Beyond the Guidelines
Perspectives on the Role of PARP Inhibition in the Management of Ovarian Cancer

Monday, May 18, 2020

Moderator
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Faculty
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**Dr Love — Disclosures**

## Dr Coleman — Disclosures

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<thead>
<tr>
<th>Category</th>
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<tr>
<td><strong>Advisory Committee and Consulting Agreements</strong></td>
<td>AbbVie Inc, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Genentech, a member of the Roche Group, GlaxoSmithKline, ImmunoGen Inc, Janssen Biotech Inc, Merck, Novocure, Roche Laboratories Inc, Takeda Oncology, Tesaro, A GSK Company</td>
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<td><strong>Data and Safety Monitoring Board/Committee</strong></td>
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## Dr Lheureux — Disclosures

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## Dr Liu — Disclosures

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Dr Moore — Disclosures

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Familiarizing yourself with the Zoom interface

How to participate in the chat

Join the chat to send in questions or troubleshoot
RTP SGO 2020 Virtual Satellite Series

• Faculty lecture series (8)
• Beyond the Guidelines program (2 – 1 hour each)
• Faculty roundtable webinar (2 – 90 minutes each)
• Breakout discussion webinar (4 – 1 hour each)
Module 1 – Dr Liu: Genetic Testing in Ovarian Cancer (OC) and Biologic Basis for the Use of PARP Inhibitors

Module 2 – Dr Moore: Integration of PARP Inhibitor Maintenance into the Management of Newly Diagnosed OC

Module 3 – Dr Lheureux: Practical Considerations with the Use of PARP Inhibitors in Advanced OC

Module 4 – Dr Coleman: Potential Role of PARP Inhibitors with Chemotherapy; Other Investigational Combination Approaches in Clinical Development for Advanced OC

Module 5: SGO Review 2020
### Survey Respondents (N = 25)

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<tr>
<td>1</td>
<td>Ronald D Alvarez, MD, MBA</td>
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<td>2</td>
<td>Andrew Berchuck, MD</td>
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<td>Michael J Birrer, MD, PhD</td>
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<td>4</td>
<td>Susana M Campos, MD, MPH</td>
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<td>5</td>
<td>Robert L Coleman, MD</td>
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<td>Stephanie L Gaillard, MD, PhD</td>
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<td>Rachel N Grisham, MD</td>
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<td>Thomas Herzog, MD</td>
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<td>9</td>
<td>Angela Jain, MD</td>
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<td>10</td>
<td>Beth Karlan, MD</td>
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<td>11</td>
<td>Professor Jonathan A Ledermann</td>
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<td>Douglas A Levine, MD</td>
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<td>Stephanie Lheureux, MD, PhD</td>
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<td>14</td>
<td>Joyce F Liu, MD, MPH</td>
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<td>15</td>
<td>Ursula Matulonis, MD</td>
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<td>16</td>
<td>Mansoor Raza Mirza, MD</td>
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<td>17</td>
<td>Bradley J Monk, MD</td>
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<td>18</td>
<td>Kathleen Moore, MD</td>
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<td>19</td>
<td>David M O’Malley, MD</td>
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<td>20</td>
<td>Ana Oaknin, MD, PhD</td>
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<td>21</td>
<td>Matthew A Powell, MD</td>
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<td>22</td>
<td>Professor Isabelle Ray-Coquard, MD, PhD</td>
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<td>23</td>
<td>Krishnansu S Tewari, MD</td>
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<td>24</td>
<td>Professor Ignace Vergote</td>
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<td>25</td>
<td>Robert M Wenham, MD</td>
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Data + Perspectives

The Current and Future Role of Immune Checkpoint Inhibitors and Other Novel Therapies in the Management of Gynecologic Cancers

Wednesday, May 20, 2020

Moderator
Neil Love, MD

Faculty
Michael J Birrer, MD, PhD
Ursula Matulonis, MD
David M O'Malley, MD
Krishnansu S Tewari, MD
Agenda

