New MTC Treatment Approved

The U.S. Food and Drug Administration (FDA) announced on April 6 the approval of vandetanib to treat adult patients with late-stage (metastatic) medullary thyroid cancer (MTC) who are ineligible for surgery and who have disease that is growing or causing symptoms. This is the first FDA-approved agent for treatment of MTC. Vandetanib is marketed by AstraZeneca Pharmaceuticals LP (Wilmington, DE).

About 44,600 new thyroid cancer cases were diagnosed in the United States during 2010, and about 1,690 people died from the disease, according to the National Cancer Institute. MTC is estimated to represent 3%–5% of all thyroid cancers. "Vandetanib's approval underscores FDA's commitment to approving treatments for patients with rare and difficult-to-treat diseases," said Richard Pazdur, MD, director of the Office of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research.

Vandetanib's safety and effectiveness were established in a single international study of 331 patients with late-stage MTC who were randomized to treatment or placebo. Patients who received vandetanib had a longer period of time without disease progression than patients receiving the placebo. Median progression-free survival was 16.4 mo in the placebo arm and at least 22.6 mo in the vandetanib arm.

Vandetanib has been associated with cardiac arrhythmia and is being approved with a Risk Evaluation and Mitigation Strategy (REMS) to inform health care professionals about serious heart-related risks. Only health care professionals and pharmacies certified through the vandetanib REMS program, a restricted distribution program, will be able to prescribe and dispense the drug. Patients will also receive an FDA-approved medication guide informing them of the potential risks.

An article by Walter et al. from University Hospital (Bern, Switzerland) in the February issue of *The Journal of Nuclear Medicine* (2011;52: 231–240) described the use of small animal PET to evaluate tumor metabolism during vandetanib treatment, effectively monitoring response to the drug as early as 3 d after initiation of therapy. The technique has promise in the clinical setting for identifying responders early in the course of therapy.

U.S. Food and Drug Administration
The Journal of Nuclear Medicine

Thyroid Shielding and Mammography

On April 4, in response to public inquiries and expressions of concern, the American College of Radiology (ACR) and the Society of Breast Imaging (SBI) released a statement on radiation received to the thyroid from mammography. In a widely viewed broadcast, television medical personality and cardiothoracic surgeon Mehmet Oz, MD, had recommended that women ask for lead thyroid shielding during mammography to minimize the risk of thyroid cancer. Numerous media outlets picked up the story, and physicians and staff at mammography centers encountered large numbers of patients seeking advice and, in some cases, patients who demanded shielding or refused unshielded imaging.

The ACR/SBI release clarified the risk, noting that concern about mammography significantly increasing the likelihood of developing thyroid cancer "simply is *not* supported in scientific literature." The report detailed the extent of exposure: "The thyroid is not exposed to the direct X-ray beam used to image the breast and receives only a tiny amount of scattered X-rays (less than 0.005 milligray)." This is equivalent to only 30 min of the routine natural background radiation received by anyone in the United States from natural sources. For annual screening mammography from ages 40 to 80 y, the cancer risk from this amount of radiation scattered to the thyroid is <1 in 17.1 million women screened. Moreover, thyroid shielding can interfere with optimal positioning and result in artifacts, leading to unnecessary reimaging. The statement concluded: "Therefore, use of a thyroid shield during mammography is *not* recommended. Patients are urged not to put off or forego necessary breast imaging care based on this erroneous media report."

In an April 25 article by Jane Brody in *The New York Times*, readers were urged to look at the facts indicating that mammography is unlikely to contribute to increased risks of thyroid cancer and to avoid "irrational fears" when making important decisions about personal health.

American College of Radiology
The New York Times

HHS Looks at ED Imaging Payments

An April 18 report from the Office of the Inspector General of the U.S. Department of Health and Human Services indicated that in 2008 Medicare erroneously allowed 19% ($29 million) of claims for interpretation and reports for CT and MR imaging and 14% ($9 million) of claims for interpretation and reports for radiography in hospital outpatient emergency departments because of insufficient documentation. The Social Security Act and the Centers for Medicare & Medicaid Services (CMS) regulations govern Medicare payments for all radiology services and require that services be ordered by physicians, have documentation to support the claims, and be medically necessary. As a condition of fee schedule payment, services are required to contribute directly to the diagnosis or treatment of an individual beneficiary.

