Research Highlights from Learning Specialist, Padmaja Genesh

Seaweed-based Therapy Approved in China for Mild to Moderate Alzheimer's, 1st New Treatment in 16 Years

Oligomannate (GV-971), a compound derived from marine brown algae that promotes a healthy gut microbiome, is now conditionally approved in China to treat mild to moderate Alzheimer's disease (AD), making it the first new disease therapy approved anywhere since Allergan's Namenda (memantine) in late 2003.

Conditional approval means that the therapy's marketing will be strictly monitored, and could be withdrawn if safety issues arise.

The decision was based on results from a 36-week Phase 3 trial, where treatment with oral Oligomannate was found to improve cognitive function in mild to moderate AD patients compared to placebo, and with sustained benefits.

Oligomannate, developed by Shanghai-based Green Valley Pharmaceuticals, is expected to be available in China by the end of 2019.

Another Phase 3 trial, called GREEN MEMORY, is planned to open in the U.S., Europe and other parts of Asia in early 2020. Positive results here will be used to support requests for Oligomannate's approval beyond China, Green Valley said in the release.

Source: https://alzheimersnewstoday.com/2019/11/05/china-approves-seaweed-based-therapy-for-mild-to-moderate-alzheimers-phase-3-trial/

Biogen to Seek Approval of Aducanumab for Early Alzheimer's based on New Analysis of Trials

Aducanumab, a human monoclonal antibody, designed to bind to and clear brain amyloid have been part of 2 Phase 3 clinical trials ENGAGE and EMERGE.

Both trials were halted in March after a monitoring committee analyzed data from the first 18 months of the studies and determined that Aducanumab was not likely to produce meaningful benefits for patients.

Biogen reconsidered the decision when an additional three months of data became available after the trials were discontinued. The new analysis showed that EMERGE met its primary endpoint, with monthly infusions of Aducanumab resulting in benefits for cognition and function, including memory, orientation, and language, as well as activities of daily living.

After meeting with the U.S. Food and Drug Administration (FDA), Biogen plans to submit a Biologics License Application in early 2020. The company is also consulting with other regulatory authorities in other countries, including Europe and Japan. If accepted, Aducanumab would become the first therapy to reduce the clinical decline of Alzheimer's disease.

Source: https://alzheimersnewstoday.com/2019/10/23/biogen-to-seek-approval-of-aducanumab-for-early-alzheimers-based-on-new-analysis-of-trials/

Nuplazid Significantly Delays Relapses in Dementia-related Psychosis, Phase 3 Study Shows

Nuplazid is a selective serotonin inverse agonist that works by binding to serotonin receptors called 5HT2A, blocking the activity of these receptors.

HARMONY (NCT03325556), the Phase 3, placebo-controlled trial was designed to evaluate the safety and efficacy of Nuplazid as a preventive treatment for delusions and hallucinations associated with dementia-related psychosis in patients with Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia spectrum disorders.

Treatment with Nuplazid (pimavanserin)was found to significantly delay time to a psychosis relapse in people with dementia-related disorders such as Alzheimer's and Parkinson's diseases, according to results from the ongoing Phase 3 HARMONY study.

Evaluation by an independent data monitoring committee recommended an early stop to this trial based on the treatment's "robust" efficacy, Acadia Pharmaceuticals, Nuplazid's manufacturer, announced in a press release.

Source: https://alzheimersnewstoday.com/2019/10/11/nuplazid-significantly-delays-relapses-dementia-related-psychosis-alzheimers-harmony-trial/

Longitudinal Blood Pressure Changes, Starting at Midlife, May Indicate Need for Earlier Treatment of Cognitive Decline

A study published in the online edition of *Lancet Neurology* found that elevated blood pressure at 53 years of age and increased systolic and diastolic blood pressure between ages 43 and 53 were associated with white matter hyper intensities and smaller brain volume at ages 69 to 71.

A 10 mm/Hg higher diastolic BP at age 43 was associated with a 6.9 mL reduction in whole-brain volume at ages 69-71. A 10 mm/Hg higher systolic BP at age 43 was associated with a 0.021 mL smaller hippocampal volume at ages 69-71. There was a statistically significant association between increasing SBP between 43 and 53 years and whole-brain volume in later life.

The blood pressure changes were not associated with amyloid status and late-life cognitive changes as measured by the Preclinical Alzheimer Cognitive Composite (PACC). This suggests that BP affects brain health through pathways not related to amyloid accumulation.

