FDA Approves Rucaparib for the Treatment of Adults With mCRPC

Key Takeaways

- Rucaparib is approved for mCRPC with BRCA mutations after androgen receptor-directed therapy, based on the TRITON3 trial results.
- The TRITON3 trial showed longer progression-free survival with rucaparib compared to control therapies in BRCA and ATM mutation subgroups.
- Common adverse events of rucaparib include fatigue, nausea, and anemia, with no reported cases of myelodysplastic syndrome or acute myeloid leukemia.
- Rucaparib's prescribing information includes warnings for myelodysplastic syndrome/acute myeloid leukemia and embryo-fetal toxicity.

The approval was supported by findings from the TRITON3 trial, which enrolled certain patients with metastatic castration-resistant prostate cancer (mCRPC).

The FDA has approved rucaparib (Rubraca; Pharmaand GmbH) for the treatment of adult patients with a deleterious BRCA mutation (BRCAm; germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) previously treated with an androgen receptor-directed therapy.[1]

What is Rucaparib?

Rucaparib is a PARP inhibitor approved for the maintenance treatment of ovarian cancer, fallopian tube cancer, or primary peritoneal cancer with a certain type of inherited (germline) or acquired (somatic) abnormal BRCA gene for patients whose cancer has come back and who are responding (complete or partial response) to a platinum-based chemotherapy. It is also approved for the treatment of CRPC that has spread to other parts of the body, in a certain type of germline or somatic abnormal BRCA gene, and in previously treated disease with certain therapies.2 Rucaparib was granted an accelerated approval for this indication in May 2020.[3]

How Did Rucaparib Receive FDA Approval?

The agent received approval following support from the TRITON3 trial (NCT02975934)4, a randomized, open-label phase 3 study that was required from the 2020 accelerated approval to confirm the efficacy and clinical benefit of rucaparib. A total of 405 patients with mCRPC—of whom 302 had BRCAm and 103 had ATM mutations (ATMm)—who progressed on a prior androgen receptor pathway inhibitor (ARPI) and did not receive prior chemotherapy in the castration-resistant setting were enrolled. Results from the TRITON3 trial were published in The New England Journal of Medicine.[1,4,5]

Patients were randomly assigned to receive either rucaparib, the physician’s choice of an ARPI that they had not previously received (enzalutamide [Xtandi; Astellas Pharma, Pfizer], abiraterone acetate [Zytiga; Janssen Biotech]), or docetaxel. Randomization was stratified by

performance status, presence of hepatic metastases, and type of mutation (BRCA1m, BRCA2m, or ATMm). Additionally, patients maintained a castrate level of testosterone via treatment with either androgen deprivation therapy or prior surgical castration.[1,4]

At the 62-month point, the duration of imaging-based progression-free survival (PFS) was significantly longer in the rucaparib group than in the control group, both in the BRCAm subgroup (median: 11.2 months and 6.4 months, respectively; HR, 0.50 [95% CI, 0.36–0.69]) and in the intention-to-treat group (median: 10.2 months and 6.4 months, respectively; HR, 0.61 [95% CI, 0.47–0.80]; P < .001 for both comparisons). Additionally, in an exploratory analysis in the ATMm subgroup, the median duration of imaging-based PFS was about 8.1 and 6.8 months in the rucaparib and control groups, respectively (HR, 0.95 [95% CI, 0.59–1.52]).[5]

The most frequent adverse events (AEs) with rucaparib were fatigue, nausea, and anemia. The TRITON3 investigators wrote that treatment interruption or dose reduction should be considered to mitigate these AEs. There were no cases of myelodysplastic syndrome or acute myeloid leukemia reported, and the risk of thromboembolic events was shown to be lower than or similar to the risk associated with control medications.5 Additionally, the FDA states that rucaparib's prescribing information includes warnings and precautions for myelodysplastic syndrome/acute myeloid leukemia and embryo-fetal toxicity.[1]

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