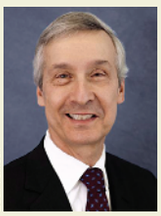
PEOPLE


Zach Veilleux

Epigenetics pioneer **C. David Allis, PhD,** will be awarded the 2014 Japan Prize in Life Sciences in April. The Japan Prize Foundation bestows the prize, worth about $500,000, annually to scientists and researchers who have made substantial contributions to their field and to "the peace and prosperity of mankind." Allis discovered that histone proteins are chemically modified in order to activate or silence nearby genes. He is a professor at The Rockefeller University in New York, NY.

Hervé Hoppenot, former president of Novartis Oncology, has been named president and CEO of Incyte (Wilmington, DE), which develops small-molecule drugs for oncology and inflammation. At Novartis, Hoppenot was responsible for translational medicine, development, and approval and commercialization, which included $11 billion in global sales. He also helped introduce new indications for Afinitor (everolimus) and Tasigna (nilotinib), and launched two new drugs, Signifor (pasireotide) for Cushing's disease and the JAK inhibitor Jakavi (ruxolitinib) for myelofibrosis.


Genentech

Roche has promoted **Sandra Horning, MD,** to chief medical officer and head of global product development. Most recently, she served as head of clinical development for the company's oncology and hematology business and helped shepherd several cancer drugs through development, including Zelboraf (vemurafenib), Erivedge (vismodegib), and Perjeta (pertuzumab). Before joining Roche in 2009, Horning worked as a practicing oncologist, clinical investigator, and professor of medicine at Stanford University School of Medicine in Palo Alto, CA.

Combination Therapy Approved for Melanoma

In January, the U.S. Food and Drug Administration (FDA) approved the targeted drug combination of trametinib (Mekinist; GlaxoSmithKline) and dabrafenib (Tafinlar; GlaxoSmithKline) for treating patients with metastatic or unresectable melanoma with *BRAF* V600K or V600E mutations. Both drugs received approval as monotherapies in May 2013.

Trametinib and dabrafenib inhibit kinases in the RAS/RAF/MEK/ERK pathway. In clinical trials, patients treated with either of these single-agent therapies develop resistance to the drugs and have disease progression within 6 or 7 months, but their combined effect extends that time.

Keith Flaherty, MD, an oncologist at the Massachusetts General Hospital Cancer Center in Boston, says combination therapies expand the efficacy of the first generation of targeted drugs, the earliest of which entered treatment regimens more than a dozen years ago.

"Numerous two-drug combinations are being evaluated in ongoing drug trials now," he says, representing the beginning of a coming wave of multidrug therapies. "I think 2014 will witness the first wave of triplet targeted regimens as well."

Targeted therapies often benefit only a small fraction of a cancer population, but combination therapies may prolong response times and benefit additional patient subgroups.

In the approval statement, the FDA cited results from a phase II open-label clinical trial, led by Flaherty, involving 162 patients with metastatic melanoma that expressed a *BRAF* mutation, most of whom were previously untreated. Participants received either dabrafenib alone or dabrafenib in combination with trametinib. Patients who received the highest combination dose—150 mg of dabrafenib twice daily with 2 mg of trametinib once daily—had an objective response rate of 76% and a median progression-free survival (PFS) of 9.4 months, compared with 54% and 5.8 months in patients treated only with dabrafenib. Overall survival data are not yet available.

On January 24, after FDA approval was granted, GlaxoSmithKline announced that the combination met its primary endpoint of PFS in a phase III trial that compared the combination to dabrafenib plus a placebo. PFS, response rate, and interim overall survival results were consistent with those seen in earlier studies, according to the company. Full results will be presented at an upcoming scientific meeting.

When targeted therapy is appropriate for a patient, the newly approved combination clearly has some advantages over single agents and "should be considered as an option for standard of care," says Mario Sznol, MD, an oncologist at the Yale Cancer Center in New Haven, CT. Data from the phase II trial, which was published in 2012, "really showed a dramatic improvement in progression-free survival for the combination," with tolerable toxicity.

The next difficult decision clinicians will face, says Sznol, is determining whether to offer the combination targeted therapy or immunotherapy to a patient with a *BRAF* mutation—or offer both, one after the other.

"We may need a randomized trial to determine which sequence of therapies, if sequencing is indeed the best approach, would lead to the best outcome in the majority of patients." ■

$540 Million Gift Boosts Cancer Research

In one of the largest single philanthropic gifts ever made to support cancer research, Ludwig Cancer Research, based in New York, NY, announced that it will disburse $540 million from the estate of the late shipping magnate Daniel K. Ludwig equally to six institutions.

In its January 6 announcement, the organization said that the money would fund cancer research at Ludwig Centers at Harvard University, Johns Hopkins University, the Massachusetts Institute of Technology, Memorial Sloan-Kettering Cancer Center, Stanford University, and the University of Chicago, based on stipulations Ludwig made before his death in 1992.

"Daniel Ludwig viewed cancer as a major challenge to mankind, which requires a comprehensive and concerted