New Agents and Emerging Strategies in the Management of Uterine Sarcomas

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

As a group, gynecologic sarcomas are relatively rare, and given their wide heterogeneity, specific histologic subtypes present even less frequently in clinical practice. As such, gynecologic and medical oncologists may lack experience caring for patients with any given uterine sarcoma, including the most common, uterine leiomyosarcoma (uLMS). Even so, and despite the fact that conventional treatment options for sarcomas of the female genital tract had remained unchanged for several years, recently published research has led to several newly approved therapies poised to disrupt established standards. With the proliferation of these research advances, it is important for any healthcare professional involved in the care of these individuals to remain up to date in order to appropriately offer patients with uLMS or other gynecologic sarcomas high-quality treatment.

As such, these video proceedings from a CME symposium held during the Society of Gynecologic Oncology's 2018 Annual Meeting on Women's Cancer blend practical perspectives with review of clinical trial data to address many of the most pertinent issues and education gaps faced by clinicians managing this unusual, challenging and heterogeneous disease.

LEARNING OBJECTIVES

- Appreciate the importance of multidisciplinary collaboration in the diagnosis and management of gynecologic sarcomas, and use this information to design a process to optimize tissue procurement, accurate histological assessment, tertiary care referral and treatment outcome.
- Develop an evidence-based strategy for the treatment of Stage I to III uterine sarcoma, considering the potential contributions of surgery, radiation therapy and/or cytotoxic therapy.
- Employ guideline-endorsed monitoring protocols and techniques to effectively screen patients with localized uLMS for the development of metastases.
- Recognize the role platelet-derived growth factor alpha (PDGFRα) expression plays in tumor proliferation and growth, and consider this information in the selection of therapeutic approach for patients with advanced uLMS.
- Appraise available safety and efficacy data with approved targeted and cytotoxic therapies used in the treatment of advanced gynecologic sarcomas, and consider how these agents can be optimally incorporated into current clinical management algorithms.

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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 1.5 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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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

Suzanne George, MD
Clinical Director, Center for Sarcoma and Bone Oncology
Dana-Farber Cancer Institute
Assistant Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Advisory Committee: Blueprint Medicines, Deciphera Pharmaceuticals Inc; **Contracted Research:** Bayer HealthCare Pharmaceuticals, Blueprint Medicines, Deciphera Pharmaceuticals Inc, Pfizer Inc; **Ownership Interest:** Abbott Laboratories.

Martee L Hensley, MD
Attending, Gynecologic Medical Oncology
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

Advisory Committee: Janssen Biotech Inc, Lilly; **Contracted Research:** Bristol-Myers Squibb Company, Janssen Biotech Inc.

David M O'Malley, MD
Professor
Director, Clinical Research
Gynecologic Oncology
Co-Director, Gynecologic Oncology Phase I Program
ORIEN Physician Liaison for OSUCCC-James
The Ohio State University and The James Cancer Center
Columbus, Ohio

Advisory Committee: Amgen Inc; **Consulting Agreement:** AstraZeneca Pharmaceuticals LP.

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 BioOncology, 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.

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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

Neil Love, MD

Drilon A et al. **Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children.** *N Engl J Med* 2018;378(8):731-9.

Goodman A et al. **Analysis of over 100,000 patients with cancer for *CD274* (*PD-L1*) amplification: Implications for treatment with immune checkpoint blockade.** *Proc ASCO* 2017;**Abstract 47**.

Love N et al. **The morbidity and mortality conference (MMC) concept applied to contemporary oncology practice: Retrospective findings on management of 233 patients (pts) who died of ovarian cancer (OC), colorectal cancer (CRC), and wild-type (no identified targetable mutation) nonsquamous non-small cell lung cancer (WTLC).** Quality Care Symposium 2017;**Abstract 241**.

Ziel K et al. **The morbidity and mortality conference (MMC) concept applied to contemporary oncology practice: Retrospective findings on management of 233 patients (pts) who died of ovarian cancer (OC), colorectal cancer (CRC) and wild-type (no identified targetable mutation) nonsquamous non-small cell lung cancer (WTLC).** *Proc ASCO* 2017;**Abstract e18195**.

David M O'Malley, MD

George S et al. **Soft tissue and uterine leiomyosarcoma.** *J Clin Oncol* 2018;36(2):144-50.

Hensley ML. **Difficult choices in stage I uterine leiomyosarcoma — It's okay to "stand there."** *Gynecol Oncol* 2017;147(1):1-2.

