NICE National Institute for Health and Care Excellence

Single Technology Appraisal

Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer (rapid review of TA1108) [ID6685]

Committee Papers

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer (rapid review of TA1108) [ID6685]

Contents:

The following documents are made available to stakeholders:

1. **Company submission** from Regeneron

2. **External Assessment Report** prepared by Newcastle NIHR TAR Team, Newcastle University

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

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Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer

Submission for a Rapid Review of TA1108 [ID6685]

File name	Version	Contains confidential information	Date
[ID6685] Rapid review of TA1108_Cemiplimab NSCLC [CON]_28_01_2026_Final (clean)	**v1.0**	**Yes**	**28 January 2026**

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Executive summary

- This abbreviated submission is made by Regeneron in support of a Rapid Review of NICE TA1108: Cemiplimab with platinum-based chemotherapy (PBC) for untreated advanced non-small-cell lung cancer (NSCLC) (1).
- Following Company discussions with NICE after the publication of TA1108, it was agreed that the Company can pursue a Rapid Review under an assumption of "…*equal efficacy between cemiplimab and pembrolizumab*" [both in combination with PBC]…*accounting for the longer time on treatment seen in the cemiplimab trials than the pembrolizumab trials*…". It was noted that "…*the committee would accept the ratio method of median PFS* [progression free survival] *to median ToT* [time on treatment] *in both arms*" (2).
- This abbreviated submission provides the agreed analyses in a cost comparison analysis framework, demonstrating fulfilment of the Committee's preferred modelling assumptions.
- As pembrolizumab is made available to the NHS in England and Wales at a confidential PAS price discount, the model results demonstrate illustrative PAS price discounts for cemiplimab to be cost equivalent to pembrolizumab.
- **The Company reiterates its previously stated aim to provide cemiplimab in this NSCLC indication at a price to the NHS that is net cost saving in the context of the current confidential PAS price in place for pembrolizumab.**
- In addition to achieving equal efficacy at a lower net cost, there is additional value for cemiplimab related to its added flexibility in accompanying chemotherapy regimens, which is not captured in the cost comparison analyses. In contrast to pembrolizumab, which is licensed for use only in metastatic disease (3), cemiplimab is licensed for use in both metastatic and locally advanced disease (4).
- The evidence provided in this abbreviated submission should provide a sufficient basis for the Company to be permitted to enter into commercial discussions with NHS England.
- To avoid further delays in NSCLC patients accessing cemiplimab, the Company respectfully requests the Rapid Review process is completed as soon as possible.

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Background

- This abbreviated submission is made by Regeneron in support of a Rapid Review of NICE TA1108: Cemiplimab with platinum-based chemotherapy (PBC) for untreated advanced non-small-cell lung cancer (NSCLC) (1).
- Following a full submission by the Company, which compared cemiplimab + PBC versus pembrolizumab + PBC using cost utility and (under an assumption of equal efficacy) cost comparison analyses, the NICE committee for TA1108 concluded that cemiplimab could not be recommended in this indication due to perceived uncertainties in comparative effectiveness and the economic model (1).
- Following further discussions with NICE, it has been agreed that the Company can pursue a Rapid Review of TA1108 under an assumption of "…*equal efficacy between cemiplimab and pembrolizumab*" [both in combination with PBC] and "…*accounting for the longer time on treatment seen in the cemiplimab trials than the pembrolizumab trials*…". To this end, "…*the committee would accept the ratio method of median PFS* [progression free survival] *to median ToT* [time on treatment] *in both arms*" (2).
- This abbreviated submission provides the agreed analyses in a cost comparison analysis framework, with the aim of demonstrating fulfilment of the Committee's preferred assumptions and forming a basis for commercial discussions between the Company and NHS England.
- This abbreviated submission is intended to be read in conjunction with the full submission made by the Company for TA1108 for details of the clinical effectiveness evidence for cemiplimab in this indication and the economic model, which is used to conduct the agreed analyses and with which the EAG and Committee are already familiar.

Methods

- Under an agreed assumption of equal efficacy and accounting for the agreed assumption of differential time on treatment, cost comparison analyses have been conducted to determine the PAS price discount required for cemiplimab to be cost equivalent to pembrolizumab.
- As pembrolizumab is made available to the NHS in England and Wales under a PAS, which includes a confidential discount on its list price, the analyses are provided

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using example pembrolizumab discounted prices (discounts of 65% to 70% to its list price).

