Practical Perspectives: Experts Review Actual Cases of Patients with Endometrial Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, October 15, 2025 5:00 PM - 6:00 PM ET

Faculty

Kathleen N Moore, MD, MS Matthew A Powell, MD



Faculty



Kathleen N Moore, MD, MS

Deputy Director

Virginia Kerley Cade Chair in Developmental Therapeutics

Co-Director, Cancer Therapeutics Program

Stephenson Cancer Center at the University

of Oklahoma HSC

Associate Director, GOG Partners

Board of Directors, GOG Foundation

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Oklahoma City, Oklahoma



MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida



Matthew A Powell, MD
Ira C and Judith Gall Professor
Division of Gynecologic Oncology
Chair, Uterine Corpus Committee
National Cancer Institute-Sponsored NRG Oncology
Washington University School of Medicine
St Louis, Missouri



Commercial Support

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



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: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Agendia Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Clovis Oncology, Coherus BioSciences, Corcept Therapeutics Inc, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Helsinn Therapeutics (US) Inc, Hologic Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Pharma America, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.



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



Dr Moore — Disclosures

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Contracted Research	Allarity Therapeutics, Daiichi Sankyo Inc, GSK, ImmunoGen Inc, Schrödinger, Verastem Inc
Data and Safety Monitoring Boards/Committees	Bicycle Therapeutics



Dr Powell — Disclosures

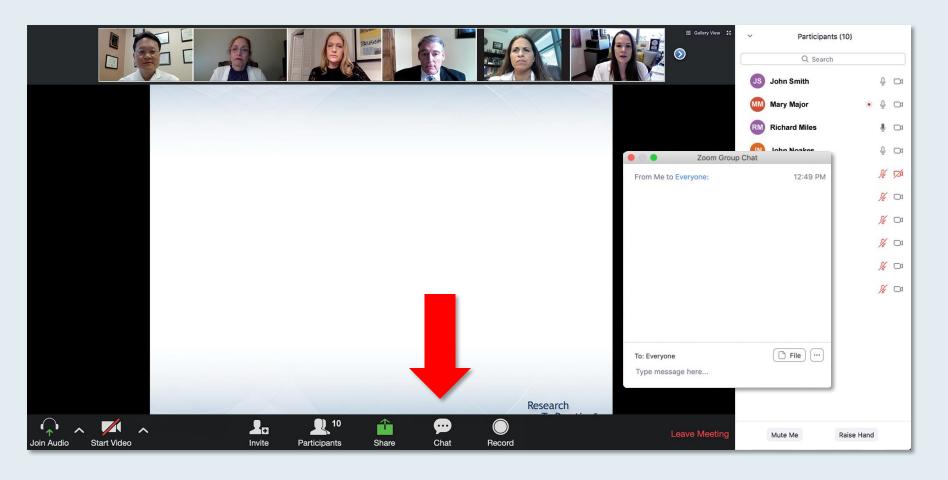
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We Encourage Clinicians in Practice to Submit Questions

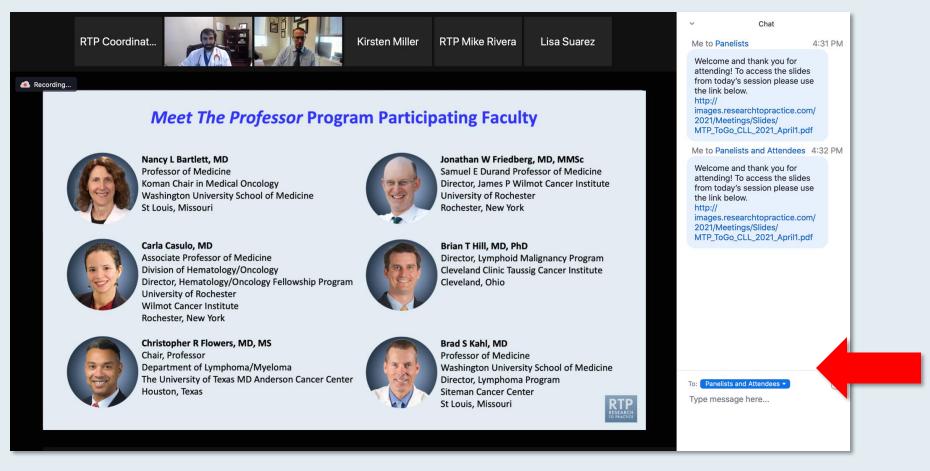


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ONCOLOGY TODAY

WITH DR NEIL LOVE

Ovarian and Endometrial Cancer — An Interview with Dr Shannon Westin on the Current Management Paradigm











Practical Perspectives: Experts Review Actual Cases of Patients with HER2-Positive Gastrointestinal Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, October 21, 2025 5:00 PM - 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD Kristen K Ciombor, MD, MSCI



Cancer Q&A: Understanding the Role and Reality of CAR (Chimeric Antigen Receptor) T-Cell Therapy for Non-Hodgkin Lymphoma

A Webinar Series for Clinicians and Patients, Developed in Partnership with CancerCare®

Patients

Wednesday, October 22, 2025 6:00 PM – 7:00 PM ET

Clinicians

Wednesday, November 12, 2025 5:00 PM – 6:00 PM ET

Faculty

Jeremy S Abramson, MD, MMSc Loretta J Nastoupil, MD



Exploring Current Patterns of Care in the Community: Optimizing the Use of Oral Selective Estrogen Receptor Degraders for HR-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, October 29, 2025 5:00 PM - 6:00 PM ET

Faculty

Rinath M Jeselsohn, MD Joyce O'Shaughnessy, MD



Join Us In Person or Virtually

Integrating New Advances into the Care of Patients with Cancer

A Multitumor Symposium in Partnership with the American Oncology Network

Saturday, November 8, 2025

Lung Cancer
Faculty
Justin F Gainor, MD
Corey J Langer, MD

Chronic Lymphocytic
Leukemia
Faculty
Kerry A Rogers, MD

Moderator Stephen "Fred" Divers, MD



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Ovarian Cancer Faculty
To be announced

Gastroesophageal Cancers
Faculty
Manish A Shah, MD

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What Clinicians Want to Know: First-Line and Maintenance Therapy for Patients with Extensive-Stage Small Cell Lung Cancer

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Tuesday, November 11, 2025 5:00 PM - 6:00 PM ET

Faculty

Luis Paz-Ares, MD, PhD Misty Dawn Shields, MD, PhD



Cancer Conference Update: 2025 ESMO Annual Meeting — Breast Cancer Highlights

CME/MOC-Accredited Live Webinar

Thursday, November 13, 2025 5:00 PM – 6:00 PM ET

Faculty

Professor Giuseppe Curigliano, MD, PhD
Priyanka Sharma, MD



Preventing and Managing Toxicities Associated with Antibody-Drug Conjugates in the Management of Metastatic Breast Cancer

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Wednesday, November 19, 2025 5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO Rita Nanda, MD



Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia 7:30 AM – 9:30 AM ET Myelofibrosis and Systemic Mastocytosis 3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia 11:30 AM – 1:30 PM ET Follicular Lymphoma and Diffuse Large B-Cell Lymphoma 7:00 PM – 9:00 PM ET



Cases from the Community: Investigators Discuss the Optimal Management of Breast Cancer

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Antibody-Drug Conjugates for Metastatic Breast Cancer
Tuesday, December 9, 2025
7:00 PM – 8:30 PM CT

HER2-Positive Breast Cancer Wednesday, December 10, 2025 7:00 PM – 9:00 PM CT

Endocrine-Based Therapy Thursday, December 11, 2025 7:00 PM – 9:00 PM CT



Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

A CME/MOC-Accredited Interactive Grand Rounds Series

October 2025 to March 2026

Steering Committee

Catherine C Coombs, MD
Matthew S Davids, MD, MMSc
Bita Fakhri, MD, MPH

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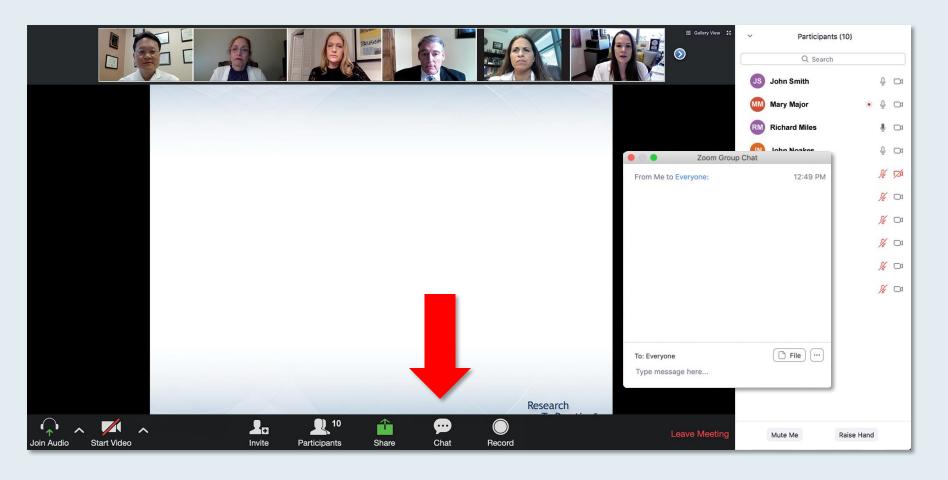
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Dr Powell — Disclosures

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Contributing General Medical Oncologists



Stephen "Fred" Divers, MD American Oncology Network Hot Springs, Arkansas



Kellie E Schneider, MD

Novant Health Cancer Institute
Charlotte, North Carolina



Karim ElSahwi, MD Hackensack Meridian Health Neptune City, New Jersey



Lyndsay J Willmott, MD Virginia G Piper Cancer Care Network Phoenix, Arizona



Victoria Giffi, MD Meritus Medical Center Hagerstown, Maryland



Syed F Zafar, MD
Florida Cancer Specialists
& Research Institute
Fort Myers, Florida



Shachar Peles, MD
Florida Cancer Specialists
& Research Institute
Lake Worth, Florida



Management of Metastatic Endometrial Cancer

Introduction: A pan-tumor perspective on MSI-high disease — Immunotherapy for localized disease

- Case 1: Dr Peles 60-year-old woman
- Case 2: Dr Divers 64-year-old woman
- Data Review: Immune Checkpoint Inhibitors
- Case 3: Dr Schneider 32-year-old woman
- Case 4: Dr Zafar 82-year-old woman
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- Data Review: Autoimmune Toxicity with Immunotherapy
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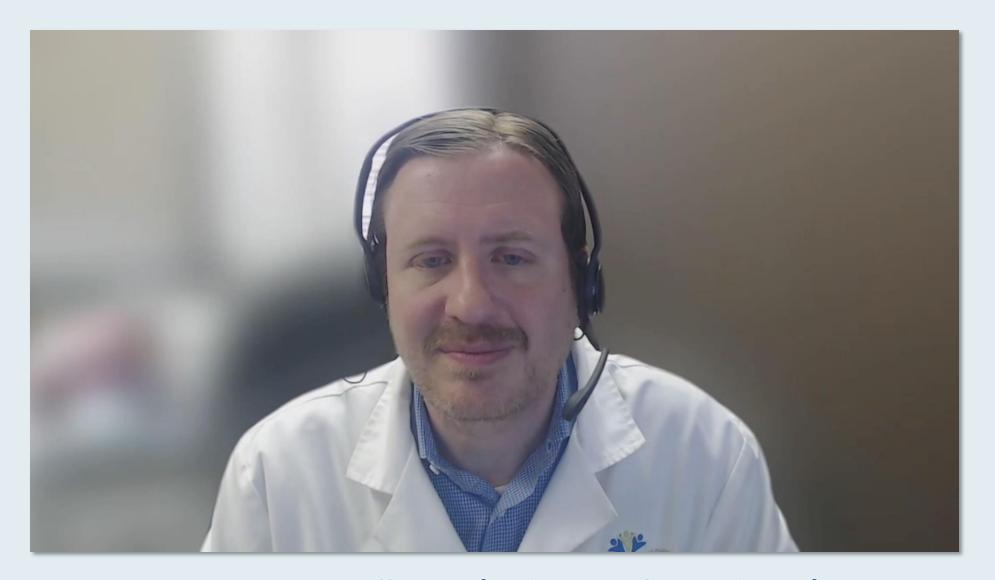


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- Data Review: Novel Antibody-Drug Conjugates





Dr Brian Mulherin (Indianapolis, Indiana)



Case Presentation: Dr Mulherin

74-year-old female who presented with dysfunctional uterine bleeding and abdominal bloating, found to have a large endometrial mass. Imaging ultimately showed an 8.4 cm endometrial mass invading the bladder and causing bilateral hydroureteronephrosis, plus several peritoneal implants and one liver metastasis.

