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Bridging the Gap Between Trial Adverse Events and Real-World Data

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We congratulate Jeon et al. [1] for their thorough analysis comparing alectinib and brigatinib as first-line therapies for advanced non-small cell lung cancer (NSCLC) with anaplastic lymphoma receptor tyrosine kinase (ALK) rearrangement in a real-world context. This study provided valuable information that both drugs are highly effective and generally well tolerated with mild side effects. Nonetheless, further investigation into adverse events (AEs) associated with brigatinib is necessary to better understand the discrepancies between clinical trial data and real-world experiences in the treatment of ALK-positive NSCLC.

The study by Jeon et al. predominantly focuses on AE profiles of alectinib with a limited exploration of those associated with brigatinib, such as hypertension, diarrhea and increased blood creatine phosphokinase, amylase and lipase [2]. Although ALK inhibitors generally share similar safety concerns, the literature indicates that each may have a unique safety profile. The Phase III ALTA-3 study, which compared brigatinib and alectinib in patients with ALK-positive NSCLC that had progressed while being treated with crizotinib, demonstrated notable differences in the safety profiles of the two drugs [3]. In this study, hypertension was reported in 22% of patients treated with brigatinib, whereas it was considerably less common in those receiving alectinib (1%). Notably, compared with other laboratory findings, hypertension as an AE is often under-recognized in clinical practice.

The advent of newer generation ALK inhibitors has markedly improved the overall survival of patients with ALK-positive NSCLC [4], making the effective management of AEs critical for ensuring successful long-term survival. Most AEs associated with ALK inhibitors can be managed by adjusting dosage or temporarily interrupting treatment. Thus, prompt recognition of the specific toxicity patterns of each ALK inhibitor can help improve treatment-related outcomes. To this end, it is important to minimize the disparity between clinical trial findings and real-world patient experiences. A more detailed, real-world study on AEs,
particularly those noted in clinical trials, is essential. Such investigations will not only broaden our understanding of AEs associated with first-line ALK inhibitors but also lead to better strategies for managing AEs that may occur during treatment. While Jeon et al.’s research significantly adds to our comprehension of ALK inhibitors in treating ALK-positive NSCLC, a pressing need remains for future research into the real-world AEs of these drugs, which may enable healthcare professionals to provide more effective patient care, ultimately leading to favorable treatment outcomes.

Author Contributions
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