A Real-World Disproportionality Analysis of Two Typical First-Generation TRK Inhibitors: Findings from the FDA Adverse Event Reporting System Database

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Abstract

Background: Although Two first-generation tropomyosin receptor kinase (TRK) inhibitors larotrectinib and entrectinib have been approved by the Food and Drug Administration (FDA), The current adverse effect profile in the real world remains unknown. Objective: The purpose of this study was to retrospectively examine the adverse effects of two typical first-generation TRK inhibitors by spontaneously mining the data from FDA Adverse Event Reporting System (FAERS) database. Methods: Four general data mining algorithms were used to conduct a disproportionate analysis of TRK inhibitors, and the time of adverse events of drugs was counted. The definition relied on the system organ class (SOC) and preferred terms (PT) by the MedDRA. Results: A total of 326 cases of 'larotrectinib' and 450 cases of 'entrectinib' as the 'primary suspect' drug were collected in this study. A total of 86 adverse drug reaction (ADR) signals involving 18 SOCs were mined. 'Dizziness' was the most common ADR, with 'glioma' as the strongest signal. The SOC with the highest number of occurrences was 'Nervous system disorders'.The median time of onset of larotinib and entertinib-related ADR was 41 days and 18 days, respectively. Most cases occurred within one month after treatment. Conclusion: The main ADRs found in this study were 'Neurotoxicity', 'Pain', 'Hepatotoxicity', 'Drug resistance', 'Nephrotoxicity' and 'Weight increased', which provide important support for clinical monitoring and risk identification of TRK inhibitors.

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`tables 1-6.docx` available at https://authorea.com/users/621526/articles/645071-a-real-world-disproportionality-analysis-of-two-typical-first-generation-trk-inhibitors-findings-from-the-fda-adverse-event-reporting-system-database