- The analyses have been conducted using the economic model submitted by the Company in TA1108. A summary of key features of the model and assumptions employed to conduct the agreed analyses is provided in Table 1.

Table 1. Key features and assumptions of the analyses

Assumption / Parameter	Value	Justification / Source
Overall survival & progression-free survival	Assumed equivalence between cemiplimab + chemotherapy and pembrolizumab + chemotherapy.	This was the agreed assumption of the NICE Committee subsequent to the publication of TA1108 final guidance (2). This aligns with UK clinical expert opinion, and international HTA precedent where the focus has been on comparing treatment costs in the absence of evidence of meaningful differences in effectiveness between cemiplimab and the relevant comparator (PBAC [Australia] (5), CADTH [Canada] (6)), as outlined in the original CS. Survival analyses used data from EMPOWER-Lung 3 – June 2022 data cut-off, which represented approximately 28 months of follow up (7), per the original CS and model*. These data were applied to the pembrolizumab arm to ensure equivalence.
Time on treatment	HR applied to PFS curves to estimate a separate ToT curve, using ratio of median TTD and median PFS data from EMPOWER Lung-3 (HR 1.30) (8) for cemiplimab and KEYNOTE-189 (9) and -407 (10) trial (HR 0.84) for pembrolizumab, to reflect relative difference in ToT.	In line with assumption of the NICE committee subsequent to the publication of TA1108 final guidance. HR for pembrolizumab (0.84) as estimated in the original CS for TA1108. HR for cemiplimab (1.30) estimated from the ratio of median TTD ([redacted] weeks) : median PFS (36.09 weeks) observed in the EMPOWER Lung-3 trial at the 5-year follow-up (6) to align with the KEYNOTE data follow-up (9,10). An alternative scenario using more robust Cox model analysis of 2-year IPD from EMPOWER-Lung 3 to estimate the HR for cemiplimab (1.17) is provided, aligned with methods used in the original CS.
Treatment waning effect	5-years from treatment initiation, with waning applied from 3-years.	To align with the TA1108 committee's preference for gradual waning of treatment effect for both arms. The discrete hazards over time from the model compared to hazards from KEYNOTE-189 and KEYNOTE-407 suggest that waning of cemiplimab + chemotherapy and pembrolizumab + chemotherapy hazards to chemotherapy hazards from 24-60 months is a conservative assumption compared to KEYNOTE-189 and KEYNOTE-407 data, which show hazards decreasing up to the end of a 5-year follow-up for PFS and OS.
Stopping rule	36-doses of cemiplimab, equivalent to 108-weeks. 18/35-doses of pembrolizumab (Q6W/Q3W).	To align with the agreed consensus during TA1108 committee discussions. This accurately reflects the rules in clinical practice for pembrolizumab (35 cycles) and to align with the EMPOWER-Lung 3 trial for cemiplimab.

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Assumption / Parameter	Value	Justification / Source
Subsequent treatment	Subsequent treatments assumed to be equal following disease progression.	To align with the assumption of equivalent clinical efficacy. Alternative scenarios accounting for trial-observed differences in subsequent IO use are provided given the differential in ToT with pembrolizumab and cemiplimab.
Adverse event rates	Grade 3 and above adverse event rates from EMPOWER-Lung 3 assumed across both cemiplimab and pembrolizumab arms.	To align with the assumption of equivalent clinical effectiveness.
Time horizon and discounting	30 years (lifetime) time horizon and discount rate 3.5%, per the model in the original CS.	Per original model in CS, in line with NICE reference case. An alternative scenario using a 5-year time horizon aligned with the maximum follow up of the EMPOWER Lung-3 (9) and KEYNOTE-189 and -407 trials (9,10) is also provided to explore the impact of a shorter time horizon on the model results.
Abbreviations: CS, company submission; DOR, duration of response; HR, hazard ratio; IPD, individual patient data; ORR, overall response rate; OS, overall survival; PFS, progression free survival; Q3W, every 3 weeks; Q6W, every 6 weeks; ToT time on treatment *5 year data from EMPOWER Lung-3 have been presented at World Conference on Lung Cancer, 6-9 September 2025 (8), and are highly consistent with the OS, PFS, ORR, DOR and safety data presented in the original CS. As the same data are used for both the cemiplimab and pembrolizumab arms of the model, the cemiplimab survival curves from the model in the original CS are retained.		

