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Cost-effectiveness of Tyrosine Kinase Inhibitors for Treatment of Locally Advanced or Metastatic ALK+ Non-Small Cell Lung Cancer in Brazil

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Abstract

Objectives

To evaluate the cost-effectiveness of ALK tyrosine kinase inhibitors (TKIs) as first and second-line treatments for adults with locally advanced or metastatic ALK-positive non-small cell lung cancer (NSCLC) in Brazil, from the public healthcare system perspective.

Methods

A Markov model was developed using TreeAge software to compare first-line ALK inhibitors (crizotinib, alectinib, brigatinib, lorlatinib) and second-line treatments including chemotherapy. Transition states included progression-free survival, second-line progression, and death. Costs (in BRL) were obtained from SIGTAP/DATASUS and pharmaceutical price submissions. Effectiveness was measured in quality-adjusted life-years (QALYs). Deterministic and probabilistic sensitivity analyses were performed. Incremental cost-effectiveness ratios (ICERs) were compared against a cost-effectiveness threshold of U$49,180.33/QALY.

Results

Among seven strategies, three were not dominated: brigatinib + chemotherapy (ICER U$47,981.02/QALY), alectinib + chemotherapy (U$182,813.02/QALY), and alectinib + lorlatinib (U$567,107.50/QALY). Deterministic sensitivity analysis showed brigatinib cost as the most influential parameter. Probabilistic analysis revealed that 47% of brigatinib + chemotherapy simulations were below the cost-effectiveness threshold.

Conclusions

Brigatinib followed by chemotherapy was the most cost-effective strategy for first-line treatment of ALK+ NSCLC in Brazil, representing an efficient use of public healthcare resources. Drug pricing remains the main determinant of cost-effectiveness.

Highlights

- **What is already known:** Targeted ALK inhibitors improve survival in ALK+ NSCLC, but high costs challenge their incorporation in public systems.
- **What this paper adds:** This study is the first to evaluate all registered ALK inhibitors in Brazil, using price proposals submitted by manufacturers.

- **Implications for decision making:** Brigatinib offers the most cost-effective balance between cost and QALY gain under Brazil's willingness-to-pay threshold.

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths globally, accounting for approximately 2 million diagnoses and 1.8 million deaths[1]. In Brazil, approximately 32,560 new cases are diagnosed annually, corresponding to an estimated risk of 15.06 cases per 100,000 inhabitants, with 18,020 cases among men and 14,540 cases among women. These values correspond to an estimated risk of 17.06 new cases per 100,000 men and 13.15 per 100,000 women[2].

LC cases are classified into two main groups, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) accounting for 85% of cases. NSCLC is frequently diagnosed when the disease is already in an advanced stage[3]. The choice of treatment for NSCLC should be based on physiological characteristics and functional capacity, histological type, clinical toxicity, patient preferences, and therapeutic protocols. Before starting any treatment, the existence of genetic mutations, such as EGFR, ALK or ROS1 genes, is confirmed by tests[4]. The American College of Pathology recommends ALK translocation testing for all patients with carcinoma on biopsy[5].

Approximately 10% of patients with NSCLC have brain metastases at the time of diagnosis, and up to 40% of patients develop this type of metastasis during the disease, with high morbidity. Brain metastases are especially common in NSCLC with ALK translocation, with a cumulative incidence of more than 50%, which is associated with a poor prognosis, high symptom burden, and decreased quality of life. The survival of patients after the diagnosis of metastasis in the central nervous system (CNS) usually does not exceed six months[6].

Global data indicate that the frequency of NSCLC with ALK translocation ranges from 1.6 to 11.6%[7] and, in Brazil, its prevalence is 3.2%, with only 16% of patients being tested[8]. In more advanced cases of NSCLC, the five-year survival rate is estimated to be extremely low, being 53.6% for localized disease, 28.9% for regional disease and 5.4% in the distant metastasis stage[9].

Current Diagnostic and Therapeutic Guidelines for lung cancer in Brazil[4] recommend radiotherapy as a therapeutic strategy for the treatment of NSCLC, which can be used for curative or palliative purposes, being indicated at all stages of the disease, and may or may not be associated with chemotherapy and surgery. For advanced or recurrent disease, the guideline recommends thoracic radiotherapy associated or not with chemotherapy; palliative chemotherapy, surgical resection of isolated brain metastasis, which may or may not be followed by cranial radiotherapy; external radiotherapy, with or without interstitial radiotherapy, for symptomatic endobronchial lesions and palliative radiotherapy, for analgesic or hemostatic purposes[10]. Targeted therapies, such as tyrosine kinase inhibitors, have demonstrated efficacy in the treatment of NSCLC patients who have genetic mutations[4].

