Addressing Current Questions and Controversies:
Emerging Treatment Strategies and Novel Approaches in Gynecologic Cancers
(Part 2 of a 2-Part Series)

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

Gynecologic cancers are comprised of 5 primary cancers affecting the ovaries, uterine corpus (endometrial cancer), uterine cervix (cervical cancer), vulva and vagina. In 2016, it is estimated 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. As with many other tumors, patient outcomes are critically dependent upon effective multidisciplinary care, which in these cases often includes contributions from gynecologic, medical and radiation oncologists as well as pathologists, diagnostic radiologists, oncology nurses and psychosocial services. In addition to the disease- and treatment-related morbidity and mortality associated with gynecologic cancers, pain, fatigue, lymphedema, depression/anxiety, infertility/childbearing and sexual dysfunction are commonly occurring issues that must also be addressed in the care of these patients. Interestingly, despite many commonalities, each of these diseases is in fact quite distinct and consequently management algorithms employed for each are varied.

These video proceedings from a CME symposium held during the Society of Gynecologic Oncology's 2016 Annual Meeting on Women's Cancer feature discussions with leading researchers with an expertise in gynecologic oncology regarding actual patient cases and related clinical research findings. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist gynecologic oncologists and other healthcare providers with the formulation of up-to-date clinical management strategies for various gynecologic cancers.

LEARNING OBJECTIVES

- Evaluate current standard therapies and emerging treatment options, and use this information to appropriately select and sequence therapeutic approaches for patients with primary and recurrent ovarian cancer (OC).
- Recognize the mechanisms of action, emerging efficacy data and toxicity profiles of investigational agents in OC to effectively prioritize clinical trial opportunities for appropriate patients.
- Describe the rationale for targeting angiogenic pathways in gynecologic cancer, and consider the role of the anti-VEGF antibody bevacizumab in the initial and long-term treatment of advanced OC, cervical cancer and endometrial cancer.
- Implement a long-term clinical plan for the management of metastatic cervical cancer and endometrial cancer, incorporating existing, recently approved and investigational treatments.
- Compare and contrast the mechanisms of action, efficacy and safety/toxicity of investigational immunotherapies for the treatment of ovarian, cervical and endometrial cancers, and counsel appropriately selected patients about the availability of ongoing clinical trials.

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 1.75 *AMA PRA Category 1 Credits™*. 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 enables the participant to earn up to 1.25 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**.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis, program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at **ResearchToPractice.com/Privacy-Policy** for more information.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should 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/GynOnc16/EmergingStrategies/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:

Michael Birrer, MD, PhD
Professor, Medicine
Harvard Medical School
Director, Gillette Center for Gynecologic Oncology
Massachusetts General Hospital
Boston, Massachusetts

Advisory Committee: Acceleron Pharma, AstraZeneca Pharmaceuticals LP, ImmunoGen Inc, Merrimack Pharmaceuticals Inc, OXiGENE Inc, Roche Laboratories Inc, Sanofi, Threshold Pharmaceuticals Inc.

Thomas J Herzog, MD
Paul and Carolyn Flory Professor
Deputy Director, UC Cancer Institute
Vice Chair, Quality and Safety
Department of Obstetrics and Gynecology
University of Cincinnati
Cincinnati, Ohio

Advisory Committee: Amgen Inc, AstraZeneca Pharmaceuticals LP, Caris Life Sciences, Pfizer Inc, Roche Laboratories Inc.

Bradley J Monk, MD
Professor and Director
Division of Gynecologic Oncology
Vice Chair, Department of Obstetrics and Gynecology
University of Arizona Cancer Center — Phoenix
Creighton University School of Medicine at Dignity Health
St Joseph's Hospital and Medical Center
Phoenix, Arizona

Consulting Agreements: Advaxis Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Cerulean Pharma Inc, Clovis Oncology, Genentech BioOncology, Gradalis Inc, ImmunoGen Inc, INSYS Therapeutics Inc, Merck, NuCana Biomed, Pfizer Inc, OXiGENE Inc, Roche Laboratories Inc, TESARO Inc, Vermillion Inc; **Contracted Research:** Amgen Inc, Array BioPharma Inc, Genentech BioOncology, Janssen Biotech Inc, Lilly, Morphotek Inc, TESARO Inc; **Speakers Bureau:** AstraZeneca Pharmaceuticals LP, Genentech BioOncology, Janssen Biotech Inc, Myriad Genetic Laboratories Inc, Roche Laboratories Inc.