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Of the allowed Medicare claims for CT and MR imaging in hospital outpatient emergency departments in 2008: 12% ($18 million) did not have physicians' orders as part of the medical record documentation, 12% ($19 million) did not have documentation to support that interpretation and reports had been performed, and 5% ($7.3 million) had overlapping errors. Of the allowed Medicare claims for x-rays in hospital outpatient emergency departments in 2008: 8.6% ($5.5 million) did not have physicians' orders as part of the medical record documentation, 8.2% ($5.4 million) did not have documentation to support the fact that interpretation and reports had been performed, and 3% ($1.9 million) had overlapping errors. Although not erroneously allowed, 12% ($19 million) of CT and MR imaging claims and 16% ($10 million) of x-ray claims were for interpretation and reports performed after beneficiaries left emergency departments. Although CMS does not offer consistent payment guidance on timing for interpretation, in written comments on the report, the agency indicated that "a uniform policy requiring that the interpretation and report be contemporaneous with, or, if not contemporaneous, demonstrably contribute to the beneficiary's diagnosis and treatment, could reduce unexplained complexity in what is already a complicated billing system for medical diagnostics." The full report is available at: http://oig.hhs.gov/oei/reports/oei-07-09-00450.pdf.

U.S. Department of Health and Human Services

FDA Strategic Priorities

The U.S. Food and Drug Administration (FDA) released on April 20 the final version of a strategic priorities document outlining goals that will guide the agency and its 12,000 employees through 2015. Titled *Strategic Priorities 2011–2015: Responding to the Public Health Challenges of the 21st Century*, the 50-page document provides a vision of the FDA that includes: a modernized field of regulatory science that draws on innovations in science and technology to help ensure the safety and effectiveness of medical products throughout their life cycles, an integrated global food safety system focused on prevention and improved nutrition, and expanded efforts to meet the needs of special populations.

"Today, it is clear that the FDA's job is fundamentally different—and far more complex—than it was even a few years ago," said FDA Commissioner Margaret A. Hamburg, MD. "We will address these challenges and aim to fulfill our mission by embracing innovation and actively pursuing partnerships with federal, state, and local agencies, international authorities, academia, nongovernment organizations, and the private sector."

The 5 cross-cutting priorities discussed in detail in the document include goals to: advance regulatory science and innovation, strengthen the safety and integrity of the global supply chain, strengthen compliance and enforcement activities to support public health, expand efforts to meet the needs of special populations, and advance medical countermeasures and emergency preparedness.

The FDA commissioner added that she would continue to act as an advocate for advancing the field of regulatory science and innovation. "Science underlies everything we do," Hamburg said. "To serve the public health, we must have the capacity to effectively oversee the translation of breakthrough discoveries in science into innovative, safe, and effective products and lifesaving therapies."

The full report is available at: www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm227527.htm.

U.S. Food and Drug Administration

IAEA Nuclear Safety Meeting

The 5th Review Meeting of the Contracting Parties to the International Atomic Energy Agency (IAEA) Convention on Nuclear Safety (CNS) met in Vienna, Austria, from April 4–14, a period that coincided with worldwide attention to the nuclear emergency at the Fukushima Daiichi Power plant in Japan. The convention, which entered into force in 1996, was designed to enhance nuclear safety. Its objectives are to achieve and maintain a high level of nuclear safety worldwide, to establish and maintain effective defenses in nuclear installations against potential radiologic hazards, and to prevent accidents having radiologic consequences.

During the 10 d of meetings, delegations from 61 of the 72 countries that are contracting parties to the convention discussed long-term safety issues, as well as the unfolding events in Japan. In addition to initiating worldwide reexaminations of nuclear power plant safety measures, the participants welcomed IAEA Director General Yukiya Amano's initiative to convene a Ministerial Conference on Nuclear Safety from June 20 to 24. The conference "will provide an opportunity to make an initial assessment of the Fukushima accident, consider lessons that need to be learned, help launch a process to strengthen global nuclear safety, and consider ways to further strengthen the response to nuclear accidents and emergencies." Although the CNS usually meets only every 3 y, it was agreed that the participants would convene an extraordinary meeting in 2012 to analyze the Fukushima accident. The assembled participants issued a statement expressing condolences to the Japanese people and a commitment to consider and act upon the lessons learned.