Tyrosine kinase inhibitors (TKIs) targeting ALK have significantly improved outcomes; however, their high cost necessitates cost-effectiveness assessment to inform public reimbursement decisions. Given the challenges faced by low- and middle-income countries in making better use of resources, efforts need to be undertaken to make cancer control more effective.

This study aims to evaluate the cost-effectiveness of ALK inhibitors available in Brazil for first-line treatment of ALK-positive advanced NSCLC, from the perspective of the Brazilian public healthcare system (SUS).

METHODS

A stochastic model based on Markov chains was built using TreeAge software. The analysis compared the drugs in the two lines of treatment, where the comparator for the first line was Crizotinib and for the second line was chemotherapy.

The model contains four mutually exclusive transition states: (a) Progression-free survival, (b) Progression to second-line treatment, and (c) Progression from second-line treatment (d) Death (Figure 1). Patients who have not yet progressed and are using first-line treatment may progress and switch to second-line treatment or die. Patients using second-line treatment, upon progression, receive palliative chemotherapy as indicated by the Diagnostic and Therapeutic Guidelines for lung cancer.

The choice of second-line drugs respected the hierarchy of the three generations of ALK inhibitor drugs. The drug eligible for second-line treatment must necessarily be from a more recent generation than the one used in first-line treatment. As first-line options, we used Crizotinib, Brigatinib, Alectinib, and Lorlatinib. For the second line, we used the same drugs, but with chemotherapy as a comparator instead of Crizotinib. In the alternative where the first line was Crizotinib (first generation), it would be possible to include any of the other 3 drugs that would be second or third generation. As a standard, Brigatinib was included because it was the lowest cost alternative. This change was considered in the sensitivity analysis.

The perspective of analysis was of the Brazilian public healthcare system, and the time horizon was lifetime (30 years), with a discount rate of 5% per year. The target population of the study were patients with NSCLC with ALK allocation.

Effectiveness data

The effective outcome used in the analysis was the quality-adjusted life years (QALY). A literature review was conducted to search for utility data for NSCLC patients, as well as economic evaluation studies of therapies used in this population. The study by Chouaid, 2013[11] presented specific utility data for the progressed and progression-free states in the different lines of treatment. A sensitivity analysis was performed using data from the study by Nafees, 2008[12].

Transition probabilities were derived from Kaplan-Meier curves. Overall survival (OS) and progression-free survival (PFS) data were extracted from Kaplan-Meier curves for crizotinib as first-line treatment, and chemotherapy and alectinib as second-line treatment. These data were estimated from the digitization of aggregated Kaplan-Meier curve data using the WebPlotDigitizer software. Based on these estimates, individual data was generated according to the algorithm proposed by Guyot, 2012[13] in the R language using the IPDfromKM package. The simulated individual data were fitted to the Exponential, Weibull, Loglogistics, Gompertz, and Lognormal survival functions using the flexsurvreg package. The meta-analysis by Zhao, 2024[14] showed very similar results in terms of PFS between alectinib, brigatinib, and lorlatinib compared to chemotherapy, with very close HR values and confidence intervals. Khan's 2019[15] meta-analysis showed no significant difference in OS between second-line treatments compared to chemotherapy. Therefore, for the probability of progression in second-line treatment, data from Alectinib were used for all proposed treatments. OS was the same as the chemotherapy comparator, as shown by the meta-analysis results. The efficacy measures of the drugs relative to their respective comparators in first and second line were extracted from the systematic review[16,17]. According to Cameron's 2022[18] the OS results for Brigatinib and Lorlatinib compared to Crizotinib did not show statistical significance and, therefore, the model considered the same OS as Crizotinib in first line for the other two drugs. Hazard ratios for PFS and OS sourced from Zhou (2024)[14], Camidge (2021)[19], Solomon (2024)[20], and Khan (2019)[15]. Table 1 shows these parameters inputs.

Costing Data

For the composition of total costs, the costs related to the interventions were considered (cost of medication, follow-up costs, and progression costs). Costs for medical procedures were extracted from SIGTAP/DATASUS. Treatment costs were calculated considering the dosage presented in the package insert. The cost of the diagnostic test was not considered since, after the incorporation of Crizotinib, which requires the diagnostic test to be performed, it was considered that all patients, regardless of treatment, had already been tested and confirmed as ALK mutation positive before the start of the model. For the costs of interventions that have not yet been incorporated into the SUS (Brazilian Unified Health System), such as Alectinib, Brigatinib, and Lorlatinib, the Department of Management and Incorporation of Health Technologies (DGITS) of the Ministry of Health sent official letters to the manufacturing companies informing them of the study, and they responded with price proposals that were considered in the analysis. For Crizotinib, the price proposal made by the company during the evaluation of its incorporation was considered. Table 1 shows these parameters inputs.