Module 1 – Dr Birrer: Checkpoint Inhibitor Therapy for Microsatellite Instability (MSI)-High and Microsatellite-Stable (MSS) Endometrial Cancer

Module 2 – Dr Tewari: Current Indications for and Future Role of Immune Checkpoint Inhibitors in Cervical Cancer

Module 3 – Dr Matulonis: Current and Potential Role of Immune Checkpoint Inhibitor Therapy in Ovarian Cancer Management

Module 4 – Dr O’Malley: Novel Targeted Agents and Strategies Under Investigation for Gynecologic Cancers
“These drugs rely on the principle of so-called synthetic sickness, which occurs when the deficiency of two or more cellular mechanisms lead to cell death, whereas if only one cellular mechanism does not. The exact mechanism for synthetic sickness with PARP inhibitors is being investigated, although described”
MODULE 1: Genetic Testing in Ovarian Cancer (OC) and Biologic Basis for the Use of PARP Inhibitors
Dr Liu: Case #1 - Frontline maintenance PARPi

• 58yo woman, newly diagnosed ovarian cancer
• Optimal cytoreductive surgery with multiple bowel resections
• Tumor testing negative for BRCA mutation, but germline testing with pathogenic mutation (deletion of BRCA1 exon 3)
• Completed 6 cycles of adjuvant carboplatin/paclitaxel chemotherapy
• Started on maintenance olaparib
Dr Liu: Case #2 - Frontline maintenance PARPi

- 52yo woman, newly diagnosed ovarian cancer
- Received neoadjuvant chemotherapy with carboplatin/paclitaxel x 3 cycles
- Optimal interval cytoreductive surgery with complete pathologic response in the omentum; residual high-grade serous carcinoma involving bilateral tubes/ovaries
- Completed 3 additional cycles of adjuvant carboplatin/paclitaxel chemotherapy
- Germline testing negative for BRCA mutation. Myriad myChoice® CDx negative for BRCA mutation but with high genomic instability score
- Started on maintenance niraparib
In general, which of the following mutation assays do you order for a patient with newly diagnosed ovarian cancer and no family history?

**Germline Testing**
- gBRCA: 6
- Multigene panel germline: 17

**Somatic Testing**
- Multigene somatic/NGS: 21

**HRD Testing**
- 7
In general, which of the following mutation assays do you order for a patient with newly diagnosed ovarian cancer and no family history?

**Germline Testing**
- gBRCA mutation: 69%
- Multigene germline panel*: 61%

**Somatic Testing**
- Multigene somatic/NGS*: 74%

**Homologous recombination deficiency (HRD) assay**
- 30%

*Includes those who responded: multigene germline and somatic/NGS

NGS, next-generation sequencing

Survey of general medical and gynecologic oncologists May 2020
Regulatory and reimbursement issues aside, have you offered or would you offer a PARP inhibitor to a patient with ovarian cancer and the following germline mutation as you would for a patient with a BRCA germline mutation?

<table>
<thead>
<tr>
<th></th>
<th>PALB2</th>
<th></th>
<th>RAD51C</th>
<th></th>
<th>ATM</th>
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<tbody>
<tr>
<td></td>
<td>Gyn Onc</td>
<td>Med Onc</td>
<td>Gyn Onc</td>
<td>Med Onc</td>
<td>Gyn Onc</td>
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<tr>
<td>I have not and would not</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>I have not, but I would for the right patient</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>4</td>
<td>11</td>
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<tr>
<td>I have</td>
<td>6</td>
<td>2</td>
<td>7</td>
<td>6</td>
<td>0</td>
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</tbody>
</table>
Regulatory and reimbursement issues aside, have you offered or would you offer a PARP inhibitor to a patient with ovarian cancer and the following germline mutations as you would for a patient with a BRCA germline mutation?

