Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer

Technology appraisal committee D 13 August 2025

ACM2 – Part 1

For public – confidential information redacted

Chair: Raju Reddy

External assessment group: Kleijnen Systematic Reviews

Technical team: Emma Bajela, Sam Slayen, Ian Watson

Company: Johnson & Johnson

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer

- ✓ ACM1 summary
- ❑ Consultation responses and key issues
- ❑ Modelling and cost effectiveness
- ❑ Summary

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Committee conclusions at 1st committee meeting (ACM1)

Recommendation "Given the uncertainty, the committee was not able to establish a plausible cost effectiveness estimate, and could not conclude that [ami-chemo] would be a cost-effective option. The committee concluded that additional evidence is needed. So [ami-chemo] should not be used…"

Committee preferred assumptions

- Recommendation applied to non-squamous only
- Use chemotherapy as the only comparator
- Weibull extrapolations: Amivantamab-chemotherapy TTD
- No vial sharing in cost effectiveness modelling
- Cost codes for most severe AEs only (non-elective stay)

Committee identified uncertainties

- Immaturity of OS data from PAPILLON trial and OS extrapolations in both arms
- Appropriate rate of dose skipping and modelling across time horizon
- Utility estimates linked to missing data

Committee requested analyses – (and how company addressed them)

- Justification of different curves for each arm with exploration of using same curve for both arms – (**Provided)**
- OS curve for ami-chemo between gompertz and weibull distributions – (**Not provided)**
- Implied OS HR to explore post progression benefit and exploration of effect waning – (**Partially provided)**
- Dose skipping by cycle in PAPILLON trial and exploration of impact of:
  - no dose skipping – **(Provided)**
  - equal dose skipping across both treatment arms – **(Provided)**
- Explore utility values from previous appraisals in NSCLC – (**Partially provided** [TA850]**)**

Abbreviations: TTD; time to treatment discontinuation, AE; adverse event, NSCLC; non small cell lung cancer, OS; overall survival

Key issues

Key issue for discussion	Resolved?	ICER impact
Plausibility of extrapolated benefits	No – for discussion	Unknown
Extrapolation of longer term OS	No – for discussion	Large
Treatment effect waning	No – for discussion	Large

Other issues

Key issue for discussion	Resolved?	ICER impact
Utilities and dose skipping	Partially	Small

Abbreviations: OS; overall survival, ICER; incremental cost effectiveness ratio

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Consultation responses

Consultation responses were received from:

- EGFR+
- Johnson & Johnson (The company)

Consultation response- patient organisation

EGFR+ UK

- Uncaptured quality of life benefits - no standard treatment pathway for exon 20 mutations and lack of treatment options
- High unmet need
- significant impact on patient quality of life, seen in terms of high levels of anxiety and depression in people with exon 20 insertion mutations compared to more common EGFR mutations
- Small population – likely low overall cost and not likely to be long term

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Abbreviations: EGFR; epidermal growth factor receptor

Overview of company's response

- Company provided a response to areas of uncertainty and additional analyses requested by committee (further detail in key issue slides) and updated base case

- New base case incorporates committee's preferred assumptions on comparator, TTDD, adverse event costs, and dosing

Consultation responses not covered in key issue slides

DG statement (section)	Company DG response (Item #)
Committee concluded that chemotherapy is the only appropriate comparator (section 3.3)	Company has modelled chemotherapy alone but argue this is conservative because IO is used in practice (1)
Committee concluded there was uncertainty on the effect of Amivantamab on OS (section 3.4)	Company note that using IPCW treatment switching results in a statistically significant OS difference (2)
Company fitted Weibull to OS for amivantamab-chemotherapy arm . . . in line with expert advisory board (27.5% at 5 years). (section 3.8)	Company note that guidance should reference full consensus as DG only referenced one part of advisory board (4)
Company fitted gamma in line with expert advisory board (10% survival at 5 years) (section 3.8)	Guidance should reference curve validated by advisory board rather than single result at one timepoint from pre-meeting survey (6)
Committee concluded that vial sharing should not be permitted in the model	Confirm no vial sharing in model. Model represents a cohort, only full vials modelled across cohort.

Abbreviations: TTDD; time to treatment discontinuation or death, IO; immuno-oncology , IPCW; inverse probability of censoring weighting, DG; draft guidance, OS; overall survival

Company response: Committee requests for additional analyses

Draft guidance (section)	Provided?	Overview of company response	Resolved?
Justifying fitting of separate curves, fitting same curves (3.9, 3.11, 3.19)	Yes	Company retain Weibull (ami-chemo) and gamma (chemotherapy) Provided clarification of curve selection and SHELF process Provided scenarios with same parametric model for both treatments	No
Exploring chemo curve between Gompertz and Weibull (3.9)	No	Alternative OS curves for amivantamab-chemotherapy between gompertz and Weibull distributions	No
Section 3.10 Exploring treatment effect waning and provision of implied hazard ratios	Partially	Company provided implied hazard ratio plots. “sufficient evidence to conclude that it is not appropriate to model a waning effect for amivantamab” Any waning is implicit in the OS curve selection. Also provided scenarios with: 1) Fixed implied HR after observed evidence 2) per cycle implied HR between OS and PFS from chemotherapy applied to amivantamab	No
Section 3.17 Dose skipping	Yes	Company provided scenarios exploring dose skipping across treatment arms based on PAPILLON trial data	Partly
Section 3.13 Exploration of alternative utility values	Yes	Company provided scenario with progression free utility value from TA850 (0.713)	No

Abbreviations: SHELF; Sheffield elicitation framework, OS; overall survival, PFS; progression free survival

Key issue: Plausibility of extrapolated benefits

ICER Impact: Unknown

Recap (**see DG section 3.7**)

- In company and EAG modelling majority of LY and QALY gains [redacted] occur in the progressed disease health state for both intervention and chemotherapy, but treatment continued until disease progression
- Committee thought this approach was associated with uncertainty. Concluded company should take this into account when extrapolating longer-term health benefits

Company

- PAPILLON data show majority of efficacy benefit for chemotherapy occurs after progression. It is appropriate for majority of QALYs to be accrued in progressed disease state for ami-chemo chemotherapy.
- Ami-chemo demonstrated 51% reduction in PFS2 compared to chemotherapy at May 2023 DCO (HR: 0.49 [95% CI: 0.32-0.76; nominal p=0.0010]). Supports notion that ratio of OS to PFS will be [redacted] times or larger
- Median PFS was reached but median PFS2 was not, suggests clear delay to second progression well beyond first progression

EAG

- EAG unsure whether this is plausible, patients treated until disease progression (or unacceptable toxicity)
- Approximately 90% of LYG are beyond the observed data period when compared with chemotherapy only.
- Assumption of no waning is uncertain. Even if there were a residual treatment effect after amivantamab discontinuation, the magnitude and duration is largely uncertain

Are the results of the modelling associated with uncertainty and if so, to what extent?

Back to key issue slide

Abbreviations: LY; life years, QALY; quality adjusted life years, DCO; data cut off, HR; hazard ratios, CI; confidence intervals, PFS2; progression free survival after subsequent therapy, OS; overall survival, PFS; progression free survival, LYG; life years gained

Key issue: Longer-term extrapolation OS- both arms

ICER Impact: Large

Recap (**see DG section 3.9**)

Committee concluded substantial uncertainty remained with OS extrapolations in both arms and requested:

- Alternative OS curves for amivantamab-chemotherapy between gompertz and Weibull distributions
- Company base case uses gamma curve and EAG uses log-logistic curve for chemotherapy OS

Company

- Gompertz scenario for ami-chemo implausible, lacks extended survival tail beyond 10 yrs (0% at 6.5 years)
- Advisory board consensus selected the Weibull and gamma curves as most plausible for ami-chemo
- The Gamma curve selection for chemotherapy OS was best match to the consensus from the advisory board. There is sufficient evidence to conclude gamma is most appropriate.
- Gamma for chemo predicts risk of death over time that closely matches PAPILLON smoothed hazard plot
- Modelling Weibull for ami-chemo and log-logistic for chemo results in crossing hazards, implausible.

EAG

- Gompertz for ami-chemo was exploratory pessimistic scenario, not base case. Committee suggested exploration of curve which gave survival estimates somewhere between Weibull and Gompertz, not provided.
- Still consider that gamma curve for chemotherapy underestimates company clinicians' responses from the advisory board pre-question. Retain log-logistic for OS chemo in EAG base case

What distributions should be used to extrapolate OS in each arm?