Model Assumptions

For the structuring of the simulation that considered the two lines of treatment, several assumptions were adopted in the model. Consultation with specialists indicated that the selection of second-line medications must adhere to the hierarchical classification of the three generations of ALK inhibitors. Specifically, the medication eligible for second-line treatment must necessarily belong to a more recent generation than that utilized in the first-line treatment.

Given the comparable progression-free survival outcomes observed among Alectinib, Brigatinib, and Lorlatinib in second-line therapy, coupled with the lack of demonstrated overall survival advantage of these treatments over chemotherapy in the second-line setting, the therapeutic options for this treatment line were consolidated to chemotherapy and ALK inhibitors. Specifically, any ALK inhibitor may be employed when Crizotinib is administered as first-line therapy, whereas Lorlatinib is designated necessarily when either Brigatinib or Alectinib is used in the first-line setting.

Dollar values were converted from BRL values using the purchasing power parity (PPP) exchange rate, where 1 USD equals 2.44 BRL.

Sensitivity Analysis

Deterministic sensitivity analysis was conducted via Tornado diagrams. Probabilistic sensitivity analysis (1,000 Monte Carlo simulations) assessed parameter uncertainty, considering cost and effectiveness distributions.

RESULTS

Cohorts treated with the 7 strategies (Table S1 - Supplementary material) were simulated using first and second-line drug combinations, producing cost-effectiveness estimates for each. Only three alternatives were not dominated: Brigatinib + Chemotherapy (ICER equal to U$34.244,90), Alectinib + Chemotherapy (ICER equal to U$159.034,41), and Alectinib + Lorlatinib (ICER equal to U$527.442,75). The Lorlatinib + Chemotherapy alternative showed extended dominance. Table 2 shows the costs and effectiveness of the non-dominated alternatives, and Table S2 shows the results for all alternatives in the supplementary material. Figure 2 shows the cost-effective relationships between all alternatives.

Deterministic sensitivity analysis was performed prioritizing the non-dominated alternatives using Tornado diagrams. In comparison between Crizotinib + Chemotherapy and Brigatinib + Chemotherapy, the ICER was more sensitive to the monthly treatment cost of Brigatinib, varying from U$9,185.25/QALY to U$86,776.61/QALY, where the price was modified by values 20% lower and higher, respectively (Fig. 3).

In the probabilistic sensitivity analysis with 1000 Monte Carlo simulations, 81.7% of the simulations for the Brigatinib + Chemotherapy strategy fell below the cost-effectiveness threshold of U$49,180.33/QALY (Fig. 4). None of the simulations for the Alectinib + Lorlatinib alternative fell below the threshold. Figures S1 and S2 show these results (Supplementary material).

In summary, Brigatinib + chemotherapy yielded the lowest ICER (U$47,981.02/QALY), falling below the national threshold. Alectinib + chemotherapy and alectinib + lorlatinib were less efficient alternatives. The model was most sensitive to brigatinib's monthly cost, which affected the ICER range (U$9,185.25–U$86,776.64/QALY). Probabilistic analysis confirmed that brigatinib-based therapy was cost-effective in 47% of simulations (Fig. 4).

DISCUSSION

This evaluation sought to study the cost-effectiveness of all ALK-1 inhibitors registered in Brazil and compare them to understand the efficiency of incorporating these treatments into the Health System. Zhang's study (2024)[21] compared 6 tyrosine kinase inhibitors as first-line treatment against NSCLC from the perspective of the Chinese health system. The results found are similar to those of the present study, where, despite the smaller number of drugs compared, brigatinib is the most efficient alternative for the health system.

The results of the analysis depend heavily on the price of the drugs, this being the variable that most impacted the analysis for all treatments studied. This work aimed to assist decision-makers in the Brazilian health system in providing the best treatment recommendation. Before it was carried out, the drug manufacturers were informed by the Ministry of Health that the study would be conducted comparing all alternatives registered in the country and a price proposal for incorporation was requested. An analysis was conducted with the initially proposed prices, and subsequently, manufacturers had access to the study results and also to the prices proposed by competitors in a public consultation. Manufacturers responded to this consultation by proposing new prices, and our analysis was carried out with these latter values. The largest discount was 75% compared to the list price. This is the first time in Brazil that this method involving the price proposals of companies through a request from the Ministry of Health has been carried out, and the final prices obtained allowed for incremental cost-effectiveness ratio results below the willingness-to-pay threshold of the health system.

