Giordano, MD, PhD, and Gary Hammer, remained unchanged since the 1970s. An agent mitotane—are palliative and have radiation, and the hormone-blocking metastatic disease—chemotherapy, 6% to 13%. Standard treatments for so its 5-year survival rate ranges from often diagnosed at an advanced stage, ACC is cancer that affects just two in every million people worldwide. ACC is cal carcinoma (ACC), a rare endocrine in six countries have joined forces to Piecing Together the companies, including Mylan Pharmaceuticals, are developing their own versions of the biologic.

Amgen’s Neupogen (filgrastim), used to treat neutropenia. In contrast to generic drugs, biosimilars are not exactly identical to their corresponding brand-name counterparts. Whereas generic drugs are copies of small-molecule drugs with relatively simple chemical compositions, biosimilars correspond to complex large-molecule biologies and must be synthesized from living organisms. Because biosimilars are impossible to precisely replicate, the FDA requires manufacturers to perform extensive analyses and conduct confirmatory clinical studies demonstrating that the products are highly similar to their branded counterparts, without any clinically meaningful differences.

“This is one of the first trials with biosimilars in oncology to demonstrate similar efficacy, safety, and immunogenicity against the reference product,” said Rugo. —Janet Colwell

FDA Approves Drug Combo for Kidney Cancer

The FDA approved the combination of lenvatinib (Lenvima; Eisai) and everolimus (Afinitor; Novartis) to treat advanced or metastatic renal cell carcinoma (RCC) in mid-May. The approval marks the first time that a tyrosine kinase inhibitor (TKI) and an mTOR inhibitor have been combined successfully as a second-line treatment for patients with RCC whose tumors advance despite previous VEGF-targeted treatment.

“We have been hoping to treat kidney cancer with this type of vertical blockade for some time, but previous combinations have been unsuccessful due to high toxicity,” says Ana Molina, MD, a medical oncologist at NewYork-Presbyterian Hospital and Weill Cornell Medicine in New York, NY.

Until recently, oncologists had two second-line treatment options: everolimus and the TKI axitinib (Inlyta; Pfizer). New approvals over the past few months have increased that number to five, including the new lenvatinib–everolimus combination; the PD-1 checkpoint inhibitor nivolumab (Opdivo; Bristol-Myers Squibb); and cabozantinib (Cabometyx; Exelixis), another TKI.

Together, lenvatinib and everolimus have a synergistic effect by blocking multiple points along the VEGF and mTOR signaling pathways that are critical to tumor growth, says Molina. In addition, lenvatinib is a strong inhibitor of FGF receptors, which have been implicated as a potential mechanism of resistance to VEGF-targeted treatments.

The approval was based on a phase II trial in which 153 patients with advanced or metastatic RCC whose disease progressed within 9 months...
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.

“The 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 Pob

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