The Implications of New Research Findings for the Management of Endometrial Cancer

A CME/MOC-Accredited Virtual Event in Partnership with the Society of Gynecologic Oncology

Wednesday, June 28, 2023

5:00 PM – 6:00 PM ET

Faculty

Bradley J Monk, MD

Matthew A Powell, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Bradley J Monk, MD
Professor
Division of Gynecologic Oncology
University of Arizona College of Medicine
Creighton University School of Medicine
Phoenix, Arizona

Moderator
Neil Love, MD
Research To Practice

Matthew A Powell, MD
Professor, Department of Obstetrics and Gynecology
Washington University School of Medicine
St Louis, Missouri

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from GSK and Merck.

RTP
RESEARCH
TO PRACTICE

Dr Love — Disclosures

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 companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

RTP
RESEARCH
TO PRACTICE

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Monk — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Eisai Inc, Genentech, a member of the Roche Group, Genmab US Inc, ImmunoGen Inc, Karyopharm Therapeutics, Merck, Myriad Genetic Laboratories Inc, Novocure Inc, Seagen Inc, Tesaro, A GSK Company
Speakers Bureau	AstraZeneca Pharmaceuticals LP, Eisai Inc, Genentech, a member of the Roche Group, ImmunoGen Inc, Merck, Myriad Genetic Laboratories Inc, Tesaro, A GSK Company

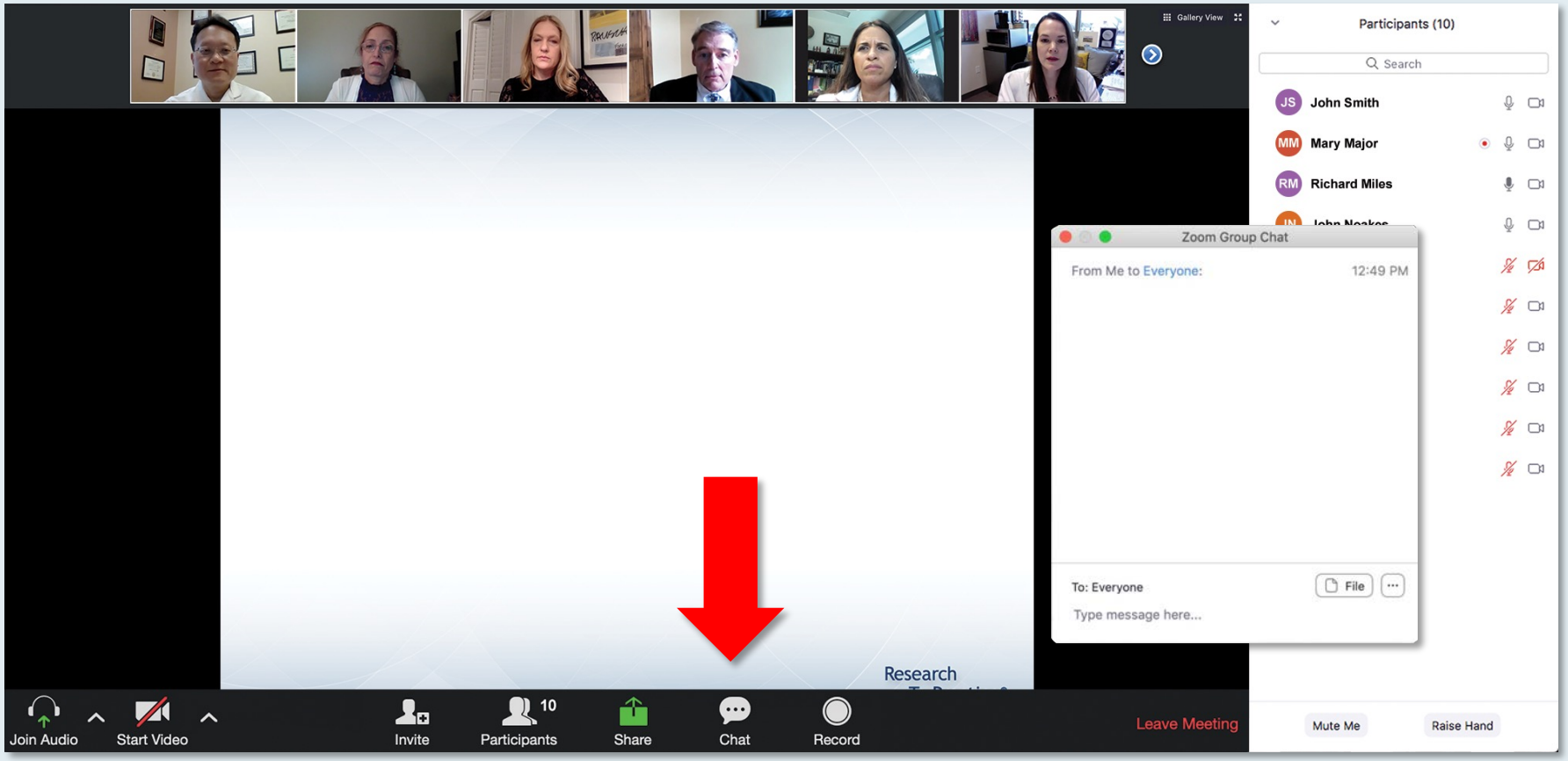
RTP
RESEARCH
TO PRACTICE

Dr Powell — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, GSK, Merck, Roche Laboratories Inc, Seagen Inc
Contracted Research	GSK

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

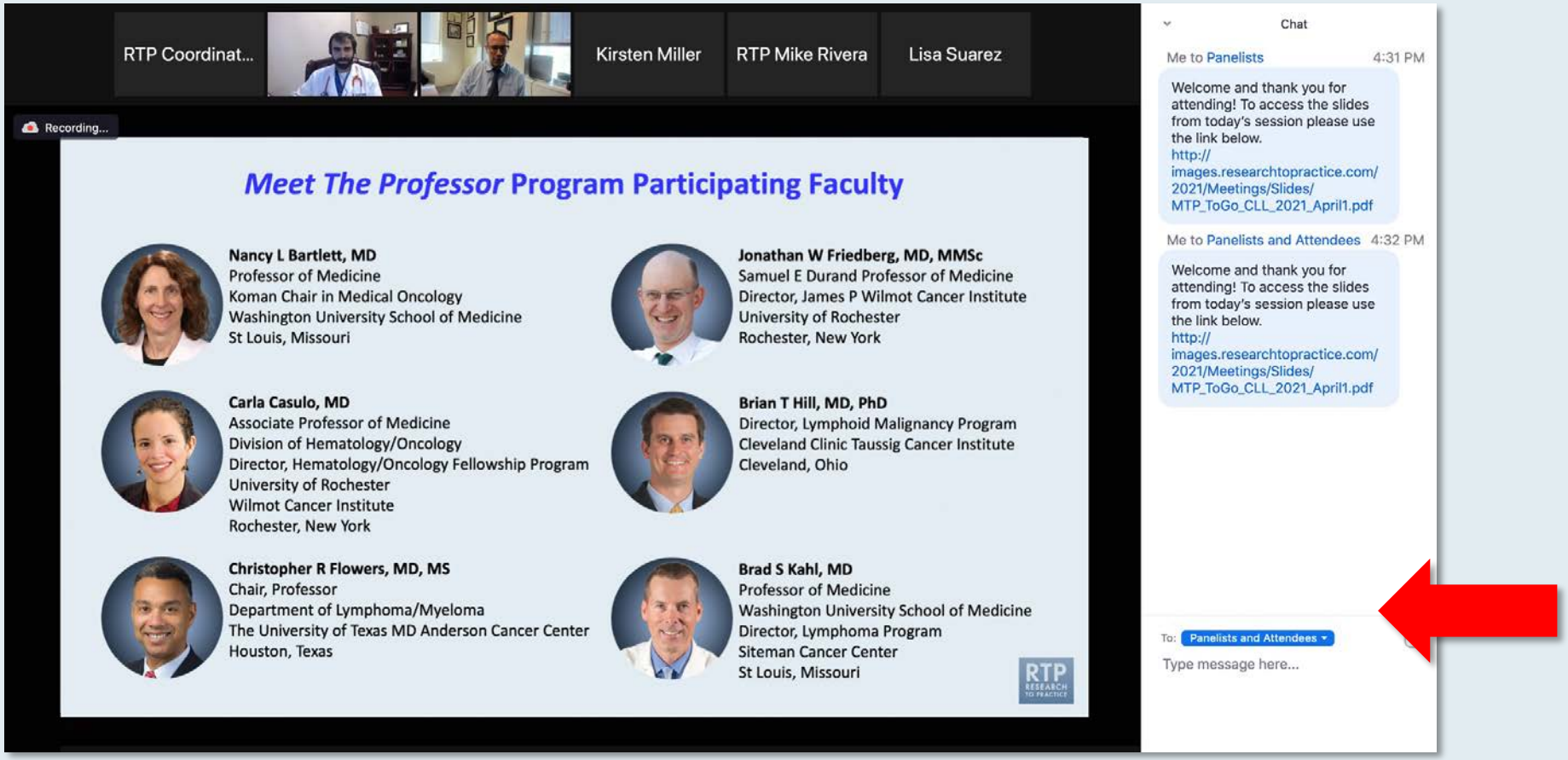


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

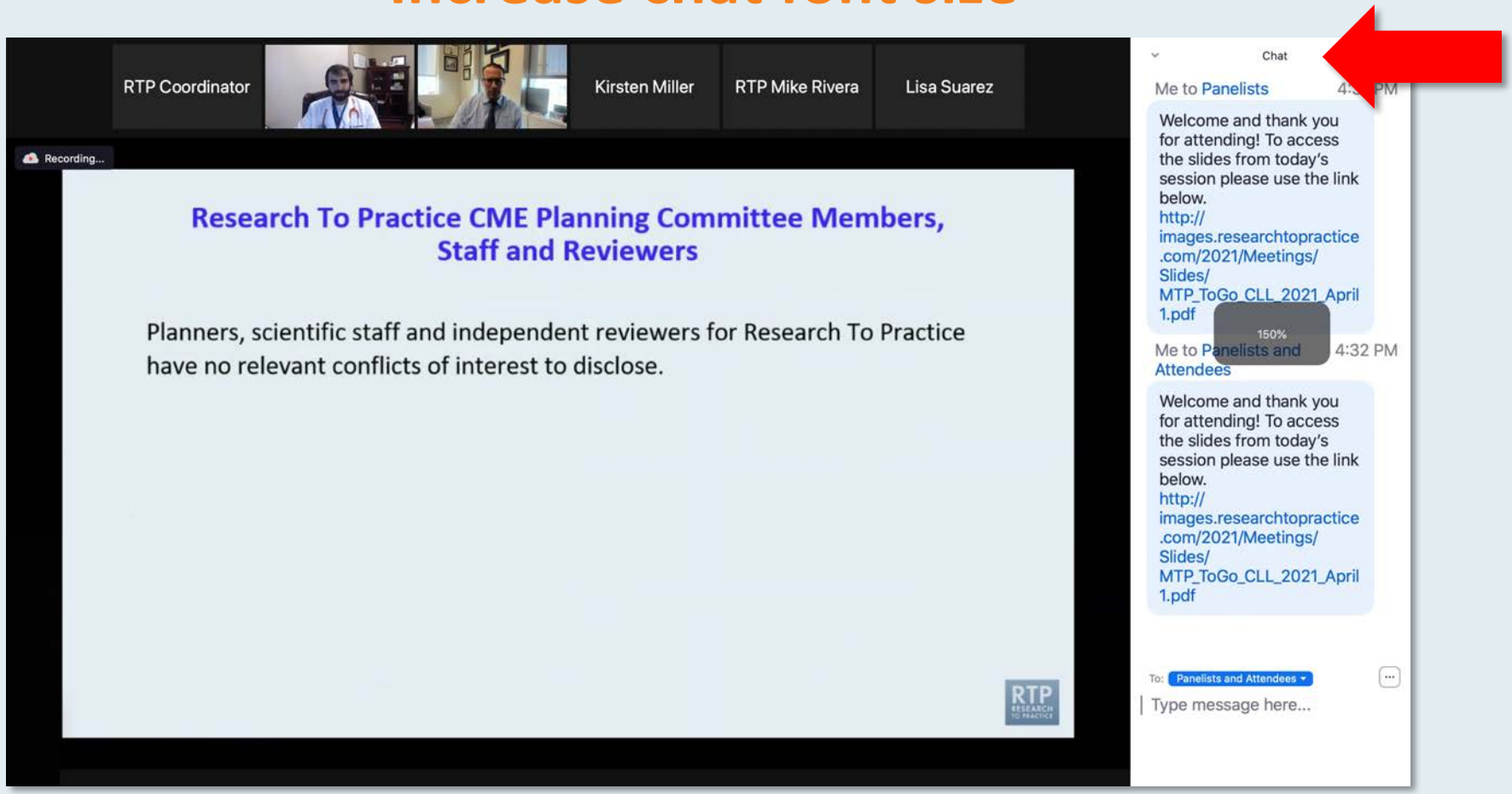


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

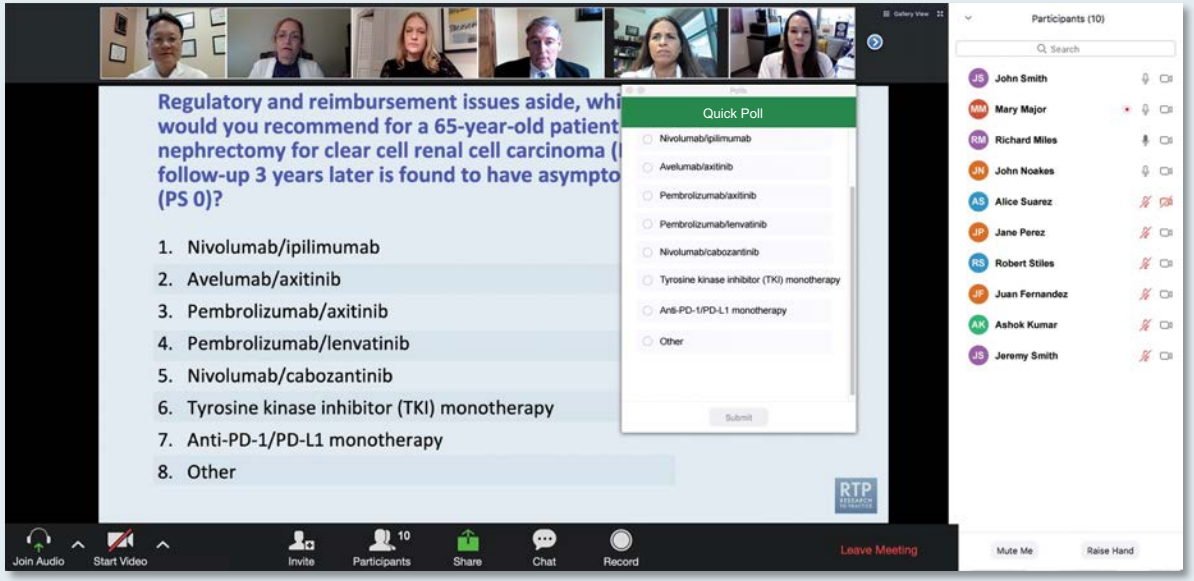
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

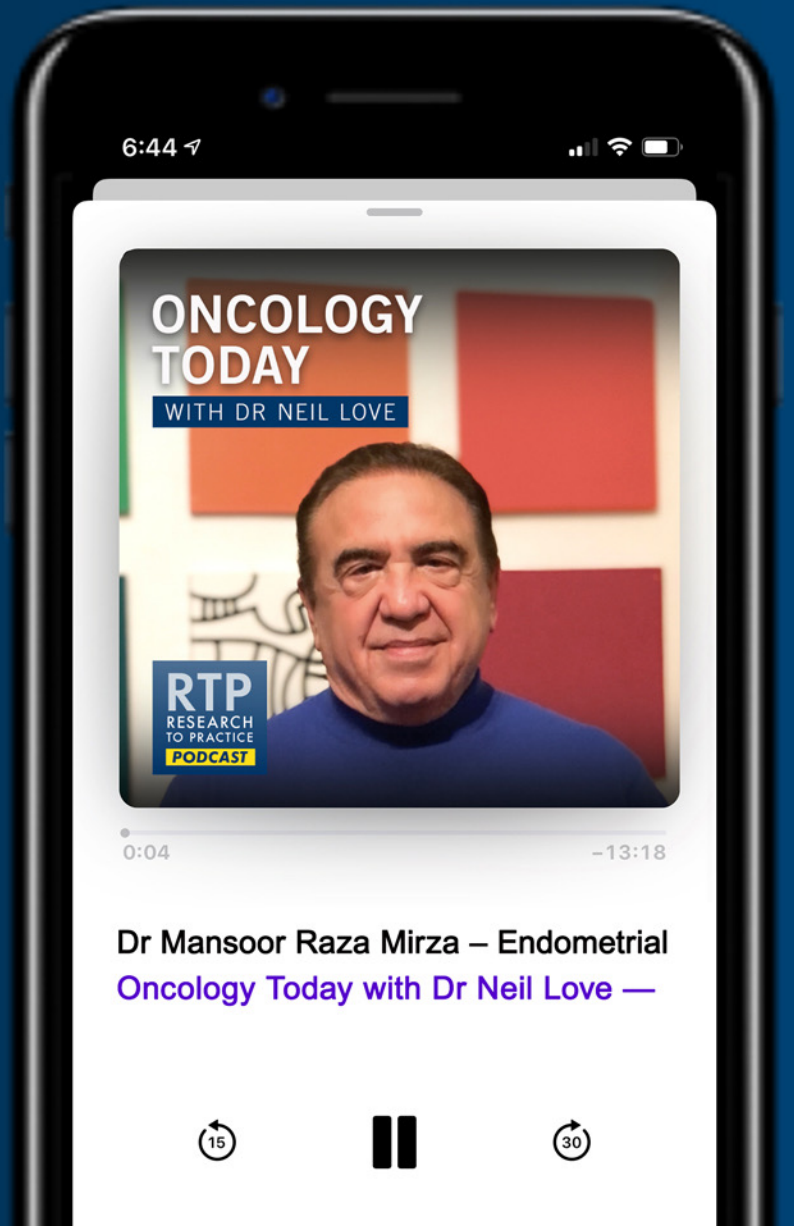
Endometrial Cancer Edition

DR MANSOOR RAZA MIRZA
COPENHAGEN UNIVERSITY HOSPITAL

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Inside the Issue: Optimizing the Management of Metastatic Urothelial Bladder Cancer

A CME/MOC-Accredited Live Webinar

Thursday, June 29, 2023
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Petros Grivas, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

What I Tell My Patients: Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Part 3 of a 3-Part Complimentary NCPD Webinar Series
in Partnership with the 2023 ONS Congress

Chronic Lymphocytic Leukemia

Thursday, July 6, 2023
5:00 PM – 6:00 PM ET

Faculty

Kristen E Battiato, AGNP-C
Jennifer Woyach, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Inside the Issue: Novel Agents, Approaches and Strategies in the Management of Higher-Risk Myelodysplastic Syndromes

A CME/MOC-Accredited Live Webinar

Tuesday, July 11, 2023
5:00 PM – 6:00 PM ET

Faculty

Guillermo Garcia-Manero, MD
David Sallman, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Melanoma and Nonmelanoma Skin Cancers

Thursday, July 13, 2023
5:00 PM – 6:00 PM ET

Faculty

Omid Hamid, MD

Evan J Lipson, MD

Moderator

Neil Love, MD

RTP Year in Review 2023

Inside the Issue: Integrating Bispecific Antibodies into the Management of Multiple Myeloma — Patient Selection and Toxicity Management

A CME/MOC-Accredited Live Webinar

Tuesday, July 18, 2023
5:00 PM – 6:00 PM ET

Faculty

Hans Lee, MD
Saad Zafar Usmani, MD, MBA

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Current and Future Management of ER-Positive Metastatic Breast Cancer After Disease Progression on a CDK4/6 Inhibitor

A CME/MOC-Accredited Live Webinar

Thursday, July 20, 2023
5:00 PM – 6:00 PM ET

Faculty

Aditya Bardia, MD, MPH
Erika Hamilton, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP
RESEARCH
TO PRACTICE

The Implications of New Research Findings for the Management of Endometrial Cancer

A CME/MOC-Accredited Virtual Event in Partnership with the Society of Gynecologic Oncology

Wednesday, June 28, 2023

5:00 PM – 6:00 PM ET

Faculty

Bradley J Monk, MD

Matthew A Powell, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Bradley J Monk, MD
Professor
Division of Gynecologic Oncology
University of Arizona College of Medicine
Creighton University School of Medicine
Phoenix, Arizona

Moderator
Neil Love, MD
Research To Practice

Matthew A Powell, MD
Professor, Department of Obstetrics and Gynecology
Washington University School of Medicine
St Louis, Missouri

RTP
RESEARCH
TO PRACTICE

Survey Participants

Ramez N Eskander, MD
Clinical Professor of Gynecologic Oncology
Fellowship Director
Co-Director, UC San Diego Health International Patient Program
Moores Cancer Center at UC San Diego
San Diego, California

Richard T Penson, MD, MRCP
Associate Professor of Medicine
Harvard Medical School
Clinical Director, Medical Gynecologic Oncology
Massachusetts General Hospital
Boston, Massachusetts

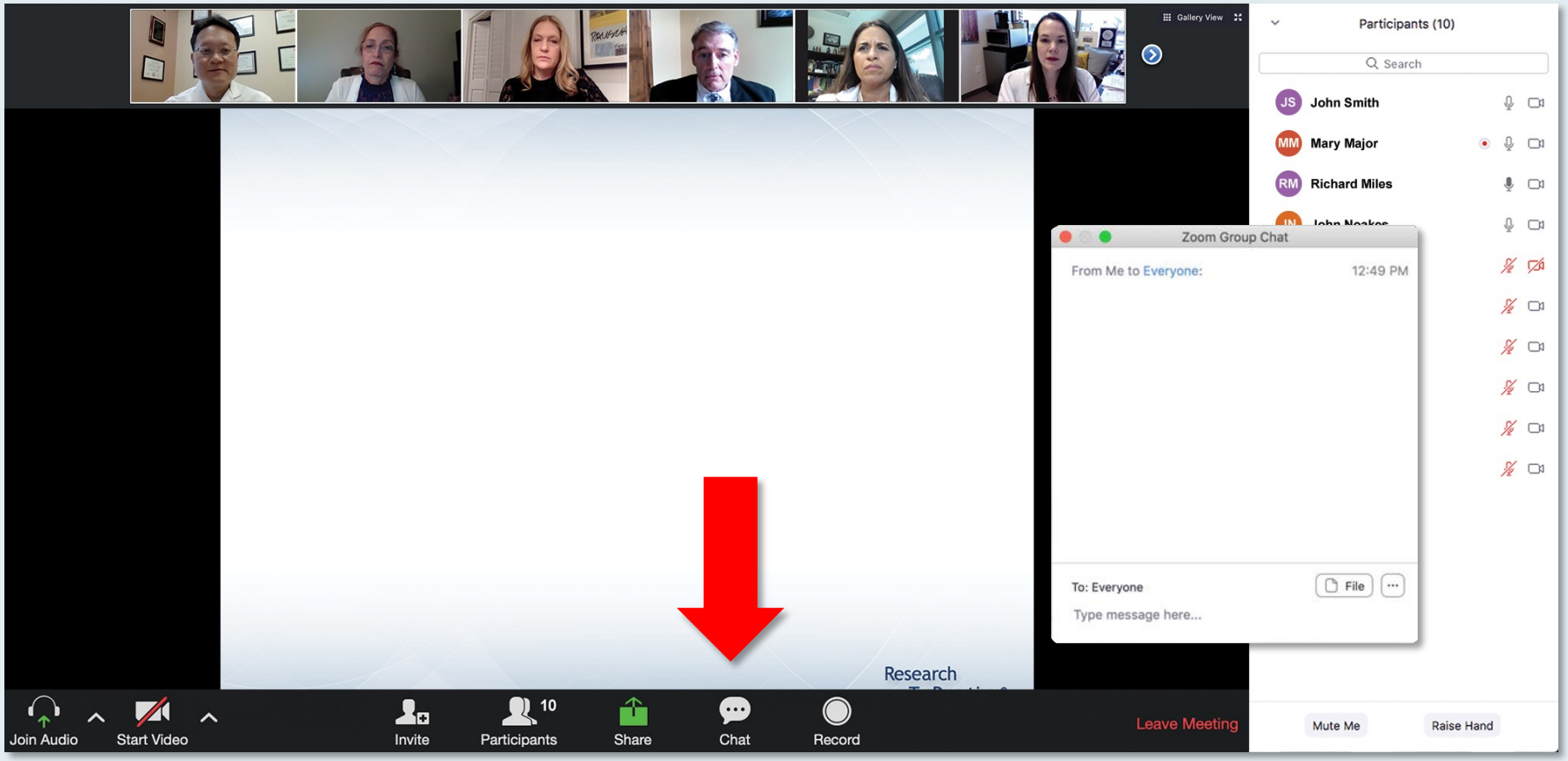
Joyce F Liu, MD, MPH
Associate Chief and Director of Clinical Research
Division of Gynecologic Oncology
Dana-Farber Cancer Institute
Boston, Massachusetts

