p-168

Saturday

Description of the Veri-T: A Phase 1 Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial of Verdiperstat in Patients with svPPA Due to FTLD-TDP

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State of the art:
Semantic variant primary progressive aphasia (svPPA) strongly predicts frontotemporal lobar degeneration (FTLD) with TAR DNA-binding protein 43 (TDP-43) mislocalization on autopsy, and is an ideal cohort for the first therapeutic trials in sporadic FTLD-TDP. One potential therapeutic target, microglial myeloperoxidase, produces oxidative stress that promotes TDP-43 mislocalization. The Veri-T trial (NCT05184569) investigates the therapeutic potential of verdiperstat, a potent myeloperoxidase inhibitor, in the first clinical trial focusing on svPPA. This trial is also the first to leverage the recruitment resources of the ARTFL LEFFTDS Longitudinal FTLD (ALLFTD) research network of clinical centers.

Methodology:
This is a phase 1, randomized, double-blind, placebo-controlled trial. N=64 participants with svPPA will be recruited at 5 ALLFTD sites and randomized 3:1 to six months of treatment with either oral verdiperstat (titrated to 600mg BID) or placebo. Psychometric, plasma, cerebrospinal fluid, and MR imaging data will be assessed before and after treatment.

Results:
The first participant was randomized April 19th, 2022 and recruitment remains ongoing. Objectives are to determine 1) the safety and tolerability and 2) the pharmacokinetic profile of verdiperstat patients with svPPA. Exploratory endpoints will include candidate pharmacodynamic measures (myeloperoxidase activity, CSF chitinase-family proteins, plasma/CSF neurofilament light chain, CSF unbiased somamer proteomics), MRI changes unique to svPPA, and psychometric measures (including language assessments via ALLFTD's smartphone app.)

Conclusion: *Veri-T* provides the first template for clinical trials in svPPA and explores novel pharmacodynamic and candidate efficacy measures that could be employed in future efficacy studies in patients with FTLD-TDP.

Conflicts of interest

N/A