azafaros

Newsletter for patients on Azafaros' current program:

Update on PRONTO and Phase 2 RAINBOW study data with nizubaglustat, for patients with Niemann-Pick disease type C (NPC) GM1 and GM2 gangliosidoses.

In September Azafaros announced positive topline data from its ongoing RAINBOW study. The double-blind, placebo-controlled Phase 2 clinical trial is investigating lead asset, nizubaglustat, in patients with either Niemann-Pick disease type C (NPC) or GM2 gangliosidosis. Because of the fast pace of drug development, we would like to use this opportunity to provide you with an update on the current status of our drug development program.

About nizubaglustat

Nizubaglustat is a small molecule, orally available in disposable tablet form which crosses the blood-brain barrier and is distributed in the brain. Its structure provides an unique dual mode of action/working mechanism that has been developed as a potential treatment for rare lysosomal storage disorders with neurological involvement, including GM1 and GM2 gangliosidoses and Niemann-Pick disease type C (NPC). This molecule inhibits two key enzymes; one which is responsible for creating the backbone structure of pathogenically overstored materials, and the other which regulates the maintenance of an acid pH inside the lysosome, which is crucial for this organelle's correct function.

PRONTO study

At the same time, Azafaros also announced 12-month follow-up data from the company's PRONTO trial, a natural history study of late-infantile/juvenile GM1 and GM2 gangliosidoses.

The PRONTO study is a prospective natural history study designed to assess the progression of neurological disease in late-infantile/juvenile GM1 and GM2 gangliosidoses. The study includes participants with those forms of the disease, genetic diagnosis, and who are between 2 and 20 years old. The main objective was to provide insight and understanding of disease progression using clinical scales and caregiver questionnaires. A total of 30 participants were recruited from 6 countries with at least 12-month follow-up data on all of them.

PRONTO is the largest prospective natural history study of these two rare diseases and is providing valuable insights for the further development of nizubaglustat, as well as for the gangliosidoses research community in general.

Data collected after one year of follow-up showed a clear deterioration in untreated patients for the ataxic (Scale for Assessment and Rating of Ataxia, SARA) and behavioural scales (Vineland v.3), providing reliable data for the expected progression in the Phase 3 placebo group.

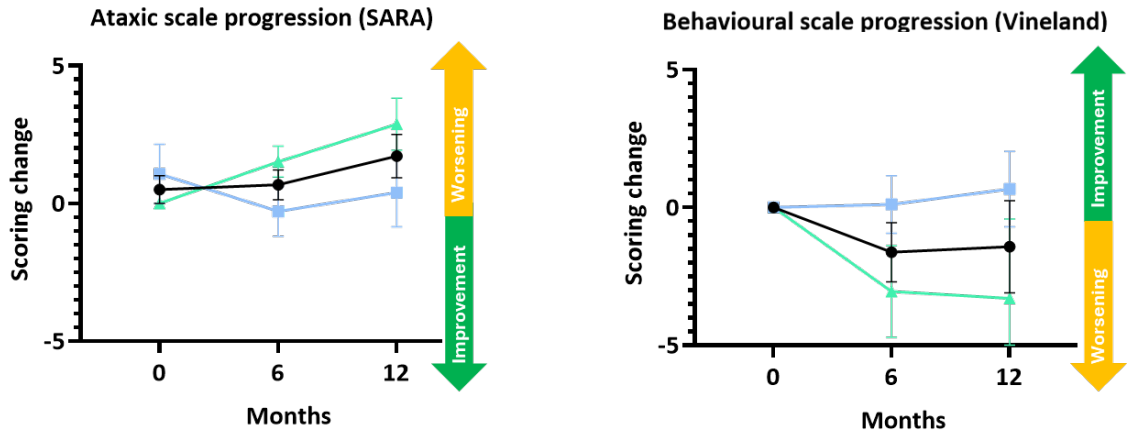

Figure 1. Change on ataxic and behavioural scoring after one year of follow-up. Data expressed as the mean and standard error of the mean for the 30 patients in the study

Phase 2 RAINBOW study

The RAINBOW trial is a Phase 2 clinical study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of nizubaglustat in patients with GM2 and Niemann-Pick disease type C (NPC) diseases.