This research implies that routine and serial blood pressure measurement might need to start earlier around 40 years of age—and decisions to start treatment might need to be based not only on absolute blood pressure but also on longitudinal blood pressure change.

Source: https://journals.lww.com/neurotodayonline/Fulltext/2019/10030/Longitudinal_Blood_Pressure_Changes,_Starting_at.2.aspx

ApoE4 and Tau in Alzheimer's: Worse than We Thought? Especially in Women

Does ApoE4 affect aspects of Alzheimer's disease other than amyloidosis? Animal studies have hinted as much, and now several brain-imaging studies seem to agree.

In a preprint posted to medRxiv on October 8, researchers led by Mark Bondi at the University of California, San Diego, report that at a given level of tau pathology, Alzheimer's Disease Neuroimaging Initiative participants with an ApoE4 allele perform worse on memory tests than non-carriers. The findings imply that ApoE4 amplifies the toxicity of tangles.

Meanwhile, researchers led by Vijay Ramanan at the Mayo Clinic in Rochester, Minnesota, examined whether ApoE genotype exerts direct effects on tangles, independent of amyloidosis. In the October 23 JAMA Network Open, they reported finding few, although, among cognitively healthy people with amyloid plaques, ApoE4 carriers did accumulate more tangles in the entorhinal cortex than did non-carriers.

In that study, women of any genotype appeared to be more susceptible to the consequences of tangles than men, with worse brain metabolism at a given tangle burden. Other recent work suggests that ApoE4 may pack the biggest punch in women, with female carriers accumulating more tangles and having worse memories than male carriers.

- ApoE4 carriers have worse memories than non-carriers with the same tau burden.
- ApoE4 carriers with amyloid plaques have more tangles than do non-carriers.
- The effects of ApoE4 are worse in women than in men.

Source: https://www.alzforum.org/news/research-news/apoe4-and-tau-alzheimers-worse-we-thought-especially-women

Childhood Cognitive Ability May Predict Cognition at Age 70

How well a child performs on neuropsychological tests may predict their cognitive scores in later life, according to a longitudinal study published online on October 30 in *Neurology.*

Children who tested at a higher cognitive ability at age 8 performed better on tests at age 70, the researchers reported. Children who scored in the top 25 per cent were more likely to stay in the top 25 per cent more than 60 years later.

Also, educational attainment and adult socioeconomic status were independently associated with late-life cognitive function.

Overall, the findings show childhood cognitive ability, education, and socioeconomic status independently all influence cognitive performance at age 70. The researchers acknowledged this has implications both for "the interpretation and analysis of cognitive data measured in later life."

For more Information you can read the results of the study here:

Lu K, Nicholas JM, Collins JD, et al. Cognition at age 70 Life course predictors and associations with brain pathologies. *Neurology* 2019; Epub 2019 Oct 30.

Source: https://journals.lww.com/neurotodayonline/blog/breakingnews/pages/post.aspx?PostID=885

Income Fluctuations in Early Adulthood May Impair Brain Aging in Midlife, Study Finds

To what extent does economic instability influence brain health? That question is at the heart of a new analysis that found that fluctuations in income and economic instability were not only associated with adverse health outcomes, they also affected cognitive abilities over time.

Previous studies have linked low socioeconomic status with poor health consequences—some have reported associations between income volatility and cardiovascular and mental health, said published in the October 2 online edition of *Neurology*

Dr Leslie Grasset, PhD, a postdoctoral associate at the Inserm Research Center in Bordeaux, France, and the lead author of the paper, decided to look more specifically at the relationship between brain ageing and fluctuations in income by pulling data from the Coronary Artery Risk Development in Young Adults study (CARDIA), an ongoing prospective study of cardiovascular disease and its risk factors in young to middle-aged adults.

The researchers found that higher income volatility and subsequent income drops were associated with a significant worsening of processing speed and executive functioning, as well as worse microstructural integrity of the total brain and total white matter findings on MRI.

The next step, she said, would be to study the mechanism behind this relationship. Future studies examining the effect of social policies aimed at mitigating the impact of unpredictable income changes on brain ageing are needed, she said.

Source: https://journals.lww.com/neurotodayonline/Fulltext/2019/11070/Income_Fluctuations_in_Early_Adulthood_May_Impair.12.aspx