRASOL (**without** treatment interaction effect)
Severity modifier	1.2	1.2 in model, but 1.7 should apply	1.2
Vial sharing – mirvetuximab	0%	50%	0% – scenarios presented
Relative dose intensity (RDI)	Cycle-specific	Mean value across timepoints	Cycle-specific
Caregiver disutility	N/A	Included – 70% patients	Not included – scenarios presented
Mirv duration of treatment	KM data + exponential	Exponential only	KM data only
Cost updates – ocular	N/A	Included	Not included
Cost updates – admin	N/A	Included	Included
AEs – management of anaemia and neutropenia	100% day case	Weighted average NHS reference costs	100% day case
AEs – disutility for alopecia	N/A	0.12	0.05
Age – years	MIRASOL (62.8)	MIRASOL (62.8)	MIRASOL (62.8)

Other considerations

Is it appropriate to consider subgroups by primary platinum-free interval (more than or less than 6 months)?

- At ACM1, the committee suggested that mirvetuximab may be more clinically effective in people with a primary platinum-free interval of more than 6 months
- Company state that results should be interpreted with caution as MIRASOL not powered to draw this conclusion. Company also highlighted non-significant results for PFS – EAG still consider this an uncertainty

Are there any uncaptured benefits?

- Uncaptured benefits highlighted by the company include the rarity of the condition, the lack of innovation, the caregiver burden (now captured in company's addendum) and inequality in the treatment pathway

Abbreviations: EAG, External Assessment Group; PFS, progression-free survival.

Cost-effectiveness results are presented in Part 2 of the committee meeting because of the confidential discount for mirvetuximab

Appendix

NICE National Institute for Health and Care Excellence

SACT report

Table: SACT report study design

	SACT report (N=7083)
Design	Cohort study
Population	Adults (aged 18+) with platinum-resistant advanced epithelial ovarian, fallopian tube or primary peritoneal cancer
Mean age	67 years
Intervention	Pegylated liposomal doxorubicin (PLD) or paclitaxel monotherapies
Comparator	N/A
Outcome	Overall survival
Time frame	Diagnosed between 1st January 2010 and 31st December 2023 PLD or paclitaxel initiated on or after 27th April 2016 (NICE TA389 publication)
Duration of follow-up	Minimum: 0.1 months Median: 8.4 months Maximum: 113 months (compared with 45 months in MIRASOL)
Locations	England

NICE

Abbreviations: SACT, Systemic Anti-Cancer Therapy.

RECAP

Committee's preferred assumptions at ACM1 (1/3)

Draft guidance section	Issue	Committee's preferred assumption	Company base case aligned?
3.3	Comparators	Pooled chemotherapy, including pegylated liposomal doxorubicin (PLD) and paclitaxel	Yes (base case updated)
3.8		Excluding the costs of topotecan	Yes (base case updated)
3.7	Subgroups	Mirvetuximab may be more clinically effective in people with a primary platinum-free interval of more than 6 months	No (other considerations)
3.9	Overall survival (OS) extrapolations	Gamma distribution for modelling mirvetuximab and chemotherapy OS	No (key issue)
3.10	Health-state utility values	Treatment-dependent health-state utility values from MIRASOL for mirvetuximab and chemotherapy	No (key issue)

Abbreviations: ACM1, first appraisal committee meeting.

RECAP

Committee's preferred assumptions at ACM1 (2/3)

Draft guidance section	Issue	Committee's preferred assumption	Company base case aligned?
3.10	Adverse events (AEs)	Including adverse event disutilities	Yes (base case updated)
3.11		Duration of grade 2 or higher ocular AEs of 4 weeks	Yes (base case already aligned at ACM1)
3.11		Frequency of ophthalmology visits of every 6 weeks	Yes (base case already aligned at ACM1)
3.11		Anaemia and neutropenia are managed as day cases	No (other issues)
3.11		Fatigue is self-managed	Yes (base case updated)
3.12	Relative dose intensity (RDI)	Using the cycle-specific approach for modelling RDI	No (key issue)
3.13	Vial sharing	No vial sharing for mirvetuximab, 50% vial sharing for chemotherapy	No (key issue)

Abbreviations: ACM1, first appraisal committee meeting.

