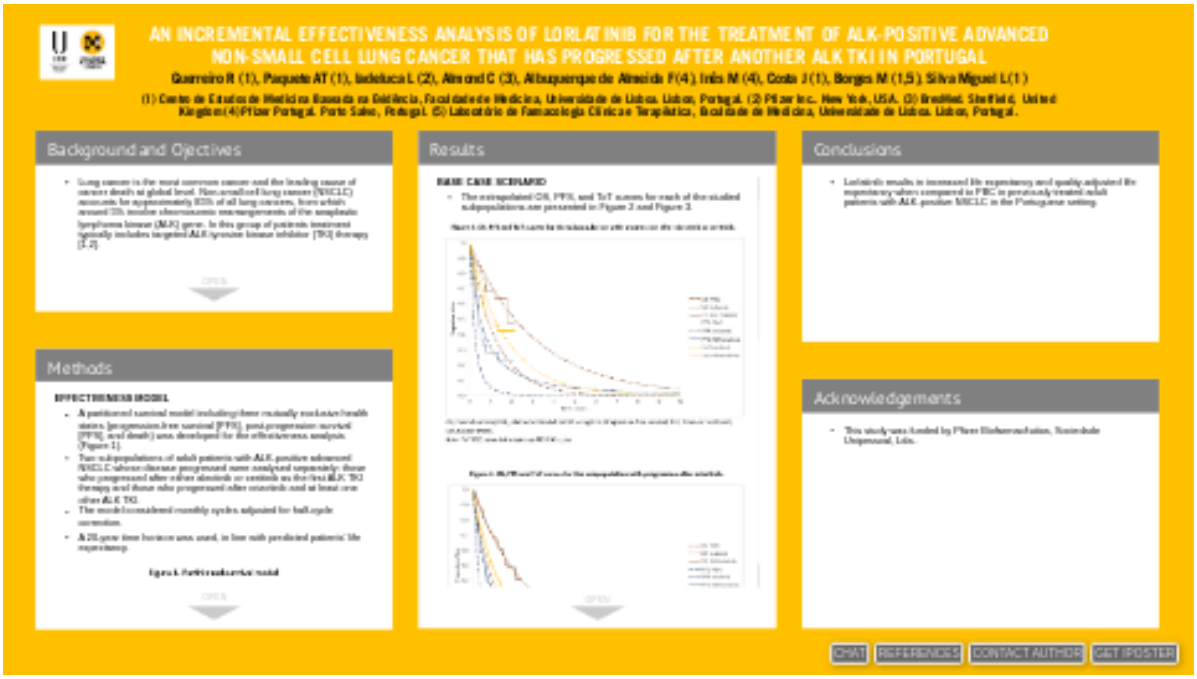
AN INCREMENTAL EFFECTIVENESS ANALYSIS OF LORLATINIB FOR THE TREATMENT OF ALK-POSITIVE ADVANCED NON-SMALL CELL LUNG CANCER THAT HAS PROGRESSED AFTER ANOTHER ALK TKI IN PORTUGAL



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PRESENTED AT:

BACKGROUND AND OJECTIVES

- Lung cancer is the most common cancer and the leading cause of cancer death at global level. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancers, from which around 5% involve chromosomic rearrangements of the anaplastic lymphoma kinase (ALK) gene. In this group of patients treatment typically includes targeted ALK tyrosine kinase inhibitor (TKI) therapy [1,2].

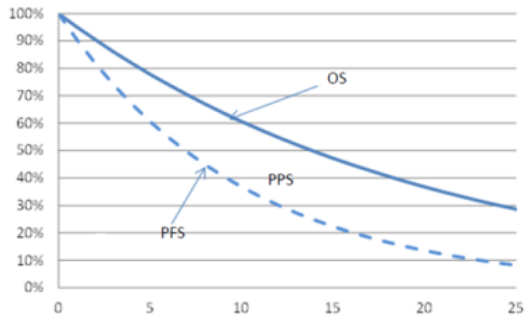
- This study aimed at evaluating the incremental effectiveness of the ALK inhibitor lorlatinib when compared to platinum-based chemotherapy (PBC) for adult patients with ALK-positive advanced NSCLC whose disease progressed after alectinib or ceritinib as the first ALK TKI therapy, or after crizotinib and at least one other ALK TKI, in the Portuguese setting.

