FDA Approves Pemazyre as First Targeted Therapy for Cholangiocarcinoma

Over a third of bile duct cancer patients treated with the kinase inhibitor experienced complete or partial tumor remission.

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On April 17, the Food and Drug Administration (FDA) granted accelerated approval of Pemazyre (pemigatinib), a targeted therapy for the treatment of locally advanced or metastatic cholangiocarcinoma that carries a specific genetic mutation.

Cholangiocarcinoma is a rare cancer that forms in the bile ducts that carry digestive fluid from the liver to the gallbladder and small intestine. It is often detected at a late stage after it has started to spread and can no longer be surgically removed. Pemazyre is the first targeted therapy approved for this type of cancer.

The new kinase inhibitor, developed by Incyte, blocks fibroblast growth factor receptor (FGFR) types 1, 2 and 3. It is indicated for adults with previously treated, inoperable cholangiocarcinoma with FGFR2 gene fusions or other genetic rearrangements. The FDA also approved the FoundationOne CDx companion diagnostic test to screen for such mutations, which occur in around 12% of patients with cholangiocarcinoma.

“With Pemazyre, we considered the observed efficacy results to be clinically meaningful and the overall risk-to-benefit assessment for patients with tumors harboring FGFR2 gene fusions and other rearrangements to be favorable, particularly when we considered that these patients have no other good options following first line treatment with chemotherapy,” Richard Pazdur, MD, director of the FDA’s Oncology Center of Excellence, said in a press release.

The approval was based on findings from the Phase II FIGHT-202 trial, which enrolled 107 people with locally advanced or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements who had received at least one prior line of treatment. Study results were presented at the 2019 European Society for Medical Oncology Congress last fall and published in Lancet Oncology.

More than half of the participants were women, and three quarters were under age 65. All were treated with Pemazyre tablets once daily for 14 days, followed by seven days off, until they

experienced disease progressed or unacceptable side effects. The trial was not randomized, and no one received a placebo or other treatment for comparison. Participants underwent scans every eight weeks to monitor cancer progression.

After a median follow-up of 15 months, the overall response rate—meaning complete or partial tumor shrinkage—was 36%, including 3% with complete remission. Another 47% had stable disease with no further progression. Among the 38 patients who responded, 24 (63%) had responses that lasted at least six months and seven (18%) had responses that lasted at least a year.

Overall survival results were still preliminary when the data were analyzed, but the median survival time of 21.1 months in this group far exceeded the 4.0 month duration seen in another patient cohort without FGFR2 fusions or rearrangements.

Treatment was generally safe and well tolerated. The most common adverse reactions observed in people taking Pemzyre were high or low phosphate levels, hair loss, diarrhea, constipation, nausea, vomiting, abdominal pain, decreased appetite, dysgeusia (abnormal taste sensations), nail problems, mouth sores, dry mouth, dry eyes, fatigue, joint pain and back pain.

The prescribing information for Pemazyre includes a warning about the risk of serious eye problems and recommends ophthalmological exams before and during treatment. Severely elevated phosphate levels (hyperphosphatemia) may also occur. Pemazyre can cause fetal harm if used during pregnancy.

Pemazyre received FDA priority review and breakthrough therapy designations, intended to expedite the development and review of medications for serious conditions that may offer substantial improvement over existing therapies. Medications that receive accelerated approval based on response rates are expected to undergo further testing in randomized trials to determine whether they improve progression-free or overall survival; the FDA can rescind approval if they don’t measure up. A Phase III study of Pemazyre versus standard chemotherapy is currently underway (ClinicalTrials.gov number NCT03656536).

“Although cholangiocarcinoma is considered a rare disease, it has been on the rise over the past three decades,” lead study investigator Ghassan Abou-Alfa, MD, of Memorial Sloan Kettering Cancer Center in New York, said in an Incyte press release. “It is encouraging to have a new targeted treatment option for patients who historically have had limited options after first-line chemotherapy or surgery, in which relapse rates remain high.”

Click here for full prescribing information for Pemazyre.
