FDA Approves Lynparza for Metastatic Prostate Cancer

PARP inhibitor delays disease progression for patients with harmful BRCA and related mutations.

May 21, 2020 By Food and Drug Administration (FDA)

FDA approves olaparib for HRR gene-mutated metastatic castration-resistant prostate cancer

On May 19, 2020, the Food and Drug Administration approved olaparib (LYNPARZA, AstraZeneca Pharmaceuticals, LP) for adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), who have progressed following prior treatment with enzalutamide or abiraterone.

Today, the FDA also approved FoundationOne CDx (Foundation Medicine, Inc.) for selection of patients with mCRPC carrying HRR gene alterations and BRACAnalysis CDx test (Myriad Genetic Laboratories, Inc.) for selection of patients with mCRPC carrying germline BRCA1/2 alterations as companion diagnostic devices for treatment with olaparib.

Efficacy was investigated in PROfound (NCT02987543), an open-label, multicenter trial randomizing (2:1) 256 patients to olaparib 300 mg twice daily and 131 patients to investigator's choice of enzalutamide or abiraterone acetate. All patients received a GnRH analog or had prior bilateral orchiectomy. Patients were divided into two cohorts based on their HRR gene mutation status. Patients with mutations in either BRCA1, BRCA2, or ATM were randomized in Cohort A (N=245); patients with mutations among 12 other genes involved in the HRR pathway were randomized in Cohort B (N=142); those with co-mutations (Cohort A gene and a Cohort B gene) were assigned to Cohort A.

The major efficacy outcome of the trial was radiological progression-free survival (rPFS) (Cohort A). Additional efficacy outcomes included confirmed objective response rate (ORR) (Cohort A) in patients with measurable disease, rPFS (combined Cohorts A+B), and overall survival (OS) (Cohort A).

A statistically significant improvement was demonstrated for olaparib compared to investigator's choice in Cohort A for rPFS with a median of 7.4 months vs 3.6 months (HR 0.34; 95% CI: 0.25, 0.47; $p<0.0001$), for OS with a median of 19.1 months vs. 14.7 months (HR 0.69; 95% CI: 0.50, 0.97, $p=0.0175$) and for ORR 33% vs 2% ($p<0.0001$). A statistically significant improvement for olaparib compared to investigator's choice was also demonstrated for rPFS in Cohort A+B, with a

median of 5.8 months vs. 3.5 months (HR 0.49; 95% CI: 0.38, 0.63; p<0.0001).

The most common adverse reactions in PROfound for olaparib (≥10% of patients) were anemia, nausea, fatigue (including asthenia), decreased appetite, diarrhea, vomiting, thrombocytopenia, cough and dyspnea. Venous thromboembolic events, including pulmonary embolism, occurred in 7% of patients randomized to the olaparib arm compared to 3.1% of those receiving enzalutamide or abiraterone.

The recommended olaparib dose is 300 mg taken orally twice daily, with or without food.

View full prescribing information for Lynparza.

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

Olaparib was granted priority review and breakthrough therapy 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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