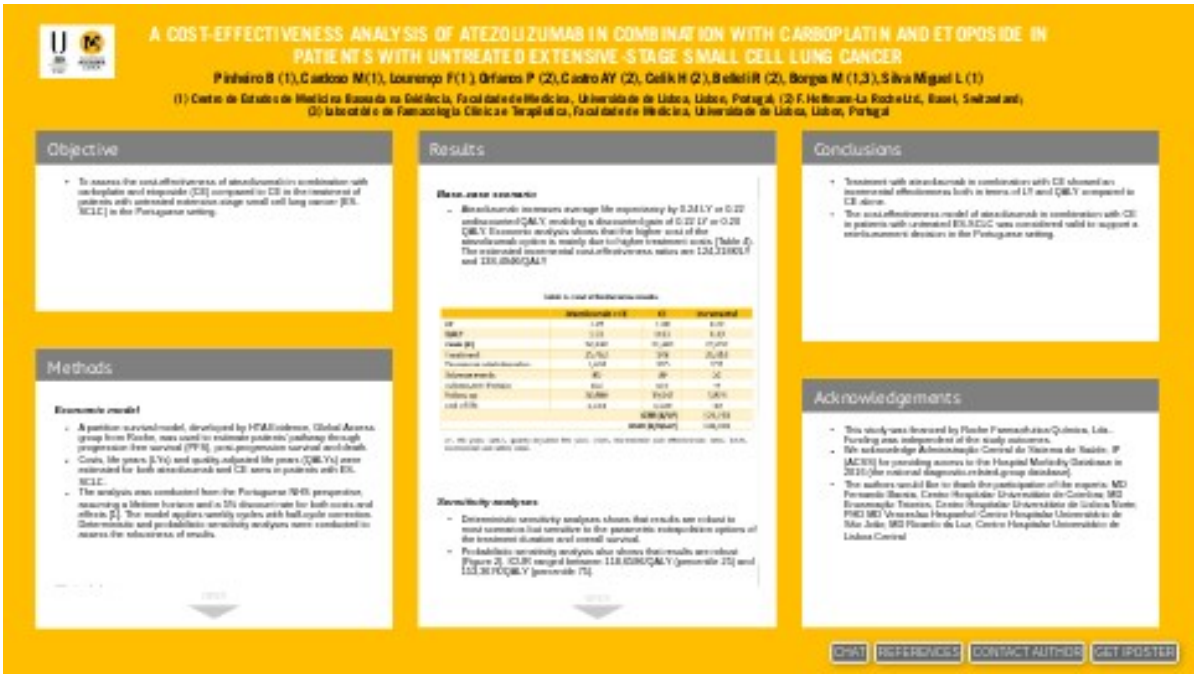
A COST-EFFECTIVENESS ANALYSIS OF ATEZOLIZUMAB IN COMBINATION WITH CARBOPLATIN AND ETOPOSIDE IN PATIENTS WITH UNTREATED EXTENSIVE-STAGE SMALL CELL LUNG CANCER



Pinheiro B (1), Cardoso M (1), Lourenço F (1), Orfanos P (2), Castro AY (2), Celik H (2), Belleli R (2), Borges M (1,3), Silva Miguel L (1)

(1) Centro de Estudos de Medicina Baseada na Evidência, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal; (2) F. Hoffmann-La Roche Ltd., Basel, Switzerland;
(3) Laboratório de Farmacologia Clínica e Terapêutica, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal

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OBJECTIVE

- To assess the cost-effectiveness of atezolizumab in combination with carboplatin and etoposide (CE) compared to CE in the treatment of patients with untreated extensive-stage small cell lung cancer (ES-SCLC) in the Portuguese setting.

METHODS

Economic model

- A partition survival model, developed by HTA Evidence, Global Access group from Roche, was used to estimate patients' pathway through progression free survival (PFS), post-progression survival and death.
- Costs, life years (LYs) and quality-adjusted life years (QALYs) were estimated for both atezolizumab and CE arms in patients with ES-SCLC.
- The analysis was conducted from the Portuguese NHS perspective, assuming a lifetime horizon and a 5% discount rate for both costs and effects [1]. The model applies weekly cycles with half-cycle correction. Deterministic and probabilistic sensitivity analyses were conducted to assess the robustness of results.

