Optimized Treatment Sequences for ALK+ Stage IV NSCLC: Cost-Effectiveness Analysis From RCT data and Real-World Evidence

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OBJECTIVES

The rising costs associated with new cancer treatment technologies have become a significant concern. Patients with ALK-mutated non-small celllung cancer (NSCLC) experience long survival rates, yet there is no established standard treatment. The lack of cost-effectiveness studies adds to the uncertainty surrounding pharmacoeconomic models. This study aims to analyze the cost-effectiveness relationship between randomized clinical trials (RCT) and real-world evidence (RWE) involving 126 patients with ALK-mutated stage IV NSCLC from Oncoclínicas&Co/MedSir, Brazil, between 2007 and 2024.

METHODS

An analytical decision model was developed, considering transitions between six health states: first-line progression-free survival (PFS) with tyrosinekinase inhibitors (TKIs; lorlatinib, alectinib, brigatinib), first-line post-progression survival (PPS), second-line PFS with TKIs, third-line PFS with chemotherapy, PPS, and death. The duration of each state was determined by the area under PFS and overall survival (OS) curves, estimated over 20 and 30 years using an exponential distribution. Costs were limited to drug purchases, as toxicity management costs were intangible for our perspective (outpatient healthcare service).

RESULTS

The QALY for brigatinib was 6.01 in RCT versus 5.10 in RWE, while the LYS was 7.73 RCT versus 7.48 RWE. For alectinib, QALY was 6.96 RCT versus 6.60 RWE, and LYS was 8.42 RCT versus 8.88 RWE. Lorlatinib had QALY and LYS of 7.71 and 9.40 in RCT, respectively. The first-line TKI costs in RCT (972,105 BRL) were higher than in RWE (644,360 BRL), while second-line TKI costs in RWE (710,014 BRL) exceeded RCT costs (140,854 BRL).

TABLE 1: INCREMENTAL COST-EFFECTIVENESS AND COST-UTILITY RATIOS

Drug	PFS1 + PPS (months) Utility	PFS2 + PPS (months) Uitility	QALY LYS	ICER (BRL)	ICUR (BRL)
Lorlatinib vs. Alectinib					
Lorlatinib	89.0 + 19.5 = 108.5 6.23 + 1.24 = 7.47	3.0 + 1.3 = 4.3 0.16 + 0.008 = 0.24	7.71 9.40	**RCT** 3.281.553 **RWD** 1.877.448	**RCT** 2.275.210 **RWD** 1.657.568
Alectinib RCT	34.8 + 16.3 = 51.1 2.44 + 1.03 = 3.47	6.6 + 3 + 45.9 + 55.5 0.46 + 0.16 + 2.87 = 3.49	6.96 8.88	-	-
Alectinib RWD	16.3 + 18.4 = 34.7 1.14 + 1.17 = 2.31	24.9 + 2.4 + 63 1.7 + 0.1 + 3.9 = 5.7	6.60 8.42	-	-
Lorlatinib vs. Brigatinib					
Lorlatinib	89.0 + 19.5 = 108.5 6.23 + 1.24 = 7.47	3.0 + 1.3 = 4.3 0.16 + 0.008 = 0.24	7.71 9.40	**RCT:** 1.442.569 **RWD** 933.733	**RCT:** 1.417.112 **RWD** 686.884
Brigatinib RCT	24.0 + 19.3 = 43.3 1.68 + 1.22 = 2.90	6.6 + 3.0 + 39.9 = 49.5 0.46 + 0.16 + 2.49 + 3.11	6,01 7.73	-	-
Brigatinib RWD	25.9 + 18.4 = 44.3 1.81 + 1.17 = 2.98	24.9 + 2.4 + 18.1 = 89.7 1.72 + 0.13 + 1.13 = 5.10	5.10 7.48	-	-

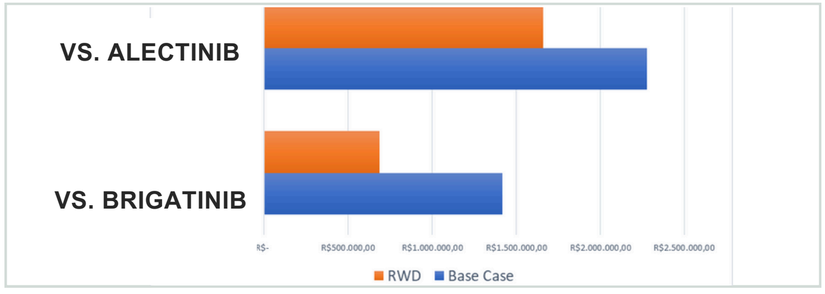

Figure 2: ICUR of lorlatinib versus alectinib and brigatinib, using real-world and RCT data.

CONCLUSIONS

RWE clarified some uncertainties in the model, especially in terms of drugs consumption, but the cost-effectiveness ratio remains unfavorable across both models, likely due to the highcosts of the evaluated technologies.