NEWS IN BRIEF

Andrew S. Kraft, MD, a nationally recognized prostate cancer physician and researcher, begins work this month as the director of the University of Arizona Cancer Center and associate vice president for oncology programs for the University of Arizona Health Sciences Center. He replaces Anne E. Cress, PhD, who has been interim director since July 2013. For the past decade, Kraft led the Hollings Cancer Center at the Medical University of South Carolina in Charleston, which earned distinction as an NCI-designated cancer center in 2009.

Bruce D. Minsky, MD, a professor of radiation oncology and the deputy division head and director of clinical research in the Division of Radiation Oncology at The University of Texas MD Anderson Cancer Center in Houston, will begin a 1-year term as president of the American Society for Radiation Oncology on September 16. A graduate of the University of Massachusetts Medical School in Worcester, Minsky has made significant contributions to the clinical management of esophageal and rectal cancer. Widely published, he serves on the editorial boards of several journals.

Joseph R. Haywood, PhD, a professor of pharmacology and toxicology and assistant vice president for regulatory affairs at Michigan State University in East Lansing, began a 1-year term as president of the Federation of American Societies for Experimental Biology in July. He has served on the Council of the Association for the Assessment and Accreditation of Laboratory Animal Care International and the Board of Governors of the International Council for Laboratory Animal Science.

Beleodaq Approved for Rare Lymphomas

The FDA approved Beleodaq (belinostat; Spectrum Pharmaceuticals) on July 3 for the treatment of patients with relapsed or refractory peripheral T-cell lymphomas (PTCL), a rare and aggressive group of diseases that accounts for 10% to 15% of all non-Hodgkin lymphomas.

PTCL is difficult to treat, and patients often relapse after first-line treatment, usually combination chemotherapy such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone). "Anything we can add to the armamentarium is helpful," says Eric D. Jacobsen, MD, an oncologist at Dana-Farber Cancer Institute in Boston, MA.

Beleodaq inhibits histone deacetylases (HDAC), enzymes involved in the regulation of genes linked to tumorigenesis and cancer progression. It is the third drug to receive FDA approval for PTCL since 2009. Folotyn (pralatrexate; Spectrum Pharmaceuticals) received accelerated approval in 2009 for patients with relapsed or refractory PTCL, and Istodax (romidepsin; Celgene), another HDAC inhibitor, was approved in 2011 for patients who had received at least one prior therapy. Beleodaq received accelerated approval, a designation given to drugs that fill an unmet medical need.

The FDA based its approval on results from a multicenter, phase II trial of 120 evaluable patients with relapsed or refractory PTCL. In the trial, 10.8% of patients experienced a complete response and 15% had a partial response. The most common adverse effects, which occurred in more than a quarter of study participants, included nausea, fatigue, pyrexia, anemia, and vomiting.

Jacobsen, an investigator on an earlier phase II trial of Beleodaq, notes that in the BELIEF trial, which led to the FDA approval, the overall response rates were comparable to those of Folotyn and Istodax. The response rate was even higher—45.5%—in patients with angioimmunoblastic T-cell lymphoma, a common subtype of PTCL. Jacobsen called those results "very encouraging."

As part of the approval process, the drug's sponsor, Spectrum Pharmaceuticals, is required to conduct a phase III trial to compare the efficacy of Beleodaq combined with CHOP versus CHOP alone, to establish whether the drug would be effective in first-line treatment as well. ∎

Analysis Finds Value in Pseudogenes

In a large, systematic analysis of the role of pseudogenes across seven types of cancer, researchers from The University of Texas MD Anderson Cancer Center in Houston have found that pseudogenes alone and in combination with other clinical and molecular markers may help define prognostic subgroups.

The findings point to new avenues of research into the roles pseudogenes may be playing in driving the growth of tumors, says principal investigator Han Liang, PhD, assistant professor of bioinformatics and computational biology (Nat Commun 2014 July 7 [Epub ahead of print]).

Pseudogenes, sometimes labeled as "junk" DNA, exist in the human genome in about the same abundance as protein-coding genes. Accumulated sequence changes prevent pseudogenes from encoding proteins, yet they are still transcribed into RNA sequences and, in turn, may play regulatory roles in cancer.

For instance, recent smaller studies have identified cases of transcribed pseudogenes acting as decoys that attract microRNAs away from tumor suppressor genes, such as *PTEN*, increasing their activity. Pseudogene transcription may also result in gene silencing, says Liang.

"People are beginning to realize that pseudogenes have functional effects," says Zhaolei Zhang, PhD, professor of molecular genetics at the University of Toronto, who did not participate in the study, but who helped characterize the abundance of pseudogenes in 2003.

To assess the role of pseudogenes in cancer more broadly, Liang analyzed data from The Cancer Genome Atlas (TCGA), which provided a snapshot of transcript levels in over 2,600 tumor samples from patients with seven types of cancer—breast, brain,

kidney, lung, colorectal, ovarian, and uterine. Liang's study, which extracted pseudogene expression levels from this data, is part of the TCGA Pan-Cancer Analysis project, an effort to look for patterns across cancer types and genomic dimensions, such as mutations (the genome) and expression levels (the transcriptome).