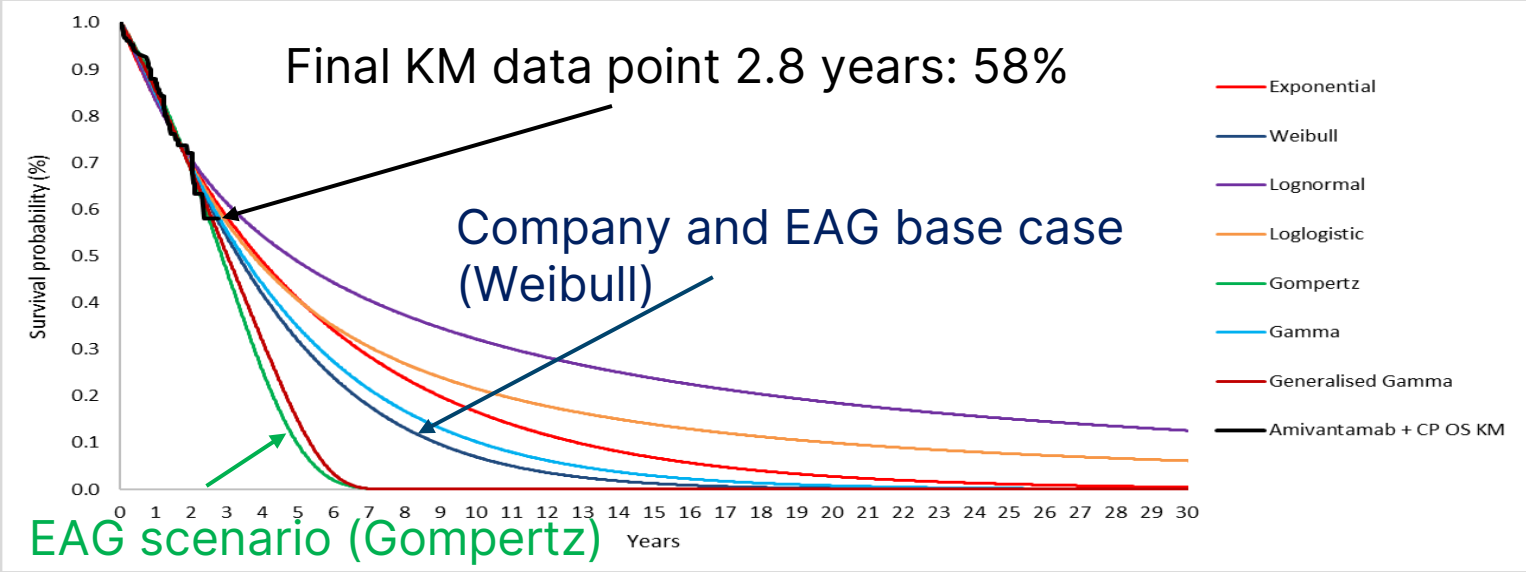
Back to key issue slide

Abbreviations:, OS: overall survival

Key Issue: OS extrapolation: ami-chemo

ICER Impact: Large

Company chooses Weibull, EAG considers it overestimates but uses it for base case



- **Company:** Advisory board consensus : Weibull or Gamma most appropriate.
- **EAG**: Weibull in base case but uses Gompertz scenario to reflect lower estimates from their expert.
- Any expert opinion should be interpreted with caution due to limited experience with amivantamab in NHS

Source	Median OS	3-year	5-year	10-year
Weibull (Company advisory board consensus)	39.8	54.4%	32.1%	7.0%
Gamma (Company advisory board consensus)	41.4	55.6%	35.0%	10.3%
Company advisory board pre-meeting questionnaire	-	50%	27.5% (25-30)	7.5% (5-10)
Gompertz (EAG scenario)	34.3	47.1%	9.9%	0.0%
EAG expert opinion	-	25-30%	10-15%	unknown

Which distribution should be used to extrapolate amivantamab plus chemotherapy OS?

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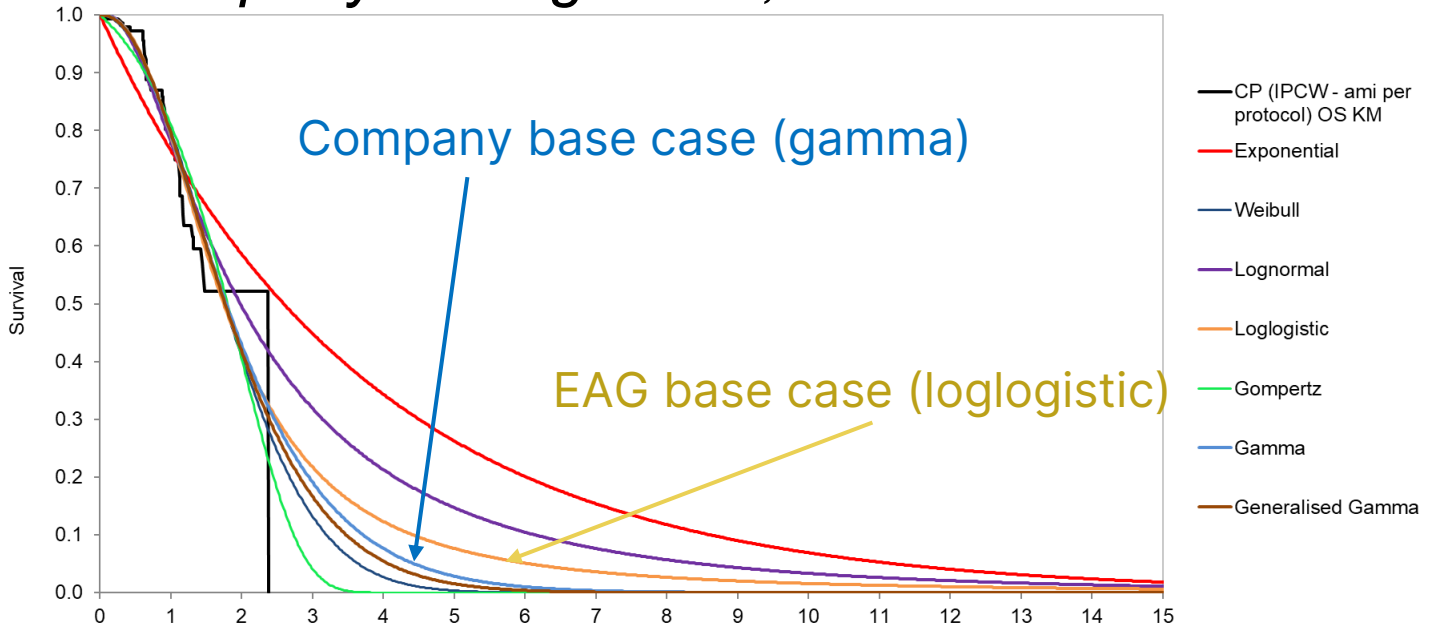
Abbreviations OS; overall survival

Key Issue: OS extrapolation: chemotherapy

ICER Impact: Large

Company uses gamma, EAG considers it underestimates and uses log-logistic



- **Company** gamma distribution based on clinical plausibility and fit to observed data
- **EAG**: gamma underestimates OS. Adopted log-logistic as EAG think it is better aligned with company advisory board pre-meeting questionnaire and EAG expert opinion.

*More information on expert opinion on chemotherapy survival estimates

Source	Median OS	3-year	5-year	10-year
Gamma (best match to advisory board consensus)	21.4	19.3%	2.9%	0.01%
Weibull [TSE*] (Company advisory board consensus)	23	21.9%	2.4%	0.0%
Company advisory board pre-meeting questionnaire	-	35% (30-40)	10%	1%
Log-logistic	21.0	21.9%	7.7%	1.6%
EAG expert		20%	5%	<1%

Which distribution should be used to extrapolate chemotherapy OS?

Abbreviations OS; overall survival

Key issue: Alternative modelling of OS- both arms

ICER Impact: Large

Recap: (see DG section 3.9)

Committee recalled TSD14 states fitting different models allows for differently shaped distributions and strong evidence is required to justify this approach.

Requested to see:

- Justification for different curves applied to different treatment arms
- Scenarios using the same curves for both arms
- Exploration of the long-term effect of treatment with amivantamab-chemotherapy

Company

- OS curves for ami-chemo (weibull) and chemotherapy (gamma) similarly shaped meaning similar risk of death over time. This mitigates risk identified in TSD14 posed by very differently shaped distributions
- Provided additional scenarios using the same models for both treatments, all of these scenarios reduced the ICER compared to the company base case.
- Explored 2 different methods for alternative modelling of long term survival benefit:
  - Using fixed (from 2.8 years) implied hazard ratio for amivantamab chemotherapy OS vs chemotherapy
  - Applying the per cycle hazard ratio between the OS and PFS of chemotherapy to the PFS of ami-chemo

EAG

- Used different distributions for OS for both treatments. Did not consider OS extrapolations using the same distributions consistent with expert opinion

What distributions should be used to extrapolate OS in each arm?

