Positive Quality Intervention: Olaparib (Lynparza®) Clinical Management

Description: This PQI will highlight its place in therapy in these disease states, safety profiles, and clinical pearls regarding dose adjustment.

Background: Olaparib is a poly ADP-ribose polymerase (PARP) enzyme inhibitor and is FDA approved for

- First-line maintenance BRCAm advanced ovarian cancer
- First-line maintenance HRD-Positive advanced ovarian cancer in combination with bevacizumab
- Maintenance BRCA-mutated recurrent ovarian cancer
- Adjuvant treatment of gBRCAm, HER2 negative, high-risk early breast cancer
- gBRCA, HER2 negative metastatic breast cancer
- First-line maintenance gBRCAm metastatic pancreatic cancer
- HRR gene-mutated metastatic castration-resistant prostate cancer
- BRCAm metastatic castration-resistant prostate cancer in combination with abiraterone and prednisone or prednisolone

A summary of the clinical trials that led to the approval of the above indications can be found in the Supplemental Information.

PQI Process:

- Verify correct dose
  - Typical starting dose for all FDA-approved indications: 300 mg orally twice daily
  - Available as 100 mg and 150 mg tablets
  - The dose of olaparib must be adjusted to 200 mg twice daily for renal dysfunction when creatinine clearance is ≤ 50 mL/minute; olaparib has not been studied in patients with creatinine clearance ≤ 30 mL/minute
- Dose adjustments for adverse reactions
  - Consider holding treatment or dose reductions if patients experience adverse reactions

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<thead>
<tr>
<th>Dose reduction</th>
<th>Recommended Dose</th>
<th>How to Supply</th>
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<tr>
<td>1st dose reduction</td>
<td>250 mg BID</td>
<td>One 150 mg tablet + one 100 mg tablet BID</td>
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<tr>
<td>2nd dose reduction</td>
<td>200 mg BID</td>
<td>Two 100 mg tablets BID</td>
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- Drug interactions
  - Avoid concomitant use with moderate and/or strong CYP3A4 inhibitors
    - If a strong CYP3A4 inhibitor must be used concomitantly, the olaparib dose should be reduced to 100 mg twice daily
    - If a moderate CYP3A4 inhibitor must be used concomitantly, the olaparib dose should be reduced to 150 mg twice daily
  - Avoid concomitant strong CYP3A4 inducers; if a moderate CYP3A inducer must be used, there is the potential for reduced efficacy of olaparib

- Laboratory monitoring
  - Complete blood counts should be performed at baseline and monthly thereafter
  - Renal function should be verified at baseline and periodically thereafter
  - Taking other anticancer agents may cause a potentiation/prolongation of myelosuppression

Patient-Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet

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1/3
• Counsel patient on side effect profile (see supplemental information and Olaparib (Lynparza®) Adverse Event Management PQI)
• Instruct patient to avoid grapefruit, grapefruit juice, Seville oranges, and/or Seville orange juice
• Advise effective contraception during treatment and for 3 months (males) or 6 months (females) of reproductive potential after the last dose
• Patient Assistance: NCODA Financial Assistance Tool

References:
1. Lynparza® (olaparib) [package insert].
10. Oya M, et al. 157O Biomarker analysis and updated results from the phase III PROpel trial of abiraterone (abi) and olaparib (ola) vs abi and placebo (pbo) as first-line (1L) therapy for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). Annals of Oncology. 2022;33:S1495. doi:https://doi.org/10.1016/j.annonc.2022.10.194.

Supplemental Information:
Current FDA-approved indications: Starting dose is 300 mg twice daily for all indications

