FDA Grants Zenocutuzumab-zbco Approval for Adults With Rare Bile Duct Cancer

Key Takeaways

- FDA authorized zenocutuzumab-zbco for NRG1 fusion–positive cholangiocarcinoma via an accelerated rare-disease pathway intended to shorten review timelines for high-unmet-need indications.
- Zenocutuzumab is a bispecific HER2/HER3 antibody that inhibits NRG1 ligand-driven HER3 activation, extending a prior 2024 approval in NRG1+ NSCLC and pancreatic adenocarcinoma.
- eNRGy enrolled 22 cholangiocarcinoma patients (median age 57), with 91% previously treated; among 19 evaluable, blinded central review per RECIST v1.1 showed 36.8% ORR.
- Safety labeling highlights infusion reactions, hypersensitivity/anaphylaxis, ILD/pneumonitis, left ventricular dysfunction, and embryo-fetal toxicity; dosing is 750 mg IV every 2 weeks until progression/toxicity.

Treatment with zenocutuzumab-zbco led to an overall response rate of 36.8% for a duration ranging from 2.8 to 12.9 months.

Zenocutuzumab-zbco (Bizengri; Merus NV) received FDA approval for treatment of patients with NRG1 fusion-positive cholangiocarcinoma, supported by data from the phase 1/2 eNRGy trial (NCT02912949). The decision marks the seventh FDA approval underneath the National Priority Voucher Pilot Program.1

“Patients with this ultra-rare type of cancer desperately need new treatment options,” said FDA Commissioner Marty Makary, MD, MPH, in an official release. “Through the national priority voucher pilot program, the FDA is accelerating therapies for rare diseases with unmet medical needs, reviewing applications in significantly shortened timelines.”[1]

Cholangiocarcinoma is a rare, aggressive type of cancer affecting the bile ducts—slender tubes responsible for carrying digestive fluids—that affects an estimated 2000 to 3000 people each year in the United States. Approximately 1% of all diagnoses are *NRG1*-positive, meaning the tumors harbor NRG1 fusion proteins. These proteins activate cancer-promoting cellular processes, contributing to disease progression.[2,3]

Zenocutuzumab-zbco is a bispecific antibody that targets and binds to HER2 and HER3 on the surface of malignant cells and tumor cells to prevent NRG1 from binding to HER3.[4] In 2024, it was approved for adults with unresectable or metastatic non-small cell lung cancer harboring *an NRG1* gene fusion with disease progression on or after prior systemic therapy or advanced, unresectable, or metastatic pancreatic ductal adenocarcinoma harboring *an NRG1* gene fusion with disease progression on or after prior systemic therapy.[5]

The phase 1/2, open-label, multi-center, multinational, dose escalation, single agent eNRGy trial assessed the safety, tolerability, pharmacokinetics, pharmacodynamics, immunogenicity, and anti-tumor activity of zenocutuzumab in patients with solid tumors harboring an *NRG1* fusion. Twenty-two patients (median age 57) were included in the cholangiocarcinoma cohort, of whom 19 were evaluable for efficacy measures. Of the patients, 91% received prior systemic therapy.

The primary end points included confirmed overall response rate (ORR) and duration of response (DOR) as determined by a blinded independent central review according to RECIST v1.1.

The data showed that patients with cholangiocarcinoma treated with zenocutuzumab-zbco achieved an ORR of 36.8% (95% CI: 16.3–61.6) and a DOR ranging from 2.8 to 12.9 months.

The label for zenocutuzumab-zbco carries warnings for infusion-related reactions, hypersensitivity and anaphylactic reactions, interstitial lung disease or pneumonitis, left ventricular dysfunction, and embryo-fetal toxicity. The most common adverse reactions include diarrhea, musculoskeletal pain, fatigue, nausea, infusion-related reactions, dyspnea, rash, constipation, vomiting, abdominal pain, and edema.

Zenocutuzumab-zbco is administered as a 750 mg intravenous infusion every 2 weeks, continuing until disease progression or unacceptable toxicity.

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