Biomarker testing showed tumor dMMR, also p53-mutated, TMB low at 4. HER2 IHC 1+. Received upfront dostarlimab/carboplatin/paclitaxel and had a partial response. However, had disease progression while still on maintenance dostarlimab at 7 months from treatment initiation.

- 1. What is the optimal therapy for this patient?
- 2. If the tumor was pMMR, with otherwise identical features, what would be the next best treatment option? What's the activity of pembrolizumablenvatinib post-I/O?



Data + Perspectives: Clinical Investigators Explore the Application of Recent Datasets in Current Oncology Care

CME/MOC, NCPD and ACPE Accredited

Saturday, October 11, 2025 7:15 AM - 12:30 PM ET



Agenda

Module 1 — Breast Cancer: *Drs Burstein, Goetz, McArthur and Nanda*

Module 2 — Prostate Cancer: *Drs Antonarakis and M Smith*

Module 3 — Colorectal Cancer: *Drs Lieu and Strickler*

Module 4 — Diffuse Large B-Cell Lymphoma and Follicular Lymphoma: Drs Lunning and S Smith



Colorectal Cancer Faculty



Christopher Lieu, MD
Professor of Medicine
Associate Director for Clinical Research
Director, GI Medical Oncology
University of Colorado Cancer Center
Aurora, Colorado



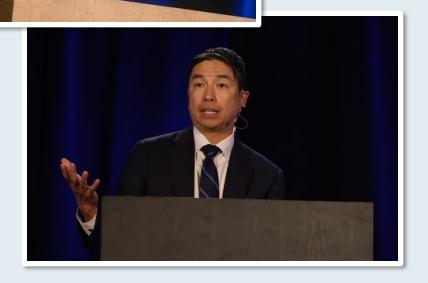
John Strickler, MD
Professor of Medicine
Associate Director, Clinical Research – GI
Co-Leader, Molecular Tumor Board
Duke University
Durham, North Carolina



Colorectal Cancer Session at FCS 2025











Phase II Study of Nivolumab for Patients with Surgically Completely Resectable Mismatch Repair (MMR)-Deficient Endometrial Cancer

Response in Patients Completing Nivolumab															
Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Clinical stage at baseline	IA	IA	IA	IA	IA	3C	IA	IB	3C	3C	IA	IA	IB	3C	1A
MMR status	PMS2	MSH2, MSH6	MSH2, MSH6	PMS2	PMS2, MLH1, MSH2, MSH6	PMS2	PMS2, MLH1, MSH2, MSH6	PMS2, MLH1, MSH2, MSH6	MLH1, PMS2	MLH1, PMS2	PMS2	MLH1, PMS2	MSH2, MSH6	MSH2, MSH6	MLH1, PMS2
Pathological best response	PR	CR	CR	CR	CR	CR	CR	CR	CR	CR	CR	PR	PR	CR	CR
Radiologic best response	NA	NE	CR	NE	NE	CR	NE	CR	CR	CR	NE	PR	PR	CR	CR

CR = complete response, PR = partial response, NE = inevaluable
*Complete Pathological Response: 0% residual viable tumor in the resected primary lesion and/or lymph nodes

A total of 7 out of 12 patients did not undergo surgery

Grade 3 adverse events were reported in 2 patients, but none led to permanent discontinuation of nivolumab

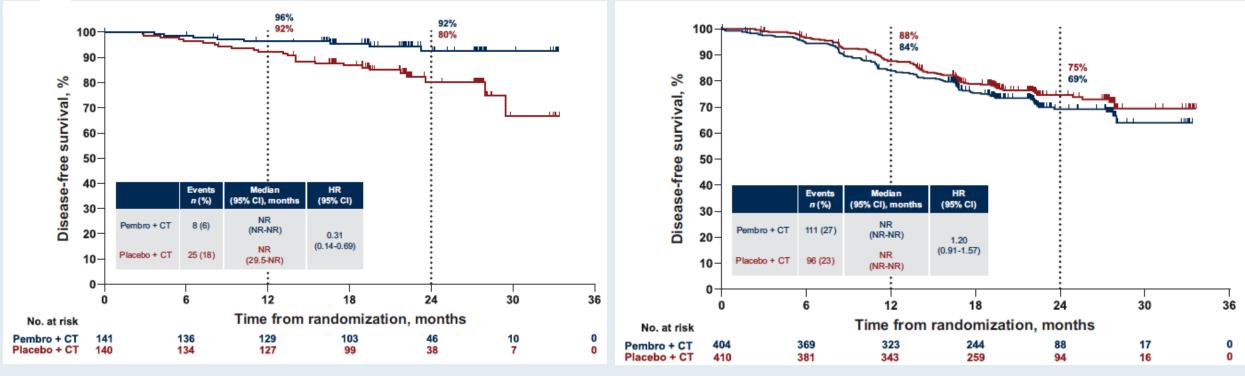


Twelve patients (80.0%) had a clinical complete response, with no evidence of tumor on imaging and biopsy

Phase III KEYNOTE-B21 Study of Pembrolizumab with Adjuvant Chemotherapy with or without Radiation Chemotherapy for Newly Diagnosed, High-Risk Endometrial Cancer



pMMR population



- In the overall population (n = 1,095), the median DFS was not reached in either treatment group and the HR for DFS was 1.02 (p = 0.570).
- Safety was manageable.



dMMR = mismatch repair-deficient; CT = chemotherapy; pMMR = mismatch repair-proficient; DFS = disease-free survival Van Gorp T et al. *Ann Oncol* 2024;35(11):968-80.

Select Ongoing Trials of Neoadjuvant Immunotherapy for Localized Endometrial Cancer

Trial identifier	Phase	Study population Treatment arms		Estimated primary completion date	
NADIA (NCT07013851)	=	Stage II–III dMMR/MSI-H	 Stage II: Dostarlimab → VBT/EBRT + adjuvant dostarlimab Stage III: Dostarlimab → concurrent EBRT + chemotherapy Dostarlimab → sequential EBRT + chemotherapy Dostarlimab → chemotherapy alone Adjuvant dostarlimab 	March 2029	
RODEO (NCT07115927)	II	Stage II–IV	Dostarlimab (2 doses) → surgery	April 2030	
PAM-UMCG-002 (NCT06180733)	П	Grade 3/CC, dMMR	Pembrolizumab → surgery	December 2027	

MSI-H = microsatellite instability-high; VBT = vaginal brachytherapy; EBRT = external beam radiation therapy



Select Ongoing Trials of Adjuvant Immunotherapy for Localized Endometrial Cancer (EC)

Trial identifier	Phase	Study population	Treatment arms	Estimated primary completion date
MMRd-GREEN (NCT05255653-2)	III	High-risk, dMMR EC after curative intent surgery	Durvalumab + RTRT	January 2030
NRG-GY020 (NCT04214067)	III	Stage II–IV	Pembrolizumab + EBRT/VBTEBRT/VBT	December 2025



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Data Review: Autoimmune Toxicity with Immunotherapy

■ Data Review: Novel Antibody-Drug Conjugates



Case Presentation: 60-year-old woman with MSI-H metastatic endometrial carcinoma has CR with dostarlimab and paclitaxel/carboplatin



Dr Shachar Peles (Lake Worth, Florida)



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Case Presentation: 64-year-old woman with MSI-H, somatic BRCA1-mutant endometrial cancer has CR with carboplatin/paclitaxel/pembrolizumab



Dr Fred Divers (Hot Springs, Arkansas)



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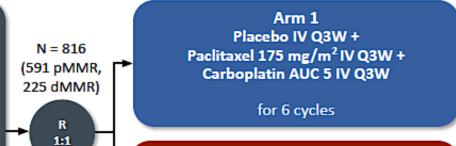
NRG-GY018 Phase III Study Design

Key Eligibility Criteria

- Measurable stage III/IVA or measurable/nonmeasurable stage IVB or recurrent endometrial cancer
- Pathology report showing results of institutional MMR IHC testing
- ECOG PS 0, 1, or 2
- No prior chemo except prior adjuvant chemo if completed ≥12 mo before study

Stratification Factors

- •dMMR vs pMMR
- ECOG PS (0 or 1 vs 2)
- Prior adjuvant chemo (yes vs no)



Arm 2
Pembrolizumab 200 mg IV Q3W +
Paclitaxel 175 mg/m² IV Q3W +
Carboplatin AUC 5 IV Q3W

for 6 cycles

Arm 1 Placebo IV Q6W

for up to 14 additional cycles

Arm 2 Pembrolizumab 400 mg IV Q6W

for up to 14 additional cycles

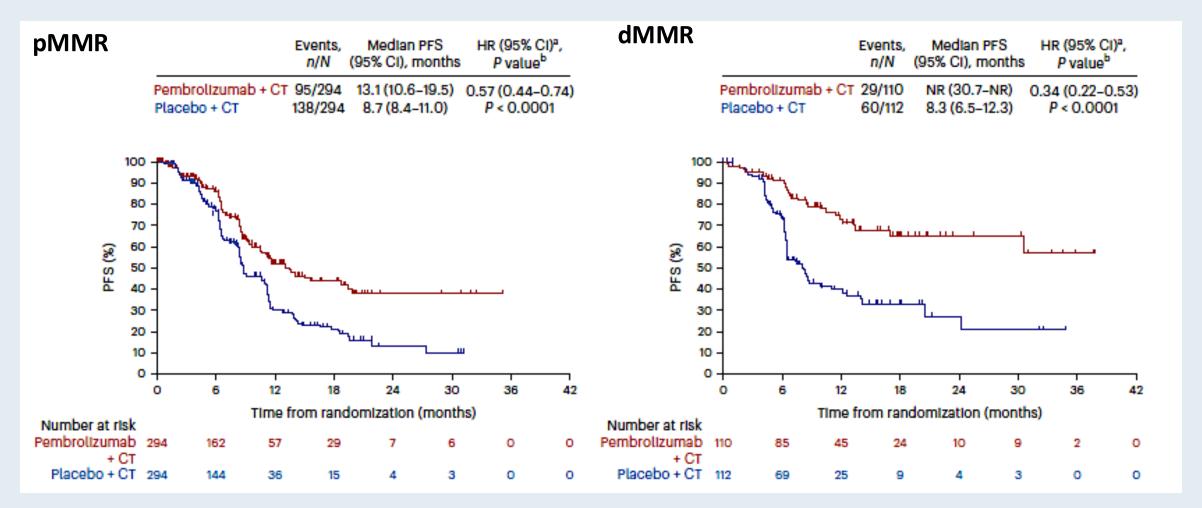
Endpoints

- Primary: PFS per RECIST v1.1 by investigator in pMMR and dMMR populations
- Secondary: Safety, ORR/DOR per RECIST v1.1 by BICR or investigator by treatment arm and MMR IHC status, OS in pMMR and dMMR populations, PRO/QoL in pMMR population, and concordance of institutional vs central MMR IHC testing results

BICR, blinded independent central review; dMMR, mismatch repair deficient; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; PRO, patient-reported outcomes; QoL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors.

