A COST-EFFECTIVENESS ANALYSIS OF ATEZOLIZUMAB AS ADJUVANT TREATMENT FOLLOWING COMPLETE RESECTION AND PLATINUM-BASED CHEMOTHERAPY IN ADULT PATIENTS WITH EARLY-STAGE NON-SMALL CELL LUNG CANCER WITH A HIGH RISK OF RECURRENCE

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Objective:

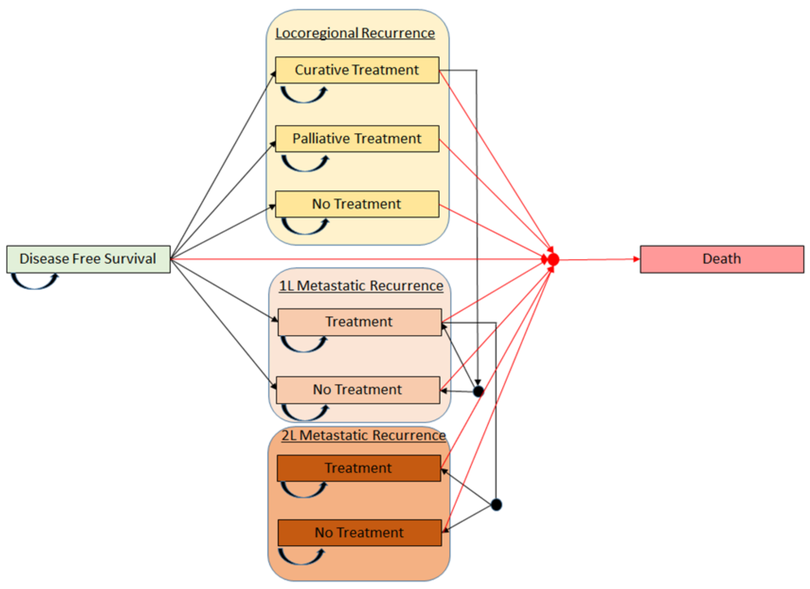
- To assess the cost-effectiveness of atezolizumab as adjuvant treatment, compared to best supportive care (BSC), following complete resection and platinum-based chemotherapy in adult patients with early-stage non-small cell lung cancer (NSCLC) with a high risk of recurrence, whose tumours have programmed death-ligand 1 (PD-L1) expression ≥50%, excluding epidermal growth factor receptor mutant or anaplastic lymphoma kinase-positive NSCLC.

Methods:

Effectiveness Model:

- A Markov model, developed by Roche (Global Access – HTA Evidence Group) was used to estimate patients' pathway through five mutually exclusive health states: disease-free survival (DFS), locoregional recurrence (LR), metastatic recurrence – first line (1LM), metastatic recurrence – second line (2LM), and death (Figure 1).
- Costs, life years (LYs) and quality-adjusted life years (QALYs) were estimated for both arms.
- The analysis was conducted from the National Health Service perspective, incorporating direct medical costs. A lifetime horizon and a 4% discount rate for both costs and effects are assumed. The model applies monthly cycles with half-cycle correction.

Figure 1. Markov model.



Clinical Data:

- The model uses data from IMpower010 for DFS. The IMpower010 is a randomized, phase III clinical trial, evaluating atezolizumab versus best supportive care (BSC) following complete resection and adjuvant platinum-based chemotherapy in stage PD-L1 >50%, Stage II-IIIA, excl. EGFR and ALK+, NSCLC population.
- Parametric functions were chosen to extrapolate DFS according to goodness-of-fit criteria (AIC and BIC) and clinical plausibility. The following hypothesis were assumed:
  - According to the literature [1], [2], the proportion of patients at risk of progression decreases linearly overtime, reaching a minimum of 8.5% at the end of the fifth year.
  - For patients not at risk of progression, it is assumed a 1.25 mortality ratio, to account for an excess mortality versus general population.
  - It is assumed the atezolizumab treatment effect lasts only 5 years.
- As there is no hazard proportionality, separate functions were estimated for each arm. The lognormal was chosen, considering goodness-of-fit for both arms.
- Transitions from other health states are based on the literature:
  - Locoregional recurrence (LR)
    - For patients on curative treatment, the model uses data from [3], that followed patients who experienced locoregional recurrence after surgery for stages I-III NSCLC, and who were treated with chemoradiotherapy or radiotherapy. The proportion of fatal events was based on [4].
    - For patients on palliative treatment, the model uses data from [5], that followed patients who had locoregional recurrence after radiotherapy for stages I-IV NSCLC, and who were re-treated with either palliative or curative radiotherapy.
  - Metastatic recurrence – first line (1LM)
    - For patients on curative treatment, the model sources data from IMpower150, a trial that compared atezolizumab in combination with carboplatin and paclitaxel with or without bevacizumab to carboplatin, paclitaxel and bevacizumab in patients with stage IV non-squamous NSCLC [6]. The proportion of patients on each type of treatment was based on a panel of Portuguese clinical experts.
    - For patients with no treatment, the model uses data from [7], who followed patients who had metastatic recurrence after surgery for stages I-III NSCLC.
  - Metastatic recurrence – second line (2LM)
    - For patients on curative treatment, the model relies on data from the OAK trial, that included patients with locally advanced or metastatic NSCLC who had failed platinum containing therapy [8]. According to the experts panel, data from docetaxel arm were considered appropriate.
    - For patients with no treatment, the model assumes the probabilities estimated for 1LM.

Table 1. Summary of monthly transition probabilities based on the literature.

Health state		Probability	Proportion of fatal events
LR	On treatment	0.036	23%
	Palliative care or off treatment	0.136	100%
1LM	On treatment	0.055	21%
	Off treatment	0.231	100%
2LM	On treatment	0.072	100%
	Off treatment	0.231	100%

Utilities:

- As patient reported outcomes were not collected during IMpower010, utility scores are based on the literature and on IMpower150. The use of this trial allowed estimating EQ-5D-3L scores with Portuguese tariffs for 1LM and 2LM patients on curative treatment. For other health states, utility scores are derived from the literature and further adjusted using the ratio between the scores obtained using Portuguese and UK tariffs on IMpower150.

Table 2. Utility scores per health state.

Health state		Without adjustment	With adjustment	Source
DFS		0.76	0.65	[9]
LR	On treatment	0.73	0.62	[10]
	Palliative care or off treatment	0.62	0.53	[11]
1LM	On treatment	0.71	0.61	IMpower150
	Off treatment	0.62	0.53	[11]
2LM	On treatment	0.69	0.57	IMpower150
	Off treatment	0.62	0.53	[11]

DFS, disease-free survival; LR, locoregional recurrence; 1LM, metastatic recurrence – first line; 2LM, metastatic recurrence – second line

Costs:

- Portuguese-specific disease management resource use was based on a panel of experts and on Portuguese 2018 DRG microdata (ACSS, 2018). 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 below:

Table 3. Estimated average monthly costs (€).

Health state		Treatment cost	Follow-up care
DFS			40
LR	On treatment (during six months)	2,216	134
	Palliative care (during six months) or off treatment	3,467	1,551
1LM	On treatment	5,545	623
	Off treatment	-	1,568
2LM	On treatment	174	1,313
	Off treatment	-	1,568

DFS, disease-free survival; LR, locoregional recurrence; 1LM, metastatic recurrence – first line; 2LM, metastatic recurrence – second line.

Results

Base-case scenario:

- Atezolizumab increases average life expectancy by 2.25 discounted life years (LY) or 1.64 discounted quality adjusted life years (QALY), being this gain due to an increase in disease free survival (see Figure 2).
- The incremental cost of 11,732€, mainly due to higher treatment costs in DFS, leads to incremental cost-effectiveness ratios of 5,212€ per LY and 7,139€ per QALY.

Figure 2. Modelled DFS curves.

