Title: Switching from Agalsidase Alfa to Pegunigalsidase Alfa to Treat Patients with Fabry Disease: 1 Year of Treatment Data from BRIDGE, a Phase 3 Open-label Study

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Background: Pegunigalsidase alfa is a novel PEGylated alpha-galactosidase A enzyme in development for the treatment of patients with Fabry disease (FD).

Methods: BRIDGE (PB-102-F30; NCT03018730) is a phase 3 open-label, switch-over study designed to assess the safety and efficacy of pegunigalsidase alfa (1 mg/kg every other week) in adults with FD, previously treated with agalsidase alfa for at least 2 years.

Results: Twenty (13 men, 7 women) of 22 enrolled patients (15 men, 7 women) completed 12 months of study treatment and were included in the efficacy analyses. Baseline characteristics (N=22): age 24–60 years; mean estimated glomerular filtration rates (eGFR), 82.5 mL/min/1.73 m^2 (men: 80.8 mL/min/1.73 m^2; women: 86.1 mL/min/1.73 m^2); mean annualized eGFR slopes, −5.3 mL/min/1.73 m^2/y (men: −5.4 mL/min/1.73 m^2/y; women: −5.0 mL/min/1.73 m^2/y); mean residual enzymatic activity in leucocytes, 12.2% (men: 4.8%; women: 27.9%) of normal laboratory means; and mean plasma lyso-Gb3, 38.30 nM (men: 49.73 nM; women: 13.81 nM). At 12 months, plasma lyso-Gb3 mean concentrations decreased from baseline by 31.5%; and mean annualized eGFR slope improved from −5.90 mL/min/1.73 m^2/y for agalsidase alfa to −1.19 mL/min/1.73 m^2/y for pegunigalsidase alfa (men: −6.36 to −1.73 mL/min/1.73 m^2/y; women: −5.03 to −0.21 mL/min/1.73 m^2/y). In this study, 75% (n/N=3/4) of progressing patients and 66.7% (n/N=6/9) of fast-progressing (eGFR slope <–5 mL/min/1.73 m^2/y) patients achieved the proposed therapeutic goals after switching to pegunigalsidase alfa.

Seven of 20 patients (35.0%) in the efficacy population were positive for IgG anti-pegunigalsidase alfa anti-drug antibodies at least at 1 timepoint. Overall, 127 treatment-emergent adverse events (TEAEs) occurred in 21 of 22 patients (95.5%). Most TEAEs (86.4%) were mild or moderate, consistent with the safety profile of the previous phase1/2 study (NCT01678898). Four severe TEAEs (3.1%) occurred in 4 patients (18.2%). Two patients (9.1%) discontinued therapy due to severe TEAEs.

Conclusion: The efficacy results suggest a potential benefit of pegunigalsidase alfa on renal function for patients with FD previously treated with agalsidase alfa. No major safety concerns were reported.

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