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Real-world pharmacokinetics of trametinib in pediatric low-grade glioma

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Abstract

Purpose: Trametinib, a MEK1/2 inhibitor, has emerged as a promising treatment for pediatric patients with low-grade gliomas (LGG). However, trametinib exhibits significant inter-individual pharmacokinetic (PK) variability, and studies in adults demonstrated an exposure-efficacy relationship. This study aimed to evaluate the PK profile of trametinib in pediatric routine care and explore potential exposure-outcome relationships.

Methods: We analyzed PK data from 65 blood samples from 19 children receiving trametinib, either as single agent or in combination with dabrafenib. A trough concentration (Cmin) range of 8-15 ng/mL was considered, based on average exposure reported in the largest pediatric study.

Results: The mean Cmin was 8.82 ng/ml, with 64.6% of samples falling within the predefined target range, while 35.4% were below it. Regarding tolerance, 84.2% of patients experienced treatment-related toxicities, predominantly skin and subcutaneous tissue disorders. Efficacy data were limited.

Conclusion: These findings underscore the necessity of therapeutic drug monitoring in pediatric patients to optimize treatment efficacy and minimize toxicity, highlighting trametinib's potential for personalized dosing strategies in this population.

Keywords: Low-grade glioma; Pediatric cancer; Pharmacokinetics; Trametinib.