Brian M Slomovitz, MD
Professor, OB-GYN, Florida International University
Director, Gynecologic Oncology
Co-Chair, Cancer Research Committee
Mount Sinai Medical Center
Miami, Florida

David M O'Malley, MD
Professor
Division Director, Gynecologic Oncology
The Ohio State University and The James Cancer Center
Columbus, Ohio

RTP
RESEARCH TO PRACTICE

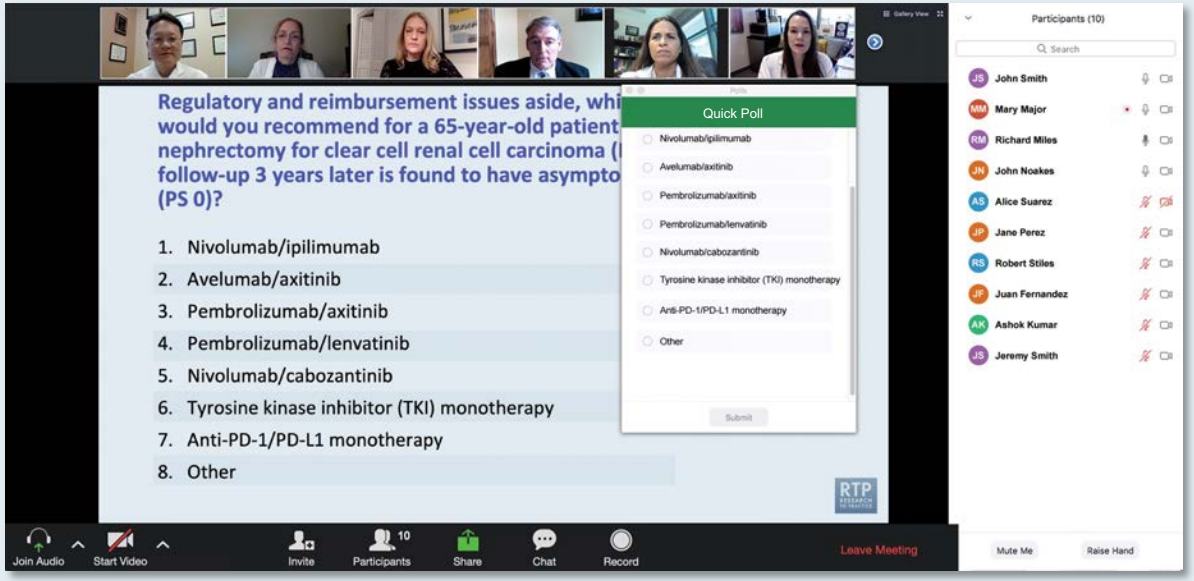
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

Inside the Issue: Optimizing the Management of Metastatic Urothelial Bladder Cancer

A CME/MOC-Accredited Live Webinar

Thursday, June 29, 2023
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Petros Grivas, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

What I Tell My Patients: Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Part 3 of a 3-Part Complimentary NCPD Webinar Series
in Partnership with the 2023 ONS Congress

Chronic Lymphocytic Leukemia

Thursday, July 6, 2023
5:00 PM – 6:00 PM ET

Faculty

Kristen E Battiato, AGNP-C
Jennifer Woyach, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Inside the Issue: Novel Agents, Approaches and Strategies in the Management of Higher-Risk Myelodysplastic Syndromes

A CME/MOC-Accredited Live Webinar

Tuesday, July 11, 2023
5:00 PM – 6:00 PM ET

Faculty

Guillermo Garcia-Manero, MD
David Sallman, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Melanoma and Nonmelanoma Skin Cancers

Thursday, July 13, 2023
5:00 PM – 6:00 PM ET

Faculty

Omid Hamid, MD

Evan J Lipson, MD

Moderator

Neil Love, MD

RTP Year in Review 2023

Inside the Issue: Integrating Bispecific Antibodies into the Management of Multiple Myeloma — Patient Selection and Toxicity Management

A CME/MOC-Accredited Live Webinar

Tuesday, July 18, 2023
5:00 PM – 6:00 PM ET

Faculty

Hans Lee, MD
Saad Zafar Usmani, MD, MBA

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Current and Future Management of ER-Positive Metastatic Breast Cancer After Disease Progression on a CDK4/6 Inhibitor

A CME/MOC-Accredited Live Webinar

Thursday, July 20, 2023
5:00 PM – 6:00 PM ET

Faculty

Aditya Bardia, MD, MPH
Erika Hamilton, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

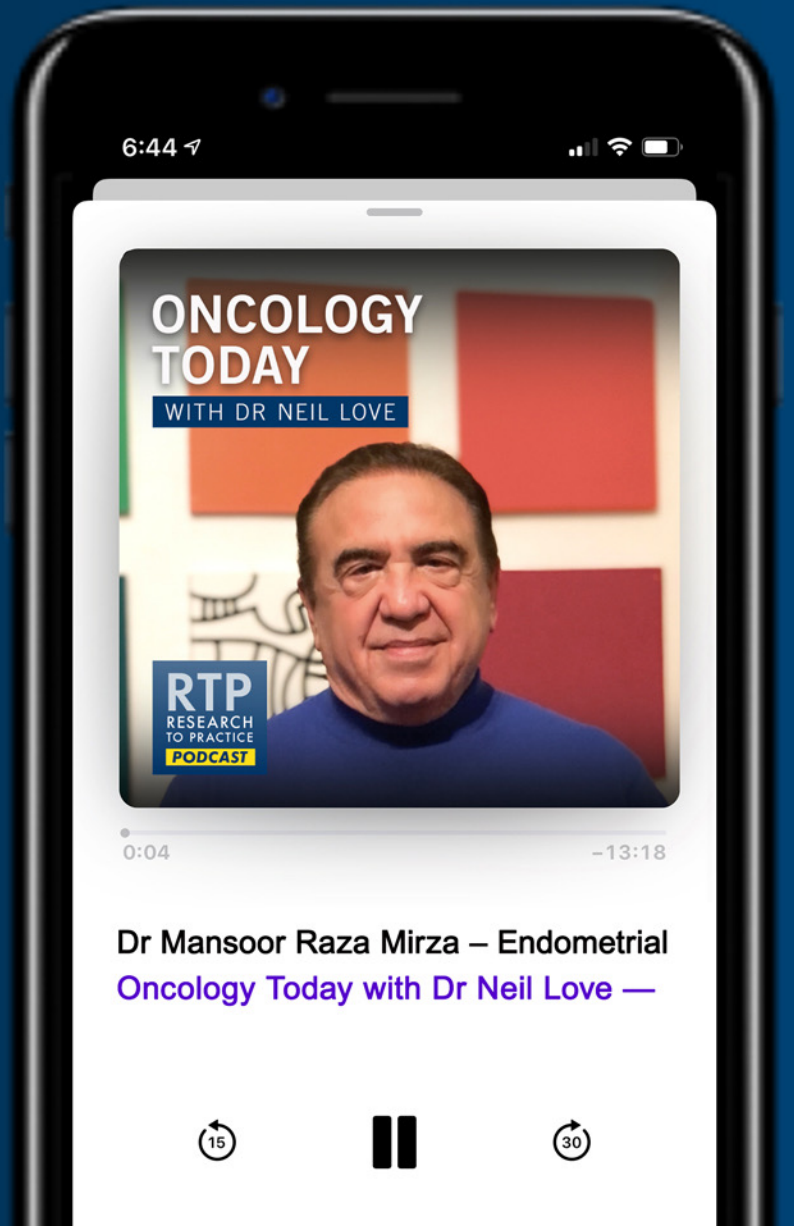
Endometrial Cancer Edition

DR MANSOOR RAZA MIRZA
COPENHAGEN UNIVERSITY HOSPITAL

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



The Implications of New Research Findings for the Management of Endometrial Cancer

A CME/MOC-Accredited Virtual Event in Partnership with the Society of Gynecologic Oncology

Wednesday, June 28, 2023

5:00 PM – 6:00 PM ET

Faculty

Bradley J Monk, MD

Matthew A Powell, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Commercial Support

This activity is supported by educational grants from GSK and Merck.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Monk — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Eisai Inc, Genentech, a member of the Roche Group, Genmab US Inc, ImmunoGen Inc, Karyopharm Therapeutics, Merck, Myriad Genetic Laboratories Inc, Novocure Inc, Seagen Inc, Tesaro, A GSK Company
Speakers Bureau	AstraZeneca Pharmaceuticals LP, Eisai Inc, Genentech, a member of the Roche Group, ImmunoGen Inc, Merck, Myriad Genetic Laboratories Inc, Tesaro, A GSK Company

RTP
RESEARCH
TO PRACTICE

Dr Powell — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, GSK, Merck, Roche Laboratories Inc, Seagen Inc
Contracted Research	GSK

RTP
RESEARCH
TO PRACTICE

Front line therapy for advanced Endometrial Cancer

Matthew A. Powell, MD
Professor and Chief, Gynecologic Oncology
Chair NRG Uterine Corpus Committee
Washington University School of Medicine, Saint Louis, MO

CURRENT OPTIONS FOR RELAPSED EC; PROMISING INVESTIGATIONAL AGENTS AND STRATEGIES

Bradley J. Monk, MD, FACS, FACOG

Director, Principal Investigator, Community Research Development, HonorHealth, Scottsdale, Arizona

Professor, Creighton University School of Medicine
University of Arizona College of Medicine
Phoenix, Arizona, USA

Co-Director GOG-Partners, Board Member GOG-Foundation

RTP RESEARCH TO PRACTICE

Key Data Sets

Matthew A Powell, MD

- Pignata S et al. Carboplatin and paclitaxel plus avelumab compared with carboplatin and paclitaxel in advanced or recurrent endometrial cancer (MITO END-3): A multicentre, open-label, randomised, controlled, phase 2 trial. *Lancet Oncol* 2023 March;24(3):286-96.
- Mirza MR et al. Dostarlimab in combination with chemotherapy for the treatment of primary advanced or recurrent endometrial cancer: A placebo-controlled randomized phase 3 trial (ENGOT-EN6-NSGO/GOG-3031/RUBY). SGO 2023;Abstract 265.
- Powell M et al. Dostarlimab for primary advanced or recurrent (A/R) endometrial cancer (EC): Outcomes by blinded independent central review (BICR) of the RUBY trial (ENGOT-EN6-NSGO/GOG-3031/RUBY). ASCO 2023;Abstract 5503.
- Eskander R et al. Pembrolizumab versus placebo in addition to carboplatin and paclitaxel for measurable stage 3 or 4a, stage 4b or recurrent endometrial cancer: The phase 3, NRG GY018 study. SGO 2023;Abstract 264.
- Eskander RS et al. Pembrolizumab plus chemotherapy in advanced endometrial cancer. *N Engl J Med* 2023 June 8;388(23):2159-70.

RTP RESEARCH TO PRACTICE

Key Data Sets

Bradley J Monk, MD

- O'Malley DM et al. Pembrolizumab in patients with microsatellite instability-high advanced endometrial cancer: Results from the KEYNOTE-158 study. *J Clin Oncol* 2022 March 1;40(7):752-61.
- Oaknin A et al. Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) or proficient/stable (MMRp/MSS) endometrial cancer: Interim results from GARNET — A phase I, single-arm study. *J Immunother Cancer* 2022 January;10(1):e003777.
- O'Malley D et al. Pembrolizumab for microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) advanced endometrial cancer: Long-term follow-up results from KEYNOTE-158. ESMO 2022;Abstract 546P.
- Makker V et al. Lenvatinib plus pembrolizumab in previously treated advanced endometrial cancer: Updated efficacy and safety from the randomized phase III Study 309/KEYNOTE-775. *J Clin Oncol* 2023 June 1;41(16):2904-10.

RTP RESEARCH TO PRACTICE

Key Data Sets

Bradley J Monk, MD (continued)

- Meric-Bernstam F et al. Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) interim results. ASCO 2023;Abstract LBA3000.
- Nishikawa T et al. Trastuzumab deruxtecan for human epidermal growth factor receptor 2-expressing advanced or recurrent uterine carcinosarcoma (NCCH1615): The STATICE trial. *J Clin Oncol* 2023 May 20;41(15):2789-99.
- Santin A et al. Preliminary results of a phase II trial with sacituzumab govitecan-hziy in patients with recurrent endometrial carcinoma overexpressing Trop-2. ASCO 2023;Abstract 294.
- Moore KN et al. Safety and efficacy of DB-1303 in patients with advanced/metastatic solid tumors: A multicenter, open-label, first-in-human, phase 1/2a study. ASCO 2023;Abstract 3023.

RTP RESEARCH TO PRACTICE

Agenda

INTRODUCTION

MODULE 1: First-Line Therapy for Advanced Endometrial Cancer (EC) — Dr Powell

MODULE 2: Current Options for Relapsed EC; Promising Investigational Agents and Strategies — Dr Monk

MODULE 3: Clinical Investigator Survey

RTP
RESEARCH
TO PRACTICE

Agenda

INTRODUCTION

MODULE 1: First-Line Therapy for Advanced Endometrial Cancer (EC) — Dr Powell

MODULE 2: Current Options for Relapsed EC; Promising Investigational Agents and Strategies — Dr Monk

MODULE 3: Clinical Investigator Survey

RTP
RESEARCH
TO PRACTICE

Front line therapy for advanced Endometrial Cancer

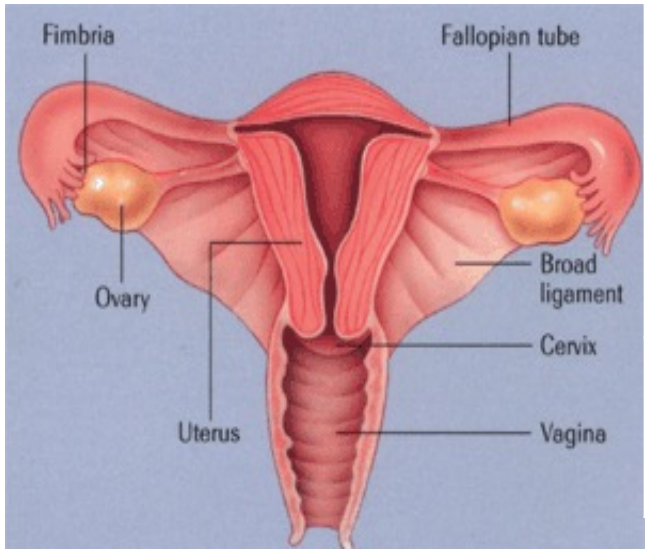
Matthew A. Powell, MD

Professor and Chief, Gynecologic Oncology

Chair NRG Uterine Corpus Committee

Washington University School of Medicine, Saint Louis, MO

Endometrial Cancer: Annual Incidence and Mortality



Year	Cases	Deaths
1987[1]	35,000	2,900
2023[2]	66,200	13,030

1. Wang Y, et al. *J Hematol Oncol.* 2016;9:112; 2. American Cancer Society. Key Statistics for Endometrial Cancer. January 12, 2023. Accessed March 24, 2023. https://www.cancer.org/cancer/endometrial-cancer/about/key-statistics.html

Courtesy of Matthew A Powell, MD

Endometrial Cancer 2022

The New York Times

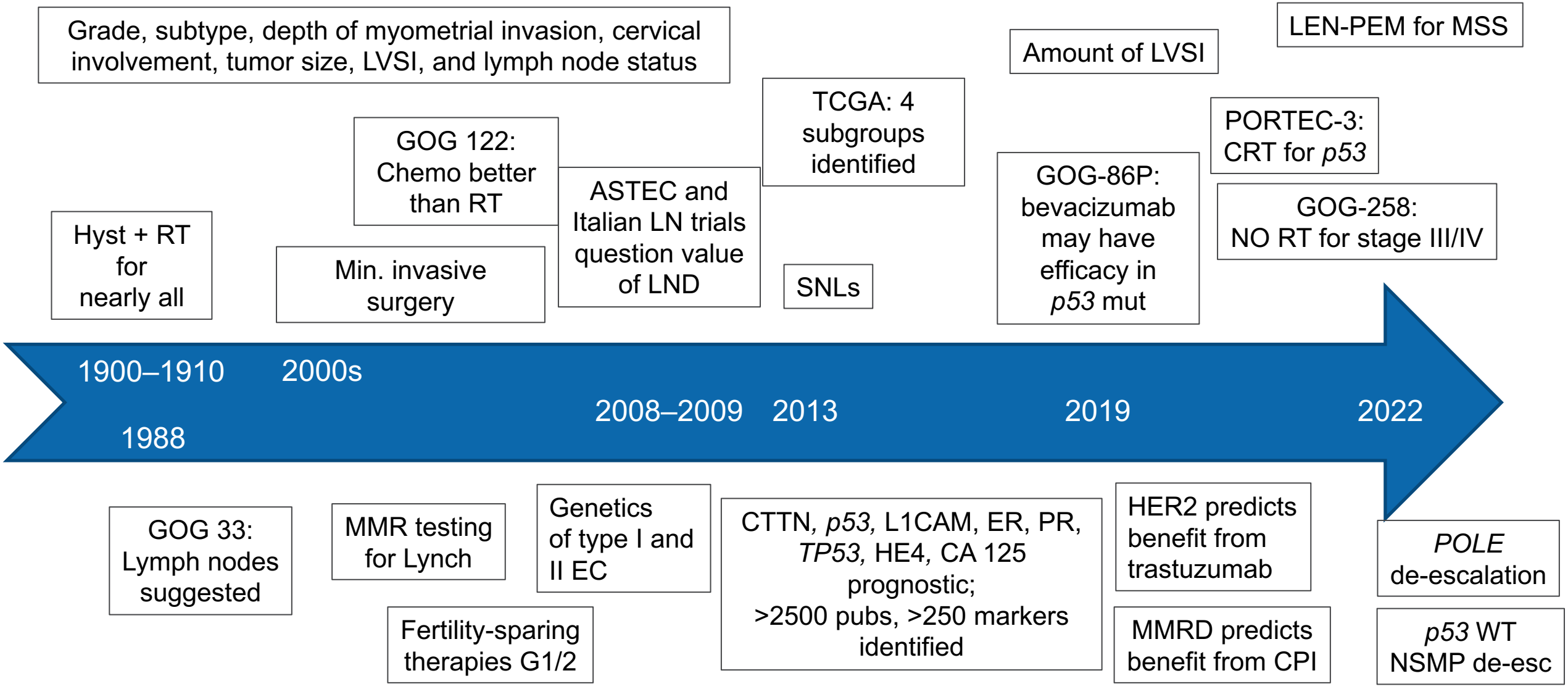
Uterine Cancer Is on the Rise, Especially Among Black Women

The cancer eventually will become the third most common type among women, experts say. The mortality rate is highest among Black Americans.

Rabin RC. *The New York Times.* June 17, 2022. Accessed March 24, 2023. https://www.nytimes.com/2022/06/17/health/uterine-cancer-black-women.html

Courtesy of Matthew A Powell, MD

History of Management of Endometrial Cancer: Journey From Prognostic to Predictive Markers



Courtesy of Matthew A Powell, MD

Agenda

INTRODUCTION

MODULE 1: First-Line Therapy for Advanced Endometrial Cancer (EC) — Dr Powell

MODULE 2: Current Options for Relapsed EC; Promising Investigational Agents and Strategies — Dr Monk

MODULE 3: Clinical Investigator Survey

RTP RESEARCH TO PRACTICE

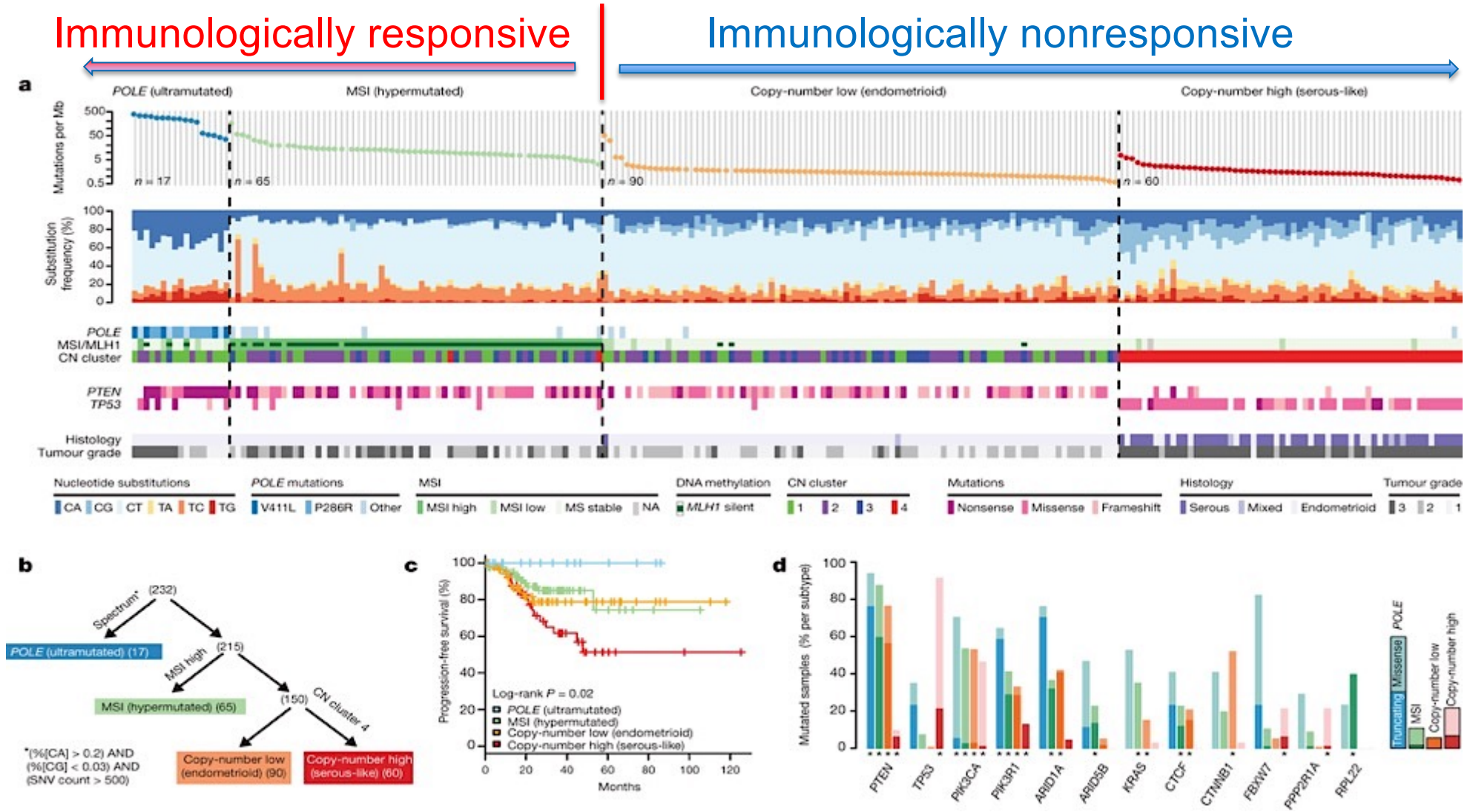
Treatment of Advanced-Stage/Recurrent Endometrial Cancer

	RT Agent vs Doublet	Single Agent vs Doublet		Doublet vs Doublet	Doublet vs Triplet	TAP vs TC
	GOG 122[1]	EORTC 55872[2]	GOG 107[3]	GOG 163[4]	GOG 177[5]	GOG 209[6]
Population (stage)	III–IV	Stage III–IV and relapsed	Stage III–IV and relapsed	Stage III–IV and relapsed	Stage III–IV and relapsed	Stage III–IV
n	396	177	299	317	273	1,328
Regimen	WART vs Dox-Cis	Dox vs Dox-Cis	Dox (A) vs Dox-Cis (AC)	Dox-Cisplat vs Dox-Paclitax	Dox-Cisplat vs Dox-Cisplat-Tax	Carbo-Tax vs Dox-Cisplat-Tax
PFS	Signif HR 0.71	NS	Signif HR 0.73	NS	Signif *P* <.01	NS
OS	Signif HR 0.68	NS	NS	NS	Signif *P* <.037	NS

1. Randall ME, et al. *J Clin Oncol*. 2006;24(1):36-44; 2. van Wijk FH, et al. *Ann Oncol*. 2003;14(3):441-448; 3. Thigpen JT, et al. *J Clin Oncol.* 2004;22(19):3902-3908; 4. Fleming GF, et al. *Ann Oncol.* 2004;15(8):1173-1178; 5. Fleming GF, et al. *J Clin Oncol.* 2004;22(11):2159-2166; 6. Miller DS, et al. *J Clin Oncol*. 2020;38(33):3841-3850.

