FDA Approves ^{18}F-Fluciclovine and ^{68}Ga-DOTATATE Products

Through its Priority Review mechanism, the U.S. Food and Drug Administration (FDA) recently approved 2 radiopharmaceutical products for use as diagnostic PET agents. The first, approved on May 27, was Axumin (^{18}F-fluciclovine) injection, indicated for use in PET imaging to identify suspected sites of prostate cancer recurrence in men with elevated levels of prostate-specific antigen (PSA) following prior treatment. The second, approved on June 1, was the NETSPOT kit for preparation of ^{68}Ga-DOTATATE injection, indicated for localization of somatostatin receptor–positive neuroendocrine tumors (NETs) in adult and pediatric patients.

^{18}F-Fluciclovine in Recurrent Prostate Cancer

Axumin (Blue Earth Diagnostics Ltd.; Oxford, UK, and Burlington, MA) is the first FDA-approved ^{18}F-labeled PET agent for use in patients with suspected recurrent prostate cancer. Axumin will be available through the national radiopharmacy network of the sole U.S. commercial manufacturer and distributor, Siemens PETNET Solutions (Malvern, PA). Initial commercial production of Axumin is underway at several regional radiopharmacies, and increasingly broader availability is planned in coming months.

"An imaging agent with sufficient diagnostic performance to adequately detect and localize recurrent prostate cancer can provide referring physicians with actionable information to guide biopsy and inform management decisions for their patients," said David M. Schuster, MD, an associate professor of Radiology and Imaging Sciences and director of the Division of Nuclear Medicine and Molecular Imaging at Emory University School of Medicine (Atlanta, GA). The fluciclovine molecule in Axumin, originally developed at Emory by Mark Goodman, PhD, detects upregulation of amino acid transport that occurs in prostate cancer, with the potential for identifying recurrent prostate cancer more reliably than conventional imaging techniques. "The product will be convenient for patients and imaging facilities, as it can be made widely available, and the entire imaging procedure can typically be completed in less than 30 minutes," said Schuster. Blue Earth reported that the fluciclovine molecule is currently being investigated for utility in other cancer indications, including glioma.

In one of the studies used as part of the approval decision-making process by FDA, ^{18}F-fluciclovine (also known in the literature as trans-1-amino-3-^{18}F-fluorocyclobutanecarboxylic acid or ^{18}F-FACBC) images acquired in 105 patients were evaluated by 3 independent physicians who were unaware of the clinical details of each patient or whether the prostate biopsy was positive or negative. On average, a correct image finding was identified in 77% of patients (range, 75%–79%). For cancer outside the region of the prostate, a correct image finding was identified in an average of 90% of patients (range, 88%–93%). Results were affected by PSA levels, with a 31% rate of inaccurate interpretation in patients with PSA levels $\leq$1 ng/mL and a 16% rate of inaccurate interpretation in patients with PSA levels $>$1 ng/mL.

^{68}Ga-DOTATATE in NETs

NETSPOT (Advanced Accelerator Applications SA [AAA]; Saint-Genis-Pouilly, France; previously marketed as Somakit-TATE) is the first approved drug using ^{68}Ga as a positron emitter. The ^{68}Ga-DOTATATE kit received an Orphan Drug designation from both the FDA and the European Medicines Agency in March 2014. Although NETs have historically been considered as rare tumors, their incidence has grown $>$500% over the last 3 decades.

AAA will commercialize the product in the United States in 2 forms: as a kit for reconstitution using a ^{68}Ga generator and as NETSPOT injection, a ready-to-use dose delivered from a local radiopharmacy in selected metropolitan areas. On June 9 and 10, AAA announced the selection of Cardinal Health, Inc. (Dublin, OH), Triad Isotopes, Inc. (Orlando, FL), and Nuclear Diagnostic Products, Inc. (Plainview, NY) to supply ^{68}Ga-DOTATATE doses prepared with the newly approved kit to U.S. hospitals and imaging centers. NETSPOT is currently approved for use with the GalliaPharm ^{68}Ga generator from Eckert and Ziegler (Berlin, Germany).

"Use of advanced imaging techniques to detect rare NETs at an early stage in patients is critical," said Libero Marzella, MD, PhD, director of the Division of Medical Imaging Products in the FDA Center for Drug Evaluation and Research. "NETSPOT provides another diagnostic tool whose results will help clinicians determine the location and extent of the tumor. This information is important for planning the appropriate course of therapy."

Three studies established the safety and effectiveness of the product. The first compared ^{68}Ga-DOTATATE PET images of NETs with images obtained with an approved drug, and then confirmed the results with CT or MR imaging. The second compared ^{68}Ga-DOTATATE PET imaging findings with histopathology and clinical follow-up. The third evaluated patients with NET recurrence using ^{68}Ga-DOTATATE PET.

"NETSPOT has the potential to significantly improve the accuracy of NET diagnosis while reducing radiation exposure for patients," said Stefano Buono, Chief Executive Officer of AAA. "We believe that the use of NETSPOT should also offer increased comfort for patients by potentially shortening a procedure that is currently performed over 24 hours or more to just a few hours."