Recent Findings Suggest New Directions for AD Diagnosis, Management

NEOPROBE LICENSES IMAGING AGENT FOR AMYLOID DETECTION

Neoprobe Corporation has in-licensed the worldwide exclusive rights from AstraZeneca to the late-stage radiopharmaceutical imaging candidate, AZD4694, for aiding the diagnosis of Alzheimer's disease.

AZD4694 is a Fluorine-18 labeled precision radiopharmaceutical candidate for use in the imaging and evaluation of patients with signs or symptoms of cognitive impairment such as AD. It works by binding to Beta-amyloid deposits in the brain that can then be imaged in PET scans.

Clinical studies in more than 70 patients have suggested AZD4694 "has the ability to image patients quickly and safely with high sensitivity," according to the company. AZD4694 exhibits low background and white matter uptake, thereby providing clear images of Beta-amyloid deposits. Neoprobe announced intentions to initiate a Phase III clinical program in early 2013, while simultaneously building the requisite safety and training database. Patents and patent applications filed around the world related to AZD4694 are effective until 2028.

ALZHEIMER'S STATS

- 5.4 million Americans have AD
- 13% of individuals 65 and older have AD
- 43% of individuals over age 85 have AD
- Almost 2/3 of all Americans with AD are women

Following is a breakdown of AD incidence by age:

Pie chart legend:
- < 55 — 4%
- 65-74 — 6%
- 75-84 — 45%
- 85+ — 45%
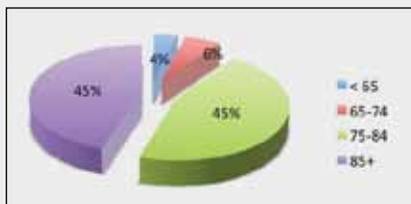
—Alzheimer's Association's 2011 Alzheimer's Disease Facts and Figures

MEDITERRANEAN DIET LINKED TO MEMORY PRESERVATION

Regular consumption of walnuts, but not of other nuts, was associated with better working memory in a recent study. (*Journal of Alzheimer's Disease*) Investigators believe that the high polyphenol content found in walnuts may be a key element in helping to preserve cognition and fight age-related cognitive decline. Coffee, virgin olive oil, and wine were also associated with better cognitive scores.

The cross-sectional study evaluated whether antioxidant-rich foods from the Mediterranean diet were associated with better cognitive performance in a subsample (447) of elderly participants (aged 55-80 years) from the landmark Spanish PREDIMED study – a dietary intervention trial in asymptomatic individuals with high cardiovascular risk. The researchers evaluated the intake of various foods and performed neuropsychological tests to assess cognitive function in relation to diet, and analyzed the urinary excretion of polyphenols as a biomarker of daily intake of antioxidants.

ORAL BEXAROTENE REVERSES Aβ LOAD IN MOUSE AD

Oral doses of the RXR agonist bexarotene cleared soluble Aβ in a mouse model of AD within hours, a new study shows. Published in *Science* (335(6075): 1503-1506), the study demonstrated enhanced clearance of soluble Aβ within hours in an apoE-dependent manner and reduction of Aβ plaque area by more than 50 percent within 72 hours. Aβc learance mediated by bexarotene was accompanied by rapid reversal of cognitive, social, and olfactory deficits and improved neural circuit function.

MRI, NEUROPSYCH TESTS BEST FORECAST AD IN OLDER PATIENTS

In most elderly patients, invasive and expensive techniques (such as lumbar puncture and PET scan) are not useful to establish the diagnosis of Alzheimer's disease, according to new research from the Journal of Alzheimer's Disease.

The researchers divided a large collaborative research product between the US and Canada, called the Alzheimer's Disease Neuroimaging Initiative, sample into two halves: a younger (<75 years) and an older half (>74 years). They found that the CSF biomarkers (amyloid and tau), and FDG-PET, are informative in the younger patients, but not in the older group.

In the older patients, MRI scans and neuropsychological tests seem to demonstrate helpful information, while CSF biomarkers and FDG-PET failed to do so. The latter two techniques were found informative only in younger patients. MRI scans and cognitive tests are not only helpful in distinguishing patients who are already demented from those who are not, but also in predicting who among older MCI patients will progress to dementia within a few years. Predictions based on CSF biomarkers may turn out to be right in the longer term, roughly five or 10 years, in patients who live that long and become demented.

Ben Schmand, one of the authors and a professor of clinical neuropsychology at the University of Amsterdam, stresses a practical implication for clinicians. "In MCI patients", he says, "particularly in older patients, it is not sufficient to base a diagnosis solely on a brief memory test, a MRI scan, and a lumbar puncture. Generally, a more thorough clinical evaluation will be necessary Cerebrospinal fluid biomarkers and PET scanning remain informative in relatively young patients."

ALZHEIMER'S MAB MAY REDUCE TAU TANGLES

New research has found treatment with the monoclonal antibody bapineuzumab significantly lowered levels of phosphorylated tau (P-tau) in the cerebrospinal fluid of Alzheimer's patients. Published online April 2 in Archives of Neurology, A pooled analysis of two phase showed P-tau levels fall significantly for those on bapineuzumab compared with controls (P=0.03) and showed a trend toward diminished total-tau levels in this group. No clear-cut differences were observed for CSF Aβ.

The two pooled phase II, multicenter, randomized, double-blind, placebo-controlled clinical trials of 12-month duration study may be the first to show that passive Aβ immunotherapy with bapineuzumab results in decreases in CSF T-tau and P-tau. This may indicate downstream effects on the degenerative process. Cerebrospinal fluid biomarkers may be useful to monitor the effects of novel disease-modifying anti-Aβ drugs in clinical trials, the authors conclude. ∎