EE72

A COST-EFFECTIVENESS ANALYSIS OF ADJUVANT OSIMERTINIB IN PATIENTS WITH RESECTED EGFR MUTATION-POSITIVE NON-SMALL CELL LUNG CANCER IN PORTUGAL

André Andrade[1], Ana Lúcia Tavares[1]

[1] AstraZeneca - Produtos Farmacêuticos Lda., Portugal

1 - BACKGROUND AND OBJECTIVE

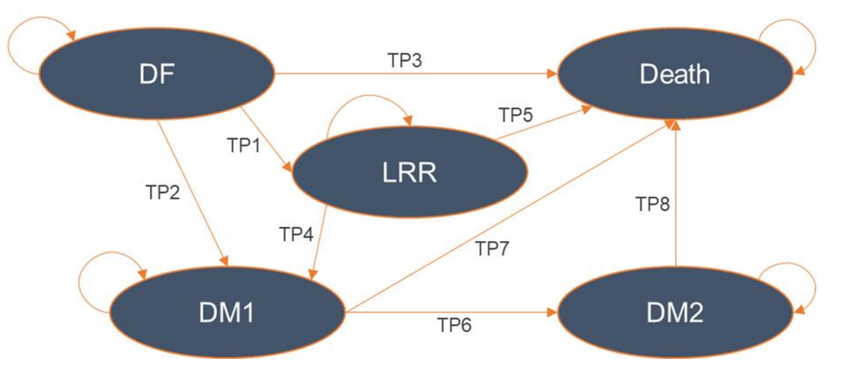
- Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer mortality in Portugal and worldwide.[1] Non-small-cell lung cancer (NSCLC) accounts for 85% of all lung cancers and the mutation of the epidermal growth factor receptor (EGFR) gene is present in approximately 12.8% of NSCLC European patients.[2] An estimated 30% of the NSCLC patients present early-stage, resectable disease (Stage IB-IIIA).[3]
- Osimertinib is a third-generation, irreversible, oral, EGFR tyrosine kinase inhibitor (TKI) that potently and selectively inhibits EGFR sensitizing mutations and the TKI resistance-conferring EGFR point mutation T790M. It is the standard of care for advanced EGFR mutation-positive (EGFRm) NSCLC and was approved for the adjuvant treatment of adult patients with early-stage NSCLC[4] [Pivotal phase III trial ADAURA (NCT02511106)].[3]
- The aim of this study was to assess the cost-effectiveness of adjuvant osimertinib compared to active surveillance in the treatment of patients with resected EGFRm NSCLC, in the Portuguese setting.

2 - METHODS

Effectiveness model

- A semi-Markov model was developed by Cytel to track the costs and survival of early-stage NSCLC patients treated with adjuvant osimertinib plus standard of care (SoC) or placebo plus SoC (active surveillance) comprising five mutually exclusive health states: 'disease-free (DF)', 'Local/Regional recurrence (LRR)', '1st line treatment for distant metastatic NSCLC (DM1)', '2nd line treatment for distant metastatic NSCLC (DM2)', and 'Death' as the absorbing state (Figure 1).
- Transitions between health states were modeled using ADAURA (NCT02511106, DCO1 January 2020)[3] and FLAURA (NCT02296125)[5] trials data, Portuguese life tables[6], and real-world data (CancerLinQ Discovery)[7]. The analysis was conducted from the Portuguese National Health Service perspective assuming a 4% discount rate for costs and consequences and a lifetime time horizon (37 years).

Figure 1. Model Structure



DF, disease-free; **DM1**, 1st line treatment for distant metastatic NSCLC; **DM2**, 2nd line treatment for distant metastatic NSCLC; **LRR**, local/regional recurrence, **TP**, transition probability.

Clinical data

- **Disease-free modelling (TPs 1 to 3):** The probability of remaining in the DFS health state was based on the ADAURA trial (DCO1).[3] Parametric distributions were fitted to the Kaplan-Meier (KM) DFS data to extrapolate it beyond the follow-up period. Note that TP3 was modeled based on the background mortality of the age-adjusted Portuguese population as the number of recorded death events in ADAURA was insufficient to fit to any distribution. Patients remaining disease-free for 5 years after treatment completion for resectable disease were considered 'cured' based on feedback from international Key Opinion Leaders (KOL) and published literature.[8,9]
- **Local/regional recurrence modelling (TP4 and TP5):** Due to limited post-recurrence follow-up data available from the ADAURA the TP4 (LRR to DM1) for both treatment arms were modelled using CancerLinQ data. As CancerLinQ data set was insufficient to fit TP5, this transition was modelled using background mortality in the age-adjusted Portuguese population.
- **Distant metastases modelling (TP6 to TP8):** For both treatment arms, the TP6, TP7 and TP8 were calculated based on the latest DCO from FLAURA trial (June 2019).
- The base case parametric distributions applied for each transition, based on goodness-of-fit criteria (Akaike and Bayesian information criteria) and clinical plausibility, and the respective data sources, are shown in Table 1.