Hensley ML et al. **GCIG consensus review: Uterine and ovarian leiomyosarcomas.** *Int J Gynecol Cancer* 2014;24(Supp 3):61-6.

Littell RD et al. **Adjuvant gemcitabine-docetaxel chemotherapy for stage I uterine leiomyosarcoma: Trends and survival outcomes.** *Gynecol Oncol* 2017;147(1):11-7.

Nasioudis D et al. **Safety of ovarian preservation in premenopausal women with stage I uterine sarcoma.** *J Gynecol Oncol* 2017;28(4):e46.

Omura GA et al. **A randomized clinical trial of adjuvant adriamycin in uterine sarcomas: A Gynecologic Oncology Group Study.** *J Clin Oncol* 1985;3(9):1240-5.

Pautier P et al. **A randomized clinical trial of adjuvant chemotherapy with doxorubicin, ifosfamide, and cisplatin followed by radiotherapy versus radiotherapy alone in patients with localized uterine sarcomas (SARCGYN study). A study of the French Sarcoma Group.** *Ann Oncol* 2013;24(4):1099-104.

Reed NS et al. **Phase III randomised study to evaluate the role of adjuvant pelvic radiotherapy in the treatment of uterine sarcomas stages I and II: A European Organisation for Research and Treatment of Cancer Gynaecological Cancer Group Study (protocol 55874).** *Eur J Cancer* 2008;44(6):808-18.

Thanopoulou E et al. **Treatment of hormone positive uterine leiomyosarcoma with aromatase inhibitors.** *Clin Sarcoma Res* 2014;4:5.

Zivanovic O et al. **A nomogram to predict postresection 5-year overall survival for patients with uterine leiomyosarcoma.** *Cancer* 2012;118(3):660-9.

Martee L Hensley, MD

A randomized, double-blind, placebo-controlled, phase 3 trial of doxorubicin plus olaratumab versus doxorubicin plus placebo in patients with advanced or metastatic soft tissue sarcoma. **NCT02451943**

Seddon B et al. **Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS): A randomised controlled phase 3 trial.** *Lancet Oncol* 2017;18(10):1397-410.

Tap WD et al. **Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: An open-label phase 1b and randomised phase 2 trial.** *Lancet* 2016;388(10043):488-97.

Suzanne George, MD

Ben-Ami E et al. **Immunotherapy with single agent nivolumab for advanced leiomyosarcoma of the uterus: Results of a phase 2 study.** *Cancer* 2017;123(17):3285-90.

D'Angelo SP et al. **Nivolumab with or without ipilimumab treatment for metastatic sarcoma (Alliance A091401): Two open-label, non-comparative, randomised, phase 2 trials.** *Lancet Oncol* 2018;19(3):416-26.

George S et al. **Soft tissue and uterine leiomyosarcoma.** *J Clin Oncol* 2018;36(2):144-50.

George S et al. **Loss of PTEN is associated with resistance to Anti-PD-1 checkpoint blockade therapy in metastatic uterine leiomyosarcoma.** *Immunity* 2017;46(2):197-204.

Select Publications

Hensley ML et al. **Efficacy and safety of trabectedin or dacarbazine in patients with advanced uterine leiomyosarcoma after failure of anthracycline-based chemotherapy: Subgroup analysis of a phase 3, randomized clinical trial.** *Gynecol Oncol* 2017;146(3):531-7.

Pautier P et al. **Trabectedin in combination with doxorubicin for first-line treatment of advanced uterine or soft-tissue leiomyosarcoma (LMS-02): A non-randomised, multicentre, phase 2 trial.** *Lancet Oncol* 2015;16(4):457-64.

Tawbi HA et al. **Pembrolizumab in advanced soft-tissue sarcoma and bone sarcoma (SARC028): A multicentre, two-cohort, single-arm, open-label, phase 2 trial.** *Lancet Oncol* 2017;18(11):1493-501.

Van der Graaf WTA et al. **Pazopanib for metastatic soft-tissue sarcoma (PALETTE): A randomised, double-blind, placebo-controlled phase 3 trial.** *Lancet* 2012;379(9829):1879-86.

Zewail-Foote M et al. **The inefficiency of incisions of ecteinascidin 743-DNA adducts by the UvrABC nuclease and the unique structural feature of the DNA adducts can be used to explain the repair-dependent toxicities of this antitumor agent.** *Chem Biol* 2001;8(11):1033-49.