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Clarivate™

October 6, 2021
Volume 32, No. 193
Special Reprint

Retrotope looks to FDA for guidance in ultra-rare pediatric dystrophy

By Lee Landenberger

Privately held Retrotope Inc., the only company currently in the clinic studying the ultra-rare and fatal neurological disorder infantile neuroaxonal dystrophy, has new data it hopes to present to the FDA early next year.

Anil Kumar, president, Retrotope

Phase II/III data along with results from a concurrent natural history study of disease onset and progression in Retrotope's study of treating infantile neuroaxonal dystrophy with RT-001 showed statistically significant improvements in overall survival and progression free survival as compared to control. The studies were conducted with participants from 14 countries on six continents who flew to treatment sites in the U.S.

Improvements were also found in the primary efficacy endpoint, which is measured by the Modified Ashworth Spasticity Scale though that outcome did not reach statistical significance. There were other single efficacy outcomes that also failed to hit statistical significance, most likely, the company said, because of the small size of the study. There are 19 patients in the study and a concurrent natural history study had 36 patients in the control arm, with no significant difference in baseline characteristics between the two.

Those in the treatment study received the drug for at least one year along with a 30-day treatment free follow-up period. Those treated with RT-001, the data showed, improved 6.42 rank points on the Modified Ashworth Spasticity Scale compared to the control group (p=0.14).

Much the same improvement in those treated with RT-001 was found, when compared to control groups, in each of the five analyzed efficacy outcome scales that ranged from 4.5 to 7.3 rank point improvements.

Data showed that a secondary endpoint, PFS, saw an 82.5% reduction in morbidity risk for those treated with the drug when compared to control (p=0.021) Data also showed a statistically significant 88.8% decrease in mortality risk for treated patients compared to control patients. Two among the 19 patients (11%) treated with RT-001 died vs. 11 of the 36 patients (36%) in the control group.

The Los Altos, Calif.-based company said it plans to submit a pre-NDA meeting request with the FDA to talk about next steps for RT-001, an isotopically stabilized, synthetic linoleic acid that has the agency's rare pediatric disease designation in infantile neuroaxonal dystrophy and Friedreich's ataxia. It also has the EMA's orphan drug designation for infantile neuroaxonal dystrophy.

"My sense is that the FDA wants to learn more, so we'll have a meeting to get deeper into this," Retrotope's president, Anil Kumar, told *BioWorld*.

Peter Milner, chief medical officer, Retrotope

The disease, which has no approved treatment, is an inborn error in children, Peter Milner, Retrotope's chief medical officer, told *BioWorld*. "It affects them at about 18 months of age, then they begin to lose vital neurologic functions, like talking, walking, and sitting up," he said.

Patients generally begin to lose their ability to balance at 1.4 years, to stand independently at 2.1 years, and to sit independently at age 3. They lose the ability to hold their head upright at about 4.5 years of age, frontotemporal function at 4.8 years and generally die at about 9.9 years, all with increased spasticity until the end of life.

RT-001 is intended to address lipid peroxidation that produces oxidative stress and cellular degeneration. A genetic defect allows for the failure of removing toxins that ultimately comes from lipid peroxidation.

The studies had a lot of moving parts, what with young participants and their parents flying frequently to participate.

"COVID got in the way and we almost thought we lost the study," Milner said. "We went to telemedicine and remote visits and that worked very well."

T-001 is also in a phase II clinical trial for treating progressive supranuclear palsy. Enrollment was completed in August and exceeded the target of 40 patients in six weeks. The primary endpoint is the change from baseline in the PSP Rating Scale at 48 weeks. The first patients were dosed in March and data are expected before the end of 2021.