FDA Approves ^{18}F-Florbetapir PET Agent

The U.S. Food and Drug Administration (FDA) on April 10 announced the approval of Amyvid (^{18}F-florbetapir injection) for PET imaging of the brain in adults under evaluation for Alzheimer disease (AD) and other causes of cognitive decline. Amyvid is manufactured for Avid Radiopharmaceuticals (Philadelphia, PA), a subsidiary of Eli Lilly & Co.

^{18}F-florbetapir PET scans are used to estimate brain β-amyloid neuritic plaque density in patients with cognitive impairment. A negative scan shows few or no neuritic plaques and reduces the likelihood that any cognitive impairment is related to AD. A positive scan shows moderate or frequent plaques and is common in patients with AD or other types of cognitive impairment and in older people with normal cognition.

In early 2011, an FDA advisory committee unanimously recommended that Amyvid be approved for use as a PET imaging agent but included a requirement that Avid develop detailed and evidence-based guidelines on the levels of plaque that could be interpreted as diagnostic for AD. The FDA final approval announcement added that Amyvid is not a test for predicting the development of AD-associated dementia and is not for monitoring patient responses to AD therapy, nor does it replace other diagnostic tests used in evaluation of cognitive impairment. Absence of uptake on the scan has a high negative predictive value for AD and excludes the disease with a high degree of confidence.

Avid Radiopharmaceuticals was founded by current chief executive officer Daniel Skovronsky, MD, PhD, a neuropathologist who trained at the University of Pennsylvania (Philadelphia) and was previously scientific director of High Throughput Screening and Drug Discovery at the school's Center for Neurodegenerative Disease Research. Amyvid was developed with research partnerships at the University of Pennsylvania, including one with Hank F. Kung, PhD, professor of radiology and pharmacology.

The product is scheduled for availability this month. "We're excited. The approval means that this product will finally be available to the patients who need and can benefit from this," Skovronsky told the *Philadelphia Inquirer.* "It's our desire to make this widely available in the United States, beginning in June. It will be up to individual physicians and their imaging center to decide whether they want to offer it."

Skovronsky and his research partners have published widely on their work with ^{18}F-florbetapir and other imaging agents, with many of these publications appearing in *The Journal of Nuclear Medicine*. The most recent article, "Performance characteristics of amyloid PET with florbetapir F18 in patients with Alzheimer disease and cognitively normal subjects," appeared in March (*J Nucl Med.* 2012;53:387–384).

Lower Doses of ^{131}I?

With results that may change standard practice in treatment after total thyroidectomy for thyroid cancer, 2 large studies reported in May indicated that low doses of radioiodine may be as effective as higher doses in reducing thyroglobulin and eliminating residual thyroid tissue. The first study, reported by Schlumberger and a consortium of French researchers (*N Engl J Med.* 2012;366:1663–173), focused on 684 thyroid cancer patients, of whom 92% had papillary cancer. Patients were assigned randomly to 1 of 4 treatment strategies: thyroid stimulation by either administration of recombinant human thyrotropin or thyroid hormone withdrawal, each paired with low (1.1 GBq) or high (3.7 GBq) ^{131}I. Ultrasonography at 8 ± 2 mo was negative in 652 (95%), and stimulated thyroglobulin levels were ≤1.0 ng/mL in the 621 patients without detectable thyroglobulin antibodies, meeting the authors' criteria for thyroid ablation. No significant differences were noted in results with the 2 doses or with the thyrotropin-stimulation approaches. The authors concluded that "the use of recombinant human thyrotropin and a low dose of ^{131}I for postoperative radioiodine ablation represents an effective and attractive option for the management of low-risk thyroid cancer that reduces the amount of whole-body irradiation and maintains the quality of life.

A separate but similar study from Ujjal Mallick, MD, from Freeman Hospital (Newcastle Upon Tyne, UK), and a consortium of investigators from 29 centers in the United Kingdom (*N Engl J Med.* 2012;366:1674–1685) included 421 patients. Ablation success rates in those receiving low- and high-dose ^{131}I were 85.0% and 88.9%, respectively. Ablation rates were similar as well for the 2 groups receiving different thyroid stimulation therapies. They concluded that for the low-risk patients, "low-dose radioiodine plus thyrotropin alfa is an effective and convenient treatment with reduced radiation exposure, providing benefits to both patients and health care providers."

An editorial (*N Engl J Med.* 2012;366:1732–1733) noted that these results raised the question of whether any radioiodine therapy is required for low-risk patients, because 21%–59% of patients in the studies had already met the goal of a low thyroglobulin level after thyroidectomy alone. Erik K. Alexander, MD, and P. Reed Larsen, MD, wrote that "the use of radioiodine to achieve effective ablation in the remainder of patients must be weighed against increasing the risk of second primary cancers through exposure to radiation and the expense and logistics of radioiodine administration." However, they added that such an approach would eliminate posttreatment whole-body scanning and the discovery of unsuspected persistent or distant metastases in some patients, leading to the challenging question: "How can the standard of care be improved for the majority without sacrificing the standard care for the minority?"