I have not and would not:
- PALB2: 37%
- RAD51C: 48%
- ATM: 48%

I have not, but I would for the right patient:
- PALB2: 35%
- RAD51C: 32%
- ATM: 32%

I have:
- PALB2: 28%
- RAD51C: 20%
- ATM: 20%

Survey of general medical and gynecologic oncologists May 2020
Has the primary approach to genetic counseling for a patient with newly diagnosed ovarian cancer and a germline BRCA mutation changed at your institution in the current era of COVID-19?

- Yes: 18
- No: 7
How has the primary approach to genetic counseling for a patient with newly diagnosed ovarian cancer and a germline BRCA mutation changed at your institution in the current era of COVID-19?

- More telehealth
- All remote (tele) visits with the genetic counselor
- All virtual visits
- Almost all use telemedicine
- The patients and family need to wait longer
- Universally, virtual-based or delayed visits
- Video visits
MODULE 2: Integration of PARP Inhibitor Maintenance into the Management of Newly Diagnosed OC
Dr Moore: Case 1

- 53 year old who presented with abdominal bloating, decreased urination and difficulty with defecation starting 10/2019. She was treated with laxatives which didn’t help and presented to her Ob/Gyn where a mass was appreciated on exam.

- TVUS demonstrated a large complex adnexal mass, free fluid
- Ca-125 = 953.6
- She was referred to gynecologic oncology where a CT was ordered.
Dr Moore: Case 1
Dr. Moore: Case 1
Pathology and Molecular Characterization

• Pathology
  • High grade serous ovarian cancer

• Comprehensive Genomic Profile:
  • Loss of heterozygosity score > 16%
  • Tumor mutational burden 4mut/Mb, MSS, BRAF D594G, NF1 loss, RB1 loss, TP53 H179R

• Genetics
  • BRCA wt
Dr Moore: Case 1 – Treatment

• Treated with carboplatin AUC 6 and paclitaxel 175mg/mg² IV every 21 days x 6 cycles
• Ca-125 was 31 post cytoreductive surgery, ended at 9
• Cycle 6 on 4/9/2020, nl Ca125 and neg CT scan = NED
• Now questions regarding maintenance?
NCCN 2020 Guidelines
Dr Moore: Case 2

- 63 year old who had surgery at an outside facility and not by a cancer specialist but was found to have advanced stage, epithelial ovarian cancer
- Chest CT with pleural effusion, mediastinal LN that did not meet RECIST criteria but were concerning
- CT Abd pelvis with multiple enlarged LN
- Pathology: HG Endometrioid
- Comprehensive Genomic Profile
  - LOH < 16%, MSS, BRAF K483E, TP53, ARID1A
- BRCA wt
Dr Moore: Case 2: Treatment

• Patient treated with carboplatin AUC 6 and paclitaxel 175mg/m² and bevacizumab 15mg/kg every 21 days x 6 completed 12/2019
• Ca-125 went from 729 to 464 after 6 cycles
• CT with partial response to therapy
• Bevacizumab discontinued after cycle 6 due to grade 3, uncontrolled HTN
• Since we had started bevacizumab – we planned to treat per PAOLA-1 but didn’t end up continuing the bev – so now just on olaparib
• Ca125 down to 187 after 4 cycles maintenance - ongoing
NCCN 2020 Guidelines
A 60-year-old woman with Stage IIIc ovarian cancer and a germline BRCA mutation is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel → olaparib: 15
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib: 6
- Carboplatin/paclitaxel → niraparib: 2
- Other: 2
A 60-year-old woman with Stage III C ovarian cancer and a germline BRCA mutation is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel → olaparib: 39%
- Carboplatin/paclitaxel + bevacizumab → olaparib: 22%
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib: 11%
- Carboplatin/paclitaxel: 11%
- Carboplatin/paclitaxel + bevacizumab → niraparib: 9%
- Other: 8%

Survey of general medical and gynecologic oncologists May 2020
A 60-year-old woman with Stage IIIc ovarian cancer and a germline BRCA mutation is status post (s/p) suboptimal debulking surgery with elevated CA-125. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
- Gynecologic oncologists: 11
- Medical oncologists: 6

