Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS
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EDITOR
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Gynecologic Oncology Update
A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY
Gynecologic cancers comprise 5 primary cancers affecting the ovaries, uterine corpus (endometrial cancer), uterine cervix (cervical cancer), vulva and vagina. In 2016, it is anticipated that approximately 105,890 new cases of gynecologic cancer will be documented in the United States and 30,890 individuals will succumb to these diseases. Patient outcomes are critically dependent upon effective multidisciplinary care, which often includes contributions from gynecologic, medical and radiation oncologists in addition to pathologists, diagnostic radiologists, oncology nurses and psychosocial services. Interestingly, despite many commonalities, each of these diseases is quite distinct, and management algorithms employed are varied. To bridge the gap between research and patient care, Gynecologic Oncology Update uses one-on-one discussion with leading investigators in these fields. By providing access to the latest scientific developments and the perspectives of experts, this CME activity assists practicing clinicians with the formulation of up-to-date management strategies.

LEARNING OBJECTIVES
• Employ current clinical guidelines and available data in the selection of treatment options for patients with commonly diagnosed gynecologic cancers.
• Consider clinical investigator perspectives regarding the indications for BRCA mutation testing, and use this information to appropriately select patients with ovarian cancer (OC) for this analysis.
• Develop an evidence-based algorithm for the initial and long-term treatment of advanced OC considering the role of the recently approved anti-VEGF antibody bevacizumab.
• Appreciate the recent approval of olaparib for patients with highly refractory advanced OC, and integrate this agent into the clinical care of appropriate individuals.
• Develop an understanding of the emerging efficacy data and toxicity profiles of investigational agents in OC to effectively prioritize clinical trial opportunities for appropriate patients.
• Implement a long-term clinical plan for the management of metastatic cervical cancer, incorporating existing, recently approved and investigational targeted treatments.

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Please note, this program has been specifically designed for the following ABIM specialty: medical oncology.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: Dr Matulonis — Advisory Committee: Momenta Pharmaceuticals Inc; Speakers Bureau: AstraZeneca Pharmaceuticals LP; Unpaid Consultant: AstraZeneca Pharmaceuticals LP. Dr Moore — Advisory Committee: Advaxis Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Genentech BioOncology, Pfizer Inc, Roche Laboratories Inc.


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SELECT PUBLICATIONS

A randomized phase II/III study of the combination of cediranib and olaparib compared to cediranib or olaparib alone, or standard of care chemotherapy in women with recurrent platinum-resistant or -refractory ovarian, fallopian tube, or primary peritoneal cancer (COCOS). NCT02502266


Disis ML et al. Avelumab (MSB0010718C), an anti-PD-L1 antibody, in patients with previously treated, recurrent or refractory ovarian cancer: A phase Ib, open-label expansion trial. Proc ASCO 2015;Abstract 5509.

Domchek SM et al. Efficacy and safety of olaparib monotherapy in germline BRCA1/2 mutation carriers with advanced ovarian cancer and three or more lines of prior therapy. Gynecol Oncol 2016;140(2):199-203.


GOG-9923: Carboplatin, paclitaxel, bevacizumab, and veliparib in treating patients with newly diagnosed stage II-IV ovarian epithelial, fallopian tube, or primary peritoneal cancer. NCT00989651


Matulonis U et al. Frequency, severity and timing of common adverse events (AEs) with maintenance olaparib in patients (pts) with platinum-sensitive relapsed serous ovarian cancer (PSR SOC). Proc ASCO 2015;Abstract 5550.


Niraparib and/or niraparib–bevacizumab combination against bevacizumab alone in HRD platinum sensitive ovarian cancer (AVANOVA). NCT02354131

Olaparib maintenance monotherapy in patients with BRCA mutated ovarian cancer following first line platinum based chemotherapy (SOLO-1). NCT0184986

Phase 1 and 2 study of MEDI4736 in combination with olaparib or cediranib for advanced solid tumors and recurrent ovarian cancer. [NCT02484404](https://clinicaltrials.gov/ct2/show/NCT02484404)


Veliparib, pegylated liposomal doxorubicin hydrochloride, carboplatin, and bevacizumab in treating patients with recurrent ovarian cancer, primary peritoneal cancer, or fallopian tube cancer. [NCT01459380](https://clinicaltrials.gov/ct2/show/NCT01459380)
1. As single agents, PARP inhibitors have shown activity in ____________.
   a. BRCA1 mutation-positive OC
   b. BRCA2 mutation-positive OC
   c. BRCA1/2 mutation-negative OC
   d. Both a and b
   e. All of the above

2. A Phase II trial reported by Liu and colleagues evaluating the combination of cediranib and olaparib versus olaparib alone for women with recurrent platinum-sensitive OC demonstrated statistically significant improvements in response rate and median progression-free survival with the combination in which of the following populations?
   a. Patients with a known deleterious germline BRCA mutation
   b. Patients without a known deleterious germline BRCA mutation
   c. Both a and b

3. The FDA approved olaparib monotherapy for patients with deleterious or suspected deleterious germline BRCA-mutated advanced OC previously treated with 3 or more lines of chemotherapy.
   a. True
   b. False