Back to key issue slide

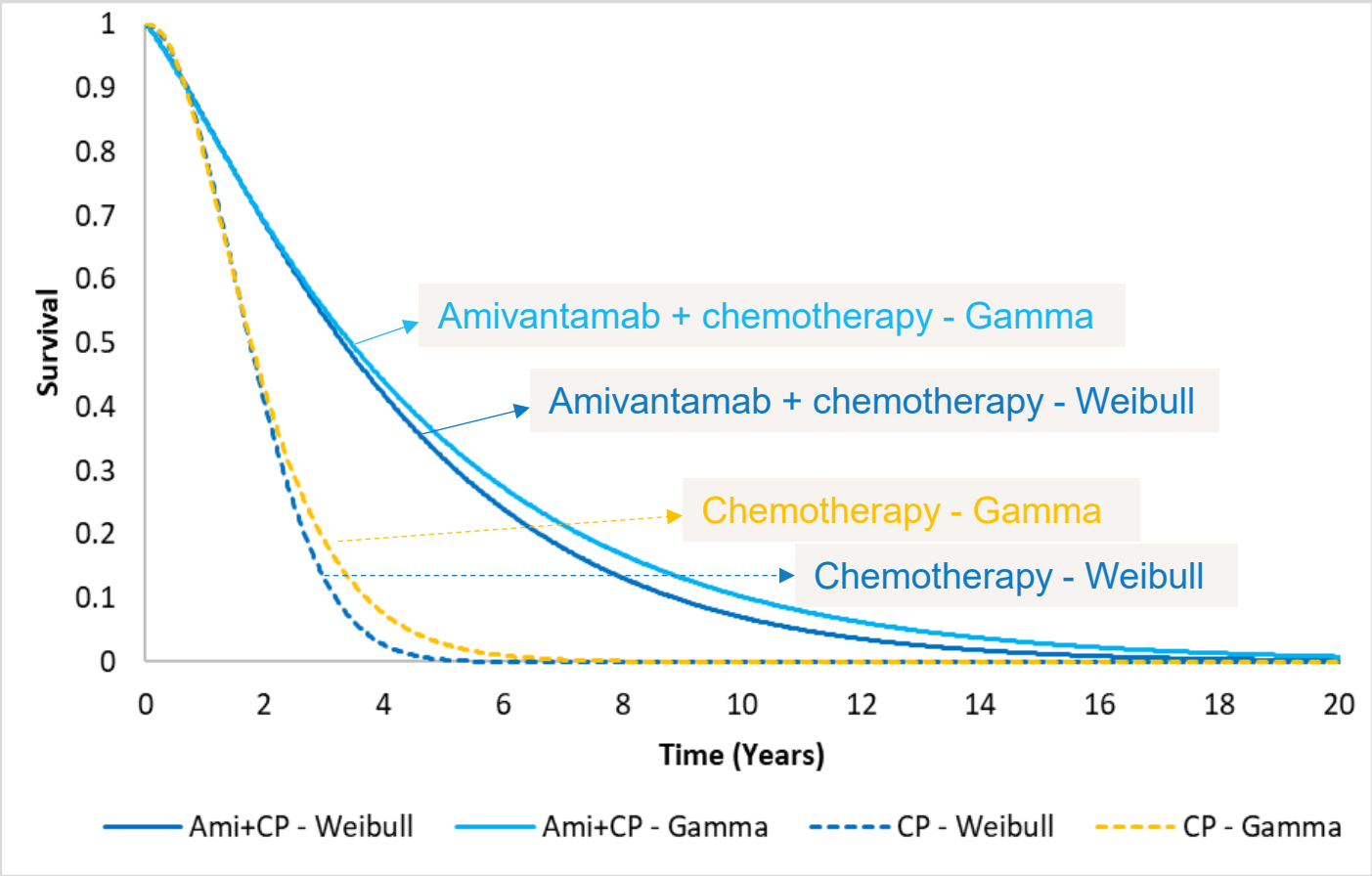
Abbreviations: OS; overall survival, PFS; progression free survival

ICER Impact: Large

Key Issue: Company OS extrapolation: chemotherapy

Company considers different curves used have similar shapes and hazard profiles

OS extrapolations for the Weibull and Gamma curves for amivantamab with chemotherapy and chemotherapy



Company: acknowledge TSD 14 recommends fitting same parametric models to all treatments, would like to highlight that, although different, the OS extrapolations selected in the company base-case are similar.

In company base-case, risk of death over time evolves in very similar way for both amivantamab with chemotherapy and chemotherapy. This mitigates the risk that "very differently shaped distributions" chosen

See supplementary appendix: IPCW adjusted data

What distributions should be used to extrapolate OS in each arm?

Abbreviations OS; overall survival

Key issue: Ami-chemo effect waning and post-progression benefit

ICER Impact: Potentially large

Recap (**see DG section 3.10**) - **Committee requested to see:**

- Exploration of the implied hazard ratio for OS referencing treatment-effect waning
- Exploration of treatment-effect waning, either modelled implicitly within OS curve selection or using an explicit modelling mechanism

Company

- PAPILLON smoothed hazard ratio does not indicate any treatment effect waning inside 28 months
- Inappropriate to model treatment effect waning given short time on treatment. Any waning implicitly captured in company base case extrapolations. (implied hazard ratio increases very gradually after 5 years)
- TA850 committee concluded appropriate to exclude modelling of treatment effect waning based on limited effect of treatment effect waning scenarios in that appraisal
- Long term survival benefit has been demonstrated in other indications
- In CHRYSALLIS (TA850 trial in heavily pre-treated population) median OS with amivantamab monotherapy was 23 months. Reasonable to expect greater OS in 1L setting, base case predicts [redacted] months median OS

EAG

- Assumption of no explicit effect waning uncertain, it would have been informative to explore this.
- Even if there was a residual treatment effect after discontinuation, magnitude and duration largely uncertain

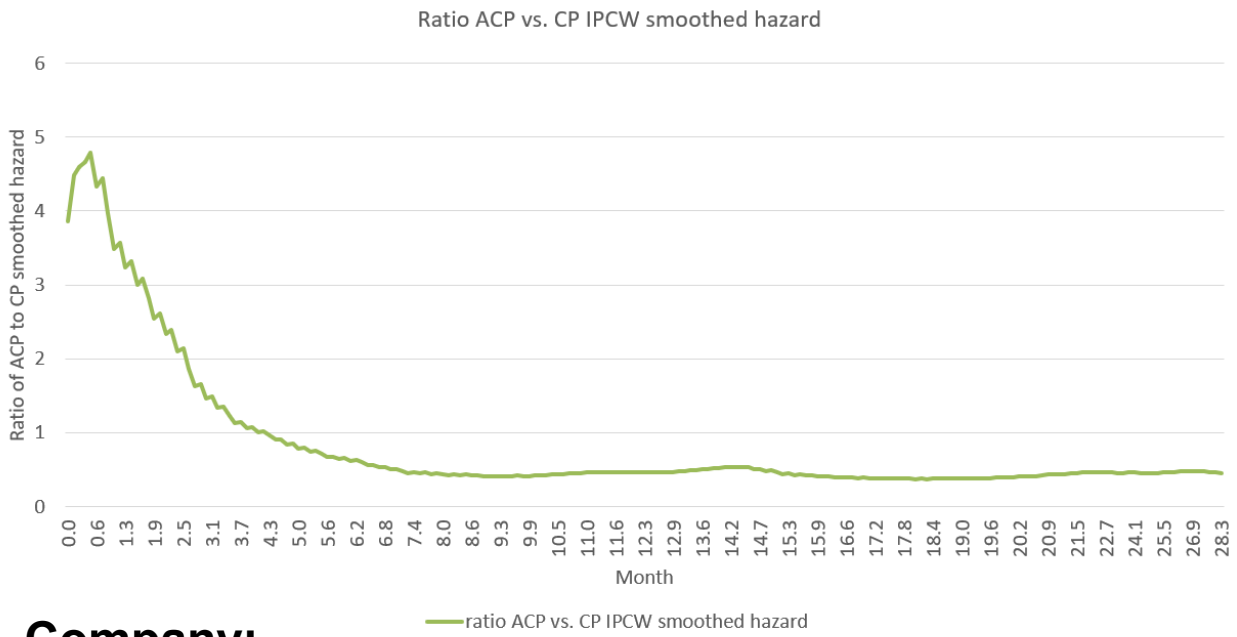
Is any specific modelling of treatment effect waning required in the model?