Carboplatin/paclitaxel + bevacizumab → olaparib
- Gynecologic oncologists: 6
- Medical oncologists: 8

Carboplatin/paclitaxel → olaparib
- Gynecologic oncologists: 8
- Medical oncologists: 6
A 60-year-old woman with Stage IIIc ovarian cancer and a germline BRCA mutation is status post (s/p) suboptimal debulking surgery with elevated CA-125. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel → olaparib: 30%
- Carboplatin/paclitaxel + bevacizumab → olaparib: 28%
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib: 24%
- Carboplatin/paclitaxel: 11%
- Other: 8%

Survey of general medical and gynecologic oncologists May 2020
Is there a patient age beyond which you would generally not administer bevacizumab for ovarian cancer?

- Yes: 2 (80 years old)
- No: 23
A 60-year-old woman with Stage III C ovarian cancer and a somatic BRCA mutation is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel → olaparib: 16
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib: 6
- Other: 3
A 60-year-old woman with Stage IIIIC ovarian cancer and a somatic BRCA mutation is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib (13)
- Carboplatin/paclitaxel → olaparib (7)
- Carboplatin/paclitaxel + bevacizumab → olaparib (3)
- Carboplatin/paclitaxel → niraparib (2)

Gynecologic oncologists
Medical oncologists
A 60-year-old woman with Stage IIIc ovarian cancer (BRCA wild type, HRD-negative) is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel + bevacizumab: 10 votes
- Carboplatin/paclitaxel → niraparib: 5 votes
- Carboplatin/paclitaxel + bevacizumab → bevacizumab: 6 votes
- Other: 4 votes

[Diagram showing the vote results for each treatment option, with options for gynecologic oncologists and medical oncologists]
A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type, HRD-negative) is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

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<th>Gynecologic oncologists</th>
<th>Medical oncologists</th>
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<td>17</td>
<td></td>
</tr>
<tr>
<td>Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Carboplatin/paclitaxel → niraparib</td>
<td>2</td>
<td></td>
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<tr>
<td>Other</td>
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A 60-year-old woman with Stage IIIIC ovarian cancer (BRCA wild type, HRD-positive) is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel → niraparib
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
- Carboplatin/paclitaxel → olaparib
- Carboplatin/paclitaxel + bevacizumab → niraparib
- Other

Gynecologic oncologists: 10 votes
Medical oncologists: 7 votes
Other: 3 votes
A 60-year-old woman with Stage IIIIC ovarian cancer (BRCA wild type, HRD-positive) is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib: 14 votes
- Carboplatin/paclitaxel → niraparib: 6 votes
- Carboplatin/paclitaxel + bevacizumab → niraparib: 2 votes
- Carboplatin/paclitaxel → olaparib: 2 votes
- Other: 1 vote

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Gynecologic oncologists: 
Medical oncologists:
Regulatory and reimbursement issues aside, which starting dose of niraparib would you use for a 125-lb patient with advanced ovarian cancer and a platelet count of 200,000 after a response to front-line platinum-based chemotherapy?

- 200 mg daily: 24
- 300 mg daily: 1
MODULE 3: Practical Considerations with the Use of PARP Inhibitors in Advanced OC
Maintenance Strategies in Phase III Clinical Trials Assessing PARP Inhibitor Treatment in Ovarian Cancer

Madariaga A et al. *Int J Gynecol Cancer* 2020;[Online ahead of print].
Dr Liu - PARPi toxicity: Case

- 74yo woman with recurrent platinum-sensitive ovarian cancer
- Germline testing with RAD51C mutation
- Received carboplatin/PLD with complete response
- Started on maintenance olaparib at 300mg BID
  - ~4 weeks after initiation, noted to have increasing fatigue, diarrhea. Platelet count decreased to 99K (from 183K at treatment initiation)
- Drug held, re-initiated with dose reduction to olaparib 250mg BID 2 weeks later after platelet recovery to 165K
  - ~4 weeks at this dose, with increasing intolerable fatigue
- Drug held, re-initiated with dose reduction to olaparib 200mg BID 2 weeks later
- Continues on maintenance olaparib at 200mg BID
Manage wisely: poly (ADP-ribose) polymerase inhibitor (PARPi) treatment and adverse events

