

## 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.<sup>1,2</sup>

**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.<sup>3</sup> The FDA has approved myChoice® CDx, which is a tumor test that determines HRD status by detecting BRCA1 and BRCA2 variants and assessing genomic instability, as a diagnostic for olaparib.<sup>4</sup> The efficacy of this combination was investigated in PAOLA-1, a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib plus 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 61.7 months and 61.9 months, the median overall survival was 56.5 months with olaparib plus bevacizumab and 51.6 months for placebo plus bevacizumab (hazard ratio (HR) for disease progression or death, 0.92; 95% CI, 0.76-1.12; p=0.4118). The HR for disease progression or death was 0.62 (95% CI, 0.45-0.85) in patients with tumors positive for HRD, including tumors that had BRCA mutations (overall survival 5 years).<sup>5</sup>

**PQI Process:** Upon receipt of an order for combination therapy with olaparib and bevacizumab:<sup>1,2</sup>

- 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 childbearing potential should undergo pregnancy testing prior to olaparib initiation
- Avoid concomitant olaparib 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, 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: Decrease to 250 mg twice daily followed by 200 mg twice daily if required
      - Renal impairment:
        - Mild (CrCl 51-80 mL/min): No dosage adjustment
        - 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

**IMPORTANT NOTICE:** NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual's sole responsibility to seek guidance from a qualified healthcare professional. *Updated 12.19.23*

- Bevacizumab 15 mg/kg IV every 3 weeks for 15 months total, including the period given with chemotherapy and given with maintenance
- Refer to [Olaparib \(Lynparza®\) Adverse Event Management](#) PQI

### Patient-Centered Activities:<sup>1,2</sup>

- 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. [Lynparza® \(Package Insert\). AstraZeneca Pharmaceuticals LP, Wilmington, DE.](#)
3. *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>.
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>.

### Supplemental Information:

- Olaparib was previously available as both a tablet and a capsule, and the two dosage forms had different bioavailability therefore are not interchangeable on a milligram-per-milligram basis
  - Capsules were discontinued August 2018; only the tablets are currently available in the United State