Neuraceq Approved in U.S. and Europe

Piramal Imaging (Berlin, Germany; Boston, MA) announced on March 20 that the U.S. Food and Drug Administration (FDA) had approved Neuraceq (^{18}F-florbetaben injection) for PET amyloid-β imaging. In February, the company received marketing authorization from the European Commission. Neuraceq is indicated for use with PET in estimation of amyloid-β neuritic plaque density in adults with cognitive impairment who are being evaluated for Alzheimer disease (AD) and other neurodegenerative decline.

The Centers for Medicare & Medicaid Services has indicated that it will cover an amyloid-β PET scan for patients under Coverage with Evidence Development programs. The objective of these programs is to assess the effect of amyloid-β scans on improving patient outcomes or advancing treatment options.

The FDA approval of Neuraceq was based on safety data from 872 patients who participated in global clinical trials, in addition to data from 3 studies that examined images from adults with a range of cognitive function, including 205 end-of-life patients who agreed to participate in a postmortem brain donation program. Images were analyzed from 82 subjects with postmortem confirmation of the presence or absence of amyloid-β neuritic plaques. Correlation of visual PET interpretation with histopathology in these 82 brains showed that ^{18}F-florbetaben accurately detected moderate to frequent amyloid-β neuritic plaques in the brain and can be useful in estimating the density of these plaques in vivo. Posted limitations and data for Neuraceq note that safety and effectiveness in PET have not been established for predicting development of dementia or other neurologic conditions or for monitoring response to therapies. Adverse reactions to date have been mild and limited to injection site reactions.

Piramal Imaging has partnered with IBA Molecular (Dulles, VA) for manufacturing and distribution of Neuraceq. IBA Molecular owns and operates a network of 49 PET isotope facilities worldwide.

Piramal Imaging

Metabolic Targeting in ALL

In an article in the March 10 issue of the *Journal of Experimental Medicine* (2014;211:473–486), Nathanson et al. from the University of California, Los Angeles (UCLA) reported on findings that advance understanding of nucleotide metabolism in leukemic cells and identify deoxycytidine triphosphate (dCTP) as a potential therapeutic target for metabolic interventions in acute lymphoblastic leukemia (ALL) and other hematologic malignancies. The study, which included UCLA molecular scientists and nuclear medicine specialists among its authors, was titled "Co-targeting of convergent nucleotide biosynthetic pathways for leukemia eradication" and was covered widely in the popular media. The study included both in vitro and in vivo mouse studies involving identification and blocking of biosynthetic pathway redundancy in ALL. dCTP can be produced by both the de novo pathway (DNP) and the nucleoside salvage pathway (NSP). The authors showed that ALL cells avoid lethal replication stress after thymidine (dT)-induced inhibition of DNP dCTP synthesis by switching to NSP-mediated dCTP production. They were able to prevent this pathway switch by using a new high-affinity small-molecule inhibitor (DI-39) of the NSP rate-limiting enzyme dC kinase (dCK). In animal studies, PET successfully monitored both the duration and degree of dCK inhibition by DI-39 treatment, serving as a validated pharmacodynamic biomarker. Not only was pharmacologic cotargeting of the DNP with dT and the NSP with DI-39 effective against ALL in mice, no accompanying toxicities were noted. Because all cancer cells utilize the DNP and NSP, the treatment strategy holds promise for a range of other hematologic malignancies.

In a press release issued by UCLA, the integrative nature of the project within the university was noted. "Usually people say that drug discovery and development cannot happen strictly in the academic environment—that discovery should be done in academia and development done elsewhere, such as in industry," said Caius Radu, MD, senior author on the report. "With this study, we show that everything can be done in the academic environment. We started this project from scratch and, with the help of UCLA scientists from many different disciplines, we have taken the drug through all the steps, and now it's nearly ready for clinical trials." The research was supported by the UCLA Scholars in Oncologic Molecular Imaging program, the Jonsson Comprehensive Cancer Center at UCLA, and the National Cancer Institute of the National Institutes of Health.