Courtesy of Matthew A Powell, MD

Disease Molecular Classification: How to test?



Cancer Genome Atlas Research Network, et al. *Nature.* 2013;497(7447):67-73.

Courtesy of Matthew A Powell, MD

“Standard of Care”

SYSTEMIC THERAPY FOR ENDOMETRIAL CARCINOMA

Primary or Adjuvant Therapy	
Chemoradiation Therapy	**Systemic Therapy**
Preferred Regimens • Cisplatin plus RT followed by carboplatin/paclitaxel[1,2]	**Preferred Regimens** • Carboplatin/paclitaxel[3] • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive uterine serous carcinoma)[a,b,4] • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive carcinosarcoma) (category 2B)[a,b,4]

No IO opportunity in the first line (to date)

SYSTEMIC THERAPY FOR ENDOMETRIAL CARCINOMA

Recurrent Disease[c,d]	
First-Line Therapy[e]	**Second-Line or Subsequent Line Therapy**
Preferred • Carboplatin/paclitaxel (category 1 for carcinosarcoma)[3] • Carboplatin/paclitaxel/trastuzumab[b] (for recurrent HER2-positive uterine serous carcinoma)[a,4] • Carboplatin/paclitaxel/trastuzumab[b] (category 2B for HER2-positive carcinosarcoma)[a,4] **Other Recommended Regimens** • Carboplatin/docetaxel[f] • Carboplatin/paclitaxel/bevacizumab[g,h,5,6]	**Other Recommended Regimens** • Cisplatin/doxorubicin[10] • Cisplatin/doxorubicin/paclitaxel[g,m,10] • Cisplatin • Carboplatin • Doxorubicin • Liposomal doxorubicin • Paclitaxel[11] • Albumin-bound paclitaxel[n] • Topotecan • Bevacizumab[h,o,12] • Temsirolimus[13] • Cabozantinib • Docetaxel[f] (category 2B) • Ifosfamide (for carcinosarcoma) • Ifosfamide/paclitaxel (for carcinosarcoma)[14] • Cisplatin/ifosfamide (for carcinosarcoma)
Useful in Certain Circumstances (Biomarker directed: after prior systemic therapy) • Lenvatinib/pembrolizumab (category 1) for mismatch repair proficient (pMMR) tumors[i,j,7] • Pembrolizumab[j] (category 1) for TMB-H[k,8] or MSI-H/dMMR[l] tumors[9]	**Useful in Certain Circumstances (Biomarker directed: after prior systemic therapy)** • Lenvatinib/pembrolizumab (category 1) for mismatch repair proficient (pMMR) tumors[i,j,7] • Pembrolizumab[j] (category 1) for TMB-H[k,8] or MSI-H/dMMR tumors[l,9] • Dostarlimab-gxly for dMMR/MSI-H tumors (category 1)[j,p,15] • Larotrectinib or entrectinib for NTRK gene fusion-positive tumors (category 2B)[g] • Avelumab for dMMR/MSI-H tumors[j] • Nivolumab for dMMR/MSI-H tumors[j,16]

IO opportunities exist in the recurrent setting

Courtesy of Matthew A Powell, MD

“Standard of Care”

SYSTEMIC THERAPY FOR ENDOMETRIAL CARCINOMA

Hormonal Therapy for Recurrent or Metastatic Endometrial Carcinoma[q]	
Preferred Regimens • Megestrol acetate/tamoxifen (alternating) • Everolimus/letrozole	**Other Recommended Regimens** • Medroxyprogesterone acetate/tamoxifen (alternating) • Progestational agents ▸ Medroxyprogesterone acetate ▸ Megestrol acetate • Aromatase inhibitors • Tamoxifen • Fulvestrant

Hormonal Therapy for Uterine limited Disease Not Suitable for Primary Surgery (ENDO-1)[q]	
Preferred Regimens • Progestational agents ▸ Medroxyprogesterone acetate ▸ Megestrol acetate	**Useful in Certain Circumstances** • Levonorgestrel intrauterine device (IUD)

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Endometrial Carcinoma

NCCN Guidelines Index
Table of Contents
Discussion

Courtesy of Matthew A Powell, MD

Single-Agent IO in pMMR/MSI-Negative Selected EC Populations

Study and Drug	Patient Population	Outcome
KEYNOTE-28: Pembrolizumab (N = 24)	Advanced-stage or metastatic PD-L1–positive EC	**ORR: 13%**
PHAEDRA trial: Durvalumab (N = 36 pMMR)	Advanced-stage or metastatic EC	**ORR in pMMR: 3%**
GARNET study: Dostarlimab (N = 94)	Previously treated, recurrent advanced-stage EC	**ORR in pMMR: 13.9%**
Ph II avelumab study (N = 16 pMMR)	Advanced-stage or metastatic EC	**ORR: 6.25%**

Ott PA, et al. *J Clin Oncol.* 2017;35(22):2535-2541; Antill YC, et al. *J Clin Oncol.* 2019;37(15 suppl):5501; Oaknin A, et al. *JAMA Oncol.* 2020;6(11):1766-1772; Konstantinopoulos PA, et al. *J Clin Oncol.* 2019;37(30):2786-2794; Oaknin A, et al. *Gynecol Oncol.* 2021;162(suppl 1):S12-S13.

Courtesy of Matthew A Powell, MD

Single-Agent IO in "Biomarker"-Selected EC Populations (dMMR/MSI Positive)

- **Response to single-agent IO in dMMR or MSI-high EC**

Study and Drug	Patient Population	Outcome
KEYNOTE-158: Pembrolizumab (N = 90)	Advanced-stage or metastatic dMMR EC	ORR: 48%
PHAEDRA trial: Durvalumab (N = 35 dMMR)	Advanced-stage or metastatic EC	ORR in dMMR: 43%
GARNET study: Dostarlimab (N = 129)	Previously treated, recurrent advanced-stage EC	ORR in dMMR: 43.5%
Ph II avelumab study (N = 15 dMMR)	Advanced-stage or metastatic EC	ORR: 26.7%

O'Malley DM, et al. *J Clin Oncol.* 2022;40(7):752-761; Antill YC, et al. *J Clin Oncol.* 2019;37(15 suppl):5501; Oaknin A, et al. *J Immunother Cancer*. 2022;10(1):e003777; Konstantinopoulos PA, et al. *J Clin Oncol.* 2019;37(30):2786-2794.

Courtesy of Matthew A Powell, MD

Endometrial Cancer: First-Line Metastatic/Recurrent

Trial	Name	Description	Status
Frontline, metastatic or recurrent PI: Eskander	NRG-GY018	Testing the addition of the immunotherapy drug pembrolizumab to the usual chemotherapy treatment (paclitaxel and carboplatin) in stage III–IV or recurrent EC	**Active, not recruiting**
Frontline, metastatic or recurrent PI: Powell *ENGOT led	GOG-3031/RUBY	A phase III, randomized, double-blind, multicenter study of dostarlimab (TSR-042) + carboplatin-paclitaxel vs placebo + carboplatin-paclitaxel in patients with recurrent or primary aEC	**Active, not recruiting**
Frontline, metastatic or recurrent PI: Westin Co-PI: Moore *GOG led	GOG-3041/DUO-E	A randomized, multicenter, double-blind, placebo-controlled, phase III study of first-line carboplatin and paclitaxel in combination with durvalumab, followed by maintenance durvalumab with or without olaparib in patients with newly diagnosed advanced or recurrent EC	**Active, not recruiting**

Courtesy of Matthew A Powell, MD

Endometrial Cancer: First-Line Metastatic/Recurrent

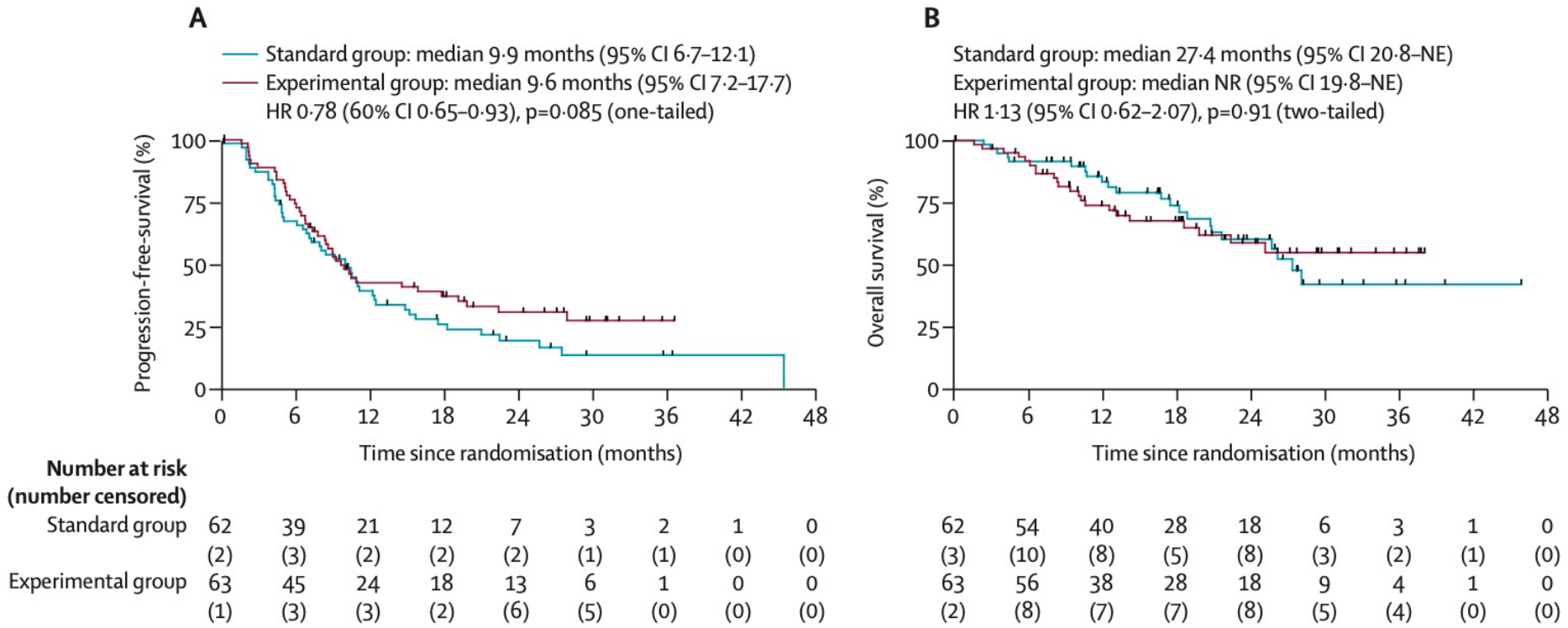
Trial	Name	Description	Status
Frontline, metastatic or recurrent PI: Marth	LEAP-001/ ENGOT-en9	A phase III randomized, open-label, study of pembrolizumab (MK-3475) + lenvatinib (E7080/MK-7902) vs chemotherapy for first-line treatment of advanced or recurrent EC	**Active, not recruiting**
Frontline, metastatic or recurrent	AtTEnd	Phase III double-blind, randomized, placebo-controlled trial of atezolizumab in combination with paclitaxel and carboplatin in women with advanced or recurrent EC	**Active, not recruiting**
Frontline, metastatic or recurrent **(dMMR only)**	KEYNOTE-C93/ GOG-3064/ ENGOT-en15	A phase III randomized, open-label, active-comparator controlled clinical study of pembrolizumab vs platinum doublet chemotherapy in participants with mismatch repair-deficient (dMMR) advanced or recurrent EC in the first-line setting	**Recruiting**

Courtesy of Matthew A Powell, MD

Carboplatin and paclitaxel plus avelumab compared with carboplatin and paclitaxel in advanced or recurrent endometrial cancer (MITO END-3): a multicentre, open-label, randomised, controlled, phase 2 trial

Lancet Oncol 2023; 24: 286–96

*Sandro Pignata, Giovanni Scambia, Clorinda Schettino, Laura Arenare, Carmela Pisano, Davide Lombardi, Ugo De Giorgi, Claudia Andreetta, Saverio Cinieri, Carmine De Angelis, Domenico Priolo, Claudia Casanova, Marta Rosati, Filippo Greco, Elena Zafarana, Ilaria Schiavetto, Serafina Mammoliti, Sabrina Chiara Cecere, Vanda Salutari, Simona Scalone, Alberto Farolfi, Marilena Di Napoli, Domenica Lorusso, Piera Gargiulo, Daniela Califano, Daniela Russo, Anna Spina, Rossella De Cecio, Paolo Chiodini, Francesco Perrone, on behalf of the MITO investigators**



Courtesy of Matthew A Powell, MD

MITO END-3

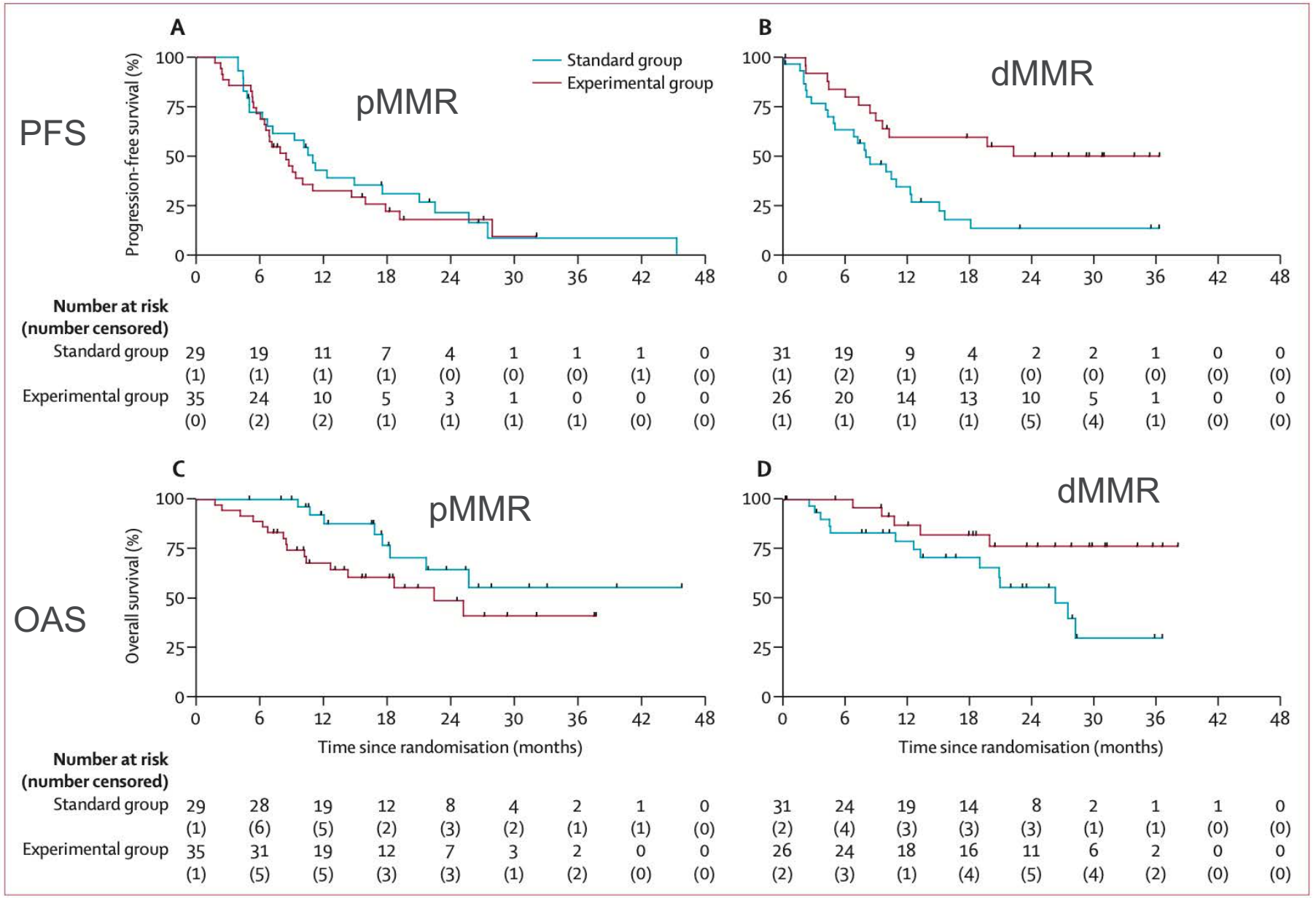


Figure 4: **Progression-free survival and overall survival curves by MMR status**
Progression-free survival in patients with pMMR (A) and dMMR (B). Overall survival in patients with pMMR (C) and dMMR (D). Vertical black lines represent censoring. Treatment groups are avelumab plus carboplatin and paclitaxel (experimental group) versus carboplatin and paclitaxel (standard group). pMMR=mismatch repair proficient. dMMR=mismatch repair deficient.

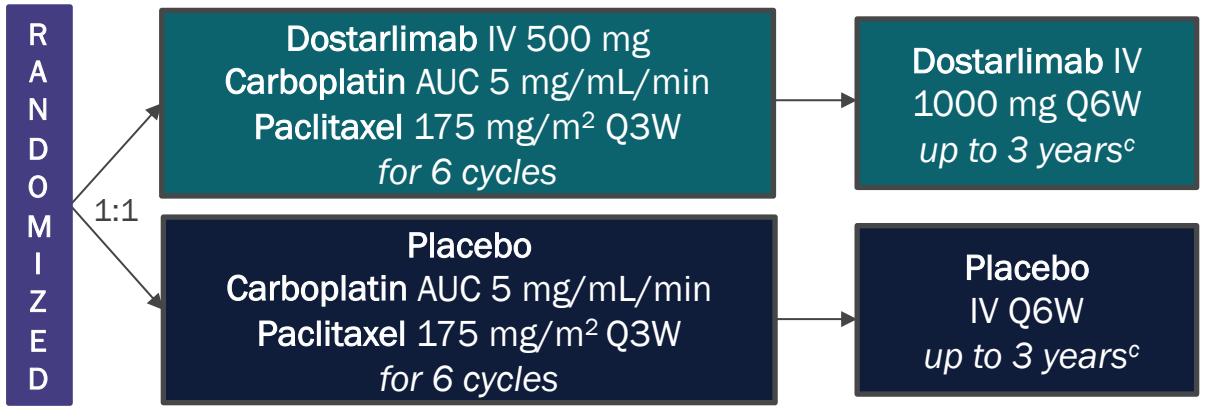
Lancet Oncol 2023; 24: 286–96

Courtesy of Matthew A Powell, MD

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – Study Design and Patients

Key Eligibility Criteria

- Histologically/cytologically proven stage III/IV or first recurrent EC
- Carcinosarcoma, clear cell, serous, or mixed histology permitted[a]
- ECOG PS 0-1
- Naïve to systemic therapy or systemic anticancer therapy and had a recurrence or PD ≥6 months after completing treatment



Stratified by MMR/MSI status[b], prior external pelvic radiotherapy, disease status

Primary endpoints: PFS by INV, OS
Secondary endpoints: PFS by BICR, PFS2, ORR, DOR, DCR, HRQOL/PRO, safety

Patient Characteristics, n(%)		dMMR/MSI-H		Overall	
		Dostar + CP (n=53)	Placebo + CP (n=65)	Dostar + CP (n=245)	Placebo + CP (n=249)
Median age (range), years		61 (45–81)	66 (39–85)	64 (41–81)	65 (28–85)
ECOG PS	0	28 (53.8)	39 (60.0)	145 (60.2)	160 (65.0)
	1	24 (46.2)	26 (40.0)	96 (39.8)	86 (35.0)
Histology					
Clear cell		0	0	8 (3.3)	9 (3.6)
Carcinosarcoma		4 (7.5)	1 (1.5)	25 (10.2)	19 (7.6)
Endometrioid		44 (83.0)	56 (86.2)	134 (54.7)	136 (54.6)
Prior systemic therapy		7 (13.2)	10 (15.4)	48 (19.6)	52 (20.9)
Carboplatin/ paclitaxel		4 (7.5)	6 (9.2)	36 (14.7)	39 (15.7)
Measurable disease at baseline		49 (92.5)	58 (89.2)	212 (86.5)	219 (88.0)

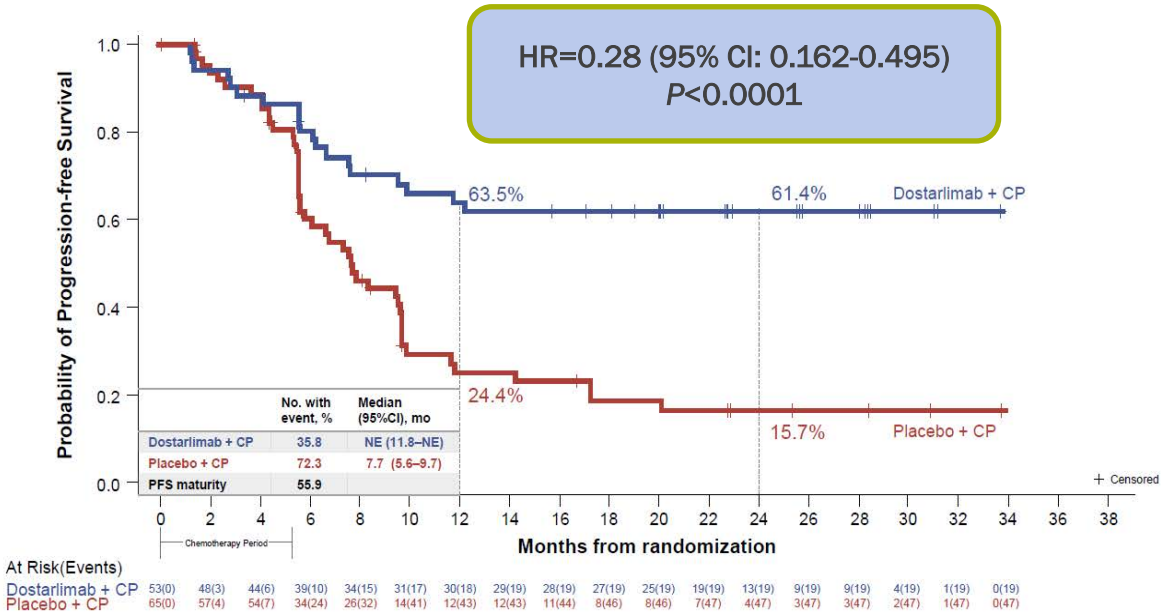
[a]Mixed histology containing at least 10% carcinosarcoma, clear cell, or serous histology. [b]Patients were randomized based on either local or central MMR/MSI testing results. For local determination of MMR/MSI status, IHC, NGS, and PCR assays were accepted. For central determination of MMR/MSI status IHC per Ventana MMR RxDxpanel was used. Central testing was used when local results were not available. [c]Treatment ends after 3 years.

