U.S., UK to Collaborate on Health IT

U.S. Department of Health and Human Services (HHS) Secretary Kathleen Sebelius and UK Secretary of State for Health Jeremy Hunt on January 23 signed a bilateral agreement for the use and sharing of health information technology (IT) data and tools. The agreement strengthens efforts to cultivate and increase the use of health IT tools and information designed to help improve the quality and efficiency of health care delivery in both countries. The 2 secretaries signed the agreement at the annual meeting of the HHS Office of the National Coordinator for Health Information Technology. "While we have very different health care delivery systems and payment models, we both face similar challenges posed by aging populations, increased levels of comorbid chronic disease, and escalating complexity of care delivery and costs," Sebelius said. "By working together, we can more effectively take on these challenges, improve the health IT economy and the health of the American and British populations." The agreement signals a formal commitment by both countries to collaborate to advance the applications of data and technology to improve health.

Originally identified at the June 5, 2013, bilateral summit meeting between the United States and United Kingdom, the collaboration focuses on 4 key areas for health IT and innovation: (1) sharing quality indicators; (2) liberating data and putting it to work; (3) adopting digital health record systems; and (4) priming the health IT market by addressing barriers to innovation. Collaborative work outputs, such as best practices for design and use of clinical quality measures, information on new datasets and expanded data catalogs, and progress made in supporting the health IT ecosystem, will be showcased at the Health Innovation Expo conference in Manchester, UK, later this month and at the Health Datapalooza to be held in June in Washington, DC.

"This is a groundbreaking agreement that will help both of our countries use information and technology more effectively to improve care, safety, and give people more control over their health, which is now even more important as we transcend care boundaries," said Secretary Hunt. "By bringing knowledge together this will not only offer insight into tackling common problems across health IT, but through innovation it will help small to medium enterprises play an effective role in our health care market. I would like to thank all involved in making this agreement happen and look forward to collaborating across our health IT economies."

The full text of the memorandum of understanding can be found at www.healthit.gov/policy-researchers-implementers/health-information-technology-use-united-states-and-united-kingdom.

U.S. Department of Health and Human Services

Trial Vaccine Targets Tau Protein

AC Immune SA (based in Lausanne, Switzerland) announced on January 9 that it had started "the world's first trial" of a vaccine against the phosphorylated tau target in Alzheimer disease (AD). In a press release that also highlighted the success of the company's most recent financing efforts, Andrea Pfeifer, AC Immune CEO said, "The recent G8 Summit on Dementia in London highlighted the commitment by policy makers and experts of significant new financial and health care resources in quest of a cure for these terrible diseases. AC Immune is proud to be part of this global effort." The company will test its ACI-35 product, an active vaccine intended to stimulate the patient's immune system to produce conformation-specific antibodies against phosphorylated tau protein. Tau protein fibrillary tangles, along with amyloid-β plaques, are considered hallmarks of AD.

During preclinical development, ACI-35 showed reduction of phosphorylated tau aggregates and total pathologic tau deposition, as well as improvement in symptomatic parameters. In a study published on August 19, 2013, in the online journal *PLoS One* (2013;8:e72301) Theunis et al. from KU Leuven (Belgium) and AC Immune, reported on testing of the liposome-based vaccine, with results showing specific, safe, and long-lasting immune responses in mouse models of rapid tauopathy generation. AC Immune has also developed an anti–amyloid-β drug, ACI-24, for which phase II trial results are expected later this year.

Numerous large and small pharmaceutical companies are currently developing active treatments and prophylactic approaches, including vaccines, for AD. Severe challenges have been met in translating these drugs to the clinic. Reuters reported in January that over the past 15 years more than 100 experimental drugs for AD have failed at some point in the developmental pipeline and cited industry analysts' estimates that a truly effective drug could have a market worth of $10 billion in annual sales. The difficulties involved in creating such a vaccine have been outlined in 2 worthwhile reviews: one by Lemere et al. in *Molecular Degeneration* (2013;8:36) and one by Panza et al. in *Immunotherapy* (2012;4:213–238).

Of note, Axon Neuroscience SE (Bratislava, Slovak Republic) has registered 2 tau-targeted vaccine trials on the ClinicalTrials.gov website within the last 6 months. A phase I trial (NCT01850238) of a tau peptide-KLH-conjugate active vaccine to treat AD was opened in 2013 and is actively recruiting patients. A second (NCT02031198), posted to the Clinical Trials.gov site in January, will be an 18-month follow-up of patients in the phase I trial.