Table 1. Distribution used for each transition

Transition	Distribution	Data source
TP1: DF -> LRR	Lognormal	ADAURA (3)
TP2: DF -> DM1	Generalized gamma	ADAURA (3)
TP3: DF -> Death	Background mortality	ADAURA / Portuguese life tables (3,6)
TP4: LRR -> DM1	Lognormal	CancerLinQ (6)
TP5: LRR -> Death	Background mortality	CancerLinQ / Portuguese life tables (7,6)
TP6: DM1 -> DM2	Weibull	FLAURA (5)
TP7: DM1 -> Death	Exponential / Background mortality	FLAURA / Portuguese life tables (5,6)
TP8: DM 2 -> Death	Weibull	FLAURA / Portuguese life tables (5,6)

Adverse Events (AEs)

- Grade ≥3 treatment-related adverse events reported in the ADAURA trial were considered in the model.

Utilities

- The quality-of-life data collected in ADAURA (SF-36) and FLAURA (EORTC QLQ-LC13) trials were mapped to EQ-5D-3L according to NICE guidelines and used in the model.

Table 2. Utility score per health state.

Health state	Mean utility value (SE)
DF	0.825 (0.018)
LRR	0.825 (0.018)
DM1	0.794 (0.0069)
DM2	0.640 (0.03)

Costs

- The model included costs associated with drug acquisition, treatment administration, healthcare resources use, subsequent therapy, and AEs obtained from Portuguese databases and literature.

Table 3. Healthcare resource cost per model cycle.

Health state	Healthcare resource cost per model cycle
DF	200.03 €
LRR	164.49 €
DM1	185.19 €
DM2	2,565.44 €

Table 4. Adverse event cost.

Grade ≥3 adverse event	Cost
Paronychia	1,509.22 €
Decreased Appetite	1,987.00 €
Diarrhoea	1,396.32 €
Stomatitis	853.18 €

3 - RESULTS

Base case scenario

- The modelled curves for each treatment arm are presented in Figures 2 and 3, and cost-effectiveness results for the base-case scenario are presented in Table 5.

Figure 2. Modelled DFS curves on the base-case scenario.

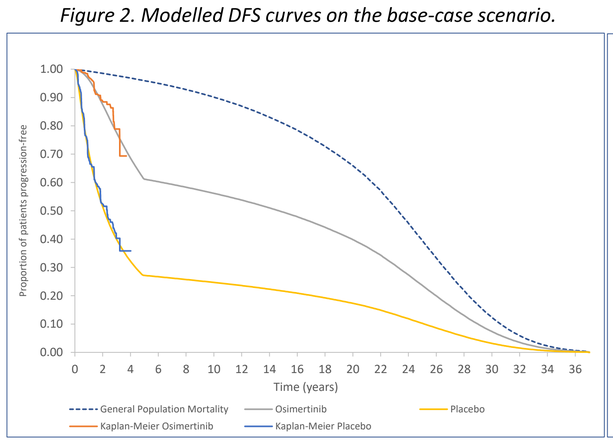
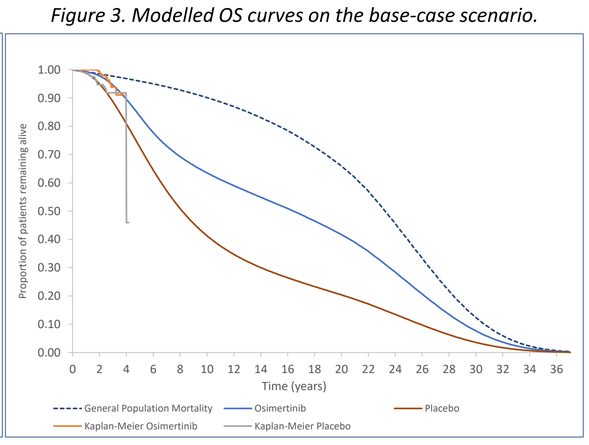


Figure 3. Modelled OS curves on the base-case scenario.



