Bizengri® (zenocutuzumab-zbco) – New orphan drug approval

- On December 4, 2024, Merus announced the FDA approval of Bizengri (zenocutuzumab-zbco), for the treatment of adults with:
    - Advanced, unresectable or metastatic non-small cell lung cancer (NSCLC) harboring a neuregulin 1 (*NRG1*) gene fusion with disease progression on or after prior systemic therapy
    - Advanced, unresectable or metastatic pancreatic adenocarcinoma harboring a *NRG1* gene fusion with disease progression on or after prior systemic therapy.
- Both indications were approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Bizengri is a bispecific antibody that binds to the extracellular domains of HER2 and HER3 expressed on the surface of cells, including tumor cells.
- The efficacy of Bizengri for NSCLC was established in an open-label, multi-cohort study in 64 adult patients with advanced or metastatic *NRG1* fusion-positive NSCLC who had disease progression following standard of care treatment for their disease. Patients received Bizengri until unacceptable toxicity or disease progression. The major outcome measures were confirmed ORR and DOR.
    - The ORR was 33% (95% CI: 22, 46) and the median DOR was 7.4 months (95% CI: 4.0, 16.6).
- The efficacy of Bizengri for pancreatic adenocarcinoma was also established in an open-label, multi-cohort study in 30 adult patients with advanced or metastatic *NRG1* fusion-positive pancreatic adenocarcinoma who had disease progression following standard of care treatment. Patients received Bizengri until unacceptable toxicity or disease progression. The major outcome measures were confirmed ORR and DOR.
    - The ORR was 40% (95% CI: 23, 59) and the DOR ranged from 3.7 to 16.6 months.
- Bizengri carries a boxed warning for embryo-fetal toxicity.
- Additional warnings and precautions for Bizengri include infusion-related reactions/ hypersensitivity/anaphylactic reactions; interstitial lung disease/pneumonitis; and left ventricular dysfunction.
- The most common adverse reactions (≥ 10%) with Bizengri use were diarrhea, musculoskeletal pain, fatigue, nausea, infusion-related reactions, dyspnea, rash, constipation, vomiting, abdominal pain, and edema. The most common grade 3 or 4 laboratory abnormalities (≥ 2%) were increased gamma-glutamyltransferase (GGT), decreased hemoglobin, decreased sodium, decreased platelets, increased aspartate transaminase (AST), increased alanine aminotransferase (ALT), increased alkaline phosphatase, decreased magnesium, decreased phosphate, increased aPTT, and increased bilirubin.
- The recommended dose of Bizengri is 750 mg as an intravenous (IV) infusion every 2 weeks until disease progression or unacceptable toxicity.

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    - Patients should be selected for treatment based on the presence of an NRG1 gene fusion in tumor specimens. An FDA-approved test for the detection of NRG1 gene fusions is not currently available.

- Merus plans to launch Bizengri in the coming weeks. Bizengri will be available as a 375 mg/18.75 mL (20 mg/mL) single-dose vial.

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