MEDCAC Meets on β-Amyloid Imaging

The Centers for Medicare & Medicaid Services (CMS) on January 30 convened a meeting of the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) in Baltimore, MD, to review available evidence and hear public testimony on the use of beta-amyloid PET imaging for management of dementia and neurodegenerative disease. In preparatory materials, CMS indicated its interest in learning more about "the clinical impact of this technology on health outcomes experienced by patients." Medicare currently does not cover beta-amyloid PET imaging. The meeting was chaired by Rita Redberg, MD, MSc, a cardiologist at the University of California–San Francisco Medical Center.

After a day that featured compelling presentations from members of the molecular imaging community representing academic, clinical, and industry experience with beta-amyloid PET imaging, the committee voted on a series of "confidence" questions. The following day, SNMMI released a formal statement indicating that the society and its members were "disappointed that the MEDCAC does not believe that adequate evidence exists to determine whether brain amyloid imaging with PET changes health outcomes. SNMMI believes that the evidence—together with Food and Drug Administration (FDA) approval—supports the ability of beta-amyloid imaging to change patient management, leading to better outcomes for patients." SNMMI urged CMS to "evaluate the evidence and provide coverage for brain amyloid imaging for the FDA-approved indication."

The lack of confidence in beta-amyloid imaging expressed by MEDCAC stemmed in part from the comments of several MEDCAC panelists who expressed concerns about possible inappropriate use of PET in cognitive decline and related indications, with special concerns about potential negative effects of false-positive reports. Earlier in the same week, SNMMI and the Alzheimer's Association released appropriate use criteria (AUC) for brain amyloid imaging that addressed these concerns. The criteria recommend the use of brain amyloid imaging in those patients already experiencing cognitive impairment but do not support its use in asymptomatic patients. SNMMI is currently developing a related education program for those who will be referring patients for beta-amyloid imaging and those who will be reading the scans. In addition, SNMMI is developing technical procedure guidelines for ensuring quality in the performance of these procedures. SNMMI added in its statement that the society is "committed to working with CMS on the continued development of further evidence of the effectiveness of brain amyloid imaging so that individuals suffering from dementia can have access to the best care possible."

Centers for Medicare & Medicaid Services
SNMMI

Priority Review for ^{223}Ra-Dichloride

Bayer HealthCare Pharmaceuticals, Inc. (Wayne, NJ) announced on February 13 that a New Drug Application (NDA) for ^{223}Ra-dichloride, an investigational oncology compound, had been accepted for filing and granted priority review by the U.S. Food and Drug Administration (FDA). The application is currently under review. "We are pleased the FDA has granted priority review of the ^{223}Ra NDA for the treatment of patients with castration-resistant prostate cancer that has metastasized to the bones," said Pamela A. Cyrus, MD, vice president and head of U.S. Medical Affairs, Bayer HealthCare Pharmaceuticals. "Receiving this designation marks another positive milestone for ^{223}Ra and underscores Bayer's ongoing commitment in oncology." The FDA grants priority review to medicines that provide a treatment where little or no adequate therapy exists. Under the Prescription Drug User Fee Act, the FDA aims to complete its review within 6 mo of the 60-d filing receipt of the NDA submission (8 mo total), rather than the standard 12-mo review cycle.

In September 2009, Bayer signed an agreement with Algeta ASA (Oslo, Norway) for the development and commercialization of ^{223}Ra. Under the terms of the agreement, Bayer will develop, apply for health authority approvals worldwide, and commercialize ^{223}Ra globally. Algeta will copromote ^{223}Ra with Bayer in the United States. ^{223}Ra is currently not approved by the FDA, the European Medicines Agency (EMA), or other health authorities. Bayer submitted a Marketing Authorization Application to the EMA for ^{223}Ra in December 2012. As noted previously in Newsline, the U.S. Nuclear Regulatory Commission in January 2013 issued a licensing decision indicating that U.S. medical sites will be able to procure and administer ^{223}Ra under 10 CFR Part 35, Subpart E, which includes 10 CFR §35.300.

Bayer HealthCare Pharmaceuticals, Inc.

Change to "Direct Supervision" Requirements

A proposed rule released on February 4 by the Centers for Medicare & Medicaid Services (CMS) included reforms to Medicare regulations identified as "unnecessary, obsolete, or excessively burdensome on hospitals and health care providers." Implementation of the reforms is projected to save nearly $676 million annually and $3.4 billion over 5 y, according to a CMS press release. The proposed rule supports President Obama's call on federal agencies to modify and streamline regulations on business. "We are committed to cutting the red tape for health care facilities, including rural providers," said Health and Human Services Secretary Kathleen Sebelius.