Regarding the results of the deterministic sensitivity analysis, the most likely variation to modify the outcome of the study's decision was the monthly cost of Brigatinib treatment, which, when varied by plus or minus 20%, produced variations in the ICER between U$9,185.25/QALY and U$86,776.61/QALY. The price of this medication is the factor that decision-makers should take most into account when evaluating the efficiency of incorporating this medication. The 20% variation in value did not change the ranking of this alternative in terms of cost-effectiveness, and it remains the most efficient. The variation made to the other parameters in the model did not produce results that would change the decision on the most efficient alternative, as it did not produce alternatives that fell below the threshold of U$49,180.33/QALY.

The parametric uncertainty with this alternative is also revealed in the probabilistic sensitivity analysis, where although the deterministic result produced an ICER lower than the cost-effectiveness threshold (U$47,981.02/QALY), the deterministic analysis revealed only 47% of the simulations below the threshold, slightly less than half. The monthly cost parameter for Brigatinib was not varied in the probabilistic sensitivity analysis, which shows that other effective parameters such as hazard ratios or utilities with their respective confidence intervals can also influence this decision.

The cost-effectiveness of ALK inhibitors is context-dependent, shaped by national drug prices, willingness-to-pay thresholds, and health system perspectives. The study of Zhang et al[21] from the

perspective of the Chinese health-care system, showed that the inclusion of drug price negotiations (2023 China National Medical Insurance) drastically changed earlier findings. Previous studies[22] had found ensartinib was a cost-effective option compared with crizotinib, and was a dominant alternative to ceritinib and brigatinib. Although lorlatinib and alectinib were associated with prolonged survival compared with ensartinib, they were less cost-effective than ensartinib due to the overwhelming total costs. After new insurance negotiations, brigatinib offered an optimal balance between efficacy and cost, outperforming alectinib and lorlatinib in economic terms. Lorlatinib, though clinically benefit, remains too expensive to be cost-effective under Chinese pricing.

Those results contrast with European analyses[23,24] (e.g., Sweden, Greece), where lorlatinib was cost-effective due to different price structures. High-income countries such as Sweden or Greece, also have high willingness-to-pay to support latest-generation TKIs. Nevertheless, in the United States (USA), none of the newer TKIs are cost-effective at prevailing prices. Despite strong efficacy, lorlatinib's high price makes it not cost-effective[25]. Even with large QALY gains (0.72), ICER $407,000/QALY is over twice the WTP limit (≈ $150,000–200,000/QALY).

Although the study shows several uncertainties and their magnitude, the Brigatinib + Chemotherapy alternative proved to be the most efficient among those registered in the country and with a deterministic result below the willingness-to-pay threshold. Treatment strategies that can offer QALY at a cost-effective price are fundamental to the sustainability of the Brazilian health system, which is characterized by universal patient care.

Brigatinib represents the most cost-effective ALK inhibitor for first-line ALK+ NSCLC within Brazil's healthcare public system. Results are consistent with international findings[21] (Zhang, 2024), supporting brigatinib as a preferred public funding option. Price negotiations were the primary determinant of affordability, highlighting the impact of manufacturer discount policies. Sensitivity analyses demonstrated robustness, with brigatinib remaining the most efficient choice across plausible cost variations.

CONCLUSIONS

Brigatinib followed by chemotherapy is the most cost-effective treatment for first-line ALK+ NSCLC in Brazil under the public healthcare perspective. Price-based negotiations and evidence-based adoption can improve sustainability in oncological care within resource-constrained systems.

Declarations

Conflicts of Interest:

The authors declare no conflicts of interest.

Funding:

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Author Contribution

Concept and design: RICARDO FERNANDES; RITA ALBUQUERQUE; TAYNÁ BANDEIRA; RAQUEL SOUZA; RODOLFO CASTRO; CARMEN ROMEROAcquisition of data: RITA ALBUQUERQUE; TAYNÁ BANDEIRA; RAQUEL SOUZA; RODOLFO CASTRO;RICARDO FERNANDESAnalysis and interpretation of data: RICARDO FERNANDES; RITA ALBUQUERQUE; TAYNÁ BANDEIRA; RAQUEL SOUZA; RODOLFO CASTRO; CARMEN ROMERODrafting of the manuscript: RICARDO FERNANDES; RITA ALBUQUERQUE; CARMEN ROMEROCritical revision of the paper for important intellectual content: RICARDO FERNANDES; RITA ALBUQUERQUE; CARMEN ROMEROStatistical analysis: RICARDO FERNANDESProvision of study materials or patients: Not applicableObtaining funding: RICARDO FERNANDESAdministrative, technical, or logistic support: Not applicableSupervision: RICARDO FERNANDES

