FDA Approves Orserdu for Certain Patients With HER2-Negative Advanced Breast Cancer

Orserdu (elacestrant) is the first treatment for people with ESR1 mutations, which can drive resistance to standard hormone therapy.

February 3, 2023 By Food and Drug Administration (FDA)

FDA approves elacestrant for ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer

On January 27, 2023, the Food and Drug Administration (FDA) approved elacestrant (Orserdu, Stemline Therapeutics, Inc.) for postmenopausal women or adult men with ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.

FDA also approved the Guardant360 CDx assay as a companion diagnostic device to identify patients with breast cancer for treatment with elacestrant.

Efficacy was evaluated in EMERALD (NCT03778931), a randomized, open-label, active-controlled, multicenter trial that enrolled 478 postmenopausal women and men with ER-positive, HER2-negative advanced or metastatic breast cancer of which 228 patients had ESR1 mutations. Patients were required to have disease progression on one or two prior lines of endocrine therapy, including one line containing a CDK4/6 inhibitor. Eligible patients could have received up to one prior line of chemotherapy in the advanced or metastatic setting.

Patients were randomized (1:1) to receive elacestrant 345 mg orally once daily (n=239) or investigator's choice of endocrine therapy (n=239), which included fulvestrant (n=166) or an aromatase inhibitor (n=73). Randomization was stratified by ESR1 mutation status (detected vs. not detected), prior treatment with fulvestrant (yes vs. no), and visceral metastasis (yes vs. no). ESR1 mutational status was determined by blood circulating tumor deoxyribonucleic acid (ctDNA) using the Guardant360 CDx assay and was limited to ESR1 missense mutations in the ligand binding domain.

The major efficacy outcome measure was progression-free survival (PFS), assessed by a blinded imaging review committee. A statistically significant difference in PFS was observed in the intention to treat (ITT) population and in the subgroup of patients with ESR1 mutations.

In the 228 (48%) patients with ESR1 mutations, median PFS was 3.8 months (95% CI: 2.2, 7.3) in the elacestrant arm and 1.9 months (95% CI: 1.9, 2.1) in the fulvestrant or aromatase inhibitor arm (hazard ratio [HR] of 0.55 [95% CI: 0.39, 0.77], 2-sided p-value=0.0005).

An exploratory analysis of PFS in the 250 (52%) patients without ESR1 mutations showed a HR 0.86 (95% CI: 0.63, 1.19) indicating that the improvement in the ITT population was primarily attributed to the results seen in the ESR1 mutated population.

The most common adverse events (≥10%), including laboratory abnormalities, were musculoskeletal pain, nausea, increased cholesterol, increased AST, increased triglycerides, fatigue, decreased hemoglobin, vomiting, increased ALT, decreased sodium, increased creatinine, decreased appetite, diarrhea, headache, constipation, abdominal pain, hot flush, and dyspepsia.

The recommended elacestrant dose is 345 mg taken orally with food once daily until disease progression or unacceptable toxicity.

View full prescribing information for Orserdu.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment. This application was granted priority review and fast track 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.

This announcement was published by the Food and Drug Administration on January 27, 2023.
