FDA Approves First Biosimilar to Treat Cancer

The FDA approved the VEGF inhibitor bevacizumab-awwb (Mvasi; Amgen/Allergan) to treat five types of cancer in adults. It is the seventh biosimilar approved by the agency since 2015, but it’s the first for the treatment of cancer.

Mvasi is a biosimilar to bevacizumab (Avastin; Genentech), which loses patent protection in the United States in 2019. The two agents have nearly identical indications, which include nonsquamous non–small cell lung cancer, metastatic colorectal cancer, cervical cancer, renal cell carcinoma, and glioblastoma. Avastin is also labeled for ovarian cancer, which was not included in Mvasi’s FDA approval. Like Avastin, Mvasi carries black box warnings for gastrointestinal perforation, severe hemorrhage, and impaired wound healing.

A biosimilar gains approval based on data demonstrating that it is highly similar to an FDA-approved biological product and that there are no clinically meaningful differences between the biosimilar product and the reference product. The agency requires rigorous physicochemical studies on the pharmacokinetics, pharmacodynamics, and immunogenicity of the biosimilar. Clinical trials play a smaller role in the process compared with approval of a novel compound.

“It’s a little bit foreign to clinicians, who have been educated to say, ‘That’s just a copycat,’ ” says James Stevenson, PharmD, professor of clinical pharmacy at the University of Michigan in Ann Arbor and president of St. Paul, MN–based Visante, a medication management-consulting firm.

Stevenson expects clinicians will have more opportunities to evaluate the studies behind biosimilars’ approvals. “Over 50% of the drugs in the pipeline are biologics,” he says. “Because of the number of drugs as well as the spend on these drugs, there’s a lot of interest in biosimilars and how they might be able to help us control expenses and improve access to care.” Amgen and Allergan have yet to release information regarding pricing or drug availability for Mvasi.

Financial impacts remain uncertain for patients—and to some extent for pharmaceutical companies as well. Stock analyst Todd Campbell, president of E.B. Capital Markets in Durham, NH, says that Amgen and Allergan are companies to watch, given their collaboration on multiple biosimilars in the pipeline, but he notes that “it’s too soon to know which company will come out on top in oncology.”

More announcements regarding cancer-treating biosimilars can be expected over the next year. Sandoz submitted a biologic license application for a new rituximab product last month, and the FDA’s Oncology Advisory Committee unanimously recommended approval of Mylan’s biosimilar of trastuzumab in July 2017. A final decision on the trastuzumab product is anticipated by the end of the year. –Jordan Calmes-Miller

Approved Drugs Might Work in More Cancers

A precision medicine trial aimed at identifying patients with rare cancers or those who have exhausted standard treatment options suggests that drugs approved for specific types of cancer might work in other tumor types that harbor the same genetic mutations. Preliminary results from the trial were presented in September at the ESMO 2017 Congress, the annual meeting of the European Society for Medical Oncology, in Madrid, Spain.

Researchers with the Center for Personalized Cancer Treatment (CPCT), a network of more than 40 hospitals in the Netherlands, performed whole-genome sequencing on biopsies taken from about 2,000 patients with all types of metastatic cancer to create a database of genetic mutations that appear in multiple tumor types. The database is being used to inform enrollment in a multiarm trial that includes 19 different approved drugs.

To date, 70 patients have been enrolled out of more than 250 cases submitted for review. To be eligible for the trial, patients must have been diagnosed with solid tumors, lymphoma, or multiple myeloma, have exhausted standard treatment options, and have actionable tumor mutations—meaning that they can be targeted by one or more of the study drugs.
Catherine Pickworth, PhD, of Cancer Research UK in London, noted that the CPCT trial involves sequencing the whole genome rather than a panel of select genes. “The wide scope of this trial allows researchers to study both common and rarer genetic mistakes,” she said. “This could reveal new ways to use existing treatments, which is particularly exciting for people with rare cancers where fewer treatments are known to work.” —Janet Colwell

**Liquid Biopsy Technique May Allow Early Screening**

A new method for performing liquid biopsies can detect the majority of early-stage tumors without large amounts of tumor DNA or foreknowledge of cancer mutations, a recent study reveals (Sci Transl Med 2017;9:eaan2415).

Liquid biopsies can be used to examine cell-free DNA in the bloodstream of patients with cancer, some of which comes from the tumor. Through DNA sequencing, researchers have been able to discern characteristic mutations in circulating tumor DNA (ctDNA). In some of the previous studies of this technique, however, researchers had already sequenced the tumor tissue, so they knew which mutations to look for in the blood. In addition, these analyses mainly included patients with late-stage cancer, who have more ctDNA than patients with early-stage disease.

Victor Velculescu, MD, PhD, of Johns Hopkins University School of Medicine in Baltimore, MD, and colleagues developed a technique to profile the smaller amounts of ctDNA present in early-stage cancer. After isolating DNA fragments from a patient’s blood, the researchers tagged each one with a different DNA barcode. These identifiers allowed the researchers to keep track of each fragment as they sequenced it around 30,000 times. By comparing many sequences at each position to each other and to a reference genome, the researchers could confirm whether a detected mutation was genuine or a false positive.

The scientists’ approach, called targeted error correction sequencing (TEC-Seq), detects 55 genes that are frequently mutated in cancer, as well as three genes that are often altered in certain benign blood conditions and can confound the identification of tumor-specific mutations. They used the technique to analyze blood samples from 194 patients with breast, colorectal, lung, or ovarian cancers. TEC-Seq correctly identified 56%, 83%, 62%, and 71% of these patients, respectively, pinpointing gene alterations in blood samples for each case. TEC-Seq was sensitive enough to detect early-stage tumors. Overall, it identified 62% of 138 patients whose tumors were stage I or II.

One concern about liquid biopsies is that mutations present in the blood may not be tumor-derived. When the researchers analyzed matched tumor and blood samples from 100 patients, however, they found that in 82% of cases, a mutation detected in the blood was also present in the tumor. In a further test, the researchers applied TEC-Seq to blood samples from 44 healthy individuals. None of them came up positive for ctDNA.

TEC-Seq may also be useful for predicting cancer recurrence. The researchers applied the method to blood samples from 38 patients with colorectal cancer who had undergone surgery to remove their tumors. Patients with large amounts of ctDNA at diagnosis had shorter progression-free survival and overall survival than did patients with less ctDNA.

The study shows that “you can use DNA changes in blood to identify cancer at an early stage,” says Velculescu. He notes that this technique can’t determine what type of tumor a patient has; further mutation analyses or imaging would be necessary to determine tumor identity and location. Velculescu and colleagues have begun clinical trials to verify TEC-Seq’s capabilities in larger groups of patients.

“What’s exciting is that they did de novo mutation calling without prior knowledge of the changes in tumor DNA,” says Pedram Razavi, MD, PhD, of Memorial Sloan Kettering Cancer Center in New York, NY. His colleague Jorge Reis-Filho, MD, PhD, agrees that this method is promising and “a significant step forward.” —Mitch Leslie
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