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References

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. 2024. https://gco.iarc.who.int/today/en
2. Nicholson AG, Tsao MS, Beasley MB, et al. The 2021 WHO Classification of Lung Tumors: Impact of Advances Since 2015. J Thorac Oncol. 2022;17(3):362–87. 10.1016/j.jtho.2021.11.003.
3. Larsson M, Ljung L, Johansson BBK. Health-related quality of life in advanced non-small cell lung cancer: correlates and comparisons to normative data: Health-related quality of life in lung cancer. Eur J Cancer Care (Engl). 2012;21(5):642–9. 10.1111/j.1365-2354.2012.01346.x.
4. Ministério da Saúde. Aprova as Diretrizes Diagnósticas e Terapêuticas Do Câncer de Pulmão.. 2014. https://bvsms.saude.gov.br/bvs/saudelegis/sas/2014/prt0957_26_09_2014.html
5. Shields MD, Marin-Acevedo JA, Pellini B. Immunotherapy for Advanced Non–Small Cell Lung Cancer: A Decade of Progress. Am Soc Clin Oncol Educ Book. 2021;41e105–27. 10.1200/EDBK_321483.
6. Detterbeck FC, Lewis SZ, Diekemper R, Addrizzo-Harris D, Alberts WM. Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice

Guidelines. Chest. 2013;143(5):S7–37. 10.1378/chest.12-2377.

7. Shaw AT, Bauer TM, De Marinis F, et al. First-Line Lorlatinib or Crizotinib in Advanced *ALK* -Positive Lung Cancer. N Engl J Med. 2020;383(21):2018–29. 10.1056/NEJMoa2027187.
8. Gridelli C, Rossi A, Carbone DP, et al. Non-small-cell lung cancer. Nat Rev Dis Primer. 2015;1(1):15009. 10.1038/nrdp.2015.9.
9. Ettinger DS, Wood DE, Akerley W, et al. NCCN Guidelines Insights: Non–Small Cell Lung Cancer, Version 4.2016. J Natl Compr Canc Netw. 2016;14(3):255–64. 10.6004/jnccn.2016.0031.
10. Calabrich A, Wainstein AJ, Melo ACD, et al. Updated Brazilian guidelines for the management of immune-related adverse events associated with checkpoint inhibitors - edition 2.0. Braz J Oncol. 2022;18(CP):2526–873220220305. 10.5935/2526-8732.20220305.
11. Chouaid C, Agulnik J, Goker E, et al. Health-Related Quality of Life and Utility in Patients with Advanced Non–Small-Cell Lung Cancer: A Prospective Cross-Sectional Patient Survey in a Real-World Setting. J Thorac Oncol. 2013;8(8):997–1003. 10.1097/JTO.0b013e318299243b.
12. Nafees B, Stafford M, Gavriel S, Bhalla S, Watkins J. Health state utilities for non small cell lung cancer. Health Qual Life Outcomes. 2008;6(1):84. 10.1186/1477-7525-6-84.
13. Guyot P, Ades A, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. BMC Med Res Methodol. 2012;12(1):9. 10.1186/1471-2288-12-9.
14. Zhao M, Shao T, Shao H, Zhou C, Tang W. Identifying optimal ALK inhibitors in first- and second-line treatment of patients with advanced ALK-positive non-small-cell lung cancer: a systematic review and network meta-analysis. BMC Cancer. 2024;24(1):186. 10.1186/s12885-024-11916-4.
15. Khan M, Lin J, Liao G, et al. ALK Inhibitors in the Treatment of ALK Positive NSCLC. Front Oncol. 2019;8:557. 10.3389/fonc.2018.00557.
16. Ministério da Saúde. Inibidores da tirosina quinase para câncer de pulmão não pequenas células com translocação em ALK em estágio localmente avançado ou metastático como 1a linha de tratamento. Brasil, Ministério da Saúde. 2025:236. https://www.gov.br/conitec/pt-br/midias/relatorios/2025/relatorio-de-recomendacao-no-993-tirosina-quinase-1a-linha
17. Ministério da Saúde. Inibidores da tirosina quinase para câncer de pulmão não pequenas células com translocação em ALK em estágio localmente avançado ou metastático como 2a linha de tratamento. Brasil, Ministério da Saúde. 2025:208. https://www.gov.br/conitec/pt-br/midias/relatorios/2025/relatorio-de-recomendacao-no-994-tirosina-quinase-1a-linha
18. Cameron LB, Hitchen N, Chandran E et al. Targeted therapy for advanced anaplastic lymphoma kinase (*ALK*)-rearranged non-small cell lung cancer. Cochrane Lung Cancer Group, ed. *Cochrane Database Syst Rev*. 2022;2022(1). 10.1002/14651858.CD013453.pub2
19. Camidge DR, Kim HR, Ahn MJ, et al. Brigatinib Versus Crizotinib in ALK Inhibitor–Naive Advanced ALK-Positive NSCLC: Final Results of Phase 3 ALTA-1L Trial. J Thorac Oncol. 2021;16(12):2091–108. 10.1016/j.jtho.2021.07.035.

