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**Veri-T: A Phase I Placebo-Controlled Trial of Verdiperstat in FTLD-TDP**

*This Phase I clinical trial will investigate the impact of a chemical compound on brain inflammation in individuals with frontotemporal dementia.*

**PI**

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**STUDY**

- CADRO category: Translational Research & Clinical Interventions

**Background**

Abnormal accumulation of the protein TAR DNA-binding protein 43 (TDP-43) in the brain, is a hallmark brain change observed in many brain diseases, including frontotemporal dementia (FTD), amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), and sometimes Alzheimer's. A form of FTD called semantic variant Primary Progressive Aphasia (svPPA) has a particularly strong association with TDP-43 accumulation, compared to other brain diseases. Individuals with svPPA may lose their ability to understand meaning of words and gradually lose familiarity with people and objects in the world around them.

Individuals with TDP-43 accumulation in the brain may experience an increase in brain inflammation due to abnormal activation of microglia, the primary immune cells of the brain. Recent studies show that an enzyme (protein) called MPO (myeloperoxidase) - that is associated with microglia - could be driving brain inflammation in brain diseases associated with TDP-43 and may be a potential therapy target for this disease. Dr. Peter Ljubenkov and colleagues will investigate whether a chemical compound called Verdiperstat, which blocks the activity of MPO, could impact brain inflammation in individuals with svPPA.

**Research Plan**

Dr. Ljubenkov and his team will conduct a Phase I clinical trial with 55 participants with svPPA from three sites including University of California, San Francisco, University of Pennsylvania, and Northwestern University. Participants in the study will receive a placebo (not the actual drug but an inactive substance that has no risk for the participant) or Verdiperstat. The individuals receiving the Verdiperstat will be split into 2 groups with one receiving a low dose and the other receiving a high dose of the compound. The researchers

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will monitor the safety and tolerability of these different dosages administered to the participants for 24 weeks.

The researchers will then perform brain scans and collect biological samples, including blood and cerebrospinal fluid (a biological fluid sample found in the brain and spinal cord), from the participants. Dr. Ljubenkov's team will study whether the dosage levels are appropriate and sufficient by testing the levels of this compound in blood and cerebrospinal fluid. They will also study changes in biological markers (biomarkers) associated with certain brain diseases including Alzheimer's and brain inflammation in order to evaluate the impact of Verdiperstat on brain changes in these participants.

**Impact**

The study results may give rise to larger clinical trials for individuals with TDP-43 accumulation in the brain. If successful, the chemical compound could reduce brain inflammation in people with FTD and other dementia associated with TDP-43 accumulation in the brain.

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