METHODS

EFFECTIVENESS MODEL

- A partitioned survival model including three mutually exclusive health states (progression-free survival [PFS], post-progression survival [PPS], and death) was developed for the effectiveness analysis (Figure 1).
- Two subpopulations of adult patients with ALK-positive advanced NSCLC whose disease progressed were analysed separately: those who progressed after either alectinib or ceritinib as the first ALK TKI therapy and those who progressed after crizotinib and at least one other ALK TKI.
- The model considered monthly cycles adjusted for half-cycle correction.
- A 20-year time horizon was used, in line with predicted patients' life expectancy.

Figure 1. Partitioned survival model



OS, Overall survival; PFS, Progression-free survival; PPS, post-progression survival.

CLINICAL DATA

- For lorlatinib, PFS, overall survival (OS), and time on treatment (ToT) were estimated through parametric survival models that were fitted to the data from the single-arm phase I/II clinical trial B7461001 [3,4].
- The parametric distributions selection was based on Akaike information criterion (AIC) and Bayesian information criterion (BIC) and on the clinical validity of long-term extrapolations (Table 1).
- For PBC, PFS was modelled using a hazard ratio (HR) estimated from a matching-adjusted indirect comparison (MAIC) based on the B7461001 trial for lorlatinib and a retrospective chart review study (Lin et al., 2020) for PBC.[5] Since no OS data were available for PBC in the relevant populations, the PFS HR was used as a proxy for the OS HR. PBC ToT was assumed to be equal to the PFS.

Table 1. PFS, OS and ToT curves per subpopulation.

	Subpopulation with progression after alectinib or ceritinib		Subpopulation with progression after crizotinib	
	Lorlatinib	**PBC**	**Lorlatinib**	**PBC**
OS	Exponential	Exponential	Exponential	Exponential
PFS	Lognormal	Lognormal	Lognormal	Lognormal
ToT	Exponential	Exponential	Exponential	Exponential

OS, Overall survival; PBC, platinum-based chemotherapy; PFS, Progression-free survival; ToT, Time on treatment.

UTILITIES

- Health related quality of life (HRQoL) was estimated for PFS and PPS after adjusting for patients' age.
- On-treatment utility weights for lorlatinib were based on the B7461001 trial, where HRQoL information had been collected using the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and its lung cancer module (QLQ LC13) [3,4]. Mapping of the EORTC QLQ-C30 utilities to EQ-5D-3L was done through an algorithm published by Young et al. (2015) and the utilities were valued according to the UK tariffs [6,7].
- PBC patients in pre-progression state were assumed to have the same utility value as lorlatinib patients.
- For the post-progression state, the utility weight was found in the literature (Zhou et al., 2015) (Table 2) [8].

Table 2. Mean utility scores per health states and corresponding sources.

	Subpopulation with progression after alectinib or ceritinib	Subpopulation with progression after crizotinib	Source
Pre-progression			
Lorlatinib	0.810	0.771	Trial B7461001 [4]
PBC			
Post-progression			
Lorlatinib (on-treatment)	0.810	0.771	Trial B7461001 [4]
Lorlatinib (post-treatment)	0,460		Zhou *et al.*, (2015) [8]
PBC			

