Written By: Ibrahim Ahsan, PharmD, BCPS
Tomah Health

Positive Quality Intervention: Olaparib (Lynparza®) Expansion with Bevacizumab (Avastin®)

Description: The purpose of this PQI is to expand on the indication of olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, when used in combination with bevacizumab, a vascular endothelial growth factor (VEGF)-directed monoclonal antibody.[1,3]

Background: The Food and Drug Administration (FDA) has expanded the indication for olaparib in combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either a deleterious or suspected deleterious BRCA mutation, and /or genomic instability.[2] The FDA has approved myChoice® CDx, which is a tumor test that determines HRD positive status by detecting BRCA1 and BRCA2 variants and assessing genomic instability, as a diagnostic for olaparib.[4] Efficacy of this combination was investigated in PAOLA-1, a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer following first-line platinum-based chemotherapy and bevacizumab. After a median follow-up of 22.9 months, the median progression-free survival was 22.1 months with olaparib plus bevacizumab and 16.6 months for placebo plus bevacizumab (Hazard ratio (HR) for disease progression or death, 0.59; 95% CI, 0.49-0.72, $p<0.001$). The HR for disease progression or death was 0.33 (95% CI, 0.25-0.45) in patients with tumors positive for HRD, including tumors that had BRCA mutations (median progression-free survival 37.2 vs 17.7 months), and 0.43 (95% CI, 0.28-0.66) in patients with HRD-positive tumors that did not have BRCA mutations (median progression-free survival, 28.1 vs 16.6 months).[5]

PQI Process: Upon receipt of an order for combination therapy with olaparib and bevacizumab:[1,3]

- Verify indication for approved treatment as first-line maintenance therapy for adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and who express HRD-positive tumors
- Consider olaparib warnings/precautions including new primary malignancies (specifically myelodysplastic syndrome & acute myeloid leukemia) and pneumonitis: Monitor CBC at baseline and monthly, and confirm hematologic toxicities from previous chemotherapies have resolved to ≤ grade 1 before starting olaparib
- Due to risk of embryofetal toxicity, women of child bearing protentional should undergo pregnancy testing prior to olaparib initiation
- Avoid olaparib concomitant use with strong or moderate CYP3A inhibitors/inducers due to risk of toxicity
- Consider bevacizumab warnings/precautions including severe hypertension and proteinuria: Monitor blood pressure regularly every 2-3 weeks during treatment and monitor renal function (SCr, BUN) and screen regularly for proteinuria via serial dipstick urine analysis
- Dosing:
    - Olaparib tablets 300 mg by mouth twice daily, continued until disease progression, unacceptable toxicity, or completion of two years of treatment
        - Dose modifications:
            - Management of adverse reactions: Recommended 250 mg twice daily followed by 200 mg twice daily if required
            - Renal impairment:
                - Mild (CrCl 51-80 mL/min): No dosage adjustment

Written By: Ibrahim Ahsan, PharmD, BCPS
Tomah Health

        - Moderate (CrCl 31-50 mL/min): Reduce dose to 200 mg twice daily
        - Severe/end-stage renal disease (CrCl ≤ 30 mL/min): No available data
    - Olaparib is only available as tablets in the US, but is available as capsules and/or tablets in other regions; due to differences in dosing and bioavailability, tablets and capsules should not be substituted on a mg-per-mg basis
- Bevacizumab 15 mg/kg IV every 3 weeks for 15 months total, including the period given with chemotherapy and given with maintenance

Patient Centered Activities:[1,3]

- Provide Oral Chemotherapy Education (OCE) Sheet for olaparib and Intravenous Cancer Treatment Education (IVE) Sheet for bevacizumab
- Patients should be counseled on warning/precautions associated with olaparib and bevacizumab
- Inform patients that olaparib can be taken with or without food
- Patients should avoid grapefruit, Seville oranges, and their juices during treatment as these can lead to drug toxicities
- Patients should be educated on common reported adverse effects of combination olaparib with bevacizumab therapy including, fatigue (including asthenia), anemia, lymphopenia, neutropenia, leukopenia, nausea & vomiting, headache, and urinary tract infection
- Educate women of reproductive age to avoid pregnancy and to use effective contraception during treatment and for at least 6 months after the last dose of any of the agents involved in olaparib and bevacizumab combination therapy
- Women should discontinue breast-feeding during olaparib and/or bevacizumab therapy and for 1 month and 6 months after final dose of agents respectively
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Avastin® (Package Insert). Genentech Inc., South San Francisco, CA.
2. *FDA approves olaparib plus bevacizumab as maintenance treatment for ovarian, fallopian tube, or primary peritoneal cancers*. (2020, May 11). U.S. Food and Drug Administration. Retrieved January 30, 2022, from https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-olaparib-plus-bevacizumab-maintenance-treatment-ovarian-fallopian-tube-or-primary.
3. Lynparza® (Package Insert). AstraZeneca Pharmaceuticals LP, Wilmington, DE.
4. *myChoice® CDx*. (2020, July 8). Myriad Genetics, Inc. Retrieved January 30, 2022, from https://myriad.com/products-services/precision-medicine/mychoice-cdx/.
5. Ray-Coquard, I., Pautier, P., Pignata, S., et al. Olaparib plus Bevacizumab as First-Line Maintenance in Ovarian Cancer. *New England Journal of Medicine*, *381*(25), 2416–2428. https://doi.org/10.1056/nejmoa1911361.