Mirza MR, et al. SGO 2023. Abstract 265. Powell M, et al. ASCO 2023; Abstract 5503.

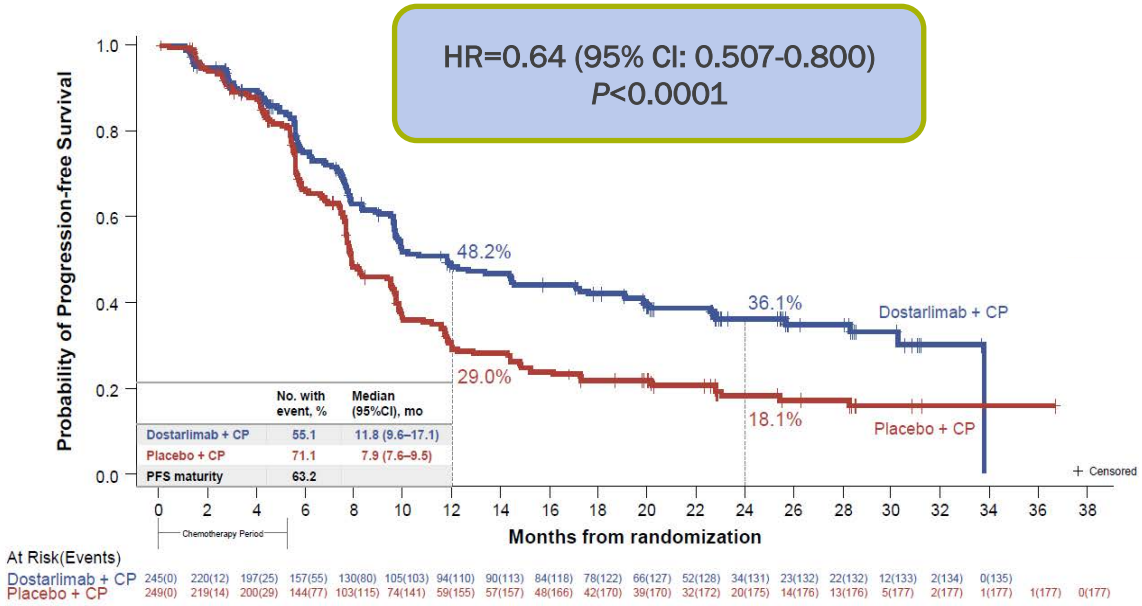
Courtesy of Matthew A Powell, MD

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – PFS

PFS in dMMR/MSI-H Population



PFS in Overall Population



- Median duration of follow-up in dMMR/MSI-H population was 24.79 months
- Median duration of follow-up in overall population was 25.38 months.

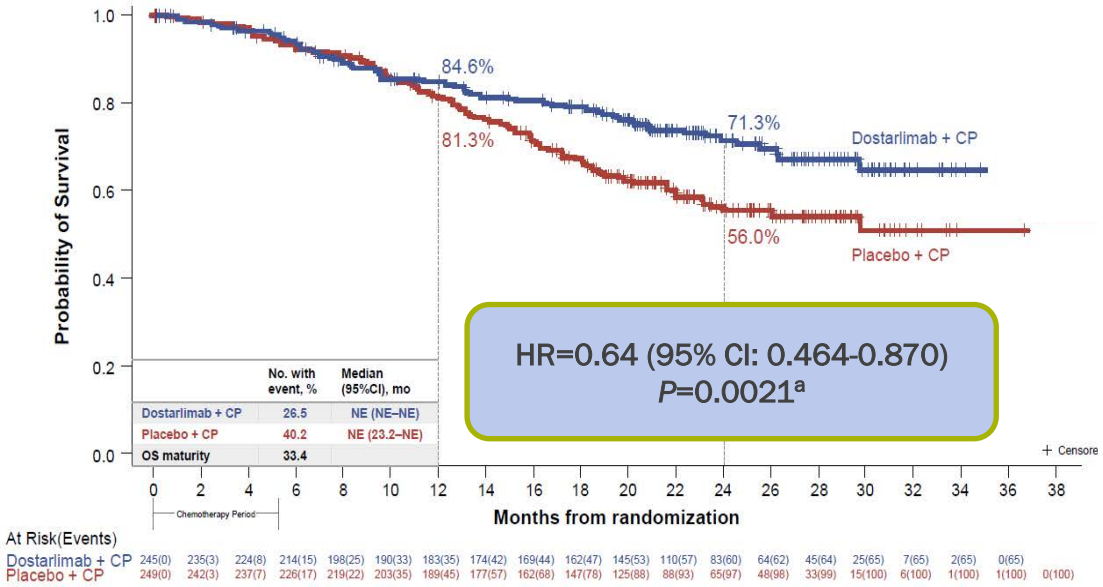
Data cutoff: September 28, 2022.

Mirza MR, et al. SGO 2023. Abstract 265. Powell M, et al. ASCO 2023; Abstract 5503.

Courtesy of Matthew A Powell, MD

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – OS

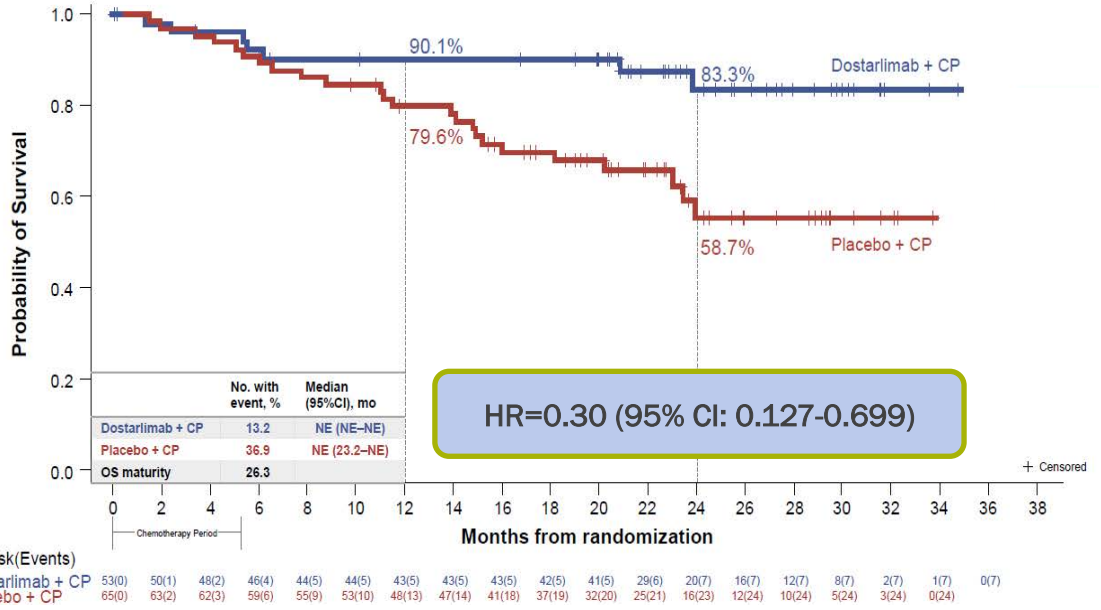
OS in Overall Population (33% maturity)



HR=0.64 (95% CI: 0.464-0.870)
P=0.0021[a]

Received subsequent immunotherapy:
- 34.5% of patients on placebo arm
- 15.5% of patients on dostarlimab arm

OS in dMMR/MSI-H Population



HR=0.30 (95% CI: 0.127-0.699)

Received subsequent immunotherapy:
- 38.5% of patients on placebo arm
- 15.1% of patients on dostarlimab arm

Data cutoff: September 28, 2022. Median duration of follow-up in overall population was 25.38 months.

[a]P≤0.00177 required to declare statistical significance at first interim analysis.

Mirza MR, et al. SGO 2023. Abstract 265.

Courtesy of Matthew A Powell, MD

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – PFS

Categories	Dostarlimab + Carboplatin/Paclitaxel (no. of events/no. of patients)	Placebo + Carboplatin/Paclitaxel (no. of events/no. of patients)	Hazard Ratio (95% CI)
All patients	135/245	177/249	0.64 (0.507–0.800)
Age			
<65 yr	69/127	72/114	0.78 (0.559–1.083)
≥65 yr	66/118	105/135	0.51 (0.376–0.704)
Race			
White	101/189	135/191	0.62 (0.481–0.808)
Other	34/56	42/58	0.67 (0.422–1.050)
Region			
North America	91/171	133/187	0.55 (0.419–0.718)
Europe	44/74	44/62	0.91 (0.602–1.390)
Eastern Europe	11/16	12/14	0.86 (0.377–1.959)
Western Europe	33/58	32/48	0.95 (0.581–1.539)
Histology category			
Endometrioid carcinoma	64/130	89/136	0.65 (0.473–0.902)
Other	71/115	88/113	0.60 (0.439–0.823)
MMR/MSI status			
dMMR/MSI-H	19/53	47/65	0.33 (0.192–0.566)
MMRp/MSS	116/192	130/184	0.76 (0.595–0.982)
dMMR status (derived)	19/53	47/63	0.31 (0.182–0.539)
Prior external pelvic radiotherapy			
Yes	21/41	31/45	0.54 (0.303–0.956)
No	114/204	146/204	0.65 (0.508–0.831)
Disease status			
Recurrent	68/117	89/119	0.56 (0.408–0.775)
Primary stage III	21/45	21/47	1.03 (0.563–1.891)
Primary stage IV	46/83	67/83	0.57 (0.392–0.836)
No disease at baseline	12/33	12/30	1.16 (0.520–2.590)

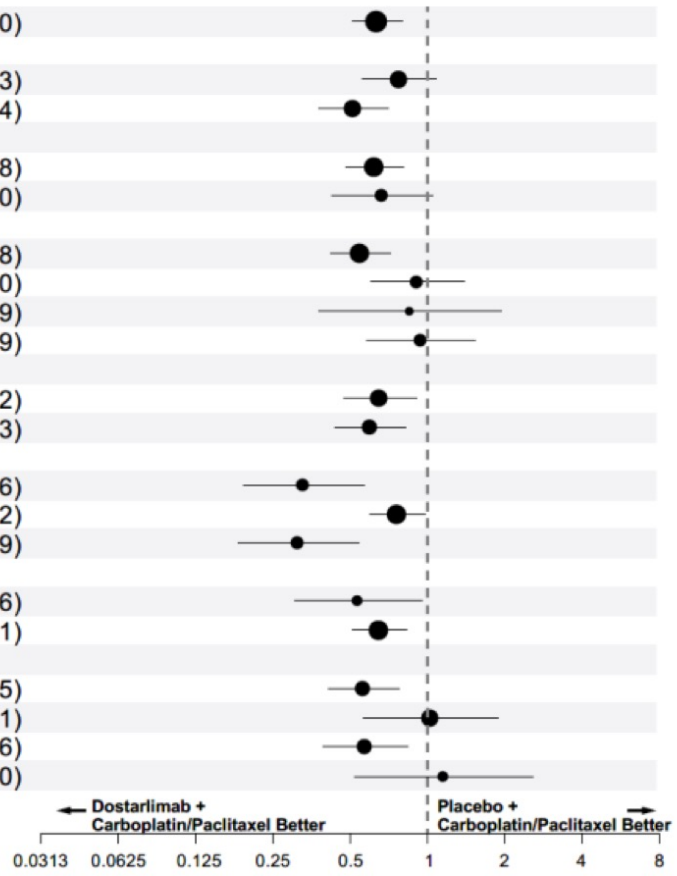
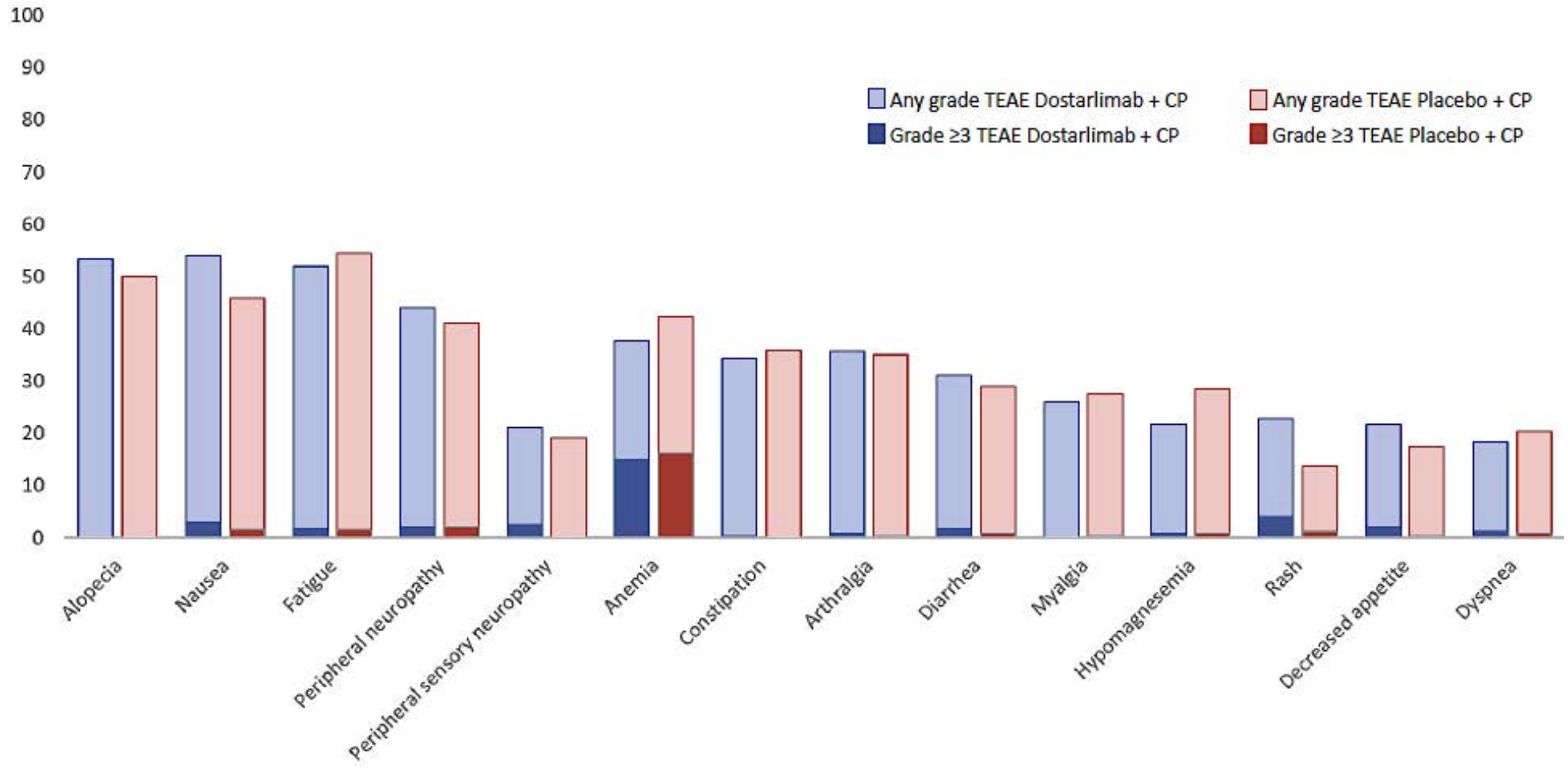


Figure S2. Forest Plot for Subgroup Analysis of PFS per Investigator Assessment

Courtesy of Matthew A Powell, MD

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – Safety

TEAEs in ≥20% of Either Arm



Data cutoff: September 28, 2022.

Mirza MR, et al. SGO 2023. Abstract 265.

Courtesy of Matthew A Powell, MD

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – Safety (cont'd) and Summary

AEs, n (%)	Dostarlimab + CP (N=241)	Placebo + CP (N=246)
Any TEAE	241 (100)	246 (100)
Any grade ≥3 TEAE	170 (70.5)	147 (59.8)
Serious TEAE	91 (37.8)	68 (27.6)
Any treatment-related irAE	92 (38.2)	38 (15.4)
Any TEAE leading to discontinuation of dostarlimab or placebo	42 (17.4)	23 (9.3)
Any TEAE leading to discontinuation of carboplatin	24 (10.0)	19 (7.7)
Any TEAE leading to discontinuation of paclitaxel	24 (10.0)	23 (9.3)
Any TEAE leading to death	5 (2.1)[a]	0
Any TEAE related to dostarlimab leading to death	2 (0.8)[b]	-
Median duration of overall treatment (range), weeks	43.0 (3.0–150.9)	36.0 (2.1–165.1)

Authors' Conclusions

- Dostarlimab + CP showed:
  - Statistically significant and clinically meaningful PFS benefit
  - Early OS trend in the overall population
  - Benefit in dMMR/MSI-H patients
  - Durable benefit in MMRp/MSS patients
- The safety profile for dostarlimab + CP was manageable and consistent with individual therapies

[a]3 deaths were not related to study treatment (opiate overdose, COVID-19, and general physical health deterioration). [b]One death was considered by the investigator as related to dostarlimab plus CP and occurred during the first 6 cycles (myelosuppression); one death was related to dostarlimab and occurred during the 90-day safety follow-up (hypovolemic shock).

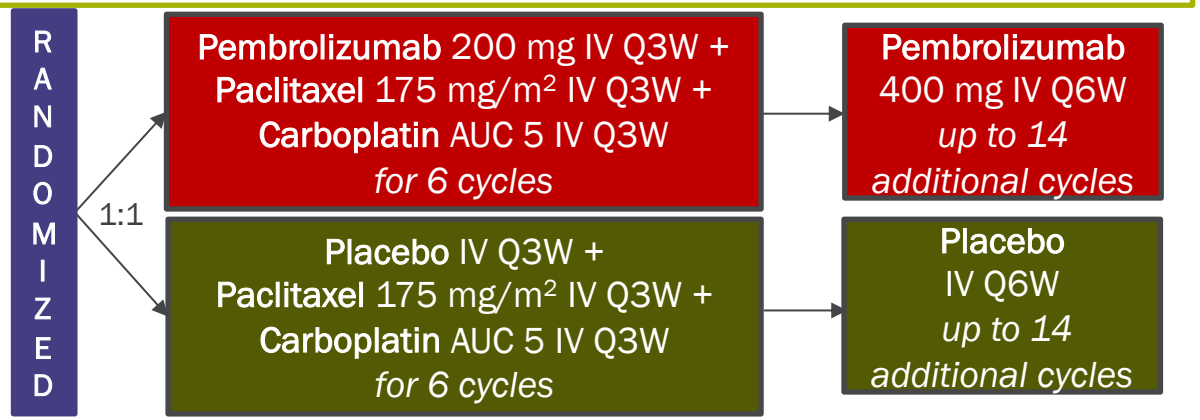
Mirza MR, et al. SGO 2023. Abstract 265. Powell M, et al. ASCO 2023; Abstract 5503.

Courtesy of Matthew A Powell, MD

NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC – Study Design and Patients

Key Eligibility Criteria

- Measurable stage III/IVA or measurable/nonmeasurable stage IVB or recurrent endometrial cancer
- MMR IHC testing
- ECOG PS 0-2
- No prior chemo except adjuvant chemo if completed ≥12 mo before study



Stratified by MMR status (pMMR vs dMMR), ECOG status, and prior adjuvant chemo

Primary endpoints: PFS per RECIST v1.1 by INV in pMMR and dMMR cohorts
Secondary endpoints: Safety, ORR/DOR, OS, PRO/QoL, concordance of MMR testing results

Patient Characteristics, n (%)		dMMR (n=225)		pMMR (n=588)	
		Pembro + CT (n=112)	Placebo + CT (n=113)	Pembro + CT (n=293)	Placebo + CT(n=295)
Median age (range), years		67 (38-81)	66 (37-85)	66 (31–93)	65 (29–90)
ECOG PS	0	72 (64.3)	73 (64.6)	196 (66.9)	198 (67.1)
	1	39 (34.8)	35 (31.0)	88 (30.0)	88 (29.8)
	2	1 (0.9)	5 (4.4)	9 (3.1)	9 (3.1)
Histology					
Clear cell		1 (0.9)	0 (0)	17 (5.8)	20 (6.8)
Endometrioid, G1		21 (18.8)	35 (31.0)	54 (18.4)	46 (15.6)
Endometrioid, G2		52 (46.4)	41 (36.3)	51 (17.4)	58 (19.7)
Endometrioid, G3		15 (13.4)	16 (14.2)	53 (18.1)	42 (14.2)
Serous		4 (3.6)	1 (0.9)	78 (26.6)	72 (24.4)
No prior chemotherapy		107 (95.5)	105 (92.9)	221 (75.4)	218 (73.9)

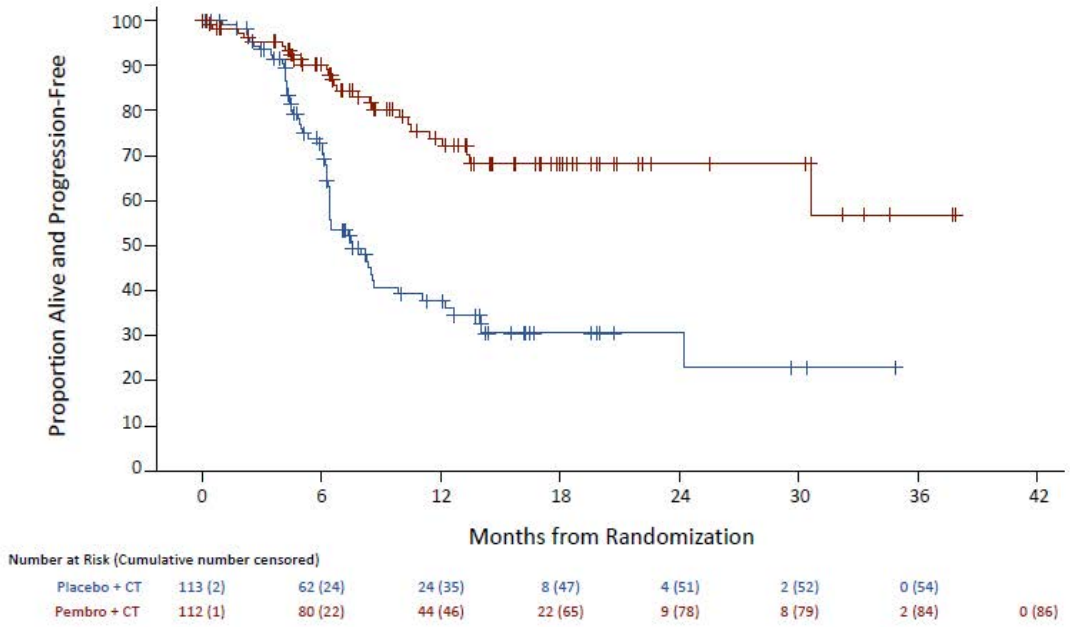
Data cutoff: December 16, 2022.

Eskander R, et al. SGO 2023. Abstract 264. Eskander RN, et al. *N Engl J Med*. 2023; 388(23):2159-2170.

