A COST-EFFECTIVENESS ANALYSIS OF ATEZOLIZUMAB FOR PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER IN PORTUGAL

Luís Silva Miguel[1], Bernardete Pinheiro[1], Joana Alarcão[1], Noman Paracha[2], Federico Felizzi[2], Catarina Pereira[3], Margarida Borges[1,4]

1 – Centro de Estudos de Medicina Baseada na Evidência, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal
2 – F. Hoffmannn-La Roche Ltd., Basel, Switzerland
3 – Roche Farmacêutica Química, Lda., Lisboa, Portugal
4 – Laboratório de Farmacologia Clínica e Terapêutica, Faculdade de Medicina, Universidade de Lisboa. Lisboa, Portugal.

Corresponding author: luis.silvamiguel@medicina.ulisboa.pt

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BACKGROUND AND OBJECTIVE

- To assess the cost-effectiveness of atezolizumab (humanised antiprogrammed death-ligand 1 [PD-L1] monoclonal antibody) compared to docetaxel in the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) in previously treated PD-L1 negative patients, in the Portuguese setting.

METHODS

ECONOMIC MODEL

- A partitioned-survival model, developed by Roche and MORSE Health Technology Assessment Group, was used to estimate patient evolution among three health states: progression-free survival (PFS), post-progression survival (PPS) and death. For atezolizumab time to treatment discontinuation (TTD) was used as a proxy of progression, once treatment was administered until clinical benefit.
- Costs, life years (LYs) and quality-adjusted life years (QALYs) were estimated for both atezolizumab and docetaxel arms in patients with NSCLC.
- The analysis was conducted from a payers' perspective, assuming a lifetime horizon and a 5% discount rate for both costs and effects. The model uses weekly cycles and half-cycle correction was implemented. Deterministic and probabilistic sensitivity analyses were conducted to assess the robustness of results.

CLINICAL DATA

- The model was parameterized using clinical data from OAK, a head-to-head phase III randomized controlled trial (Rittmeyer et al., 2017)[1].
- For all outcomes (OS, PFS and TTD), Kaplan-Meier (KM) data were used until at least 10% of patients were still at risk of event, and onwards a parametric curve was used for extrapolation **(Table 1)**. In docetaxel arm, TTD was only used for cost calculation.

Outcome		KM duration (weeks)	Parametric curve and duration (weeks)
PFS	Docetaxel	0-44	Generalized gamma: >44
TTD	Atezolizumab	0-85	Generalized gamma: >85
	Docetaxel	0-27	Generalized gamma: >27
OS	Atezolizumab	0-95	Generalized gamma: >95
	Docetaxel	0-96	Generalized gamma: >96

Table 1. Modelling summary of survival outcomes.

KM, Kaplan-Meier; PFS, progression-free survival; TTD, time to treatment discontinuation; OS, overall survival

- For TTD, PFS and OS, separate models were adjusted after rejecting proportional hazards assumption[2] and considering the different drug mechanisms and expected long-term efficacy. Once the usual statistical criterion (AIC e BIC) were very similar across models and therefore uninformative[2], the choice of the parametric curves was based on clinical plausibility. Choices conducted to an intermediate scenario. Clinical validation of OS extrapolation was based on external data from clinical trial POPLAR.

UTILITIES

- Health related quality of life (HRQoL) was measured in the OAK trial using the EuroQol (EQ-5D-3L) questionnaire. Utility weights were derived according to time to death approach[3,4,5], and stratified by on and off treatment. UK tariffs were used for utility calculation **(Table 2)**.

Time to death (weeks)	On treatment	Off Treatment
≤5	0.39 (0.08)	0.35 (0.04)
]5, 15)	0.61 (0.04)	0.43 (0.03)
]15, 30)	0.71 (0.01)	0.58 (0.01)
>30	0.77 (0.01)	0.68 (0.01)

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

- Adverse events' disutilities were taken from the literature[6,7].

