

# Cost-Effectiveness Analysis of Cemiplimab for Patients with Advanced Non-Small Cell Lung Carcinoma in Spain

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## INTRODUCTION

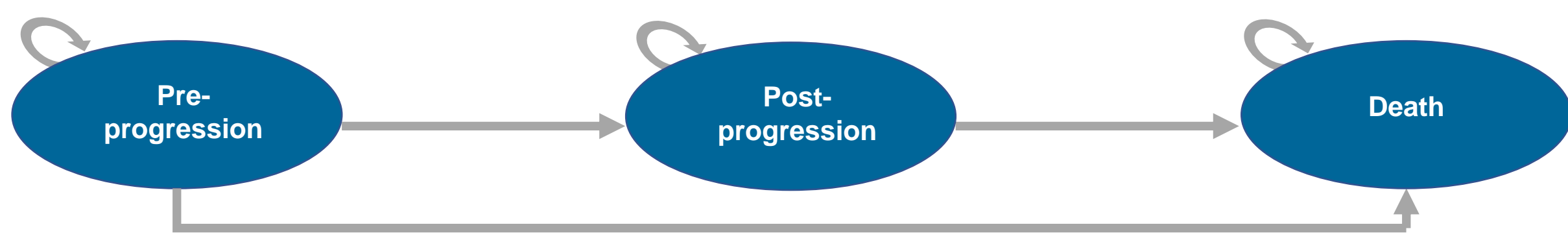
- Lung cancer is the leading cause of cancer mortality in Spain<sup>1</sup>. Approximately 85% of all lung cancers are non-small cell lung carcinoma (NSCLC)<sup>2</sup> and it is estimated that 20-30% of these cases are programmed death ligand 1 (PD-L1) positive in  $\geq 50\%$  of tumor cells<sup>3-5</sup>.
- EMPOWER-LUNG 1 trial demonstrated that cemiplimab as monotherapy significantly improved overall survival (OS) and progression-free survival (PFS) compared with chemotherapy in patients with advanced NSCLC PD-L1  $\geq 50\%$ , providing a potential new treatment option for this patient population.
- Cemiplimab, pembrolizumab and atezolizumab are currently the only drugs reimbursed in Spain for the treatment of first line metastatic NSCLC in adults whose tumors express PD-L1 in a proportion  $\geq 50\%$ <sup>7</sup> but pembrolizumab is generally considered the standard of care.
- The aim of this study was to evaluate the cost-effectiveness of cemiplimab versus pembrolizumab in the first line treatment for patients with advanced NSCLC expressing PD-L1 in  $\geq 50\%$  of tumor cells in Spain.

## METHODS

### Model structure

- A partitioned survival model was adapted considering the Spanish National Healthcare System perspective (only direct medical costs, euros 2021), over a lifetime horizon (30 years) and using monthly cycles (Figure 1).
- The population was based on the patients included in the EMPOWER-LUNG 1 study (mean age: 63 years old; proportion of males: 87.6%)<sup>6</sup>.
- Results were expressed in life years (LY) and quality-adjusted life-years (QALY) gained, costs and incremental cost-effectiveness ratio (ICER).
- A discount annual rate of 3% was applied to both costs and health outcomes.

Figure 1. Markov model structure



### Modelling OS, PFS and duration of treatment

- OS and PFS were estimated from the studies EMPOWER-LUNG 1 (cemiplimab)<sup>6</sup> and KEYNOTE-024 (pembrolizumab)<sup>8</sup>. Since there was no head-to-head study of cemiplimab compared to pembrolizumab, time-varying hazard ratios from a network meta-analysis of randomized clinical trials were considered for survival outcomes.
- Extrapolation of PFS and OS was adjusted by second-order fractional polynomials.
- EMPOWER-LUNG 1<sup>6</sup> and KEYNOTE-024<sup>8</sup> allowed treatment switching between both arms (crossover) after progression. Curves were adjusted by two-stage method.
- For cemiplimab, the treatment duration curve from the EMPOWER-LUNG 1 study<sup>6</sup> was extrapolated to the time horizon of the model, using a Weibull distribution. For pembrolizumab, treatment duration was assumed to be equal to PFS after analyzing their similarity.

