

Cases from the Community

Clinical Investigators Provide Their Perspectives on Emerging Research and Actual Patients with Ovarian Cancer

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 American Cancer Society estimates that in 2018, approximately 22,240 new cases of ovarian cancer (OC) will be diagnosed in the United States and more than 14,000 individuals will die of the disease, making it the most lethal of the various gynecologic cancers. As with many other tumors, patient outcomes are critically dependent upon effective multidisciplinary care, which 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 OC, pain, fatigue, lymphedema, depression/anxiety, infertility/child-bearing and sexual dysfunction are commonly occurring issues that must also be addressed in the care of these patients.

These video proceedings from a CME symposium held during the Society of Gynecologic Oncology's 2018 Annual Meeting on Women's Cancer explore significant therapeutic advances in the field of OC treatment by using the perspectives of leading experts on challenging cases and questions submitted by gynecologic and medical oncologists in the community to frame a relevant discussion of how this information has aided in the refinement of current routine clinical practice and ongoing research. This CME activity will help gynecologic oncologists, medical oncologists, gynecologists and other healthcare providers find answers to the individualized questions and concerns that they frequently encounter and in turn provide high-quality cancer care.

LEARNING OBJECTIVES

- Review available efficacy and safety data with the use of neoadjuvant chemotherapy followed by surgical cytoreduction for patients with Stage IIIC or IV OC, and identify patients who may be suitable for this approach.
- Summarize existing research data and ongoing clinical trials documenting the risks and benefits of angiogenesis inhibition in the management of newly diagnosed advanced

OC, and identify individuals who may benefit from this treatment strategy.

- Develop a treatment algorithm for the management of progressive epithelial OC, considering the response to prior therapy, genomic profile, goals of treatment and the relative efficacy and safety of evidence-based therapeutic strategies.
- Recognize the toxicities associated with therapeutic agents and regimens commonly used in the care of patients with OC, and offer supportive management strategies to minimize and/or ameliorate these side effects.
- Develop an understanding of the mechanisms of action, available data and potential clinical roles of compounds under investigation for patients with advanced OC in preparation for their potential introduction into clinical practice.

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 2 *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, which includes participation in the evaluation component, enables the participant to earn up to 2 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**.

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 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/GynOnc18/CommunityCases/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:

Don S Dizon, MD

Director, Women's Cancers
Lifespan Cancer Institute
Director, Medical Oncology
Rhode Island Hospital
Associate Professor of Medicine
Alpert Medical School of Brown University
Providence, Rhode Island

Consulting Agreement: Fujibio.

Lainie P Martin, MD

Chief, Gynecologic Medical Oncology
Assistant Professor, Department of Hematology/Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Advisory Committee: ImmunoGen Inc, Tesaro Inc; **Contracted Research:** Novartis.

Bradley J Monk, MD

Professor
Division of Gynecologic Oncology
Arizona Oncology (US Oncology Network)
University of Arizona College of Medicine - Phoenix
Creighton University School of Medicine at
St Joseph's Hospital
Phoenix, Arizona

Consulting Agreements: Amgen Inc, AstraZeneca Pharmaceuticals LP, Genentech, Incyte Corporation, Merck, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Roche Laboratories Inc; **Speakers Bureau:** AstraZeneca Pharmaceuticals LP, Genentech, Janssen Biotech 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: Alexion Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Genentech, Janssen Biotech Inc, Myriad Genetic Laboratories Inc, Roche Laboratories Inc, Tesaro Inc; **Contracted Research:** Boehringer Ingelheim Pharmaceuticals Inc, Merck.

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, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals 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, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genomic Health Inc, Gilead Sciences Inc, 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, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals 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, ImmunoGen Inc and Merck.

