Title: Safety and Efficacy of Pegunigalsidase Alfa Administered Every 4 Weeks in Patients with Fabry Disease: Results from the Phase 3, Open-label, BRIGHT Study

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Background: Fabry disease is caused by reduced activity of the lysosomal enzyme α-galactosidase A (α-Gal A), leading to an accumulation of sphingolipids that can cause organ failure. Current treatments include enzyme replacement therapies (ERTs) that require infusions every 2 weeks. Pegunigalsidase alfa is a PEGylated α-Gal A enzyme with a much longer half-life than other ERTs for Fabry disease developed to reduce infusion frequency. The study objective was to evaluate the safety and efficacy of 2.0 mg/kg pegunigalsidase alfa administered once every 4 weeks for 1 year to patients with Fabry disease, who previously received commercially available ERTs every 2 weeks.

Methods: BRIGHT (NCT03180840) was a phase 3, open-label, switchover study of adults (aged 18–60 years old) with Fabry disease who previously received agalsidase alfa or agalsidase beta every other week for ≥ 3 years. Patients received 2.0 mg/kg pegunigalsidase alfa every 4 weeks for 1 year. Safety outcomes included treatment-emergent (TEAEs) and treatment-related adverse events (TRAEs); efficacy outcomes included eGFR changes and plasma lyso-Gb3 concentration.

Results: This study enrolled 30 adults (mean age of 40.5 years old; 24 males, 6 females). 27 Patients (90%) reported 183 TEAEs with no serious or severe TEAEs attributed to pegunigalsidase alfa treatment. No patients developed de novo antidrug antibodies, and no new safety concerns were identified. Among 413 total infusions, 22 caused 27 mild to moderate infusion-related reactions (IRRs), with no serious or severe IRRs reported. In the efficacy analysis (n=29), eGFR values (mean [SE] change from baseline of −1.27 [1.39] mL/min/1.73m^2), mean [SE] eGFR slope (−1.6 [0.8] mL/min/1.73m^2/year) and plasma lyso-Gb3 concentrations remained stable throughout the study.

Conclusion: Patients with Fabry disease receiving ERT every other week can be successfully transitioned to pegunigalsidase alfa 2.0 mg/kg every 4 weeks as an effective maintenance-therapy schedule with a positive safety profile in this study.

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References: N/A

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