NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: A Multicenter, Multicountry, Postmarketing Active Surveillance Taliglucerase Alfa Registry in Patients With Gaucher Disease

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Rationale and background: In the United States (US), taliglucerase alfa for injection received initial approval for treatment of adult patients with Type 1 Gaucher disease in 2012 and subsequent approval for treatment of pediatric patients in 2014. This taliglucerase alfa exposure registry is a Post-Marketing Requirement issued by the US Food and Drug Administration (FDA) on approval in 2012. This interim report was prepared after completion of approximately 5 years of study including data collected from First Participant First Visit (18 September 2013) to the data cutoff date for this interim analysis (07 January 2019).

Research question and objectives: The primary objective of this study is to characterize the safety profile of taliglucerase alfa through the solicited collection and summary of non-serious and serious adverse event data. The secondary objective is to characterize the effectiveness of taliglucerase alfa through the collection and analysis of Gaucher disease measures, including hematologic (hemoglobin and platelet count) and organ volume (spleen and liver) assessments.

Study design: This non-interventional prospective cohort study is an ongoing drug registry of patients with Gaucher disease receiving taliglucerase alfa. This drug registry is planned to remain active for 10 years. All treatments, clinical assessments and information collected for each participant are undertaken according to the standard of care of his/her enrolling physician.

Setting: Eligible participants are required to complete a baseline visit and are being followed up to the end of study. Duration of follow-up depends on time of enrollment which is to occur during the first 8 years of the drug registry.

Subjects and study size, including dropouts: Patients with confirmed diagnosis of Gaucher disease who plan to or have been receiving treatment with taliglucerase alfa are eligible to participate in the drug registry. As of the data cut-off date (07 January 2019) for this interim report, a total of 106 participants have been treated in this study (90 adults and 16 children). Nine (9) participants discontinued from the study (all adults), four of them due to death.

Variables and data sources: Detailed data on taliglucerase alfa are being collected. The safety profile of taliglucerase alfa is characterized by collection and analyses of treatment-emergent adverse events (TEAEs) which are defined as any adverse events occurring following the start of the primary treatment period (on or after Day 1) through 28 days after the end of the primary treatment period.

The effectiveness variables include hemoglobin level, platelet count, spleen volume (absolute values and by multiples of normal [MN]), and liver volume (absolute values and MN).

The primary data source is the participant's medical record and participant interviews. All data are captured in an electronic case report form (eCRF).

Results:

Safety

A total of 95 all-causality TEAEs were reported in 39 participants. The system organ class (SOC) with the highest percentage of participants was General disorders and administration site conditions (11.3%), followed by Infections and infestations (8.5%), Musculoskeletal and connective tissue disorders, Nervous system disorders, and Respiratory, thoracic and mediastinal disorders (7.5% each).

A total of 21 treatment-related TEAEs were reported in 12 participants, including 3 TEAEs (chest pain, back pain, and systemic lupus erythematosus) which were deemed severe by the treating physician and also reported as serious adverse events (SAEs).

SAEs were reported in 15 participants (including 4 deaths), and all occurred in adult participants. The majority of the SAEs were considered not related to taliglucerase alfa treatment by the treating physicians. All 4 deaths occurred in adult participants, and were considered not related to taliglucerase alfa treatment.

Effectiveness

The treatment effects on effectiveness variables observed in this real-world registry were generally similar to previous controlled studies.

At baseline, both hemoglobin level and platelet count in previously treated participants were higher than among Treatment Naïve participants, which may reflect the therapeutic effects of prior treatments which mainly consisted of taliglucerase alfa. During follow-up, both hemoglobin level and platelet count were increased in the Treatment Naïve group; in the Prior enzyme replacement therapy (ERT) group, hemoglobin level and platelet count remained relatively constant or increased slightly during follow-up, suggesting taliglucerase alfa is effective in improving hemoglobin level and platelet count, and such effects can be sustained.

During follow-up, both spleen volume by MN and liver volume by MN were reduced for the Prior ERT group: at the Year 2 visit, the median spleen volume by MN decreased by 25.0%, and the median liver volume by MN decreased by 3.0%. In the Treatment Naïve group, comparison to baseline organ volume was available only in 2 participants at the Year 1 visit:

both spleen volume by MN (decrease by 61.3%) and liver volume by MN (decrease by 5.3%) were reduced in 1 participant; spleen volume by MN was reduced by 81.0% and liver volume by MN was increased by 132.1% in the other participant.

Discussion: A total of 106 participants have been treated with taliglucerase alfa in this drug registry by the data cutoff date of 07 January 2019 for the interim analysis.

The interim data showed that taliglucerase alfa is generally safe and well-tolerated and no new or emergent safety information was observed in this study utilizing real-world data. Each of the treatment-related TEAEs occurred in a small number of participants and the majority of them were mild or moderate in severity. Overall, safety data in this study were consistent with the known risk profile of taliglucerase alfa treatment. Additionally, despite small sample size, the interim data suggest that taliglucerase alfa is effective in improving standard clinical disease markers of effectiveness in treatment naïve patients, and either improving or maintaining the clinical markers in previously treated patients with Gaucher disease.

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