FDA approves talazoparib for gBRCAm HER2-negative locally advanced or metastatic breast cancer

On October 16, 2018, the Food and Drug Administration approved talazoparib (TALZENNA, Pfizer Inc.), a poly (ADP-ribose) polymerase (PARP) inhibitor, for patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative locally advanced or metastatic breast cancer. Patients must be selected for therapy based on an FDA-approved companion diagnostic for talazoparib.

Approval was based on EMBRACA (NCT01945775), an open-label trial randomizing 431 patients (2:1) with gBRCAm HER2-negative locally advanced or metastatic breast cancer to receive talazoparib (1 mg) or physician's choice of chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine). All patients were required to have a known deleterious or suspected deleterious gBRCA mutation and must have received no more than 3 prior cytotoxic chemotherapy regimens for locally advanced or metastatic disease. Patients were required to have received treatment with an anthracycline and/or a taxane (unless contraindicated) in the neoadjuvant, adjuvant, and/or metastatic treatment setting.

The primary efficacy outcome was progression-free survival (PFS) according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, as assessed by blinded independent central review. Estimated median PFS was 8.6 and 5.6 months in the talazoparib and chemotherapy arms, respectively (HR 0.54; 95% CI: 0.41, 0.71; p<0.0001).

The prescribing information includes warnings and precautions for myelodysplastic syndrome/acute myeloid leukemia, myelosuppression, and embryo-fetal toxicity. Most common (≥20%) adverse reactions of any grade were fatigue, anemia, nausea, neutropenia, headache, thrombocytopenia, vomiting, alopecia, diarrhea, decreased appetite.

FDA also approved the BRACAnalysis CDx test (Myriad Genetic Laboratories, Inc.) to identify patients with breast cancer with deleterious or suspected deleterious gBRCAm who are eligible for talazoparib. The effectiveness of the BRACAnalysis CDx test was based on the EMBRACA trial population for whom deleterious or suspected deleterious gBRCAm status was confirmed with either prospective or retrospective testing with BRACAnalysis CDx.

The recommended talazoparib dose is 1 mg taken as a single oral daily dose, with or without food.

View full prescribing information for TALZENNA (https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf).

FDA granted this application priority review. FDA expedited programs are described in the **Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics (http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf)**.

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 (http://www.fda.gov/medwatch/report.htm)** or by calling 1-800-FDA-1088.

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