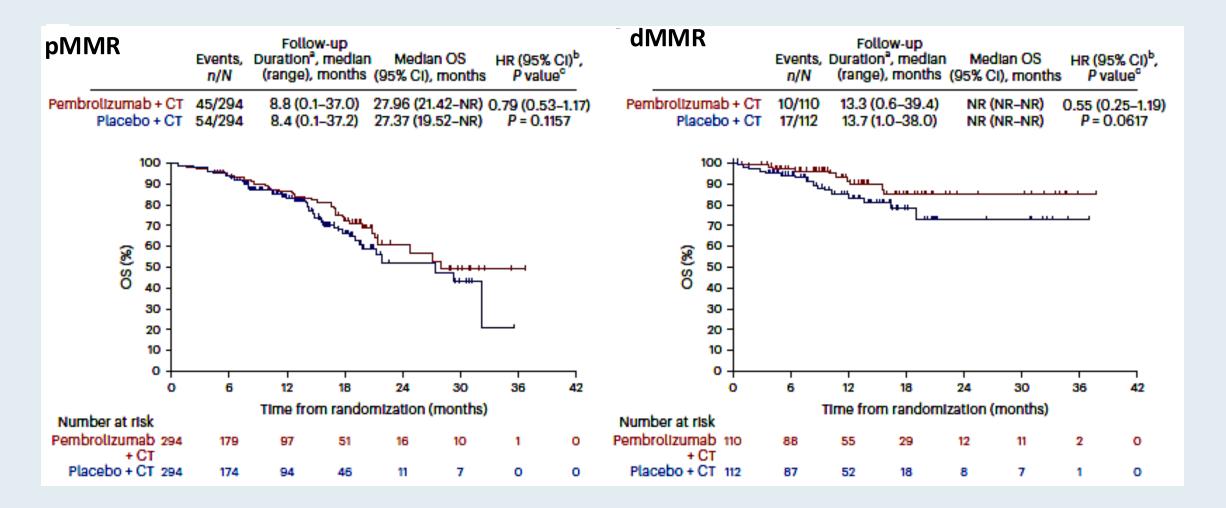


NRG-GY018: Investigator-Assessed Progression-Free Survival (PFS) by Mismatch Repair (MMR) Status



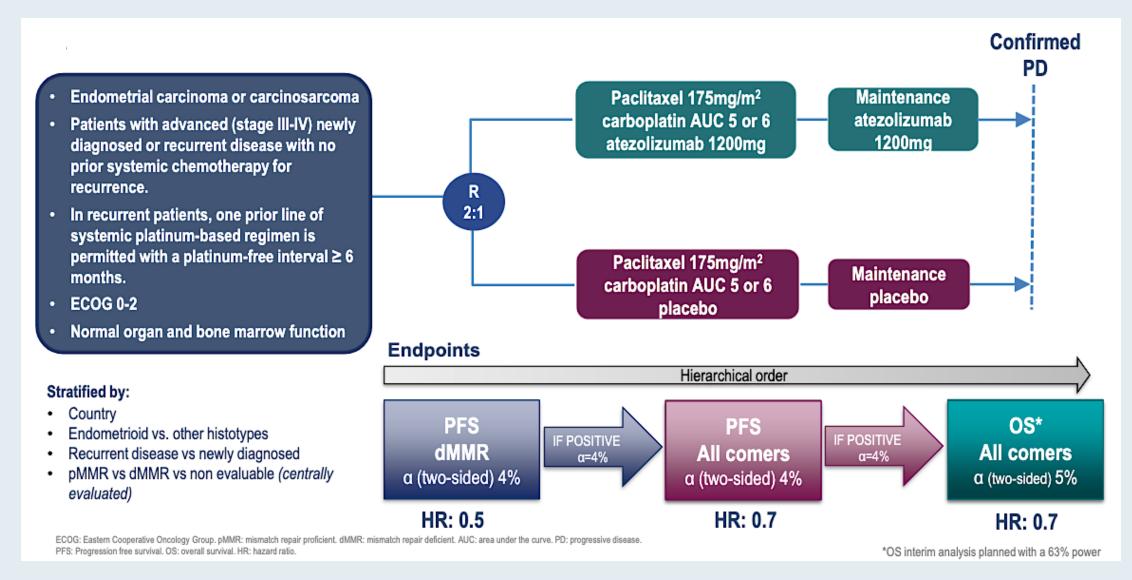


NRG-GY018: Interim Analysis of Overall Survival (OS) by MMR Status





AtTEnd Phase III Study Design

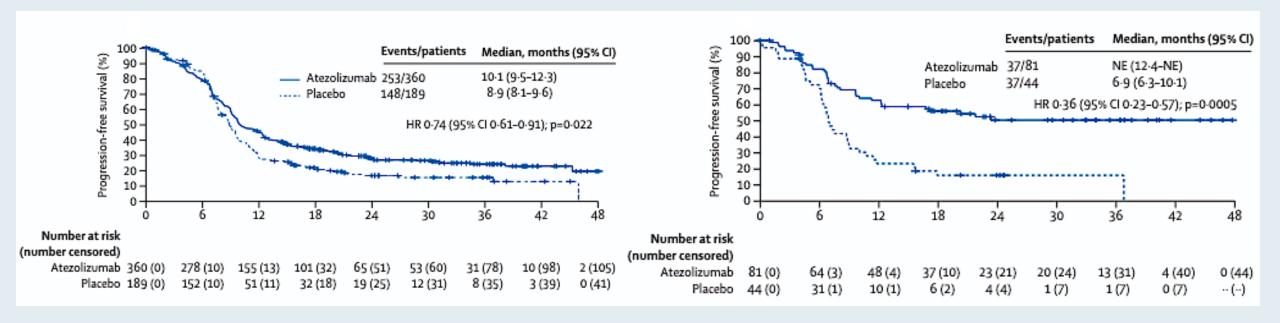




AtTEnd: PFS in the Overall and dMMR Populations

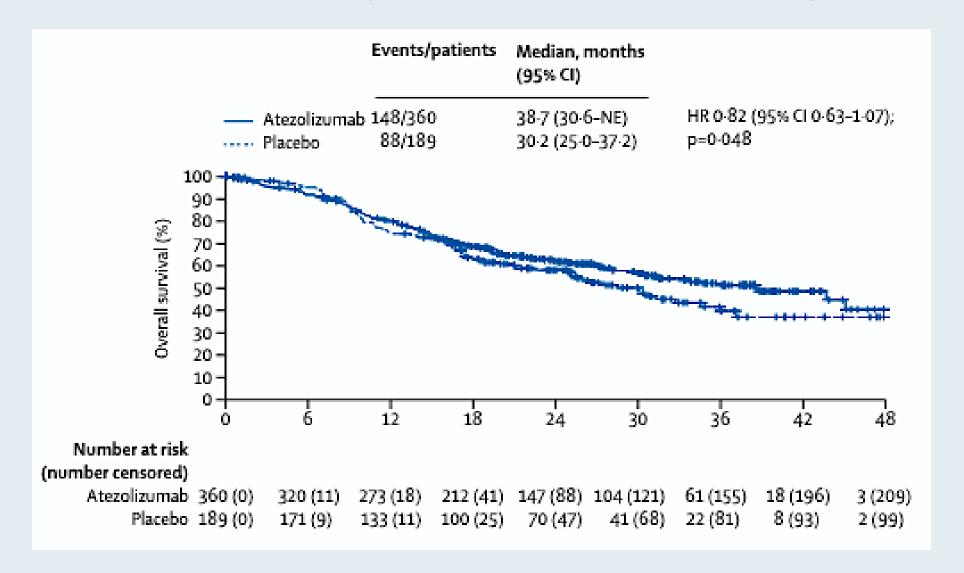
Overall population

dMMR population





AtTEnd: Interim Analysis of OS in the Overall Population





Final Overall Survival (OS) Results from the Randomized Double-Blind Phase III AtTEnd/ENGOT-EN7 Trial Evaluating Atezolizumab in Combination with Paclitaxel and Carboplatin in Women with Advanced/Recurrent Endometrial Cancer

Ginesta MPB et al.

ESMO 2025; Abstract LBA39.

PROFERRED PAPER | SUNDAY, OCTOBER 19 | 14:55 CEST



WES-Derived Aneuploidy Score (W-AS) Identifies MMRd Patients with Reduced Benefit from Immunotherapy in Endometrial Cancer: Multi-omic Analysis of the Phase III AtTEnd/ENGOT-EN7 Trial

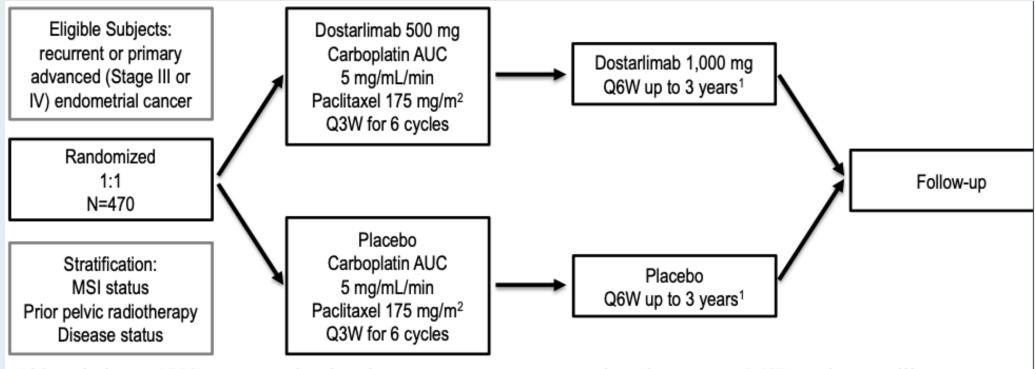
Mazarella L et al.

ESMO 2025; Abstract LBA40.

PROFERRED PAPER | SUNDAY, OCTOBER 19 | 10:15 CEST



Phase III RUBY Part 1 Study Design

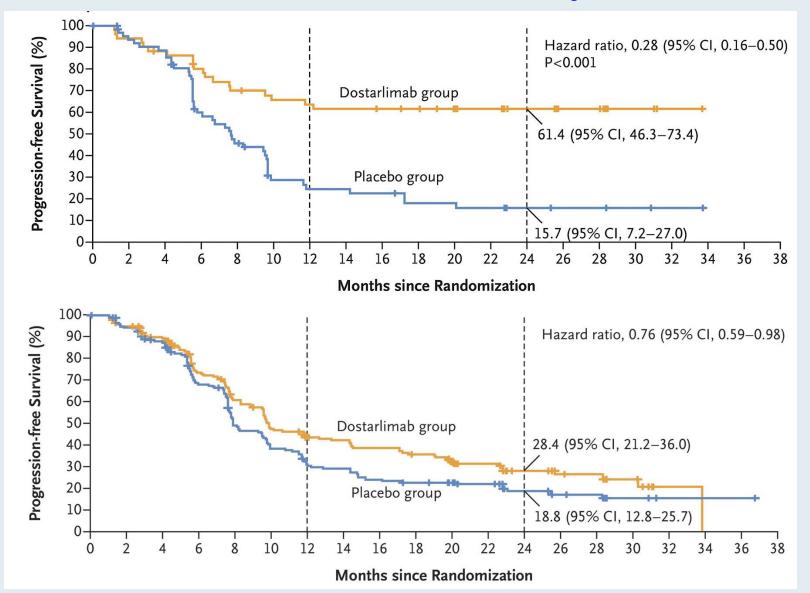


Abbreviations: AUC = area under the plasma or serum concentration-time curve; MSI = microsatellite instability; QxW = every x weeks.

