Abstract: PB3373

Title: LONG-TERM SAFETY OUTCOMES OF ELIGLUSTAT IN PATIENTS WITH GAUCHER DISEASE: PROSPECTIVE, MULTICENTER, OBSERVATIONAL, POST AUTHORIZATION SAFETY SUB-REGISTRY STUDY

Abstract Type: Publication Only

Topic: Platelet disorders

Background:

Eliglustat, a potent and specific inhibitor of glucosylceramide synthase acts as substrate reduction therapy (SRT) and is approved for the long-term treatment of adult Gaucher disease type 1 (GD1) patients, who are CYP2D6 poor, intermediate, or extensive metabolisers.

Aims:

To report post-authorization, real-world data on long-term safety and utilization of eliglustat from safety sub-registry of the International Collaborative Gaucher Group (ICGG) Gaucher Registry in adult GD1 patients enrolled as of December 30, 2022.

Methods:

Overall, 166 patients treated with eliglustat (n=110) and imiglucerase (n=56) were enrolled; since treatment could be changed, 127 and 63 patients received at least one dose of eliglustat and imiglucerase, respectively. For eliglustat and imiglucerase treatments, 122 (96.1%) and 58 (92.1%) patients respectively had one treatment episode.

Results:

For any exposure, 87 (68.5%) patients on eliglustat and 30 (47.6%) patients on imiglucerase reported at least one adverse event (AE). The exposure-adjusted incidence rate (IR) of AEs for eliglustat and imiglucerase was 0.440 (197.8 patient-years at risk) and 0.286 (105.0 patient-years at risk) respectively (**Table 1**). Musculoskeletal and connective tissue disorders (eliglustat: arthralgia, bone pain; imiglucerase: arthralgia, back pain) were the most common AEs reported with both the treatments (eliglustat, 25.2%, [IR: 0.096]; imiglucerase, 14.3% [IR: 0.060]). Exposure-adjusted IR of serious AEs was 24 events in 13 participants (0.034) for eliglustat and 5 events in 3 participants (0.018) for imiglucerase (**Table 1**). Eliglustat-related AEs were reported in 25 (19.7%) patients with gastrointestinal disorders (16 [12.6%]) being the most frequent. Imiglucerase-related AEs, reported in 2 (3.2%) patients were anaphylactic reaction, drug hypersensitivity, dizziness, paraesthesia, and infusion site extravasation, none appeared in >1 patient. One death was reported on eliglustat treatment due to Covid-19 pneumonia. Compliance/adherence of HCPs to eliglustat was >96%.

Summary/Conclusion: Eliglustat was well-tolerated by GD1 patients in real-world and safety profile was consistent with that observed during clinical development.

Table 1. Exposure-adjusted incidence rate of AEs and SAEs for any eliglustat and imiglucerase treatments

Parameters	Any eliglustat treatment (N=127)			Any imiglucerase treatment (N=63)		
	n (%)	Patient-years at risk	Events (Exposure-adjusted IR)	n (%)	Patient-years at risk	Events (Exposure-adjusted IR)
Patients with any AE	87 (68.5%)	197.8	261 (0.440)	30 (47.6%)	105.0	90 (0.286)
Patients with any AE related to treatment	25 (19.7%)	346.8	38 (0.072)	2 (3.2%)	164.5	6 (0.012)
Patients with any AE leading to treatment withdrawn	7 (5.5%)	396.0	7 (0.018)	1 (1.6%)	166.9	1 (0.006)
Patients with any AE leading to death	1 (0.8%)*	397.1	1 (0.003)	0 (0%)	166.9	0 (0.000)
Patients with any SAE	13 (10.2%)	378.5	24 (0.034)	3 (4.8%)	165.1	5 (0.018)

Note: Any eliglustat treatment in ELISAFE includes treatment with eliglustat at enrollment and changes in treatment from imiglucerase to eliglustat. Any imiglucerase treatment in ELISAFE includes treatment with imiglucerase at enrollment and changes in treatment from eliglustat to imiglucerase.
*Death due to Covid-19 pneumonia.
AE, adverse event; IR, incidence rate; n, number of patients; SAE, serious adverse event.

Disclosures:

• Pilar Giraldo has been involved in premarketing studies with Genzyme, Protalix and Idorsia, and has received grants from Sanofi-Genzyme and Takeda.

• Isabela Batsu, Beverly Accomando, Sefika Uslu are employees of Sanofi and may hold shares and/or stock options in the company.

• Maurizio Scarpa has received honoraria, consulting fees, and/or research support for participating in conferences related to Pompe disease.

Keywords: Real world data, Safety, Gaucher disease, Treatment