PARP Inhibitors in the Management of Ovarian Cancer
ASCO Guideline Rapid Recommendation Update

Tew, W et al.
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Background & Methodology
Introduction

- In 2020, ASCO published a guideline on PARPi therapy in the management of ovarian cancer.¹
- In June 2022, the ATHENA-MONO² phase III multinational, double-blind RCT evaluating rucaparib monotherapy reported on the efficacy of rucaparib maintenance therapy compared with placebo in patients with stage III-IV epithelial ovarian cancer (EOC) who are in complete or partial response to first-line platinum-based chemotherapy.
- A significant improvement in PFS constituted a strong signal for an update of the 2020 ASCO guideline recommendation for first-line maintenance therapy.
- Furthermore, reports of detrimental OS from the ARIEL4 trial³ (rucaparib), SOLO3 trial (olaparib),⁴ and ENGOT-OV16/NOVA trial⁵ (niraparib) constituted safety signals for recommendation updates for treatment in recurrent platinum-sensitive EOC (BRCA mutation or HRD positive status) and in unselected patient population second-line maintenance treatment, respectively.
Development Methodology

• A targeted electronic literature search was conducted to identify any additional phase III RCTs of PARPi in this patient population.

• The Expert Panel reconvened to assess evidence and to review and approve the amended guideline.

• The ASCO Guideline methodology manual can be found at: www.asco.org/guideline-methodology
Rapid Recommendation Update
Rapid Recommendation Update

Recommendation 2.1.

• Patients with newly diagnosed stage III-IV EOC who are in complete or partial response to first-line platinum-based chemotherapy should be offered PARPi maintenance therapy in HGS or endometrioid ovarian cancer. For those with germline or somatic pathogenic or likely pathogenic variants in BRCA1 or BRCA2 genes, options should include olaparib (300 mg orally every 12 hours for 2 years), niraparib (200-300 mg orally daily for 3 years) or rucaparib (600 mg twice a day for 2 years). Longer duration could be considered in selected individuals after discussion of risks. For those who are HRD positive, determined using FDA-approved companion diagnostic tests, rucaparib and niraparib are options. Niraparib or rucaparib may be offered for non-BCRAmut/HRDneg patients.
Rapid Recommendation Update

Recommendation 3.0.

• PARPi monotherapy maintenance (second-line or more) may be offered to patients with EOC who have not already received a PARPi and who have responded to platinum-based therapy regardless of BRCA mutation status; treatment is continued until progression of disease or toxicity despite dose reductions and best supportive care. Options include: olaparib 300 mg every 12 hours, rucaparib 600 mg every 12 hours or niraparib 200-300 mg once daily.

• Maintenance treatment with niraparib for patients without germline or somatic BRCA mutation should weigh potential PFS benefit against possible overall survival decrement.
Rapid Recommendation Update

Recommendation 3.1./3.2

- PARPi monotherapy should not be routinely offered to patients for the treatment of recurrent platinum sensitive EOC.

- Evidence on PARPi use in this setting is evolving and data are continuing to emerge. Any decision to proceed with PARPi treatment in select populations (BRCA mutation, No prior PARPi use, Platinum Sensitive, Advanced Lines of Treatment) should be based on individualized patient and provider assessment of risks, benefits, and preferences.
Rapid Recommendation Update

Recommendation 3.3

- PARPi monotherapy is not recommended for treatment for patients with either BRCA wild-type or platinum-resistant recurrent EOC.
Summary of Previous Recommendations
Summary of Previous Recommendations

• Recommendations that are unchanged are provided in the following slides
Summary of Previous Recommendations

Recommendation 1.0.

• Repeating PARPi therapy in the treatment of EOC is not recommended at this time. Consideration should be made as to the best time in the life cycle of an individual patient’s EOC in which to use PARPi; clinical trial participation is encouraged.

