Challenges in Projecting Treatment Journeys for ALK-mutated NSCLC: Addressing Uncertainty in PPS and Immature Overall Survival Data

RWD94

Author Block: Rahyssa R. Sales, Bruna Carvalho Silva, Sr., MD, Rafael Duarte Paes, BSc, Rodrigo Dienstmann, PhD, MD, Deborah Marta dos Santos Oliveira,MSc, Mariana Tosello Laloni, PhD, MD , Ana Caroline Zimmer Gelatti, PhD, MD, William Nassib William Junior, PhD, MD, Carlos Gil Moreira Ferreira Gil, PhD,MD, Pedro Nazareth Aguiar Junior, PhD, MD

Oncoclínicas&Co/MedSir, São Paulo, Brazil.

OBJECTIVES

In ALK-mutated stage IV Non-Small Cell Lung Cancer (NSCLC), randomized clinical trials (RCTs) often provide immature overall survival (OS) data, leading to challenges in predicting long-term outcomes. The gap between progression-free survival (PFS) and OS with first-line tyrosine kinase inhibitors (TKIs) complicates post-progression survival (PPS) assessments, especially when treatment patterns are unclear. This "grey area" poses difficulties for economic modeling. Real World Evidence (RWE) can help address these gaps, but its use in health technology assessment (HTA) presents challenges. We aimed to evaluate the incorporation of RWE to address the PPS using data from 126 patients with ALK-mutated stage IV NSCLC from Oncoclínicas&Co/MedSir, Brazil between 2007 and 2024.

METHODS

We analyzed long-term survival estimates from RCTs and RWE for patients with ALK-mutated stage IV NSCLC treated with ALK TKIs: lorlatinib, alectinib, and brigatinib. We estimated PFS and OS curves from RCTs (CROWN, ALEX, and ALTA-1) and RWE (imputed data) over 20 and 30 years using an exponential distribution.

RESULTS

First-line PFS was 34.8 months (RCT) vs. 16.3 months (RWE) for alectinib and 24 months (RCT) vs. 25.9 months (RWE) for brigatinib. First-line PPS was similar across treatments. The PFS for the second TKI was 6.6 months (RCT) and 24.9 months (RWE). For post-TKI chemotherapy, PFS was 3 months (RCT) and 2.4months (RWE). Estimated PPS was 45.9 months (RCT) and 39 months (RWE) for alectinib, and 39.9 months (RCT) and 18.1 months (RWE) for brigatinib. We assessed lorlatinib data only from RCT. Limitations include reliance on immature data and the challenge of distinguishing treatment lines in real-world settings. The 'grey area' is the longest period of the journey for many patients.

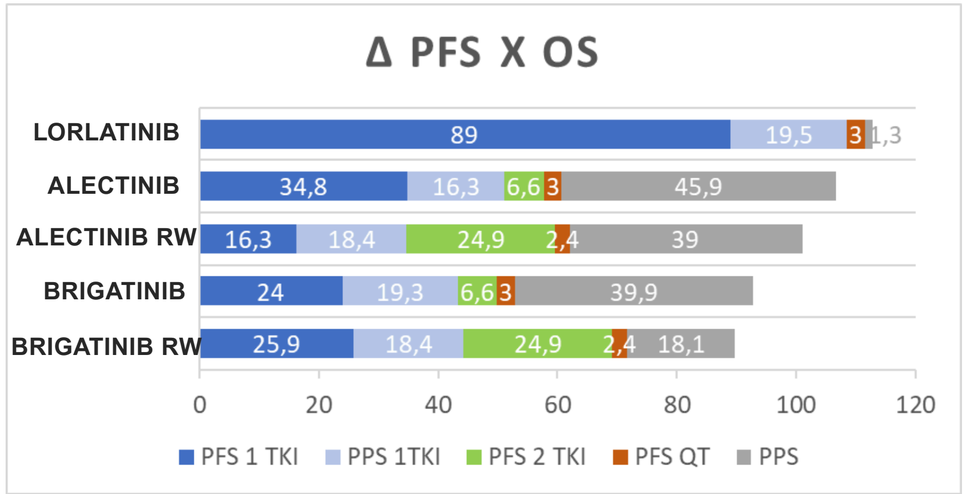

Figure 1: Progression-free survival (PFS) and post-progression survival (PPS) per drug. Grey areas (PPS) indicate uncertainty in the economic modelling.

CONCLUSIONS

The lack of a defined PPS standard and immature OS data increases uncertainty in treatment projections. While RWE mitigates gaps, robust sensitivity analyses remain critical to account for variability in post-progression outcomes.