- Adjuvant osimertinib treatment was more effective than active surveillance leading to a mean 2.16 additional quality-adjusted life-years (QALYs) (8.53 vs 6.37) per patient. Osimertinib was associated with mean added costs of 30,514 € per patient and a cost/QALY (incremental cost-effectiveness ratio) of 14,130 € *versus* active surveillance.

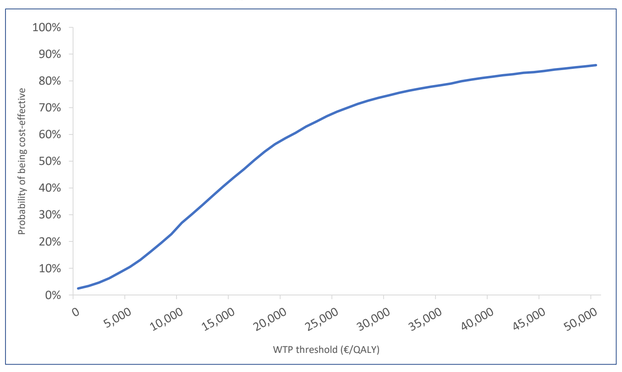
Table 5. Cost-effectiveness results for the base-case scenario.

QALY	Osimertinib	Placebo	Incremental	*Costs*	Osimertinib	Placebo	Incremental
DFS	7.61	3.95	3.65	DFS	130,917.72 €	5,832.02 €	125,085.71 €
LR	0.40	0.66	-0.26	LR	1,341.86 €	3,586.24 €	- 2,244.38 €
DM1	0.17	1.08	-0.91	DM1	3,716.44 €	78,517.92 €	- 74,801.49 €
DM2	0.36	0.68	-0.32	DM2	17,939.45 €	35,419.33 €	- 17,479.88 €
AE	0.00	0.00	0.00	AE	246.48 €	292.42 €	- 45.94 €
Total	8.53	6.37	2.16	Total	154,161.95 €	123,647.94 €	30,514.02 €

Sensitivity analysis

- Model robustness was demonstrated through scenario analyses. Probabilistic sensitivity analysis (PSA) also showed that results are robust with all PSA iterations showing similar results. The results from the cost-effectiveness acceptability curve show that at willingness-to-pay threshold of 20,000 € osimertinib has a probability of cost-effectiveness of approximately 58% increasing thereafter.

Figure 4. Cost-effectiveness acceptability curve.



4 - CONCLUSIONS

- Osimertinib was considered cost-effective compared with active surveillance and is recommended for the adjuvant treatment of patients with completely resected stage IB–IIIA EGFRm NSCLC in the Portuguese National Health Service. The cost-effectiveness model was considered valid to support a reimbursement decision in the Portuguese setting.

5 - REFERENCES

1. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [20 June 2022]. **2.** Melosky B, Kambartel K, Häntschel M, Bennetts M, Nickens DJ, Brinkmann J, *et al.* Worldwide Prevalence of Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer: A Meta-Analysis. Mol Diagn Ther. 2022 Jan;26(1):7-18. **3.** Wu Y-L, Tsuboi M, He J, John T, Grohe C, Majem M, *et al.* Osimertinib in Resected EGFR -Mutated Non–Small-Cell Lung Cancer . N Engl J Med. 2020 Oct;383(18):1711–23. **4.** European Medicines Agency: Enhertu SmPC Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/tagrisso, accessed [20 June 2022]. **5.** Soria J-C, Ohe Y, Vansteenkiste J, Reungwetwattana T, Chewaskulyong B, Lee KH, *et al.* Osimertinib in Untreated EGFR -Mutated Advanced Non–Small-Cell Lung Cancer . N Engl J Med. 2018;378(2):113–25. **6.** National life tables 2018-2020. Statistics Portugal. Available from: https://www.ine.pt, accessed [20 June 2022]. **7.** CancerLinQ. ADAURA-like patient characteristics. Data on file. 2020. **8.** Winton T, Livingston R, Johnson D, Rigas J, Johnston M, Butts C, et al. Vinorelbine plus Cisplatin vs. Observation in Resected Non-Small-Cell Lung Cancer. Vol. 352, N Engl J Med. 2005 **9.** Douillard JY, Rosell R, De Lena M, Carpagnano F, Ramlau R, Gonzáles-Larriba JL, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIA non-small-cell lung cancer. Lancet Oncol. 2006;7(9):719–27.

Corresponding author: andre.andrade@astrazeneca.com