Novel Agents and Emerging Strategies in the Management of Gynecologic Cancers

CME Information

TARGET AUDIENCE

This activity is intended for gynecologic oncologists, medical oncologists, gynecologists and other healthcare providers involved in the treatment of gynecologic cancers.

OVERVIEW OF ACTIVITY

The pace of oncology drug development has accelerated in recent years to previously unmatched levels. Fueled by an increased understanding of the biologic underpinnings of tumor development and progression, clinical research platforms largely focused on the evaluation of potential benefits with novel targeted therapeutics possessing unique mechanisms of action and safety profiles have led to improved outcomes in myriad large and rigorous clinical trials across many tumor types. The successes yielded by this rational approach to the design and evaluation of new therapies have in turn provided oncology healthcare professionals and patients with many additional and beneficial FDA-endorsed treatment options. Although this dynamic appears to be prevalent in many corners of oncology, recent advancements in the management of gynecologic cancers — including ovarian, cervical and endometrial cancer — have made it particularly relevant for this area of medicine. A plethora of extremely promising data sets related to the management of these diseases have recently emerged, providing significant enthusiasm that several more novel approaches may soon become available to practicing clinicians. Existing management algorithms for patients with these gynecologic cancers are poised for further change, and it is therefore critical that continuing education be offered to all practitioners involved in their care.

This CME program developed from the proceedings of a satellite symposium held during the Society of Gynecologic Oncology's 2019 Annual Meeting on Women's Cancer features video slide presentations given by leading researchers with an expertise in gynecologic cancers. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, gynecologic oncologists and other healthcare providers with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Review the mechanisms of action of, emerging efficacy data with and toxicity profiles of novel targeted agents under investigation in ovarian, endometrial and cervical cancer, and effectively prioritize clinical trial opportunities or expanded access programs for eligible patients.
- Recall the biologic rationale for, published research data with and ongoing research evaluating the use of immune checkpoint inhibitors in the management of ovarian, endometrial and cervical cancer, and identify patients who may be eligible for this strategy in or outside of a protocol setting.
- Appraise early research data and recently activated clinical trials evaluating anti-PD-1/PD-L1 antibodies in combination with targeted agents or other immune checkpoint inhibitors for gynecologic cancers, and use this information to identify patients who may be eligible for study participation.
- Recognize the incidence of folate receptor alpha overexpression in patients with gynecologic cancers, and consider the potential role of novel agents designed to exploit this therapeutic target.
- Design and implement a plan of care to recognize and manage side effects and toxicities associated with novel and recently approved systemic therapies for patients with ovarian, endometrial and cervical cancer to support quality of life and continuation of therapy.
- Counsel appropriately selected patients with ovarian, endometrial and cervical cancer about participation in ongoing research protocols.

ACCREDITATION STATEMENT

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Research To Practice designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance

of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

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

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HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/GynOnc19/NovelAgents/Video/CME**.

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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:

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later
Adobe Flash Player 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

Matthew A Powell, MD

Baik CS et al. **Immuno-oncology clinical trial design: Limitations, challenges, and opportunities.** *Clin Cancer Res* 2017;23(17):4992-5002.

Castellano T et al. **An overview of immune checkpoint inhibitors in gynecologic cancers.** *Clin Ther* 2018;40(3):372-88.

Chen DS, Mellman I. **Oncology meets immunology: The cancer-immunity cycle.** *Immunity* 2013;39(1):1-10.

Disis ML et al. **Avelumab (MSB0010718C; anti-PD-L1) in patients with recurrent/refractory ovarian cancer from the JAVELIN Solid Tumor phase 1b trial: Safety and clinical activity.** *Proc ASCO* 2016;**Abstract 5533**.

Fleming GF et al. **Clinical activity, safety and biomarker results from a phase Ia study of atezolizumab (atezo) in advanced/recurrent endometrial cancer (rEC).** *Proc ASCO* 2017;**Abstract 5585**.

Frenel JS et al. **Pembrolizumab in patients with advanced cervical squamous cell cancer: Preliminary results from the phase 1b KEYNOTE-028 study.** *Proc ASCO* 2016;**Abstract 5515**.

Hamanishi J et al. **Safety and antitumor activity of anti-PD-1 antibody, nivolumab, in patients with platinum-resistant ovarian cancer.** *J Clin Oncol* 2015;33(34):4015-22.

Hanahan D, Weinberg RA. **Hallmarks of cancer: The next generation.** *Cell* 2011;144(5):646-74.

Hollebecque A et al. **An open-label, multicohort, phase I/II study of nivolumab in patients with virus-associated tumors (CheckMate 358): Efficacy and safety in recurrent or metastatic (R/M) cervical, vaginal, and vulvar cancers.** *Proc ASCO* 2017;**Abstract 5504**.

Lheureux S et al. **A phase I/II study of ipilimumab in women with metastatic or recurrent cervical carcinoma: A study of the Princess Margaret and Chicago N01 Consortia.** *Proc ASCO* 2015;**Abstract 3061**.

