of undergoing VEGF-targeted therapy received daily doses of either lenvatinib plus everolimus; lenvatinib alone; or everolimus alone (Lancet Oncol 2015;16:1473–82). The combination significantly prolonged median progression-free survival (PFS) compared with everolimus alone (14.6 vs. 5.5 months)—the current standard of care. Lenvatinib alone also prolonged PFS compared with standard of care (7.4 months).

Despite the combination's promising results, Molina says that the anti–PD-1 drug nivolumab may be even more appealing to many oncologists and patients given its favorable side-effect profile. In addition, FDA approval of nivolumab for advanced RCC was based on more robust phase III data.

"With the approval of lenvatinib plus everolimus, nivolumab, and cabozantinib, we have a number of promising second-line treatment options," says Molina. "However, we don't yet know what the best sequence should be." *–Janet Colwell* ■

Treating Tumors by Molecular Profile, Not Type

Preliminary findings from MyPathway, an ongoing Genentech-sponsored phase II basket trial, indicate that matching molecular abnormalities of patients' tumors to relevant targeted therapies—albeit outside a given drug's FDA-approved indication—is both feasible and promising. The results were presented by John Hainsworth, MD, a senior investigator at Sarah Cannon Research Institute in Nashville, TN, during the annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago, IL, June 3–7.

"The same mutations for which targeted agents have been approved for specific cancers can be found in other tumor types—but usually at a lower incidence," Hainsworth said. "With an increase in comprehensive genomic profiling over the last few years, identifying sufficient patients to test these drugs' potential efficacy in nonindicated tumors has become easier."

Hainsworth reported data on MyPathway's first 129 patients, who had molecular abnormalities in HER2, *BRAF*, Hedgehog, or *EGFR*. They were matched to corresponding Genentech drugs: dual HER2 blockade with trastuzumab (Herceptin) plus pertuzumab (Perjeta); the BRAF inhibitor vemurafenib (Zelboraf); the Hedgehog inhibitor vismodegib (Erivedge); and the EGFR inhibitor erlotinib (Tarceva). All patients had tumor types outside of current indications for these therapies and were refractory to standard treatment options.

Twenty-nine patients with 12 types of advanced cancer achieved an objective response—tumor shrinkage of 30% or more—to their matched therapy, and another 40 saw their disease stabilize. There were responders in each of the four treatment arms, Hainsworth noted, and overall, no new side effects were observed with these therapies.

The most promising results were observed in patients with HER2-amplified tumors—seven of 20 with colorectal cancer, three of eight with bladder cancer, and three of six with biliary cancer had objective responses to trastuzumab plus pertuzumab.

Encouraging data was also seen in patients with *BRAF*-mutant non–small cell lung cancer (NSCLC): Three of 15 patients responded to vemurafenib, and two more had stable disease.

Based on these findings, the study investigators are enrolling additional patients with HER2-amplified colorectal, bladder, and biliary cancers, as well as patients with *BRAF*-mutant NSCLC. They'll also add the MEK inhibitor cobimetinib (Cotellic) to vemurafenib—a combination currently approved for advanced or unresectable melanoma—for the study's *BRAF*-mutant arm. Using ado-trastuzumab emtansine (T-DM1; Kadcyla) in the HER2-amplified arm is another possibility.

Sumanta Kumar Pal, MD, a medical oncologist at City of Hope Comprehensive Cancer Center in Duarte, CA, noted that trials like MyPathway include NCI-MATCH and ASCO's TAPUR study. "It's too early to draw any firm conclusions, but if the results hold, we may see a shift in the long-standing paradigm of treating patients based on their cancer type," he said. *–Alissa Poh* ■

NOTED

Technology entrepreneur **Larry Ellison announced that he will give $200 million to the University of Southern California** in Los Angeles to create the Lawrence J. Ellison Institute of Transformative Medicine, which will focus on cancer research. The gift will help fund the construction of a state-of-the-art building with interdisciplinary laboratories in which cancer researchers will draw upon the knowledge of experts from fields such as mathematics, physics, and engineering.

A recent study questioned the FDA's Accelerated Approval program for new cancer drugs. The analysis found that of 25 drugs approved between 2009 and 2014, 56% lacked supporting evidence aligning the surrogate measures used—including objective response rate and progression-free survival—with a survival benefit (Mayo Clin Proc 2016;91:713–25).

The NIH awarded $142 million over 5 years to the Rochester, MN–based Mayo Clinic to create a biobank for the Precision Medicine Initiative cohort program. The funds will be used to collect, store, and distribute more than 35 million biospecimens for comprehensive genomic analyses.

The FDA issued a new form for physicians to request expanded access to an investigational drug or biologic for patients who suffer from serious or life-threatening diseases and for whom no comparable or satisfactory alternative therapy or clinical trial is available. "We know that navigating this process can be challenging and time-consuming, and we are committed to reducing the procedural burdens on physicians and patients whenever possible," said FDA Commissioner Robert Califf, MD.

Former FDA Commissioner Margaret Hamburg, MD, and Sanofi research head Elias Zerhouni, MD, called for international harmonization of drug regulations. In an editorial, they wrote that "the mosaic of regulations that govern drug development and oversight nation by nation are creating unnecessary barriers to the efficient delivery of safe, innovative, and effective treatments to patients in need" (Sci Transl Med 2016;8:338ed6).

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/content/early/by/section.