4. The Phase III SOLO-1 trial is evaluating olaparib maintenance monotherapy for patients with ____________ advanced OC after first-line platinum-based chemotherapy.
   a. BRCA wild-type
   b. Germline BRCA-mutated
   c. Both a and b

5. Studies investigating anti-PD-1/PD-L1 antibodies have shown these agents to produce response rates of approximately ____________ for patients with relapsed/refractory OC.
   a. <5%
   b. 20%
   c. 40%
   d. 80%

6. Both the GOG-0218 and ICON7 trials demonstrated an improvement in progression-free survival with the addition of bevacizumab to standard chemotherapy for patients with newly diagnosed OC.
   a. True
   b. False

7. Bevacizumab is FDA approved for which of the following gynecologic cancers?
   a. Platinum-resistant recurrent epithelial OC
   b. Persistent, recurrent or metastatic cervical cancer
   c. Platinum-sensitive recurrent OC
   d. Both a and b
   e. None of the above

8. NCCN guidelines recommend that ____________ undergo BRCA testing.
   a. All patients with epithelial OC
   b. Only patients with an Ashkenazi Jewish background
   c. Only patients with a strong family history of breast cancer or OC at a young age

9. Mirvetuximab soravtansine (IMGN853) is ____________.
   a. An anti-angiogenic agent
   b. An antibody-drug conjugate
   c. A PARP inhibitor

10. Which of the following toxicities has been observed with mirvetuximab soravtansine?
    a. Alopecia
    b. Blurred vision
    c. Peripheral neuropathy
    d. All of the above
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**PART 1 — Please tell us about your experience with this educational activity**

**How would you characterize your level of knowledge on the following topics?**

<table>
<thead>
<tr>
<th>Topic</th>
<th>BEFORE</th>
<th>AFTER</th>
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</thead>
<tbody>
<tr>
<td>Clinical trials investigating the addition of anti-angiogenic agents (ie, bevacizumab, cediranib) to PARP inhibition for patients with advanced OC</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>Efficacy of PARP inhibitors in patients with advanced OC with and without germline BRCA1/2 mutations</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>NCCN guideline recommendations regarding BRCA testing for patients with epithelial OC</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>Mechanism of action and available data with the folate receptor alpha-targeting antibody-drug conjugate mirvetuximab sorav坦sine (IMGN853) in advanced OC</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>Available data and ongoing trials evaluating anti-PD-1/PD-L1 antibodies in advanced OC</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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**Practice Setting:**
- [ ] Academic center/medical school
- [ ] Community cancer center/hospital
- [ ] Group practice
- [ ] Solo practice
- [ ] Government (eg, VA)
- [ ] Other (please specify)

**Approximately how many new patients with the following do you see per year?**
- Ovarian cancer:...
- Cervical cancer:...
- Endometrial cancer:...

**Was the activity evidence based, fair, balanced and free from commercial bias?**
- [ ] Yes
- [ ] No

If no, please explain:

**Please identify how you will change your practice as a result of completing this activity (select all that apply).**
- [ ] This activity validated my current practice
- [ ] Create/revise protocols, policies and/or procedures
- [ ] Change the management and/or treatment of my patients
- [ ] Other (please explain):

If you intend to implement any changes in your practice, please provide 1 or more examples:

**The content of this activity matched my current (or potential) scope of practice.**
- [ ] Yes
- [ ] No

If no, please explain:

**Please respond to the following learning objectives (LOs) by circling the appropriate selection:**

<table>
<thead>
<tr>
<th>LO</th>
<th>4 = Yes</th>
<th>3 = Will consider</th>
<th>2 = No</th>
<th>1 = Already doing</th>
<th>N/M = LO not met</th>
<th>N/A = Not applicable</th>
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<tr>
<td>1. Employ current clinical guidelines and available data in the selection of treatment options for patients with commonly diagnosed gynecologic cancers.</td>
<td>4 3 2 1</td>
<td>N/M</td>
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<td>2. Consider clinical investigator perspectives regarding the indications for BRCA mutation testing, and use this information to appropriately select patients with ovarian cancer (OC) for this analysis.</td>
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<td>N/M</td>
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<td>3. Develop an evidence-based algorithm for the initial and long-term treatment of advanced OC considering the role of the recently approved anti-VEGF antibody bevacizumab.</td>
<td>4 3 2 1</td>
<td>N/M</td>
<td>N/A</td>
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As a result of this activity, I will be able to:

• Appreciate the recent approval of olaparib for patients with highly refractory advanced OC, and integrate this agent into the clinical care of appropriate individuals. 4 3 2 1 N/M N/A

• Develop an understanding of the emerging efficacy data and toxicity profiles of investigational agents in OC to effectively prioritize clinical trial opportunities for appropriate patients. 4 3 2 1 N/M N/A

• Implement a long-term clinical plan for the management of metastatic cervical cancer, incorporating existing, recently approved and investigational targeted treatments. 4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

Would you recommend this activity to a colleague?
☒ Yes ☐ No If no, please explain:

PART 2 — Please tell us about the faculty and editor for this educational activity

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<tr>
<td>Ursula A Matulonis, MD</td>
<td>4 3 2 1</td>
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<td>Neil Love, MD</td>
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Signature: ___________________________ Date: ___________________________

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