RECAP

Committee's preferred assumptions at ACM1 (3/3)

Draft guidance section	Issue	Committee's preferred assumption	Company base case aligned?
3.14	Clinical management costs	Gynaecological oncology consultations once every 6 weeks in both the pre- and post-progression health states	Yes (base case updated)
3.15	Mirvetuximab duration of treatment	Observed Kaplan–Meier (KM) data up to 120 weeks, followed by exponential extrapolation	No (other issues)
3.16	Subsequent treatment	Adjusting for treatment crossover and removing the cost of mirvetuximab in the post-progression state	Yes (base case updated)
3.17	Age	Using the mean baseline age in MIRASOL (62.8 years) for the starting age in the model	Yes (base case updated)
3.17	Severity modifier	Severity weight of 1.2 (based on QALY shortfall calculated from ACM1 assumptions)	?
3.19	ICER threshold	Not stated – more information needed on the 3 key uncertainties (utilities, survival and age) to understand the extent of the uncertainty	N/A

NICE

Abbreviations: ACM1, first appraisal committee meeting; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

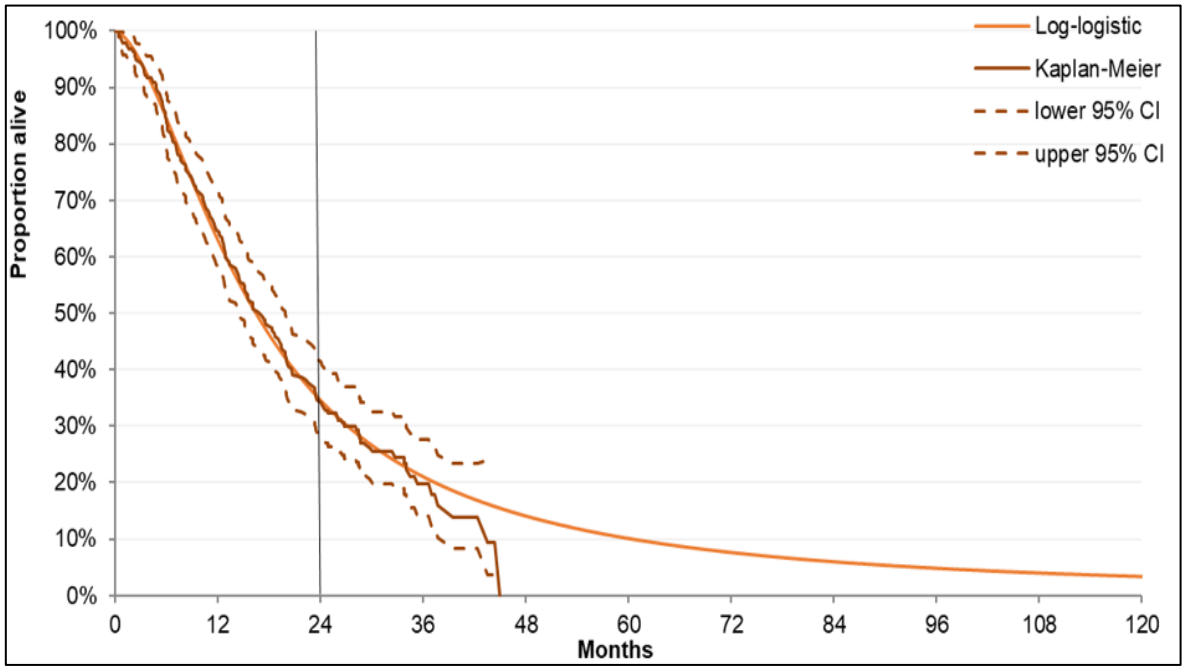
Key issue 1: OS extrapolations – MIRASOL

