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Analysis of the baseline characteristics of Fabry disease patients screened for the pegunigalsidase alfa phase III BALANCE study

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Enzyme replacement therapy (ERT) may lead to formation of anti-drug antibodies (ADA) in "classical" patients with Fabry disease (FD). Recent studies provided evidence that neutralizing antibodies (nAb) may interfere with ERT efficacy. Higher doses of ERT have been recently shown to overcome the activity inhibition caused by ADAs. BALANCE (PB-102-F20 NCT02795676) is a double blind head-to-head study comparing the effect of pegunigalsidase-alfa to agalsidase-beta (1mg/kg every 2 weeks) on renal function. The screening strategy selected FD patients with progressive loss of kidney function despite long-term ERT (1-16 years). The current analysis describes the baseline characteristics of FD patients screened for this study. Among male patients currently screened for the study, 55% were positive for both binding and neutralizing ADA to agalsidase-beta, with in-vitro mean enzyme activity inhibition of ~80% and IgG titers of 60 to 127,933. One female was ADA-positive (binding ADA only). In-vitro evaluation of the cross-reactivity of the nAb-positive samples toward pegunigalsidase-alfa showed a lower mean enzyme activity inhibition of ~64%, resulting in a greater amount of effective (non-inhibited) enzyme of ~40% vs ~20%. The lower enzyme activity inhibition combined with ~40-fold longer plasma half-life of pegunigalsidase-alfa compared to agalsidase-beta (~80 h vs ~2h) are expected to result in a greater amount of effective enzyme available in the circulation of patients switching from a long-standing treatment with agalsidase-beta to pegunigalsidase-alfa. Further evaluation of ADA status and renal function of this cohort indicates that 64% (14/22) of the ADA-positive FD male patients also have significant proteinuria (UPCR≥ 500 mg/gr). The unique characteristics of pegunigalsidase-alfa, encompassing an improved pharmacokinetic profile, lower immunogenicity, and lower cross reactivity to pre-existing anti-agalsidase nAb, may result in higher levels of effective enzyme reaching target organs, with the potential to improve long-term clinical outcomes and attenuation of renal function deterioration in FD patients.

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