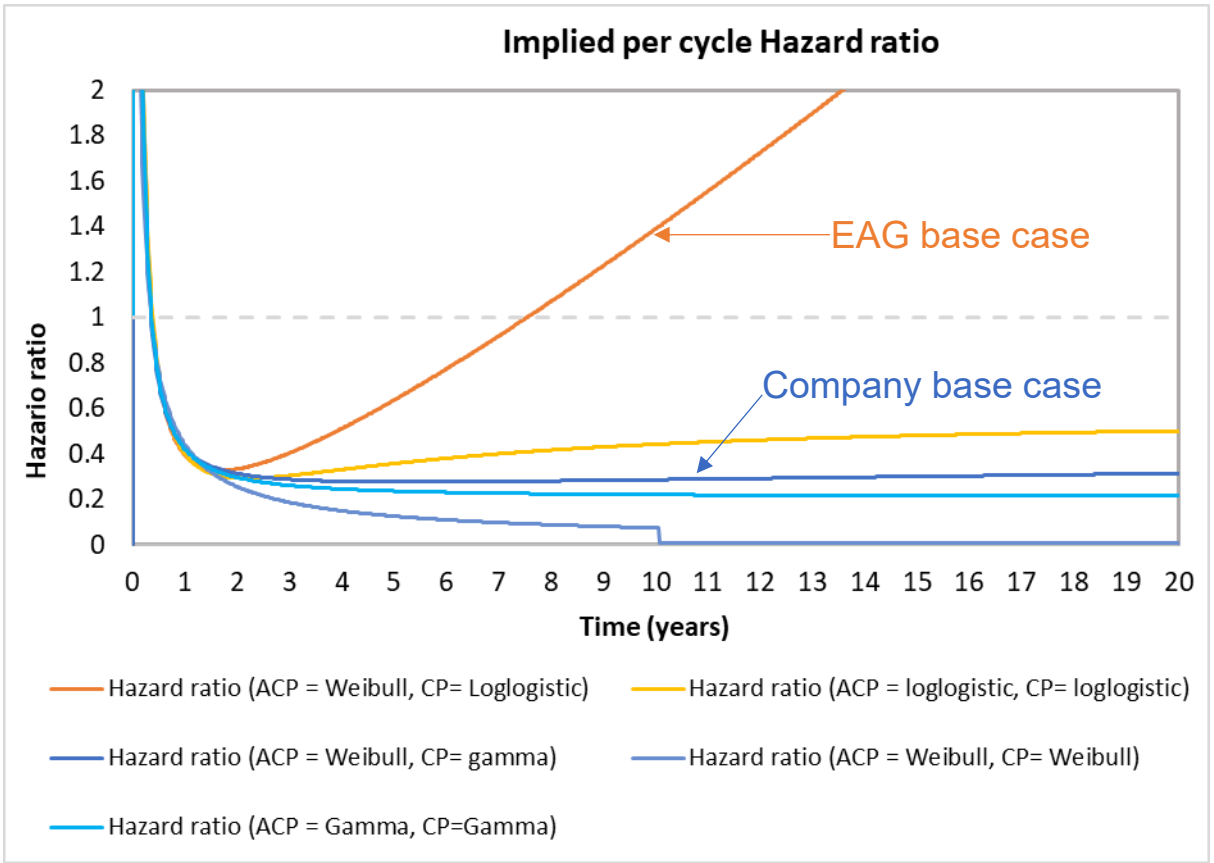
Back to key issue slide

Abbreviations OS; overall survival; 1L, first line

Key issue: Ami-chemo effect waning and post-progression benefit

ICER Impact: Large





Company:

- Smoothed HR from PAPILLON falls below 1 and does not rise above 1 or indicate an upwards trend
- Supported by biological rationale, amivantamab uses MET receptor degradation, inhibition of ligand binding and immune cell recruitment in parallel to achieve prolonged tumour inhibition

Is any specific modelling of treatment effect waning required in the model?

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Abbreviations: HR; hazard ratios, ACP; amivantamab with chemotherapy, CP; chemotherapy, IPCW; inverse probability of censoring weighting

Key Issue: Utility values and dose skipping

ICER Impact: Small

Utility values

- At ACM1 EAG noted missing data from both health states, with substantial missing from the progressed-disease health state. If data not missing at random then utility values might not be accurate
- Committee concluded that utility values from other NSCLC appraisals should be used
- Company response states there is sufficient data to conclude that missingness was random, reducing the risk that trial utility values are not accurate
- no empirical evidence that data was missing at random but both arms had similar degrees of missingness and no discernible pattern over cycles 0 to 27.
- EAG did not find supporting evidence for the statement "*missingness was not associated with any prognostic baseline characteristic*"

Dose skipping

- Committee concluded it would like to see dose skipping modelled from first and subsequent cycles in PAPILLON with scenarios to model:
  1. cycle specific dose skipping (Cycle 1 and subsequent cycles separated)
  2. exploring no dose skipping across both treatment arms
  3. equal dose skipping across all treatments and arms
- Company retain base case but provide scenarios 1 and 2: minimal effect on ICER compared to base case.
- Considered no dose skipping and scenarios inappropriate
- EAG consider company scenario sufficient to address committee request

NICE Supplementary appendix: PAPILLON dose skipping data

Abbreviations: NSCLC: non small cell lung cancer , ICER: incremental cost effectiveness ratio

Other Issue: Costs of amivantamab administration

ICER Impact: Large

Inappropriate HRG codes might be used in the base cases

Background

- Company apply SB12Z (30-60 minutes chair time) for amivantamab with pemetrexed (post carboplatin)
- Summary of product characteristics for amivantamab suggestes an infusion time of ≥2 hours
- In ID6256 CDF lead gave HRG codes verified by NHSE clinical pharmacist. Committee concluded:
  - Day case costs should be used for decision making (not outpatient costs)
  - SB14Z (day 1 doses) and 15Z (day 2 & 8 doses) should be used in the induction phase and SB13Z after

HRG code	Definition	NHS Reference cost	NHS Payment Scheme
SB12Z	Simple parenteral chemotherapy	OP: £133, DC: £418	£182
SB13Z	More complex parenteral chemotherapy	OP: £184, DC: £528	£365
SB14Z	Complex chemotherapy, including prolonged infusional treatment	OP: £337, DC: £570	£547
SB15Z	Subsequent elements of a chemotherapy cycle	OP: £198, DC: £426	£365

Which administration costs should be applied to amivantamab?

Abbreviations: HRG; healthcare resource group, CDF; cancer drugs fund, IV; intravenous; OP, outpatient; DC, day case

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ✓ **Other considerations**
- ❑ Summary

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Managed access

Criteria for a managed access recommendation

Recap: (see DG section 3.11)
The committee concluded that it was unable to establish a plausible approach for extrapolating OS. It needed additional evidence including: Exploring the value of more mature OS data from the PAPILLON trial (for example, through a period of managed access, if the criteria for managed access were fulfilled)

The committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to **5 years**) without **undue burden**.

"Johnson & Johnson consider that the clinical and economic evidence is sufficiently robust to support routine NHS commissioning of amivantamab in combination with carboplatin and pemetrexed… However, Johnson & Johnson are open to discuss the potential for managed access with the NICE committee if needed."

Additional OS data will be available from the final OS analysis of the Phase 3 PAPILLON study [redacted]

NICE Abbreviations: OS; overall survival

QALY weightings for severity (2/2)

Company

- QALY shortfall analysis indicates that amivantamab is eligible for a 1.2x severity modifier
- Criteria are met when considering the total discounted QALYs calculated for people in the NCRAS dataset (England-specific RWE)

EAG comments

- No concerns regarding the QALY shortfall analysis, agree that 1.2x severity modifier is appropriate for both company and EAG base cases and regardless of the comparator selected

	QALYs of people without condition (57.8% female, 59.6 years old)	QALYs with the condition on current treatment	**Absolute QALY shortfall (has to be >12)**	**Proportional QALY shortfall (has to be >0.85)**
Company base case	12.58	[redacted]	[redacted]	[redacted]

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Abbreviations: QALY; quality adjusted life year, NCRAS; national cancer registry and analysis service, RWE; real world evidence

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer

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Cost-effectiveness results:

- Cost effectiveness results cannot be reported here because of confidential discounts for included technologies
- Company base case ICER is above £30,000 per QALY gained
- EAG base case ICER is above £30,000 per QALY gained
- All results are presented in Part 2 slides for committee

Abbreviations: ICER; incremental cost effectiveness ratio, QALY; quality adjusted life year

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer

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- ✓ **Summary**

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Equality considerations

Committee conclusion at ACM1:

- No equalities issues identified which can be addressed in a technology appraisal

No equalities issues were identified in the draft guidance consultation.