- NHS England has agreed in principle (05 Jan 2026 (11)) that cemiplimab in this NSCLC indication fulfils its criteria for consideration of an indication-specific PAS discount price. Analyses have been conducted to determine an indication-specific PAS discount at which cemiplimab + PBC would be cost equivalent versus pembrolizumab + PBC.
- The base case assumes equivalent subsequent therapy following disease progression. As time on treatment is modelled to differ and observed receipt of post progression immunotherapy differed between the EMPOWER Lung-3 trial of cemiplimab + PBC (6) and the KEYNOTE-189 and -407 trials of pembrolizumab + PBC, (9,10) scenario analyses explore plausible alternative assumptions on subsequent immunotherapy use following disease progression with cemiplimab + PBC and pembrolizumab + PBC, based on the distribution of subsequent immunotherapies observed in the 5-year follow up of the EMPOWER Lung-3 trial of cemiplimab + PBC (8) and the proportion of patients experiencing disease progression in that trial and the KEYNOTE trials of pembrolizumab + PBC (9,10).
- As requested by NICE, the base case estimates ToT in both arms of the model using a HR based on the ratio of median TTD : PFS applied to their respective PFS curves. This is a crude approach, adopted in the absence of individual patient data (IPD)

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from the KEYNOTE trials of pembrolizumab. A scenario analysis explores a more robust approach using a Cox model-based on 2-year IPD from EMPOWER-Lung 3 to estimate the HR for for ToT with cemiplimab, in line with the methodology used in the original CS for TA1108.

Results

- Table 2 provides illustrative, indication-specific PAS price discounts required for cemiplimab to be cost equivalent versus example PAS price discounts for pembrolizumab.

Table 2. Cemiplimab PAS discount required to achieve cost equivalence versus pembrolizumab in this NSCLC indication

Scenario	Pembrolizumab PAS = 65%	Pembrolizumab PAS = 70%
Base case: Equal subsequent therapies across both cemiplimab and pembrolizumab model arms. 30-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 1: Equal subsequent therapies across both cemiplimab and pembrolizumab model arms. 5-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 2: Subsequent IO using ITT values from KN and EL3 as denominator 30-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 3: Subsequent IO using only progressed pts from KN and EL3 as denominator 30-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 4: Equal subsequent therapies across both cemiplimab and pembrolizumab model arms. 30-year time horizon Cox model method to estimate HR applied to PFS for cemiplimab ToT curve, and median TTD:PFS ratio to estimate HR applied to PFS for pembrolizumab ToT curve	[redacted]	[redacted]
Abbreviations:; EL3, EMPOWER Lung-3 trial of cemiplimab + PBC; HR, hazard ratio; IO, immune-oncology therapy; ITT, intention to treat population; KN, KEYNOTE trials of pembrolizumab + PBC; PAS, Patient access scheme; PBC, platinum-based chemotherapy; ToT, time on treatment; TTD, time to discontinuation		

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- The base case assumes a 30-year time horizon, equivalent subsequent treatments following disease progression, and ToT estimated using the ratio of median TTD : median PFS in both arms. These assumptions are explored in scenario analyses:
    - Scenario analysis 1 uses a 5-year time horizon aligned with the maximum follow up of the EMPOWER Lung-3 and the KEYNOTE-189 and -407 trials,(8-10) and yields highly similar results to the base case, which demonstrates that the time horizon is not a driver of the model outputs.
    - Scenario analyses 2 and 3 demonstrate that, given the assumed much longer time on treatment modelled for cemiplimab, accounting for trial-observed differences in subsequent immunotherapies may be appropriate and would lower the PAS discount required for cemiplimab to achieve cost equivalence with pembrolizumab.
    - Scenario 4 shows that, using a more robust analysis of IPD from EMPOWER-Lung 3 to estimate ToT, the NICE-requested assumption used in the base case may overestimate ToT for cemiplimab, leading to an overestimation of the cemiplimab PAS price discount required to achieve cost equivalence versus pembrolizumab.

