FDA AD Drug Development Guidance

On February 7, the U.S. Food and Drug Administration (FDA) issued draft guidance that the agency said was designed "to assist companies developing new treatments for patients in the early stages of Alzheimer's disease [AD], before the onset of noticeable (overt) dementia." The document addresses current FDA thinking on selection of patients for clinical trials, the selection of endpoints for clinical trials in these populations, and the ways in which disease modification should be demonstrated. The document, titled "Guidance for Industry, Alzheimer's Disease: Developing Drugs for the Treatment of Early Stage Disease," is intended to serve "as a focus for continued discussions among representatives of the [FDA] Division of Neurology Products, pharmaceutical sponsors, the academic community, and the public."

"The scientific community and the FDA believe that it is critical to identify and study patients with very early AD before there is too much irreversible injury to the brain," said Russell Katz, MD, director of the Division of Neurology Products. "It is in this population that most researchers believe that new drugs have the best chance of providing meaningful benefit to patients."

Although the draft guidance recognizes the potential role of biomarkers as both single primary and supportive secondary outcome measures, no such definitive measures are included. Nowhere in the report is imaging mentioned as a potential biomarker of AD or other causes of cognitive decline. The document states that, without evidence-based agreement on the beneficial effects associated with any specific biomarker, the agency "will not be in a position to consider an approval based on the use of a biomarker as a surrogate outcome measure in AD (at any stage of the illness)." For support of secondary outcomes, the agency said, "there is currently no consensus as to what particular biomarkers would be appropriate to support clinical findings in trials in early AD."

"We are hopeful that the FDA will revisit in the near future the role of AD imaging results in providing acceptable primary or secondary biomarker data," said Michael Graham, MD, PhD, past president of SNMMI. "A growing number of radiotracers and imaging techniques are already providing not only qualitative but quantitative data illuminating the significance of beta-amyloid and other markers in early AD."

FDA is seeking public comment on the draft guidance, with the comment period to end in early April. The proposal is part of the U.S. Department of Health and Human Services (HHS) efforts under the National Plan to Address Alzheimer's Disease, which calls for both the government and the private sector to intensify efforts to treat or prevent AD and related dementias and to improve care and services. It responds to recommendations from a May 2012 HHS and National Institutes of Health Alzheimer research summit to conduct clinical trials in at-risk individuals without symptoms and to develop and validate new measures so that AD can be identified at the earliest possible time in the course of the disease. The complete draft guidance is available at: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM338287.pdf.

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Zhaowei Meng, MD, PhD, from Tianjin Hospital (China); Erica Cohen, DO, MPH, from Loyola University Medical Center (Maywood, IL); and Guido Davidzon, MD, from Stanford University Medical Center (Palo Alto, CA). All the presenters deserve congratulations for their excellent work.

The Chinese delegation also had an opportunity to tour Tulane University School of Medicine under the direction of Harold Neitzschman, MD, professor and chair of radiology and Tulane Health Sciences Center section head, nuclear medicine; visit beautiful mansions in New Orleans; attend a Hornets basketball game; and enjoy the entertainment in the French Quarter.

As Alessio and Iagaru noted in their conference welcome message: "Together, the SNMMI and CSNM have worked to further develop education in the United States and in China, assisted with the growth of young professionals and residents within the respective societies, and traveled great distances to ensure that the relationship between these 2 world-leading organizations continues for many years to come. CSNM leaders have been instrumental in continuing this important relationship, and we believe that the continuation of this biannual conference will reinforce the importance and value of global collaboration."

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