### Adverse events and end-of-life

- Utility values were assigned to pre-progression and post-progression states. The utilities were derived from EMPOWER-LUNG 1<sup>6</sup>, which collected patient quality of life data from the EORTC QLQ-C30 questionnaire (Table 1).
- Disutility due to grade 3 and 4 adverse events in the pre-progression state was incorporated. The values of disutility considered in the model were identified in the literature<sup>9</sup> (Table 1).
- Costs associated with the end of life of patients (last weeks before death) were identified in the literature<sup>11</sup> and correspond to € 3,905.01.

Table 1. Utilities, frequency and cost of adverse events

Health state	Utility (mean [SD]) <sup>9</sup>			
Pre-progression	0.779 [0.0082]			
Post-progression	0.693 [0.0294]			
Adverse events	Disutility <sup>9</sup>	Frequency (Cemiplimab) <sup>8</sup>	Frequency (Pembrolizumab) <sup>8</sup>	Unit cost <sup>10</sup>
Rash	-0.03	0.85%	1.30%	€ 1,152.75
Increased AST	NA	1.41%	0.00%	€ 3,600.10
Increased ALT	NA	0.85%	0.00%	€ 3,600.10
Diarrhoea	-0.05	0.00%	3.90%	€ 901.76
Fatigue	-0.05	0.85%	1.95%	€ 178.64
Anaemia	-0.07	0.56%	1.30%	€ 576.84
Neutropenia	-0.09	0.56%	0.00%	€ 1,047.51

Abbreviations. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; NA: Not applicable.

### Pharmacological and administration costs

- Pharmacological costs were calculated using the estimated reimbursed price of each treatment applying the corresponding deduction according to the mandatory Royal Decree Law (RDL) 8/2010 deduction<sup>12,13</sup>.
- The recommended dosing regimens were used in accordance with the summary of product characteristics of cemiplimab and pembrolizumab<sup>14</sup>.
- The dosage and distribution of chemotherapy combinations used after progression were validated with clinical experts. In treatments where the dose to be administered depended on the patient's weight or body surface area, it was assumed that the amount left over from the vials is not wasted.
- For treatments administered intravenously, the cost of administration was assumed to be the cost associated with day hospital administration, which is estimated at € 222.72<sup>10</sup>.

### Use of resources

- Use of resources was validated by an expert panel. Unit cost were obtained from Spanish healthcare cost databases<sup>10</sup>.
- In each of the health states, use of resources was equal for cemiplimab and pembrolizumab (Table 2).

Table 2. Health resources used monthly in pre- and post-progression states

	Pre-progression		Post-progression		Unit cost
	N	%	N	%	
Oncologist visit	1.40	95.00%	1.80	90.00%	€ 86.12
Radiography (Chest)	0.30	40.00%	0.70	50.00%	€ 27.96
CT scan (Chest)	0.40	100.00%	0.30	70.00%	€ 235.20
Nursing visit (hospital)	0.70	85.00%	0.80	85.00%	€ 29.79
Nursing visit (PC)	NA	NA	0.50	45.00%	€ 29.79
Medical visit (PC)	0.40	50.00%	0.80	55.00%	€ 51.95
Medical visit (PHC)	0.30	10.00%	0.40	55.00%	€ 52.38
Blood analysis	1.30	100.00%	NA	NA	€ 5.96
Emergency room visit	1.00	20.00%	NA	NA	€ 173.20

Abbreviations. N: Number of resources per month; %: Percentage of patients; CT: Computed tomography; PC: Primary care; NA: Not applicable; PHC: Primary home care.

### Sensitivity analysis

- In addition to the base case analysis, scenario analyses as well as deterministic and probabilistic sensitivity analyses were performed to assess the robustness of the results.

## RESULTS

### Base case

- Cemiplimab provided an alternative with lower overall associated costs (€ 6,301/patient) compared to pembrolizumab, primarily as a result of reduced pharmacological and administration costs (Table 3).
- In terms of health outcomes, treatment with cemiplimab provided 0.93 LYG versus pembrolizumab (3.70 vs 2.77). Therefore, the ICER of cemiplimab was dominant versus pembrolizumab (Table 3).
- Expressing health outcomes in QALY, cemiplimab was associated with a gain of 0.64 QALY vs. pembrolizumab (2.65 vs. 2.01). The resulting cost-utility ratio was also dominant over pembrolizumab (Table 3).