Discussion

- In the course of Company discussions with NICE following the negative recommendation for cemiplimab + PBC in TA1108, the Committee expressed its preferred assumptions for modelling equal efficacy of cemiplimab + PBC versus pembrolizumab + PBC (2).
- The Company believes the modelling provided in this abbreviated submission fulfils these Committee-preferred assumptions. The cost comparison analyses demonstrate the PAS price discount required for cemiplimab to be cost equivalent to pembrolizumab, taking into account the drug acquisition and administration costs associated with the longer time on treatment under these assumptions.
- Throughout the appraisal process for TA1108, the Company stated its aim to provide cemiplimab + PBC in this NSCLC indication at a price to the NHS that is net cost saving in the context of the current confidential PAS price in place for pembrolizumab. The analyses provided herein reflect illustrative cemiplimab PAS price discounts required to achieve cost equivalence versus example pembrolizumab PAS price discounts.

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- **The Company reiterates its aim to provide cemiplimab in this NSCLC indication at a price to the NHS that is net cost saving in the context of the current confidential PAS price in place for pembrolizumab.**
- The base case analysis is conservative versus the original model provided in the CS for TA1108, in assuming a much longer ToT versus pembrolizumab and not accounting for the impact this may have on subsequent treatments.
- In addition to achieving equal efficacy at a lower cost, there is additional value for cemiplimab over pembrolizumab related to its added flexibility in accompanying chemotherapy regimens compared with the current commissioning policy for pembrolizumab in this indication (12). In contrast to pembrolizumab, which is licensed in this indication only in patients with metastatic disease (3), cemiplimab is licensed and supported by trial data in patients with locally advanced as well as metastatic disease (4).
- The evidence provided in this abbreviated submission should provide a sufficient basis for the Company to be permitted to enter into commercial discussions with NHS England.
- To avoid further delays in NSCLC patients accessing cemiplimab, the Company respectfully requests the Rapid Review process is completed as soon as possible.

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Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer [ID3949]

Evidence Assessment Group Rapid Review Report

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Report reference:	Jayachandran L, Robinson T, Eastaugh C, Rice S. Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer [ID3949]. Evidence Assessment Group Rapid Review. Newcastle upon Tyne: Population Health Sciences Institute, Faculty of Medical Sciences, Newcastle University 2026
Report key:	Commercial in confidence (CiC) data are highlighted in blue throughout the report. Any de-personalised data are highlighted in pink throughout the report.

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1 Background

Following a full submission by the company (Regeneron) as part of TA1108[1] (Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer), the NICE committee for TA1108 concluded that cemiplimab could not be recommended for this indication, due to uncertainties in the economic model and the cost-effectiveness estimates being above the range normally considered an acceptable use of NHS resources.

Following discussions[2] between the company (Regeneron) and NICE following the publication of TA1108, it was agreed that the company could pursue a Rapid Review under an assumption of "…*equal efficacy between cemiplimab and pembrolizumab*" [both in combination with PBC] and "…*accounting for the longer time on treatment seen in the cemiplimab trials than the pembrolizumab trials*…". To this end, "…*the committee would accept the ratio method of median PFS* [progression free survival] *to median ToT* [time on treatment] *in both arms*".

The company subsequently submitted an abbreviated submission to NICE, along with an updated company economic model (CEM) containing the agreed analysis in a cost-comparison framework, reportedly fulfilling the Committee's preferred assumptions.

In this document, the Newcastle EAG (who authored the original EAG report for TA1108[3]) review the rapid review documentation provided by the company, including the CEM adjusted to incorporate the updated cost-comparison framework.

In a separate document, the EAG have replicated the analysis provided by the company using up to date Patient Access Scheme (PAS) prices for both cemiplimab and comparator treatments. These PAS prices are confidential so cannot be reported in this document.

2 Methods

In the Rapid Review submission, the company reported having updated the CEM to incorporate an assumption of equal efficiency, accounting for differential time on treatment between cemiplimab and pembrolizumab for this indication. Furthermore, the company provided analysis showing the PAS price discount required for cemiplimab to be cost equivalent to pembrolizumab given example discounted prices for pembrolizumab.[1]

Table 2.1 presents the company key assumptions, justifications and sources of the updated CEM within a cost comparison framework.

