Lorlatinib as a first-line treatment of adult patients with anaplastic lymphoma kinase-positive advanced non-small cell lung cancer: A cost-effectiveness analysis in Greece.

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Background

- Lung cancer is a major public health problem worldwide in terms of diagnosis and mortality. In Greece, lung cancer was responsible for an estimated 8,960 new cases and 7,662 deaths in 2020[1].
- 3-7% of patients with advanced non-small cell lung cancer (aNSCLC) are anaplastic lymphoma kinase positive (ALK+) and may benefit from first-line treatment with an ALK Tyrosine Kinase Inhibitor (TKI) [2-3].
- Despite the efficacy of 1st and 2nd generation TKIs, emergence of ALK resistance mutations and variable brain penetration pose significant treatment challenges, affecting survival and causing clinical and economic burden [4].
- Lorlatinib is a potent, brain-penetrant, 3rd generation ALK and ROS1 TKI, providing broad coverage of ALK mutations[5].
- The efficacy and safety of lorlatinib have been evaluated in the CROWN trial (NCT03052608)[5] where lorlatinib demonstrated significant clinical benefits vs crizotinib in patients with previously untreated ALK+ aNSCLC.

Objective

- **The aim of this study was to evaluate the cost-effectiveness of lorlatinib compared to currently marketed and commonly used ALK TKIs (alectinib, brigatinib, crizotinib) as first-line treatment option for adult patients with ALK+ aNSCLC in Greece.**

Methods

Model structure

- A published[6] four health-state partitioned survival model (progression-free state, central nervous system (CNS) progression, non-CNS progression and death) was locally adapted, from a public (EOPYY) payer perspective (Figure 1).

Clinical inputs

- Efficacy inputs were overall survival (OS), intracranial progression-free survival (IC-PFS), progression-free survival (PFS) and time-on-treatment (ToT).
- CROWN study informed the efficacy in the lorlatinib and crizotinib arms of the model, while indirect relative efficacy estimates for alectinib and brigatinib were derived through a network meta-analysis (NMA).[6].
- Safety and health state utilities data were sourced from published studies[7,8-9].

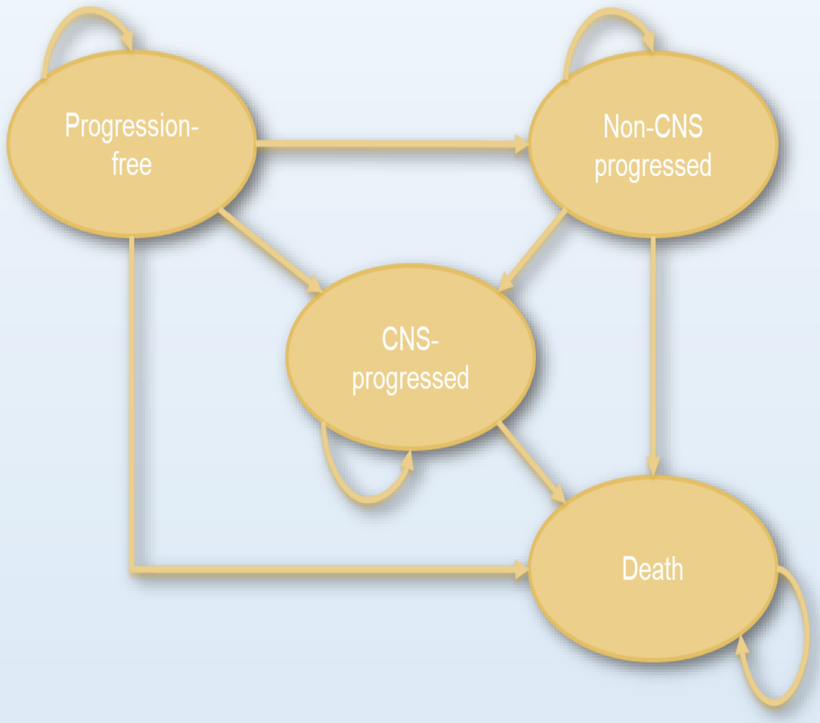
Cost inputs

- Only direct medical costs related to drug acquisition, monitoring costs that split into progression-free and progressed disease health state costs per cycle, post-progression treatment costs and end-of-life care were considered. All costs reflect the year 2023 in Euro (€).