Clinical data

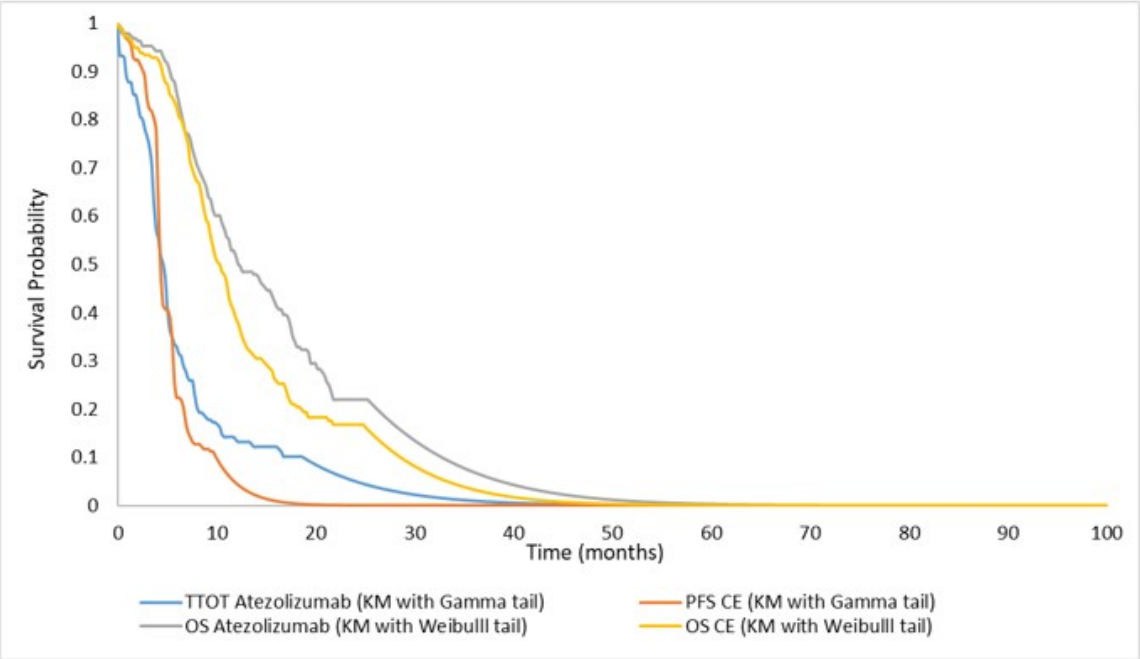
- The model was parameterized using clinical data from IMpower133, a phase I/III, randomized controlled trial[2].
- For overall survival (OS) and PFS, Kaplan-Meier (KM) data were used until at least 10% of patients were still at risk of event, being a parametric curve used for extrapolation (Table 1). Time to off treatment (TTOT) with atezolizumab, that was assumed to be a PFS proxy for patients on atezolizumab plus CE, followed the same approach. For TTOT with CE in both arms, only KM data was used, as there was no need to extrapolate.
- As the proportional hazards assumption does not hold, separate models were fitted to each curve. Moreover, once the usual statistical criterion (AIC and BIC) were very similar across models, the choice of parametric curves was based on clinical plausibility. Choices conducted to an intermediate scenario.

Table 1. Modelling summary of survival outcomes.

Outcome		KM duration (weeks)	Parametric curve and duration (weeks)
OS	Atezolizumab + CE	0-110	Weibull: ≥ 111
	CE	0-108	Weibull: ≥ 109
PFS	CE	0-42	Generalized gamma: ≥ 43
	Atezolizumab	0-81	Generalized gamma: ≥ 82
TTOT	CE, intervention arm	0-16[a]	-
	CE	0-17[a]	-

KM, kaplan-meier; CE, carboplatin and etoposide; PFS, progression-free survival; TTOT, time to of treatment; OS, overall survival.
[a] As all patients had discontinue the treatment with CE before the clinical trial was finished, no parametric extrapolation was needed.

Figure 1. Modelled curves.



KM, kaplan-meier; TTOT, time to of treatment; OS, overall survival; CE, carboplatin and etoposide; PFS, progression-free survival.

Utilities

- Utility weights were estimated (Table 2) using the proximity to death approach[4,5] separately for on/off treatment and applying the EQ-5D-5L Portuguese[6] value set to the patient reported outcomes from the IMpower133 trial[2].

Table 2. Mean utility (standard error) score per health state.

Time to death (weeks)	On treatment	Off Treatment
≤5	0.742 (0.026)	0.448 (0.046)
]5, 15)	0.803(0.016)	0.647 (0.037)
]15, 30)	0.818 (0.009)	0.807 (0.027)
>30	0.836 (0.008)	0.865 (0.029)

Costs

- Portuguese-specific disease management resource use was based on a panel of clinical experts and on Portuguese 2017 DRG microdata (ACSS, 2017). Resources were valued according to national legislation (Portaria nº 207/2017) and official national drug cost databases (Infomed and ACSS Catalog).
- The average weekly follow-up cost per health state is presented on Table 3.