Angeles Alvarez Secord, MD, MHSc
Professor
Department of Obstetrics and Gynecology
Division of Gynecologic Oncology
Duke Cancer Institute
Durham, North Carolina

Advisory Committee: AstraZeneca Pharmaceuticals LP, Genentech BioOncology, Janssen Biotech Inc; **Contracted Research:** Amgen Inc, Astellas Pharma Global Development Inc, Astex Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Eisai Inc, Endocyte Inc, Exelixis Inc, Genentech BioOncology, Incyte Corporation, Morphotek Inc, Prima BioMed, TESARO Inc.

CONSULTING GYNECOLOGIC ONCOLOGISTS — The following consulting gynecologic oncologists (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

Ioannis Alagkiozidis, MD
Chief of Gynecologic Oncology
Bronx Lebanon Hospital
Bronx, New York

No relevant conflicts of interest to disclose.

Barbara Buttin, MD
Practice Leader, Gynecologic Oncology
Northwestern Medicine Regional Medical Group
Winfield, Illinois

No relevant conflicts of interest to disclose.

Joanie Mayer Hope, MD
Medical Director, Providence Infusion Center
Managing Partner, Alaska Women's Cancer Care
Director of Gynecologic Oncology
Native Alaska Medical Center
Anchorage, Alaska

No relevant conflicts of interest to disclose.

Lynn D Kowalski, MD
Nevada Surgery and Cancer Care
Medical Director, Las Vegas Institute for Robotic Surgery
Vice Chief of Staff, Mountainview Hospital
Las Vegas, Nevada

Consulting Agreement: IntegraGen; **Speakers Bureau:** AstraZeneca Pharmaceuticals LP.

Lyndsay J Willmott, MD
Assistant Professor
Division of Gynecologic Oncology
Creighton University School of Medicine at Dignity Health
St Joseph's Hospital and Medical Center
Phoenix, Arizona

No relevant conflicts of interest to disclose.

MODERATOR — **Dr Love** is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Agendia Inc, Amgen Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, ImmunoGen Inc, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate Inc.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

This activity is supported by educational grants from Genentech BioOncology and ImmunoGen Inc.

Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: July 2016

Expiration date: July 2017

Select Publications

Thomas J Herzog, MD

Alberts DS et al. **Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer.** *N Engl J Med* 1996;335(26):1950-5.

Chan JK et al. **Weekly versus every-3-week paclitaxel and carboplatin for ovarian cancer.** *N Engl J Med* 2016;374(8):738-48.

Chan J et al. **Phase III trial of every-3-weeks paclitaxel vs dose dense weekly paclitaxel with carboplatin +/- bevacizumab in epithelial ovarian, peritoneal, fallopian tube cancer: GOG 262 (NCT01167712).** *Int J Gynecol Cancer* 2013;23:9-10. **No abstract available**

du Bois A et al. **Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: A combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: By the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO).** *Cancer* 2009;115(6):1234-44.

Katsumata N et al; Japanese Gynecologic Oncology Group. **Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer: A phase 3, open-label, randomised controlled trial.** *Lancet* 2009;374(9698):1331-8.

Kehoe S et al. **Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): An open-label, randomised, controlled, non-inferiority trial.** *Lancet* 2015;386(9990):249-57.

Markman M et al. **Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: An intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group.** *J Clin Oncol* 2001;19(4):1001-7.