Table 3. Base case results

	Cemiplimab	Pembrolizumab	Differential (cemiplimab vs. pembrolizumab)
<b>Costs results</b>			
Pharmacological and administration	€ 45,207	€ 54,824	- € 9,617
Disease monitoring	€ 16,577	€ 13,308	€ 3,268
Management of adverse events	€ 108.57	€ 61.08	€ 47.50
<b>Total</b>	<b>€ 61,893</b>	<b>€ 68,194</b>	<b>- € 6,301</b>
<b>Effectiveness results</b>			
LY	3.70	2.77	0.93
QALY	2.65	2.01	0.64
<b>Incremental results</b>			
ICER (costs/LY gained)		<b>Dominant</b>	
ICUR (costs/QALY gained)		<b>Dominant</b>	

Abbreviations. LY: life year; QALY: quality-adjusted life-years; ICER: incremental cost-effectiveness ratio; ICUR: incremental cost-utility ratio.

### Sensitivity analyses

- A scenario analysis was carried out by proposing different methodological alternatives to the base case of the analysis and testing certain assumptions made. The results of all scenarios showed a dominant incremental cost-effectiveness ratio (ICUR), therefore, in all scenarios, cemiplimab would be more effective and less costly than pembrolizumab (Table 4).

Table 4. Scenario analysis results

	Differential (cemiplimab vs. pembrolizumab)	QALY increase (cemiplimab vs. pembrolizumab)	ICUR (€/QALY)
<b>Base case</b>	<b>- € 6,301</b>	<b>0.64</b>	<b>Dominant</b>
Time horizon: 5 years	- € 8,139	0.16	Dominant
Time horizon: 10 years	- € 7,184	0.44	Dominant
Time horizon: 15 years	- € 6,554	0.57	Dominant
Discount rate: 0%	- € 5,286	0.83	Dominant
Discount rate: 5%	- € 6,689	0.54	Dominant
Duration of cemiplimab treatment equal to PFS	- € 9,355	0.64	Dominant
Efficacy curves not adjusted to the crossover	- € 7,369	0.35	Dominant
Utilities based on UK McKenzie algorithm	- € 6,301	0.66	Dominant

Abbreviations. QALY: quality-adjusted life-years; ICUR: incremental cost-utility ratio; PFS: progression-free survival.

- Deterministic univariate analyses showed that the results of the analysis were robust to changes in input parameters and reinforced that cemiplimab was dominant over pembrolizumab.
- Potential variations in the ICUR result were analysed by univariate modification of several parameters. Table 5 shows the results of the 10 parameters that generated the greatest variations.
- In particular, the improved PFS of pembrolizumab produced a non-dominant but still cost-effective result for cemiplimab, generating a reduced cost that remained below the willingness to pay threshold commonly used in Spain (€ 30,000 per QALY gained)<sup>15-17</sup>.

