FDA Approves Nerlynx for Metastatic HER2-Positive Breast Cancer

A third of people treated with Nerlynx plus capecitabine experienced remission.

February 26, 2020 By Food and Drug Administration (FDA)

On February 25, 2020, the Food and Drug Administration approved neratinib (NERLYNX, Puma Biotechnology, Inc.) in combination with capecitabine for adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Efficacy of neratinib with capecitabine was investigated in NALA (NCT01808573), a randomized, multicenter, open-label clinical trial in 621 patients with metastatic HER2-positive breast cancer who received two or more prior anti-HER2 based regimens in the metastatic setting. Patients were randomized (1:1) to receive neratinib 240 mg orally once daily on days 1-21 with capecitabine 750 mg/m^2 given orally twice daily on days 1-14 for each 21-day cycle (n=307) or lapatinib 1250 mg orally once daily on days 1-21 with capecitabine 1000 mg/m^2 given orally twice daily on days 1-14 for each 21-day cycle (n=314). Patients were treated until disease progression or unacceptable toxicity.

The primary efficacy outcome measures were progression-free survival (PFS), assessed by a blinded independent central review per RECIST v1.1, and overall survival (OS). Key secondary outcome measures were objective response rate (ORR) and response duration. Median PFS was 5.6 months (95% CI: 4.9, 6.9) for patients who received neratinib with capecitabine and 5.5 months (95% CI: 4.3, 5.6) for those receiving lapatinib with capecitabine (hazard ratio 0.76; 95% CI: 0.63, 0.93; p=0.0059). The PFS rate at 12 months was 29% (95% CI: 23, 35) vs 15% (95% CI: 10, 20), respectively.

Median OS was 21 months (95% CI: 17.7, 23.8) for patients receiving neratinib with capecitabine compared to 18.7 months (95% CI: 15.5, 21.2) for those receiving lapatinib plus capecitabine (HR 0.88; 95% CI: 0.72, 1.07; p=0.2086). The ORR was 32.8% (95% CI: 27.1, 38.9) vs 26.7% (95% CI: 21.5, 32.4), respectively. Median response duration was 8.5 (95% CI: 5.6, 11.2) vs 5.6 months (95% CI: 4.2, 6.4), respectively.

The most common adverse reactions of any grade (>5%) in the neratinib plus capecitabine arm were diarrhea, nausea, vomiting, decreased appetite, constipation, fatigue/asthenia, weight decreased, dizziness, back pain, arthralgia, urinary tract infection, upper respiratory tract

infection, abdominal distention, renal impairment, and muscle spasms. The most frequently reported Grade 3 or 4 adverse reactions were diarrhea, nausea, vomiting, fatigue and decreased appetite.

The recommended neratinib dose for advanced or metastatic breast cancer is 240 mg (6 tablets) given orally once daily with food on days 1-21 of a 21-day cycle plus capecitabine (750 mg/m^2 given orally twice daily) on days 1-14 of a 21-day cycle until disease progression or unacceptable toxicities.

View full prescribing information for NERLYNX.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment. This application was approved 2 months prior to the FDA goal date.

Neratinib 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.

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