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Phase 1 Clinical Trial of Innate Immunity Stimulation via TLR9 in Early AD

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STUDY

- CADRO category: Translational Research & Clinical Interventions

This Phase 1 clinical trial will evaluate whether a chemical compound can reduce brain changes observed in mild cognitive impairment and Alzheimer's.

Background

Microglia are the primary immune cells of the brain. Microglia help maintain healthy nerve cells in the brain. Individuals with Alzheimer's typically experience brain inflammation caused by dysregulation of the immune system, including increased activity of microglia, which can damage nerve cells. Researchers have been studying ways to reduce brain inflammation, while increasing the ability of microglia to clear brain changes observed in Alzheimer's, to help preserve nerve cell function and communication.

Immune cells use proteins on their surfaces to sense molecules in their environment and respond appropriately. Toll-like receptor 9 (TLR9) is a protein located inside immune cells that can help microglia detect molecules in the surrounding environment and help activate an immune response to these surroundings. Using genetically engineered Alzheimer's-like mouse models and non-human primate models, Dr. Thomas Wisniewski's team has studied a chemical compound which activates TRL9 and found that this could be associated with a beneficial immune response, which reduced brain changes observed in Alzheimer's.

Research Plan

Based on these preliminary findings, Dr. Wisniewski and colleagues will conduct a Phase 1 clinical trial with 30 older adults who have either mild Alzheimer's or mild cognitive impairment (a condition with subtle memory loss that may precede dementia, including Alzheimer's dementia). Participants in the study will receive either the experimental drug or a placebo (not the actual drug but an inactive substance that has no benefits and also no risk for the participant) over 14 months. The researchers will test the safety of their compound using several

measures that include physical examination, cognitive tests and brain (Magnetic Resonance Imaging) scans.

Additionally, they will collect both blood and cerebrospinal fluid (a biological fluid found in the brain and spinal cord) samples and brain scans (using Positron Emission Tomography) to study the impact of their compound on brain changes associated with Alzheimer's and cognition in the participants. They will then prepare for larger clinical trials.

Impact

If successful, the study results could help potentially help advance a novel therapeutic approach in order to prevent or slow the progression of Alzheimer's.

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