Alzheimer's Vaccine Found Safe, Effective in Patients with Mild Forms of the Disease, Phase 2 Study Finds

AXON Neuroscience's investigational AADvac1 vaccine against tau protein, a hallmark of Alzheimer's disease, was found safe and effective at lessening signs of neurodegeneration in patients with mild Alzheimer's, according to the results of a Phase 2 trial.

Immunotherapy using the AADvac1 vaccine is intended to induce the patient's immune system to produce specific antibodies against abnormal forms of tau, with the ultimate goal of protecting neurons from degeneration.

The Phase 2 ADAMANT study randomized 196 patients with mild Alzheimer's to receive ADDvac1 or a placebo. Patients were enrolled at 42 clinical centers in eight countries around Europe. The vaccine was given in a total of 11 doses.

The results showed that AADvac1 was safe and well-tolerated. The vaccine induced a robust immune response, with 98.2% of patients generating antibodies against toxic forms of the tau protein.

Moreover, treatment with AADvac1 significantly lessened nerve cells' death and neurodegeneration, as shown by the blood levels of neurofilament light chain (NfL) – a biomarker measured in the blood or in the cerebrospinal fluid that reflects nerve cell damage in neurodegenerative diseases.

AADvac1-treated patients also showed a trend for reduced specific Alzheimer's disease biomarkers, including the pathogenic variants of tau protein. The vaccine also seemed to improve cognitive outcomes in younger subjects, and lessened brain shrinkage associated with disease progression.

Source: ***https://alzheimersnewstoday.com/2019/09/20/alzheimers-vaccine-safe-effective-mild-forms-of-disease-phase-2-study/***

Phase 3 Trial Suggests Pimavanserin Assuages Psychosis in Dementia

A Phase 3 trial of Pimavanserin was halted early when the study met its primary endpoint of delaying relapse to psychosis in people with dementia, according to a press release by its sponsor, Acadia Pharmaceuticals.

Pimavanserin—a selective serotonin inverse agonist—is approved to treat psychosis in Parkinson's, and the company is gunning for approval in people who suffer from psychosis associated with all-cause dementia. Trial data is yet to be released.

The announcement comes nearly two years after a Phase 2 study that was inconclusive.

As with many anti-psychotic drugs, Pimavanserin, marketed as Nuplazid, comes with a black box warning against use in elderly people with dementia, owing to increased mortality.

Source: ***https://www.alzforum.org/news/research-news/phase-3-trial-suggests-pimavanserin-assuages-psychosis-dementia***

Bryostatin-1 Fails to Ease Dementia in Moderate-to-Severe Alzheimer's Patients in Phase 2 Trial

An investigational Alzheimer's treatment called bryostatin-1 failed to meet its primary goal — lesser evidence of dementia in people with more severe disease — in a Phase 2 clinical trial, Neurotrope, the company developing the therapy, announced in a press release.

Bryostatin-1 is a molecule that activates protein kinase C (PKC), which plays an important role in learning, memory, and maintaining the health of synapses — the places where neurons (nerve cells) come into contact with, and send signals to, each other.

Prior studies — including another Phase 2 clinical trial — indicated that bryostatin-1 might be helpful in the clinical management of Alzheimer's disease.

In this most recent trial (NCT03560245), 108 people with moderate to severe Alzheimer's disease were randomly assigned to intravenous (directly into the vein) treatment with either 20 mg of bryostatin-1 or a placebo, given seven times over the course of 12 weeks.

The study's primary endpoint, or goal, was the change in total score for the Severe Impairment Battery (SIB) — a test designed to assess cognitive function in people with

dementia who are unable to complete other psychological tests — from the study's start to week 13.

Data found that treatment with bryostatin-1 did not ease dementia symptoms relative to placebo.

The average total SIB score increased by 1.3 points in the bryostatin-1-treated group, while it increased by 2.1 points in the placebo group. Higher scores indicate better functionality (i.e., less evidence of dementia).

No statistically significant differences were seen between the bryostatin-1 and placebo groups for any of the study's secondary endpoints that were assessed. This included changes in SIB score at different points in time over the course of the study (at two, five, nine, and 15 weeks after the start of treatment).

Source: ***https://alzheimersnewstoday.com/2019/09/18/bryostatin-1-fails-to-ease-dementia-in-phase-2-clinical-trial/***

End of the BACE Inhibitors? Elenbecestat Trials Halted Amid Safety Concerns

Marking the fall of the only remaining BACE inhibitor currently tested for AD, Biogen and Eisai announced today the discontinuation of two Phase 3 studies of elenbecestat in people with mild cognitive impairment and mild AD.

The companies have yet to release details about the decision, but noted it was based on a safety review.

