Abstract: PB2512

Title: SAFETY OF CRIZANLIZUMAB IN PATIENTS WITH SICKLE CELL DISEASE: INTEGRATED POST-MARKETING SURVEILLANCE ANALYSIS

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Session Title: Sickle cell disease

Background:

Crizanlizumab, a first-in-class humanized monoclonal antibody that blocks P-selectin, is approved in 52 countries/regions worldwide in patients (pts) with sickle cell disease (SCD) aged ≥16 years. Reports on infusion-related reactions (IRRs), hemostasis, infection, and immunogenicity due to crizanlizumab are limited.

Aims:

We used data from post-marketing sources to assess the risk of IRR, hemorrhage, infection, and immunogenicity in pts who received crizanlizumab worldwide up to 14 November 2022.

Methods:

In the cumulative analysis, data were collected between 15 November 2019 and 14 November 2022 from post-marketing sources, including post-marketing studies (PMS), spontaneous reports, and scientific literature. We included a separate analysis of recent data reported between 15 May–14 November 2022 (current reporting interval). Adverse events (AEs) were summarized by preferred term (PT)/system organ class and seriousness/severity per MedDRA Version 25.1. Detailed searches and follow-ups were performed for previously identified important risks with crizanlizumab (specifically, IRRs) and previously recognized potential important risks (effect on hemostasis [hemorrhage], immunogenicity, and infections). Analysis per 100 patient-treatment years (PTY) was performed for identified and potential important risks.

Results:

Post-marketing exposure was estimated at 5655 PTY. Cumulatively, 937 serious AEs (SAEs) were reported (321 in PMS and 616 in spontaneous reports/literature). In total, a fatal outcome was reported in 40 cases (21 in PMS and 19 in spontaneous reports/literature). None of the post-marketing fatal outcome reports was determined to be causally related to the crizanlizumab treatment. The most frequently reported AE PTs were pain (206), back pain (104), sickle cell anemia with crisis (90), arthralgia (56), chest pain (55), pain in extremity (51), pyrexia (44), nausea (41), headache (34), fatigue (32). Reports in the current reporting interval included 109 SAEs (22 in PMS; 87 in spontaneous reports/literature). The cumulative reporting rate (RR) for IRR was 5.31/100 PTY. There were 73 cumulative cases of effects on hemostasis (hemorrhage) (cumulative RR=0.99/100 PTY), most of which were confounded by underlying disease or other risk factors. No cases of immunogenicity were reported. There were 172 cumulative cases of all types of infections (cumulative RR=1.20/100 PTY). All relevant cases of infections were confounded or did not have sufficient information for meaningful medical assessment. Three cases with infections were reported with fatal outcomes; however, the reports did not have sufficient information for meaningful medical assessment. Overall, the AE profile of crizanlizumab was consistent with previous reports.

Summary/Conclusion:

This post-marketing surveillance analysis showed that crizanlizumab was well tolerated. The review of the data on the AEs of special interest did not reveal any new safety concerns for crizanlizumab.

Keywords: P-selectin, Safety, Sickle cell disease