Summary of base case assumptions at ACM2

Assumption	Committee preference at ACM1	Company base case ACM2	EAG base case ACM2
Amivantamab-chemotherapy OS	Additional analysis needed between gompertz and weibull	Weibull	Weibull (consider this uncertain)
Chemotherapy OS	Additional analysis needed	Gamma distribution	Log logistic
Amivantamab TTDD (for amivantamab-chemotherapy)	Weibull	Weibull	Weibull
Chemotherapy TTDD (for amivantamab-chemotherapy)	Weibull	Weibull	Weibull
AE unit costs	Use of most severe AE unit costs for non-elective short stay	Use of most severe AE unit costs for non-elective short stay	Use of most severe AE unit costs for non-elective short stay

Abbreviations: OS; overall survival, PFS; progression free survival, TTDD; time to treatment discontinuation or death, AE; adverse event

Key issues

Key issue for discussion	Resolved?	ICER impact
Plausibility of extrapolated benefits	No – for discussion	Unknown
Extrapolation of longer term OS	No – for discussion	Large
Treatment effect waning	No – for discussion	Unknown

Other issues

Key issue for discussion	Resolved?	ICER impact
Utilities and dose skipping	Partially	Small

Abbreviations: OS; overall survival, ICER; incremental cost effectiveness ratio

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer

Supplementary appendix

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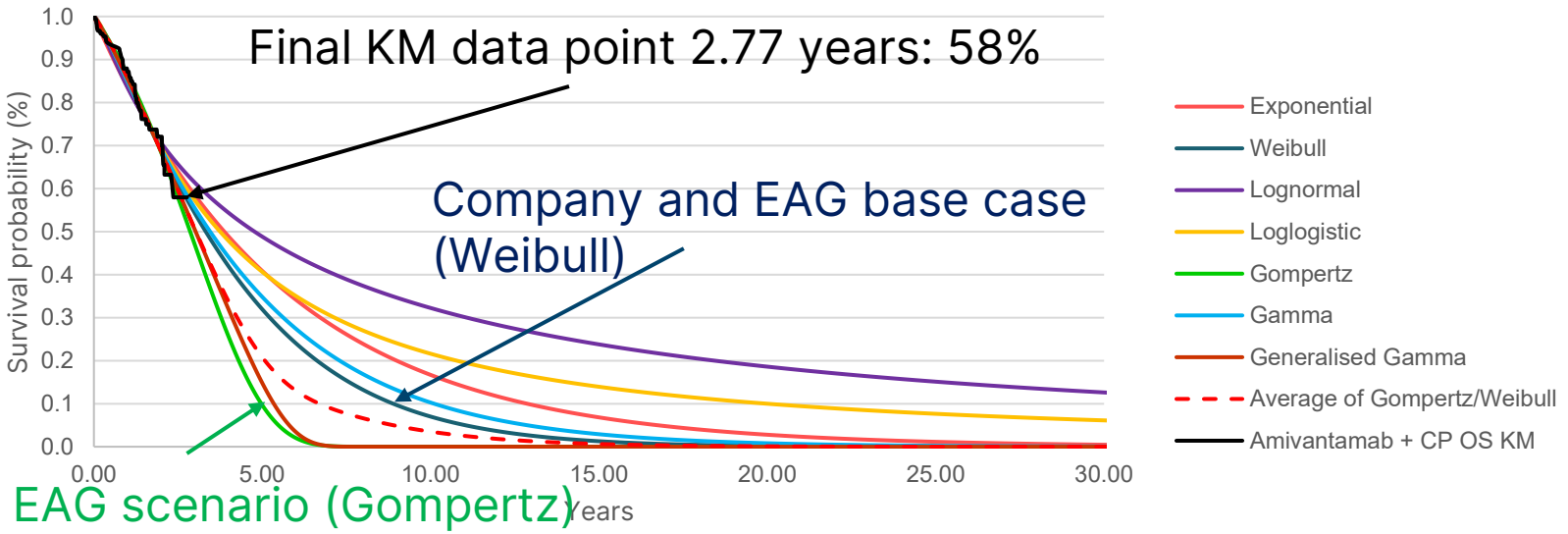
ICER Impact: Large

Back to key issue slide

Additional info: OS extrapolation: ami-chemo

Committee explicitly requested exploration of curves between Gompertz and Weibull



Recap: (see DG section 3.9) – "The committee concluded that it was unable to establish a plausible approach for extrapolating OS. It needed additional evidence including: Exploring OS curves for amivantamab-chemotherapy that might give estimates of OS between those of the Gompertz and Weibull distributions"

Source	Median OS	3-year	5-year	10-year
Weibull (Company advisory board consensus)	39.8	54.4%	32.1%	7.0%
Gompertz (EAG scenario)	34.3	47.1%	9.9%	0.0%
Weibull/Gompertz average (illustrative only)		50.7%	21.0%	3.5%
Weibull 75% / Gompertz 25% (illustrative only)		52.6%	26.5%	5.3%
Company advisory board pre-meeting questionnaire	-	50%	27.5% (25-30)	7.5% (5-10)
EAG expert opinion	-	25-30%	10-15%	unknown

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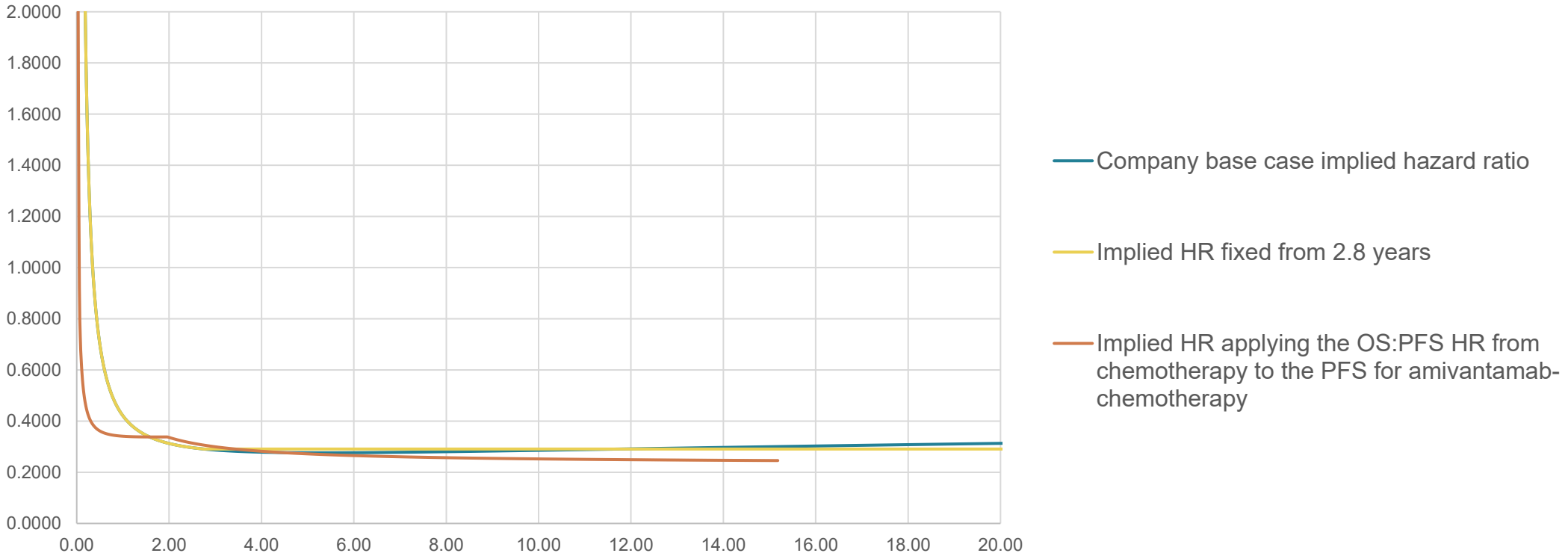
Which distribution should be used to extrapolate amivantamab plus chemotherapy OS?