Informal consensus

Evidence Quality
Insufficient

Strength of Recommendation
Strong
Summary of Previous Recommendations

Recommendation 2.0.

• PARPis are not recommended for use in initial treatment of early stage (stage I-II) EOC because there is insufficient evidence to support use in this population.
Summary of Previous Recommendations

Recommendation 2.2.

- The addition of olaparib to bevacizumab maintenance may be offered to patients who have stage III-IV HGS or endometrioid ovarian cancer and germline or somatic pathogenic or likely pathogenic variants in BRCA1 or BRCA2 genes and/or genomic instability, as determined by Myriad myChoiceCDx, and who have had a partial or complete response to chemotherapy plus bevacizumab combination.

Evidence-based

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<th>Evidence Quality</th>
<th>Strength of Recommendation</th>
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<td>High</td>
<td>Strong</td>
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Summary of Previous Recommendations

Recommendation 2.3.

- Inclusion of the PARPi veliparib with combination chemotherapy followed by veliparib maintenance therapy cannot be recommended at this time. There are no data that this approach is superior, equal, or less toxic than a switch maintenance.

Note: As of this writing, veliparib is not commercially available.
Summary of Previous Recommendations

Recommendation 4.0.

- PARPi are not recommended for use in combination with chemotherapy, other targeted agents, or immune-oncology agents in the recurrent setting outside the context of a clinical trial. Clinical trial participation is encouraged.
Summary of Previous Recommendations

Recommendation 5.0.

• Management of Toxicities - Anemia:
  a. Patients requiring a blood transfusion for symptom relief and/or hemoglobin level < 8 g/dL should be monitored. PARPi dose should be reduced with evidence of repeated anemia to avoid multiple transfusions.
  b. Patients with progressive anemia may be offered growth factor per ASCO guidelines and physician and patient comfort.
Summary of Previous Recommendations

Recommendation 5.1.

• Management of Toxicities - Neutropenia:
  a. Growth factor is not indicated for use in patients receiving daily PARPi.
  b. Neutropenia (grade 4 lasting at least 5-7 days or associated with fever) should result in dose hold until recovery of infection and granulocyte count, followed by dose reduction. Growth factor support may be used in this setting to support patient safety during the drug hold.
Summary of Previous Recommendations

Recommendation 5.2.

- Management of Toxicities - Platelets:
  a. Thrombocytopenia is most common with niraparib. Niraparib dosing guidelines should be used to lower starting dose (200 mg) based on weight and platelet count.
  b. Discontinue PARPi for persistent thrombocytopenia or significant bleeding despite dose reduction.
Summary of Previous Recommendations

Recommendation 5.3.

- Management of Toxicities – Persistent cytopenia:
  a. Evaluation for treatment-related myelodysplastic syndrome/acute myeloid leukemia should be initiated in patients with persistent cytopenia that occurs despite drug hold

Informal consensus

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<td>Insufficient</td>
<td>Moderate</td>
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Summary of Previous Recommendations

Recommendation 5.4.

- Management of Toxicities – Nausea:
  a. Many patients will have tachyphylaxis of nausea symptoms over the first cycle of therapy.
  b. Persistent nausea requiring daily antiemetic intervention, causing a reduction in performance status, and/or resulting in > 5% weight loss should result in dose reduction.
Additional Information
Additional Resources

• More information, including clinical tools and resources, is available at www.asco.org/gynecologic-cancer-guidelines

• Patient information is available at www.cancer.net
## Guideline Panel Members

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Abbreviations

- ASCO, American Society of Clinical Oncology
- EOC, epithelial ovarian cancer
- HRD, homologous recombination deficiency
- HRDpos, homologous recombination deficiency positive
- HRDneg, homologous recombination deficiency negative
- HGS, high-grade serous;
- OS, overall survival
- PARPi, poly(ADP-ribose) polymerase inhibitor
- PFS, progression-free survival
- RCT, randomized controlled trial
References


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