AC Immune SA
ClinicalTrials.Gov

GalioMedix and Orphan Drug Status

RadioMedix, Inc., a clinical-phase biotechnology company based in Houston, TX, commented on January 5 on an earlier U.S. Food and Drug Administration (FDA) announcement of Orphan Drug status for ^{68}Ga-DOTATATE as a diagnostic agent for management of patients with neuroendocrine tumors (NETs) (see Newsline, *J Nucl Med.* 2014;55:10N). The company's ^{68}Ga-DOTATATE product, GalioMedix, is covered under the designation. "This approval will significantly expedite and facilitate the commercialization process and access of the NET patients to the ^{68}Ga PET/CT technology," said Ebrahim Delpassand, MD, chair and CEO of RadioMedix. "Preliminary results on GalioMedix are highly promising and have shown superior sensitivity and image resolution compared to other currently available modalities. Also, the test is completed in 2 hours and provides quantification capability that is not available by Octreoscan, which is the currently approved agent." Orphan drug status is granted to drugs for effective treatment, diagnosis, or prevention of rare diseases/disorders that affect fewer than 200,000 people in the United States. "This is a significant achievement of our clinical and scientific teams at RadioMedix and our sister institution, Excel Diagnostics and Nuclear Oncology Center. The Orphan Drug designation awarded for ^{68}Ga-DOTATATE (GalioMedix) radiotracer will significantly help in expedited and less expensive regulatory pathway for the final approval of the drug by FDA," said Delpassand. "The successful collaboration between the Excel Diagnostics and Nuclear Oncology Center and RadioMedix will have a positive impact on expansion of ^{68}Ga radiotracers beyond management of NETs."

RadioMedix, Inc.

Online FDA Committee Nomination Portal

The U.S. Food and Drug Administration (FDA) launched on January 22 an advisory committee membership nomination portal that allows interested individuals to submit nominations for membership to any of the agency's 33 advisory committees. The portal will enable nominees to submit applications for membership on an advisory committee from the FDA's website, creating a paperless, streamlined process that will enable the agency to accept, evaluate, and nominate qualified individuals for membership in a timely fashion. Advisory committees provide the FDA with independent, expert advice on a range of complex scientific, technical, and policy issues.

"The portal allows applicants to complete their entire application online," said Jill Hartzler Warner, JD, acting associate commissioner of the FDA Office of Special Medical Programs. "Applicants will experience an interactive, step-by-step process that eliminates confusion and accelerates the timeframe for submitting and processing an application." The system will securely store all applicant information and enable the FDA to develop metrics for assessing the entire applicant pool to identify qualified candidates to fill specific vacancies on advisory committees. Nominations for scientific members and consumer and industry representatives may be submitted by professional societies, industry and consumer groups, and other interested persons and organizations. Potential candidates are asked to provide detailed information about financial holdings, employment, and research grants and/or contracts to permit evaluation of possible sources of conflict of interest. In conjunction with the launch of the nomination portal, the FDA is also posting a set of presentation slides on conflicts of interest for potential members.

The new portal can be accessed at: www.accessdata.fda.gov/scripts/FACTRSPortal/FACTRS/index.cfml.

U.S. Food and Drug Administration

Genetic Changes and Rhabdomyosarcoma

The National Cancer Institute (NCI) announced on January 23 that in mapping the genetic changes associated with rhabdomyosarcoma, scientists had identified 2 distinct genotypes characterizing the disease. Results of the study, led by Javed Khan, MD, head of the Oncogenomics Section, Pediatric Oncology, NCI Center for Cancer Research, and lead author Jack Shern, MD, an NCI clinical fellow, was published on January 16 ahead of print in *Cancer Discovery.* The research collaboration included scientists from the Children's Oncology Group and the Broad Institute of the Massachusetts Institute of Technology and Harvard University (Cambridge, MA).

Khan's team used a number of advanced sequencing techniques to investigate the genetic changes in a total of 147 rhabdomyosarcoma tumors that were paired with normal tissue samples. These sequencing tools allowed them to unravel the complex molecular events that occur in tumor cells, compare normal DNA with tumor DNA, identify mutations in genes, and determine exactly which genes are activated or deactivated in disease progression. The researchers identified 2 distinct genotypes of tumors: one characterized by either a PAX3 or PAX7 fusion gene and a second lacking a PAX fusion gene but with mutations in key signaling pathways. The researchers also found that, as in other types of pediatric cancers, the overall number of alterations in tumor DNA that develop over a child's lifespan (somatic mutations) are relatively low compared with DNA alterations with which a child is born. The somatic mutation rate was especially low in tumors with a PAX fusion gene. The researchers identified relatively frequent somatic mutations in several genes, including NRAS, KRAS, HRAS, FGFR4, PIK3CA, CTNNB, all of which had previously been found to be mutated in rhabdomyosarcoma, as well as the genes FBXW7 and BCOR, which had not been previously associated with this disease. They also identified mutations in additional genes in the RAS/PIK3CA signaling pathway. Overall, altera-

tions in this pathway were found in 93% of rhabdomyosarcoma tumors. Many of the genes mutated in the tumors without a PAX fusion gene were found to be activated or deactivated by proteins produced by PAX fusion genes.