Liang found that unique sets of pseudogene transcripts were expressed in each form of cancer. In addition, subtypes defined by pseudogene expression levels corresponded closely with subtypes defined by other molecular markers, such as estrogen receptor expression in breast cancer.

In kidney cancer, by joining pseudogene markers with clinical variables, such as disease stage, Liang was able to divide patients into prognostic risk groups. Without pseudogenes, three groups emerge, but adding pseudogenes separates the middle group into two that differ in overall survival. Liang did not investigate the mechanistic roles of pseudogenes, but, he says, "pseudogenes are a novel dimension that we can use to further understand the subtypes."

"The study included almost 10 times more samples than previous work, which really drives home the validity of the conclusions that pseudogenes can be used as cancer markers," says Zhang.

Liang hopes to find another large dataset to validate his findings, and also to expand his current analysis across additional types of cancer. "If these patterns are robust, we can consider using pseudogene expression data to build prognostic models that have clinical value," he says. ■

3D Imaging Finds More Breast Cancers

Adding 3D imaging to traditional digital mammography finds more invasive breast cancers and reduces false positives, a new study finds, although it is not yet known whether the new technology improves breast cancer survival.

Researchers retrospectively reviewed 454,850 mammograms from 13 breast centers. More than a third used 3D imaging, or digital breast tomosynthesis, done at the same time as traditional mammography, whereas the rest used traditional mammography alone.
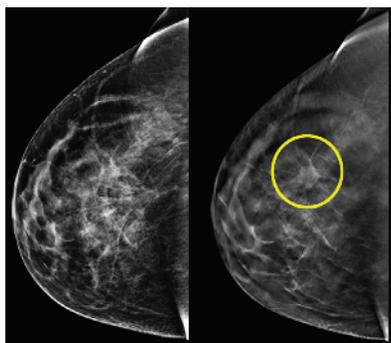
The 3D mammography image on the right reveals a 15 mm mass (circled), which is hidden in the traditional digital image on the left.

The invasive cancer detection rate increased from 2.9 per 1,000 traditional mammograms to 4.1 per 1,000 combined 3D mammograms, researchers reported (JAMA 2014;311:2499–507). False positives were 15% less likely using the 3D approach, and there were 16 fewer callbacks for additional imaging per 1,000 screenings.

"Conventional mammography is far from ideal," says senior author Emily Conant, MD, chief of breast imaging at the University of Pennsylvania's Perelman School of Medicine in Philadelphia. "3D mammography is an improvement because it addresses two of the major limitations of mammographic screening—there are too many false positives and the sensitivity is not what we'd like, so we miss cancers."

The FDA approved the Selenia Dimensions digital breast tomosynthesis system (Hologic; Bedford, MA) in 2011 in combination with traditional mammography for breast cancer screening. Using multiple low-dose X-rays taken at different angles, thin "slices" of breast tissue are reconstructed into a 3D image that gives a clearer view of breast tissue.

In an accompanying editorial, Etta Pisano, MD, and Martin Yaffe, PhD, called for more research, noting that it is still uncertain whether tomosynthesis should replace traditional digital mammography (JAMA 2014;311:2488–9).

Conant notes that because the study was not designed to follow women over time, it is not known whether 3D mammography saves lives. It is also unclear which women benefit the most from 3D scans, she says.

"We need research that looks at patient-level data such as breast density, patient age, and the types of cancer detected with 3D mammography that weren't detected with conventional mammography," Conant says. "We need to better understand what each woman needs." ■

Improved Survival Ends Nivolumab Trial Early

A phase III trial testing Bristol-Myers Squibb's (BMS) immunotherapeutic drug nivolumab to treat advanced melanoma was stopped early after the treatment demonstrated a clear improvement in overall survival (OS) compared with standard chemotherapy.

The control group in the randomized, double-blind study—dubbed CheckMate-066—was invited to switch to nivolumab after an independent data-monitoring committee found evidence of superior OS in patients who took nivolumab, BMS reported. The trial was comparing nivolumab 3 mg/kg every 2 weeks with dacarbazine 1,000 mg/m² every 3 weeks in 418 patients with previously untreated BRAF wild-type unresectable late-stage melanoma. It was conducted primarily in Canada and Europe, where dacarbazine is a standard first-line therapy.

"The outcome of CheckMate-066 is an important milestone in the field of immuno-oncology as it represents the first well-controlled, randomized phase III trial of an investigational PD-1 checkpoint inhibitor to demonstrate an overall survival benefit," says Michael Giordano, MD, head of oncology development at BMS.

Nivolumab is a monoclonal antibody that targets PD-1, a receptor on activated T-cells that inhibits the immune system from attacking cancer cells. BMS is testing the therapy in melanoma, non–small cell lung cancer, and renal cell carcinoma, for which the drug received fast track designation from the FDA last year.

In March, investigators published results from a 107-patient phase I trial showing that nivolumab led to tumor regression and increased OS in patients with advanced melanoma (J Clin Oncol 2014;32:1020–30). The median OS was 16.8 months, with a median response of 2 years among the 33 patients who experienced tumor regressions.

CANCER DISCOVERY

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