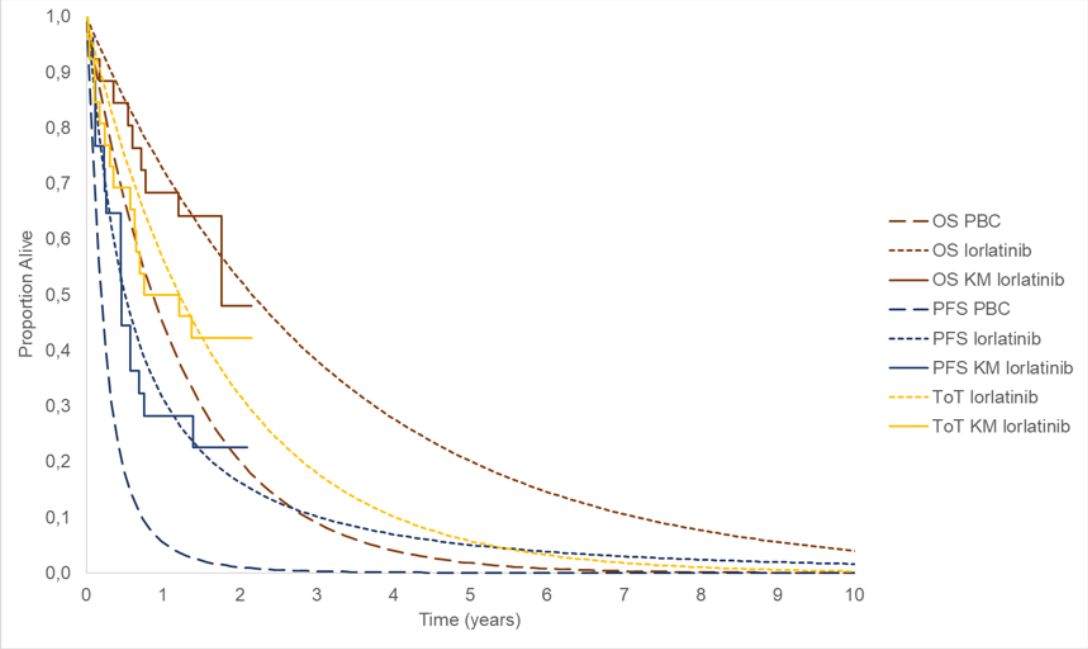
PBC, platinum-based chemotherapy.

RESULTS

BASE CASE SCENARIO

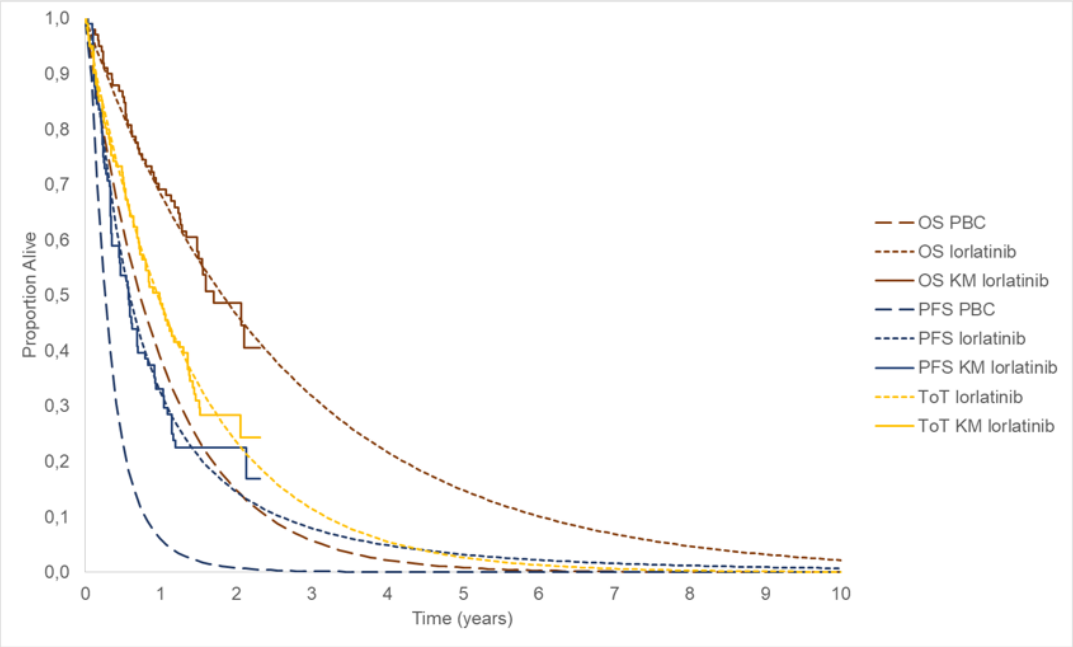
- The extrapolated OS, PFS, and ToT curves for each of the studied subpopulations are presented in Figure 2 and Figure 3.