University of California, Los Angeles

ASCO Breast SLN Biopsy Guideline Updates

The American Society of Clinical Oncology (ASCO) on March 24 issued new recommendations for the use of sentinel lymph node (SLN) biopsy in patients with early-stage breast cancer. "Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology Clinical Practice Guideline update," was published online on March 24 ahead of print in the *Journal of Clinical Oncology.*

ASCO issued an original guideline on this topic in 2005. To update the guideline, the society convened experts in medical oncology, pathology,

radiation oncology, surgical oncology, guideline implementation, and advocacy. The committee conducted a systematic review of the literature published from 2004 to 2013 and based recommendations on review of the evidence. "The updated guideline incorporates new evidence from more recent studies—9 randomized controlled trials and 13 cohort studies since 2005," said Armando Giuliano, MD, cochair of the ASCO expert panel that updated the guideline. "Based on these studies, we're saying more patients can safely get sentinel node biopsy without axillary lymph node dissection. These guidelines help determine for whom sentinel node biopsy is appropriate." The guideline updates 3 specific recommendations based on evidence from randomized controlled trials:

- Women without SLN metastases should not receive axillary lymph node dissection (ALND);
- Most women with 1 or 2 metastatic SLNs planning to receive breast-conserving surgery with whole breast radiotherapy should not undergo ALND; and
- Women with SLN metastases who will receive mastectomy may be offered ALND.

The guideline updates 2 groups of recommendations based on cohort studies and/or informal consensus:

- Women with operable breast cancer and multicentric tumors, and/or ductal carcinoma in situ (DCIS), who will have mastectomy and/or had prior breast and/or axillary surgery and/or had preoperative/neoadjuvant systemic therapy may be offered SLN biopsy; and
- Women who have large or locally advanced invasive breast cancers (T3/T4) and/or inflammatory breast cancer and/or DCIS, when breast-conserving surgery is planned, and/or are pregnant, should not receive SLN biopsy.

The ASCO committee noted that, in some cases, evidence was insufficient to update previous recommendations. "We strongly encourage patients to talk with their surgeon and other members of their multidisciplinary team to understand their options and make sure everybody's on the same page," said Gary Lyman, MD, MPH, cochair of the expert panel. "The most critical determinant of breast cancer prognosis is still the presence and extent of lymph node involvement and, therefore, the lymph nodes need to be evaluated so we can understand the extent of the disease." More information on the new guideline and clinical tools and resources can be found at www.asco.org/guidelines/breastsnb.

American Society of Clinical Oncology

Representation of Women in Medical Journals

In an article published online on February 24 in the *Journal of the American Medical Association Internal Medicine* (*JAMA Inter Med*), Erren et al. from the University Hospital of Cologne (Germany) and the University of Basel (Switzerland) reported on a study assessing the "Representation of women as authors, reviewers, editors in chief, and editorial board members at 6 general medical journals in 2010 and 2011." The researchers looked at 2 y of publication for 6 prominent journals: *Annals of Internal Medicine (Ann Intern Med), British Medical Journal* (*BMJ*), *JAMA, JAMA Intern Med, The Lancet, and The New England Journal of Medicine (NEJM).* They found that the percentage of women who were first authors of original research articles ranged from 23.7% (*NEJM*) to 46.7% (*BMJ*). For senior (last) authorship, these figures ranged from 18.3% (*Lancet*) to 28.8% (*BMJ*). Women were first authors in from 18.0% (*NEJM*) to 27.4% (*BMJ*) of editorials and were senior (last) authors in from 19.6% (*NEJM*) to 32.3% (*Ann Intern Med*) of editorials. Women made up only 16.6% (*NEJM*) to 28.8% (*BMJ*) of reviewers, and the percentage of women on editorial boards ranged from 22.2% (*NEJM*) to 41.7% (*JAMA Intern Med*). In an accompanying editorial, titled "Shattering the glass ceiling," Marcia Angell, MD, the first woman to serve as editor of *NEJM*, noted that women's representation in scientific publication seems to have lagged behind the equities implied by the growing numbers of women in academic medical settings. She pointed to seniority as one explanatory factory: in 2004, only 19% of associate and full professors on clinical faculties in U.S. medical schools were women, whereas women made up 38% of assistant professors. "The problem," Angell wrote, "is not so much at the journals as it is at the medical schools." Angell suggested that women may be less flexible than men in their early careers (unable to devote as large a percentage of time to dedicated research projects and publication) and that some women may focus on and excel at teaching and mentoring rather than research. She suggested that the "reward system" in academic medicine be changed: "Research productivity should no longer be considered the primary measure of academic success. If teaching and mentoring are rewarded commensurately with research, women will do very well. In fact, men might well have to work harder than they are now to catch up with women in these areas. In any case, I have no doubt that physicians would be better educated and that the medical literature would be less voluminous but of higher quality."

