Title: Long-term Safety and Efficacy of Pegunigalsidase Alfa: A Multicenter Extension Study in Adult Patients with Fabry Disease

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Background: Fabry disease (FD), a rare, X-linked lysosomal storage disorder, is caused by deficiency of the enzyme α-galactosidase A (α-Gal-A), leading to low residual enzymatic activity and accumulation of glycosphingolipids such as globotriaosylsphingosine (lyso-Gb3) and progressive end organ failure. Pegunigalsidase alfa is a novel PEGylated α-Gal-A enzyme replacement therapy (ERT) in development for FD, and previous studies report its enhanced bioavailability and favorable safety and efficacy for up to 12 months. The study objective was to investigate long-term safety, tolerability, and efficacy of pegunigalsidase alfa in adults with FD for up to 72 months.

Methods: Patients with FD (ERT-naïve or not receiving ERT for 6 months before inclusion) who completed two phase 1/2 studies were subsequently enrolled in an open-label extension study (NCT01981720). Patients received 1.0 mg/kg pegunigalsidase alfa via intravenous infusion every other week for up to 72 months.

Results: Of 15 patients enrolled, 10 (6 males; 4 females) completed the study. Median age (range: 17–54 years) was 32. Most (97.5%) treatment-emergent adverse events (TEAEs) were mild or moderate. Three patients experienced 4 serious AEs unrelated to treatment. One patient experienced a single clinical event (non-cardiac-related death) following chronic obstructive pulmonary disorder exacerbation unrelated to the treatment. Immunogenicity results showed that 4 patients were transiently positive for anti-pegunigalsidase alfa IgG, and 1 patient was positive from 48 months until study completion. At 60 months, there was a continuous reduction from baseline in plasma lyso-Gb3 concentration (mean [SE] change from baseline was 68.4 [25.0] ng/mL); renal (mean [SE] estimated glomerular filtration rate slope of −1.6 [0.8] mL/min/1.73m^2/year), and cardiac function remained relatively stable.

Conclusion: This is the first assessment of long-term administration of pegunigalsidase alfa. Results are consistent with favorable safety and efficacy findings from earlier studies and suggest long-term pegunigalsidase alfa treatment may provide continued benefits in patients with FD.

Support: This study was sponsored by Protalix Biotherapeutics. Medical writing support was provided by Oxford PharmaGenesis, Inc., and was funded by Chiesi USA, Inc.

References: N/A

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