Figure 2. OS, PFS and ToT curves for the subpopulation with progression after alectinib or ceritinib.



OS, Overall survival; PBC, platinum-based chemotherapy; PFS, Progression-free survival; ToT, Time on treatment; KM, Kaplan-Meier.
Note: ToT PBC curve is the same as PFS PBC curve.

Figure 3. OS, PFS and ToT curves for the subpopulation with progression after crizotinib.



OS, Overall survival; PBC, platinum-based chemotherapy; PFS, Progression-free survival; ToT, Time on treatment, KM; Kaplan-Meier.

Note: ToT PBC curve is the same as PFS PBC curve.

- Treatment with lorlatinib results in a gain of:
  - 1.87 life years (LY) or 1.40 quality-adjusted life years (QALY) in patients whose disease progressed after alectinib or ceritinib (Table 3);
  - 1.57 LY or 1.04 QALY in patients whose disease progressed after crizotinib and another ALK TKI (Table 4).

Table 3. QALY and LY results for the subpopulation with progression after alectinib or ceritinib.

	Lorlatinib	PBC	Δ
QALY			
Pre-progression	1.05	0.27	0.78
Post-progression: on treatment	0.48	0.00	0.48
Post-progression: not on treatment	0.56	0.42	0.14
Total	**2.09**	**0.69**	**1.40**
LY			
Pre-progression	1.28	0.32	0.96
Post-progression: on treatment	0.60	0.00	0.60
Post-progression: not on treatment	1.24	0.92	0.32
Total	**3.12**	**1.25**	**1.87**

LY, Life years; PBC, platinum-based chemotherapy; QALY, Quality-adjusted life years.

Table 4. QALY and LY results for the subpopulation with progression after crizotinib.

	Lorlatinib	PBC	Δ
QALY			
Pre-progression	0.87	0.29	0.58
Post-progression: on treatment	0.25	0.00	0.25
Post-progression: not on treatment	0.53	0.31	0.22
Total	**1.64**	**0.60**	**1.04**
LY			
Pre-progression	1.14	0.38	0.76
Post-progression: on treatment	0.32	0.00	0.32
Post-progression: not on treatment	1.16	0.67	0.49
Total	**2.62**	**1.05**	**1.57**

LY, Life years; PBC, platinum-based chemotherapy; QALY, Quality-adjusted life years.

SENSITIVITY ANALYSES

- Deterministic and probabilistic sensitivity analyses showed that the model was robust to the variation of most parameters, with exception of the parametric distributions used for extrapolating OS and ToT for lorlatinib.
- For the subpopulation whose disease progressed after alectinib or ceritinib, the QALY gain obtained in the deterministic analysis was highest when the Gompertz distribution was used for extrapolating OS, while the lowest increment was observed when lorlatinib ToT was assumed to be equal to PFS. For the subpopulation whose disease progressed after crizotinib, the highest QALY gain was observed when the lognormal curve was selected for lorlatinib ToT and the lowest when a Gompertz curve was chosen for OS for lorlatinib.

CONCLUSIONS

- Lorlatinib results in increased life expectancy and quality-adjusted life expectancy when compared to PBC in previously treated adult patients with ALK-positive NSCLC in the Portuguese setting.

ACKNOWLEDGEMENTS

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