Ainhoa Madariaga, Valerie Bowering, Soha Ahrari, Amit M Oza, Stephanie Lheureux

Int J Gynecol Cancer 2020;[Online ahead of print].
How would you respond to a patient with Stage III ovarian cancer who is about to begin a PARP inhibitor as maintenance therapy after suboptimal debulking surgery and chemotherapy and asks you to estimate the chance that during the first year of treatment she will...

- "Sail through" treatment:
  - Gyn Oncs: 50%
  - Med Oncs: 64%

- Experience side effects that lead to dose reduction:
  - Gyn Oncs: 50%
  - Med Oncs: 40%

- Experience side effects that require discontinuation:
  - Gyn Oncs: 11%
  - Med Oncs: 10%
How would you respond to a patient with Stage III ovarian cancer who is about to begin a PARP inhibitor as maintenance therapy after suboptimal debulking surgery and chemotherapy and asks you to estimate the chance that during the first year of treatment she will...
A woman in her mid-60s with recurrent high-grade serous ovarian cancer begins rucaparib monotherapy (600 mg BID). Within a few weeks, her serum creatinine increases from 0.86 mg/dL to 1.6 mg/dL. What would be the optimal management approach?

- Continue rucaparib at the same dose: 15
- Hold rucaparib until creatinine returns to normal, and restart at the same dose: 5
- Hold rucaparib until creatinine returns to normal, and restart at a reduced dose: 3
- Other: 1
A woman in her mid-60s with recurrent high-grade serous ovarian cancer begins rucaparib monotherapy (600 mg BID). Within a few weeks, her serum creatinine increases from 0.86 mg/dL to 1.6 mg/dL. What would be the optimal management approach?

<table>
<thead>
<tr>
<th>Management Approach</th>
<th>Percentage</th>
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<td>Hold rucaparib until creatinine returns to normal, and restart at a reduced dose</td>
<td>39%</td>
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<tr>
<td>Continue rucaparib at a reduced dose</td>
<td>22%</td>
</tr>
<tr>
<td>Continue rucaparib at the same dose</td>
<td>15%</td>
</tr>
<tr>
<td>Hold rucaparib until creatinine returns to normal, and restart at the same dose</td>
<td>13%</td>
</tr>
<tr>
<td>Discontinue rucaparib</td>
<td>11%</td>
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Survey of general medical and gynecologic oncologists May 2020
In general, what is your approach to antiemetic therapy for a patient with ovarian cancer who is starting treatment on a PARP inhibitor?

Recommend antiemetic if the patient experiences nausea

Prophylactic antiemetic therapy prior to administration of PARP inhibitor

- Gynecologic oncologists: 21
- Medical oncologists: 4
In general, what is your approach to antiemetic therapy for a patient with ovarian cancer who is starting treatment on a PARP inhibitor?

- **Recommend antiemetic/reduce dose of PARP inhibitor if the patient experiences nausea**
  - 50%

- **Prophylactic antiemetic therapy prior to administration of PARP inhibitor**
  - 50%

Survey of general medical and gynecologic oncologists May 2020
For a patient with Stage IIIC ovarian cancer and a germline BRCA mutation who has undergone optimal debulking surgery followed by chemotherapy and 2 years of PARP inhibitor maintenance therapy, do you believe the risk of developing MDS or AML is increased by the PARP inhibitor?

Yes: 18
No: 2
It is not known: 5

**Median Risk Estimate:**
- Gyn Onc: 1%
- Med Onc: 1%
According to your clinical experience, do PARP inhibitors cause insomnia?

