Novel Agents and Emerging Strategies in the Management of Gynecologic Cancers

Audio Program

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 rates. Fueled by an increased understanding of the biologic underpinnings of tumor development and growth, clinical research focused on the potential benefits of novel targeted therapeutic agents with unique mechanisms of action and safety profiles has 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 therapies have in turn provided oncology healthcare professionals and patients with new FDA-endorsed treatment options. Although this dynamic is evident in many areas of oncology, recent advances in the management of gynecologic cancers (ovarian, cervical and endometrial cancer) have made it particularly important in this corner of medicine. A plethora of extremely promising data sets have recently emerged, stirring significant enthusiasm for the possibility that several more novel approaches may soon become available to practicing clinicians. Existing management algorithms for these gynecologic cancers are poised for further change, and it is therefore critical that continuing education be offered to all practitioners involved in patient care.

This CME program was developed from the proceedings of a satellite symposium held during the Society of Gynecologic Oncology's 2019 Annual Meeting on Women's Cancer. It features leading gynecologic cancer researchers discussing actual cases from their practices and the published data that drive clinical decision-making for patients in those and diverse other situations. 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 and emerging efficacy data with novel targeted agents under investigation for ovarian, endometrial and cervical cancer, and effectively prioritize clinical trial opportunities or expanded access programs for eligible patients.
- 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.
- Recall the biologic rationale for, published research data with and ongoing clinical trials evaluating the use of immune checkpoint inhibitors in the management of gynecologic cancers, and identify patients who may be eligible for this strategy in or outside of a protocol setting.
- 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.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 1.25 *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 1.25 Medical Knowledge MOC points 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 an audio component. To receive credit, the participant should review the CME information, listen to the MP3s, 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/CME**.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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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MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genmab, Genomic Health Inc, Gilead Sciences Inc, Guardant Health, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, Teva Oncology, Tokai Pharmaceuticals Inc and Tolero Pharmaceuticals.

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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**.

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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.

Varga A et al. **Pembrolizumab in patients with programmed death ligand 1-positive advanced ovarian cancer: Analysis of KEYNOTE-028.** *Gynecol Oncol* 2019;152(2):243-50.

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**.

de Goeij BE et al. **High turnover of tissue factor enables efficient intracellular delivery of antibody-drug conjugates.** *Mol Cancer Ther* 2015;14(5):1130-40.

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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.

Vanneman M, Dranoff G. **Combining immunotherapy and targeted therapies in cancer treatment.** *Nat Rev Cancer* 2012;12(4):237-51.

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