The Phase 2 trial, called Study 202 (NCT02322021), that evaluated elenbecestat's safety and efficacy in early Alzheimer's found that elenbecestat effectively reduced amyloid buildup in the brain while being safe and well-tolerated. Results were announced in 2018.

The Phase 3 elenbecestat clinical program, called MISSION AD, comprised two global, multicenter trials with identical protocols. MISSION AD1 and AD2 aimed to enroll a total of 2,100 participants diagnosed with mild cognitive impairment or mild AD and confirmed Aβ pathology. Participants were randomized to receive placebo or 50 mg elenbecestat daily for two years.

This decision does not impact the development of Eisai and Biogen's candidate BAN2401, a monoclonal antibody against a form of beta-amyloid protein that accumulates in the brain of Alzheimer's patients.

BAN2401 is being tested in the Phase 3 Clarity AD (NCT03887455) study, currently enrolling participants with early Alzheimer's and testing the antibody's safety and effectiveness. Early data from an ongoing Phase 2 trial (NCT01767311) support BAN2401's potential to slow cognitive decline.

Sources: ***https://www.alzforum.org/news/research-news/end-bace-inhibitors-elenbecestat-trials-halted-amid-safety-concerns***

https://alzheimersnewstoday.com/2019/09/23/phase-3-trials-of-elenbecestat-in-early-alzheimers-stopped-for-lack-of-benefit-eisai-and-biogen-say/

ADvance II Study Testing Deep Brain Stimulation in Mild Alzheimer's Started, Enrollment Ongoing

The first patient enrolled in the ADvance II Study has been implanted with a deep brain stimulation (DBS) device to start treatment for mild Alzheimer's disease.

The double-blind trial (NCT03622905) is currently recruiting up to 210 participants, ages 65 or older, across 14 sites in the U.S., Toronto in Canada, and Germany.

The study is expected to be completed by October 2024. For more information on participating, and on the study's steps, visit its webpage here.

The trial was specifically designed to assess the safety and efficacy of Deep Brain Stimulation (DBS) on the fornix (DBS-f), a brain area implicated in memory. All participants will have the DBS-f device implanted, but one-third — the "off" group — will only have it turned on after the 12-month visit.

Preclinical work in sheep and mice has suggested that targeting the fornix can improve memory and increase the activity of the hippocampus, a critical brain region for cognitive function.

This system also is being used in people with Parkinson's. DBS is a common approach for treating patients no longer responding effectively to medications. Epilepsy and essential tremor are two other neurological disorders also being treated with this technique.

ADvance II is based on findings of the previous ADvance study (NCT01608061), which demonstrated that DBS-f could benefit patients older than 65.

Source: ***https://alzheimersnewstoday.com/2019/09/13/advance-ii-trial-testing-deep-brain-stimulation-mild-alzheimers-started-enrollment-ongoing/***

Diet Directly Affects Gut Bacteria and May Contribute to Alzheimer's Progression, Pilot Study Suggests

A modified Mediterranean-ketogenic diet can regulate bacteria in the gut that may contribute to the development and progression of cognitive impairment and Alzheimer's disease, results from a pilot study suggest.

Those findings come from a small study by researchers at Wake Forest School of Medicine, which was published in *The Lancet* journal *EBioMedicine*.

Several factors can influence neuro-inflammation, including the bacteria that reside in the intestines, which are collectively named the gut microbiome.

Although it is not fully understood how gut microbiome may affect Alzheimer's progression, it is widely acknowledged that dietary patterns may play a role.

Western diets, rich in saturated fats and simple carbohydrates, have been associated with increased risk of Alzheimer's. In contrast, other dietary patterns with high mono- and poly-unsaturated fats, vegetables, fruits, and lean proteins, are associated with reduced Alzheimer's risk.

Wake Forest researchers explored the impact of the so-called Mediterranean diet in the gut microbiome and the overall risk for Alzheimer's disease.

The study (NCT02984540) enrolled 17 participants, of whom 11 had mild cognitive impairment and six had no cognitive problems. They were divided randomly into two groups to receive a modified Mediterranean diet or the American Heart Association Diet (AHAD) for six weeks. At the end of that period they stopped taking the dietary intervention for six weeks, after which they started the other diet for an additional six weeks.

After completion of the six-week dietary intervention, no major changes were reported on the overall microbiome diversity between the two groups, regardless of the diet. Still, the different dietary patterns led to some significant changes in the specific pattern of gut microbiome, with some bacteria family being reduced or increased with either the modified Mediterranean diet or the AHAD.

Importantly, the bacterial changes induced by the modified Mediterranean diet were linked reduced levels of Alzheimer's biomarkers, such as tau protein and beta-amyloid molecules.

Source: ***https://alzheimersnewstoday.com/2019/09/11/diet-gut-bacteria-alzheimers-progression/***