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IRB Approved at the
Protocol Level
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ADVANCE II

Have You Or Someone You Know Been Diagnosed With Mild Alzheimer's Disease?

A study researching a different approach for mild Alzheimer's Disease is seeking participants who:

- ✓ ≥ 65 years old
- ✓ Are in good general health
- ✓ Are currently taking medication for Alzheimer's
- ✓ Have a caregiver or family member who can accompany the patient to doctor visits

Discover The ADvance II Study

Caution: Investigational Device. Limited by Federal law to investigational use.

Need for More Alzheimer's Treatments

Alzheimer's disease is a type of dementia that causes problems with memory, thinking and behavior. Symptoms usually develop slowly and get worse over time, becoming severe enough to interfere with daily tasks. There are a few medications available that provide moderate relief of symptoms for a limited period of time, but there is currently no cure for Alzheimer's Disease.

ADvance II Study Using Electrical Stimulation for Alzheimer's Disease

The ADvance Study is researching the use of a surgically implanted device that delivers mild electrical pulses to specific areas of the brain in people with Alzheimer's. This deep brain stimulation (known as DBS) will be given to the fornix, a place in the brain that plays a central role in memory. Based on results of a study of 42 patients with Alzheimer's*, the ADvance study is designed to determine if DBS of the fornix (DBS-f) is safe and has potential clinical benefit for patients with mild Alzheimer's.

The study will involve about 210 subjects ≥ 65 years of age that have been diagnosed with mild Alzheimer's disease. The study is being conducted at sites in the U.S. and Europe. The neurosurgeons participating in this study have extensive experience with DBS surgery. All subjects in the study will have a DBS-f system implanted, with the stimulation device turned on for two-thirds of the subjects, and off for one-third. For those with the device left off at the start of the study, they will have it turned on after 12 months. All study participants will be regularly assessed for at least 48 months to measure their rate of Alzheimer's progression. The DBS-f system or certain components of the system are likely to remain in the body of study participants for the rest of their lives.

About Deep Brain Stimulation

More than 135,000 people worldwide have received DBS therapy, with stimulation of other areas of the brain to treat other medical conditions. The ADvance Study is using a DBS system produced by Boston Scientific. DBS technology was first approved by the FDA in 1997 and is now used for the treatment of Parkinson's Disease and Essential Tremor. The use of DBS in the fornix for Alzheimer's is investigational (being studied) and not currently approved by the FDA.

DBS-f is an adjustable therapy that uses an implanted device that electrically stimulates the brain. The system includes a neurostimulator, similar to a heart pacemaker, that is implanted beneath the skin in the patient's chest and two attached wires that deliver electrical pulses directly to a specific area in the brain.

* Lozano AM, Fosdick L, Chakravarty MM, et al. A Phase II Study of Fornix Deep Brain Stimulation in Mild Alzheimer's Disease. 2016;54:777-787. doi:10.3233/JAD-160017.

Discover The ADvance II Study

Visit www.ADvanceStudy4AD.com

Who Can Participate in This Study?

You may be eligible for the ADvance Study if you meet several factors, including:

- Are ≥65 years old
- Have been diagnosed with mild Alzheimer's
- Have a reliable informant (spouse, relative, caregiver) who can attend all study visits and report on your daily activities and function
- Are in good general health
- Are on a stable dose for at least two months of an FDA approved drug for Alzheimer's — Aricept (donepezil), Razadyne (galantamine), or Exelon (rivastigmine)

You will be interviewed and standard screening tests will be performed to ensure that you are an appropriate candidate for this study.

What Are Volunteers Asked to Do During This Study?

The research staff will meet with you and your caregiver/family member to review the process for the study in detail. If you choose to participate, there are a few steps involved in the study, including:

Screening Visit

You and your caregiver/family member will participate in a screening visit that involves a physical exam along with several memory tests and psychological assessments to determine whether you are a candidate for the study.

Baseline Assessment

If you have completed the screening visit and are selected as appropriate for the study, you will next undergo a baseline assessment. This assessment is done during one or more visits before the scheduled implantation surgery and is conducted to establish your baseline levels and ensure that you are safe and prepared before undergoing the DBS-f implantation surgery.

Implantation Surgery

If the baseline assessment establishes that you are eligible for surgery, you will have the DBS-f device implanted while under anesthesia. All steps in this procedure will be explained to you in advance.

Setting the Device

About 2 to 4 weeks after the implant procedure you will be assigned by chance to one of three groups :

Brain Stimulation On$_{(low)}$ – the device will be activated
Brain Stimulation On$_{(high)}$ – the device will be activated
Brain Stimulation OFF – the device will be left off

If you are in the "On" group, your device will be turned on for the duration of the study. If you are in the "Off" group, your device will be turned on after your 12-month visit. Neither you nor your doctor will know whether you are in the "On" group or "Off" group.

Monitoring and Assessment

After the device is set, you will return to the clinic for several regularly scheduled visits to assess your physical health, psychological state, and level of physical skills, memory and thinking patterns during the course of the study. You will be followed up for 48 months.

Progress Through Research

With a lack of effective long-term treatments, researchers are working hard to find new and better future treatments for patients with Alzheimer's. Advances in treatment are possible through volunteers participating in clinical research studies like ADvance II. At this time, it is unknown whether you will benefit from participating in this study. As with all clinical research, there are potential benefits and risks associated with participating. Your study physician will review all these with you and your caregiver before being enrolled in the ADvance II Study.

The ADvance II Study is sponsored by Functional Neuromodulation.

How To Participate

If you or someone you know is interested in additional information about the ADvance II Study, please contact:

Or visit www.ADvanceStudy4AD.com