¹ Treatment ends after 3 years, progression of disease, toxicity, withdrawal of consent, Investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered following discussion between the Sponsor and the Investigator.



Phase III RUBY Part 1: PFS by Mismatch Repair (MMR) Status

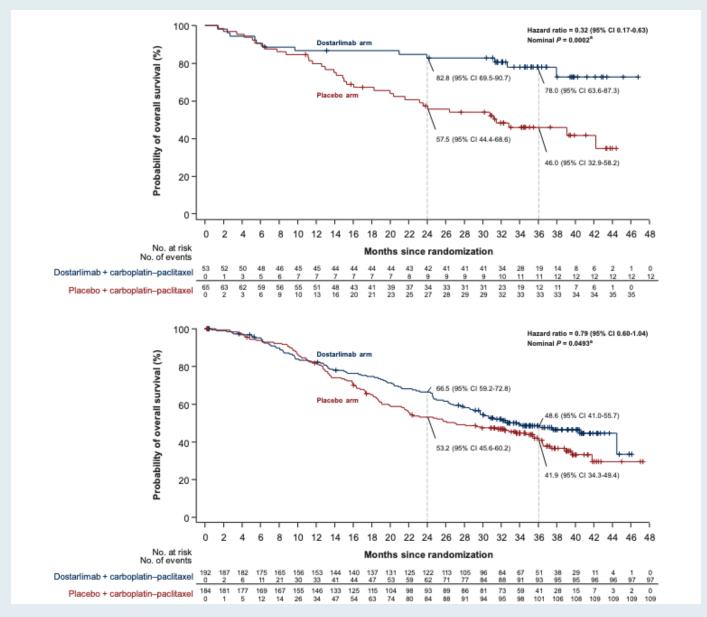


dMMR/MSI-H population

pMMR/MSS population



Phase III RUBY Part 1: Overall Survival by MMR Status



dMMR/MSI-H population

pMMR/MSS population



Post Hoc Survival Outcomes Based on Initial and Subsequent Treatment in Patients (pts) with Mismatch Repair Proficient/Microsatellite Stable (MMRp/MSS) Primary Advanced or Recurrent Endometrial Cancer (pA/R EC) in the ENGOT-EN6-NSGO/GOG-3031/RUBY Trial

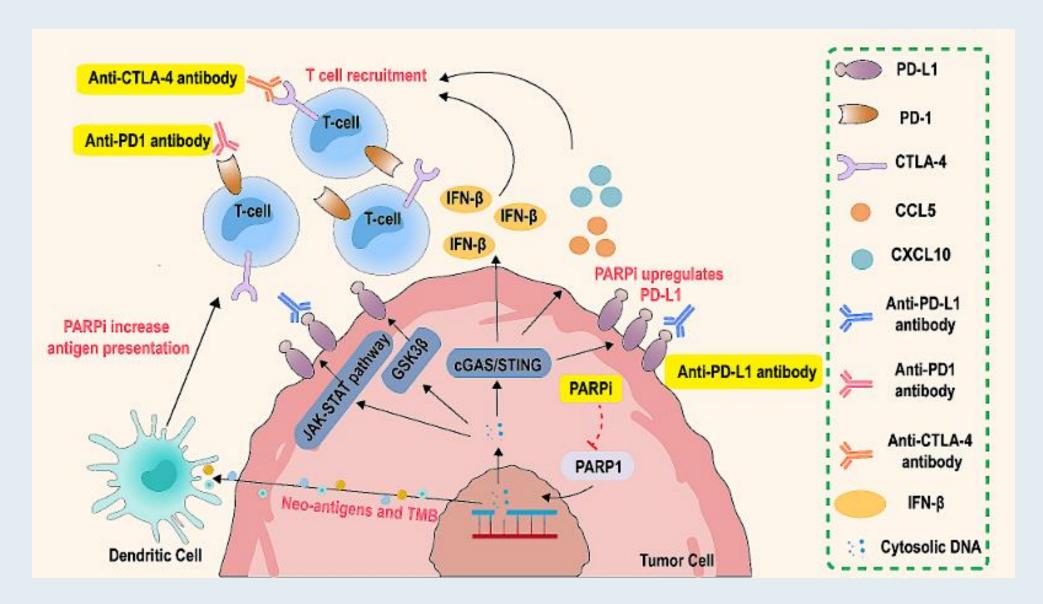
Monk BJ et al.

ESMO 2025; Abstract 1113P.

POSTER SESSION 1 | SATURDAY, OCTOBER 18



Interaction Between PARP Inhibitors and Immune Checkpoint Inhibitors





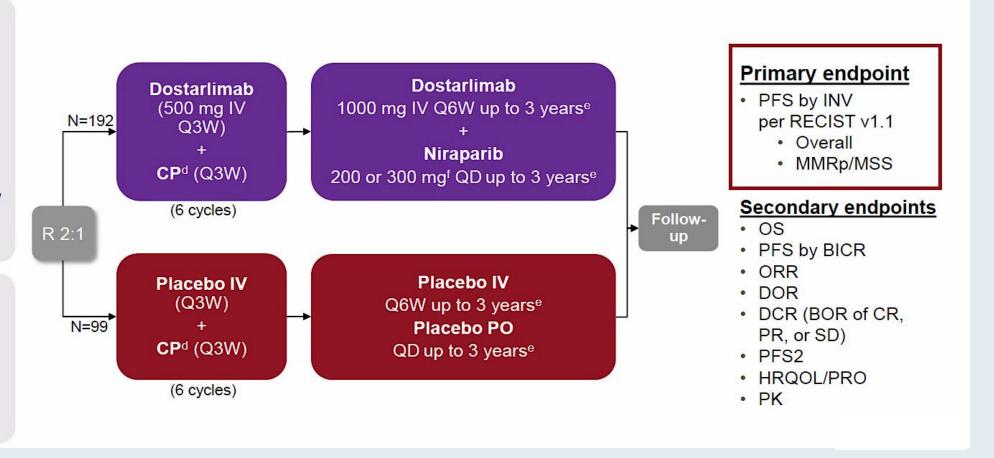
Phase III RUBY Part 2 Study Design

Eligible patients

- Stage III/IV disease or first recurrent EC^a
 - All histologies except sarcomas^b
- Naive to systemic anticancer therapy or had a recurrence or PD ≥6 months after completing systemic anticancer therapy
- Naive to PARP inhibitor therapy

Stratification

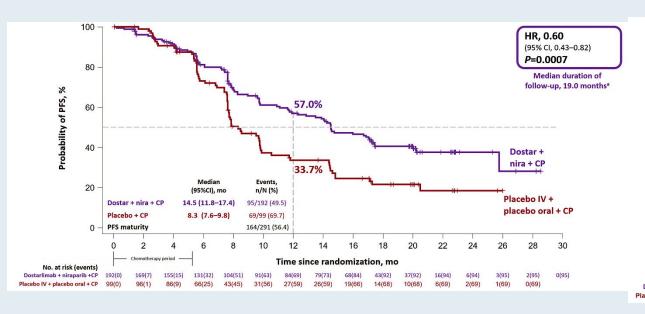
- MMR/MSI status^c
 - 25% dMMR/MSI-H
 - 75% MMRp/MSS
- Prior external pelvic radiotherapy
- · Disease status



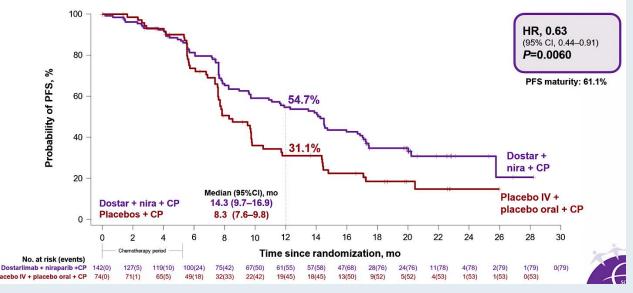


Phase III RUBY Part 2 Coprimary Endpoints: PFS in the Overall and pMMR Populations

Overall population

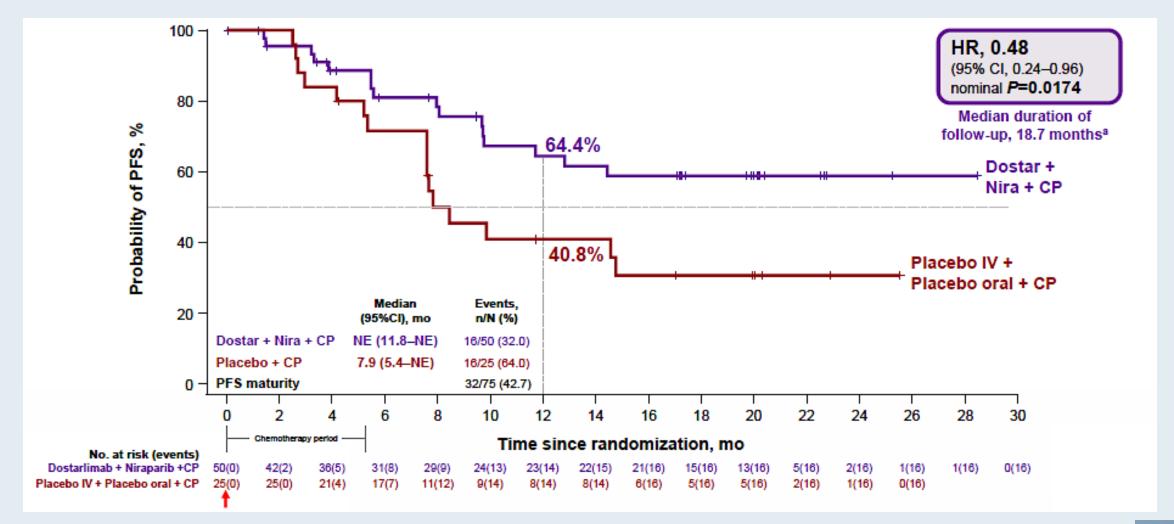


pMMR/MSS population



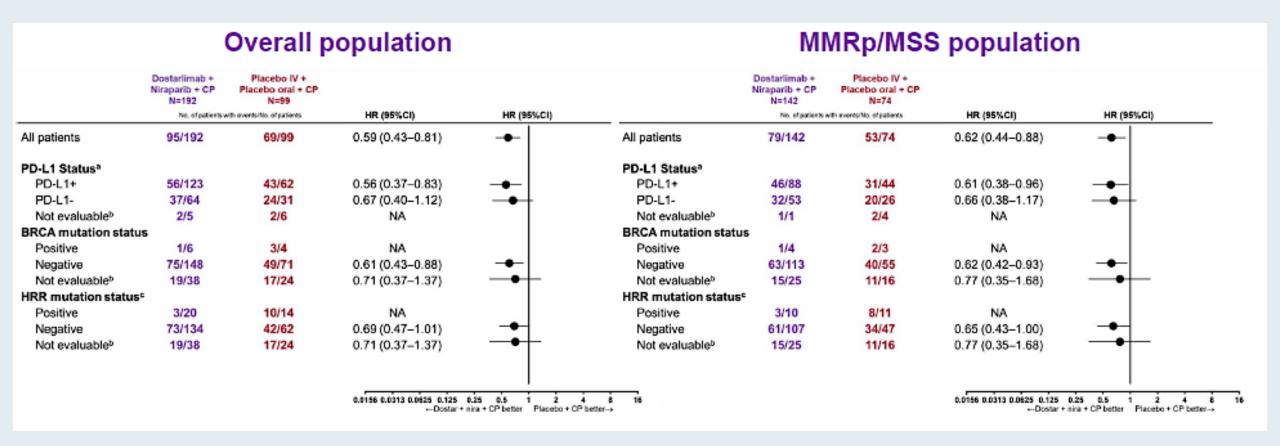


Phase III RUBY Part 2 Exploratory Analysis: PFS in the dMMR/MSI-H Population





Phase III RUBY Part 2 Exploratory Analysis: PFS by PD-L1, BRCA and Homologous Recombination Repair (HRR) Status