Data analysis

- Model outcomes were patients' life years (LYs), quality-adjusted life years (QALYs), total lifetime costs and incremental cost-effectiveness ratios (ICERs).
- An annual discounting of 3.5% was applied for both health outcomes and costs.
- Probabilistic sensitivity analysis (PSA) and one-way sensitivity analysis (OWSA) were performed.
- While there is no official willingness-to-pay (WTP) threshold in Greece, a WTP of €63,000 per QALY was used in present analysis, aligning with public literature (~3 times the GDP per capita)[10-11].

Figure 1: Model structure



Results

Base case results

- Over a lifetime horizon, the total cost per patient with lorlatinib, alectinib, crizotinib and brigatinib was estimated to be €188,205, €183,343, €75,028, and €145,454 respectively (Table 1).
- In terms of health outcomes, lorlatinib was associated with 1.13, 3.33 and 2.58 increment in LYs compared with alectinib, crizotinib, and brigatinib respectively (Table 1).
- In addition, lorlatinib gained 5.47 QALYs, while alectinib, crizotinib and brigatinib gained 4.37, 3.12 and 3.84 QALYs respectively (Table 1).
- Lorlatinib resulted in ICERs of €4,315 per LY gained and €4,422 per QALY gained compared to alectinib, €34,032 per LY gained and €48,256 per QALY gained versus crizotinib and €16,587 per LY gained and €26,271 per QALY gained compared to brigatinib (Table 1).

Sensitivity analyses results

- OWSA indicated that the parameters that have the biggest impact on cost-effectiveness results were the utility values reported in Roughley et al. (2014)[9] for contralateral lung metastases and brain metastases; the alectinib and brigatinib OS HRs versus crizotinib; and the alectinib and brigatinib median reported treatment durations.
- In the PSA, lorlatinib was associated with a 74%, 65% and 70% probability of being a cost-effective option compared to alectinib (Figure 2), crizotinib (Figure 3) and brigatinib (Figure 4) respectively, at a WTP threshold of €63,000 per QALY gained.

Table 1 : Cost effectiveness base case results

Parameters	Lorlatinib	Crizotinib	Alectinib	Brigatinib
Total cost	€188,205	€75,028	€183,343	€145,454
LYs	9.21	5.89	8.09	6.64
QALYs	5.47	3.12	4.37	3.84
ICER per LY gained		€34,032	€4,315	€16,587
ICER per QALY gained		€48,256	€4,422	€26,271

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

Conclusion

Present analysis indicates that lorlatinib provides substantial clinical benefits versus current therapeutic alternatives and appears to be a cost–effective treatment option compared to 1st and 2nd generation TKIs for previously untreated patients with ALK+ aNSCLC in Greece.