Table 2.1: Key assumptions in the company economic model

Assumption / Parameter	Value	Justification / Source
Overall survival & progression-free survival	Assumed equivalence between cemiplimab + chemotherapy and pembrolizumab + chemotherapy.	This was the agreed assumption of the NICE Committee subsequent to the publication of TA1108 final guidance. [2] This aligns with UK clinical expert opinion, and international HTA precedent where the focus has been on comparing treatment costs in the absence of evidence of meaningful differences in effectiveness between cemiplimab and the relevant comparator (PBAC [Australia],[4] CADTH [Canada],[5]) as outlined in the original CS. Survival analyses used data from EMPOWER-Lung 3 – June 2022 data cut-off, which represented approximately 28 months of follow up,[6] per the original CS and model*. These data were applied to the pembrolizumab arm to ensure equivalence.
Time on treatment	HR applied to PFS curves to estimate a separate ToT curve, using ratio of median TTD and median PFS data from EMPOWER Lung-3 (HR 1.30)[7] for cemiplimab and	In line with assumption of the NICE committee subsequent to the publication of TA1108 final guidance.[10] HR for pembrolizumab (0.84) as estimated in the original CS for TA1108. HR for cemiplimab (1.30) estimated from the ratio of median TTD [redacted] weeks): median PFS (36.09 weeks) observed in

Assumption / Parameter	Value	Justification / Source
	KEYNOTE-189[8] and -407[9] trial (HR 0.84) for pembrolizumab, to reflect relative difference in ToT.	the EMPOWER Lung-3 trial at the 5-year follow-up to align with the KEYNOTE data follow-up.[8,9] An alternative scenario using more robust Cox model analysis of 2-year IPD from EMPOWER-Lung 3 to estimate the HR for cemiplimab (1.17) is provided, aligned with methods used in the original CS.
Treatment waning effect	5-years from treatment initiation, with waning applied from 3-years.	To align with the TA1108 committee's preference for gradual waning of treatment effect for both arms. The discrete hazards over time from the model compared to hazards from KEYNOTE-189 and KEYNOTE-407 suggest that waning of cemiplimab + chemotherapy and pembrolizumab + chemotherapy hazards to chemotherapy hazards from 24-60 months is a conservative assumption compared to KEYNOTE-189 and KEYNOTE-407 data, which show hazards decreasing up to the end of a 5-year follow-up for PFS and OS.
Stopping rule	36-doses of cemiplimab, equivalent to 108-weeks. 18/35-doses of pembrolizumab (Q6W/Q3W).	To align with the agreed consensus during TA1108 committee discussions. This accurately reflects the rules in clinical practice for pembrolizumab (35 cycles) and to align with the EMPOWER-Lung 3 trial for cemiplimab.
Subsequent treatment	Subsequent treatments assumed to be equal following disease progression.	To align with the assumption of equivalent clinical efficacy. Alternative scenarios accounting for trial-observed differences in subsequent IO use is provided given the differential in ToT with pembrolizumab and cemiplimab.
Adverse event rates	Grade 3 and above adverse event rates from EMPOWER-Lung 3 assumed across both cemiplimab and pembrolizumab arms.	To align with the assumption of equivalent clinical effectiveness.
Time horizon and discounting	30 years (lifetime) time horizon and discount rate 3.5%, as per the model in the original CS.	As per original model in CS, in line with NICE reference case. An alternative scenario using a 5-year time horizon aligned with the maximum follow up of the EMPOWER Lung-3 and KEYNOTE-189 and -407 trials[10] is also provided to explore the impact of a

Assumption / Parameter	Value	Justification / Source
		shorter time horizon on the model results.

Source: Company RR submission, Table 1, Pg. 4-5[10]
Abbreviations: CS, company submission; DOR, duration of response; HR, hazard ratio; IPD, individual patient data; ORR, overall response rate; OS, overall survival; PFS, progression free survival; Q3W, every 3 weeks; Q6W, every 6 weeks; ToT time on treatment
*5 year data from EMPOWER Lung-3 have been presented at World Conference on Lung Cancer, 6-9 September 2025, and are highly consistent with the OS, PFS, ORR, DOR and safety data presented in the original CS. As the same data are used for both the cemiplimab and pembrolizumab arms of the model, the cemiplimab survival curves from the model in the original CS are retained.

EAG Comment: The EAG has reviewed the different parameters and assumptions in the CEM[11]and found them to be appropriate. The key parameters that have an impact on costs are discussed below.

