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Gynecologic Oncology™ UPDATE

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

FACULTY INTERVIEWS

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ABIM CME MOC ACCREDITED

CME Certified

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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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

Armstrong DK et al. **Intraperitoneal cisplatin and paclitaxel in ovarian cancer.** *N Engl J Med* 2006;354(1):34-43.

Burger RA et al. **Incorporation of bevacizumab in the primary treatment of ovarian cancer.** *N Engl J Med* 2011;365(26):2473-83.

Burger RA et al. **Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian cancer (EOC), primary peritoneal cancer (PPC), or fallopian tube cancer (FTC): A Gynecologic Oncology Group study.** *Proc ASCO* 2010;**Abstract LBA1**.

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.

Eccles DM et al. **BRCA1 and BRCA2 genetic testing — Pitfalls and recommendations for managing variants of uncertain clinical significance.** *Ann Oncol* 2015;26(10):2057-65.

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

Gunderson CC, Moore KN. **BRACAnalysis CDx as a companion diagnostic tool for Lynparza.** *Expert Rev Mol Diagn* 2015;15(9):1111-6.

Herzog TJ et al. **A state by state analysis of BRCA1 and BRCA2 testing in patients with ovarian cancer.** *Proc SGO* 2015;**Abstract 443**.

Kaufman B et al. **Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation.** *J Clin Oncol* 2015;33(3):244-50.

Ledermann J et al. **Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: A preplanned retrospective analysis of outcomes by BRCA status in a randomized phase 2 trial.** *Lancet Oncol* 2014;15(8):852-61.

Ledermann J et al. **Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer.** *N Engl J Med* 2012;366(15):1382-92.

Lheureux S et al. **Genomic characterization of long-term responders to olaparib.** *Proc ASCO* 2015;**Abstract 5566**.

Liu JF, Matulonis UA. **Bevacizumab in newly diagnosed ovarian cancer.** *Lancet Oncol* 2015;[Epub ahead of print].

Liu JF et al. **Combination cediranib and olaparib versus olaparib alone for women with recurrent platinum-sensitive ovarian cancer: A randomised phase 2 study.** *Lancet Oncol* 2014;15(11):1207-14.

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**.

Matulonis UA et al. **Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer and a BRCA mutation: Overall survival adjusted for post-progression PARP inhibitor therapy.** *Proc SGO* 2015;**Abstract 13**.

Moore KN et al. **Preliminary single agent activity of IMGN853, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in platinum-resistant epithelial ovarian cancer (EOC) patients (pts): Phase I trial.** *Proc ASCO* 2015;**Abstract 5518**.

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). NCT01844986

Oza AM et al. **Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): Overall survival results of a phase 3 randomised trial.** *Lancet Oncol* 2015;16(8):928-36.

Phase 1 and 2 study of MEDI4736 in combination with olaparib or cediranib for advanced solid tumors and recurrent ovarian cancer. NCT02484404

Saeed Rafii et al. **What clinical factors influence advanced BRCA1/2 mutant ovarian cancer patient (BMOC pt) outcomes to poly(ADP-ribose) polymerase inhibitor (PARPi) treatment?** *Proc ASCO* 2015;**Abstract 5546**.

Tewari D et al. **Long-term survival advantage and prognostic factors associated with intraperitoneal chemotherapy treatment in advanced ovarian cancer: A gynecologic oncology group study.** *J Clin Oncol* 2015;33(13):1460-6.

Varga A et al. **Antitumor activity and safety of pembrolizumab in patients (pts) with PD-L1 positive advanced ovarian cancer: Interim results from a phase Ib study.** *Proc ASCO* 2015;**Abstract 5510**.

Veliparib, pegylated liposomal doxorubicin hydrochloride, carboplatin, and bevacizumab in treating patients with recurrent ovarian cancer, primary peritoneal cancer, or fallopian tube cancer. NCT01459380

QUESTIONS (PLEASE CIRCLE ANSWER):

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. Platinium-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

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Gynecologic Oncology Update — Issue 2, 2015

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — Please tell us about your experience with this educational activity

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

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Clinical trials investigating the addition of anti-angiogenic agents (ie, bevacizumab, cediranib) to PARP inhibition for patients with advanced OC	4 3 2 1	4 3 2 1
Efficacy of PARP inhibitors in patients with advanced OC with and without germline BRCA1/2 mutations	4 3 2 1	4 3 2 1
NCCN guideline recommendations regarding BRCA testing for patients with epithelial OC	4 3 2 1	4 3 2 1
Mechanism of action and available data with the folate receptor alpha-targeting antibody-drug conjugate mirvetuximab soravtansine (IMGN853) in advanced OC	4 3 2 1	4 3 2 1
Available data and ongoing trials evaluating anti-PD-1/PD-L1 antibodies in advanced OC	4 3 2 1	4 3 2 1

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:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- Employ current clinical guidelines and available data in the selection of treatment options for patients with commonly diagnosed gynecologic cancers. . . 4 3 2 1 N/M N/A
- 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. . . . . 4 3 2 1 N/M N/A
- 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. . . . . 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Ursula A Matulonis, MD	4 3 2 1	4 3 2 1
Kathleen Moore, MD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

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