- Yes: 18
- No: 5
- I don’t know: 2
MODULE 4: Potential Role of PARP Inhibitors with Chemotherapy; Other Investigational Combination Approaches in Clinical Development for Advanced OC
Dr Coleman: Case

• Hx: 60 y/o woman with recurrent high grade serous ovarian cancer (BRCA-wt)
  – Initial diagnosis 2/2012: Stage IIIC (gross intraperitoneal disease, ascites); CA125: 2151 U/mL
    • Cytoreduction to < 1cm
    • IV: Paclitaxel/Carboplatin q 3 week x 6 cycles [clinical CR]
  – First recurrence: 3/2015: multifocal pelvic and abdominal disease, CA125: 367 U/mL
    • IV: Paclitaxel/carboplatin x 8; [PR], consolidated with IV: Carboplatin AUC5 x 6 months [SD] but developed HSR
    • CA125: 69 U/mL
  – Persistent small volume measurable disease: Eligible for Phase II trial (ARIEL2: Rucaparib)
• Hx: 60 y/o woman with recurrent high grade serous ovarian cancer
  – Started rucaparib 600 mg BID, sCr: 0.8, CA125: 69 U/mL
  – Gr 1 GI controlled with anti-emetics
  – Cycle 2 – sCR: 1.83 (Gr2) – dose held 1 week sCr: 0.97
  – Cycle 3 – imaging [SD], sCr: 1.65 (Gr2), CA125: 44 U/mL, dose reduction, held – sCr: 1.19
Dr Coleman: Case (Cont’d)

- Hx: 60 y/o woman with recurrent high grade serous ovarian cancer
  - Cycle 4 – imaging [PR], sCr: 1.67 (Gr2), CA125: 32 U/mL, dose held – renal function studies
sCr: 1.51
Est CrCl: 44 mL/min

GFR: 97.9
• Hx: 60 y/o woman with recurrent high grade serous ovarian cancer
  – Patient went on to receive 22 total cycles of therapy
  – One further dose delay and dose reduction
  – Close of trial estimated CrCl: 45 ml/min coincided with renal scan (42 ml/min)
Dr Coleman: Case

Patient Receiving Concomitant Therapy

• 56 y.o. with high grade serous ovarian cancer
  – gBRCA-wt
  – Heavy disease burden with involvement of omentum, diaphragm, and peritoneal lining
  – Grossly enlarged pelvic nodes
  – Ovarian masses bilaterally

• CA-125: 6713 U/mL

• Enrolled onto VELIA/GOG-3005
Dr Coleman: Case
Patient Receiving Concomitant Therapy

• 56 y.o. with high grade serous ovarian cancer
  – NACT: Paclitaxel 80 mg/m² + carboplatin AUC6 + placebo/veliparib
  – 3 cycles of therapy (CA-125: 72 U/mL)

• Imaging prior to surgery
  – Near complete resolution of omental/diaphragm disease, post-treatment peritoneal thickening
  – Nodal disease near normal (largest short axis dimension: 1.2 cm)
  – Ovaries irregular but markedly smaller

• Interval resection accomplished with near complete gross resection
  – Small volume miliary mesenteric disease
Dr Coleman: Case
Patient Receiving Concomitant Therapy

• 56 y.o. with high grade serous ovarian cancer
  – Completed 6 cycles of chemotherapy plus placebo/veliparib
  – CA-125: 15 U/mL
  – Initiated and completed maintenance phase
  – NED

• Sequencing from interval cytoreduction: Rad51D mutation
A 70-year-old woman with advanced ovarian cancer and a germline BRCA mutation undergoes debulking surgery followed by chemotherapy with carboplatin/paclitaxel and experiences disease relapse 1 year later. Which treatment would you likely recommend?

