Presentation Title:

Pexidartinib risk evaluation and mitigation strategy program: 3-year safety data assessment

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ABSTRACT:

Objective: Pexidartinib (Turalio®) is a first-in-class colony-stimulating factor-1 receptor blocker indicated for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery. Due to potential risk of hepatotoxicity, pexidartinib (400 mg orally twice daily) was approved by the US Food and Drug Administration on the condition of establishing a Risk Evaluation and Mitigation Strategy (REMS) program. 3-year (August 2019-June 2022) cumulative safety data collected from patients enrolled in the Turalio® REMS are described here.

Methods: The Turalio® REMS consists of elements to ensure safe pexidartinib use. Healthcare providers, dispensing pharmacies, and pexidartinib distributers were certified in the REMS. Scheduled safety assessments were collected on patient access forms.

Results: During the 3-year period, 451 patients, 369 prescribers, 2 wholesalers/distributors, and 2 pharmacies were certified/enrolled in the REMS. Of the adverse events (AEs) reported, the majority (94.2%) were nonserious. Hair color changes were the most frequently reported nonserious AE (4.4%); increased aspartate aminotransferase (AST; 0.5%) was the most frequently reported serious AE.

Of 451 patients enrolled, 51 (2.4%) lab tests had ALT or AST liver enzymes >3×ULN and TBIL >2×ULN, 17 (0.8%) had ALT or AST >10×ULN with/without TBIL elevation, and 12 (0.6%) had TBIL ≥2×ULN without changes in ALT or AST. Twenty-one (4.7%) patients met the criteria for a liver AE or laboratory abnormalities suggestive of serious and potentially fatal liver injury; the pattern of reported hepatic injury was consistent with the phase 3 ENLIVEN trial results. There were no events of irreversible liver injury. After starting pexidartinib, treatment interruption (n=106) was seen in 98 (21.7%) patients, primarily due to hepatic AEs (n=24; 22.6%), nonhepatic AEs (n=15; 14.2%), disease progression (n=2; 1.9%), and death (n=1; 0.9%). In patients resuming treatment, all were at a lower dose. Treatment discontinuation was reported in 132 patients (29.3%; 137 events), primarily due to hepatic AEs (n=26; 19%), nonhepatic AEs (n=23; 16.8%), disease progression (n=13; 9.5%), confirmed pregnancy (n=2; 1.5%), and death (n=1; 0.7%; not related to hepatotoxicity).

Conclusion: Safety data from the Turalio® REMS were consistent with data from the ENLIVEN trial. Furthermore, no new hepatic safety signals were identified. These results indicate that careful monitoring of liver enzymes and early intervention using dose modifications/permanent discontinuation are being actively conducted to mitigate the risk of potential hepatotoxicity. This 3-year cumulative safety data assessment indicates that the Turalio® REMS is ensuring safe pexidartinib use.