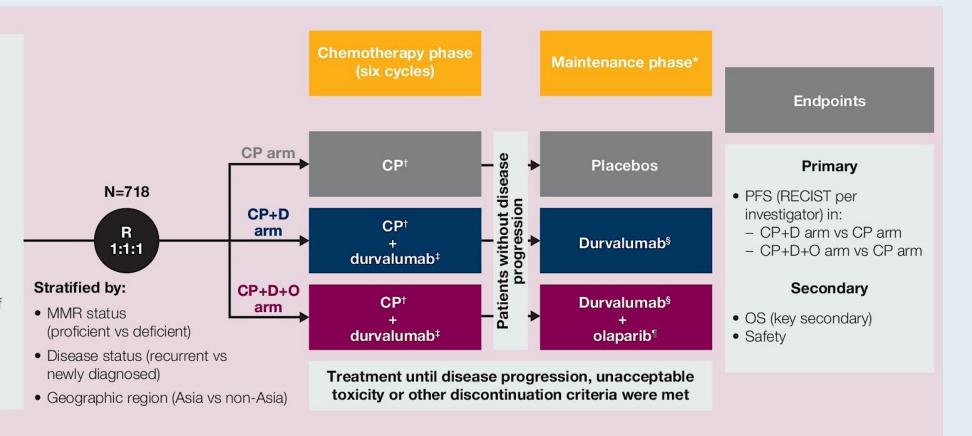


Phase III DUO-E Study Design

Durvalumab (D) with Carboplatin (C) and Paclitaxel (P) Followed by Maintenance D with or without Olaparib (O) for Advanced Endometrial Cancer (EC)

Patients

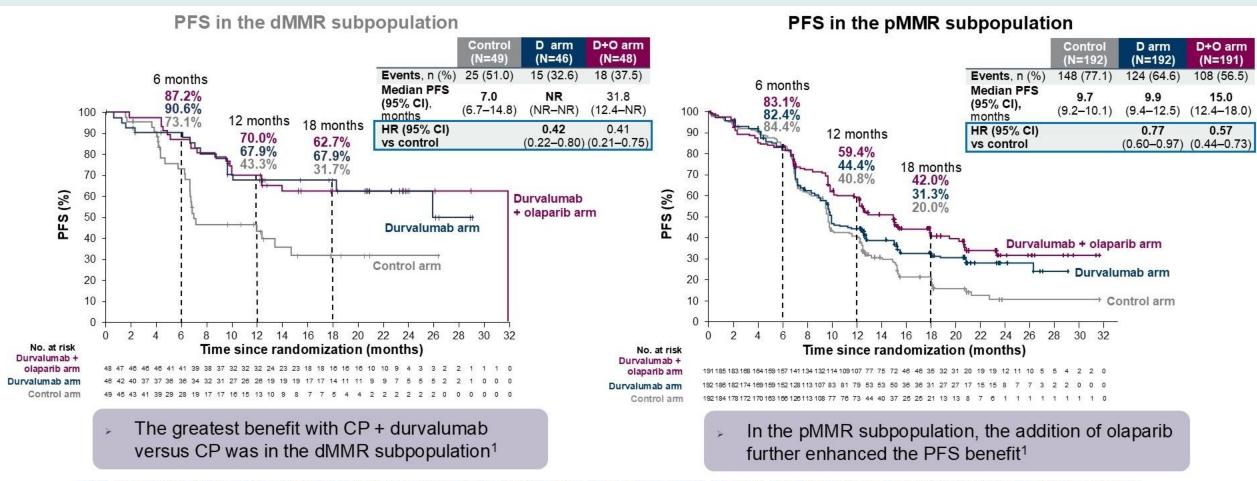
- Newly diagnosed FIGO 2009 stage III/IV or recurrent EC (measurable disease if newly diagnosed stage III disease)
- Known MMR status
- Naïve to first-line systemic anticancer treatment for advanced disease
- Naïve to PARP inhibitors and immune-mediated therapy
- Adjuvant chemotherapy allowed if ≥12 months from last treatment to relapse
- All histologies except sarcomas



*The start of the maintenance phase (defined as having received at least one dose of olaparib/placebo) was 3–9 weeks after the last chemotherapy infusion; †Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg/mL/min q3w and paclitaxel 175 mg/m² q3w; †Durvalumab 1120 mg IV q3w; *Durvalumab 1500 mg IV q4w; *Olaparib 300 mg tablets bid. bid, twice daily; D, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; IV, intravenously; O, olaparib; OS, overall survival; PARP, poly(ADP-ribose) polymerase; q3(4)w, every 3(4) weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.



DUO-E: PFS by MMR Status



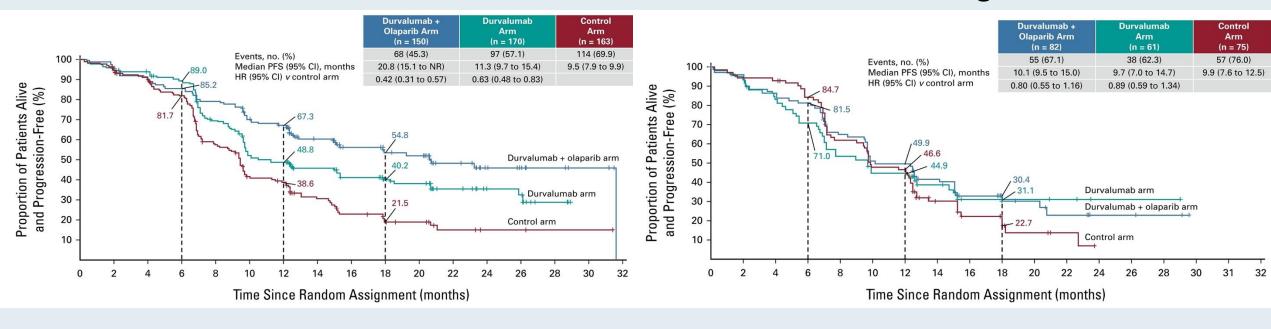
dMMR, mismatch repair deficient; NR, not reported; pMMR, mismatch repair proficient. 1. Westin SN, et al. *J Clin Oncol* 2024;42:283–99. Kaplan–Meier figure borrowed with permission from Westin SN, et al. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: the phase III DUO-E trial. *J Clin Oncol* 2024;42:283–99: https://ascopubs.org/doi/full/10.1200/JCO.23.02132. © American Society of Clinical Oncology.



DUO-E: PFS by PD-L1 Status

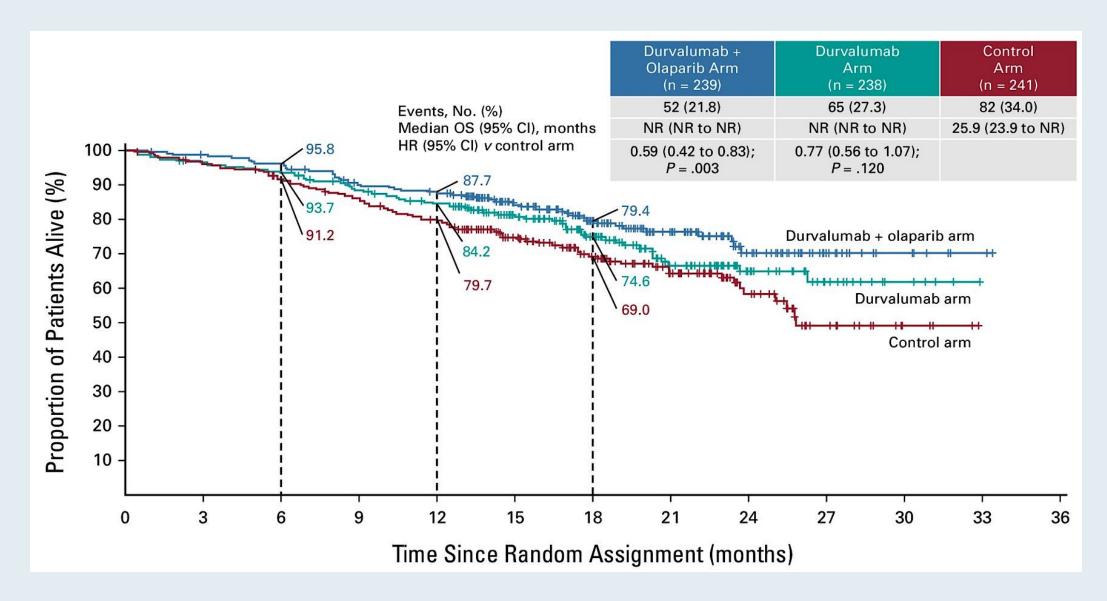
PD-L1-Positive

PD-L1-Negative



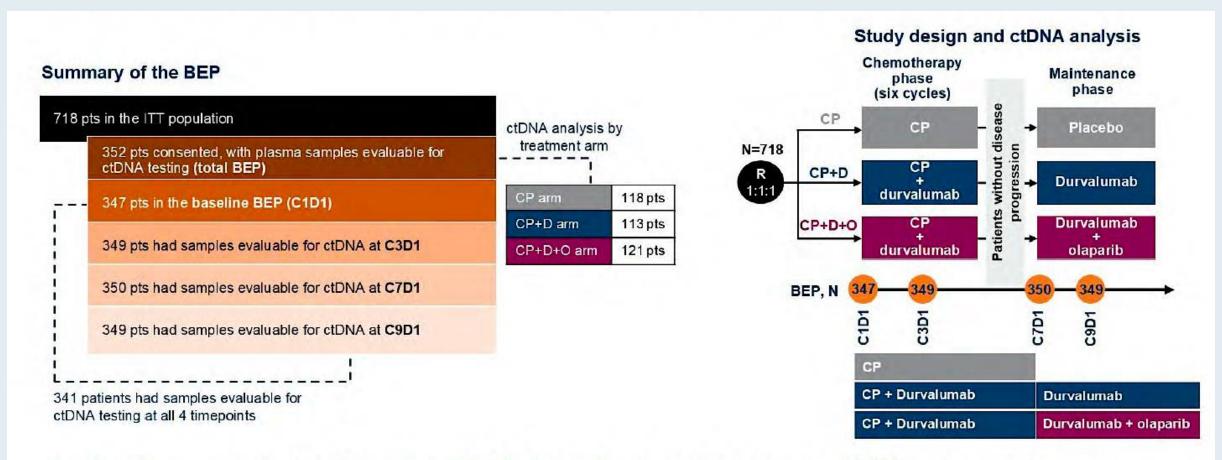


DUO-E: Interim Overall Survival





Circulating Tumor DNA (ctDNA) Analysis in DUO-E



- Samples were collected at baseline (C1D1), during the chemotherapy phase (C3D1), prior to maintenance initiation (C7D1), and during the maintenance phase (C9D1)
- ctDNA was analyzed using the methylation-based Guardant Infinity™ assay (Guardant Health, Palo Alto, CA)

C, cycle, D, day, pts, patients.