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

Release date: May 2018

Expiration date: May 2019

Select Publications

Angeles Alvarez Secord, MD, MHSc

- Burger RA et al; Gynecologic Oncology Group. **Incorporation of bevacizumab in the primary treatment of ovarian cancer.** *N Engl J Med* 2011;365(26):2473-83.
- Chan JK et al. **Weekly vs every-3-week paclitaxel and carboplatin for ovarian cancer.** *N Engl J Med* 2016;374(8):738-48.
- Clamp AR et al. **ICON8: A GCIG phase III randomised trial evaluating weekly dose-dense chemotherapy integration in first-line epithelial ovarian/fallopian tube/primary peritoneal carcinoma (EOC) treatment: Results of primary progression-free survival (PFS) analysis.** *Proc ESMO* 2017;Abstract 9290_PR.
- du Bois A et al; AGO Study Group led Gynecologic Cancer Intergroup/European Network of Gynaecologic Oncology Trials Groups Intergroup Consortium. **Standard first-line chemotherapy with or without nintedanib for advanced ovarian cancer (AGO-OVAR 12): A randomised, double-blind, placebo-controlled phase 3 trial.** *Lancet Oncol* 2016;17(1):78-89.
- du Bois A et al. **Incorporation of pazopanib in maintenance therapy of ovarian cancer.** *J Clin Oncol* 2014;32(30):3374-82.
- Fagotti A et al. **Phase III randomised clinical trial comparing primary surgery versus neoadjuvant chemotherapy in advanced epithelial ovarian cancer with high tumour load (SCORPION trial): Final analysis of peri-operative outcome.** *Eur J Cancer* 2016;59:22-33.
- Katsumata N et al; Japanese Gynecologic Oncology Group. **Long-term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): A randomised, controlled, open-label trial.** *Lancet Oncol* 2013;14(10):1020-6.
- 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.
- Meyer L et al. **Use and effectiveness of neoadjuvant chemotherapy for treatment of ovarian cancer.** *J Clin Oncol* 2016;34(32):3854-63.
- Onda T et al; Japan Clinical Oncology Group. **Comparison of treatment invasiveness between upfront debulking surgery versus interval debulking surgery following neoadjuvant chemotherapy for stage III/IV ovarian, tubal, and peritoneal cancers in a phase III randomised trial: Japan Clinical Oncology Group Study JCOG0602.** *Eur J Cancer* 2016;64:22-31.
- Oza AM et al. **Olaparib combined with chemotherapy for recurrent platinum-sensitive ovarian cancer: A randomised phase 2 trial.** *Lancet Oncol* 2015;16(1):87-97.
- Perren TJ et al; ICON7 Investigators. **A phase 3 trial of bevacizumab in ovarian cancer.** *N Engl J Med* 2011;365(26):2484-96.
- Pignata S et al. **Carboplatin plus paclitaxel once a week versus every 3 weeks in patients with advanced ovarian cancer (MITO-7): A randomised, multicentre, open-label, phase 3 trial.** *Lancet Oncol* 2014;15(4):396-405.
- Trial on radical upfront surgery in advanced ovarian cancer. NCT02828618**
- van Driel WJ et al. **Hyperthermic intraperitoneal chemotherapy in ovarian cancer.** *N Engl J Med* 2018;378(3):230-40.
- 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.
- Wright AA et al. **Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline.** *J Clin Oncol* 2016;34(28):3460-73.

Bradley J Monk, MD

- Aghajanian C et al. **OCEANS: A randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer.** *J Clin Oncol* 2012;30(17):2039-45.
- Alvarez RD et al. **Moving beyond the platinum sensitive/resistant paradigm for patients with recurrent ovarian cancer.** *Gynecol Oncol* 2016;141(3):405-9.
- Coleman RL et al; ARIEL3 Investigators. **Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet* 2017;390(10106):1949-61.
- Gonzalez-Martín AJ et al. **Randomized phase II trial of carboplatin versus paclitaxel and carboplatin in platinum-sensitive recurrent advanced ovarian carcinoma: A GEICO (Grupo Español de Investigación en Cáncer de Ovario) study.** *Ann Oncol* 2005;16(5):749-55.
- Parmar MK et al; ICON and AGO Collaborators. **Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: The ICON4/AGO-OVAR-2.2 trial.** *Lancet* 2003;361(9375):2099-106.

Select Publications

Pfisterer J et al; AGO-OVAR; NCIC CTG; EORTC GCG. **Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: An intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG.** *J Clin Oncol* 2006;24(29):4699-707.

Pujade-Lauraine E et al. **Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): A double-blind, randomised, placebo-controlled, phase 3 trial.** *Lancet Oncol* 2017;18(9):1274-84.

Pujade-Lauraine E et al. **Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse.** *J Clin Oncol* 2010;28(20):3323-9.

Raja FA et al. **Platinum versus platinum-combination chemotherapy in platinum-sensitive recurrent ovarian cancer: A meta-analysis using individual patient data.** *Ann Oncol* 2013;24(12):3028-34.

Mirza MR et al. **Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer.** *N Engl J Med* 2016;375(22):2154-64.

Don S Dizon, MD

Alici S et al. **Oral etoposide (VP16) in platinum-resistant epithelial ovarian cancer (EOC).** *Am J Clin Oncol* 2003;26(4):358-62.

Brewer CA et al. **Cisplatin plus gemcitabine in platinum-refractory ovarian or primary peritoneal cancer: A phase II study of the Gynecologic Oncology Group.** *Gynecol Oncol* 2006;103(2):446-50.

Burger RA et al. **Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: A Gynecologic Oncology Group Study.** *J Clin Oncol* 2007;25(33):5165-71.

Cannistra SA et al. **Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer.** *J Clin Oncol* 2007;25(33):5180-6.

Coleman RL et al. **A phase II evaluation of nanoparticle, albumin-bound (nab) paclitaxel in the treatment of recurrent or persistent platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer: A Gynecologic Oncology Group study.** *Gynecol Oncol* 2011;122(1):111-5.