Figure 2: Cost-effectiveness acceptability curve of Lorlatinib versus Alectinib

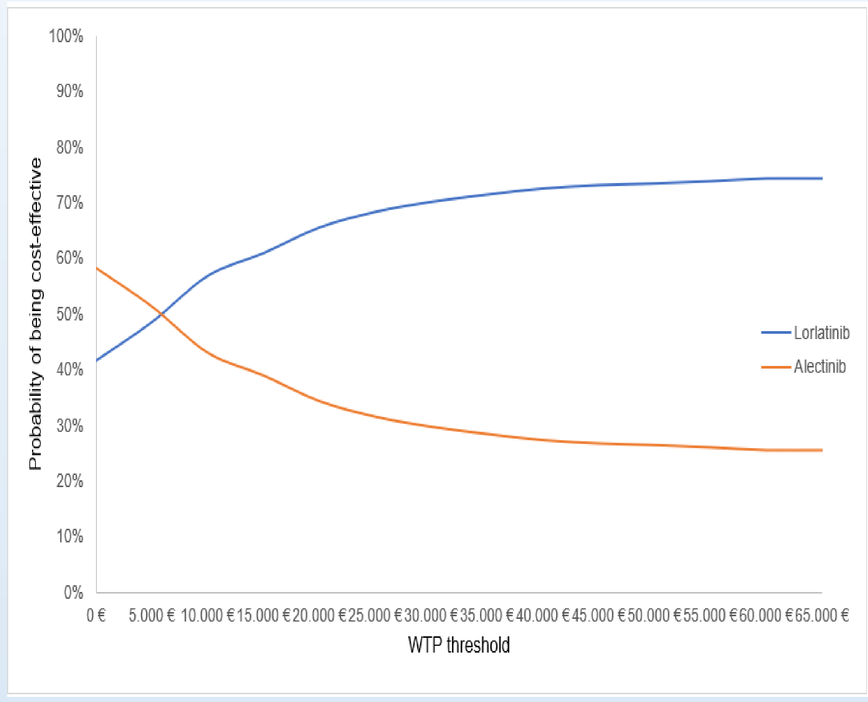


Figure 3: Cost-effectiveness acceptability curve of Lorlatinib versus Crizotinib

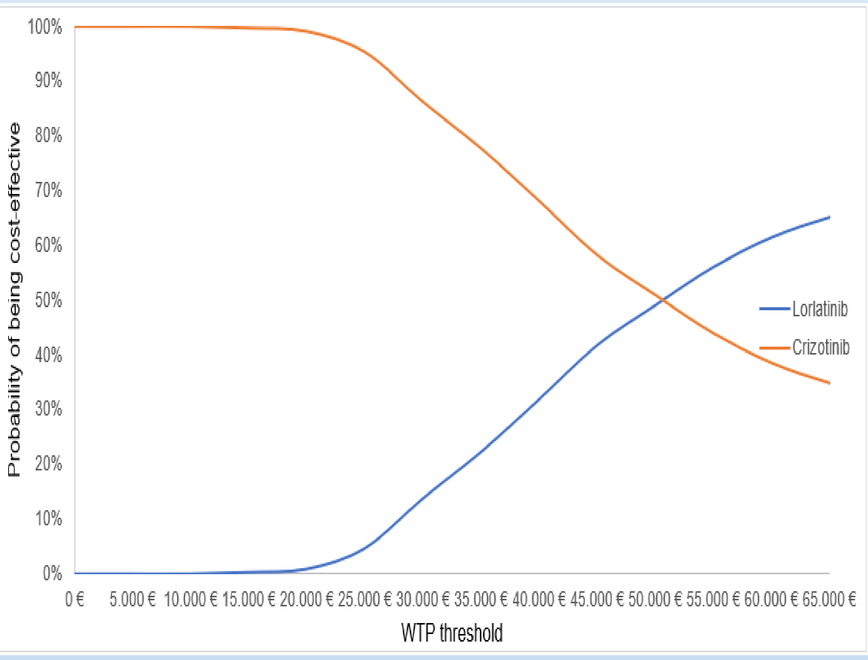
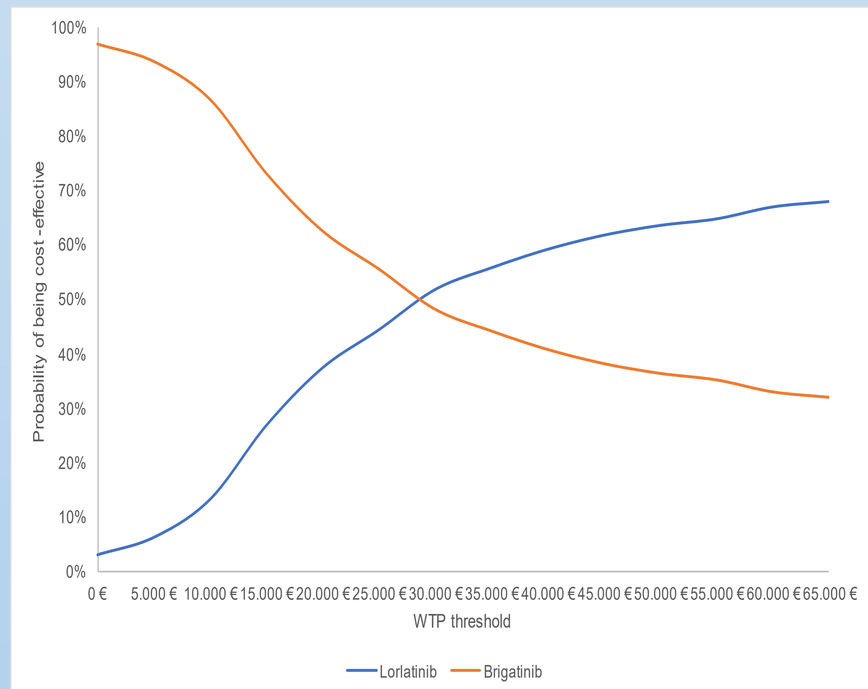


Figure 4: Cost-effectiveness acceptability curve of Lorlatinib versus Brigatinib



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Disclosures

This study was sponsored by Pfizer Hellas SA. OZ and AL are employees of Pfizer Hellas SA. GG and CT are owners of Health Through Evidence, which was a paid consultant to Pfizer in connection with the development of this study.

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