20. Solomon BJ, Liu G, Felip E, et al. Lorlatinib Versus Crizotinib in Patients With Advanced *ALK* -Positive Non–Small Cell Lung Cancer: 5-Year Outcomes From the Phase III CROWN Study. J Clin Oncol. 2024;42(29):3400–9. 10.1200/JCO.24.00581.
21. Zhang M, Zheng B, Yang W, et al. Cost-Effectiveness Analysis of 6 Tyrosine Kinase Inhibitors as First-Line Treatment for ALK-Positive NSCLC in China. Clin Med Insights Oncol. 2024;18:11795549241257234. 10.1177/11795549241257234.
22. Luo X, Zhou Z, Zeng X, Peng L, Liu Q. Cost-effectiveness of ensartinib, crizotinib, ceritinib, alectinib, brigatinib and lorlatinib in patients with anaplastic lymphoma kinase-positive non-small cell lung cancer in China. Front Public Health. 2022;10:985834. 10.3389/fpubh.2022.985834.
23. Naik J, Beavers N, Nilsson FOL, Iadeluca L, Lowry C. Cost–Effectiveness of Lorlatinib in First-Line Treatment of Adult Patients with Anaplastic Lymphoma Kinase (ALK)–Positive Non–Small–Cell Lung Cancer in Sweden. Appl Health Econ Health Policy. 2023;21(4):661–72. 10.1007/s40258-023-00807-7.
24. Gourzoulidis G, Kastanioti C, Mavridoglou G, et al. Real-World Prevalence, Treatment Patterns, and Economic Impact of EGFR- and ALK-Targeted Therapies in Non-Small Cell Lung Cancer: A Nationwide Analysis from Greece. Curr Oncol. 2025;32(10):542. 10.3390/curroncol32100542.
25. Li S, Li J, Peng L, Li Y, Wan X. Cost-Effectiveness of Lorlatinib as a First-Line Therapy for Untreated Advanced Anaplastic Lymphoma Kinase-Positive Non-Small Cell Lung Cancer. Front Oncol. 2021;11:684073. 10.3389/fonc.2021.684073.

Tables

Tables are available in the Supplementary Files section.

Figures

Figure 1. Markov Model Structure

Description: Transition states in the Markov model representing progression-free, post-progression, and death states.

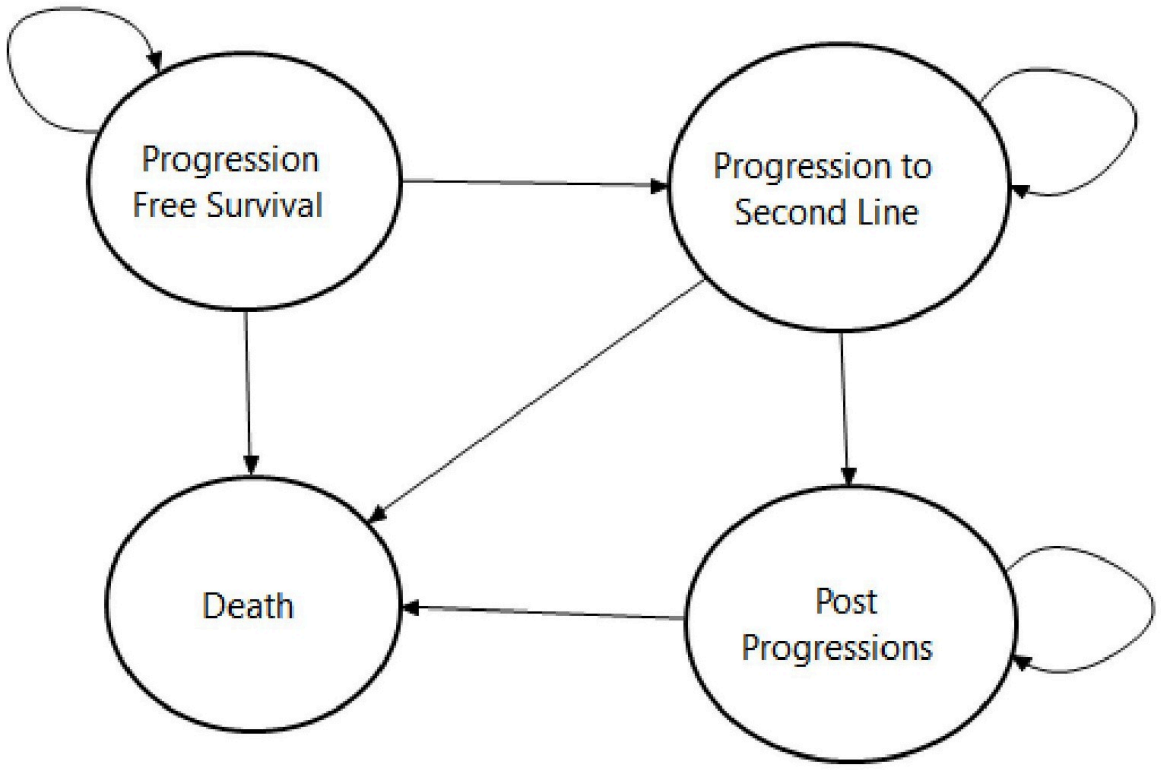


Figure 1

See image above for figure legend.

