Abstract: P1588

Title: LONG-TERM REAL-WORLD EFFECTIVENESS OF ELIGLUSTAT IN TREATMENT-NAÏVE AND SWITCH PATIENTS ENROLLED IN THE INTERNATIONAL COLLABORATIVE GAUCHER GROUP (ICGG) GAUCHER REGISTRY

Abstract Type: Poster Presentation

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Background:

Eliglustat, a potent inhibitor of glucosylceramide synthase, is a first-line oral substrate reduction therapy for adults with Gaucher disease type 1 (GD1) dosed according to CYP2D6 metabolizer status. Extensive clinical trials have established long-term clinical benefit in *de novo* treatment of GD1 and in assuring stability in patients switching from another therapy. In a clinical trial setting, patients are of relatively homogenous phenotypes, whereas GD1 is renowned for its heterogeneity, underscoring the importance of outcome of treatment in the real-world setting.

Aims:

We aimed to assess the hematologic and visceral response to eliglustat in patients enrolled in the ICGG Gaucher Registry across long-term follow-up.

Methods:

We included 381 GD1 patients enrolled in the ICGG Gaucher Registry (NCT00358943) as of June 2022 who initiated eliglustat at ≥18 years of age and had baseline and ≥1 follow-up assessment for at least one hematologic (hemoglobin, platelet count) or visceral (liver volume, spleen volume) parameter. We used linear mixed models to estimate the annual change in each parameter following initiation of eliglustat; models for hemoglobin and platelet count were adjusted for patient sex. Non-splenectomized patients (N=290) and splenectomized patients (N=57) who switched to eliglustat from another Gaucher therapy were modelled separately. In addition, descriptive statistics are provided for 34 eliglustat-naïve patients

Results:

The median age (25^{th}, 75^{th} percentile) at eliglustat initiation was 41.4 years (28.3, 54.8) in non-splenectomized switch patients, 52.1 years (45.9, 58.4) in splenectomized switch patients, and 38.7 years (24.8, 51.6) in naïve patients. Overall, the majority of patients were extensive CYP2D6 metabolizers (76%), followed by intermediate metabolizers (18%). Non-splenectomized switch patients had mean baseline values of 14.79 g/dL (males) and 13.28 g/dL (females) for hemoglobin, 167.8 $x10^3/mm^3$ (males) and 190.0 $x10^3/mm^3$ (females) for platelet count, 0.95 multiples of normal (MN) for liver volume, and 3.46 MN for spleen volume. They were followed for a median (25^{th}, 75^{th} percentile) of 3.2 years (1.7, 5.1) and 3.0 years (1.6, 4.6) for hematologic and visceral parameters, respectively. Platelet count increased an average of 2.74 $x10^3/mm^3$ per year, 95% confidence interval (CI): 1.07, 4.41 (n=247; 1529 records) following eliglustat initiation, while hemoglobin decreased slightly (-0.04 g/dL per year, 95% CI: -0.06, -0.01; n=257; 1599 records); liver volume (-0.01 MN, 95% CI: -0.02, 0.00; n=102; 420 records) and spleen volume (-0.06 MN, 95% CI: -0.14, 0.03; n=106; 438 records) were stable. Splenectomized switch patients maintained stability in all parameters. In treatment-naïve patients with data at baseline and 4 years of follow-up, median hemoglobin increased from 12.2 to 13.6 g/dL (n=8) in 4 years following eliglustat initiation, platelet count increased from 91.5 to 165.0$x10^3/mm^3$ in those with intact spleen (n=8), spleen volume decreased from 6.6 to 3.7 MN (n=6), and liver volume decreased from 1.2 to 1.1 MN (n=6).

Summary/Conclusion:

GD1 patients who switched from another therapy to eliglustat maintained stability in hematologic and visceral parameters. In treatment-naïve patients, treatment with eliglustat resulted in clinically meaningful improvements

in hematologic and visceral parameters. These long-term real-world data from the ICGG Gaucher Registry are consistent with those reported in eliglustat clinical trials and establish its role as a first-line therapy dosed according to CYP2D6 metabolizer status.

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Keywords: Lysosomal storage disease, Real world data, Gaucher disease