Abbreviations OS; overall survival

Additional info: Scenarios exploring implied OS HR

Company submitted 2 scenarios exploring the implied HR for long term OS

1. Using fixed (from 2.8 years) implied hazard ratio for amivantamab chemotherapy OS vs chemotherapy (HR = 0.29)
2. Applying the per cycle hazard ratio between the OS and PFS of chemotherapy to the PFS of ami-chemo



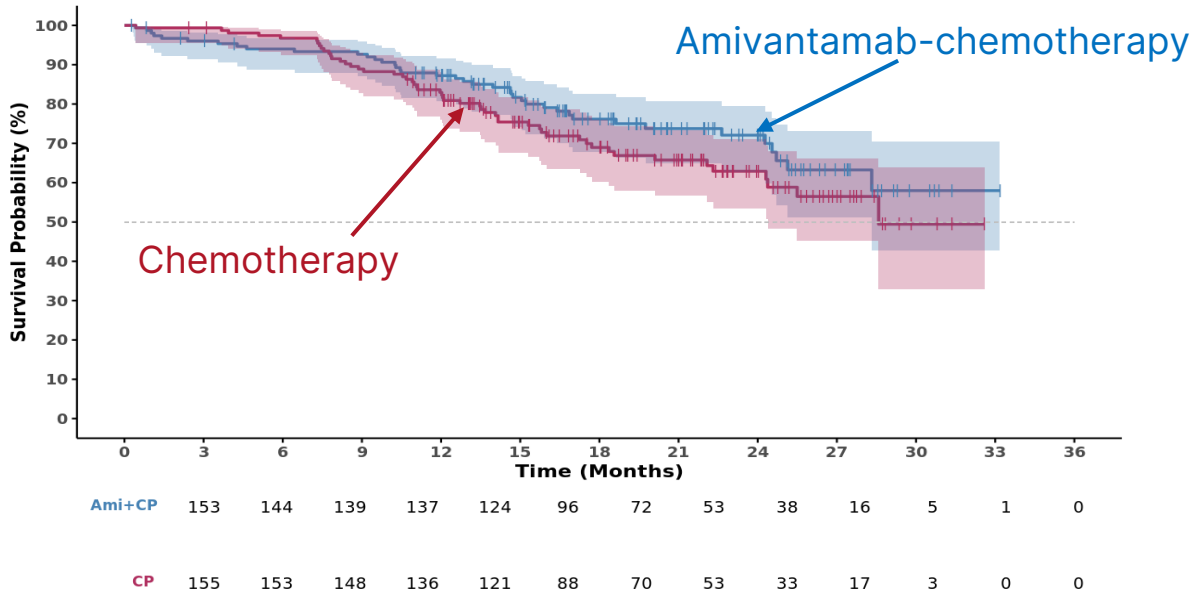
Abbreviations: OS; overall survival, HR; hazard ratio, PFS; progression free survival

Additional info: Plausibility of extrapolated benefits

Company argument to support majority of gains in PD health state

Treatment	Median OS (months)	Median PFS (months)	Ratio
Chemotherapy	[redacted] (IPCW adjusted)	6.7	[redacted]
Amivantamab-chemotherapy	Not reached after 20.9 months median follow up	11.37	?

Amivantamab-chemotherapy vs chemotherapy OS (Oct 2023 DCO)



Company

- Post progression benefit seen clearly in the chemotherapy arm of PAPILLON
- Median OS not yet reached in ami-chemo arm however likely it will exceed the ratio for chemotherapy
- This supports the idea of a post-progression benefit for ami-chemo

Are the results of the modelling plausible?

Back to key issue slide

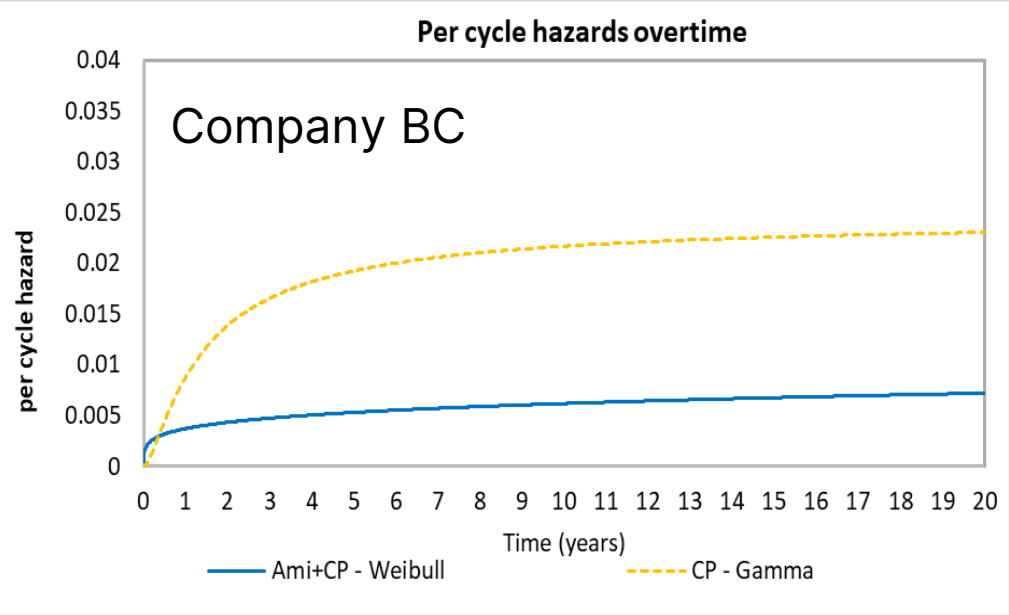
Abbreviations: IPCW; inverse probability of censoring weighting, CP; chemotherapy, ACP; Amivantamab with chemotherapy, TSE; two stage elimination

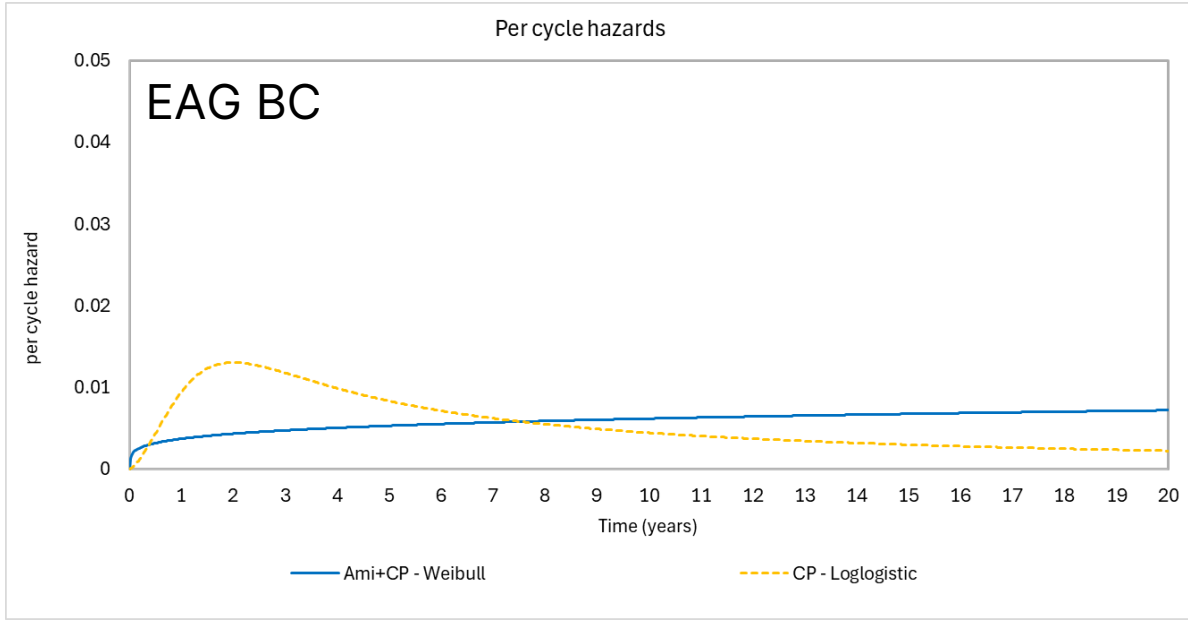
Additional info: Extrapolation of longer-term OS

Company rationale for selecting gamma for chemotherapy

Extrapolation	Treatment switching adjustment	3 year	5 year	10 year
Weibull	TSE	22%	2%	0%
Gamma	IPCW	19%	3%	0%

- At time of August 2024 advisory board, TSE was preferred method of switching adjustment.
- Advisory board consensus was Weibull was the most appropriate to fit to the TSE adjusted OS
- Company later selected IPCW as the preferred method of treatment switching
- Gamma distribution fitted to IPCW adjusted most closely aligned with the advisory board consensus