Company: log-logistic is most appropriate extrapolation for mirvetuximab

Company

- Log-logistic curve is a good visual fit up to 36 months
- Log-logistic hazards follow the shape of the observed hazards consistently, until 24 months (at which time the committee note the data should be interpreted with caution)
- Clinical experts invited to the first committee meeting, all support the plausibility of the log-logistic 5-year survival rate, with the gamma 5-year survival rate being pessimistic

Figure: Log-logistic extrapolation and mirvetuximab OS KM



Number at risk:
24 months = 70
36 months = 12

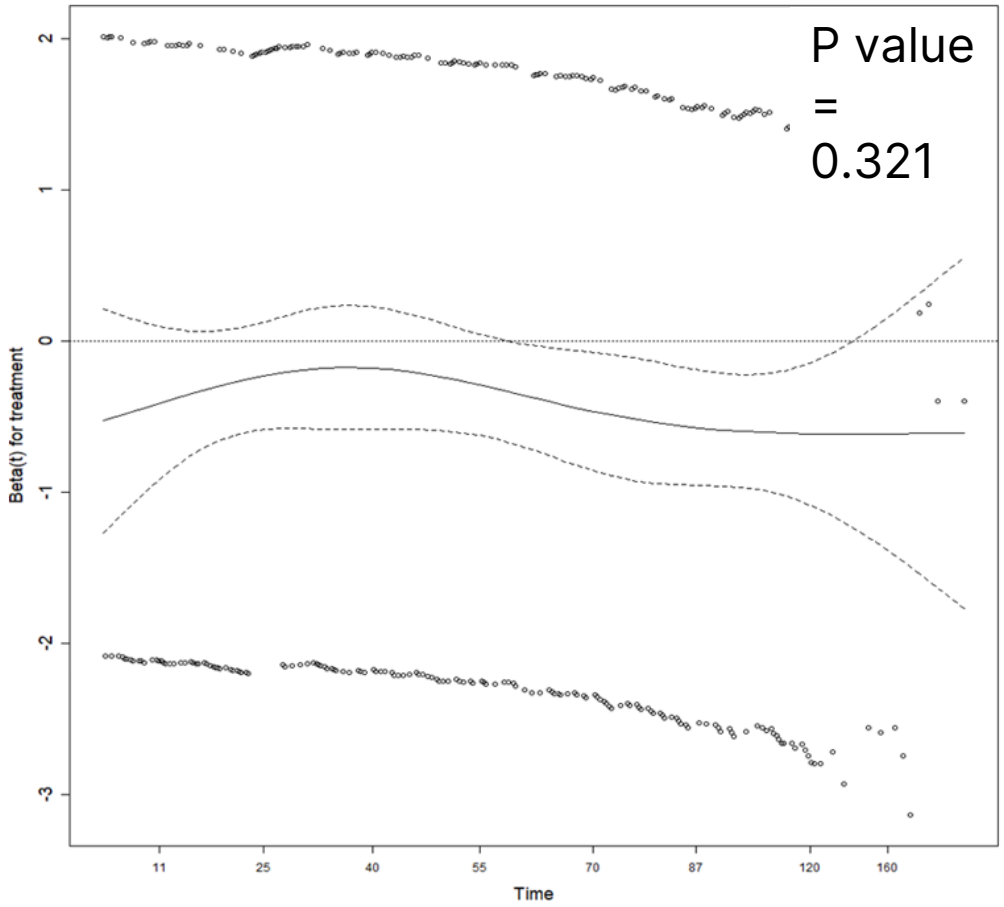
Abbreviations: CI, confidence interval; KM, Kaplan–Meier; OS, overall survival.

Key issue 1: OS extrapolations – median and landmark survival estimates across all approaches

Scenario	Treatment arm	Median OS (months)	1-year OS (%)	2-year OS (%)	3-year OS (%)	5-year OS (%)	10-year OS (%)
EAG base case - MIRASOL	Mirvetuximab (MIRASOL log-logistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Chemotherapy (MIRASOL log-logistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Company base case - MIRASOL	Mirvetuximab (MIRASOL log-logistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Chemotherapy (MIRASOL Weibull)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
SACT + HR scenario	Mirvetuximab (HR from MIRASOL applied to SACT)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Chemotherapy (SACT loglogistic)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Key issue 1: OS extrapolations – Schoenfeld residuals plot MIRASOL OS, mirvetuximab vs chemotherapy

Figure 2: Schoenfeld residuals plot for OS – mirvetuximab vs pooled chemotherapy



Notes on interpretation: If the plotted smoothed line is horizontal, the PH assumption holds. If the line shows a trend, the hazard ratio changes over time. A significant p-value indicates the PH assumption is violated.

