FDA Approves Akeega for Metastatic Prostate Cancer

Patients taking the combination with prednisone saw an improvement in progression-free survival.

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FDA approves niraparib and abiraterone acetate plus prednisone for BRCA-mutated metastatic castration-resistant prostate cancer

On August 11, 2023, the Food and Drug Administration approved the fixed dose combination of niraparib and abiraterone acetate (Akeega, Janssen Biotech, Inc.), with prednisone, for adult patients with deleterious or suspected deleterious BRCA-mutated castration-resistant prostate cancer (mCRPC), as determined by an FDA-approved test.

View full prescribing information for Akeega.

Efficacy was evaluated in Cohort 1 of MAGNITUDE (NCT03748641), a randomized, double-blind, placebo-controlled trial enrolling 423 patients with homologous recombination repair (HRR) gene-mutated mCRPC. Patients were randomized (1:1) to receive niraparib 200 mg and abiraterone acetate 1,000 mg plus prednisone 10mg daily or placebo and abiraterone acetate plus prednisone daily.

Patients were required to have a prior orchiectomy or be receiving gonadotropin-releasing hormone (GnRH) analogues. Patients with mCRPC were eligible if they had not received prior systemic therapy in the mCRPC setting except for a short duration of prior abiraterone acetate plus prednisone (up to four months) and ongoing ADT.

Patients could have received prior docetaxel or androgen-receptor (AR) targeted therapies in earlier disease settings. Randomization was stratified by prior docetaxel, prior AR targeted therapy, prior abiraterone acetate plus prednisone, and BRCA status. Of the 423 patients enrolled, 225 (53%) had prospectively determined BRCA gene mutations (BRCAm). No benefit was observed in mCRPC patients without an HRR gene mutation (Cohort 2 of MAGNITUDE) as the criterion for futility was met.

The major efficacy outcome measure was radiographic progression-free survival (rPFS) per RECIST version 1.1 for soft tissue and Prostate Cancer Working Group 3 criteria for bone, assessed by blinded independent central review. Overall survival (OS) was an additional endpoint.

A statistically significant improvement in rPFS for niraparib and abiraterone acetate plus prednisone compared to placebo and abiraterone acetate plus prednisone was observed in BRCAm patients with a median of 16.6 months vs 10.9 months (HR 0.53; 95% CI 0.36, 0.79; p=0.0014). An exploratory OS analysis in the BRCAm patients demonstrated a median of 30.4 vs 28.6 months (HR 0.79; 95% CI: 0.55, 1.12) favoring the investigational arm. While a statistically significant improvement in rPFS was seen in the overall Cohort 1 intention to treat (ITT) HRR population (HR 0.73; 95% CI 0.56, 0.96; p=0.0217), in the subgroup of 198 (47%) patients with non-BRCA HRR mutations, the rPFS hazard ratio was 0.99 (95% CI: 0.67, 1.44) and the OS hazard ratio was 1.13 (95% CI: 0.77, 1.64), indicating that the improvement in the ITT HRR gene-mutated population was primarily attributed to the results seen in the subgroup of patients with BRCAm.

The most common adverse reactions (≥20%), including laboratory abnormalities, were decreased hemoglobin, decreased lymphocytes, decreased white blood cells, musculoskeletal pain, fatigue, decreased platelets, increased alkaline phosphatase, constipation, hypertension, nausea, decreased neutrophils, increased creatinine, increased potassium, decreased potassium, and increased AST. Among all patients with mCRPC treated with niraparib and abiraterone acetate plus prednisone in Cohort 1 of MAGNITUDE (n=423), 27% required a blood transfusion, including 11% who required multiple transfusions.

The recommended Akeega dose is 200 mg niraparib and 1,000 mg abiraterone acetate taken orally once daily in combination with 10 mg of prednisone daily until disease progression or unacceptable toxicity. Patients receiving niraparib and abiraterone acetate plus prednisone should also receive a GnRH analog concurrently or should have had bilateral orchiectomy.

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

This application was granted priority review. 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.

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