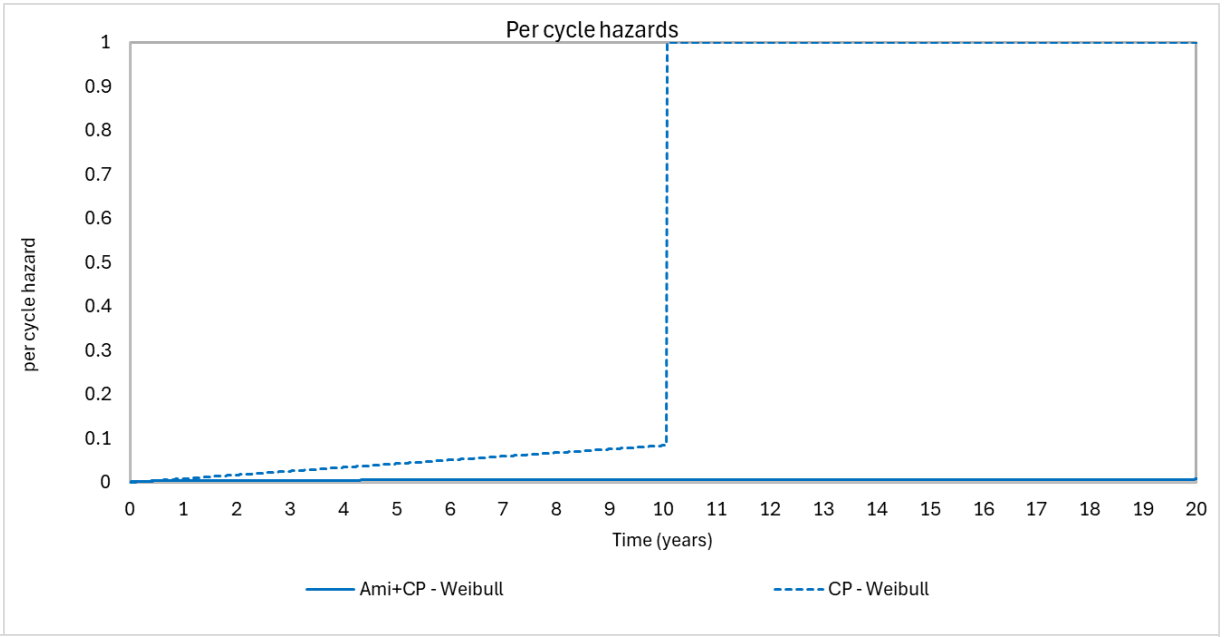


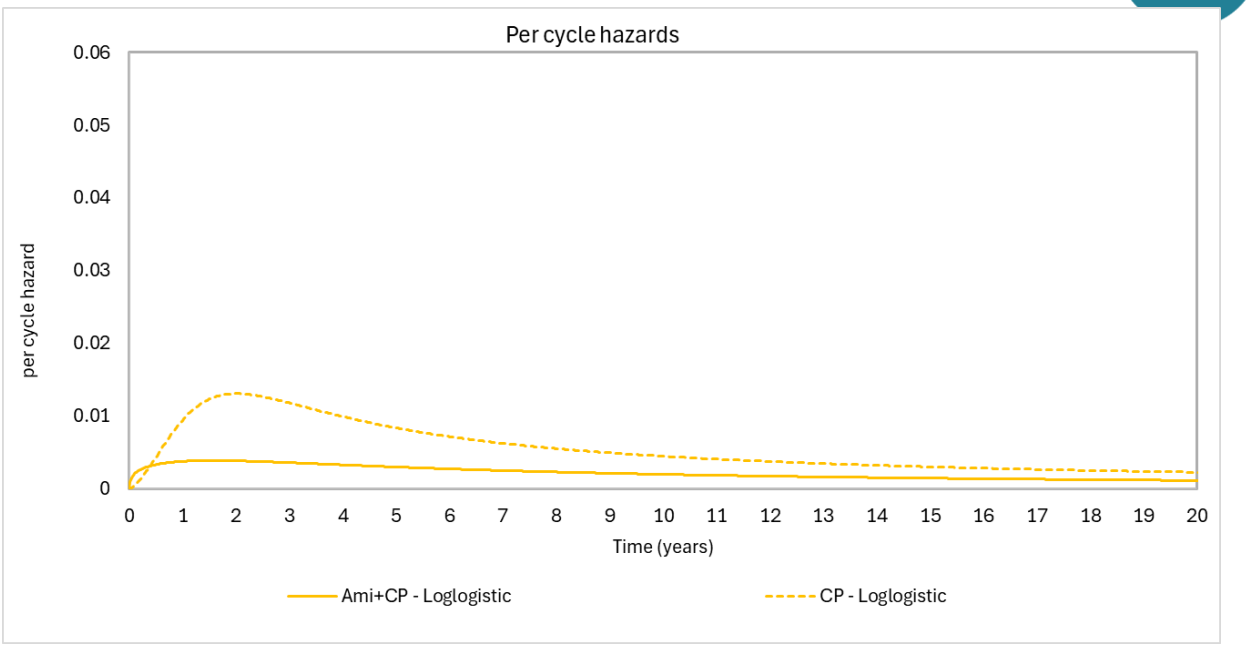


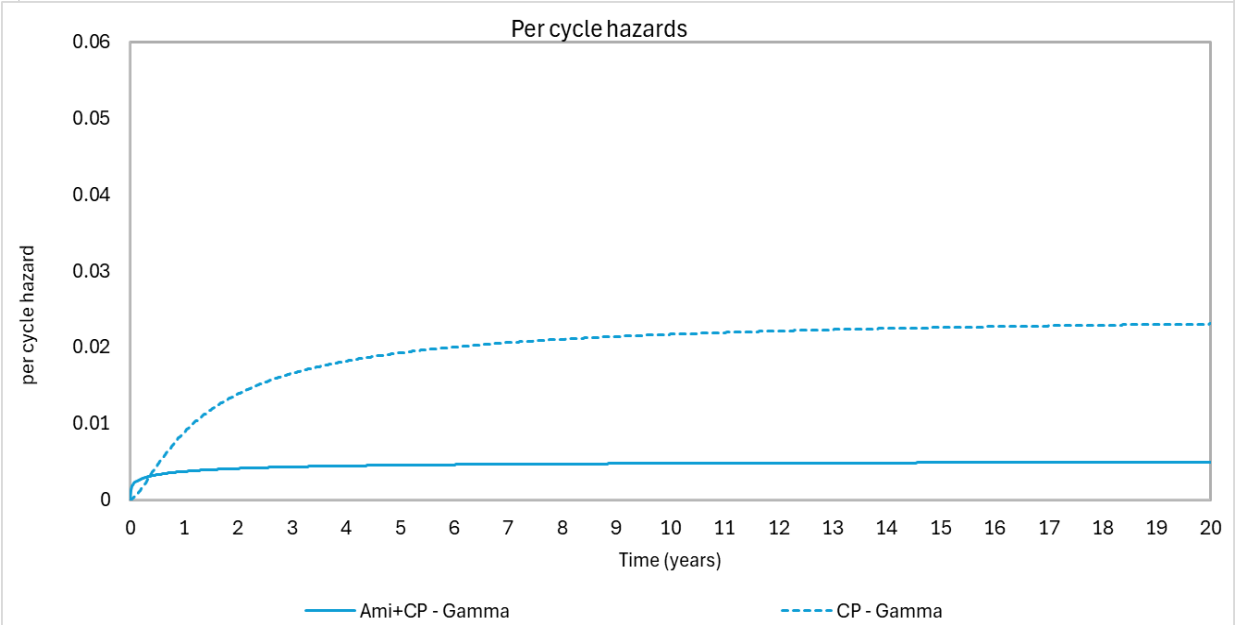
Back to key issue slide

Abbreviations: OS; overall survival, IPCW; inverse probability of censoring weighting, CP; chemotherapy, ACP; Amivantamab with chemotherapy, TSE; two stage elimination

Additional info: Exploration of alternative modelling of OS







Abbreviations: OS: overall survival, CP: chemotherapy, ACP: Amivantamab with chemotherapy

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Dose skipping data for the first and subsequent cycles of amivantamab-chemotherapy arm of PAPILLON trial

Scenario

Component	Dose skipping all cycles (Company BC)	Dose skipping Week 1 cycle	Dose skipping subsequent cycles
Amivantamab <80kg	[redacted]	[redacted]	[redacted]
Amivantamab >80kg	[redacted]	[redacted]	[redacted]
Pemetrexed	[redacted]	[redacted]	[redacted]
Carboplatin	[redacted]	[redacted]	[redacted]