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<tr>
<th>Indication</th>
<th>Efficacy</th>
<th>Safety</th>
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<td>First-line maintenance treatment for deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients who are in a complete or partial response to first-line platinum-based chemotherapy (SOLO-1)</td>
<td>mPFS results: olaparib 56 months vs placebo 13.8 months 5-Year PFS: olaparib 48% vs placebo 21%</td>
<td>Most common AEs with olaparib: nausea, vomiting, fatigue, anemia, diarrhea Serious AEs occurred in 21% of olaparib patients vs 12% of placebo patients, most commonly anemia</td>
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<td>In combination with bevacizumab for maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients who are in a 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 deleterious or suspected deleterious BRCA mutation and/or genomic instability PAOLA-1 trial</td>
<td>Reduced the risk of disease progression or death by 67% (equal to HR of 0.33) and improved progression-free survival to a median of 37.2 months vs 17.7 months with bevacizumab alone Higher Risk: mPFS olaparib 36.0 vs. 16.0 bevacizumab Lower Risk: mPFS olaparib Not Reached vs. 22.1 bevacizumab</td>
<td>Adverse reactions (Grade 1-4) occurring in ≥10% of patients treated with olaparib/bevacizumab in PAOLA-1 compared with the placebo/bevacizumab arm were nausea (53%), fatigue (including asthenia) (53%), anemia (41%), lymphopenia (24%), vomiting (22%), and leukopenia (18%), diarrhea (18%), neutropenia (18%), urinary tract infection (15%), and headache (14%)</td>
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<td>Maintenance treatment for recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer for patients who are in a complete or partial response to platinum-based chemotherapy – 2 randomized trials completed SOLO-2 trial</td>
<td>SOLO-2: PFS: olaparib 19.1 months vs placebo 5.5 months OS: olaparib 51.7 months vs placebo 38.8 months Study 19: PFS: olaparib 8.4 months vs placebo 4.8 months;</td>
<td>SOLO-2: Most common Grade 1/2 AEs in both groups: nausea, fatigue, vomiting, abdominal pain, and diarrhea Most common ≥ Grade 3 AE: anemia</td>
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<td>SOLO-2:</td>
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<th>Study 19</th>
<th>OS: olaparib 29.8 months vs placebo 27.8 months</th>
<th>63%), vomiting (35%), diarrhea (28%), anemia (23%), constipation (22%), respiratory tract infection (22%), decreased appetite (21%), and headache (21%)</th>
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<td>Deleterious or suspected deleterious gBRCAm advanced ovarian cancer after ≥3 prior lines of chemotherapy</td>
<td>Single arm trial PFS results: ORR: 34%; Median DoR: 7.9 months</td>
<td>Serious AEs reported in 30% of patients, most frequently anemia, abdominal pain</td>
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<td><strong>Breast Cancer</strong></td>
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<td>Deleterious or suspected deleterious gBRCAm, HER2-negative metastatic breast cancer after treatment with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting</td>
<td>PFS: olaparib 7 months vs chemotherapy 4.2 months; ORR: olaparib 52% vs chemotherapy 23%; OS: olaparib 19.3 months vs chemotherapy 17.2 months</td>
<td>Rate of ≥ Grade 3 AEs olaparib (36.6%) vs chemotherapy (50.5%); AEs that occurred more frequently with olaparib: anemia, nausea, vomiting, fatigue, headache, and cough</td>
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<td>OlympiAD trial⁷</td>
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<td><strong>Pancreatic Cancer</strong></td>
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<td>Maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen POLO trial⁸</td>
<td>PFS: olaparib vs. placebo: median 7.4 months vs 3.8 months ORR: 23% in olaparib vs 12% in placebo OS: olaparib 19.3 months vs placebo 17.1 months</td>
<td>Most common AE at grades 3-4 for olaparib: anemia (11%); All grades AE &gt;30% for olaparib: Fatigue (60%), nausea (45%), abdominal pain (34%); All grade diarrhea occurred at a rate of 29%</td>
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<td><strong>Prostate Cancer</strong></td>
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<td>Treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone PROfound trial⁹</td>
<td>Reduced risk of disease progression or death by 66% (HR 0.34) Radiographic PFS median of 7.4 months vs 3.6 months with enzalutamide or abiraterone in men with BRCA1/2 or ATM gene-mutated mCRPC OS: olaparib 19.1 months vs placebo 14.7 months</td>
<td>PROfound: Most common AE (Grade 1-4) occurring in ≥10% in the olaparib arm were anemia (46%), fatigue (41%), nausea (41%), vomiting (30%), decreased appetite (25%), thrombocytopenia (12%), cough (11%) and dyspnea (10%); Venous thromboembolic events, including pulmonary embolism occurred in 7% of patients with mCRPC who received olaparib plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT</td>
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<td>PROpel trial¹⁰</td>
<td>Radiographic PFS: olaparib + abiraterone 30% vs placebo + abiraterone 74%; OS: olaparib + abiraterone 28% vs placebo + abiraterone 66%</td>
<td>Most common AE (≥10%) in patients receiving olaparib plus abiraterone were anemia (48%), fatigue (38%), nausea (30%), diarrhea (19%), decreased appetite (16%), lymphopenia (14%), dizziness (14%), and abdominal pain (13%). Seventy-two patients (18%) required at least one blood transfusion and 46 (12%) required multiple transfusions.</td>
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PFS: progression free survival; AEs: adverse events; ORR: objective response rates; DoR: duration of response

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 States