Overall survival (OS) and progression-free survival (PFS)

The company used the survival analysis data from EMPOWER-Lung 3 trial as per the original CS submission, which had a follow-up of approximately 28 months, to model the overall survival in the cemiplimab treatment arm. [12] The same estimates were applied to the pembrolizumab treatment arm to adopt the NICE preferred assumption of an equivalence in clinical effectiveness between the two groups. The mean overall survival was 3.51 years in both the arms.[11] Similarly, the PFS modelled in the cemiplimab arm from the trial data was applied to the pembrolizumab arm, and the mean progression free survival was 1.87 years.[11]

EAG Comment: The company approach ensured that effectiveness was equal. The source of PFS data will affect the cost difference given that the ToT is related to PFS in this rapid review model.

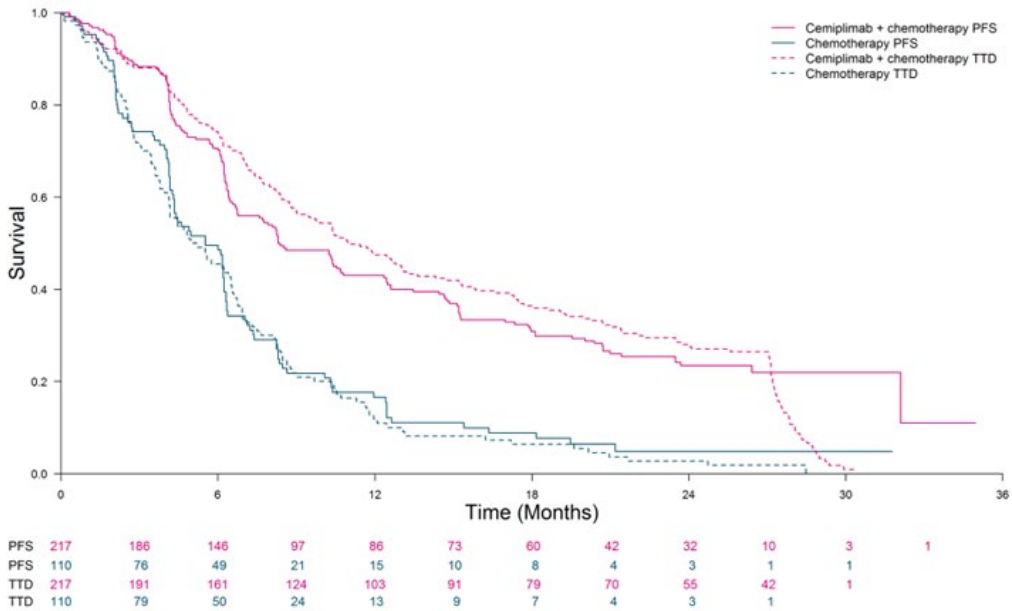
Time to treatment discontinuation (TTD)

The HRs calculated from median TTD and median PFS are applied to the PFS curve to derive time to treatment (ToT) curve in the CEM. For cemiplimab, the HR is calculated from the ratio of median TTD ([redacted]weeks)

and median PFS (36.09 weeks), taken from the 5-year follow-up data of EMPOWER-Lung 3 trial.[12] For pembrolizumab, the HR 0.84 was estimated using the same method from the KEYNOTE-189[13] and KEYNOTE-407 trials,[14] as in the original CS.[10] The calculated HRs are then used to transform the cycle PFS probabilities to on-treatment probabilities to derive the respective ToT curves.

EAG Comment: The company also provided a scenario with a Cox model analysis HR estimate as in the original submission. In the original CS, the company noted the independence of observations assumption was violated. Time ratios derived from Kaplan-Meier curves can vary significantly across survival probabilities as illustrated in Fig 1 (a reproduction of Figure 30 from the CS[15]). But selecting the median is unbiased and consistent across comparators. EAG could not verify the original source of median TTD value of [redacted] weeks for cemiplimab (provided in the company RR submission[15] from the references in the reference pack.