Abbreviations: BC, base case

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Dose skipping data for the first and subsequent cycles of chemotherapy arm of PAPILLON trial

Chemotherapy				
Number of patients	155			
	Doses given	Doses expected	Doses missed	% missed
Pemetrexed				
Cycle 1	[redacted]	155	[redacted]	[redacted]
Cycles 2+	[redacted]	1706	[redacted]	[redacted]
Carboplatin				
Cycle 1	[redacted]	155	[redacted]	[redacted]
Cycles 2+	[redacted]	456	[redacted]	[redacted]

Key issue: Utility Values

Patient level data for the degree of missingness against key events

[redacted]

Health state	Utility value
Progression free	[redacted]
Progressed disease	[redacted] 0.713 scenario (TA850, PF)

Abbreviations: CP; chemotherapy

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Additional info: Administration costs for amivantamab

EAG concerned that administration costs for amivantamab in the model may be underestimated

Table - Chemotherapy delivery HRGs

HRG code	Definition	Explanation	NHS Reference cost	NHS Payment scheme
SB12Z	Deliver simple parenteral chemotherapy	Overall time of 30min nurse time and 30 to 60min chair time for the delivery of a complete cycle.	OP: £133 DC: £418	£182
SB13Z	Deliver more complex parenteral chemotherapy	Overall time of 60min nurse time and up to 120 min chair time for the delivery of a complete cycle.	OP: £184 DC: £528	£365
SB14Z	Deliver complex chemotherapy, including prolonged infusional treatment	Overall time of 60min nurse time and over two hours chair time for the delivery of a complete cycle.	OP: £337 DC: £570	£547
SB15Z	Deliver subsequent elements of a chemotherapy cycle	Delivery of any pattern of outpatient chemotherapy regimen, other than the first attendance, for example day 8 of a day 1 and 8 regimen	OP: £198 DC: £426	£365
SB17Z	Deliver chemotherapy for regimens not on the National List	Delivering chemotherapy regimens not included on the National List. All prices negotiated locally.	OP: £287 DC: £496	N/A

Abbreviations: DC, day-case; HRG, Healthcare Resource Group, OP, out-patient

Recap – Committee's key conclusions from ACM1

Amivantamab should not be used

Key Issue	Committee's preferred assumptions (accepted in updated company base case)
Population	• Recommendation applied to non-squamous histology only (section 3.2)
Comparator	• Use chemotherapy as the only comparator (section 3.4)
TTDD	• Weibull extrapolations for Amivantamab-chemotherapy (section 3.6)
Vial sharing	• No vial sharing in cost effectiveness modelling
Adverse events	• Cost codes for most severe AEs only (non-elective stay)

Key areas of uncertainty

Key Issue	Uncertainty
Overall Survival	• OS extrapolations in both arms and appropriate parametric models (section 3.8)
Overall Survival	• Immaturity of OS data from PAPILLON trial (section 3.8)
Dose Skipping	• Appropriate rate of dose skipping and modelling across time horizon (section 3.18)
Utility Values	• Estimates of health state utility linked to missing data (section 3.13)

Abbreviations: TTDD; time to treatment discontinuation or death, AE; adverse event, OS; overall survival

Amivantamab (Rybrevant, Johnson & Johnson)

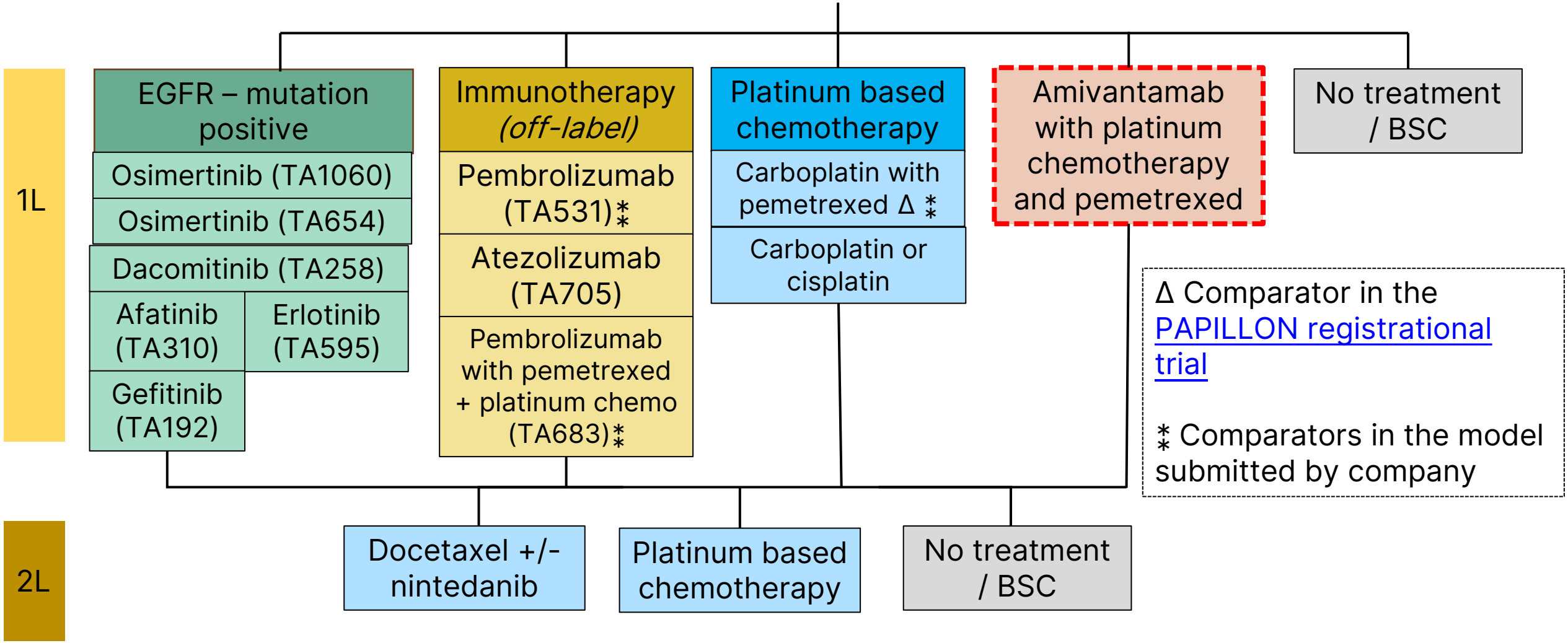
Amivantamab offered until progression (post-progression use allowed in trial)

Marketing authorisation	• In combination with carboplatin and pemetrexed for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) Exon 20 insertion mutations • UK MA granted July 2024
Mechanism of action	• Binds EGFR and MET receptors to disrupt signalling functions • This enhances degradation of EGFR and MET, reducing tumour growth and progression
Duration of treatment	• Amivantamab 'until disease progression or unacceptable toxicity' • Pemetrexed to disease progression • Platinum based chemotherapy every 3 weeks for up to 12 weeks
Administration	• Intravenous infusion • Dosage (body weight at baseline) ➢ Less than 80kg: 1400 mg (4 vials) weekly for first 4 doses then 1750 mg every 3 weeks ➢ 80kg or above: 1750 mg weekly (5 vials) for first 4 doses then 2100 mg every 3 weeks
Price	• Amivantamab 350mg per 7ml vial • List price £1,079.00 per vial • A confidential discount is in place for amivantamab

Abbreviations: NSCLC; non small cell lung cancer, EGFR; epidermal growth factor receptor, MA; marketing authorisation, MET; MET proto-oncogene

Treatment pathway – Untreated EGFR exon20+ NSCLC

Numerous options for NSCLC and EGFR+ disease but limited options for exon20+



Abbreviations: EGFR; epidermal growth factor receptor, exon20+; exon 20 insertion mutation positive, NSCLC; non small cell lung cancer, BSC; best supportive care

Notes: 1L immunotherapy licences exclude EGFR positive NSCLC; post chemotherapy immunotherapy options not shown (e.g TA428)

Chemotherapy overall survival - IPCW- adjusted

Statistically significant improvement shown compared with chemotherapy after adjusting for treatment switching.

Scenario	Median OS (months)
EAG base case	[redacted]
Company base case	[redacted]
IPCW adjusted PAPILLON	[redacted]

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Abbreviations: IPCW; inverse probability of censoring weighting, CP; chemotherapy, ACP; Amivantamab with chemotherapy, TSE; two stage elimination