Courtesy of Matthew A Powell, MD

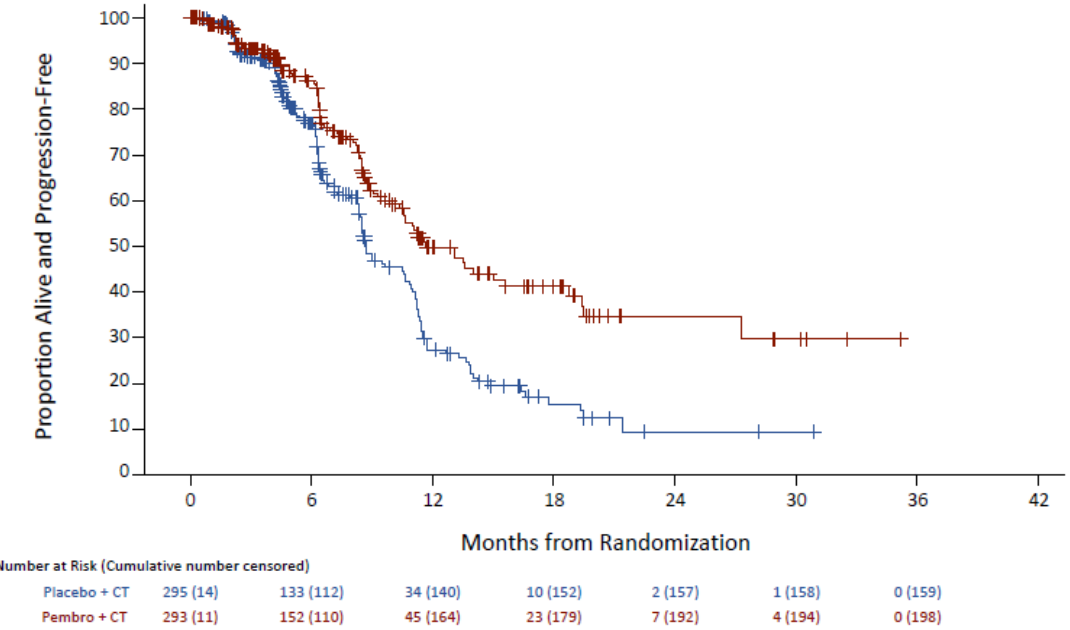
NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC - PFS

PFS per RECIST v1.1 in dMMR Population



	Events, n/N	Median (95% CI), mo	HR (stratified; 95% CI)
Pembro + CT	26/112	NR (30.6-NR)	**0.30 (0.19-0.48)** ***P*<0.00001**
Placebo + CT	59/113	7.6 (6.4-9.9)	

PFS per RECIST v1.1 in pMMR Population



	Events, n/N	Median (95% CI), mo	HR (stratified; 95% CI)
Pembro + CT	95/293	11.7 (10.5-15.6)	**0.57 (0.44-0.74)** ***P*<0.0001**
Placebo + CT	136/295	8.7 (8.4-10.7)	

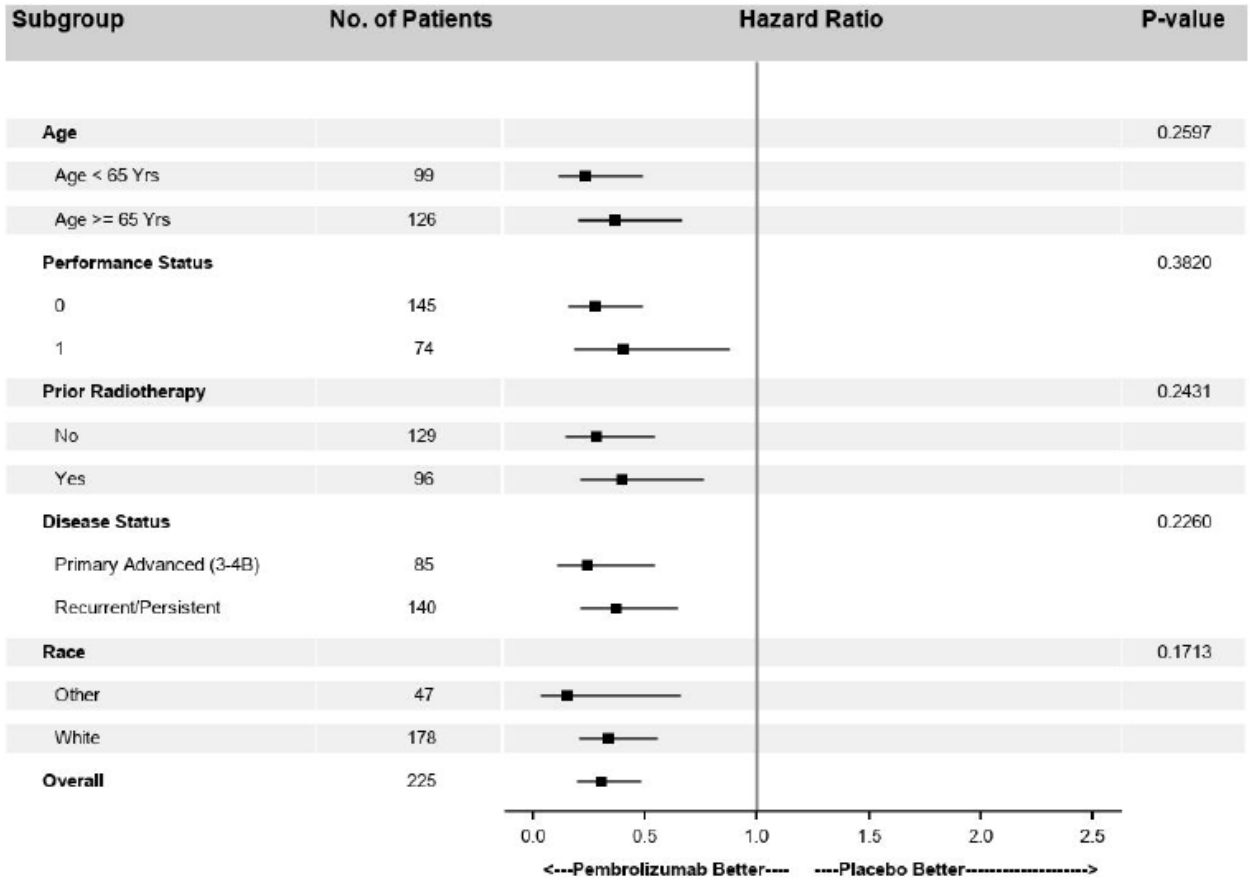
Data cutoff: December 16, 2022.

Eskander R, et al. SGO 2023. Abstract 264. Eskander RN, et al. *N Engl J Med*. 2023; 388(23):2159-2170.

Courtesy of Matthew A Powell, MD

NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC – Subgroup Analyses of PFS

PFS per RECIST v1.1 in dMMR Population



PFS per RECIST v1.1 in pMMR Population

Eskander R, et al. SGO 2023. Abstract 264. Eskander RN, et al. *N Engl J Med*. 2023; 388(23):2159-2170.

Courtesy of Matthew A Powell, MD

NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC – AEs and Summary

AEs, n (%)		dMMR (n=225)		pMMR (n=550)	
		Pembro + CT (n = 109)	Placebo + CT (n = 106)	Pembro + CT (n = 276)	Placebo + CT (n = 274)
Any AE	All-cause	107 (98.2)	105 (99.1)	258 (93.5)	256 (93.4)
	Grade 3-5	69 (63.3)	50 (47.2)	152 (55.1)	124 (45.3)
	AE leading to death	1 (0.9)[a]	2 (1.9)[a]	6 (2.2)[b]	2 (0.7)[b]
AEs of interest[c]	Any[d]	42 (38.5)	28 (26.4)	92 (33.3)	54 (19.7)
	Grade 3-5	9 (8.3)	6 (5.7)	10 (3.6)	7 (2.6)

Authors' Conclusions

- Pembro + SOC chemo followed by Pembro maintenance led reduced risk of disease progression or death in patients with dMMR and pMMR endometrial cancer by 70% and 43%, respectively
  - This benefit was seen in all evaluable subgroups
- The frequency of AEs commonly associated with Pembro + SOC chemo were not increased with the addition of Pembro
- The incidence of immune-mediated AEs were similar to prior EC studies of Pembro monotherapy

[a]These AEs included one each of: cardiac arrest, sepsis, and lower gastrointestinal hemorrhage. [b]These AEs included sepsis in 4 patients, cardiac arrest in 2 patients; and small intestinal obstruction, sudden death not otherwise specified in 1 patient each. [c]The AEs of interest are those with a possible immune-related cause and are considered regardless of attribution to a trial drug by the investigator. [d]Total number of patients who experienced an irAE. Some patients experienced multiple irAEs.

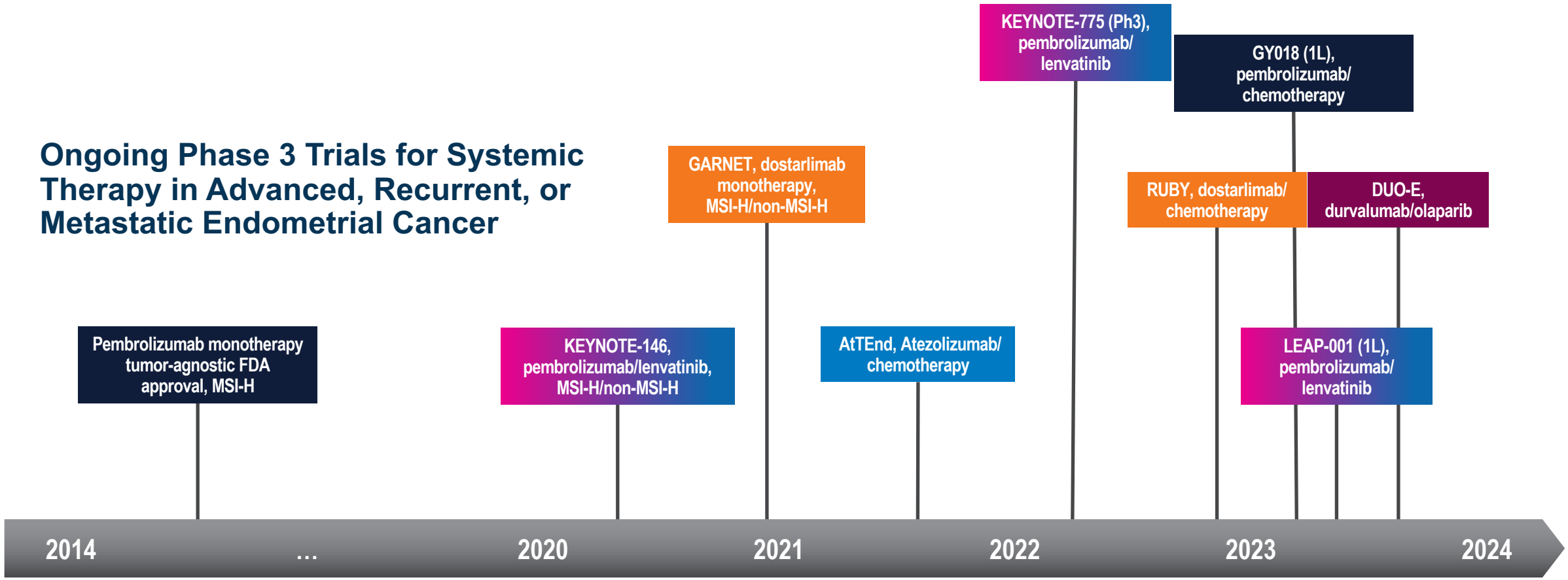
Eskander R, et al. SGO 2023. Abstract 264. Eskander RN, et al. *N Engl J Med*. 2023; 388(23):2159-2170.

Courtesy of Matthew A Powell, MD

Conclusions: Endometrial Cancer Future Treatment Landscape

Molecularly driven therapy for early-/late-stage endometrial cancer

Serous: IO +systemic therapy→>Add VEGFi or PARP or HER-directed?



Courtesy of Matthew A Powell, MD

Conclusions

- Importance of molecular subtypes in EC
- Key trials of immunotherapy agents reporting
- dMMR/MSI-positive tumors with robust response to CPIs
- pMMR/MSI-negative tumors may need dual therapy
  - Chemo + CPI
  - TKI + CPI
- Not all CPIs may be the same. Anti–PD-1 vs PD-L1?

Courtesy of Matthew A Powell, MD

Positive High-Level Results Announced from DUO-E: The First Global Phase III Trial of Immunotherapy with PARP Inhibition to Demonstrate Clinical Benefit for Endometrial Cancer

Press Release: May 26, 2023

"Positive high-level results from the DUO-E Phase III trial showed durvalumab in combination with platinum-based chemotherapy followed by either durvalumab plus olaparib or durvalumab alone as maintenance therapy both demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to standard-of-care chemotherapy alone in patients with newly diagnosed advanced or recurrent endometrial cancer. There was a greater clinical benefit observed with the combination of durvalumab and olaparib as maintenance treatment.

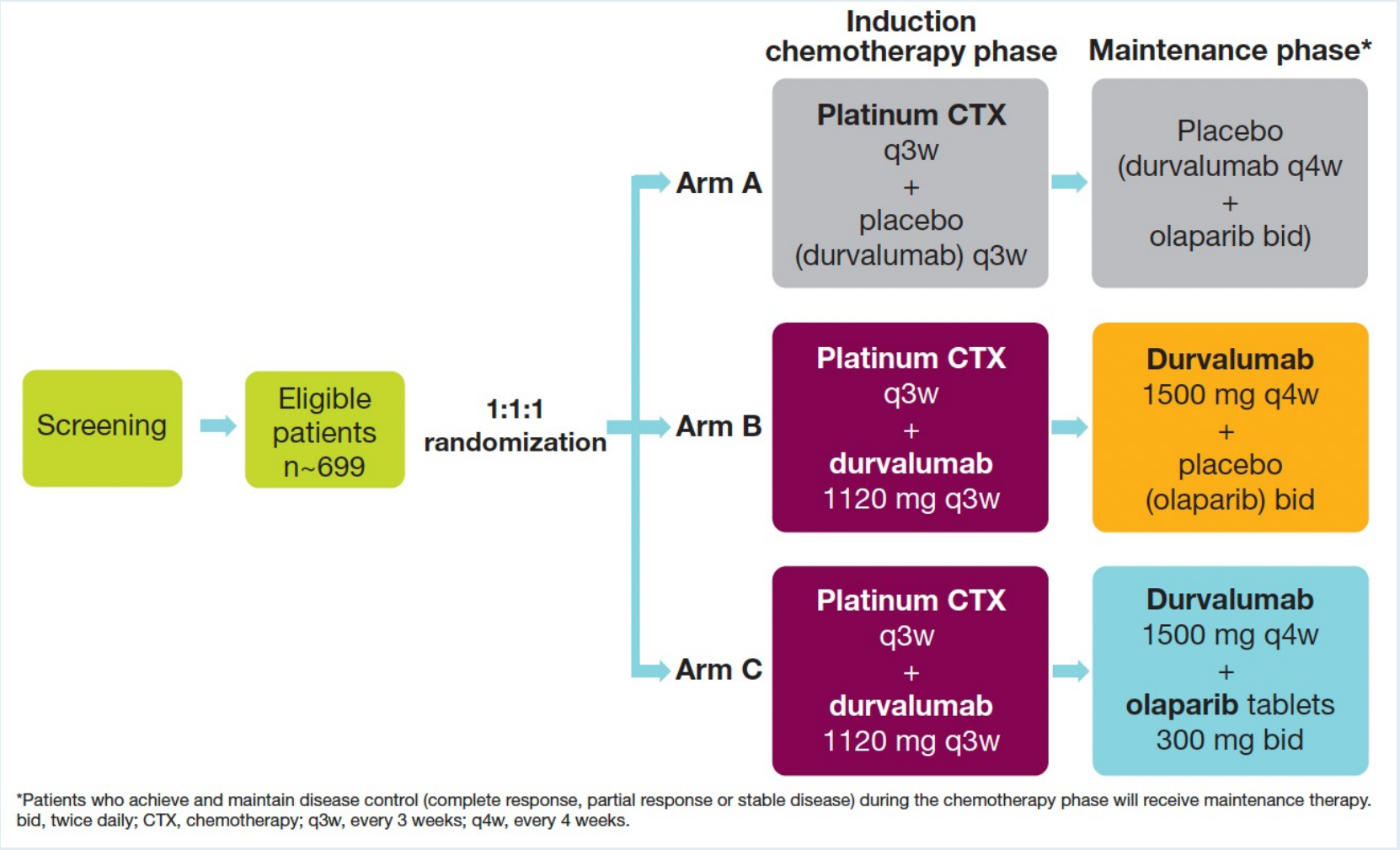
Overall survival (OS) data were immature at the time of this analysis however, a favourable trend was observed for both treatment regimens.

The safety and tolerability profile of durvalumab plus chemotherapy and of durvalumab in combination with olaparib was broadly consistent with that observed in prior clinical trials and the known profiles of the individual medicines. These data will be presented at a forthcoming medical meeting, and we look forward to discussing them with health authorities."

https://www.astrazeneca.com/media-centre/press-releases/2023/imfinzi-lynparza-prolonged-pfs-in-endometrial-cancer.html

RTP RESEARCH TO PRACTICE

DUO-E: A Phase III Trial of First-Line Chemotherapy in Combination with Durvalumab Followed by Maintenance Durvalumab with or without Olaparib for Advanced or Recurrent Endometrial Cancer



*Patients who achieve and maintain disease control (complete response, partial response or stable disease) during the chemotherapy phase will receive maintenance therapy.
bid, twice daily; CTX, chemotherapy; q3w, every 3 weeks; q4w, every 4 weeks.

Westin SN et al. ASCO 2020;Abstract TPS6108.

RTP RESEARCH TO PRACTICE

Agenda

INTRODUCTION

MODULE 1: First-Line Therapy for Advanced Endometrial Cancer (EC) — Dr Powell

MODULE 2: Current Options for Relapsed EC; Promising Investigational Agents and Strategies — Dr Monk

MODULE 3: Clinical Investigator Survey

RTP
RESEARCH
TO PRACTICE

CURRENT OPTIONS FOR RELAPSED EC; PROMISING INVESTIGATIONAL AGENTS AND STRATEGIES

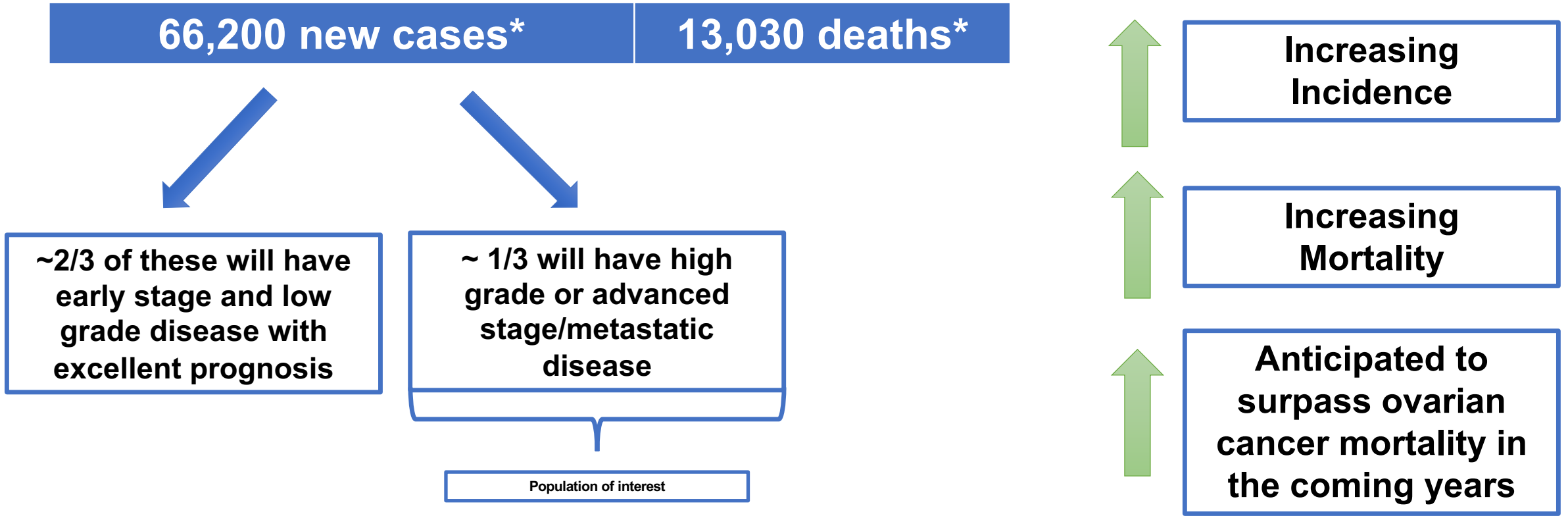
Bradley J. Monk, MD, FACS, FACOG

Director, Principal Investigator, Community Research Development, HonorHealth, Scottsdale, Arizona

Professor, Creighton University School of Medicine
University of Arizona College of Medicine
Phoenix, Arizona, USA

Co-Director GOG-Partners, Board Member GOG-Foundation

Endometrial Cancer 2023

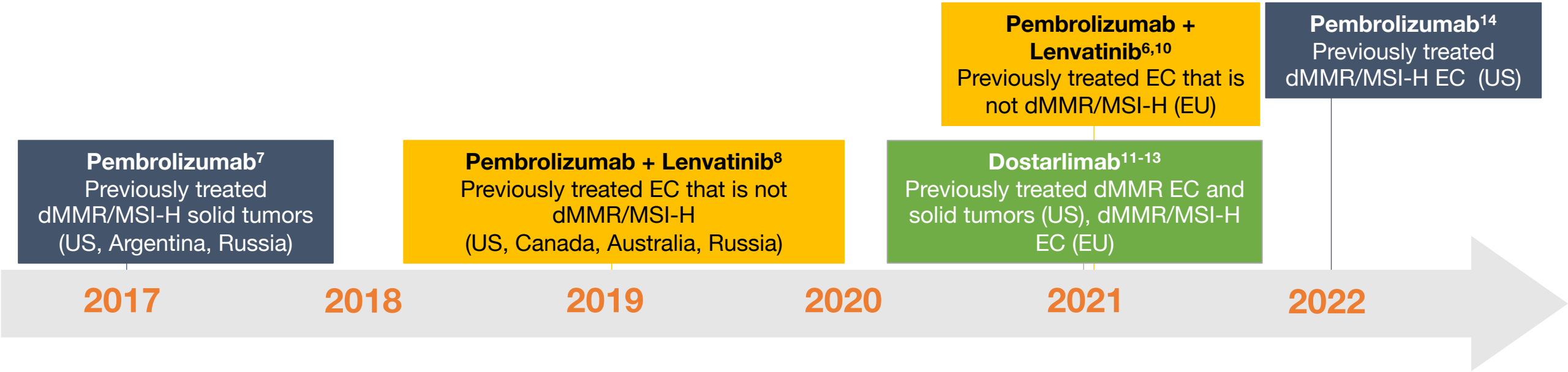


Siegel et al. Cancer Statistics 2023
Cancer Facts & Figures 2023. American Cancer Society. Available at https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf. Accessed January 31, 2023.

Courtesy of Bradley J Monk, MD

Evolving Treatment Landscape for Advanced/Recurrent or High-risk Endometrial Carcinoma

- Treatment guidelines recommend platinum-based chemotherapy (carboplatin + paclitaxel) as preferred 1L treatment of advanced/recurrent EC[1,2,a]
- In 2L treatment, guidelines recommend PD-1 regimens based on biomarker (MMR/MSI) status[2]
- Guideline recommendations are based on recent approvals of PD-1 agents in previously treated EC[3-5,6]



[a]Hormone therapy is included as a preferred 1L therapy In low grade carcinomas without rapidly progressive disease. 1L, first line; 2L, second line; CRC, colorectal cancer; dMMR, mismatch repair deficient; EC, endometrial cancer; EU, European Union; MMR, mismatch repair; MSI, microsatellite instability; MSI-H, microsatellite instability-high; PD-1, programmed death 1; US, United States.

1. Colombo N et al. *Ann Oncol*. 2016;27:16–41. 2. Concin N et al. *Int J Gynecol Cancer*. 2021;31:13–39. 3. Keytruda [prescribing information]. Whitehouse Station. NJ: Merck Sharp & Dohme Corp.; 2021. 4. Jemperli (dostarlimab-gxly) injection, for intravenous use [prescribing information]. Research Triangle Park, NC, USA: GlaxoSmithKline LLC; 2021. 5. Jemperli (Dostarlimab 500 mg solution for infusion) [Summary of product characteristics]. Dublin, Ireland: GlaxoSmithKline (Ireland) Limited; 2021. 6. Keytruda (pembrolizumab) [Summary of product characteristics]. Merck Sharp & Dohme B.V. Netherlands: 2021. 7. US FDA. Press Release. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature. Accessed May 14, 2021. 8. US FDA. Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/simultaneous-review-decisions-pembrolizumab-plus-lenvatinib-australia-canada-and-us. Accessed May 14, 2021. 9. US FDA. Press Release. Available at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-pembrolizumab-first-line-treatment-msi-hdmmr-colorectal-cancer. Accessed December 13, 2021. 10. Merck. Press Release. Available at: https://www.merck.com/news/european-commission-approves-keytruda-pembrolizumab-plus-lenvima-lenvatinib-for-patients-with-certain-types-of-endometrial-carcinoma/ Accessed: March 29, 2022.11. FDA Approves Immunotherapy for Endometrial Cancer with Specific Biomarker | FDA. | FDA Accessed June 7, 2021. 12. EMA: Jemperli. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/jemperli. Accessed June 7, 2021. 13. US FDA. Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-advanced-solid-tumors. Accessed September 22, 2021. 14. US FDA Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-advanced-endometrial-carcinoma. Accessed March 28, 2022.