- **Platinum doublet → maintenance olaparib**: 14
- **Platinum doublet → maintenance rucaparib**: 6
- **Platinum doublet → maintenance niraparib**: 3
- **Other**: 2

Gynecologic oncologists: 14
Medical oncologists: 6

14 participants were surveyed.
A 70-year-old woman with advanced ovarian cancer and a germline BRCA mutation undergoes debulking surgery followed by chemotherapy with carboplatin/paclitaxel and experiences disease relapse 1 year later. Which treatment would you likely recommend?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum doublet → maintenance olaparib</td>
<td>51%</td>
</tr>
<tr>
<td>Platinum doublet → maintenance niraparib</td>
<td>14%</td>
</tr>
<tr>
<td>Platinum doublet + bevacizumab → maintenance bevacizumab + olaparib</td>
<td>12%</td>
</tr>
<tr>
<td>Platinum doublet + bevacizumab → maintenance bevacizumab</td>
<td>8%</td>
</tr>
<tr>
<td>Platinum doublet → maintenance rucaparib</td>
<td>6%</td>
</tr>
<tr>
<td>Other</td>
<td>9%</td>
</tr>
</tbody>
</table>

Survey of general medical and gynecologic oncologists May 2020
A 70-year-old woman with advanced ovarian cancer (BRCA wild type, HRD-negative) undergoes debulking surgery followed by chemotherapy with carboplatin/paclitaxel and experiences disease relapse 1 year later. Which treatment would you likely recommend?

- Platinum doublet + bevacizumab → maintenance bevacizumab [8] (Gynecologic oncologists)
- Platinum doublet → maintenance olaparib [2]
- Platinum doublet → maintenance niraparib [5]
- Platinum doublet → maintenance rucaparib [2]
- Platinum doublet + bevacizumab → maintenance bevacizumab + PARP inhibitor [3]
- Other [2] (Medical oncologists)
A 70-year-old woman with advanced ovarian cancer (BRCA wild type, HRD-negative) undergoes debulking surgery followed by chemotherapy with carboplatin/paclitaxel and experiences disease relapse 1 year later. Which treatment would you likely recommend?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum doublet + bevacizumab → maintenance bevacizumab</td>
<td>31%</td>
</tr>
<tr>
<td>Platinum doublet → maintenance olaparib</td>
<td>29%</td>
</tr>
<tr>
<td>Platinum doublet</td>
<td>16%</td>
</tr>
<tr>
<td>Platinum doublet → maintenance niraparib</td>
<td>14%</td>
</tr>
<tr>
<td>Platinum doublet → maintenance rucaparib</td>
<td>6%</td>
</tr>
<tr>
<td>Platinum doublet + bevacizumab → maintenance bevacizumab + olaparib</td>
<td>4%</td>
</tr>
</tbody>
</table>

Survey of general medical and gynecologic oncologists May 2020
Based on available data, do you believe that chemotherapy/veliparib → veliparib should be an FDA-endorsed initial treatment option for patients with Stage IIIIC ovarian cancer?

- Yes: 15
- No: 10

Gynecologic oncologists
Medical oncologists
A patient with advanced ovarian cancer and a germline BRCA mutation who is receiving PARP-inhibitor maintenance therapy is scheduled to undergo hip replacement surgery. Would you discontinue the PARP inhibitor in advance of the surgery?

Median Number of Days PARP Inhibitor Discontinued Prior to Surgery:
Gyn Onc: 12 days
Med Onc: 7 days
A patient with advanced ovarian cancer and a germline BRCA mutation who is receiving PARP-inhibitor maintenance therapy is scheduled to undergo hip replacement surgery. Would you discontinue the PARP inhibitor in advance of the surgery?

- Yes: 46%
- No: 54%

Median number of days to discontinue PARP inhibitor prior to surgery: 7 days

Survey of general medical and gynecologic oncologists May 2020
MODULE 5: SGO Review 2020
Genetic Testing in Ovarian Cancer (OC) and Biologic Basis for the Use of PARP Inhibitors – Dr Liu

- D'Indinosante M et al. BRCA tumor-testing in a tertiary referral center: Are we missing something or not? SGO 2020; Abstract 59.