Abbreviations: PH, proportional hazards; OS, overall survival

Key issue 3: Severity modifier

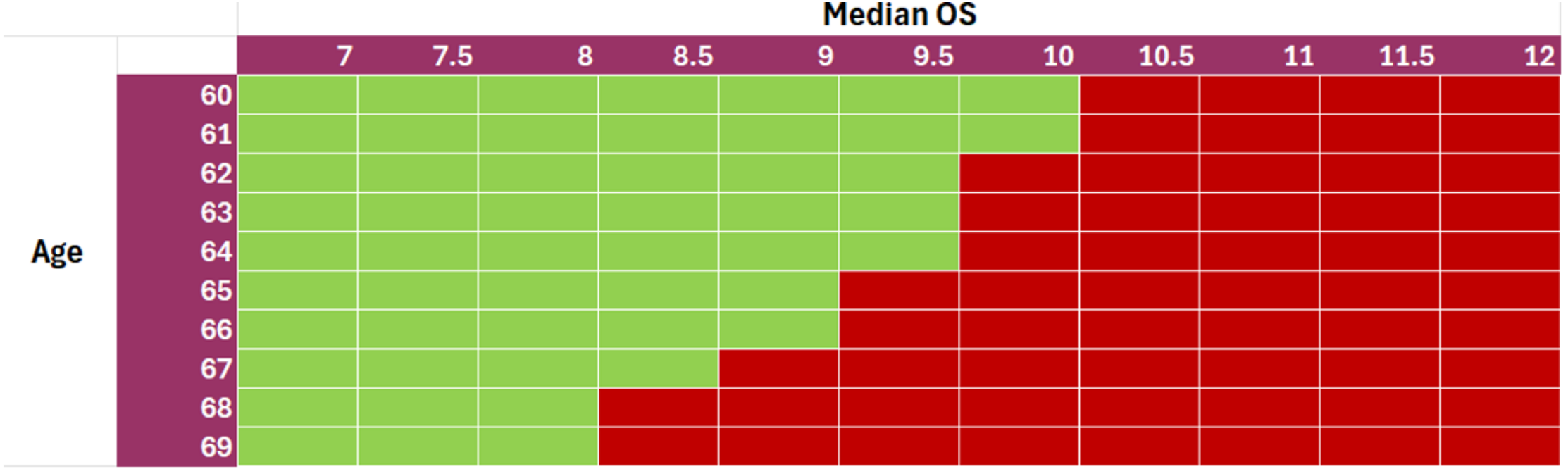
Table: Proportional and absolute shortfall and corresponding QALY weights

QALY weight	Proportional QALY shortfall	Absolute QALY shortfall
1	Less than 85%	Less than 12
x1.2	85 to 95%	12 to 18
x1.7	At least 95%	At least 18

Abbreviations: QALY, quality-adjusted life year.

Key issue 3: Severity modifier

Figure: Exploring severity modifier weights at different median OS and age assumptions



Green: x1.7 applies, Red: x1.2 applies

Abbreviations: OS, overall survival.

Small ICER impact

Other issues 8: Cost updates in company's addendum

Company

Ocular assessment costs

- SPC states that: *"an ophthalmic exam including visual acuity and slit lamp exam should be conducted before the initiation of ELAHERE"*
- AbbVie is working with a major high-street provider to fund the costs of the baseline eye exam. As a result, this cost should no longer be included in the economic model

Administration costs for first administration of paclitaxel in each 28-day cycle:

- Existing SB12Z HRG code –*"overall time of 30 minutes nurse time and 30 to 60 minutes chair time for the delivery of a complete cycle"*
- Updated SB13Z HRG code – *"60 minutes nurse time and up to 120 minutes chair time for the delivery of a complete cycle".*

EAG comments

Ocular assessment costs – EAG does not accept this change

- No evidence that the company-funded arrangement has been formally agreed and will apply for the full duration of branded drug availability within the NHS

Administration costs – EAG accepts this change

- Notes that this issue was recently considered for tisotumab (ID3753), where CDF lead advised that the SB13Z cost code could be used for weekly paclitaxel, as it appropriately captures the time required to cannulate, administer premedication and paclitaxel, flush the line and remove the cannula.