Courtesy of Bradley J Monk, MD

Clinical Data of Immunotherapy in 2L Endometrial Cancer

Pembrolizumab (KN-158): Robust Antitumor Activity in Patients With MSI-H Advanced EC

Variable	MSI-H EC n = 79	EC (biomarker unselected) n = 107
ORR % (95% CI)	**48** (37-60)	**11.2** (5.9-18.8)
Complete response	11 (14)	0
Partial response	27 (34)	12 (11.2)
Stable disease	14 (18)	26 (24.3)
Progressive disease	23 (29)	56 (52.3)
Not evaluable	1 (1)	2 (1.9)
Not assessed	3 (4)	11 (10.3)

O'Malley DM et al. J Clin Oncol. 2022 Mar 1;40(7):752-761.

Dostarlimab (GARNET Cohorts A1 & A2): Clinical Benefit in dMMR and MMRp EC Patients

Variable	dMMR EC n = 103	MMRp EC n = 142
ORR % (95% CI)	**46** (34.9-54.8)	**19** (8.3-20.1)
Complete response	11 (10.7)	3 (2.1)
Partial response	35 (34.0)	16 (11.3)
Stable disease	13 (12.6)	31 (21.8)
Progressive disease	39 (37.9)	77 (54.2)
Not evaluable	3 (2.9)	0
Not done	2 (1.9)	15 (10.6)

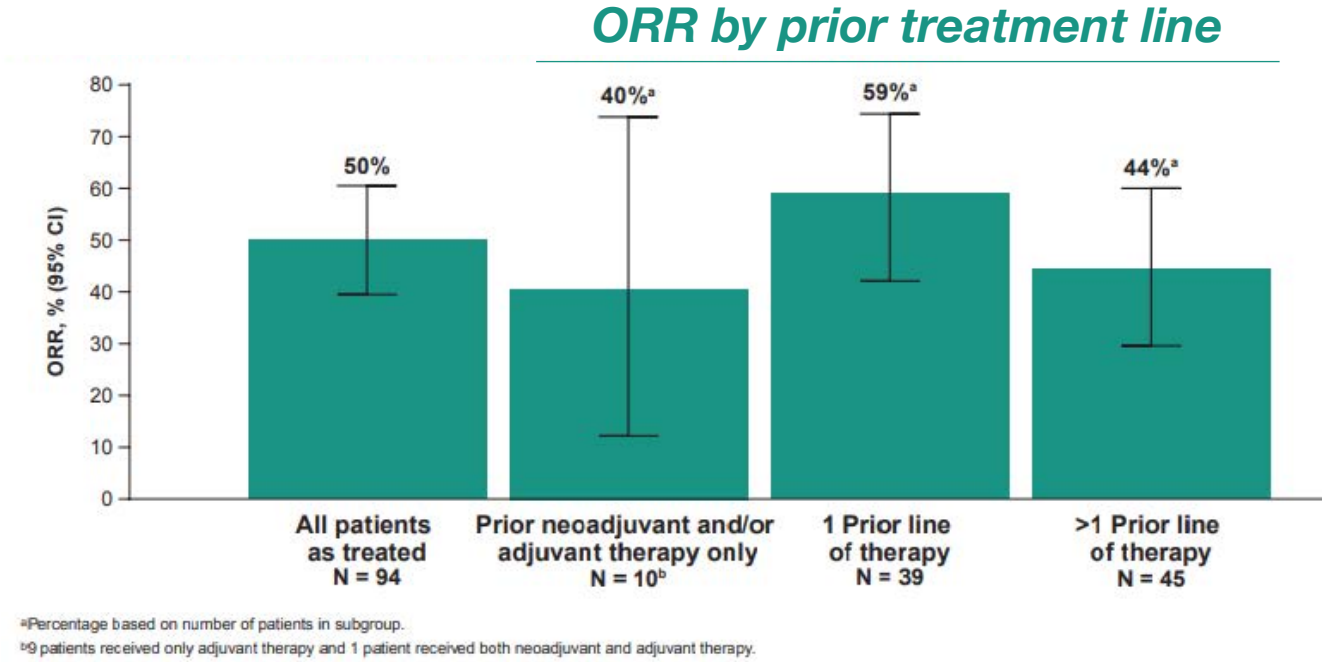
Oaknin A et al. J Immunother Cancer. 2022 Jan;10(1):e003777.

Courtesy of Bradley J Monk, MD

Phase 2 KEYNOTE-158 Study: Updated Responses[a]

Data cutoff: 12 JAN, 2022; median time from first dose to data cutoff: 54.5 mo

ORR (ICR)



[a]Percentage based on number of patients in subgroup.
[b]9 patients received only adjuvant therapy and 1 patient received both neoadjuvant and adjuvant therapy.

Best ORR and DOR (ICR)

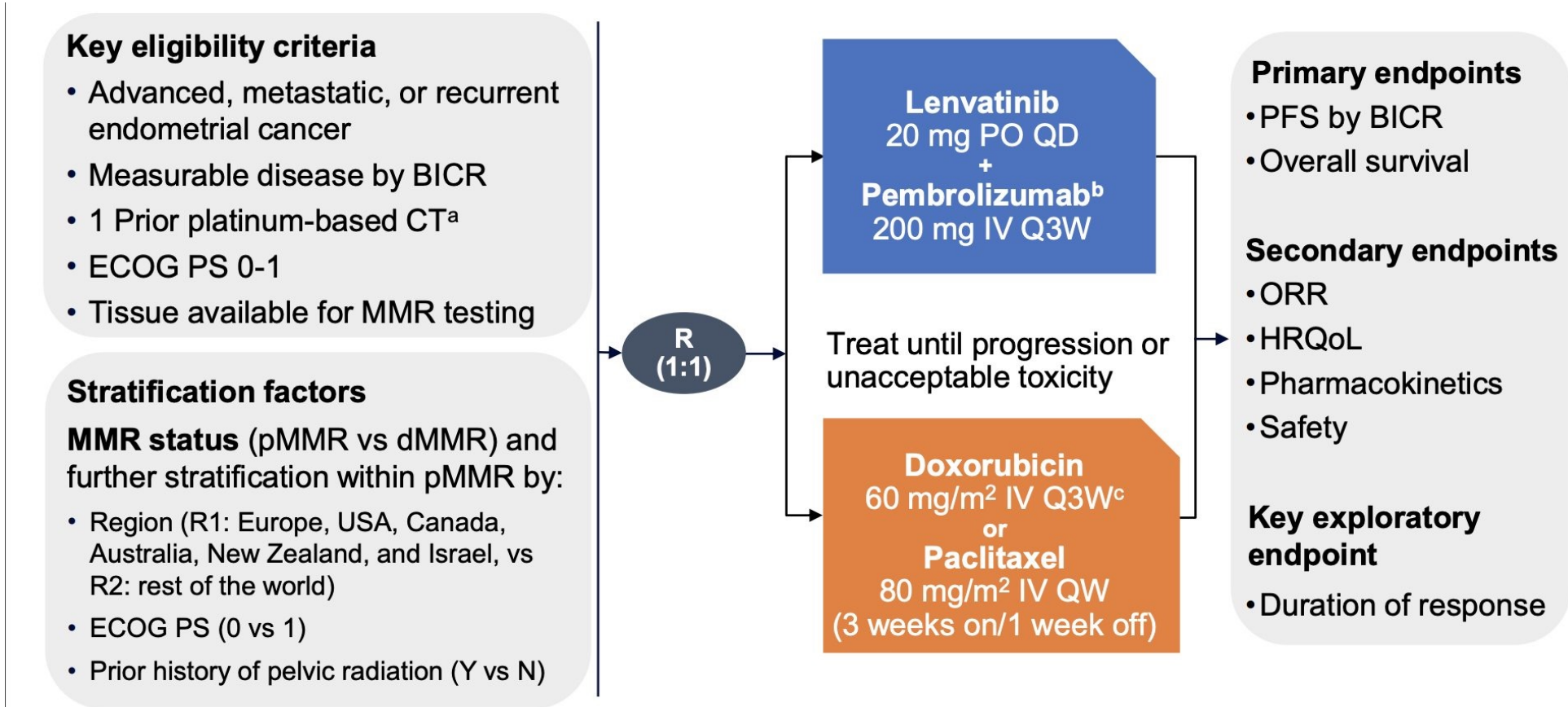
	Analysis population (n = 94)
ORR, % (95% CI)	50 (39.5–60.5)
CR, n (%)	16
PR, n (%)	34
SD, n (%)	18
mDOR, mo	63.2
DOR ≥1 y, %	87
DOR ≥2 y, %	71
DOR ≥3 y, %	66
DOR ≥4 y, %	66

a. At 42.6 mo follow up: ORR, 48%; mDOR NR.

O'Malley D, et al. ESMO 2022. Abstract 546P.

Courtesy of Bradley J Monk, MD

Phase 3 309/KEYNOTE 775 Study of Lenvatinib + Pembrolizumab

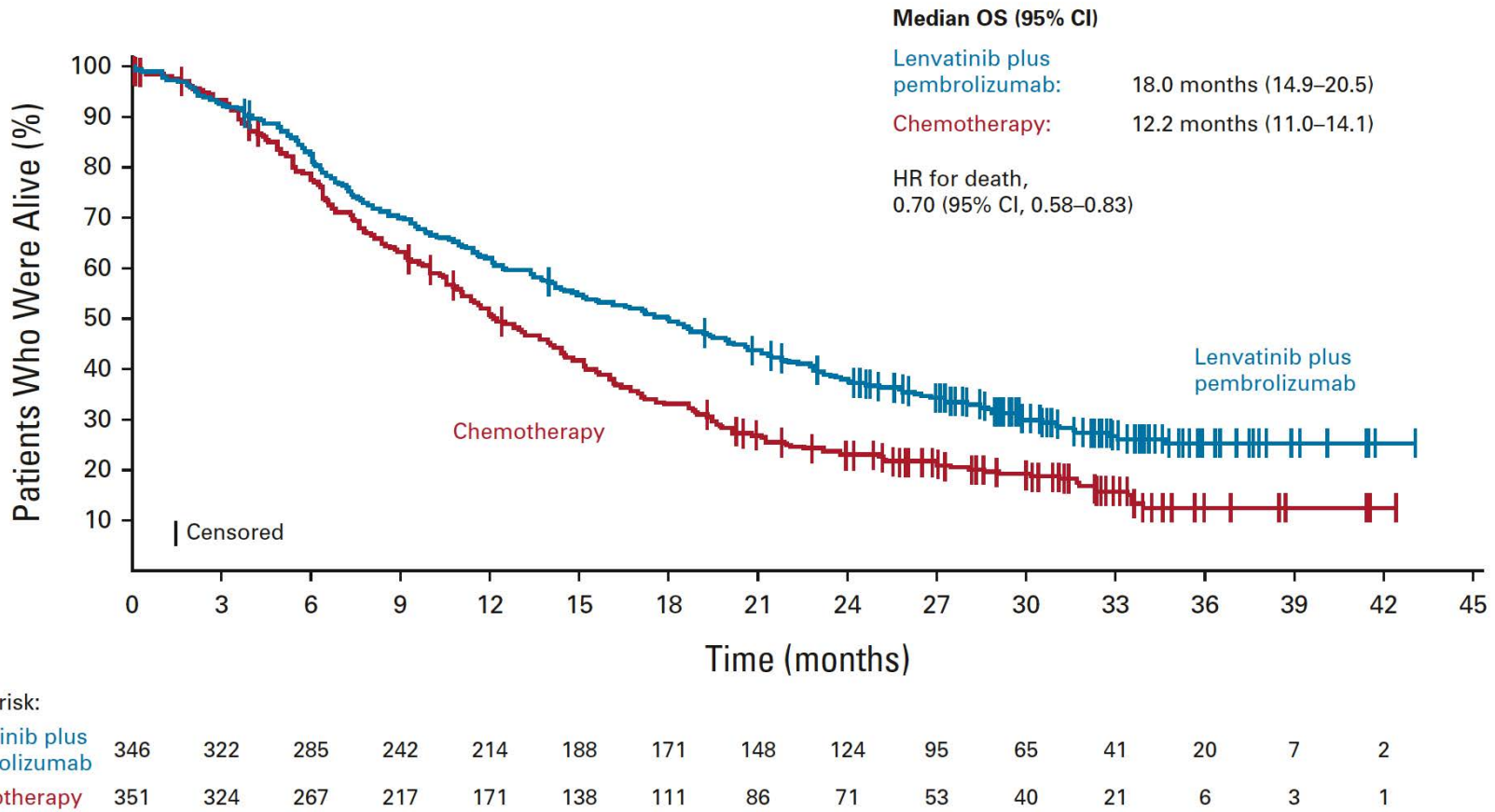


[a]Patients may have received up to 2 prior platinum-based CT regimens if 1 is given in the neoadjuvant or adjuvant treatment setting. [b]Maximum of 35 doses. [c]Maximum cumulative dose of 500 mg/m².

NCT03517449.

Courtesy of Bradley J Monk, MD

Lenvatinib Plus Pembrolizumab in Previously Treated Advanced Endometrial Cancer: Updated Efficacy and Safety From the Randomized Phase III Study 309/KEYNOTE-775



ORR in pMMR patients: 32.4% *v* 15.1%

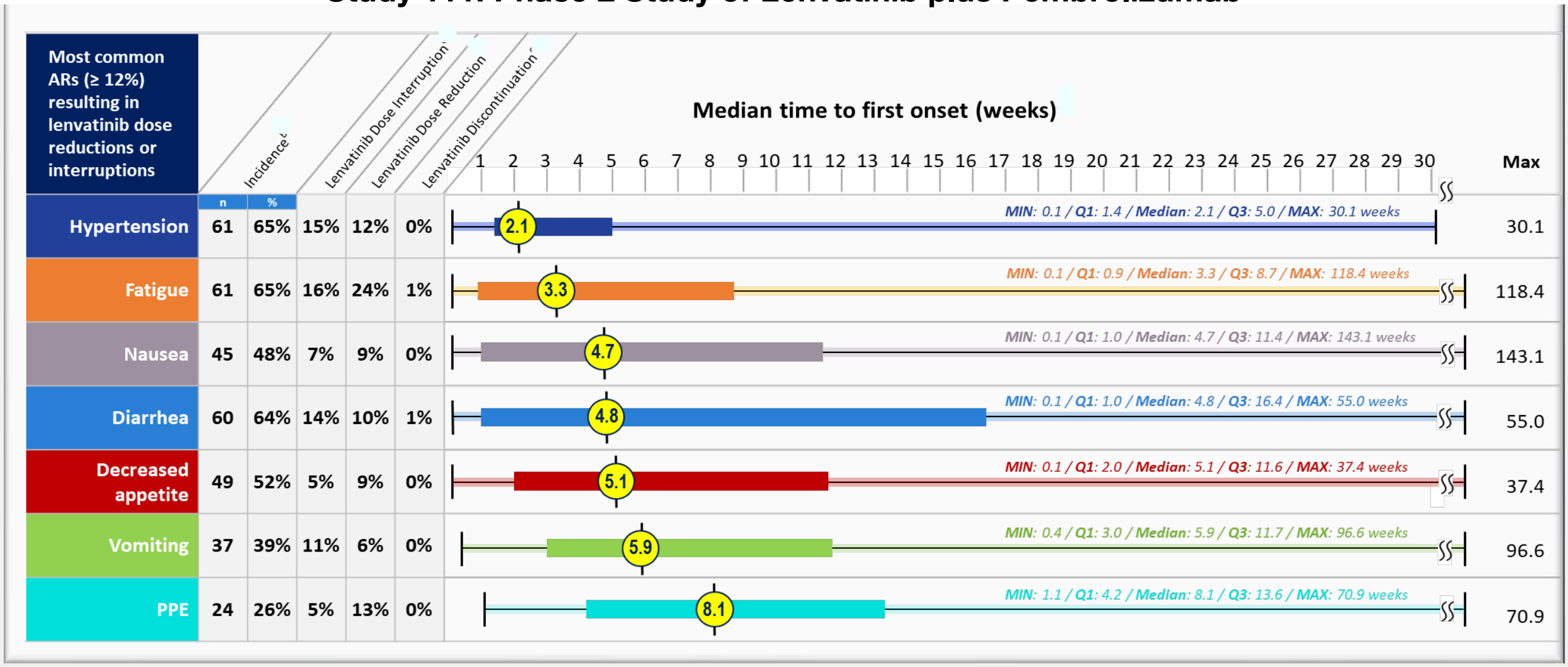
Median follow-up was 18.7 months in the lenvatinib plus pembrolizumab arm and 12.2 months in the chemotherapy arm (14.7 months overall)

Makker V, Colombo N, Herráez AC, Monk BJ, Mackay H, Santin AD, Miller DS, Moore RG, Baron-Hay S, Ray-Coquard I, Ushijima K, Yonemori K, Kim YM, Guerra Alia EM, Sanli UA, Bird S, Orlowski R, McKenzie J, Okpara C, Barresi G, Lorusso D. J Clin Oncol. 2023 Jun 1;41(16):2904-2910.

Courtesy of Bradley J Monk, MD

Most Common Adverse Reactions, All Grades, Time to first onset, weeks

Previously Treated pMMR Subgroup (n=94), Study 111: Phase 2 Study of Lenvatinib plus Pembrolizumab



Makker V, Taylor MH, Oaknin A, et al. Characterization and Management of Adverse Reactions in Patients with Advanced Endometrial Carcinoma Treated with Lenvatinib Plus Pembrolizumab. Oncologist. 2021;26(9):e1599-e1608

Courtesy of Bradley J Monk, MD

Pembrolizumab + Lenvatinib Safety Profile in Patients With Advanced EC Consistent With Individual Monotherapies

Safety	Pembrolizumab + lenvatinib n=406	Physician's choice n=388
Median duration of treatment (range), days	231 (1-817)	104.5 (1-785)
TEAEs, %	99.8	99.5
Grade ≥3 TEAEs, %	88.9	72.7
TEAEs leading to dose reductions, %[a]	66.5	12.9
Any-grade TEAEs leading to interruptions, %[b]	69.2	27.1
Lenvatinib[c]	58.6	--
Pembrolizumab[c]	50.0	--
Pembrolizumab + lenvatinib	30.8	--
Any-grade TEAEs leading to discontinuation, %[b]	33.0	8.0
Lenvatinib[c]	30.8	--
Pembrolizumab[c]	18.7	--
Pembrolizumab + lenvatinib	14.0	--

Most frequent TEAEs for pembrolizumab + lenvatinib (≥40% of All-comers) included

- Hypertension (64%), hypothyroidism (57%),[d] diarrhea (54%), nausea (50%), and decreased appetite (45%)

Most frequent (≥5%) Grade ≥3 TEAEs included

- Hypertension (38%), weight decrease (10%), diarrhea (8%), decreased appetite (8%), anemia (6%), asthenia (6%), fatigue (5%), and proteinuria (5%)

Most frequent TEAEs for physician's choice (≥40% of All-comers) included

- **Anemia (49%) and nausea 46%**

Most frequent (≥5%) Grade ≥3 TEAEs included

- **Neutropenia (26%) and anemia (15%)**

In the lenvatinib + pembrolizumab arm, 5.7% of patients died due to grade 5 events (gastrointestinal disorders, 1.2%; cardiac disorders, 0.5%; general disorders, 1.5%; infections, 0.7%; decreased appetite, 0.2%; neoplasms, nervous system, psychiatric, renal, reproductive, or respiratory disorders, 0.2% each. In the physician's choice arm, 4.9% of patients died due to grade 5 events (cardiac disorders: 1%, general disorders: 1.3%, infections, 1.5%, subdural hematoma: 0.3%, respiratory disorders: 0.8%).

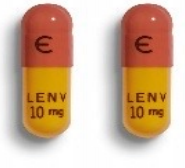
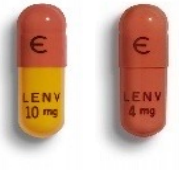
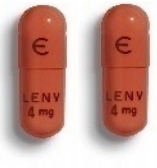
Makker V, Taylor MH, Oaknin A, et al. Characterization and Management of Adverse Reactions in Patients with Advanced Endometrial Carcinoma Treated with Lenvatinib Plus Pembrolizumab. Oncologist. 2021;26(9):e1599-e1608

Courtesy of Bradley J Monk, MD

Lenvatinib + Pembrolizumab
Recommended Dosage and Administration

When administering Lenvatinib and Pembrolizumab in combination for the treatment of endometrial carcinoma, interrupt one or both drugs or dose reduce Lenvatinib as appropriate.

Recommended dose reduction for Lenvatinib in endometrial carcinoma

Recommended dosage	First dosage reduction	Second dosage reduction	Third dosage reduction
			
20 mg orally once daily	14 mg orally once daily	10 mg orally once daily	8 mg orally once daily

Capsules may not be shown at actual size.

Continue treatment with Lenvatinib + Pembrolizumab until disease progression, unacceptable toxicity, or for Pembrolizumab, up to 24 months in patients without disease progression.

https://www.lenvima.com/-/media/Project/Eisai/Lenvima/PDF/prescribing-information.pdf?v=2020-12-22

Courtesy of Bradley J Monk, MD

Chemotherapy ± Immune checkpoint inhibitor currently investigated in Primary Advanced/Recurrent EC

	Dostarlimab RUBY Part 1	ENGOT-en6[1]	Pembrolizumab NRG-GY018[2,3]	Durvalumab DUO-E	ENGOT-en10[5]	Atezolizumab ATTEND	ENGOT-en7[6]
N	494		819	699		550	
Study Chair	Mirza		Eskander	Westin		Colombo	
Treatment arms	Dostarlimab + C/P then dostarlimab **vs** C/P then PBO		Pembrolizumab + C/P then pembrolizumab **vs** C/P then PBO	Durvalumab + C/P then durvalumab + olaparib **&** Durvalumab + C/P then durvalumab + PBO **vs** C/P then PBO		Atezolizumab + C/P then atezolizumab **vs** C/P then PBO	
Patient population	All comers		All comers	All comers		All comers	
Primary outcome(s)	PFS (IA), **OS**		PFS	PFS (IA)		PFS, **OS**	

There are no completed direct head-to-head trials of these products in EC. There are inherent limitations in cross-study comparisons; caution should be exercised in comparing trials. This slide is for information purposes only and is not intended to imply or infer the noninferiority or superiority of any product, in terms of efficacy or safety.

BICR: blinded independent central radiology review; C/P: carboplatin/paclitaxel; DFS: disease-free survival; EC: endometrial cancer; ENGOT: European Network of Gynecological Oncological Trial Groups; IA: investigator-assessed; ICI: immune checkpoint inhibitor; MSI-H: microsatellite instability high; OS: overall survival; PBO: placebo; PFS: progression-free survival.

1. https://clinicaltrials.gov/ct2/show/NCT03981796 . 2. https://clinicaltrials.gov/ct2/show/NCT03914612. 3. Merck News Release. Merck's KEYTRUDA® (pembrolizumab) https://www.merck.com/news/mercks-keytruda-pembrolizumab-plus-chemotherapy-met-primary-endpoint-of-progression-free-survival-pfs-as-first-line-therapy-for-advanced-or-recurrent-endometrial-carcinoma . Accessed February 7, 2023. 4. https://clinicaltrials.gov/ct2/show/NCT04634877 . 5. https://clinicaltrials.gov/ct2/show/NCT04269200 . 6. https://clinicaltrials.gov/ct2/show/NCT03603184 . All ClinicalTrials.gov sites accessed January 31, 2023.

