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2020 Part the Cloud: Translational Research Funding for Alzheimer's Disease (PTC) - \$745,836

ALSENLITE: An Open-Label Pilot Study of Senolytics for Alzheimer's Disease

This Phase IIa clinical trial will determine if a novel drug is successful in potentially alleviating age-related brain disorders including Alzheimer's disease.

PI

- Ph.D., University of Toronto, Canada, 1990
- President-Elect, American Federation of Aging Research, 2016
- Clinical Trials Advisory Panel, National Institute on Aging, Bethesda, MD, 2015

STUDY

- CADRO category: Translational Research & Clinical Interventions

Background

Aging is the biggest risk factor for Alzheimer's disease. Researchers have been studying the use of drugs that impact aging process as a potential strategy to tackle Alzheimer's. One of the processes underlying aging is called "cellular senescence" - which means that as one ages, the cells in the body cease to divide. The senescent cells tend to accumulate in multiple tissues with aging and are present in areas of the body where many age-related diseases develop. Over time, accumulation of these senescent cells may slow or stop cell regeneration and maintenance of tissue, thereby contributing to tissue aging. Past studies show that in Alzheimer's disease, senescent cells may be present in brain regions and could impact cognition, language, memory among others.

Dr. James Kirkland believes that clearing these senescent cells from the brain and other tissues may benefit brain diseases, specifically Alzheimer's. To this end, Dr. Kirkland and colleagues recently developed special type of drugs called "senolytic drugs" that targets the removal of senescent cells. The researchers have shown that in genetically engineered Alzheimer's-like mice, the senolytic drugs were able to partially alleviate brain changes associated with the disease, restore memory and other aspects of brain function. Furthermore, Dr. Kirkland and his research team conducted a small pilot clinical trial for individuals with a progressive, fatal lung disease caused by senescent cells. The researchers found that these trial participants had improved physical function after a brief course of the experimental drugs.

Research Plan

Building on their prior work, Dr. Kirkland and colleagues will perform a phase IIa clinical trial in individuals with confirmed Alzheimer's. The researchers will recruit up to 75 older adult individuals with Alzheimer's disease from the Robert and Arlene Kogod Center on Aging at the Mayo Clinic. The participants will first be observed over a 90-day period to collect baseline information and then given 12 doses of the experimental

drugs over a period of 90 days. Dr. Kirkland's team will assess the safety and tolerability of the senolytic drugs. To measure the impact of the experimental drugs Dasatinib and Quercetin, the researchers will measure blood-based and cerebrospinal fluid (a biological fluid surrounding the brain and spinal cord) based biological markers associated with Alzheimer's and cell senescence, as well as brain scans in the participants before, during and after 3-months of the clinical trial.

Furthermore, Dr. Kirkland and colleagues will also measure the impact of these experimental drugs to assess potential cognitive (including memory, attention, processing speed, mood and behavior) and physical (such as improved balance, walking) benefits in the study participants.

Impact

If successful, the clinical trial may provide vital information about the efficacy and impact of these experimental drugs, which may enable researchers to plan a larger clinical trial and recruit more participants.

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