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New Study Shows Beta-Amyloid Imaging is Associated with Altered Diagnosis and Management of Alzheimer's Disease

Study Results Presented at the Alzheimer's Association International Conference 2014

INDIANAPOLIS, July 16, 2014 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced new data showing that beta-amyloid imaging was associated with altered diagnosis and management of patients with Alzheimer's disease. Change in management was observed in both patients who met and did not meet the Appropriate Use Criteria (AUC), which were developed by the Society of Nuclear Medicine and Molecular Imaging and the Alzheimer's Association to provide guidance on which patients are most appropriate for imaging and how best to use the results. These data were presented today at the Alzheimer's Association International Conference 2014 (AAIC 2014) in Copenhagen, Denmark by Andrew Siderowf, M.D., MSCE, medical director, Avid Radiopharmaceuticals, a wholly owned subsidiary of Lilly. The data were also featured by the AAIC in a research media tips sheet.

"This study included patients in which there was diagnostic uncertainty by the treating physician and found that changes in diagnosis and management of Alzheimer's disease did not vary between patients depending on whether they met the Appropriate Use Criteria or not. In addition, analysis of beta-amyloid scans conducted post-diagnosis indicated that many patients being treated with medications may have potentially been misdiagnosed and inappropriately treated," said Dr. Siderowf. "While we support the development of the Appropriate Use Criteria, one of the clearest insights resulting from these data is that we need to continue to fine tune our understanding of the appropriate use of these tools and their utility for patients facing a diagnosis of Alzheimer's disease."

The objective of the study was to evaluate which patients are most likely to receive different care if they had an amyloid PET scan as part of their diagnostic work-up. In particular, the study evaluated if patients who met the working definition of the AUC would be more affected than those who did not. The AUC guidelines propose that patients who are being evaluated for dementia with atypical presentations, younger patients, and patients with unexplained mild cognitive impairment, are most appropriate for amyloid PET imaging. For the patient to be included in the study, Alzheimer's disease had to be under consideration and the treating physician had to have uncertainty regarding the diagnosis.

Results showed that 59 percent of subjects met the working definition of AUC. Forty-seven percent of the AUC-like cases were amyloid positive compared to 62 percent of non-AUC cases. Diagnosis changed after PET scan for 58 percent of AUC cases versus 45 percent of non-AUC cases (p=0.10). The proportion of patients with change in management plan was high for both AUC (88 percent) and non-AUC (77 percent) cases. In particular, the use of Alzheimer's disease medications including cholinesterase inhibitors, or memantine, declined after a negative florbetapir F 18 scan by 20 percent (from 26/54 to 15/54 cases; p=0.002) in AUC cases and by 33 percent (from 17/27 to 8/27 cases; p=0.004) in non-AUC cases. Diagnoses for non-AUC cases in which Alzheimer's disease medications were withdrawn after a negative scan included prodromal Alzheimer's disease/mild cognitive impairment due to Alzheimer's disease (n=8), or mild cognitive impairment of uncertain etiology (n=1). This study found that patients with an uncertain diagnosis, but who are not otherwise explicitly captured by AUC, may be reasonable candidates for amyloid imaging.

"Alzheimer's disease is one of many possible causes of cognitive impairment, which can make diagnosis challenging. In fact, it is estimated that up to one in five patients clinically diagnosed with probable Alzheimer's disease during life do not exhibit Alzheimer's disease pathology upon autopsy[1],[2]," said Dr. Siderowf. "These results reinforce how knowledge of the presence or absence of amyloid pathology can substantially affect both diagnosis and management in these patients being evaluated for Alzheimer's disease or other possible causes of cognitive decline."

Study Methods

The impact of amyloid PET on actual patient care was examined in a previous study.[3]

In the prior study, performed at 19 clinical sites, treating physicians provided a provisional diagnosis and management plan prior to receiving results of amyloid PET imaging with florbetapir F 18. Participants' medical records for the three months immediately after imaging were abstracted to capture their actual diagnosis and management. For the current study, participants were classified as meeting an operational definition of AUC-like or not, based on pre-scan diagnosis and demographic features.