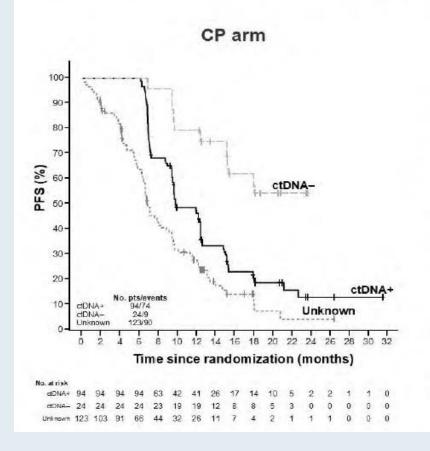
ctDNA Analysis in DUO-E: Baseline Characteristics

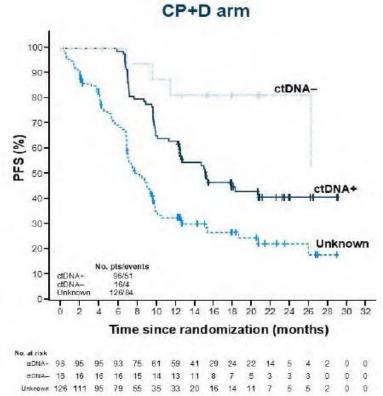
		ITT (N=718)			BEP (N=352)		
		CP (n=241)	CP+D (n=238)	CP+D+O (n=239)	CP (n=118)	CP+D (n=113)	CP+D+O (n=121)
Age, years	Median (range)	64 (31–85)	64 (22–84)	63 (27–86)	64 (36–85)	64 (28–78)	64 (29–84)
MMR status, n (%)	dMMR	49 (20)	46 (19)	48 (20)	14 (12)	23 (20)	28 (23)
	pMMR	192 (80)	192 (81)	191 (80)	104 (88)	90 (80)	93 (77)
ctDNA status, n (%)	ctDNA+	94 (39)	96 (40)	88 (37)	94 (80)	96 (85)	88 (73)
	ctDNA-	24 (10)	16 (7)	29 (12)	24 (20)	16 (14)	29 (24)
	Unknown	123 (51)	126 (53)	122 (51)	0 (0)	1 (1)	4 (3)
Disease type, n (%)	Newly diagnosed	115 (48)	113 (48)	114 (48)	56 (48)	60 (53)	65 (54)
	Recurrent	126 (52)	125 (53)	125 (52)	62 (53)	53 (47)	56 (46)
Region, n (%)	Asia	68 (28)	68 (29)	67 (28)	34 (29)	33 (29)	36 (30)
	Rest of the world	173 (72)	170 (71)	172 (72)	84 (71)	80 (71)	85 (70)
ECOG, n (%)	Normal activity	156 (65)	156 (66)	166 (70)	88 (75)	84 (74)	92 (76)
	Restricted activity	85 (35)	81 (34)	73 (31)	30 (25)	29 (26)	29 (24)

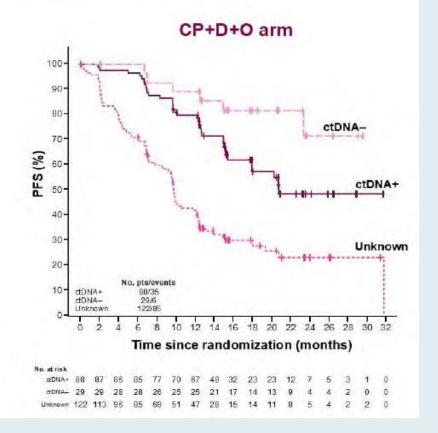


ctDNA Analysis in DUO-E: PFS by ctDNA status in ITT Population

Baseline ctDNA positivity was associated with higher risk of progression across treatment arms



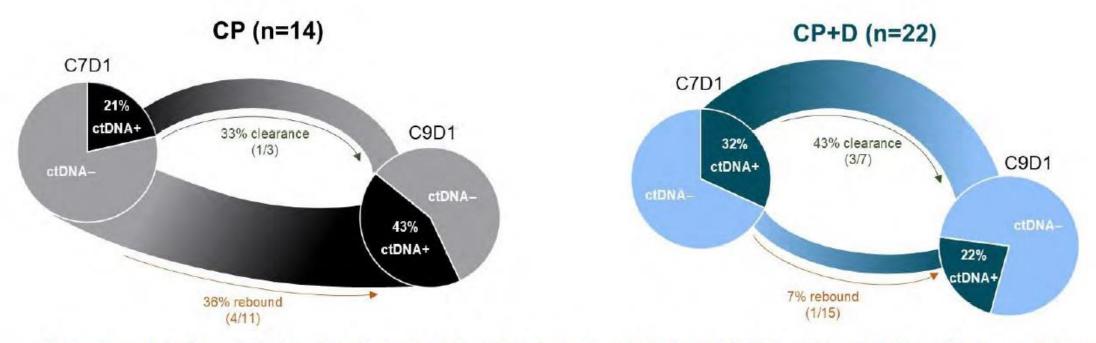






ctDNA Analysis in DUO-E: Durvalumab-Mediated ctDNA Changes During Maintenance Phase (C7D1-C9D1) in Patients with dMMR Disease

Continued durvalumab treatment maintained existing responses established during the chemotherapy phase

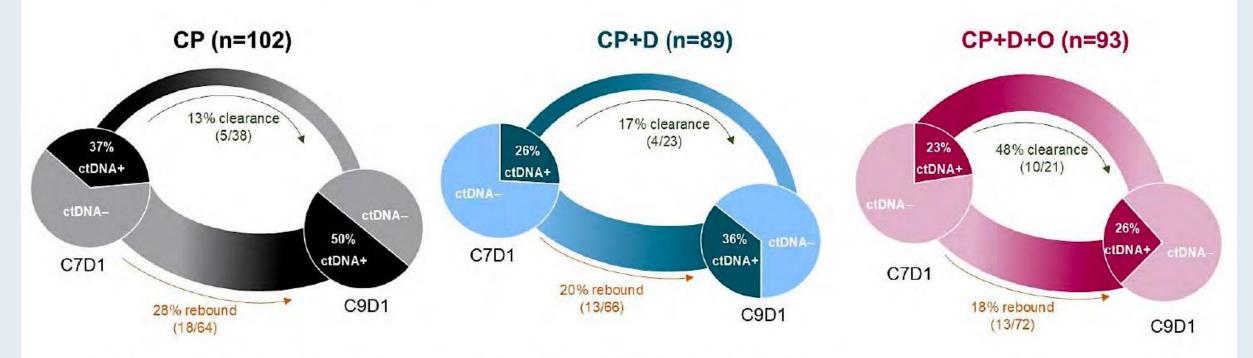


- Durvalumab led to 10% greater clearance of ctDNA between C7D1 and C9D1 within dMMR patients, vs CP arm
- Durvalumab led to 29% less ctDNA rebound between C7D1 and C9D1 within dMMR patients, vs CP arm



ctDNA Analysis in DUO-E: Durvalumab/Olaparib-Mediated ctDNA Changes During Maintenance Phase in Patients with pMMR Disease

Addition of olaparib may be driving novel anti-tumor activity in pMMR tumors not seen with durvalumab alone



- Durvalumab led to 4% more clearance of ctDNA and 8% less rebound, vs CP arm
- Addition of olaparib to durvalumab led to 35% more clearance of ctDNA and 10% less rebound, vs CP arm



ctDNA Analysis in DUO-E: Author's Conclusions

- DUO-E met its dual primary endpoints in the ITT population
 - The greatest benefit with CP + durvalumab vs CP was observed in the dMMR population
 - The addition of olaparib maintenance to durvalumab further enhanced PFS benefit in the pMMR population
- ctDNA+ status at baseline was associated with shorter PFS in all treatment arms, compared with ctDNA- status at baseline
- The addition of durvalumab was associated with rapid reductions in ctDNA detection during chemotherapy phase and less rebound of ctDNA during maintenance phase, compared with CP arm
- The addition of maintenance olaparib was associated with additional ctDNA clearance, resulting in a further reduction of detectable ctDNA in patients with pMMR tumors
 - Addition of olaparib may be driving novel anti-tumor activity in pMMR tumors not seen with durvalumab alone



Phase III KEYNOTE-775 Study Design

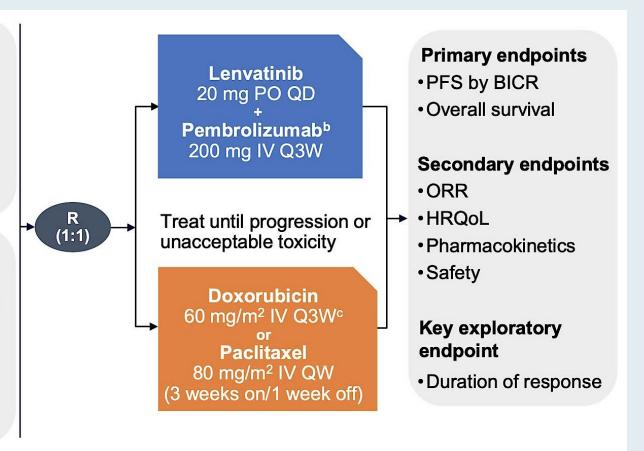
Key eligibility criteria

- Advanced, metastatic, or recurrent endometrial cancer
- Measurable disease by BICR
- 1 Prior platinum-based CT^a
- ECOG PS 0-1
- Tissue available for MMR testing

Stratification factors

MMR status (pMMR vs dMMR) and further stratification within pMMR by:

- Region (R1: Europe, USA, Canada, Australia, New Zealand, and Israel, vs R2: rest of the world)
- ECOG PS (0 vs 1)
- Prior history of pelvic radiation (Y vs N)

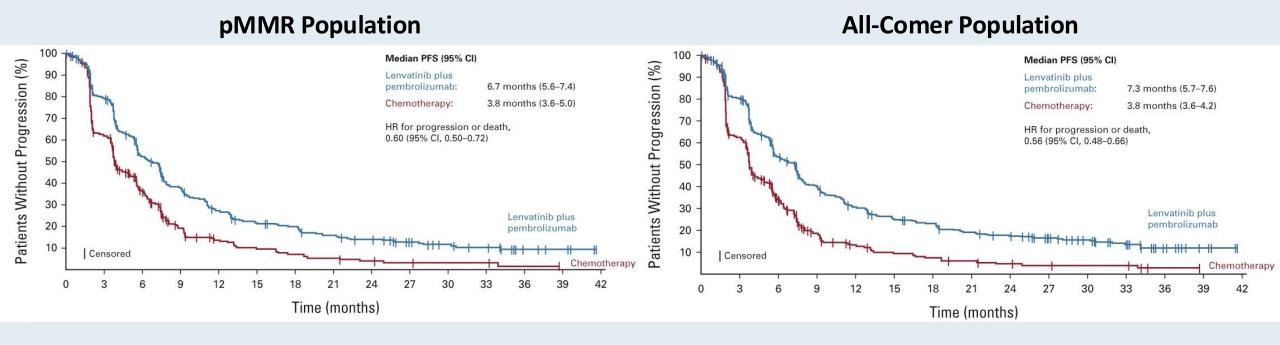


^aPatients may have received up to 2 prior platinum-based CT regimens if 1 is given in the neoadjuvant or adjuvant treatment setting. ^bMaximum of 35 doses. ^cMaximum cumulative dose of 500 mg/m².

BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IV, intravenous; PFS, progression-free survival; pMMR, mismatch repair-proficient; ORR, objective response rate; PO, per os (by mouth); QD, once daily; Q3W, every 3 weeks; QW, once weekly.