Matulonis UA et al. **Antitumor activity and safety of pembrolizumab in patients with advanced recurrent ovarian cancer: Interim results from the phase 2 KEYNOTE-100 study.** *Proc ASCO* 2018;**Abstract 5511**.

Ott PA et al. **Safety and antitumor activity of pembrolizumab in advanced programmed death ligand 1-positive endometrial cancer: Results from the KEYNOTE-028 study.** *J Clin Oncol* 2017;35(22):2535-41.

Oaknin A et al. **Preliminary safety, efficacy, and PK/PD characterization from GARNET, a phase 1 clinical trial of the anti–PD-1 monoclonal antibody, TSR-042, in patients with recurrent or advanced MSI-H endometrial cancer.** *Proc ESMO* 2018;**Abstract 935PD**.

Tang J et al. **Comprehensive analysis of the clinical immuno-oncology landscape.** *Ann Oncol* 2018;29(1):84-91.

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Zehir A et al. **Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients.** *Nat Med* 2017;23(6):703-13.

Zhang L et al. **Intratumoral T cells, recurrence, and survival in epithelial ovarian cancer.** *N Engl J Med* 2003;348(3):203-13.

Michael J Birrer, MD, PhD

Moore KN et al. **IMGN853 (mirvetuximab soravtansine), a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC): Single agent activity in platinum-resistant epithelial ovarian cancer (EOC) patients (pts).** *Proc ASCO* 2016;**Abstract 5567**.

Naumann RW et al. **PRECEDENT: A randomized phase II trial comparing EC145 and pegylated liposomal doxorubicin (PLD) in combination, versus PLD alone, in subjects with platinum-resistant ovarian cancer.** *J Clin Oncol* 2010;28(Supp 18):LBA5012b.

David M O'Malley, MD

Breij EC et al. **An antibody-drug conjugate that targets tissue factor exhibits potent therapeutic activity against a broad range of solid tumors.** *Cancer Res* 2014;74(4):1214-26.

Cocco E et al. **Expression of tissue factor in adenocarcinoma and squamous cell carcinoma of the uterine cervix: Implications for immunotherapy with hI-con1, a factor VII-IgGFc chimeric protein targeting tissue factor.** *BMC Cancer* 2011;11:263.

Concin N et al. **A phase IIa study of tisotumab vedotin in patients with previously treated recurrent or metastatic cervical cancer: Updated analysis of full cervical expansion cohort.** *Proc ESMO* 2018;**Abstract 963P**.

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Shannon N Westin, MD, MPH

Bouzin C et al. **Effects of vascular endothelial growth factor on the lymphocyte-endothelium interactions: Identification of caveolin-1 and nitric oxide as control points of endothelial cell anergy.** *J Immunol* 2007;178(3):1505-11.

Chen DS, Mellman I. **Oncology meets immunology: The cancer-immunity cycle.** *Immunity* 2013;39(1):1-10.

Chen L, Flies DB. **Molecular mechanisms of T cell co-stimulation and co-inhibition.** *Nat Rev Immunol* 2013;13(4):227-42.

Coukos G et al. **The role of dendritic cell precursors in tumour vasculogenesis.** *Br J Cancer* 2005;92(7):1182-7.

Galluzzi L et al. **The secret ally: Immunostimulation by anticancer drugs.** *Nat Rev Drug Discov* 2012;11(3):215-33.

Gavalas NG et al. **VEGF directly suppresses activation of T cells from ascites secondary to ovarian cancer via VEGF receptor type 2.** *Br J Cancer* 2012;107(11):1869-75.

Hannani D et al. **Prerequisites for the antitumor vaccine-like effect of chemotherapy and radiotherapy.** *Cancer J* 2011;17(5):351-8.

Jiao S et al. **PARP inhibitor upregulates PD-L1 expression and enhances cancer-associated immunosuppression.** *Clin Cancer Res* 2017;23(14):3711-20.

Konstantinopoulos PA et al. **TOPACIO/Keynote-162 (NCT02657889): A phase 1/2 study of niraparib + pembrolizumab in patients (pts) with advanced triple-negative breast cancer or recurrent ovarian cancer (ROC) — Results from ROC cohort.** *Proc ASCO* 2018;**Abstract 106**.

Makker V et al. **Lenvatinib + pembrolizumab in patients with advanced endometrial cancer: Updated results.** *Proc ASCO* 2018;**Abstract 5596**.

Makker V et al. **A phase Ib/II trial of lenvatinib (LEN) plus pembrolizumab (Pembro) in patients (Pts) with endometrial carcinoma.** *Proc ASCO* 2017;**Abstract 5598**.

Rotte A et al. **Mechanistic overview of immune checkpoints to support the rational design of their combinations in cancer immunotherapy.** *Ann Oncol* 2018;29(1):71-83.

Shrimali RK et al. **Antiangiogenic agents can increase lymphocyte infiltration into tumor and enhance the effectiveness of adoptive immunotherapy of cancer.** *Cancer Res* 2010;70(15):6171-80.

Terme M et al. **VEGFA-VEGFR pathway blockade inhibits tumor-induced regulatory T-cell proliferation in colorectal cancer.** *Cancer Res* 2013;73(2):539-49.

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