Journal of the American Medical Association Internal Medicine

Minority Clinical Trial Participation

Two articles appearing in an April 1 special supplement to *Cancer* outlined the current state and challenges to improvement in inclusion of minorities in clinical oncologic research. The first study, by Chen et al.

from the University of California, Davis (UC Davis) (*Cancer.* 2014;120 [suppl 7]:1091–1096), looked at the frequency with which minorities were the primary focus of National Cancer Institute (NCI)–sponsored clinical trials, documented citations from the PubMed database focusing on the search terms "NIH Revitalization Act of 1993" and "enhancing minority accrual to cancer clinical trials," and supplemented the review with expert commentary on National Institutes of Health (NIH)–funded research related to minority accrual in cancer clinical trials. They found that reporting and analysis of data on minorities in clinical trials remains "inadequate": <2% of NCI clinical trials focus specifically on racial or minority populations. In a literature review, 1.5%–58% of authors included race/ethnicity in describing their study populations, and only 20% of randomized controlled studies in high-impact oncology journals included results analyses with race/ethnicity data. "The proportion of minorities in clinical research remains very low and is not representative of the U.S. population with cancer," said Moon Chen, PhD, MPH, associate director, Population Research and Cancer Disparities, UC Davis Comprehensive Cancer Center. "What is needed is deliberate effort. Minorities are not hard to reach. They are hardly reached." The authors concluded that: "The solution is not changing the attitudes of minorities but rather in ensuring access to health research," including design of clinical trials to include and focus on specific populations and efforts by scientific journals to insist on appropriate representation and analyses of NIH-funded research by race and ethnicity.

In a second study (*Cancer.* 2014;120 [suppl 7]:1113–1121), Hawk, from The University of Texas MD Anderson Cancer Center (Houston), and researchers from 4 other NCI-designated cancer centers compared data reported to the NCI for their most recent Cancer Center Support Grant competitive renewal to assess catchment area designations, data definitions and elements, collection processes, reporting, and performance regarding proportional representation of race/ethnicity. They found that not only were data and data collection widely heterogeneous across the cancer centers, but racial and ethnic categories were defined differently, making informative comparisons challenging. Accrual of minorities was rated as "less than desired" for at least 1 racial/ethnic subcategory at 4 of the 5 participating cancer centers. The investigators recommended efforts toward harmonization of data definition, collection, and reporting as an essential first step toward expanding minority participation in clinical trials. They also advised collection of more socioeconomic data by cancer centers, including income and education levels, and collection of patient zip codes and insurance status so that researchers can explore differences in access to clinical trials that may be related to geography or availability of health insurance coverage.

Cancer
University of California, Davis

New TRIUMF Director Named

TRIUMF, Canada's national laboratory for particle and nuclear physics, announced on March 18 the appointment of Jonathan Bagger, PhD, as its next director. Bagger is Krieger–Eisenhower Professor, vice provost, and former interim provost at Johns Hopkins University (Baltimore, MD). TRIUMF focuses on the structure and origins of matter and the advancement of isotopes for science and medicine. Located on the Vancouver campus of the University of British Columbia, TRIUMF is owned and operated by a consortium of 18 Canadian universities and supported by the Canadian and provincial governments.

Bagger received his PhD from Princeton University (NJ) in 1983 and then was a postdoctoral researcher at the Stanford Linear Accelerator Center (Menlo Park, CA). From 1986 to 1989, he was an associate professor at Harvard University (Cambridge, MA), before assuming a professorship at Hopkins. Bagger has twice been a member of the Institute for Advanced Study in Princeton. He held a Sloan Foundation Fellowship and a National Science Foundation Presidential Young Investigator award. Bagger is a general councilor and fellow of the American Physics Society and a member of the Fermilab Board of Overseers. He is also on the editorial boards of the Johns Hopkins University Press, as well as *Physics Reports*, the *Physical Review,* and the *Journal of High Energy Physics*. His research interests center on high-energy physics at the interface of theory and experiment, including research on supersymmetry and supergravity.

In a press release accompanying the announcement of his appointment, Bagger expressed enthusiasm for his transition to TRIUMF, planned for this summer: "TRIUMF is known internationally for its impressive capabilities in science and engineering, ranging from rare-isotope studies on its Vancouver campus to its essential contributions to the Higgs boson discovery at CERN. All rest on the legendary dedication and commitment of TRIUMF's researchers and staff. I look forward to working with this terrific team to advance innovation and discovery in Vancouver, in Canada, and on the international stage."

TRIUMF