National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Katie Carter, PharmD, BCPS
Indiana University Health
Updated 9.29.2020

Positive Quality Intervention: Olaparib Clinical Management

Description:

Olaparib (Lynparza) is a poly ADP-ribose polymerase (PARP) enzyme inhibitor and is FDA approved as a targeted therapy for *BRCA*-mutated breast cancer, ovarian, and pancreatic cancer as well as prostate cancer. This PQI will highlight its place in therapy in these disease states, safety profiles, and clinical pearls regarding dose adjustment.

Background:

Breast Cancer

About 5-10% of breast cancers can be associated with gene mutations inherited from a parent, most commonly mutations in the *BRCA*1 and *BRCA*2 genes.

Lifetime Risk of Developing Breast Cancer		
Mutation	Women	Men
BRCA1	Up to 72%	6.8%
BRCA2	69%	Less frequent cause

Ovarian Cancer

Currently, ovarian cancer is primarily treated with surgery and systemic chemotherapy. About 22% of ovarian cancer cases are related to a BRCA mutation (15% germline and 7% somatic).[14,15]

Pancreatic Cancer

Up to 7% of patients with pancreatic cancer have a g*BRCA* mutation. [16,17]

Prostate Cancer

Olaparib approved in May 2020 for patients with homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (Full indication list in *Supplemental Information)*

PQI Process:

- Verify the dosage form is correct
  - Olaparib was previously available as both a tablet and a capsule, and the two dosage forms had different bioavailability and therefore were not interchangeable on a milligram-per-milligram basis. The capsules were discontinued as of August 2018, and only the tablets are currently available.
  - Olaparib is available as 100 mg and 150 mg tablets.
- Verify the dose is correct
  - Typical starting dose for all FDA-approved indications: 300 mg orally twice daily
    - See Supplemental Information Section for current FDA-approved indications
  - The dose of olaparib must be adjusted to 200 mg twice daily for renal dysfunction when creatinine clearance is $\leq$ 50 mL/minute. Olaparib has not been studied in patients with creatinine clearance $\leq$ 30 mL/minute.

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PQI Process continued:

- Dose adjustments for adverse reactions
  - Consider holding treatment or dose reductions if patients experience adverse reactions.

Dose reduction	Recommended Dose	How to Supply
1st dose reduction	250 mg BID	One 150 mg tablet + one 100 mg tablet BID
2nd dose reduction	200 mg BID	Two 100 mg tablets BID

- 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 CYP3A 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

Patient Centered Activities:

- Provide Oral Chemotherapy Education Sheet
- Storage: Olaparib should be stored at room temperature and protected from moisture
- Handling: though not on the NIOSH list, Olaparib is considered hazardous due to its toxicity profile. Appropriate handling should be advised.
- Instruct patient to avoid grapefruit, grapefruit juice, Seville oranges, and/or Seville orange juice.

Copay Assistance:

- Commercially insurance patients who qualify can enroll in a $0 copay card assistance program through AstraZeneca's Access 360 program: www.MyAccess360.com

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Supplemental Information:

Current FDA-approved indications: (Starting dose is 300 mg twice daily for all indications)

Indication	Efficacy	Safety
Ovarian cancer		
First-line maintenance treatment for deleterious or suspected deleterious germline or somatic *BRCA*-mutated (g*BRCA*m or s*BRCA*m) 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 trial)	• PFS results (p-value <0.0001): olaparib vs placebo: NR vs 13.8 months • 70% lower risk of disease progression or death with olaparib than with placebo.	• 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
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)	• 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	• Adverse reactions (Grade 1-4) occurring in ≥10% of patients treated with olaparib/bevacizumab in PAOLA-1 and at ≥5% frequency compared with the placebo/bevacizumab arm were nausea (53%), fatigue (including asthenia) (53%), anemia (41%), lymphopenia (24%), vomiting (22%), and leukopenia (18%). • Most common adverse reactions (≥10%) for patients receiving olaparib/bevacizumab were diarrhea (18%), neutropenia (18%), urinary tract infection (15%), and headache (14%).
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 (SOLO-2 trial)	• PFS (p-value <0.0001): olaparib vs placebo: 19.1 months vs 5.5 months	• Most common grade 1-2 AEs in both groups: nausea, fatigue, vomiting, abdominal pain, and diarrhea • Most common grade 3 or higher AE with olaparib: anemia
Deleterious or suspected deleterious *gBRCAm* advanced ovarian cancer after ≥ 3 prior lines of chemotherapy	Single arm trial PFS results: • ORR: 34% • Median DoR: 7.9 months	• Serious AEs reported in 30% of patients, most frequently anemia, abdominal pain, intestinal obstruction, and pleural effusion

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Breast Cancer		
Deleterious or suspected deleterious g*BRCA*m, HER2-negative metastatic breast cancer after treatment with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting (OlympiAD trial)	• PFS (p-value 0.0009): • Olaparib vs chemotherapy: 7 months vs 4.2 months	• Rate of grade 3 or higher AEs was lower with olaparib (36.6%) vs chemotherapy (50.5%) • AEs that occurred more frequently in the olaparib group: anemia, nausea, vomiting, fatigue, headache, and cough
Pancreatic Cancer		
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 trial)	• PFS results (p-value 0.0035): olaparib vs. placebo: median 7.4 months vs. 3.8 months • ORR: 23% in olaparib arm (12% in placebo arm)	• Most common AE at grades 3-4 for olaparib: anemia (11%) • All grades AE that were >30%: Fatigue (60%), Nausea (45%), Abdominal pain (34%) • All grade Diarrhea at 29%
Prostate Cancer		
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 trial)	• Reduced risk of disease progression or death by 66% (HR 0.34, p-value <0.0001) • Radiographic PFS maiden of 7.4 months vs. 3.6 months with enzalutamide or abiraterone in men with *BRCA1/2* or *ATM* gene-mutated mCRPC	• Most common AE (Grade 1-4) occurring in ≥10% in the olaparib arm (N=256) were anemia (46%), nausea (41%), fatigue including asthenia (41%), decreased appetite (30%), diarrhea (21%), vomiting (18%), thrombocytopenia (12%), cough (11%) and dyspnea (10%).[1] • 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

PFS – progression free survival; AEs – adverse events; ORR – objective response rates; DoR – duration of response

Based on current February 2020 ASCO Guidelines[13]:

- Women diagnosed with epithelial ovarian cancer
  - Offer germline genetic testing for BRCA1/2 and other ovarian cancer susceptibility genes at time of diagnoses
  - First or second-degree blood relatives with a known germline susceptible gene mutation or variant
    - Should be offered individualized genetic risk evaluation/counseling and genetic testing
  - Genetic evaluations can be conducted in conjunction with HCPs including genetic counselors