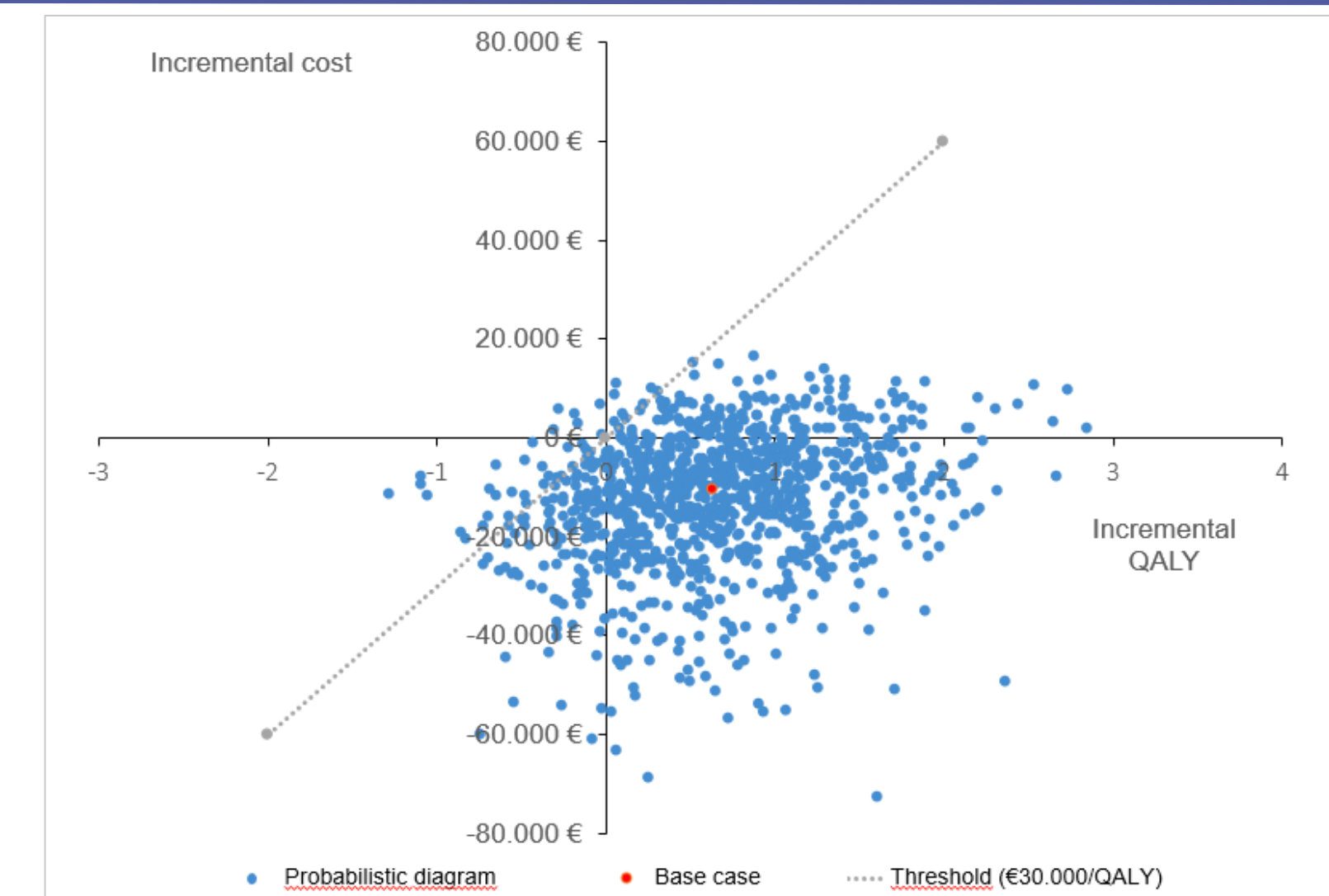
Table 5. Results of deterministic univariate analysis

	Lower limit	Upper limit
Cemiplimab OS	Dominant	Dominant
Pembrolizumab PFS	Dominant	€ 2,042
Reference curve OS	Dominant	Dominant
Pembrolizumab OS	Dominant	Dominant
Utility PD	Dominant	Dominant
Cemiplimab PFS	Dominant	Dominant
Reference curve PFS	Dominant	Dominant
Disease management cost - PF	Dominant	Dominant
Utility PF	Dominant	Dominant
Disease management cost - PD	Dominant	Dominant

Abbreviations. OS: Overall survival; PFS: Progression-free survival; PD: Progressed disease; PF: Progression-free.

- Probabilistic sensibility analyses (Figure 2) revealed that 94% of the simulations performed would be below the willingness to pay threshold commonly considered in Spain (€ 30,000/QALY gained)<sup>15-17</sup>, showing cemiplimab as a cost-effective option compared to pembrolizumab. Cemiplimab would also be a dominant alternative in 60% of the iterations.

Figure 2. Incremental cost-effectiveness (cemiplimab vs pembrolizumab)



## CONCLUSIONS

Findings suggest that cemiplimab compared with pembrolizumab is a cost-effective first-line treatment option for advanced NSCLC patients with PD-L1 expression  $\geq 50\%$  in Spain.

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### Disclosures

LL receives honoraria for lectures from Pfizer, Boehringer, Novartis, Astra Zeneca, Sanofi, Bristol, MSD, Takeda. The author receives honoraria for advisory board from Sanofi, Lilly, Novartis, Boehringer, Amgen. LL receives support for attending meetings from MSD and Astra Zeneca. ASH Advisory role, speaking bureau or travel and accommodations: Roche, BMS, MSD, Janssen, Lilly, Takeda, Sanofi, Astra-Zeneca. JSM, EU and DN are employees of Pharmalex, an independent contract health economic organization that received consultancy fees from Sanofi to conduct this research.

### Funding Source

This research was funded by Sanofi.