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Modulating neuroinflammation by targeting microglia with CSF1Ri EI-1071

This Phase 2 trial will examine the safety and efficacy of a chemical compound that may reduce brain inflammation in people with Alzheimer's

Background

Microglia are the primary immune cells of the brain and help maintain the health of nerve cells in the brain. During Alzheimer's, microglia can become activated in response to brain changes in Alzheimer's, and release substances that promote brain inflammation that may lead to nerve cell damage.

Studies have shown that a protein called Colony Stimulating Factor-1 Receptor (CSF-1R) plays an important role in the growth and survival of microglia cells. Initial experiments on the effect of the CSF-1R in Alzheimer's were conducted in genetically engineered Alzheimer's-like mouse models by Dr. Hung-Kai Chen's team, and other groups. These studies showed that if CSF-1R on microglia is blocked, the number of microglia in the brain decreases. Additionally, these studies revealed a reduced amount of brain inflammation and other brain changes associated with Alzheimer's.

Building on the preliminary findings in mice, Dr. Chen and colleagues moved onto a Phase 1 clinical trial in humans to evaluate if the compound is safe and tolerable in cognitively unimpaired adults. Individuals were given either the drug or a placebo (not the actual drug, but an inactive substance that has no risk for the participant). Encouraging safety and tolerability results from the Phase 1 clinical trial support proceeding to a Phase 2 clinical trial.

Research Plan

The main objective of the Phase 2 clinical trial, conducted by Dr. Chen and colleagues, is to investigate the effects of EI-1071, which blocks CSF-1R, in individuals with Alzheimer's. The trial will include 15 individuals with either mild cognitive impairment due to Alzheimer's, or those with mild, moderate, or severe Alzheimer's.

The researchers will collect brain scan images, and samples of blood and cerebrospinal fluid (or, CSF, the biological fluid surrounding the brain and

spinal cord), from all participants using routine procedures. In addition, they will monitor individuals closely, to continue to evaluate the safety of the drug and any potential side effects.

Brain scans will be used to determine the effect of the compound on brain inflammation. Blood and CSF will be used to evaluate the impact of the compound in terms of biological markers (biomarkers) associated with inflammation. Although it is not the main focus of this Phase 2 trial, with its relatively short treatment schedules as a proof-of-concept study, Dr. Chen and colleagues will also use various brain function tests to assess the impact of the compound on cognition and other brain functions.

Impact

The knowledge gained from this study will aid in understanding if EI-1071 is safe and effective in individuals with Alzheimer's. If successful, this study may allow for a larger Phase 3 trial with a longer treatment to determine whether or not EI-1071 has the potential to slow or halt cognitive decline in individuals with Alzheimer's as well explore potential benefits in other brain diseases.

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