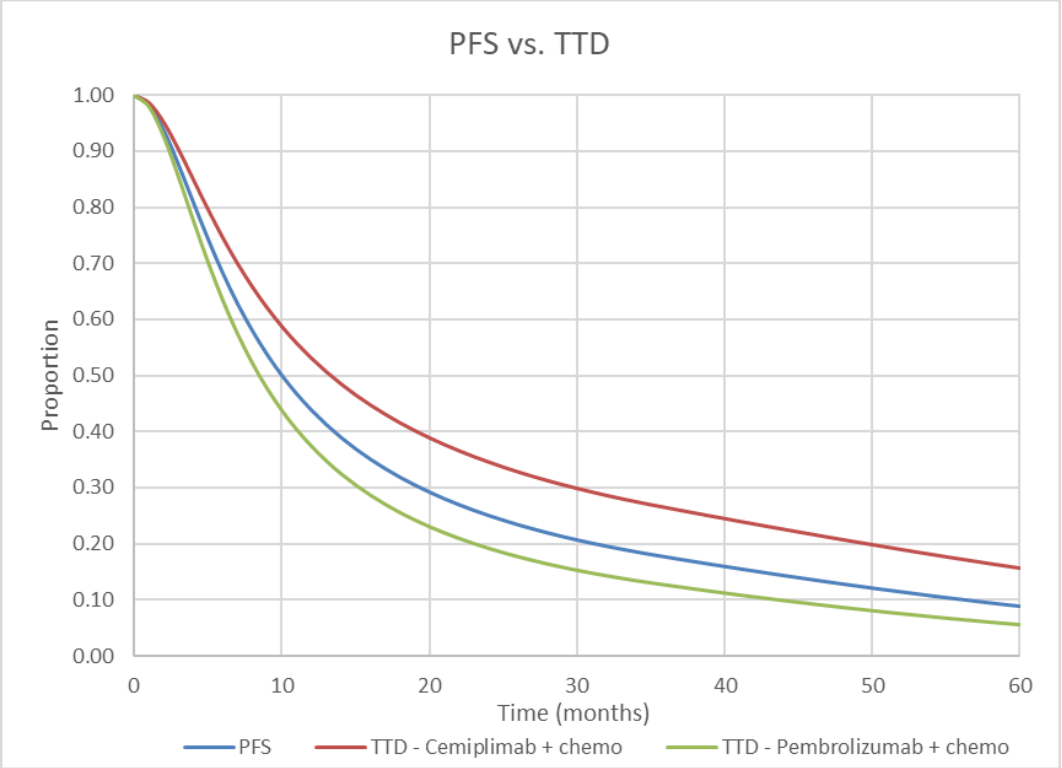
Figure 1: PFS and TTD for cemiplimab + chemotherapy and chemotherapy from EMPOWER-Lung 3 (June 2022 DCO) in the PD-L1 ≥1%, any histology population



Reproduced from Figure 30, CS[15].

To illustrate the relationship between the TTD and PFS for cemiplimab and pembrolizumab, the EAG have produced a plot of the predicted decision model ToT curves in the new company base case (see Figure 2).

Figure 2: PFS curve and TTD curves for cemiplimab + SoC and pembrolizumab + SoC



Source: Generated by EAG using updated CEM[11]
Abbreviations: PFS, progression free survival; TTD, time to treatment discontinuation; vs., versus; chemo, chemotherapy.

Treatment Waning

In the updated CEM, the cemiplimab + SoC treatment effect was modelled for 5 years from initiation, with a waning of this treatment effect applied from year 3 until 5 years. The same treatment waning was modelled for pembrolizumab + SoC. This is consistent with the preferences of the NICE committee.

EAG Comment: Assuming equal clinical effectiveness means that the treatment waning assumptions have very little impact on the costs. Subsequent treatment costs are tiny.

Subsequent treatments

In the updated company base-case, the subsequent treatments were assumed to be equal for patients who have progressed in the cemiplimab and pembrolizumab treatments arms. The subsequent treatment distribution is informed by the EMPOWER-Lung 5-year data,[16] and then recalculated to restrict the choice of immunotherapies (IOs) to pembrolizumab, nivolumab and atezolizumab to better reflect the UK clinical practise.[17] All other post-progression treatment distributions for both the treatment arms were retained from the cemiplimab arm of the original company submission[15] (See Table 2.2). The company undertook scenario analyses of subsequent treatment using KEYNOTE – 189 and - 407 trials[8,9] in the pembrolizumab arm (scenario 2 and 3).

EAG Comment: Assuming equal subsequent treatments and equal effectiveness assumptions means that subsequent treatment has no impact on the cost analysis. An assumption of equal subsequent treatment makes sense if cemiplimab and pembrolizumab have a similar effect on subsequent treatment options. This is independent of effectiveness. The company base case is conservative compared to the two alternative subsequent treatment scenarios they presented.