Figure 2. Cost-Effectiveness Plane

Description: Incremental costs versus incremental effectiveness for each strategy.

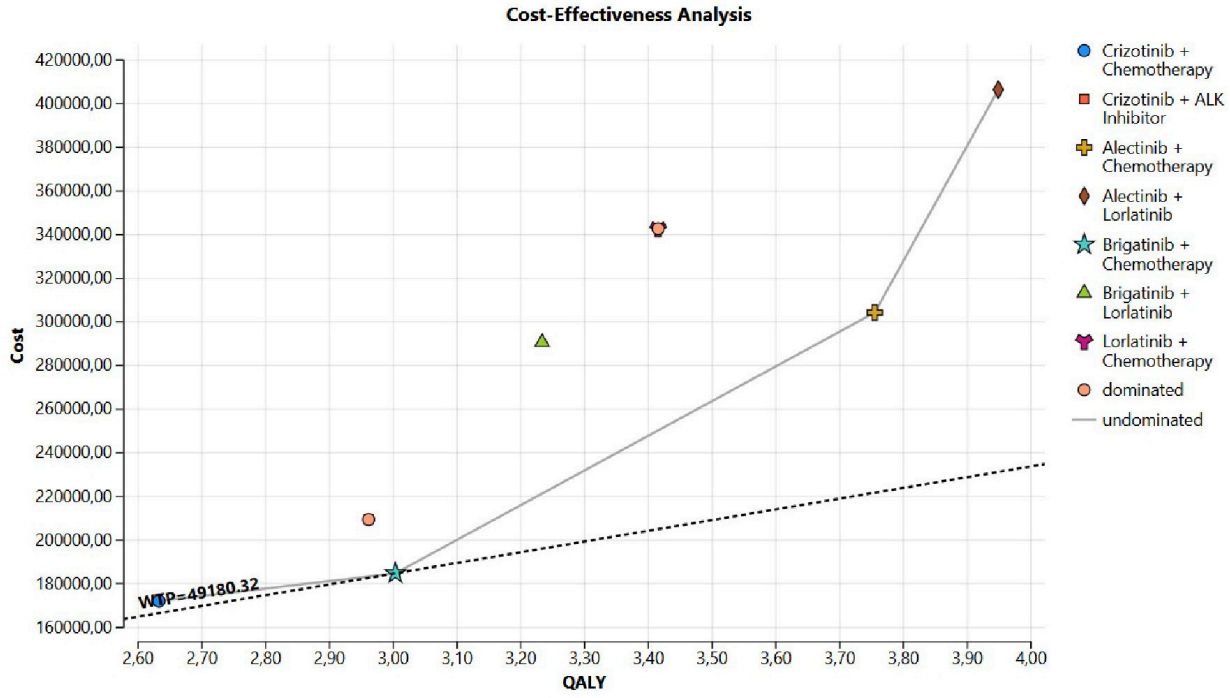


Figure 2

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Figure 3. Deterministic Sensitivity Analysis Results (Tornado Diagram Inputs)

Description: Main parameters influencing ICER in deterministic sensitivity analysis.