COSTS

- Portuguese-specific disease management resource use was based on a panel of clinical experts on NSCLC and on Portuguese 2016 DRG microdata (ACSS, 2015).
- Resources were valued according to national legislation (Portaria 234/2015, Portaria nº20/2015 and Portaria 353/2017) and official drug cost databases (Infomed and ACSS Catalog). Only direct costs were imputed.
- Patient transportation costs were considered for outpatient visits, emergency visits and radiotherapy treatment. Official prices for non-urgent transportation (Despacho nº 7702-A/2012) and a study estimating costs supported by patients in Portugal were used[8].
- The average weekly cost per health state is presented on **Table 3**.

2nd line	3rd line	Best supportive care
187	271	364

Table 3. Estimated weekly costs (€).

ACKNOWLEDGMENTS

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RESULTS

BASE CASE SCENARIO

- Treatment with atezolizumab was projected to prolong OS and PFS in patients with NSCLC **(Figure 1)**.

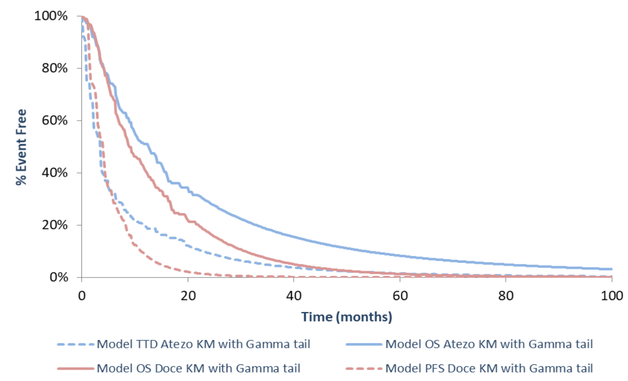

Figure 1. Modelled curves.

- Atezolizumab increases average life expectancy by 0.74 undiscounted life years (LY) enabling a discounted gain of 0.58 LY or 0.44 quality-adjusted life years (QALY). Economic analysis shows that the higher costs of the atezolizumab option is mainly due to higher treatment costs **(Table 4**). The estimated incremental cost-effectiveness ratios (ICER) are 59,295€/LY and 78,977€/QALY.

	Atezolizumab	Docetaxel	Incremental
LY (undiscounted)	1.90	1.16	0.74
LY	1.67	1.09	0.58
PFS	0.74	0.43	0.31
PPS	0.94	0.66	0.28
QALY	1.10	0.66	0.44
Costs (€)	57,568	23,080	34,488
Treatment	30,381	174	30,207
Treatment administration	450	430	20
PFS Follow-up	6,467	5,566	902
PPS Follow-up	18,847	12,355	6,493
Subsequent therapy	1,118	3,164	-2,046
Adverse events	13	1,091	-1,078
End of life	291	301	-9
		ICER (€/LY)	59,295
		ICUR (€/QALY)	78,977

Table 4. Cost-effectiveness results.

PFS, progression-free survival; PPS, post-progression survival; LY, Life year; QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio.

SENSITIVITY ANALYSIS

- Deterministic sensitivity analyses show that results are robust to most scenarios but sensitive to treatment duration and parametric extrapolation options.
- Probabilistic sensitivity analysis was conducted (1,000 simulations), also showing that results are robust **(Figure 2)**. ICUR ranged between 65,690€/QALY (percentile 25) and 98,088€/QALY (percentile 75) .

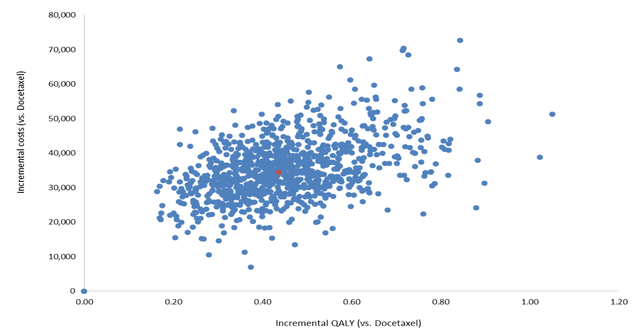

Figure 2. Cost-effectiveness plane.

CONCLUSIONS

- The cost-effectiveness model of atezolizumab in the treatment of PD-L1 negative patients with locally advanced or metastatic NSCLC after prior chemotherapy was considered valid to support a reimbursement decision in the Portuguese setting.
- Atezolizumab is recommended for routine use in the Portuguese National Health Service.

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