The study is being conducted at three sites in Brazil, involving patients older than 12 years of age with a genetic diagnosis of one of the diseases, neurological involvement and who are not prescribed miglustat. In the main phase of the study, patients were randomized to receive either a high dose or low dose of nizubaglustat or placebo. All patients who progressed onto the extension phase of the study and those who had received the placebo at baseline, were randomized to receive either a high or a low dose of nizubaglustat. The extension of this study will continue until an open-label study is in place to continue treating these patients.

The results of the main phase of RAINBOW involved 13 patients (6 NPC and 7 GM2) and demonstrated a positive safety profile, with no severe adverse events (AE). Skin reactions were the most common mild or moderate AE, with a frequency of 33% of treated patients. Also, the pharmacodynamic and pharmacokinetic data obtained allows us to demonstrate dose-dependent enzyme inhibition and to identify the most suitable dose for our upcoming Phase 3 clinical trial.

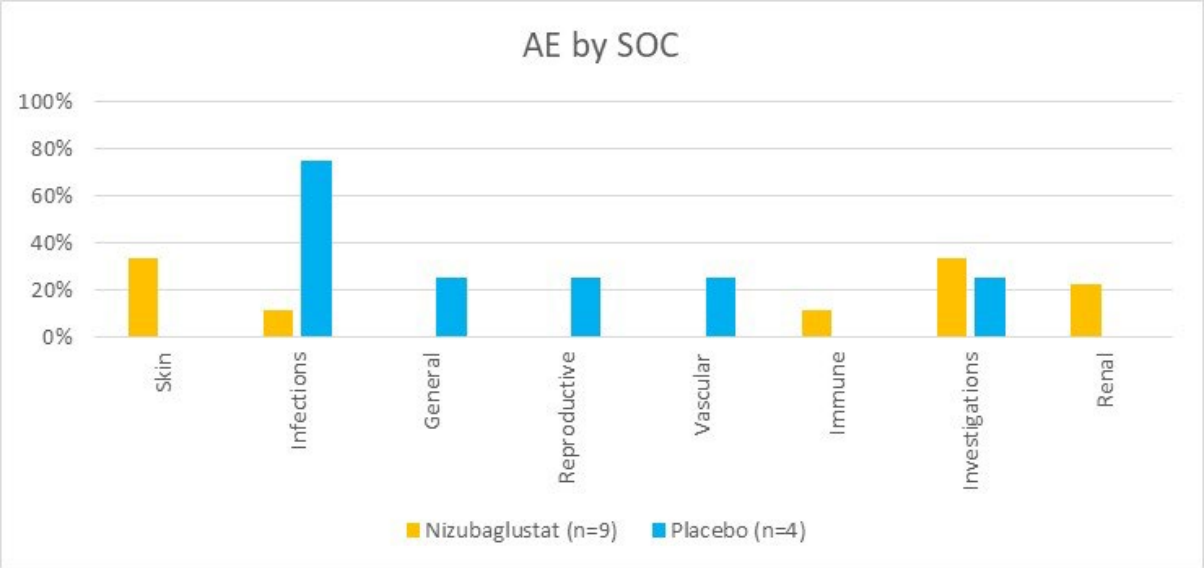

Figure 1. % of patients with adverse events depending on which dose of nizubaglustat or placebo they received.

Of the main phase participants, only two decided not to continue to the extension phase because they had gained access to an approved treatment.

Data on this phase from 11 patients (4 NPC and 7 GM2), maintained a similar safety profile with moderate or mild skin reactions as the most prevalent AE in 38% of participants. Diarrhoea, a common AE in treatments with similar mode of action has not been reported by any participant.

Despite not being an efficacy study, the extension phase has provided some clinical insights. For example, a slight reduction in daily seizure frequency and a reduction in the ataxic progression rate, compared to PRONTO data. This data is encouraging as we move forward with the Phase 3 pivotal studies, although it cannot be considered a claim of efficacy for nizubaglustat because of the reduced number of participants, among other reasons.

Follow-up towards Phase 3

Data from the RAINBOW study will be used to inform the target dose for Azafaros' planned Phase 3 pivotal studies. A master study will be intended to harmonize two independent studies, one for NPC and the other for GMx (gangliosidosis). Phase 3 study is planned to be initiated worldwide in mid-2025.

Azafaros is grateful to the patients and their families for their engagement and participation in the RAINBOW and PRONTO study.

For further information about our clinical trials and assets, contact us via email at: info@azafaros.com or talk with your clinician.