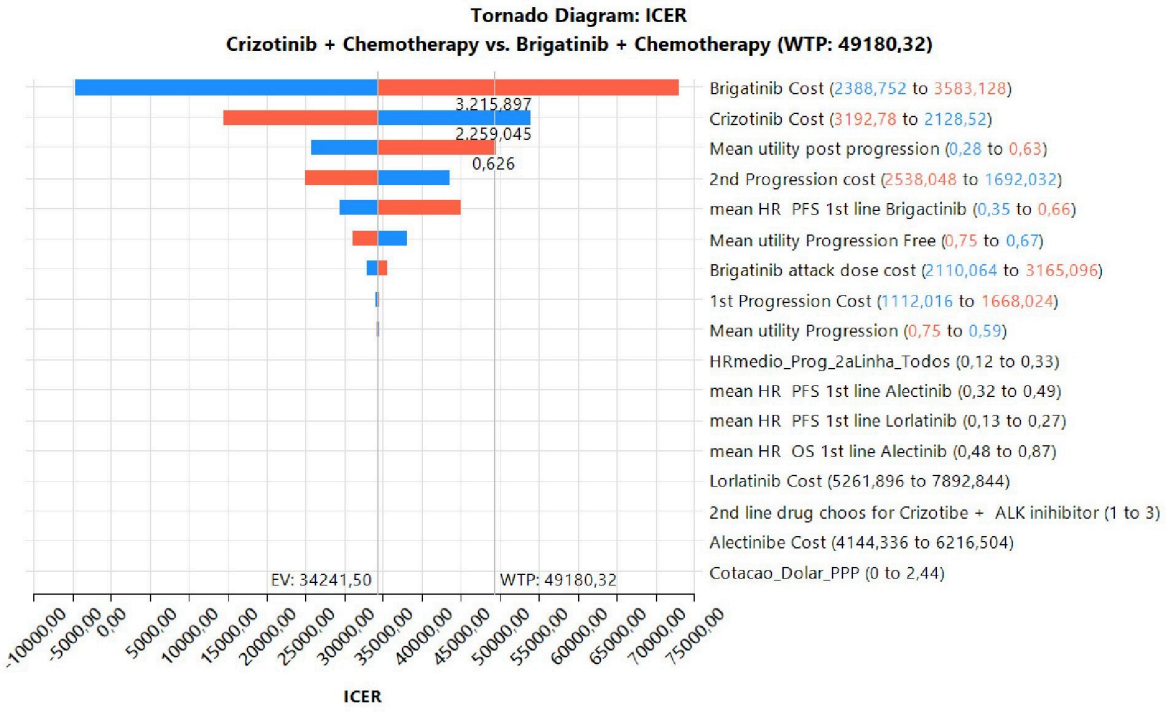


Figure 3

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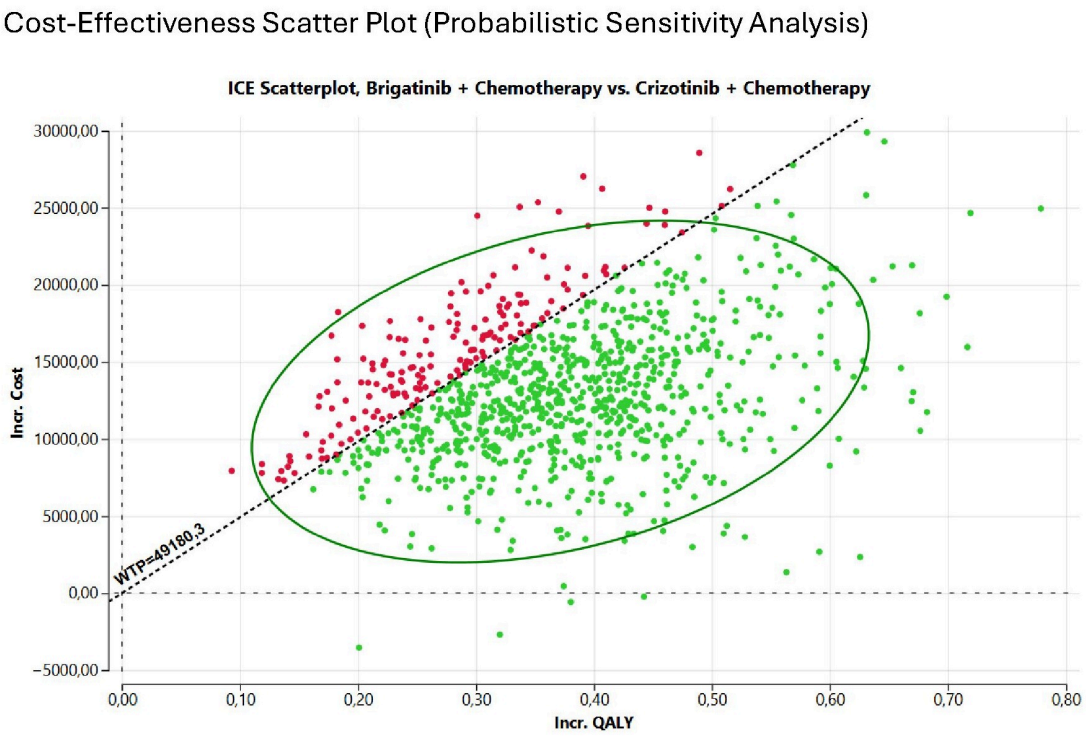


Figure 4

See image above for figure legend.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1ModelParametersandInputs.docx
- Table2.CostEffectivenessResultsforNonDominatedAlternatives.docx
- CORASupplementaryMaterial11.12.15reviewed.docx