"By eliminating outdated or overly burdensome requirements, hospitals and health care professionals can focus on treating patients."

Of direct interest to molecular medicine is the proposal to permit trained nuclear medicine technicians in hospitals to prepare radiopharmaceuticals for procedures without the supervising physician or pharmacist being present, a measure designed to speed services to patients, particularly during off hours or at remote facilities. The proposed change was based on suggestions provided by SNMMI. CMS estimated the first-year and recurring savings or benefits from this change to be ~$39 million.

In the past, in-house preparation of radiopharmaceuticals could be performed only by or under the direct supervision of an appropriately trained registered pharmacist or a doctor of medicine or osteopathy. Direct supervision required that one of these professionals be physically present in the hospital and immediately available during the preparation of all radiopharmaceuticals. Hospitals reported to CMS that this requirement was extremely burdensome when the presence of a pharmacist or physician was required for provision of off-hour nuclear medicine tests that required only minimal in-house preparation of radiopharmaceuticals. The revision from "direct supervision" to ''supervision'' will allow for other appropriately trained hospital staff to prepare in-house radiopharmaceuticals. The proposed changes would allow hospitals to establish their own policies on supervision of nuclear medicine personnel and the in-house preparation of radiopharmaceuticals. CMS added that "Absent a requirement for 'direct' supervision, we would expect most hospitals to follow the Society of Nuclear Medicine and Molecular Imaging recommendations on this issue and to no longer require a registered pharmacist or MD/DO to be on site for direct supervision when radiopharmaceuticals are prepared in-house." The full text of the proposed rules was published on February 7 in the *Federal Register* and is available at www.gpo.gov/fdsys/pkg/FR-2013-02-07/pdf/2013-02421.pdf.

Centers for Medicare & Medicaid Services

Stroke Imaging and Outcomes

The use of advanced imaging shortly after the onset of acute stroke failed to identify a subgroup of patients who could benefit from a clot-removal procedure, according to study results released on February 8 by the National Institute of Neurological Disorder and Stroke (NINDS) and published online on the same day in the *New England Journal of Medicine*. Kidwell et al. reported on "A trial of imaging selection and endovascular treatment for ischemic stroke intervention" as part of the NINDS-funded Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE) trial.

Patients in the trial were enrolled in 22 centers in the United States. The MR RESCUE study looked at whether brain imaging can identify patients most likely to benefit from therapies for acute ischemic stroke and whether endovascular thrombectomy improves clinical outcomes in such patients. The study included 118 patients (mean age, 65.5 y), all of whom underwent pretreatment CT or MR imaging of the brain. Patients were randomly assigned within 8 h (median, 5.5 h) after onset of large-vessel, anterior-circulation stroke to undergo mechanical embolectomy or receive standard care. Randomization was stratified according to whether the patient had a favorable penumbral pattern (substantial salvageable tissue and small infarct core) or a nonpenumbral pattern (large core or small or absent penumbra). Outcomes were assessed at 90 d, at which timepoint mortality was at 21% and symptomatic intracranial hemorrhage was at 4% in both the embolectomy and standard care groups. Mean scores on the modified Rankin scale did not differ between these groups, regardless of penumbral pattern, nor did pretreatment imaging provide benefits in assigning individuals to embolization. The authors summarized their findings by stating that "a favorable penumbral pattern on neuroimaging did not identify patients who would differentially benefit from endovascular therapy for acute ischemic stroke, nor was embolectomy shown to be superior to standard care."

"Despite a lack of evidence showing that these clot-removal devices improve outcomes, they are already widely used in patients who are not able to get to the hospital in time to receive t-PA," said Walter J. Koroshetz, MD, deputy director of NINDS. "Though some patients have had dramatic improvements with clot removal, it has not been shown effective in this or another larger study, the Interventional Management of Stroke, which was halted early because it did not find the procedure to be of significant benefit."

The results of the MR RESCUE study are not consistent with the conclusions of a separate NINDS-funded observational study called DEFUSE-2, which suggested that a slightly different brain imaging strategy could predict patients who benefited from the clot-removal procedure. In addition to other imaging techniques "it's possible that newer intra-arterial devices that were not available when the [MR-RESCUE] study started could improve functional outcomes," said Scott Janis, PhD, program director, NINDS. "But an important message from MR RESCUE is that those newer devices still need to go head to head with standard therapy."