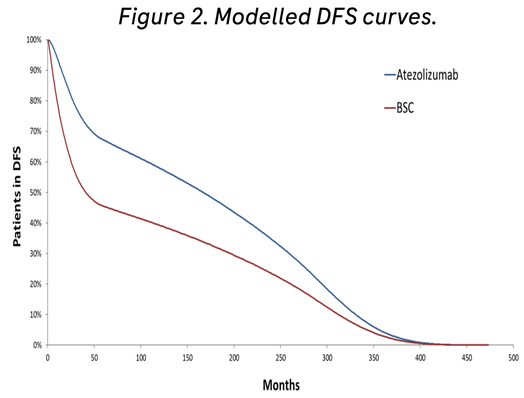


Table 4. Cost-effectiveness results for the base-case scenario (probabilistic results).

	Atezolizumab	BSC	Atezolizumab vs. BSC
Cost per LY (€)			5.212
Cost per QALY (€)			7.139
LY	9.96	7.71	2.25
Disease-free survival	9.24	6.61	2.63
Locoregional recurrence	0.33	0.32	0.01
Metastatic recurrence – 1st line	0.28	0.54	-0.27
Metastatic recurrence – 2nd line	0.12	0.24	-0.12
QALYs	6.95	5.30	1.64
Disease-free survival	6.51	4.64	1.87
Locoregional recurrence	0.20	0.20	0.01
Metastatic recurrence – 1st line	0.17	0.33	-0.16
Metastatic recurrence – 2nd line	0.07	0.13	-0.07
Costs (€)	61,274	49,543	11,732
Disease-free survival	35,549	1,963	33,586
Locoregional recurrence	2,994	2,918	75
Metastatic recurrence – 1st line	20,079	39,572	-19,493
Metastatic recurrence – 2nd line	2276	4435	-2159
End of life	378	655	-277

BSC, best supportive care; LY, life years; QALY, quality-adjusted life years.

Sensitivity Analysis

- Deterministic sensitivity analyses showed that the results were robust to most hypotheses and estimates, except the ones related to duration of treatment effect with atezolizumab and 1LM treatment costs. Nevertheless, cost per QALY is inferior to 12 thousand euros in all evaluated scenarios.
- Probabilistic sensitivity analysis also shows that results are robust (figures 3 and 4), with atezolizumab being dominant in more than 5% of the simulations and cost effective in 96% of the simulations when a willingness to pay of 30 thousand euros is assumed.

Figure 3. Incremental cost-effectiveness plane.

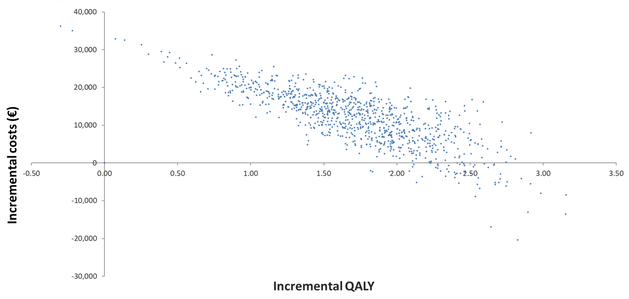
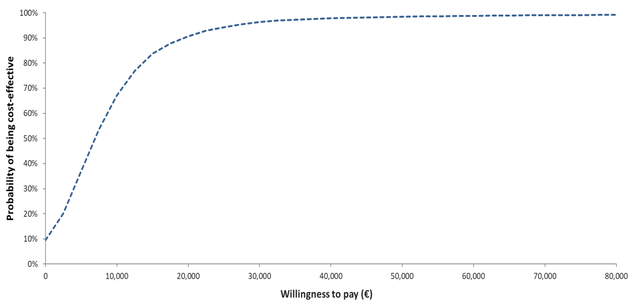


Figure 4. Cost-effectiveness acceptability curve.



Conclusions:

- Treatment with atezolizumab allows for an increase of LY and QALY compared to BSC, with an ICER that is usually considered cost-effective in the Portuguese setting.

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