The meeting's conclusions also included detailed technical discussions about enhancing safety cultures, overcoming challenges in recruiting a new generation of nuclear professionals, managing aging nuclear facilities and safely extending their lifetimes, nuclear power plant designs, siting of new plants, periodic safety reviews, international cooperation, and networking on emergency management and operating experience. In addition, conference attendees discussed country reports

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on nuclear safety that all countries with operating nuclear power plants are required to submit.

For the 2012 special meeting, participant countries are being urged to address 9 topics in their reports: nuclear power plant design against external events, offsite response to emergency situations (e.g., station blackout), emergency management and preparedness following worst case accident scenarios, safety consideration for operation of multiunits at the same nuclear power plant site, cooling of spent fuel storage in severe accident scenarios, training of nuclear power plant operators for severe accident scenarios, radiological monitoring following nuclear power plant accident involving radiological release, public protection emergency actions, and communications in emergency situations.

International Atomic Energy Agency

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. We have added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of diagnostic and therapeutic progress in this area. 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.

MOLECULAR IMAGING/ THERAPY

Multimodality Monitoring of Breast Ca Therapy

In an article e-published on April 1 ahead of print in *Breast Cancer Research and Treatment*, Jacobs et al. from the Johns Hopkins University School of Medicine (Baltimore, MD) reported on a study determining the utility of advanced MR and PET/CT imaging in identifying radiologic biomarkers for treatment response in patients receiving preoperative systemic therapy (PST) for locally advanced breast cancer. The study included 6 women who were enrolled both in a study correlating PET/CT imaging and response to chemotherapy and in a study of advanced MR imaging parameters and response to chemotherapy. Each received 4 cycles of docetaxel at 14 d intervals, with or without 4 additional cycles of doxorubicin and cyclophosphamide. Patients underwent diagnostic breast MR, ^{23}Na MR, and ^{18}F-FDG PET/CT evaluation of breast lesions before and within 7 d after administration of the first cycle. Core biopsy samples were taken at baseline and after the first drug cycle for correlation of histopathologic and radiologic markers. Five patients experienced a pathologic partial response, and 1 experienced a pathologic nonresponse. Total tissue sodium concentration decreased by 21% in responders but increased in the nonresponder. Responders also saw a greater reduction (38%) in standardized uptake values on PET than did the nonresponder. MR imaging volumes decreased after the first drug cycle by 42% in responders and 35% in the nonresponder. The proliferation index declined in responders but increased in the nonresponder. The authors concluded that these results "demonstrate the feasibility of using multimodality proton, ^{23}Na MRI, and PET/CT metrics as radiological biomarkers for monitoring response to PST in patients with operable breast cancer."

Breast Cancer Research and Treatment

Multimodal Prostate SLN Guidance

van der Poel et al. from The Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital (Amsterdam) reported on March 30 ahead of print in *European Urology* on a pilot study designed to demonstrate combined preoperative, intraoperative, and postoperative sentinel lymph node (SLN) imaging in laparoscopic lymph node dissection using a multimodal tracer. The study included 11 men scheduled for robot-assisted laparoscopic prostatectomy with an increased risk of nodal metastasis. Before surgery, each participant underwent injection with a radioactive and fluorescent tracer, indocyanine green (ICG)–^{99m}Tc-NanoColl, into the prostate. This was followed by lymphoscintigraphy and SPECT/CT imaging of pelvic nodes to preoperatively identify the location of sentinel lymph nodes. A fluorescence laparoscope, optimized for detection in the near infrared range, was used during surgery to visualize nodes identified on SPECT/CT. The authors found that SPECT/CT successfully identified SLNs and that fluorescence imaging enhanced intraoperative identification of these nodes, especially in areas with high radioactive background noise (such as the injection site). Histopathologic analysis showed a strong correlation between radioactive and fluorescent tracer content in excised lymph nodes. The authors cautioned that fluorescent tracers cannot take the place of radiotracers

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