PEOPLE

Benjamin G. Neel, MD, PhD, became director of the Laura and Isaac Perlmutter Cancer Center at NYU Langone Medical Center, an NCI-designated cancer center in New York, NY, in January. He succeeds William L. Carroll, MD. A renowned cancer biologist and expert in cell signal transduction, Neel previously served as director of the Ontario Cancer Institute at Princess Margaret Cancer Center, Canada’s largest cancer research center, a position he held for 14 years. He was also a professor of medical biophysics at the University of Toronto. His research focuses on cell signaling in cancer and developmental disease, the functional genomics of breast cancer, and ovarian cancer tumor-initiating cells.

In his new role, Neel will oversee the building of world-class translational programs in immunotherapy; cancer genetics, targeted therapies and epigenetics; imaging; community outreach; and supportive care.

Bristol-Myers Squibb announced that Giovanni Caforio, MD, the company’s current chief operating officer, will become its CEO effective May 5. He will succeed Lamberto Andreotti, who will become executive chairman of the board, a position he will retain after he retires in August.

After earning his medical degree at the University of Rome in Italy, Caforio began his career in medical affairs at Abbott Laboratories, where he spent 12 years in various leadership positions. He joined Bristol-Myers Squibb in 2000 as vice president and general manager, Italy, in the Worldwide Medicines Group. In 2007, he was named senior vice president, U.S. Oncology. In 2010, he was named senior vice president, Global Commercialization, Oncology and Immunology, before becoming president of U.S. operations in 2011.

Olaparib Approved for Advanced Ovarian Cancer

The FDA’s recent approval of olaparib (Lynparza; AstraZeneca) provides a new treatment for some women with advanced ovarian cancer and may bring personalized medicine for the disease one step closer.

On December 19, the FDA endorsed olaparib, a PARP inhibitor, for patients with ovarian cancer who carry germline BRCA mutations and who have had at least three lines of therapy. A diagnostic test developed by Myriad Genetics that detects BRCA mutations in blood samples also received approval.

To support its action, the FDA cited a single-arm trial in which the drug induced objective responses in 34% of 137 women with advanced ovarian cancers. The median duration of response was 7.9 months. Whether olaparib improves overall survival in these patients remains unclear.

About 20% of patients with ovarian cancer have the hereditary BRCA mutations that make them eligible for olaparib, notes Ursula Matulonis, MD, of Dana-Farber Cancer Institute in Boston, MA, although some of these women can be cured by platinum-based therapies such as carboplatin.

“Approval of olaparib is a very positive step. It really expands the options for women with germline BRCA mutations,” Matulonis says. Several of her patients meet the criteria for the drug, and she plans to prescribe it for them. Before olaparib’s approval, these women had only two treatment choices: join a clinical trial or receive chemotherapy with agents such as doxorubicin and paclitaxel.

Trials have also evaluated olaparib in breast, pancreatic, and prostate cancers. “The safety profile of this drug is reasonable, and it is mostly well tolerated,” says Eileen O’Reilly, MD, of Memorial Sloan Kettering Cancer Center in New York, NY, who has participated in studies of olaparib in patients with pancreatic cancer. It can trigger side effects that include fatigue and nausea, and there’s a small risk of myelodysplasia, the decreased production of blood cells, she says.

The FDA’s decision marks olaparib’s first approval in the United States; European regulators sanctioned its use for advanced ovarian cancer in December, too. The approval also breaks new ground in another way: Olaparib is the only treatment for ovarian cancer that targets a specific genomic defect, Matulonis notes. Personalized medicine is the norm for breast cancer, she says, but “this is a first step toward personalized medicine for ovarian cancer.”

Organoid Model Advances Pancreatic Cancer Research

Researchers in the Netherlands and the United States have developed a culture system for pancreatic cancer capable of rapidly generating three-dimensional (3-D) organoid models from normal and diseased pancreatic tissue, providing a window into the molecular underpinnings of tumor progression and a potential path to identifying new drug targets.

In a recent study, researchers established normal and neoplastic pancreatic organoids—tiny 3-D organ-like structures comprised of hundreds to thousands of cells—from mouse and human pancreatic ductal cells (Cell 2015;160:324–38). The 3-D culture strategy enabled researchers to grow normal pancreatic cells—which has not been possible in 2-D culture conditions—and study them alongside diseased pancreatic cells in order to analyze the molecular pathways that correlate with disease progression.

“By growing the cancer as an organoid we were able to capture the earliest stages of disease,” says study co–senior author Hans Clevers, MD, PhD, professor of molecular genetics at the HEBRECHT Institute, Royal Netherlands Academy of Arts and Sciences, who first developed organoids representing a variety of tissues, including the small intestine, colon, stomach, liver, and prostate. “Furthermore, this allows us to identify molecular pathways that are altered in the cancer compared to normal cells.”

