FDA Approves Margenza for Metastatic HER2-Positive Breast Cancer

Monoclonal antibody delays disease progression in people with previously treated HER2-positive tumors.

December 18, 2020 By Food and Drug Administration (FDA)

On December 16, 2020, the Food and Drug Administration approved margetuximab-cmkb (Margenza, MacroGenics) in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

Efficacy was evaluated in SOPHIA (NCT02492711), a randomized, multicenter, open-label trial of 536 patients with IHC 3+ or ISH-amplified HER2+ metastatic breast cancer who had received prior treatment with other anti-HER2 therapies. Patients were randomized (1:1) to plus chemotherapy or trastuzumab plus chemotherapy. Randomization was stratified by chemotherapy choice (capecitabine, eribulin, gemcitabine, or vinorelbine), number of lines of therapy in the metastatic setting (≤ 2, > 2), and number of metastatic sites (≤ 2, > 2).

The main efficacy outcome measures were progression-free survival (PFS) by blinded independent central review (BICR) and overall survival (OS). Additional efficacy outcome measures were objective response rate (ORR) and duration of response (DOR) assessed by BICR.

Median PFS in the margetuximab arm was 5.8 months (95% CI: 5.5, 7.0) compared with 4.9 months (95% CI: 4.2, 5.6) in the control arm (HR 0.76; 95% CI: 0.59, 0.98; p=0.033). Confirmed ORR was 22% (95% CI: 17, 27) with a median DOR of 6.1 months (95% CI: 4.1, 9.1) in the margetuximab arm compared to an ORR of 16% (95% CI: 12, 20) and median DOR of 6.0 months (95%CI: 4.0, 6.9) in the control arm.

The most common adverse drug reactions (>10%) with margetuximab in combination with chemotherapy are fatigue/asthenia, nausea, diarrhea, vomiting, constipation, headache, pyrexia, alopecia, abdominal pain, peripheral neuropathy, arthralgia/myalgia, cough, decreased appetite, dyspnea, infusion-related reactions, palmar-plantar erythrodysesthesia, and extremity pain. The Prescribing Information includes a Boxed Warning to advise health professionals of the risks of left ventricular dysfunction and embryo-fetal toxicity.

The recommended margetuximab dose is 15 mg/kg by intravenous infusion over 120 minutes for the initial dose, then over a minimum of 30 minutes every 3 weeks for all subsequent doses. On

days when both margetuximab and chemotherapy are to be administered, margetuximab may be administered immediately after chemotherapy completion. Refer to the respective Prescribing Information for each therapeutic agent administered in combination with margetuximab for the recommended dosage information, as appropriate.

View full prescribing information for Margenza.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

This application was granted fast-track designation. A description of FDA expedited programs is 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.

This announcement was originally published on the Food and Drug Administration website on December 16, 2020.
