Another Targeted Therapy for ERBB2-Positive Breast Cancer
The FDA recently granted accelerated approval to an antibody-drug combination for adults who’ve already received at least 2 treatment regimens for unresectable or metastatic breast cancer that is positive for human epidermal growth factor receptor 2 (ERBB2; formerly HER2/neu).

Marketed as Enhertu, fam-trastuzumab deruxtecan-nxki is an anti-ERBB2 antibody with a cytotoxic topoisomerase I inhibitor attached. It is administered via intravenous infusion. According to the FDA, about 20% of breast cancers have a genetic mutation that results in ERBB2-positive tumors, which are very aggressive.

The newly approved drug was evaluated in a 2-part phase 2 clinical trial to establish a recommended dose (5.4 mg/kg) and to assess safety and efficacy. Trial participants included 184 women whose previous treatment involved another antibody-drug conjugate, trastuzumab emtansine, which is standard second-line therapy for ERBB2-positive breast cancer. The investigators noted that if patients develop trastuzumab emtansine resistance, there’s no uniform agreement on which treatment to use next.

Among women in the trial who received the recommended dose of fam-trastuzumab deruxtecan-nxki, the overall response rate was 60.9% and treatment response lasted for a median of 14.8 months. The median progression-free survival was 16.4 months.

The investigators noted that results from their study appeared to substantially exceed those of currently available anti-ERBB2 treatments as well as new agents being developed. They pointed out that compared with trastuzumab emtansine, fam-trastuzumab deruxtecan-nxki has a higher concentration of drug relative to antibody. It’s also more likely than trastuzumab emtansine to kill adjacent tumor cells that don’t express the ERBB2 protein, and its short half-life reduces potential toxicity to healthy tissue.

However, the drug carries a boxed warning about the risk of developing interstitial lung disease and pneumonitis, which have caused deaths. The warning advises physicians to monitor for signs and symp-toms including cough, dyspnea, fever, and other respiratory symptoms.

New Migraine Drug Gains Approval
A small-molecule drug that blocks pain transmission in the trigeminovascular system is the first in its class to be approved for adults who have migraine headaches with or without aura.

Ubrogepant, marketed as Ubrelvy, is an oral calcitonin gene–related peptide receptor antagonist. The drug represents a new mechanism of action for the acute treatment of migraine compared with currently used medications such as triptans, ergot, opioids, and ibuprofen.

Two phase 3 clinical trials of ubrogepant were conducted between July 2016 and February 2018. In one of the trials, 1465 randomized patients received 25 mg or 50 mg of the drug or placebo. In the other trial, 1372 randomized patients in the modified intention-to-treat population received 50 mg or 100 mg of ubrogepant or placebo.

Both trials evaluated treatment for a single migraine episode. The primary end points were being free of migraine pain and relief from the most troubling symptom (sensitivity to light or sound or nausea) at 2 hours after taking ubrogepant. In both trials, patients in the treatment groups had significantly greater freedom from pain compared with those in the placebo groups. But only those who took a 50-mg or 100-mg dose got relief from their most troubling symptom at 2 hours after taking the drug.

Billy Dunn, MD, acting director of the Office of Neuroscience at the FDA, noted in a statement that disabling migraines affect an estimated 37 million people in the United States. “The FDA…will continue to work with stakeholders to promote the development of new safe and effective migraine therapies,” he added.

Adverse events reported in the trials included nausea, dizziness, and sleepiness.

FDA’s New Effort to Improve Compounded Drug Quality
Inspections of compounding facilities in recent years that have turned up unsanitary conditions and prompted some compounders to recall their products or cease operations have led the FDA to launch a new initiative: the Compounding Quality Center of Excellence.

The effort is aimed at outsourcing facilities that produce compounded drugs for hospitals, clinics, and other health care providers and must comply with current good manufacturing practices (CGMP). “By providing comprehensive, accessible learning tools, we will support outsourcing facilities in reliably producing high-quality compounded products that meet FDA’s standards,” Janet Woodcock, MD, director of the FDA’s Center for Drug Evaluation and Research, said in a statement.

In-person training sessions for outsourcing facility staff will cover aspects of CGMP including environmental monitoring, sterile drug compounding, and clean room conditions. The courses begin in March and will offer continuing education credits. Free online training also will be available on topics including the regulatory framework for compounded drugs, sterility assurance, and investigations and corrective and preventive actions.

In September, the Center of Excellence will host a conference in Dallas where members of the compounding industry, state and federal regulators, and other stakeholders can discuss key topics and best practices. – Rebecca Voelker, MSJ

Note: Source references are available through hyperlinks embedded in the article text.