When the cancerous organoid cells were transplanted into mice, they successfully replicated the full spectrum
of pancreatic tumor development, allowing researchers to isolate and analyze each stage of disease.

“Using this progression model is very different from implanting cancer cell lines into mouse models and watching them grow as cancer cells,” says study co-senior author David Tuveson, MD, PhD, director of the Lustgarten Foundation Pancreatic Cancer Research Laboratory at Cold Spring Harbor Laboratory in New York. “With this new system, the cells appear to be reprogrammed so that they start out as a low-grade and become, over time, a high-grade neoplasm.”

The model also allows organoids to be generated rapidly from tiny needle biopsies, eliminating a barrier for researchers. To date, there has been limited access to tissue samples because 85% of pancreatic cancer patients are ineligible for surgical resection due to the advanced stage of their disease at diagnosis or because their tumor is enmeshed in critical vasculature.

Gene expression and proteomic analyses conducted as part of the study revealed that nucleoporins—a family of proteins that make up the nuclear core complex—were broadly upregulated in the neoplastic mouse organoid models and that the expression increased measurably along with cancer progression, says Tuveson. The unexpected finding suggests that nucleoporins, which have been previously implicated in cancer, should be a focus of future pancreatic cancer research.

The investigators also established an organoid with a wild-type KRAS gene, an uncommon manifestation of pancreas cancer, says Clevers. Studying these organoids may help identify new driver genes and molecular pathways with therapeutic relevance.

“We’re hoping that organoid technology will provide a platform from which researchers will be able to identify actionable mutations for pancreas cancer,” says Clevers. Concurring, Tuveson notes that “the organoid model may be a way to actually deliver on the promise of personalized medicine.”

**AACR, ASCO Call for E-cigarette Regulation**

Use of electronic cigarettes (e-cigarettes) and other electronic nicotine delivery systems (ENDS) has skyrocketed in recent years. However, robust and conclusive data on the products’ health effects and efficacy as smoking cessation tools—as they’re often marketed—are lacking, say the American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO) in a joint policy statement (Clin Cancer Res 2015 Jan 8 [Epub ahead of print]).

While some states and local governments have restricted the sale or use of ENDS, the products aren’t currently regulated by the FDA. They should be, according to the organizations, which call for more ENDS-related research, particularly on their health effects and impact on smoking behavior. In addition, the statement says manufacturers should be required to report ingredient lists to the FDA and be prohibited from selling products flavored like fruit or candy that appeal to children.

Roy Herbst, MD, PhD, chief of medical oncology at Yale Comprehensive Cancer Center in New Haven, CT, chaired the committee that wrote the joint statement. He says the AACR and ASCO have become alarmed at the sharply increasing use of ENDS, both among patients and in the general population.

“We don’t know the long-term health consequences of e-cigarettes,” he says. “People are selling ENDS under false pretenses—as smoking cessation tools—but there are insufficient data to support that benefit.”

Herbst says cancer patients and their oncologists need to know that people who smoke should be aggressive in their cessation efforts, but should use FDA-approved medications like nicotine gum or patches, varenicline (Chantix), or bupropion (Zyban or Wellbutrin) instead of ENDS.

Radiation oncologist Graham Warren, MD, PhD, from the Medical University of South Carolina in Charleston, serves on the AACR’s tobacco and cancer subcommittee, chairs the ASCO tobacco control subcommittee, and helped draft the policy statement. He notes that ENDS need to be regulated, in part, because they raise complicated, contextual questions that will be difficult for researchers to answer.

For example, “smoking is so detrimental that almost anything would be better, and arguably e-cigarettes might be safer than smoking, but we just don’t know,” he says. “But if people who have never smoked before start using e-cigarettes, you’ve got to think that breathing these chemical vapors is going to be harmful.”

Warren notes he rarely heard about the products from his cancer patients 4 or 5 years ago. “Now, probably more than 80% of smokers I see have used e-cigarettes or want to try them,” he says. He tells those patients that because the effects of ENDS on overall health or on cancer treatment are unknown, using FDA-approved products for smoking cessation is a better strategy.

When the FDA finalizes the deeming document (available at www.fda.gov) it released last April, which classifies ENDS as tobacco products, ENDS will be regulated at the federal level. In the meantime, both Warren and Herbst say they hope the policy statement will encourage further regulation of ENDS at other levels of government and lead to research on the behavioral and clinical effects of ENDS.

**IOM Report Calls for Culture of Data Sharing**

A new report from the Institute of Medicine (IOM) recommends that sharing clinical trial data—supported by new technology platforms and shared funding—should become the norm in the medical research community to encourage secondary analyses and maximize trial participants’ contributions.

Noting that a large proportion of clinical trial data is never published or made public, the authors of *Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk* propose a practical framework that provides incentives for
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