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Saturday

Results from the phase 2 study of latozinemab (AL001) in frontotemporal dementia patients carrying a granulin mutation

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State of the Art:

A loss-of-function mutation in the progranulin gene (*GRN),* which reduces progranulin (PGRN) levels by >50%, are a common cause of familial FTD. Latozinemab is a human monoclonal IgG1 antibody that blocks and downregulates sortilin, a receptor in the primary degradation pathway of progranulin. Restoring PGRN levels may be an effective therapeutic approach in treating FTD-*GRN* patients.

Methodology:

INFRONT-2 is an open-label, Phase 2 study in *GRN* mutation carriers to investigate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of latozinemab administered intravenously every four weeks. Participants 18 – 85 years, with a CDR® plus NACC FTLD (CDR-FTLD) global score of 0.5 – 2 underwent lumbar punctures and MRI scans at baseline and every 6 months thereafter. Clinical assessments were completed every 3 months. Fluid biomarkers were analyzed in plasma and CSF.

Results:

Latozinemab was generally safe and well-tolerated in INFRONT-2. Chronic dosing led to a sustained increase in PGRN levels to a normal range. Clinical assessment data and biomarker data related to key aspects of FTD-*GRN* pathophysiology will be presented for INFRONT-2 participants who have received latozinemab for up to 12 months.

Conclusion:

In INFRONT-2, latozinemab normalized CSF and plasma PGRN levels and biomarkers of the disease cascade in FTD-*GRN* carriers. Latozinemab is being evaluated in a Phase 3 study for the treatment of FTD-*GRN* to reduce the rate of neurodegeneration by increasing levels of PGRN and disrupting the pathophysiological disease cascade associated with FTD-*GRN*.

Conflicts of interest

All authors are equity stakeholders in Alector, Inc and/or employees of Alector, LLC