Courtesy of Bradley J Monk, MD

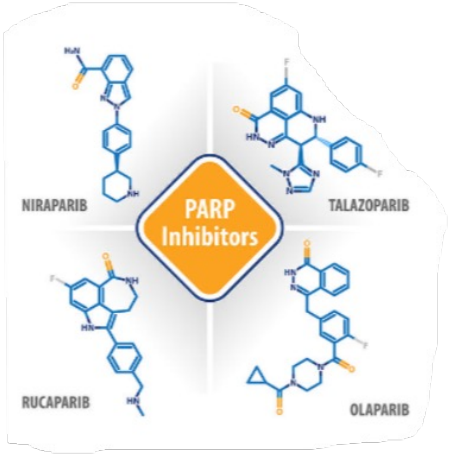
Antibody Drug Conjugates: Continuing the Paradigm Shift Towards Individualized Therapy

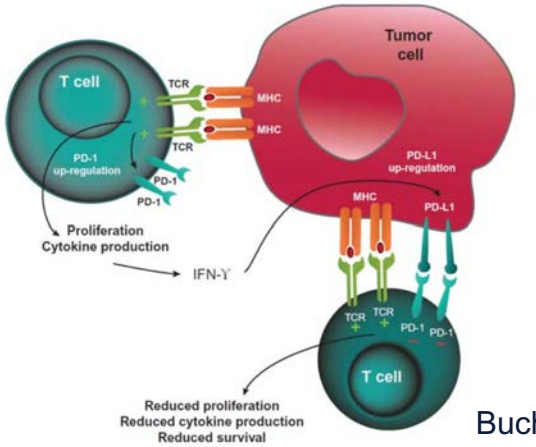
Treatment for Gynecologic Malignancies is becoming more individualized

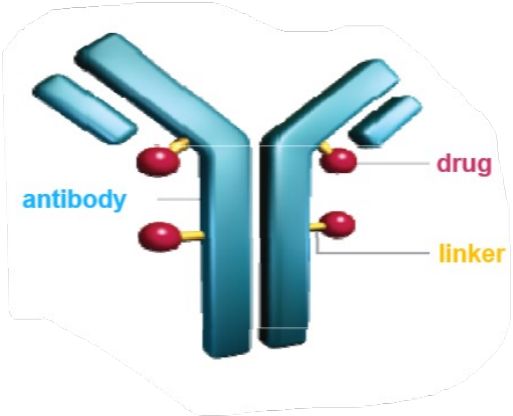
- PARP inhibition for BRCA and HRD
- Immune checkpoint inhibition for MSI-Hi/MMRd

Antibody Drug Conjugates are the next frontier in personalized therapy, allowing us to

- target specific tumor associated antigens
- deliver highly potent chemotherapy directly to the tumor
- offer patients a differentiated safety profile
- offer combination therapies in the near future which may replace standard, systemic chemotherapy







Buchbinder et al. Am J Clin Oncol. 2016

Courtesy of Bradley J Monk, MD

ADCs Under Evaluation in Gynecologic Cancers

In Phase 3 Registration Trials

Generic Name	Conjugate	Indication	Target	Phase	NCT
Mirvetuximab soravtansine	Maytansinoid (DM4)	Ovary	Folate Receptor α	3: Gloriosa 3: MIRASOL 2: SORAYA 2: PICCOLO	NCT05445778 NCT04209855 NCT04296890 NCT05041257
STRO-002 Luveltamab Tazevibulin	SC209 (tubulin targeting)	Ovary	Folate Receptor α	1	NCT03748186 NCT05200364
MORAb-202	Eribulin	Ovary	Folate Receptor α	2	NCT05613088
Upifitamab Rilsodotin	AF-HPA (DolaLOck-controlled bystander effect)	Ovary	NaPi2b	2 UPLIFT 3: UP-NEXT	NCT03319628 NCT05329545
Sacituzumab Govitecan (IMMU-132)	SN-38 (metabolite of topo 1 inhibitor)	Solid tumor (endo)	TROP2	2	NCT04251416
KL 264 01/SKB264	Belotecan (novel camptothecin derivative)	Solid tumors	TROP2	1	NCT04152499
BDC-1001	TLR 7/8 dual agonist	Solid tumor	HER2	1	NCT04278144
DB1303	Topoisomerase 1 inhibitor (P1003)	Solid tumor (endo)	HER2	1	NCT05150691
Ado-trastuzumab emtansine	DM1	Solid tumor (endo & ovary)	HER2	2	NCT04439110
Trastuzumab Deruxtecan	Deruxtecan	Solid tumor (endo, ovary, cervix)	HER2	2	NCT04482309
Trastuzumab duocarmycin	Duocarmycin	Solid tumor (endo)	HER2	2	NCT04205630
DS6000a	deruxtecan	Solid tumor	CDH6	1	NCT04707248
XB002	auristatin	Solid tumor	TF	1	NCT04925284
Tisotumab vedotin	MMAE	Cervix	TF	3	NCT04697628

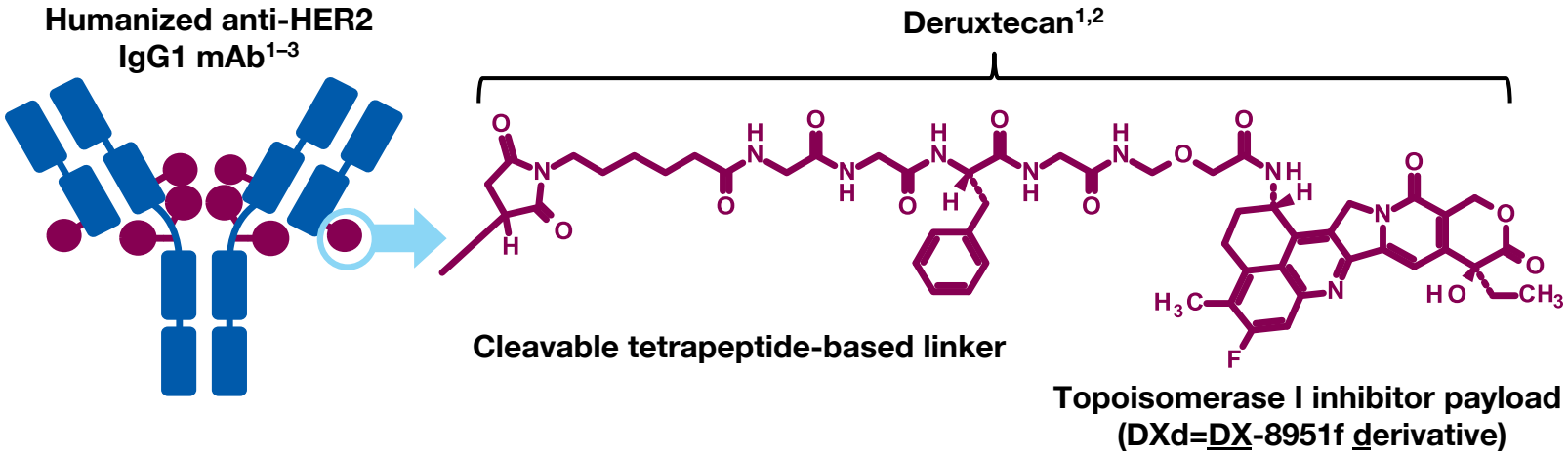
Courtesy of Bradley J Monk, MD

2023 ASCO ANNUAL MEETING

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

T-DXd is an ADC with three components:

1. A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
2. A topoisomerase I inhibitor payload, an exatecan derivative
3. A tetrapeptide-based cleavable linker



[a]The clinical relevance of these features is under investigation.

ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; T-DXd, trastuzumab deruxtecan.

1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173–185. 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097–5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126–142.
4. Okamoto H, et al. *Xenobiotica*. 2020;50(10):1242–1250. 5. Nagai Y, et al. *Xenobiotica*. 2019;49(9):1086–1096.

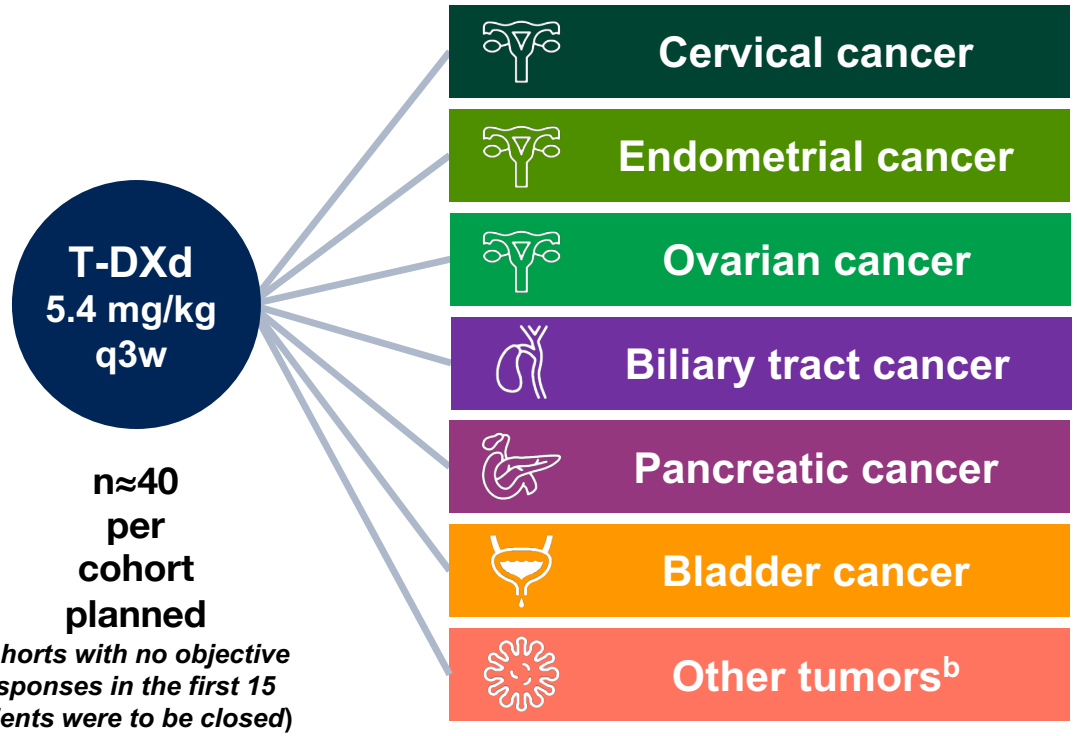
Courtesy of Bradley J Monk, MD

2023 ASCO ANNUAL MEETING

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

An open-label, multicenter study (NCT04482309)

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1



n≈40 per cohort planned
(***Cohorts with no objective responses in the first 15 patients were to be closed***)

Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

- DOR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

Funda Meric-Bernstam, MD et al.
ASCO 2023

[A] Patients were eligible for either test. All patients were centrally confirmed. [b]Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.
[c]Investigator-assessed per Response Evaluation Criteria In Solid Tumors version 1.1.
2L, second-line; ASCO, American Society of Clinical Oncology; DCR, disease control rate; CAP, College of American Pathologists; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2;
IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.
1. Hofmann M, et al. *Histopathology 2008*;52(7):797–805.

Courtesy of Bradley J Monk, MD

2023 ASCO ANNUAL MEETING

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

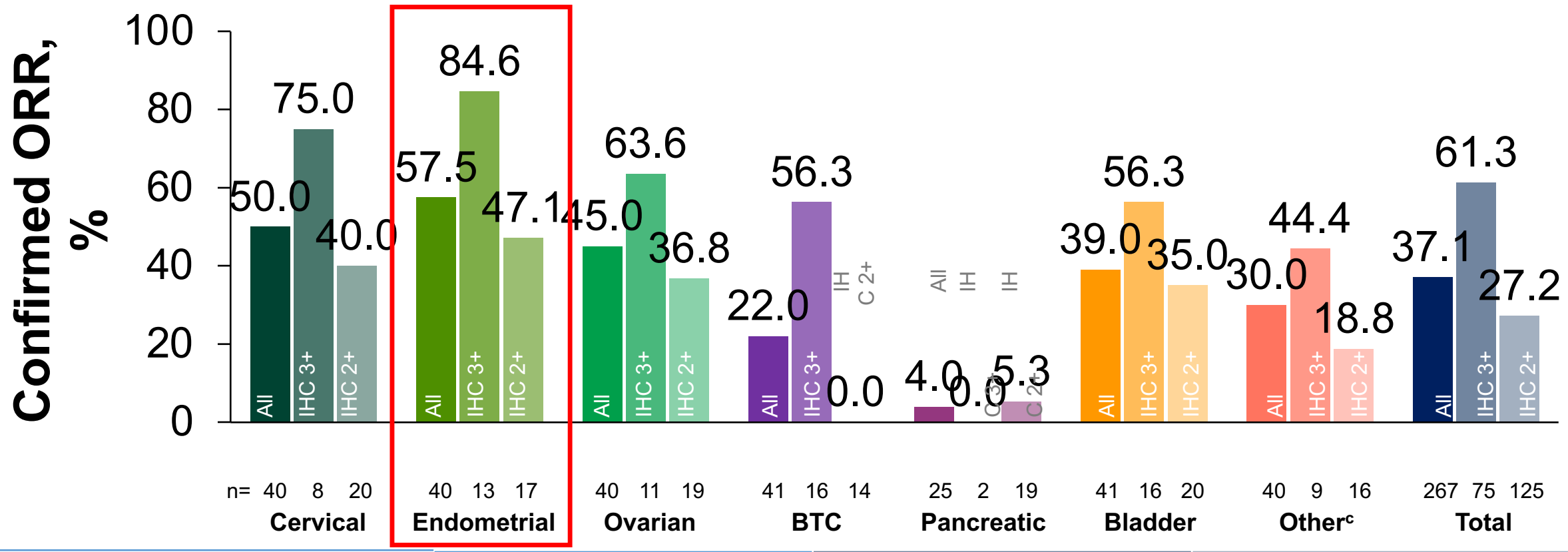
		Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)	BTC (n=41)	Pancreatic (n=25)	Bladder (n=41)	Other (n=40)	All patients (N=267)
Investigator assessment									
ORR, n (%)		**20 (50.0)**	**23 (57.5)**	**18 (45.0)**	**9 (22.0)**	**1 (4.0)**	**16 (39.0)**	**12 (30.0)**	**99 (37.1)**
Best overall response, n (%)	Complete response	2 (5.0)	7 (17.5)	4 (10.0)	1 (2.4)	0	1 (2.4)	0	15 (5.6)
	Partial response	18 (45.0)	16 (40.0)	14 (35.0)	8 (19.5)	1 (4.0)	15 (36.6)	12 (30.0)	84 (31.5)
	Stable disease	12 (30.0)	13 (32.5)	14 (35.0)	25 (61.0)	17 (68.0)	18 (43.9)	24 (60.0)	123 (46.1)
	PD	7 (17.5)	4 (10.0)	7 (17.5)	7 (17.1)	7 (28.0)	7 (17.1)	3 (7.5)	42 (15.7)
	Not evaluable	1 (2.5)	0	1 (2.5)	0	0	0	1 (2.5)	3 (1.1)
DCR[a] at 12 weeks, n (%)		27 (67.5)	32 (80.0)	28 (70.0)	27 (65.9)	9 (36.0)	29 (70.7)	30 (75.0)	182 (68.2)
Median DOR, months (95% CI)		9.8 (4.2–NE)	NR (9.9–NE)	11.3 (4.1–NE)	8.6 (2.1–NE)	NR	8.7 (4.3–11.8)	NR (4.1–NE)	11.8 (9.8–NE)
Independent central review: ORR, n (%)		16 (40.0)	21 (52.5)	17 (42.5)	11 (26.8)	3 (12.0)	17 (41.5)	13 (32.5)	98 (36.7)

Funda Meric-Bernstam, MD et al.
ASCO 2023

Courtesy of Bradley J Monk, MD

2023 ASCO ANNUAL MEETING

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results



	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

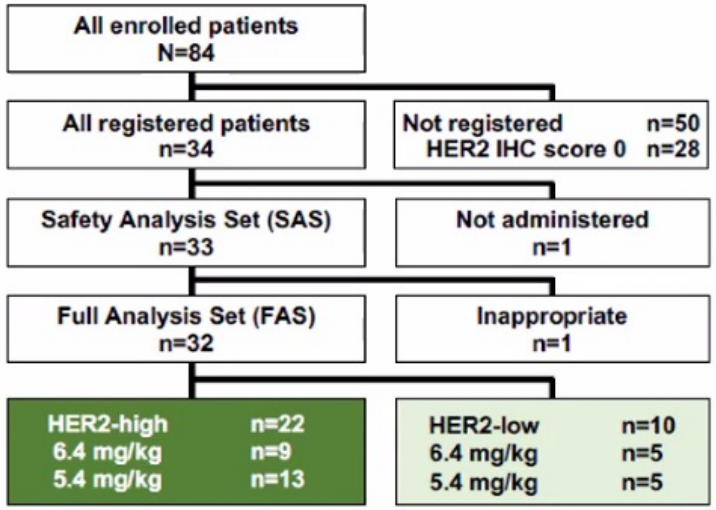
Funda Meric-Bernstam, MD et al.
ASCO 2023

Courtesy of Bradley J Monk, MD

Trastuzumab deruxtecan in carcinosarcoma

Patient Flow Diagram

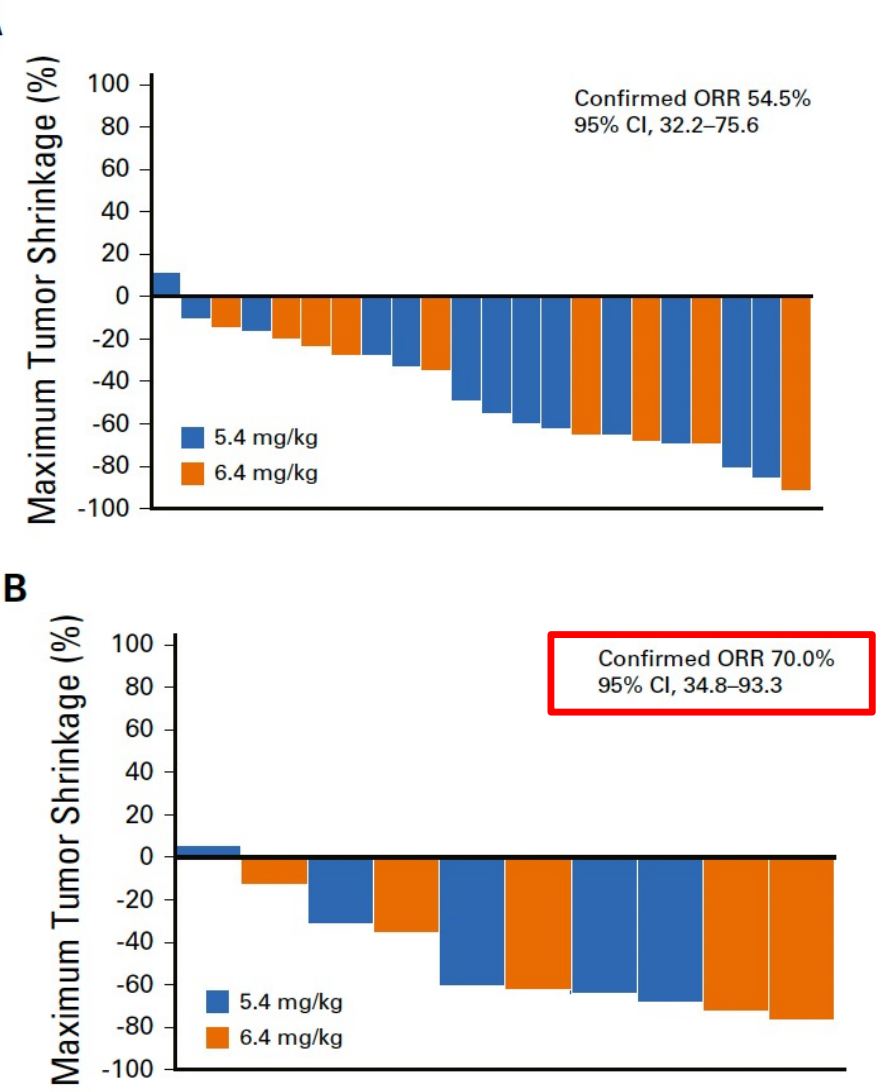
- Patients were enrolled from February 2018 to June 2020 at 7 institutions in Japan
- Data cut-off was done in December 2020
- Twenty-eight patients (33.3%) were excluded from registration due to HER2 IHC score 0
- One patient did not receive T-DXd due to progression of UCS
- One patient was excluded from FAS due to central review with no measurable target lesion



Patient Characteristics

HER2 IHC score (N=84)
0: 28 (33%), 1: 24 (29%)
2: 22 (26%), 3: 10 (12%)

		All (n=34)	(%)	FAS (n=32)	(%)
Age (years)		45- 81	65.5 (median)	45-81	64.5 (median)
PS (ECOG)	0	25	(73.5)	24	(75)
	1	9	(26.5)	8	(25)
HER2 (IHC)	1	11	(32.4)	10	(31.3)
	2	16	(47.1)	15	(46.9)
	3	7	(20.6)	7	(21.9)
HER2 (FISH)	Negative	26	(76.5)	24	(75)
	Positive	8	(23.5)	8	(25)
Prior regimens	1			17	(53.1)
	2			9	(28.1)
	≥3			6	(18.8)



Nishikawa et al. J Clin Oncol 2023

Courtesy of Bradley J Monk, MD

2023 ASCO ANNUAL MEETING

Preliminary results of a Phase II trial with sacituzumab govitecan (SG) in patients with recurrent endometrial carcinoma overexpressing Trop-2 (NCT04251416)

SG is an ADC directed against Trop-2:

1. Conjugated with SN-38 (govitecan), an active metabolite of irinotecan and a topoisomerase I inhibitor
2. Utiilizes a hydrolysable linker
3. SG is FDA-approved for use in metastatic urothelial cancer and metastatic triple-negative breast cancer

Trop-2 is overexpressed in several EC histologies, including grade 3 endometrioid adenocarcinoma (96%) and uterine serous carcinoma (65%)

Trop-2 over expression is prognostic for poor disease outcomes

Stage 1 of an open label non randomized phase 2 trial evaluating the activity of SG in patients with persistent or recurrent Trop-2 overexpressing EC

Primary endpoint: ORR

Required:

50% or **Any staining intensity of Trop-2 in more of tumor cells**

RECIST v1.1 measurable disease

A. Santin, MD et al. ASCO 2023 Poster #294

Courtesy of Bradley J Monk, MD

2023 ASCO ANNUAL MEETING

Preliminary results of a Phase II trial with sacituzumab govitecan (SG) in patients with recurrent endometrial carcinoma overexpressing Trop-2 (NCT04251416)

Table 1. Demographics and clinical characteristics	SG (n = 21)
Median age at study entry, y (range)	63 (47-77)
Race, n (%)	
White	15 (71.4)
Black or African-American	0
Asian	2 (9.5)
Other	4 (19.0)
Histological/cytological diagnosis, n (%)	
Serous	10 (47.6)
Endometrioid	6 (28.6)
Carcinosarcoma	3 (14.3)
Other	2 (9.5)
Number of prior anticancer regimen, n (%)	
1-3	11 (52.4)
> 3	10 (47.6)
Median prior anticancer regimens, n (range)	3 (1-6)
Median follow up duration, m (IQR)	17 (7.6-35.2)

Table 2. Overall response rate and durable disease control	SG (n = 21) n (%)
Best overall response	
Confirmed complete response (CR)	1 (4.8)
Confirmed partial response (PR)	6 (28.5)
Stable disease	11 (47.6)
Progressive disease	3 (14.3)
Objective response rate (confirmed CR + PR)	7 (33.3)
Durable disease control (confirmed CR + PR + SD ≥ 6 months)	7 (35.0)*

*Out of 20 patients evaluable for durable disease control

Table 3. Most Common Treatment-Related Adverse Events	Grade ≥ 3 (≥ 10% of patients)
Neutropenia	9 (43%)
Fatigue	4 (19%)
Anemia	3 (14%)
Diarrhea	3 (14%)
Febrile neutropenia	2 (10%)

- **Median PFS was 5.7 months**
- **Median OS was 22.2 months**

Conclusions:

Sacituzumab govitecan shows encouraging clinical activity against **Trop-2** overexpressing **endometrial cancer** in stage 1 of an **open-label phase 2 trial**; stage 2 is now open/recruiting an all-comer population.