About Alzheimer's Disease

Alzheimer's disease is a fatal illness that causes progressive decline in memory and other aspects of cognition.[4] It is the most common form of dementia, accounting for 60 to 80 percent of dementia cases.[4] There are currently an estimated 44 million people living with dementia worldwide.[5] The number of people affected by dementia is expected to be more than 75 million in 2030 and 135 million in 2050.[5]

About Florbetapir F 18 Injection[6]

Florbetapir F 18 is indicated for Positron Emission Tomography (PET) imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline. A negative florbetapir F 18 scan indicates sparse to no neuritic plaques and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD. A positive florbetapir F 18 scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Florbetapir F 18 is an adjunct to other diagnostic evaluations.

Limitations of Use:

- A positive florbetapir F 18 scan does not establish a diagnosis of AD or other cognitive disorder
- Safety and effectiveness of florbetapir F 18 have not been established for:
  - Predicting development of dementia or other neurologic condition
  - Monitoring responses to therapies

WARNINGS AND PRECAUTIONS

Risk for Image Misinterpretation and Other Errors

- Errors may occur in the florbetapir F 18 estimation of brain neuritic plaque density during image interpretation
- Image interpretation should be performed independently of the patient's clinical information. The use of clinical information in the interpretation of florbetapir F 18 images has not been evaluated and may lead to errors. Other errors may be due to extensive brain atrophy that limits the ability to distinguish gray and white matter on the florbetapir F 18 scan as well as motion artifacts that distort the image
- Florbetapir F 18 scan results are indicative of the brain neuritic amyloid plaque content only at the time of image acquisition and a negative scan result does not preclude the development of brain amyloid in the future

Radiation Risk

- Florbetapir F 18, similar to other radiopharmaceuticals, contributes to a patient's overall long‑term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure

MOST COMMON ADVERSE REACTIONS

- The most common adverse reactions reported in clinical trials were headache (1.8%), musculoskeletal pain (0.7%), blood pressure increased (0.7%), nausea (0.7%), fatigue (0.5%), and injection site reaction (0.5%)

For more information about florbetapir F 18, please see the Prescribing Information at http://pi.lilly.com/us/amyvid-uspi.pdf.

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About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and http://newsroom.lilly.com/social-channels.

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This press release contains certain forward-looking statements about florbetapir F 18, a radioactive diagnostic agent indicated for brain imaging of beta-amyloid plaques in patients with cognitive impairment who are being evaluated for Alzheimer's Disease and other causes of cognitive decline. This release reflects Lilly's current beliefs; however, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that florbetapir F 18 will be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

[1] Petrovitch H, White LR, Ross GW, et al. Accuracy of clinical criteria for AD in the Honolulu-Asia Aging Study, a population-based study. Neurology. 2001;57(2):226-234.

[2] Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. J Am Geriatr Soc. 1999;47(5):564-569.

[3] Grundman M, Pontecorvo MJ, Salloway SP, et al. Potential impact of amyloid imaging on diagnosis and intended management in patients with progressive cognitive decline. *Alzheimer Dis Assoc Disord*. 2013 Jan;27(1):4-15.

[4] Alzheimer's Association. 2014 Alzheimer's Disease Facts and Figures. http://www.alz.org/downloads/facts_figures_2014.pdf. Accessed on June 4, 2014.

[5] Alzheimer's Disease International. Policy Brief for Heads of Government: The Global Impact of Dementia 2013 - 2050. http://www.alz.co.uk/research/GlobalImpactDementia2013.pdf. Published December 2013. Accessed on June 4, 2014.

[6] Amyvid [package insert]. Indianapolis, IN: Lilly USA, LLC; 2012.

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