Should the model apply the cost updates in the company's addendum?

Small ICER impact

Other issues 9a: Adverse events – management of anaemia and neutropenia

Committee conclusion at ACM1 (draft guidance section 3.11)

- Preferred to assume that anaemia and neutropenia are managed as day cases

Company

- Maintains a weighted average cost (for day case, inpatient long stay and inpatient short stay procedures)
- This is consistent with approach used in previous NICE appraisals in ovarian cancer (TA1007, TA962 and TA946)

EAG comments

- Company's weighted average cost is taken from NHS reference costs which reflects all diseases – not necessarily representative of chemotherapy side effects in platinum-resistant ovarian cancer
- In 5 out of 6 cases, costs used in prior appraisals were lower than the updated company base case
- Clinical expert advice to the EAG is that the vast majority of grade 3+ anaemia and neutropenia AEs would be treated as day cases
- Rates of febrile neutropenia and neutropenic sepsis in MIRASOL, which would require admission, were very low
- Maintains assumption that anaemia and neutropenia are managed as day cases in base case

Should the EAG's day case or company's weighted average cost be assumed for managing anaemia and neutropenia?

NICE

Abbreviations: AE, adverse event; ICER, incremental cost-effectiveness ratio.

Small ICER impact

Other issues 9b: Adverse events – disutility for alopecia

Committee conclusion at ACM1 (draft guidance section 3.10)

- Adverse event (AE) disutilities should be included to capture the impact of side effects on HRQoL

Company

- Updated base case to include AE disutilities – a disutility for alopecia has also been included
- The model uses a disutility of 0.12 based on difference between best and worst health states in TA958 (severe alopecia areata)

EAG comments

- The company's disutility for alopecia may be too high as it assumes all people experience full hair loss on chemotherapy
  - Paclitaxel causes full hair loss although with weekly scheduling it falls out quite slowly – scalp cooling can be partially successful in preventing hair loss where this is available
  - Pegylated liposomal doxorubicin (PLD) generally only causes very mild hair thinning
- EAG updated base case includes a disutility for alopecia for people having paclitaxel but assumes a lower decrement (0.05 rather than 0.12) – based on values for moderate alopecia in TA958
- Reiterated potential for double counting when applying the AE disutilities on top of values from MIRASOL

What is the appropriate disutility for alopecia? A disutility of 0.12 (company) or 0.05 (EAG)?

Abbreviations: HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio.

Equality considerations – at ACM1

Company raised equality issues relating to gender health gap, rarity and equity of access:

- **Women experience an additional 3 years of ill health and disability compared with men**
  - In July 2024, 46% of gynaecology patients were on waiting lists longer than the NHS target of 18 weeks, and nearly 30,000 women were waiting for over a year
  - Longer wait times lead to delayed diagnosis and worse outcomes
- **Mirvetuximab granted orphan designation by FDA and EMA**
  - Indicative of rarity of condition
- **People from more deprived areas less likely to receive surgery or chemotherapy**
  - 50% more likely to die within 2 months of diagnosis in most deprived areas vs least deprived

EAG commented that it was unclear how introducing mirvetuximab alone would reduce health inequalities:

- Company did not present evidence or rationale to demonstrate that mirvetuximab would lead to earlier detection of those eligible for treatment
- However, EAG agrees that availability of alternative to chemotherapy would be valuable to people with platinum-resistant ovarian cancer

Abbreviations: EAG, external assessment group; EMA, European Medicines Agency; FDA, Food and Drug Administration