Pignata S et al. **A randomized multicenter phase III study comparing weekly versus every 3 weeks carboplatin (C) plus paclitaxel (P) in patients with advanced ovarian cancer (AOC): Multicenter Italian Trials in Ovarian Cancer (MITO-7) — European Network of Gynaecological Oncological Trial Groups (ENGOT-ov-10) and Gynecologic Cancer Intergroup (GCIG) trial.** *Proc ASCO* 2013;**Abstract LBA5501**.

Suidan RS et al. **A multicenter prospective trial evaluating the ability of preoperative computed tomography scan and serum CA-125 to predict suboptimal cytoreduction at primary debulking surgery for advanced ovarian, fallopian tube, and peritoneal cancer.** *Gynecol Oncol* 2014;134(3):455-61.

Vergote I et al; European Organization for Research and Treatment of Cancer-Gynaecological Cancer Group; NCIC Clinical Trials Group. **Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer.** *N Engl J Med* 2010;363(10):943-53.

Walker KL et al. **A phase III trial of bevacizumab with IV versus IP chemotherapy in ovarian, fallopian tube, and peritoneal carcinoma: A GOG/NRG trial (GOG 252).** Society of Gynecologic Oncology Annual Meeting 2016;**Late-breaking abstract 6**.

Angeles Alvarez Secord, MD, MHSc

Aghajanian C et al. **A randomized phase II study of paclitaxel/carboplatin/bevacizumab, paclitaxel/carboplatin/temsirolimus and ixabepilone/carboplatin/bevacizumab as initial therapy for measurable stage III or IVA, stage IVB or recurrent endometrial cancer, GOG-86P.** *Proc ASCO* 2015;**Abstract 5500**.

Fagotti A et al. **A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: A pilot study.** *Ann Surg Oncol* 2006;13(8):1156-61.

Lorusso D et al. **Randomized phase II trial of carboplatin-paclitaxel (CP) compared to carboplatin-paclitaxel-bevacizumab (CP-B) in advanced (stage III-IV) or recurrent endometrial cancer: The MITO END-2 trial.** *Proc ASCO* 2015;**Abstract 5502**.

Zorn KK et al. **Gene expression profiles of serous, endometrioid, and clear cell subtypes of ovarian and endometrial cancer.** *Clin Cancer Res* 2005;11(18):6422-30.

Michael Birrer, MD, PhD

Borghaei H et al. **Phase 1 study of IMGN853, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC) in patients (Pts) with epithelial ovarian cancer (EOC) and other FRA-positive solid tumors.** *Proc ASCO* 2015;**Abstract 5558**.

Cheung LW et al. **High frequency of PIK3R1 and PIK3R2 mutations in endometrial cancer elucidates a novel mechanism for regulation of PTEN protein stability.** *Cancer Discov* 2011;1(2):170-85.

Select Publications

D'Incalci M, Galmarini CM. **A review of trabectedin (ET-743): A unique mechanism of action.** *Mol Cancer Ther* 2010;9(8):2157-63.

Monk BJ et al. **Trabectedin plus pegylated liposomal doxorubicin in recurrent ovarian cancer.** *J Clin Oncol* 2010;28(19):3107-14.

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**.

Bradley J Monk, MD

Brahmer JR et al. **Safety and activity of anti-PD-L1 antibody in patients with advanced cancer.** *N Engl J Med* 2012;366(26):2455-65.

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**.

Eskander RN, Tewari KS. **Immunotherapy: An evolving paradigm in the treatment of advanced cervical cancer.** *Clin Ther* 2015;37(1):20-38.

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**.

Longoria TC, Tewari KS. **Pharmacologic management of advanced cervical cancer: Antiangiogenesis therapy and immunotherapeutic considerations.** *Drugs* 2015;75(16):1853-65.

Mellman I et al. **Cancer immunotherapy comes of age.** *Nature* 2011;480(7378):480-9.

Ribas A. **Adaptive immune resistance: How cancer protects from immune attack.** *Cancer Discov* 2015;5(9):915-9.

Ribas A. **Tumor immunotherapy directed at PD-1.** *N Engl J Med* 2012;366(26):2517-9.

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**.

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