FDA Approves Vyloy for Advanced Stomach Cancer

Zolbetuximab is a monoclonal antibody targeting claudin 18.2, a protein expressed on gastric and gastroesophageal junction tumors.

October 22, 2024 By Food and Drug Administration (FDA)

FDA approves zolbetuximab-clzb with chemotherapy for gastric or gastroesophageal junction adenocarcinoma

On October 18, 2024, the Food and Drug Administration approved zolbetuximab-clzb (Vyloy, Astellas Pharma US, Inc.), a claudin 18.2 (CLDN18.2)-directed cytolytic antibody, with fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are CLDN18.2 positive, as determined by an FDA-approved test.

Today, FDA also approved the VENTANA CLDN18 (43-14A) RxDx Assay (Ventana Medical Systems, Inc./Roche Diagnostics) as a companion diagnostic device to identify patients with gastric or GEJ adenocarcinoma who may be eligible for treatment with zolbetuximab.

Full prescribing information for Vyloy will be posted on Drugs@FDA.

Efficacy and Safety

Efficacy was evaluated in trials SPOTLIGHT (NCT03504397) and GLOW (NCT03653507). Both were randomized (1:1), double-blind, multicenter trials that enrolled patients with CLDN18.2 positive advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma. The major efficacy outcome measure in both trials was progression-free survival (PFS), as assessed per RECIST v1.1 by an independent review committee. Overall survival (OS) was an additional efficacy outcome measure.

In SPOTLIGHT, 565 patients were randomized to receive zolbetuximab-clzb with mFOLFOX6 chemotherapy or placebo with mFOLFOX6 chemotherapy. Median PFS was 10.6 months (95% CI: 8.9, 12.5) in the zolbetuximab-clzb/chemotherapy arm and 8.7 months (95% CI: 8.2, 10.3) in the placebo/chemotherapy arm (hazard ratio [HR] 0.751 [95% CI: 0.598, 0.942]; 1-sided p-value=0.0066). Median OS was 18.2 months (95% CI: 16.4, 22.9) and 15.5 months (95% CI: 13.5, 16.5), respectively, (HR 0.750 [95% CI: 0.601, 0.936]; 1-sided p-value=0.0053).

In GLOW, 507 patients were randomized to receive either zolbetuximab-clzb with CAPOX chemotherapy or placebo with CAPOX chemotherapy. Median PFS was 8.2 months (95% CI: 7.5, 8.8) in the zolbetuximab-clzb/chemotherapy arm and 6.8 months (95% CI: 6.1, 8.1) in the placebo/chemotherapy arm (hazard ratio [HR] 0.687 [95% CI: 0.544, 0.866]; 1-sided p-value=0.0007). Median OS was 14.4 months (95% CI: 12.3, 16.5) and 12.2 months (95% CI: 10.3, 13.7), respectively (HR 0.771 [95% CI: 0.615, 0.965]; 1-sided p-value=0.0118).

The most common serious adverse reactions in SPOTLIGHT (≥2%) were vomiting, nausea, neutropenia, febrile neutropenia, diarrhea, intestinal obstruction, pyrexia, pneumonia, respiratory failure, pulmonary embolism, decreased appetite, and sepsis. The most common serious adverse reactions in GLOW (≥2%) were vomiting, nausea, decreased appetite, decreased platelet count, upper gastrointestinal hemorrhage, diarrhea, pneumonia, pulmonary embolism, and pyrexia.

The recommended zolbetuximab-clzb dosage with fluoropyrimidine- and platinum-containing chemotherapy is:

- First dose: 800 mg/m^2 intravenously,
- Subsequent dosages:
  - 600 mg/m^2 intravenously every 3 weeks, or
  - 400 mg/m^2 intravenously every 2 weeks.

Expedited Programs
This review used the Real-Time Oncology Review (RTOR) pilot program, which streamlined data submission prior to the filing of the entire clinical application, and the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

This application was granted priority review, fast track, and orphan drug designation. FDA expedited programs are described in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

For assistance with single-patient INDs for investigational oncology products, healthcare professionals may contact OCE's Project Facilitate at 240-402-0004 or email OncProjectFacilitate@fda.hhs.gov.

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