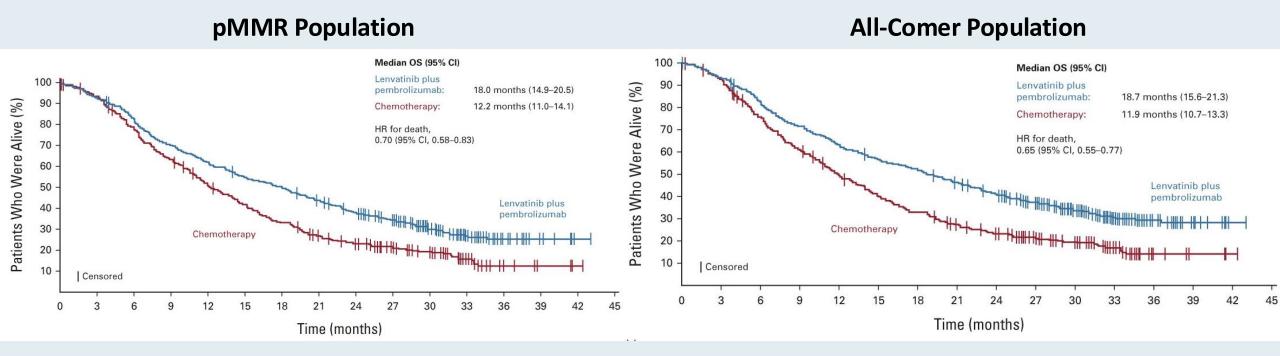


Phase III KEYNOTE-775: Progression-Free Survival





Phase III KEYNOTE-775: Overall Survival





Phase III KEYNOTE-775: Safety

	LEN Plus Pem	bro (n = 406)	Chemotherapy (n = 388)	
Preferred Term ^a	Any Grade	Grade ≥ 3 ^b	Any Grade	Grade $\geq 3^{\text{b}}$
TEAEs, No. (%)	405 (99.8)	366 (90.1)	386 (99.5)	286 (73.7)
Hypertension	264 (65.0)	159 (39.2)	20 (5.2)	10 (2.6)
Hypothyroidism	239 (58.9)	6 (1.5)	3 (0.8)	0 (0.0)
Diarrhea	226 (55.7)	33 (8.1)	79 (20.4)	8 (2.1)
Nausea	210 (51.7)	14 (3.4)	180 (46.4)	5 (1.3)
Decreased appetite	189 (46.6)	31 (7.6)	83 (21.4)	2 (0.5)
Vomiting	153 (37.7)	12 (3.0)	82 (21.1)	10 (2.6)
Weight decreased	144 (35.5)	44 (10.8)	23 (5.9)	1 (0.3)
Fatigue	138 (34.0)	22 (5.4)	107 (27.6)	12 (3.1)
Arthralgia	131 (32.3)	7 (1.7)	31 (8.0)	0 (0.0)
Proteinuria	124 (30.5)	21 (5.2)	13 (3.4)	1 (0.3)
Constipation	115 (28.3)	3 (0.7)	95 (24.5)	2 (0.5)
Anemia	114 (28.1)	28 (6.9)	189 (48.7)	60 (15.5)
Urinary tract infection	112 (27.6)	17 (4.2)	40 (10.3)	4 (1.0)
Headache	107 (26.4)	2 (0.5)	35 (9.0)	1 (0.3)
Neutropenia	37 (9.1)	8 (2.0)	132 (34.0)	101 (26.0)
Alopecia	24 (5.9)	0 (0.0)	120 (30.9)	1 (0.3)
Treatment-related TEAEs, No, (%) ^c	395 (97.3)	320 (78.8)	364 (93.8)	233 (60.1)
AEOSIs, No. (%)d	279 (68.7)	54 (13.3)	17 (4.4)	1 (0.3)
CSAEs, No. (%) ^d	386 (95.1)	227 (55.9)	149 (38.4)	51 (13.1)



TEAEs = treatment-emergent adverse events; AEOSIs = adverse events of special interest; CSAEs = clinically significant adverse events

Lenvatinib plus Pembrolizumab (L + P) vs Treatment of Physician's Choice (TPC) for Advanced Endometrial Cancer (EC): 5-Year Outcomes from Study 309/KEYNOTE-775

Makker V et al.

ESMO 2025; Abstract 1119P.

POSTER SESSION 1 | SATURDAY, OCTOBER 18



First-Line Lenvatinib + Pembrolizumab (L + P) vs Chemotherapy (CT) for Advanced or Recurrent Endometrial Cancer (EC): Additional 1-Year Follow-Up Results from ENGOT-en9/LEAP-001

Marth C et al.

ESMO 2025; Abstract 1114P.

POSTER SESSION 1 | SATURDAY, OCTOBER 18



Management of Metastatic Endometrial Cancer

Introduction: A pan-tumor perspective on MSI-high disease — Immunotherapy for localized disease

Case 1: Dr Peles – 60-year-old woman

Case 2: Dr Divers – 64-year-old woman

■ Data Review: Immune Checkpoint Inhibitors

Case 3: Dr Schneider – 32-year-old woman

Case 4: Dr Zafar – 82-year-old woman

Case 5: Dr Willmott – 67-year-old woman

■ Data Review: HER2-Targeted Treatment

Case 6: Dr Giffi – 73-year-old woman

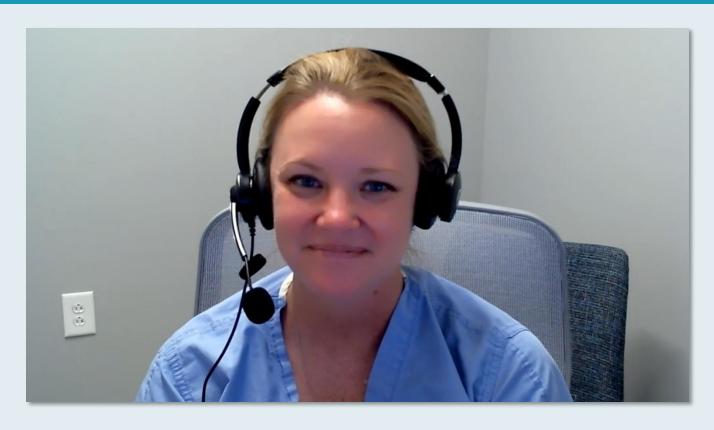
Case 7: Dr ElSahwi – 68-year-old woman

Data Review: Autoimmune Toxicity with Immunotherapy

Data Review: Novel Antibody-Drug Conjugates



Case Presentation: 32-year-old woman with metastatic recurrence of pMMR endometrial carcinoma has partial response to carboplatin/paclitaxel/pembrolizumab



Dr Kellie Schneider (Charlotte, North Carolina)



Management of Metastatic Endometrial Cancer

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Case 7: Dr ElSahwi – 68-year-old woman

■ Data Review: Autoimmune Toxicity with Immunotherapy

■ Data Review: Novel Antibody-Drug Conjugates



Case Presentation: 82-year-old woman with recurrent MSS endometrial carcinoma s/p chemotherapy receives pembrolizumab/lenvatinib



Dr Syed Zafar (Fort Myers, Florida)



Management of Metastatic Endometrial Cancer

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Case 7: Dr ElSahwi – 68-year-old woman

■ Data Review: Autoimmune Toxicity with Immunotherapy

Data Review: Novel Antibody-Drug Conjugates



Case Presentation: 67-year-old woman with HER2-positive metastatic uterine serous carcinoma with progression after carboplatin/paclitaxel/trastuzumab → trastuzumab maintenance receives trastuzumab deruxtecan



Dr Lyndsay Willmott (Phoenix, Arizona)



Management of Metastatic Endometrial Cancer

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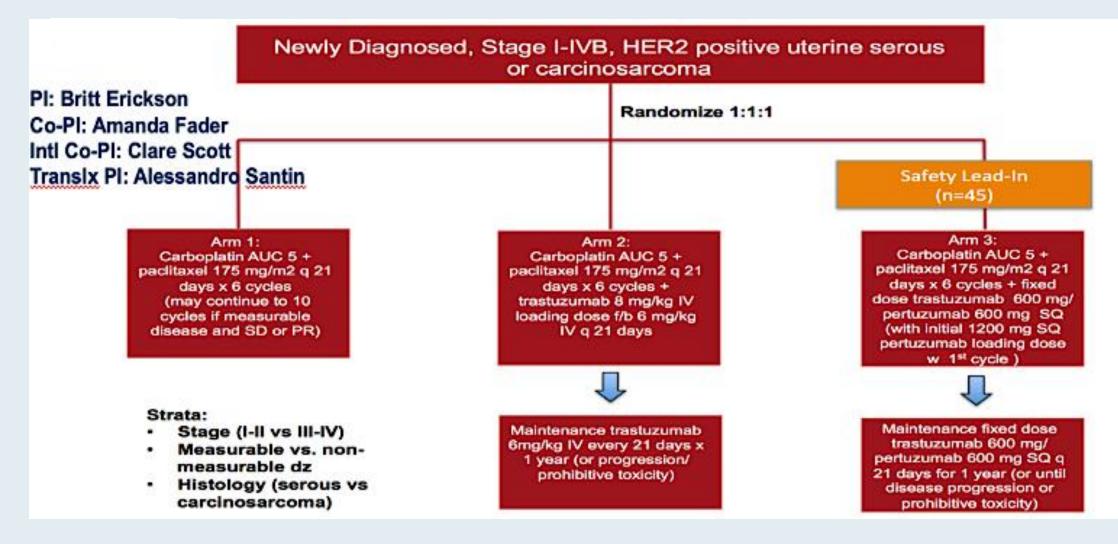
Case 7: Dr ElSahwi – 68-year-old woman

■ Data Review: Autoimmune Toxicity with Immunotherapy

■ Data Review: Novel Antibody-Drug Conjugates



NRG-GY026: An Ongoing Phase II/III Trial of Paclitaxel/Carboplatin Alone or with Either Trastuzumab or Trastuzumab/Pertuzumab for HER2-Positive Endometrial Cancer





Original Reports | Gynecologic Cancer

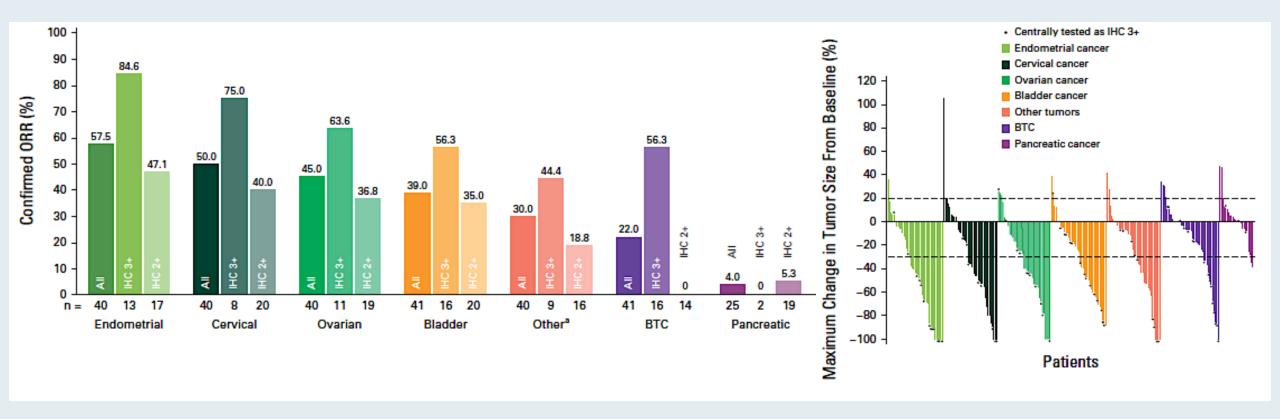
©Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

Funda Meric-Bernstam, MD¹ (D); Vicky Makker, MD^{2,3} (D); Ana Oaknin, MD⁴ (D); Do-Youn Oh, MD⁵ (D); Susana Banerjee, PhD⁶ (D); Antonio González-Martín, MD⁷ (D); Kyung Hae Jung, MD⁸ (D); Iwona Ługowska, MD⁹; Luis Manso, MD¹⁰ (D); Aránzazu Manzano, MD¹¹; Bohuslav Melichar, MD¹²; Salvatore Siena, MD¹³ (D); Daniil Stroyakovskiy, MD¹⁴ (D); Anitra Fielding, MBChB¹⁵; Yan Ma, MSc¹⁶; Soham Puvvada, MD¹⁵; Norah Shire, PhD¹⁵; and Jung-Yun Lee, MD¹⁷ (D)

J Clin Oncol 2024;42(1):47-58.