Table 3. Estimated weekly follow-up costs (€).

Treatment arm	PFS	PPS
Atezolizumab + CE	176.22 €	425.77€
CE	193.30€	425.41€

PFS, progression-free survival; PPS, Post-progression survival; CE, carboplatin and etoposide.

RESULTS

Base-case scenario

- Atezolizumab increases average life expectancy by 0.24 LY or 0.22 undiscounted QALY, enabling a discounted gain of 0.22 LY or 0.20 QALY. Economic analysis shows that the higher cost of the atezolizumab option is mainly due to higher treatment costs (Table 4). The estimated incremental cost-effectiveness ratios are 124,218€/LY and 138,494€/QALY

Table 4. Cost-effectiveness results.

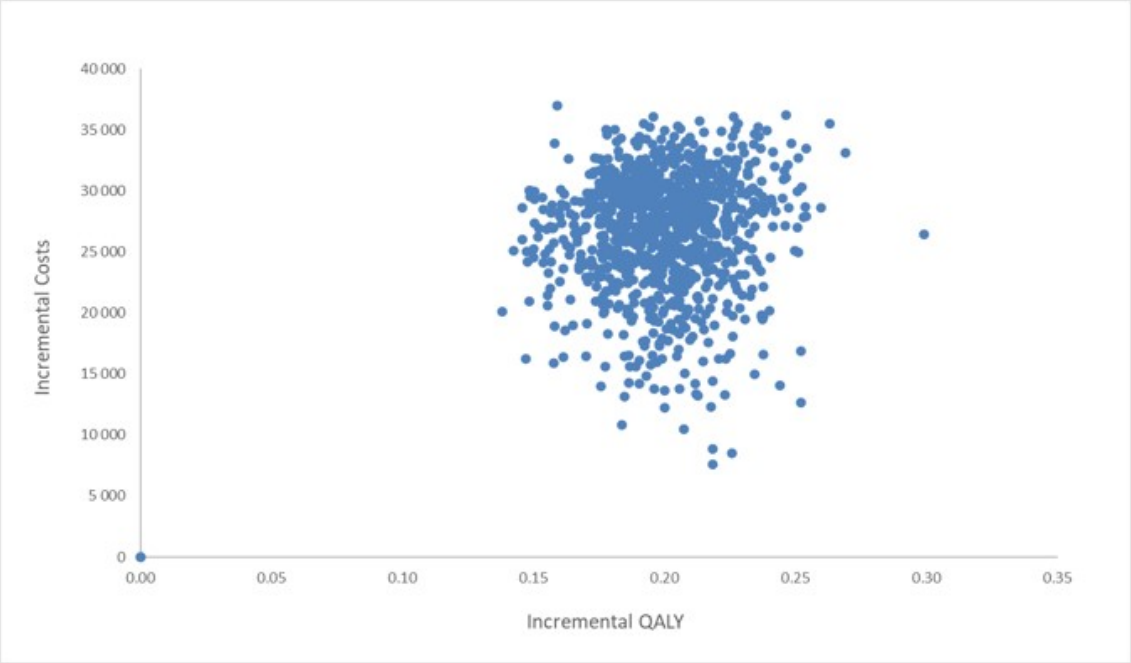
	Atezolizumab + CE	CE	Incremental
LY	1.29	1.06	0.22
QALY	1.03	0.83	0.20
Costs (€)	50,108	22,409	27,699
Treatment	25,452	143	25,310
Treatment administration	1,496	959	537
Adverse events	90	39	51
Subsequent therapy	603	607	-4
Follow-up	20,866	19,042	1,824
End of life	1,601	1,620	-19
		ICER (€/LY)	124,218
		ICUR (€/QALY)	138,494

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

Sensitivity analyses

- Deterministic sensitivity analyses shows that results are robust to most scenarios but sensitive to the parametric extrapolation options of the treatment duration and overall survival.
- Probabilistic sensitivity analysis also shows that results are robust (Figure 2). ICUR ranged between 118,658€/QALY (percentile 25) and 153,367€/QALY (percentile 75).

Figure 2. Cost-effectiveness plane.



QALY, quality-adjusted life year

CONCLUSIONS

- Treatment with atezolizumab in combination with CE showed an incremental effectiveness both in terms of LY and QALY compared to CE alone.
- The cost-effectiveness model of atezolizumab in combination with CE in patients with untreated ES-SCLC was considered valid to support a reimbursement decision in the Portuguese setting.

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AUTHOR INFORMATION

Corresponding author: francisco.lourenco@medicina.ulisboa.pt

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