"Advances in neuroimaging are promising and may someday help to identify who will benefit from a device-based approach. But the MR RESCUE results show that more work needs to be done," Koroshetz said.

National Institute of Neurological Disorder and Stroke

ECRI and Hospital Technology Watch List

ECRI, an independent nonprofit that researches patient care improvement strategies, issued a white paper on February 19 addressing 10 technology issues that "health care leaders should have on their radar in 2013 and beyond." Called the "ECRI Institute's Top 10

C-Suite Watch List: Hospital Technology Issues for 2013," the report covers a range of technologies, with electronic health records topping the list of areas for concern. Imaging and image procedure–related concerns account for more than half of the items on the list. These include: (1) imaging and surgery, with a focus on placement of full-scale angiography, CT, MR, and other imaging systems in operating rooms (ORs) as adjuncts to interventional radiology and minimally invasive procedures; (2) minimally invasive cardiac surgery, specifically transcatheter aortic valve implantation, requiring hybrid OR imaging environments; (3) PET MR, with a focus on when a hospital should decide to acquire this technology and considerations in this decision; (4) added supply expenses associated with MR-compatible pacemakers; (5) issues associated with CT radiation dose safety; and (6) questions about lung cancer screening, particularly about the inherent costs of false-positive results. The report is available for free download at: https://www.ecri.org/Forms/Pages/2013-C-Suite-Watch-List.aspx.

ECRI

AAAS Honors Nuclear Medicine Researcher

Nasima Akhter, PhD, was recognized by the American Association for the Advancement of Science (AAAS) for early-career excellence on February 16 at the AAAS Minority and Women Scientists and Engineers Networking Breakfast at the society's 2013 Annual Meeting in Boston, MA. Akhter is a senior medical officer at the Center for Nuclear Medicine and Ultrasound, Dhaka Medical College Hospital, Bangladesh. Her work has spanned a broad range of radionuclide applications, including bone scintigraphy in breast cancer, imaging in Alzheimer disease, and cardiac imaging. She is currently conducting clinical research on nuchal translucency–based fetal screening for congenital anomalies during the first trimester of pregnancy. She is also investigating the usefulness of nonradioactive iodine adjunct medication with radioiodine therapy in Graves disease. Her work, recognized with the Society of Nuclear Medicine, Bangladesh, 2011 Young Scientist Award gold medal, was praised by the AAAS for its focus on the specific needs of developing countries.

American Association for the Advancement of Science

Demographic Patterns of PET Use

In a study published online on February 15 in *Radiology*, Dinan et al. from the Duke University School of Medicine (Durham, NC) reported on an exploration of demographic and regional factors associated with changing patterns of use of PET in patients with non–small cell lung cancer (NSCLC). The authors used Surveillance Epidemiology and End Results Medicare data on individuals who received a diagnosis of NSCLC between 1998 and 2007. They looked at changes in the number of PET studies in the period from 2 mo before to 4 mo after diagnosis. The final study group included 46,544 patients with 46,935 cases of NSCLC. By 2005, more than half of these patients had undergone at least 1 PET study, regardless of demographic subgroup. The authors found that patients who underwent PET were more likely to be married, nonblack, younger than 80 y, and to live in census tracts with higher education levels and/or in the northeast United States. Although living in relative proximity (within 40 miles) was a factor associated with higher use in the earliest years of the study, this association was no longer significant in 2007. Over the total study period, imaging rates increased more rapidly in patients who were nonblack, younger than 81 y, and/or who lived in the northeast or southern United States.

Radiology

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

Selumetinib and ^{131}I Uptake

In an article in the February 14 issue of the *New England Journal of Medicine* (2013;368:623–632), Ho et al. from the Memorial Sloan–Kettering Cancer Center and Weill Cornell Medical College (New York, NY) reported on a study designed to determine whether the MAPK kinase (MEK) 1 and MEK2 inhibitor selumetinib could reverse radioiodine refractory status in patients with metastatic thyroid cancer. The study included 20 evaluable patients (11 men, 9 women; median age, 61 y, range, 44–77 y). Tumors in 9 patients showed BRAF mutations and in 5 patients showed NRAS mutations. All patients underwent thyrotropin-α stimulation as well as ^{124}I PET dosimetry, performed before and 4 wk after treatment with selumetinib (75 mg BID). When the second dosimetric results indicated that a dose ≥2,000 cGy ^{131}I could be administered to a metastatic lesion, the dose was administered along with selumetinib.