- Li L et al. Clinical indication of BRCA1 variation: Time for reassessment. SGO 2020; Abstract 60.


- Weiss AS et al. Inherited mutations in fallopian tube, ovarian, and primary peritoneal carcinoma: Changes in diagnoses and mutational frequency over 20 years. SGO 2020; Abstract 62.
Integration of PARP Inhibitor Maintenance into the Management of Newly Diagnosed OC – Dr Moore

• Poveda A et al. Final overall survival (OS) results from SOLO2/ENGOT-ov21: A phase III trial assessing maintenance olaparib in patients (pts) with platinum-sensitive, relapsed ovarian cancer and a BRCA mutation. ASCO 2020; Abstract 6002.

• Vergote IB et al. Population adjusted indirect comparison of the SOLO1 and PAOLA-1/ENGOTov25 studies of olaparib with or without bevacizumab, bev alone and placebo in the maintenance treatment of women with newly diagnosed stage III/IV ovarian cancer with BRCA mutation. SGO 2020; Abstract 35.

Integration of PARP Inhibitor Maintenance into the Management of Newly Diagnosed OC (continued) – Dr Moore

- Grimm C et al. Maintenance olaparib plus bevacizumab (bev) after platinum-based chemotherapy plus bev in patients (pts) with newly diagnosed advanced high-grade ovarian cancer (HGOC): Efficacy by timing of surgery and residual tumor status in the Phase III PAOLA-1 trial. SGO 2020; Abstract 34.

- Loverix L et al. Randomized phase II CLIO study on olaparib monotherapy versus chemotherapy in platinum-sensitive recurrent ovarian cancer. SGO 2020; Abstract 30.
Practical Considerations with the Use of PARP Inhibitors in Advanced OC – Dr Lheureux


- Han SN et al. Time to first subsequent therapy (TFST) and progression-free survival 2 (PFS2) from the phase 3 randomized, double-blind PRIMA/ENGOT-OV26/GOG-3012 study in patients with newly diagnosed ovarian cancer. SGO 2020; Abstract 32.

- Pothuri B et al. Patient-reported outcomes (PRO) in patients receiving niraparib in the PRIMA/ENGOT-OV26/GOG-3012 trial. SGO 2020; Abstract 83.
Potential Role of PARP Inhibitors with Chemotherapy; Other Investigational Combination Approaches in Clinical Development for Advanced OC – Dr Coleman

- Coleman RL. Integration of veliparib (V) with front-line chemotherapy and maintenance in women with high-grade serous carcinoma of ovarian, fallopian tube, or primary peritoneal origin (HGSC). SGO 2020; Abstract 36.


- Swisher EM et al. Safety of veliparib in combination with chemotherapy and as maintenance in front-line ovarian cancer: Results in BRCAm, hrd, and whole populations from the VELIA trial. SGO 2020; Abstract 37.
Potential Role of PARP Inhibitors with Chemotherapy; Other Investigational Combination Approaches in Clinical Development for Advanced OC (continued) – Dr Coleman

• Gillen J et al. Tolerability and adverse events experienced by women with ovarian cancer treated with intravenous or intraperitoneal chemotherapy plus veliparib and bevacizumab based on BRCA status. SGO 2020; Abstract 26.

• Washington CR et al. Outcomes based on treatment regimen in newly diagnosed ovarian, primary peritoneal and fallopian tube cancer receiving intravenous or intraperitoneal platinum-based chemotherapy in combination with veliparib and bevacizumab. SGO 2020; Abstract 27.

Has the approach to primary debulking surgery for patients with Stage III ovarian cancer changed at your institution during the COVID-19 pandemic?

Yes: 15
No: 10
Are you currently administering more neoadjuvant treatment for patients with Stage III ovarian cancer at your institution than you were before the COVID-19 pandemic?

Yes: 15
No: 10

Gynecologic oncologists: 15
Medical oncologists: 10
Thank you for joining us!

CME credit information will be emailed to each participant tomorrow morning.