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Positive Quality Intervention: Use of Rucaparib (Rubraca®) and Indications

Description: The purpose of this PQI is to discuss the various indications and management of rucaparib (Rubraca®).

Background: Rucaparib is an oral tricyclic indole and inhibitor of poly(ADP-ribose) polymerases (PARPs) PARP 1, PARP 2 and PARP 3, with antineoplastic activity.[1] PARPs are a group of enzymes activated by single-strand DNA breaks. PARP inhibitors block the ability of PARP to repair DNA that has been damaged including the recruitment of other DNA repair proteins.[2] Rucaparib selectively binds to PARP 1, 2 and 3 and inhibits PARP mediated DNA repair. The enhanced accumulation of DNA strand breaks ultimately promotes genomic instability and leads to cell arrest and apoptosis. This activity may also increase the cytotoxicity of DNA-damaging agents possibly reversing resistance to chemotherapy and radiation therapy. Rucaparib is indicated as maintenance treatment in adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Rucaparib is also indicated in adult patients with a deleterious BRCA mutation- associated metastatic castration resistant prostate cancer who have been previously treated with androgen receptor-directed therapy and taxane-based chemotherapy. Rucaparib has also been given an NCCN category 2A rating in the maintenance treatment of adult patients with metastatic pancreatic cancer that is associated with a pathogenic germline or somatic variant in BRCA1, BRCA2, or PALB2 mutation who did not have disease progression following their most recent platinum-based chemotherapy.[3,4]

PQI Process:

- Rucaparib starting dose for any indication is 600 mg (2 x 300 mg tabs) taken twice daily
- No initial dose adjustment required for renal or hepatic impairment
- May be taken with or without food
- Treatment should be continued until disease progression or toxicity
- If the patient is receiving rucaparib for metastatic castration-resistant prostate cancer (mCRPC) they should also be receiving a gonadotropin-releasing hormone (GnRH) analog
- If the mCRPC patient is not receiving a GnRH they should have had a bilateral orchiectomy
- Most common ADR's requiring dose adjustment in ovarian cancer based on ARIEL 3 study[4]
    - Thrombocytopenia
    - Anemia
    - Nausea
    - Fatigue/asthenia
- Most common ADR's requiring dose adjustment in mCRPC based on TRITON2 study[4]
    - Anemia
    - Asthenia/fatigue
    - Thrombocytopenia
    - Nausea

Table 1. Recommended Dose Modification Schedule for Adverse Reactions[4]

Dose Reduction	Dose
Starting Dose	600 mg twice daily (2 x 300 mg tablets)
First Dose Reduction	500 mg twice daily (2 x 250 mg tablets)
Second Dose Reduction	400 mg twice daily (2 x 200 mg tablets)
Third Dose Reduction	300 mg twice daily (1 x 300 mg tablet)

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Available Tablet Strengths:

- 200 mg tablet – blue, round, film coated, "C2" imprint
- 250 mg tablet – white, diamond, film coated "C25" imprint
- 300 mg tablet – yellow, oval, immediate release, film coated "C3" imprint

Patient Centered Activities:

- Patient Education
  - Provide Oral Chemotherapy Education (OCE) Sheet
  - Patients may have their dose adjusted several times during their course of treatment
  - If the patient misses a dose they should skip the missed dose and resume their regular dosing schedule
  - Rucaparib should be stored at room temperature, away from heat, moisture and light

- Monitoring
  - Myelodysplastic syndrome/ acute myeloid leukemia have occurred, Grades 3 or 4 (8%) in patients taking rucaparib[4]
  - Monitor for hematologic toxicity at baseline and monthly
  - Monitor for symptoms of fatigue, anemia and AST/ALT elevation
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. National Center for Biotechnology Information. "PubChem Compound Summary for CID 9931954, Rucaparib" *PubChem*, https://pubchem.ncbi.nlm.nih.gov/compound/Rucaparib. Accessed 25 June, 2021.
2. NCI, S., May 20, 2021, & April 22, 2021. (2020, June 11). *FDA Approves Olaparib, Rucaparib to Treat Prostate Cancer*. National Cancer Institute. https://www.cancer.gov/news-events/cancer-currents-blog/2020/fda-olaparib-rucaparib-prostate-cancer.
3. Reiss KA, Mick R, O'Hara MH, et al. Phase II study of maintenance rucaparib in patients with platinum-sensitive advanced pancreatic cancer and a pathogenic germline or somatic variant in BRCA1, BRCA2, or PALB2. J Clin Oncol. 2021;39(22):2497-2505.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Cancer V.1.2022. © National Comprehensive Cancer Network, Inc. 2022.
5. Rubraca (rucaparib) [Package Insert].