Dizon DS et al. **Retrospective analysis of carboplatin and paclitaxel as initial second-line therapy for recurrent epithelial ovarian carcinoma: Application toward a dynamic disease state model of ovarian cancer.** *J Clin Oncol* 2002;20(5):1238-47.

Foote J et al. **Predicting 6- and 12-month risk of mortality in patients with platinum-resistant advanced-stage ovarian cancer: Prognostic model to guide palliative care referrals.** *Int J Gynecol Cancer* 2018;28(2):302-7.

Galluzzi L et al. **Systems biology of cisplatin resistance: Past, present and future.** *Cell Death Dis* 2014;5:e1257.

Gordon AN et al. **Recurrent epithelial ovarian carcinoma: A randomized phase III study of pegylated liposomal doxorubicin versus topotecan.** *J Clin Oncol* 2001;19(14):3312-22.

Gynecologic Oncology Group et al. **Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: A Gynecologic Oncology Group study.** *Gynecol Oncol* 2006;101(3):436-40.

Lortholary A et al; GINECO group France. **Weekly paclitaxel as a single agent or in combination with carboplatin or weekly topotecan in patients with resistant ovarian cancer: The CARTAXHY randomized phase II trial from Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO).** *Ann Oncol* 2012;23(2):346-52.

Matulonis UA et al. **Olaparib monotherapy in patients with advanced relapsed ovarian cancer and a germline BRCA1/2 mutation: A multistudy analysis of response rates and safety.** *Ann Oncol* 2016;27(6):1013-9.

Miller DS et al. **Phase II evaluation of pemetrexed in the treatment of recurrent or persistent platinum-resistant ovarian or primary peritoneal carcinoma: A study of the Gynecologic Oncology Group.** *J Clin Oncol* 2009;27(16):2686-91.

Mutch DG et al. **Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer.** *J Clin Oncol* 2007;25(19):2811-8.

Pujade-Lauraine E et al. **Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial.** *J Clin Oncol* 2014;32(13):1302-8.

Sehouli J et al. **Topotecan weekly versus conventional 5-day schedule in patients with platinum-resistant ovarian cancer: A randomized multicenter phase II trial of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group.** *J Clin Oncol* 2011;29(2):242-8.

Shoji T et al. **A phase II study of irinotecan and pegylated liposomal doxorubicin in platinum-resistant recurrent ovarian cancer (Tohoku Gynecologic Cancer Unit 104 study).** *Cancer Chemother Pharmacol* 2017;80(2):355-61.

Smolle E et al. **Malignant ascites in ovarian cancer and the role of targeted therapeutics.** *Anticancer Res* 2014;34(4):1553-61.

Select Publications

Stuart GC et al; Participants of 4th Ovarian Cancer Consensus Conference (OCCC); Gynecologic Cancer Intergroup. **2010 Gynecologic Cancer InterGroup (GCIG) consensus statement on clinical trials in ovarian cancer: Report from the Fourth Ovarian Cancer Consensus Conference.** *Int J Gynecol Cancer* 2011;21(4):750-5.

Verschraegen CF et al. **Docetaxel for patients with paclitaxel-resistant Müllerian carcinoma.** *J Clin Oncol* 2000;18(14):2733-9.

Wilson MK et al. **Fifth Ovarian Cancer Consensus Conference of the Gynecologic Cancer InterGroup: Recurrent disease.** *Ann Oncol* 2017;28(4):727-32.

Lainie P Martin, MD

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* 2017;Abstract 5533.

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.

Infante J et al. **Safety, clinical activity and biomarkers of atezolizumab (atezo) in advanced ovarian cancer (OC).** *Proc ESMO* 2016;Abstract 871P.

Matulonis UA et al. **Initial safety and activity findings from a phase IB escalation study of mirvetuximab soravtansine, a folate receptor alpha (FR α)-targeting antibody-drug conjugate (ADC), with pembrolizumab in platinum-resistant epithelial ovarian cancer (EOC) patients.** *Proc SGO* 2018;Abstract 74.

Martin LP et al. **Characterization of folate receptor alpha (FR α) expression in archival tumor and biopsy samples in a phase I study of mirvetuximab soravtansine, a FR α -targeting antibody-drug conjugate (ADC), in relapsed epithelial ovarian cancer patients.** *Proc SGO* 2017;Abstract 61.

Moore KN et al. **FORWARD I: A phase III study of mirvetuximab soravtansine versus chemotherapy in platinum-resistant ovarian cancer.** *Future Oncol* 2018;[Epub ahead of print].

Ponte JF et al. **Mirvetuximab soravtansine (IMGN853), a folate receptor alpha-targeting antibody-drug conjugate, potentiates the activity of standard of care therapeutics in ovarian cancer models.** *Neoplasia* 2016;18(12):775-84.

Varga A et al. **Pembrolizumab in patients (pts) with PD-L1–positive (PD-L1⁺) advanced ovarian cancer: Updated analysis of KEYNOTE-028.** *Proc ASCO* 2017;Abstract 5513.