A. Santin, MD et al. ASCO 2023 Poster #294

Courtesy of Bradley J Monk, MD

Abstract 3023

Safety and efficacy of DB-1303 in patients with advanced/metastatic solid tumors: A multicenter, open-label, first-in-human, phase 1/2a study

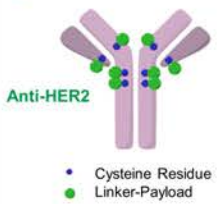
Kathleen Moore,[1] Dhanusha Sabanathan,[2] Yiqun Du,[3] Huaxin Duan,[4] Xiumin Li,[5] Feng Wang,[6] Omkar Marathe,[7] Hua Yang,[8] Vicky Makker,[9] Whitfield B. Growdon,[10] Jim Coward,[11] Peng Zhao,[12] Liming Liu,[13] Rong Shi,[13] Shengxue Liu,[13] Wei Gu,[13] Yang Qiu,[13] Zhongyuan Zhu,[13] Jian Zhang,[14,15] Erika Hamilton[16]

[1] Stephenson Cancer Center at the University of Oklahoma, Oklahoma City, OK, USA; [2] Macquarie University Cancer Institute, Sydney, NSW, Australia; [3] Fudan University Shanghai Cancer Center, Shanghai, China; [4] Hunan Provincial People's Hospital, Changsha, China; [5] Linyi Cancer Hospital, Shandong, China; [6] The First Affiliated Hospital of Zhengzhou University, Henan, China; [7] The Oncology Institute of Hope and Innovation, Lakewood, CA, USA; [8] Affiliated Hospital of Hebei University, Hebei, China; [9] Memorial Sloan Kettering Cancer Center, New York, NY, USA; [10] Perlmutter Cancer Center at NYU Langone Health, New York, NY, USA; [11] ICON Cancer Centre, Brisbane, Australia; [12] The First Affiliated Hospital, Zhejiang University School of Medicine, Zhejiang, China; [13] Duality Biologics, Shanghai, China; [14] Phase I Clinical Trial Center, Fudan University Shanghai Cancer Center, Shanghai, China; [15] Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China; [16] Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA

BACKGROUND

- DB-1303 is an antibody-drug conjugate (ADC) consisting of a humanized anti-HER2 IgG1 monoclonal antibody, covalently linked to proprietary DNA topoisomerase I inhibitor (P1003) via a maleimide tetrapeptide-based cleavable linker, with a high drug-to-antibody ratio (~8) (Figure 1).
- Preclinical studies of DB-1303 showed a favorable safety profile and potent antitumor activity compared with approved HER2-ADC.
- For more information, please visit ClinicalTrials.gov (NCT05150691).

Figure 1 DB-1303 structure and attributes



Key Attributes of DB-1303:

- Payload mechanism of action: topoisomerase I inhibitor
- High potency of payload
- High drug-to-antibody ratio: ~8
- Stable linker-payload
- Tumor-selective cleavable linker
- Selectively endocytosed into the lysosome of HER2-positive cell
- ADCC activity and bystander antitumor effect

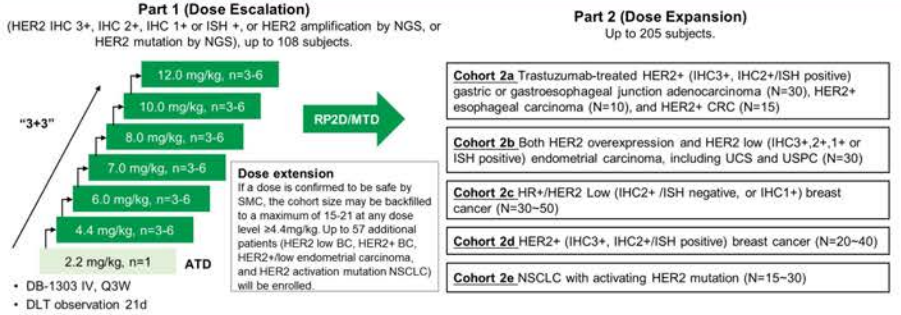
Abbreviations

ADA, Anti-drug antibody; ADC, Antibody-drug conjugate; ADCC, Antibody dependent cellular cytotoxicity; AE, Adverse event; AESI, Adverse event of special interest; ATD, Accelerated titration design; AUC, The area under the concentration-time curve; BC, Breast cancer; Cmax, Peak observed concentration; CRC, Colorectal cancer; DCR, Disease control rate; DLT, Dose-limiting toxicity; DoR, Duration of response; EC, Esophageal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EsC, Esophageal squamous cell carcinoma; HER2, Human epidermal growth factor receptor 2; IHC, Immunohistochemistry; ISH, In situ hybridization; IV, Intravenous; MTD, Maximum tolerated dose; NGS, Next generation sequencing; NSCLC, Non-small cell lung cancer; OC, Ovarian cancer; ORR, Objective response rate; OS, Overall survival; PFS, Progression free survival; PK, Pharmacokinetic; Q3W, Once every 3 weeks, RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, Recommended phase 2 dose; SAE, Serious adverse event; SMC, Safety monitoring committee; SOD, Sum of longest diameters; TEAE, Treatment emergent adverse event; TRAE, Treatment related adverse event; TKI, Tyrosine Kinase inhibitor; TTR, Time to response; UCS, Uterine carcinosarcoma; USPC, Uterine serous papillary carcinoma

Scan Quick Response (QR) Code via a barcode reader application.
Copies of this poster obtained through QR Code are for personal use only and may not be reproduced without permission from ASCO® or the author of this poster.

METHODS

- This is a global first-in-human, dose-escalation and -expansion study in patients with advanced/metastatic solid tumors
  - **Part 1:** primary endpoints including DLTs, SAEs, TEAEs, MTD and/or RP2D; secondary endpoints including ORR, DoR, DCR, TTR, PFS, OS, PK, ADA
  - **Part 2:** primary endpoints including SAEs, TEAEs, ORR; secondary endpoints including percent change in target lesions, DoR, DCR, TTR, Time on therapy, PK, ADA



RESULTS

- At the January 13, 2023, data cutoff, 85 patients received DB-1303 at 6 dose levels (2.2, 4.4, 6.0, 7.0, 8.0, and 10.0 mg/kg) (Table 1). Here we report the results from dose-escalation
  - A total of 68 patients (80.0%) remained on treatment
- The unconfirmed **ORR was 44.2% (23/52)** and DCR was 88.5% (46/52) per RECIST v1.1 in heavily pretreated patients with 7 prior systemic regimens including HER2 ADCs. Among patients with post-baseline tumor scan (n = 52) (Figure 2-4),
  - Encouraging activity of DB-1303 was observed in HER2 expression BC
    - ✓ **HER2 positive BC**: ORR, 50% (13/26); DCR, 96.2% (25/26); **HER2 positive BC with brain metastases**: ORR, 55.6% (5/9); DCR, 100.0% (9/9)
    - ✓ **HER2 low BC**: ORR, 38.5% (5/13), DCR, 84.6% (11/13)
  - Antitumor activity of DB-1303 was also observed in non-BC tumor types: ORR, **CRC** (2/3), **EsC** (1/2), **OC** (1/2), and **EC** (1/3)
- Antitumor activity was observed in heavily pretreated patients with HER2-expressing solid tumors (Figure 2 and 3)

Table 1 Baseline and characteristics

	Total (n = 85)
Age, median (range)	52.0 (30.0-79.0)
Female, n (%)	78 (91.8%)
Region, n (%)	
US/AUS	30 (35.3%)
CHN	55 (64.7%)
ECOG PS, n (%)	
0	22 (25.9%)
1	63 (74.1%)
Number of prior systemic regimens in the metastatic disease, median (range)	7.0 (1-27)
Cancer types, n (%)	
HER2 positive breast cancer	42 (49.4%)
HER2 low breast cancer	21 (24.7%)
Endometrial carcinoma	6 (7.1%)
Colorectal cancer	3 (3.5%)
Ovarian cancer	3 (3.5%)
Esophageal cancer	2 (2.4%)
Gastric cancer	1 (1.2%)
Gastroesophageal junction adenocarcinoma	1 (1.2%)
Non-small cell lung cancer	1 (1.2%)
Vaginal cancer	1 (1.2%)
Site of metastasis, n (%)	
Lungs	43 (50.6%)
Liver	34 (40.0%)
Brain	18 (21.2%)
HER2 IHC results, n (%)	
1+	8 (9.4%)
2+	29 (34.1%)
ISH Positive	10 (11.8%)
ISH Negative or NE	18 (21.2%)
3+	40 (47.1%)
Prior anti-HER2 ADC therapy, n (%)	28 (32.9%)
Prior anti-HER2 antibody therapy, n (%)	47 (55.3%)
Prior anti-HER2 TKI therapy, n (%)	35 (41.2%)
SOD in target lesion, median (n, range)	55.0 (81, 10.5-206.0)

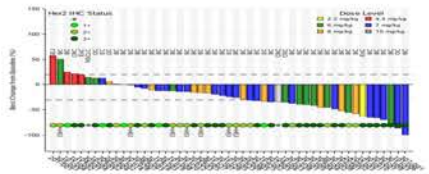


Figure 2 Best tumor response for all patients with post-baseline scans

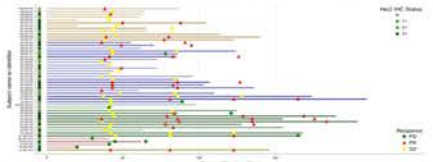


Figure 3 Response over time

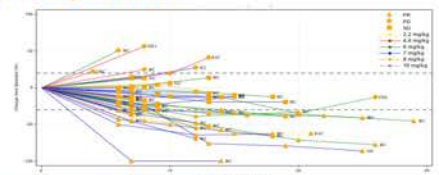


Figure 4 Response with changes of tumor size

SAFETY

- DB-1303 was well tolerated and all AEs were manageable so far (Table 2 and 3)
  - No DLT was observed in 6 dose levels during dose escalation
  - No TEAEs associated with death occurred
  - Interstitial lung disease occurred in 2 patients (2.4%, grade 1), without any ≥grade 2
  - Few patients experienced neutropenia (10 [11.8]; grade ≥3 in 1 [1.2%] patients,) and alopecia (3 [3.5%], grade 1)
- The median duration of treatment was 63.0 (range, 21-211) days, and the median duration of follow-up was 77.0 (range, 7-350) days

Table 2 Summary of overall safety

	2.2 mg/kg (n = 1)	4.4 mg/kg (n = 5)	6.0 mg/kg (n = 15)	7.0 mg/kg (n = 29)	8.0 mg/kg (n = 32)	10.0 mg/kg (n = 3)	Total (n = 85)
Any TEAEs	1 (100.0%)	5 (100.0%)	14 (93.3%)	26 (89.7%)	26 (81.2%)	2 (66.7%)	74 (87.1%)
Associated with treatment withdrawal	0	0	0	1 (3.4%)	0	0	1 (1.2%)
Associated with treatment dose reduction	0	0	0	2 (6.9%)	1 (3.1%)	0	3 (3.5%)
Associated with treatment dose interruption	0	0	4 (26.7%)	8 (27.6%)	5 (15.6%)	0	17 (20.0%)
Grade ≥3	0	3 (60.0%)	3 (20.0%)	9 (31.0%)	2 (6.2%)	1 (33.3%)	18 (21.2%)
Serious AEs	0	3 (60.0%)	4 (26.7%)	4 (13.8%)	2 (6.2%)	0	13 (15.3%)
Treatment-related TEAEs	1 (100.0%)	3 (60.0%)	12 (80.0%)	26 (89.7%)	25 (78.1%)	2 (66.7%)	69 (81.2%)
Grade ≥3	0	1 (20.0%)	2 (13.3%)	6 (20.7%)	1 (3.1%)	1 (33.3%)	11 (12.9%)
Serious AEs	0	0	2 (13.3%)	0	0	0	2 (2.4%)

Table 3 Summary of AEs occurring in ≥20% of patients and AESI (n = 85)

	TEAEs		TRAEs		AESI	
	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3
Nausea	44 (51.8%)	3 (3.5%)	42 (49.4%)	2 (2.4%)	-	-
Vomiting	37 (43.5%)	1 (1.2%)	32 (37.6%)	0	-	-
Platelet count decreased	30 (35.3%)	3 (3.5%)	30 (35.3%)	3 (3.5%)	-	-
Anemia	25 (29.4%)	5 (5.9%)	23 (27.1%)	5 (5.9%)	-	-
Aspartate aminotransferase increased	22 (25.9%)	0	21 (24.7%)	0	-	-
Decreased appetite	22 (25.9%)	0	21 (24.7%)	0	-	-
Fatigue	18 (21.2%)	1 (1.2%)	15 (17.6%)	0	-	-
Alanine aminotransferase increased	17 (20.0%)	0	17 (20.0%)	0	-	-
Ejection fraction decreased	-	-	-	-	3 (3.5%)	0
Infusion related reaction	-	-	-	-	2 (2.4%)	0
Interstitial lung disease	-	-	-	-	2 (2.4%)	0
Electrocardiogram QT prolonged	-	-	-	-	1 (1.2%)	0

PK

- The exposure parameters (C_{max} and AUC) of DB-1303 ADC increased with dose in the dose range of 2.2 to 10.0 mg/kg.
- The half-life of DB-1303 ADC is approximately 6-7 days for therapeutic dose range of 6.0-8.0 mg/kg.
- The exposure of release payload was magnitudes lower than that of DB-1303 ADC, with ADC/payload molar ratio of approximately 80, demonstrating stability of the ADC in systemic circulation.

CONCLUSION

- DB-1303 was well tolerated and all AEs were manageable
- Encouraging preliminary activity of DB-1303 was observed in heavily pretreated patients with advanced/metastatic solid tumors,
  - HER2 positive BC: unconfirmed ORR, 50%; HER2 positive BC with brain metastases: unconfirmed ORR, 55.6%
  - HER2 low BC: unconfirmed ORR, 38.5%
  - Antitumor activity is also observed in non-BC tumor types (e.g., CRC, EsC, OC, EC).
- Expansion is ongoing in selected tumor patients treated at the RP2D.

Funding

- This study is sponsored by Duality Biologics and BioNTech

Acknowledgements

- We thank the patients who participating in this study, as well as their families and caregivers.

Courtesy of Bradley J Monk, MD

Summary and conclusions

- **Lines of therapy, prior treatment, and biomarkers key to personalizing therapy**

❖In endometrial cancer, 2-L IO is the standard of care (SOC) in dMMR/MSI;
in pMMR/MSS pembrolizumab + lenvatinib is SOC

❖In endometrial cancer, 1-L IO + chemotherapy is SOC in dMMR/MSI. PDUFA date for RUBY Sept 23, 2023 [1]

❖In pMMR/MSS benefit from IO is marginal

❖Multiple ADCs in development

❖Clinical trial preferred

1. https://www.gsk.com/en-gb/media/press-releases/gsk-receives-us-fda-file-acceptance-for-jemperli/

Courtesy of Bradley J Monk, MD

Agenda

INTRODUCTION

MODULE 1: First-Line Therapy for Advanced Endometrial Cancer (EC) — Dr Powell

MODULE 2: Current Options for Relapsed EC; Promising Investigational Agents and Strategies — Dr Monk

MODULE 3: Clinical Investigator Survey

RTP
RESEARCH
TO PRACTICE

For patients undergoing evaluation for first-line treatment of metastatic EC, what type of genomic evaluation do you routinely order?

 Dr Monk	NGS, IHC for MMR, TP53, HER2, ER and RNA fusions
 Dr Powell	NGS, IHC for MMR, TP53, HER2 and ER
 Dr Eskander	NGS, IHC for MMR, TP53, HER2 and ER
 Dr Liu	NGS, IHC for MMR, TP53, HER2 and ER
 Dr O'Malley	NGS, IHC for MMR, TP53, and HER2
 Dr Penson	IHC for MMR, TP53, HER2 and ER
 Dr Slomovitz	NGS, IHC for MMR, TP53, HER2 and ER

IHC = immunohistochemistry; MMR = minimal residual disease; NGS = next-generation sequencing

RTP RESEARCH TO PRACTICE

What is your recommended first-line therapy for a patient with MSI-high/dMMR metastatic EC?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Carboplatin/paclitaxel + pembrolizumab*	Carboplatin/paclitaxel + pembrolizumab*
 Dr Powell	Carboplatin/paclitaxel + pembrolizumab or dostarlimab	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Eskander	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab
 Dr Liu	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab
 Dr O'Malley	Carboplatin/paclitaxel + pembrolizumab or dostarlimab	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Penson	Pembrolizumab	Pembrolizumab
 Dr Slomovitz	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab

* Depends on stage

What is your recommended second-line treatment for a patient with MSI-high/dMMR metastatic EC who experiences disease progression on carboplatin/paclitaxel?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Pembrolizumab	Pembrolizumab
 Dr Powell	Pembrolizumab or dostarlimab	Pembrolizumab or dostarlimab
 Dr Eskander	Pembrolizumab	Pembrolizumab
 Dr Liu	Pembrolizumab	Pembrolizumab
 Dr O'Malley	Pembrolizumab or dostarlimab	Pembrolizumab or dostarlimab
 Dr Penson	Pembrolizumab	Pembrolizumab
 Dr Slomovitz	Pembrolizumab	Pembrolizumab

What is your recommended first-line therapy for a patient with MSS/pMMR metastatic EC? What is your recommendation if carboplatin or cisplatin is not available?

	Usual recommendation	Carboplatin or cisplatin not available
 Dr Monk	Carboplatin/paclitaxel*	Oxaliplatin
 Dr Powell	Carboplatin/paclitaxel + pembrolizumab or dostarlimab	Oxaliplatin
 Dr Eskander	Carboplatin/paclitaxel + pembrolizumab	Lenvatinib/pembrolizumab
 Dr Liu	Carboplatin/paclitaxel	Lenvatinib/pembrolizumab
 Dr O'Malley	Carboplatin/paclitaxel + pembrolizumab	Lenvatinib/pembrolizumab
 Dr Penson	Carboplatin/paclitaxel	Lenvatinib/pembrolizumab or AC
 Dr Slomovitz	Carboplatin/paclitaxel + pembrolizumab	Doxorubicin/paclitaxel

* Depends on stage

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a patient with MSS/pMMR metastatic EC?

 Dr Monk	Carboplatin/paclitaxel*
 Dr Powell	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Eskander	Carboplatin/paclitaxel + pembrolizumab
 Dr Liu	Carboplatin/paclitaxel
 Dr O'Malley	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Penson	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Slomovitz	Carboplatin/paclitaxel + pembrolizumab

* Depends on stage

RTP RESEARCH TO PRACTICE

If you chose to use an anti-PD-1 antibody as first-line therapy for a patient with MSS/pMMR metastatic EC, do you generally prefer pembrolizumab or dostarlimab?

 Dr Monk	No preference
 Dr Powell	No preference
 Dr Eskander	Pembrolizumab
 Dr Liu	Pembrolizumab
 Dr O'Malley	No preference
 Dr Penson	No preference
 Dr Slomovitz	Pembrolizumab

RTP RESEARCH TO PRACTICE

If you chose to use an anti-PD-1 antibody as first-line therapy for a patient with MSS/pMMR metastatic EC, for how long would you continue treatment?

 Dr Monk	2 years
 Dr Powell	2 or 3 years, depending on agent
 Dr Eskander	2 years
 Dr Liu	2 years
 Dr O'Malley	2 years
 Dr Penson	2 years
 Dr Slomovitz	2 years

RTP RESEARCH TO PRACTICE

What is your recommended second-line treatment for a patient with MSS/pMMR metastatic EC who experiences disease progression on carboplatin/paclitaxel?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Powell	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Eskander	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Liu	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr O'Malley	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Penson	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Slomovitz	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab

For a patient with recurrent metastatic EC to whom you are about to administer second-line lenvatinib/pembrolizumab, in general, what is your usual starting dose of lenvatinib? What proportion of these patients require dose modification?

	Lenvatinib starting dose	Patients requiring dose modification
 Dr Monk	20 mg	80%
 Dr Powell	14 mg	30%
 Dr Eskander	20 mg	90%
 Dr Liu	20 mg	50%
 Dr O'Malley	20 mg	65%
 Dr Penson	14 mg	60%
 Dr Slomovitz	20 mg	40%

Regulatory and reimbursement issues aside, in general, what would be your treatment approach for a patient with metastatic EC who received carboplatin/paclitaxel/dostarlimab and experienced disease progression 8 months after completing 3 years of maintenance dostarlimab?

	MSS/pMMR EC	MSI-high/dMMR EC
 Dr Monk	Carboplatin/paclitaxel	Rechallenge with dostarlimab
 Dr Powell	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Eskander	Rechallenge with same dostarlimab-based regimen	Rechallenge with same dostarlimab-based regimen
 Dr Liu	Switch to lenvatinib/pembrolizumab	Rechallenge with dostarlimab
 Dr O'Malley	Rechallenge with dostarlimab	Rechallenge with dostarlimab
 Dr Penson	Lenvatinib/pembrolizumab	Rechallenge with dostarlimab
 Dr Slomovitz	Weekly paclitaxel or doxorubicin	Pembrolizumab

Which adjuvant systemic treatment, if any, would you recommend for a patient with localized microsatellite stable (MSS)/MMR-proficient (pMMR) EC who has undergone hysterectomy and has 2 positive lymph nodes?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Carboplatin/paclitaxel	Carboplatin/paclitaxel
 Dr Powell	Carboplatin/paclitaxel	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Eskander	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab
 Dr Liu	Carboplatin/paclitaxel	Carboplatin/paclitaxel
 Dr O'Malley	Carboplatin/paclitaxel	Carboplatin/paclitaxel
 Dr Penson	Carboplatin/paclitaxel	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Slomovitz	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab

Which adjuvant systemic treatment, if any, would you recommend for a patient with localized microsatellite instability (MSI)-high/MMR-deficient (dMMR) EC who has undergone hysterectomy and has 2 positive lymph nodes?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Carboplatin/paclitaxel	Carboplatin/paclitaxel
 Dr Powell	Carboplatin/paclitaxel	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Eskander	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab
 Dr Liu	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab
 Dr O'Malley	Carboplatin/paclitaxel	Carboplatin/paclitaxel + pembrolizumab or dostarlimab
 Dr Penson	Carboplatin/paclitaxel	Carboplatin/paclitaxel + pembrolizumab
 Dr Slomovitz	Carboplatin/paclitaxel + pembrolizumab	Carboplatin/paclitaxel + pembrolizumab

What is your recommended first-line therapy for a patient with MSS/pMMR, HER2-positive metastatic EC?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Carboplatin/paclitaxel + trastuzumab*	Carboplatin/paclitaxel + trastuzumab*
 Dr Powell	Carboplatin/paclitaxel + trastuzumab deruxtecan	Carboplatin/paclitaxel + trastuzumab
 Dr Eskander	Carboplatin/paclitaxel + trastuzumab	Carboplatin/paclitaxel + trastuzumab deruxtecan
 Dr Liu	Carboplatin/paclitaxel + trastuzumab	Carboplatin/paclitaxel + trastuzumab
 Dr O'Malley	Carboplatin/paclitaxel + trastuzumab	Carboplatin/paclitaxel + trastuzumab deruxtecan
 Dr Penson	Carboplatin/paclitaxel + trastuzumab	Carboplatin/paclitaxel + trastuzumab deruxtecan
 Dr Slomovitz	Carboplatin/paclitaxel + trastuzumab	Carboplatin/paclitaxel + trastuzumab

* Depends on stage

What is your recommended second-line treatment for a patient with MSS/pMMR, HER2-positive metastatic EC who experiences disease progression on carboplatin/paclitaxel?

	Usual recommendation	Regulatory and reimbursement issues aside
 Dr Monk	Lenvatinib/pembrolizumab	Trastuzumab deruxtecan
 Dr Powell	Lenvatinib/pembrolizumab	Pembrolizumab or dostarlimab
 Dr Eskander	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Liu	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr O'Malley	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab
 Dr Penson	Trastuzumab deruxtecan	Trastuzumab deruxtecan
 Dr Slomovitz	Lenvatinib/pembrolizumab	Lenvatinib/pembrolizumab

Inside the Issue: Optimizing the Management of Metastatic Urothelial Bladder Cancer

A CME/MOC-Accredited Live Webinar

Thursday, June 29, 2023
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Petros Grivas, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP
RESEARCH
TO PRACTICE