"Although more work is needed, our study may provide researchers with the rationale to develop genomics-guided therapeutic interventions with greater efficacy and fewer side effects than the treatment options currently available for pediatric patients with rhabdomyosarcoma," Shern said. Building on this research, Khan and his team will design and test interventions that target the genetic drivers identified in this genomic analysis of rhabdomyosarcoma.

National Cancer Institute

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.

Single-Dose ^{131}I in Advanced Papillary Thyroid Cancer

In an article e-published on January 3 ahead of print in *Annals of Surgical Oncology*, Hughes et al. from the University of Michigan (Ann Arbor) reported on a study designed to evaluate the effectiveness of total thyroidectomy with therapeutic central and lateral neck dissection in patients with regionally advanced papillary thyroid cancer, using posttherapeutic serum thyroglobulin levels as metrics of treatment success. The study included 61 patients previously treated with total thyroidectomy and therapeutic central and lateral neck dissection for papillary thyroid cancer involving the lateral cervical nodes (median number of lymph nodes excised, 27 [range, 5–112]; median number of positive lymph nodes, 9 [range, 1–67]). Extranodal extension was found in 48% of patients. All patients underwent ^{131}I therapy after resection (median total dose, 150 mCi [range, 30–244 mCi]). Recurrent or persistent cervical disease was identified in 8 (13%) and 3 (5%) patients, respectively, with additional ^{131}I treatment in 2 and reoperative neck dissection in 10. Over the median follow-up period of 20 mo (range, 1–109 mo), 3 patients developed new distant metastases and 1 died. Undetectable unstimulated serum thyroglobulin ($<$1.0 ng/mL) without clinically detectable recurrence occurred in 68% of patients with initial treatment. The authors concluded that "biochemical remission can be experienced in most patients presenting with regionally advanced papillary thyroid cancer with total thyroidectomy and compartment-based therapeutic neck dissection followed by a single dose of radioiodine."

Annals of Surgical Oncology

Noncontrast Perfusion SPECT/CT and Pulmonary Embolism

Lu et al. from Memorial Sloan–Kettering (New York, NY) reported on January 2 ahead of print in *Chest* on a study comparing the diagnostic accuracy of noncontrast perfusion SPECT/CT (Q-SPECT/CT) with that of planar ventilation/perfusion (V/Q) imaging in patients at high risk for pulmonary embolism (PE). A total of 106 patients met criteria of cancer diagnoses, mean Wells scores of 4.4, and sufficient follow-ups. All patients underwent both Q-SPECT/CT and conventional planar V/Q scintigraphy. All images were reviewed retrospectively by 4 observers, who used established criteria for the planar scans. For Q-SPECT/CT, all wedge-shaped peripheral perfusion defects occupying $\geq$50% of a segment without corresponding pulmonary parenchymal or pleural disease were considered positive for PE. Final diagnoses were varied and supported by a combination of data from electrocardiography, ultrasound of lower extremity veins, D-dimer levels, CT pulmonary angiography (when available), and $\geq$ 3-mo clinical follow-up. These final diagnoses indicated that 22 patients had PEs and 84 did not. On V/Q imaging, the sensitivity and specificity using PIOPED2 criteria were 50% and 98%, respectively, and using PISA-PED criteria were 86% and 93%, respectively. These respective figures for Q-SPECT/CT were 91% and 94%. Additional relevant findings were made by the CT portion of Q-SPECT/CT in 72 patients. The authors concluded that "noncontrast Q-SPECT/CT has higher accuracy than planar V/Q imaging using PIOPED2 criteria in cancer patients with high risk for PE."

Chest

SPECT vs. PET in Bone Healing and Biomaterial

In an article e-published on January 6 ahead of print in the *Journal of Tissue Engineering and Regenerative Medicine*, Venture et al. from the Radboud University Nijmegen Medical Centre (The Netherlands) reported on a comparison of the ability of ^{99m}Tc-hydroxymethylene diphosphonate (^{99m}Tc-HDP) SPECT/CT and ^{18}F-fluoride to monitor in vivo bone defect healing and radiopaque biomaterial