Table 2.2: Subsequent treatment distribution in updated company base-case

Post-progression treatment	Post-progression treatment distribution
Post-progression immunotherapy (IO)	
Pembrolizumab	0.92%
Nivolumab	0.92%
Atezolizumab	2.76%

Post-progression chemotherapy	
Docetaxel	4.5%
Carboplatin	5.4%
Cisplatin	1.9%
Gemcitabine	3.5%
Paclitaxel	3.2%
Pemetrexed	1.9%
Total	**25.1%**
Source: Company RR model[11]	

Adverse events (AEs)

The company has assumed equivalent safety profile for both cemiplimab and pembrolizumab treatment regimes. The adverse events of Grade 3 and above data from the EMPOWER-Lung 3 trial (~28 months follow-up) were assumed across both the arms in the updated CEM.[12]

EAG Comment: The EAG notes that equal efficacy does not necessarily imply equal safety. It depends on the association between duration of treatment and incidence of adverse events. If adverse events are not related to duration and are likely to occur at the start of treatment then equal safety is a reasonable assumption. But the costs modelled for adverse events were very small in the CS and the assumption of equal safety has a negligible effect on the results. Therefore, the EAG are satisfied with this assumption.

3 Results

Table 3.1 shows the results of the company analyses. The company estimated the PAS price discount on the list price of cemiplimab required for cemiplimab to be cost-equivalent compared to pembrolizumab when assuming either a 65% or 70% discount PAS price for pembrolizumab and other los.

In the base-case, cemiplimab PAS discount is required to be [redacted]% and [redacted]% to be cost equivalent to pembrolizumab cost, with PAS discounts of [redacted]%, [redacted]%, respectively.[11] The four company scenarios with plausible alternative assumptions for subsequent immunotherapy use have a negligible impact on the results.[11] All analyses were verified by the EAG.

EAG Comment: The EAG is satisfied with the company's base case and scenario analyses. The EAG has produced a confidential cPAS appendix which presents the scenario results with the correct cPAS prices for the drugs other than cemiplimab.

Table 3.1: Cemiplimab PAS discount required for it to be cost equivalent versus pembrolizumab in NSCLC

Scenario	Pembrolizumab PAS = 65%	Pembrolizumab PAS = 70%
Base case: Equal subsequent therapies across both cemiplimab and pembrolizumab model arms. 30-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 1: Equal subsequent therapies across both cemiplimab and pembrolizumab model arms. 5-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]

Scenario	Pembrolizumab PAS = 65%	Pembrolizumab PAS = 70%
Scenario analysis 2: Subsequent IO using ITT values from KN and EL3 as denominator 30-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 3: Subsequent IO using only progressed pts from KN and EL3 as denominator 30-year time horizon Median TTD:PFS ratio to estimate HR applied to PFS for ToT in both arms	[redacted]	[redacted]
Scenario analysis 4: Equal subsequent therapies across both cemiplimab and pembrolizumab model arms. 30-year time horizon Cox model method to estimate HR applied to PFS for cemiplimab ToT curve, and median TTD:PFS ratio to estimate HR applied to PFS for pembrolizumab ToT curve	[redacted]	[redacted]

Source: Company rapid review submission[10]
Abbreviations: EL3, EMPOWER Lung-3 trial of cemiplimab + PBC; HR, hazard ratio; IO, immune-oncology therapy; ITT, intention to treat population; KN, KEYNOTE trials of pembrolizumab + PBC; PAS, Patient access scheme; PBC, platinum-based chemotherapy; ToT, time on treatment; TTD, time to discontinuation

4 Conclusion

Overall, the EAG is satisfied that the updated company submission has adopted the committee's preferred assumptions regarding equal efficacy. The EAG have also validated the cost-comparison analyses presented by the company in the submission with example PAS price discounts for pembrolizumab and other IOs required to achieve cost equivalence between cemiplimab + SoC and pembrolizumab + SoC, which take into account the additional drug acquisition and administration costs associated with longer time on treatment.

The results presented by the company in their updated submission are not appropriate for decision making, as only example PAS prices have been used for pembrolizumab and other IOs. Results using the confidential PAS prices for all other IOs and chemotherapies will be presented in an accompanying confidential PAS appendix.

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