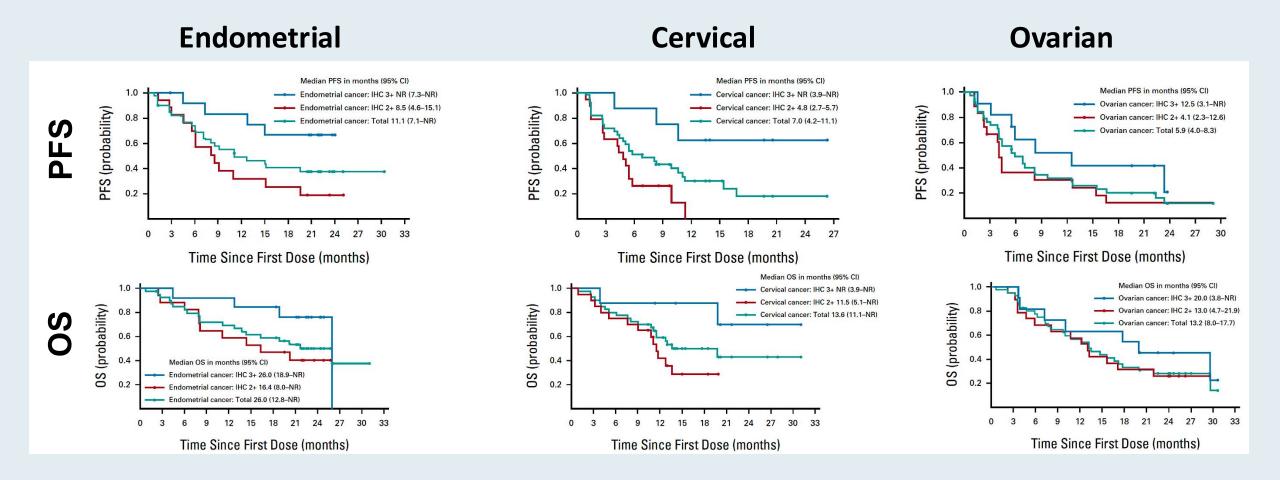
DESTINY-PanTumor02: A Phase II Trial of Trastuzumab Deruxtecan for Patients with HER2-Expressing Solid Tumors



ORR = objective response rate

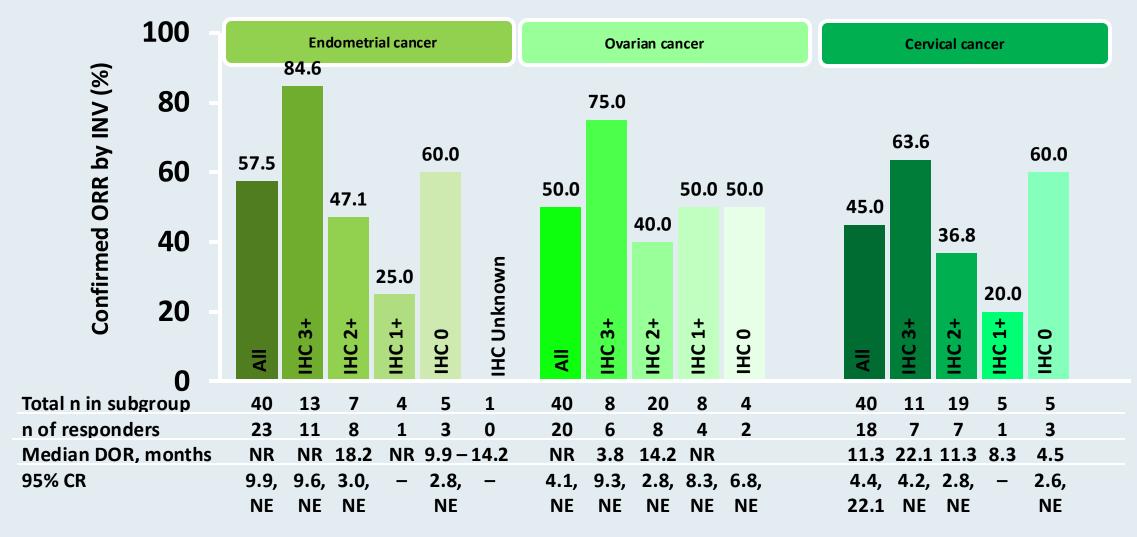


DESTINY-PanTumor02: Survival





DESTINY-PanTumor02: Response by HER2 Expression Level (Central)





INV = investigator; NR = not reached; NE = not estimable
Lee J-Y et al. International Gynecologic Cancer Society (IGCS) 2023; Makker V et al. SGO 2024.

DESTINY-PanTumor02: Adverse Events

Adverse Event	Endometrial Cancer (n = 40)	Cervical Cancer (n = 40)	Ovarian Cancer (n = 40)
Drug-related adverse events, No. (%)	36 (90.0)	36 (90.0)	34 (85.0)
Grade ≥3	14 (35.0)	19 (47.5)	21 (52.5)
Serious adverse events	4 (10.0)	3 (7.5)	11 (27.5)
Leading to discontinuation	3 (7.5)	3 (7.5)	1 (2.5)
Leading to dose modification ^a	13 (32.5)	13 (32.5)	18 (45.0)
Associated with death	2 (5.0)	0	0
Most common drug-related adverse events (>10% of total patients), No. (%)			
Nausea	29 (72.5)	26 (65.0)	22 (55.0)
Anemia	7 (17.5)	15 (37.5)	15 (37.5)
Diarrhea	16 (40.0)	15 (37.5)	8 (20.0)
Fatigue	10 (25.0)	9 (22.5)	11 (27.5)
Vomiting	16 (40.0)	10 (25.0)	7 (17.5)
Neutropenia	4 (10.0)	8 (20.0)	5 (12.5)
Decreased appetite	8 (20.0)	7 (17.5)	8 (20.0)
Asthenia	11 (27.5)	9 (22.5)	6 (15.0)
Alopecia	9 (22.5)	8 (20.0)	5 (12.5)
Thrombocytopenia	2 (5.0)	2 (5.0)	5 (12.5)

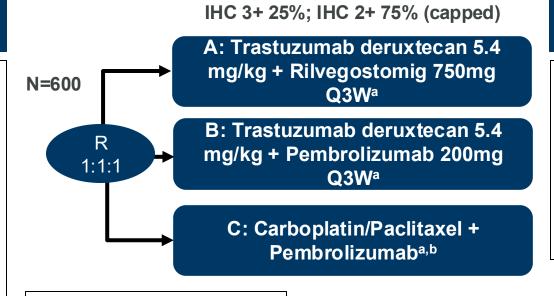
Adjudicated drug-related events of interstitial lung disease (ILD)/pneumonitis: 28 patients overall (10.5%) Majority were low grade (grade 1, n = 7 [2.6%]; grade 2, n = 17 [6.4%]), but there were 3 fatal adjudicated drug-related cases of ILD/pneumonitis, one each in the biliary tract, endometrial and other tumors cohorts



DESTINY-Endometrial01/ GOG-3098/ ENGOT-EN24: A Phase III Study of Trastuzumab Deruxtecan Plus Rilvegostomig or Pembrolizumab as First-Line Treatment of HER2-Expressing (IHC 3+/2+), Mismatch Repair Proficient (pMMR) Endometrial Cancer

Patient Population

- HER2 expressing (IHC 3+/2+) EC by central test
- pMMR EC by central test
- Stage III, Stage IV, or recurrent, histologically-confirmed endometrial cancer
- Stage III must have measurable disease
- Any histological subtype except for sarcomas
- May have received 1 prior line of adjuvant/ neoadjuvant chemotherapy (chemotherapy and/or chemoradiation) if recurrence ≥ 6 months after last dose of chemo
- No prior exposure to ADCs or ICIs
- ECOG PS 0 or 1



Endpoints

Primary:

PFS (BICR) in ITT

Secondary:

- OS (key secondary endpoint)
- PFS (Investigator)
- ORR
- PFS2
- HRQoL

Stratification factors:

- HER2 IHC 3+ vs 2+
- PD-L1 TAP ≥1% vs TAP <1%
- Asia vs Non-Asia

^{*} At the discretion of the treating Investigator, participants may continue to receive carboplatin, paclitaxel and pembrolizumab Q3W for up to 10 cycles.







^a Treatment will continue until objective disease progression according to RECIST v1.1 as assessed by the Investigator and confirmed by BICR or until other discontinuation criterion is met, whichever occurs first.

^b Carboplatin AUC5, paclitaxel 175 mg/m2, and pembrolizumab 200 mg IV once Q3W x 6 cycles*, followed by maintenance with pembrolizumab 400 mg IV Q6W. Treatment with pembrolizumab will continue for up to 20 total cycles (approximately 24 months, accounting for combination and maintenance phases) or until other discontinuation criteria is met, whichever occurs first.

A Randomized Phase 3 Study of First-Line (1L)
Trastuzumab Deruxtecan (T-DXd) with Rilvegostomig or
Pembrolizumab in Patients with HER2-Expressing,
Mismatch Repair-Proficient (pMMR), Primary Advanced
or Recurrent Endometrial Cancer (EC): DESTINYEndometrial01/GOG-3098/ENGOT-EN24

Slomovitz BM et al.

ESMO 2025; Abstract 1223TiP.

POSTER SESSION 1 | SATURDAY, OCTOBER 18



Management of Metastatic Endometrial Cancer

Introduction: A pan-tumor perspective on MSI-high disease — Immunotherapy for localized disease

Case 1: Dr Peles – 60-year-old woman

Case 2: Dr Divers – 64-year-old woman

■ Data Review: Immune Checkpoint Inhibitors

Case 3: Dr Schneider – 32-year-old woman

Case 4: Dr Zafar – 82-year-old woman

Case 5: Dr Willmott – 67-year-old woman

■ Data Review: HER2-Targeted Treatment

Case 6: Dr Giffi – 73-year-old woman

Case 7: Dr ElSahwi – 68-year-old woman

■ Data Review: Autoimmune Toxicity with Immunotherapy

■ Data Review: Novel Antibody-Drug Conjugates



Case Presentation: 73-year-old woman with MSS metastatic endometrial carcinoma has disease progression after multiple regimens, including IO/chemotherapy with carboplatin/gemcitabine/pembrolizumab; biopsy: weak to moderate ER staining, FGFR and PIK3CA mutations



Dr Victoria Giffi (Hagerstown, Maryland)



Management of Metastatic Endometrial Cancer

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■ Data Review: Autoimmune Toxicity with Immunotherapy

■ Data Review: Novel Antibody-Drug Conjugates



Case Presentation: 68-year-old woman with dMMR metastatic endometrial carcinoma receives carboplatin/paclitaxel/pembrolizumab and develops pericarditis



Dr Karim ElSahwi (Neptune City, New Jersey)



Management of Metastatic Endometrial Cancer

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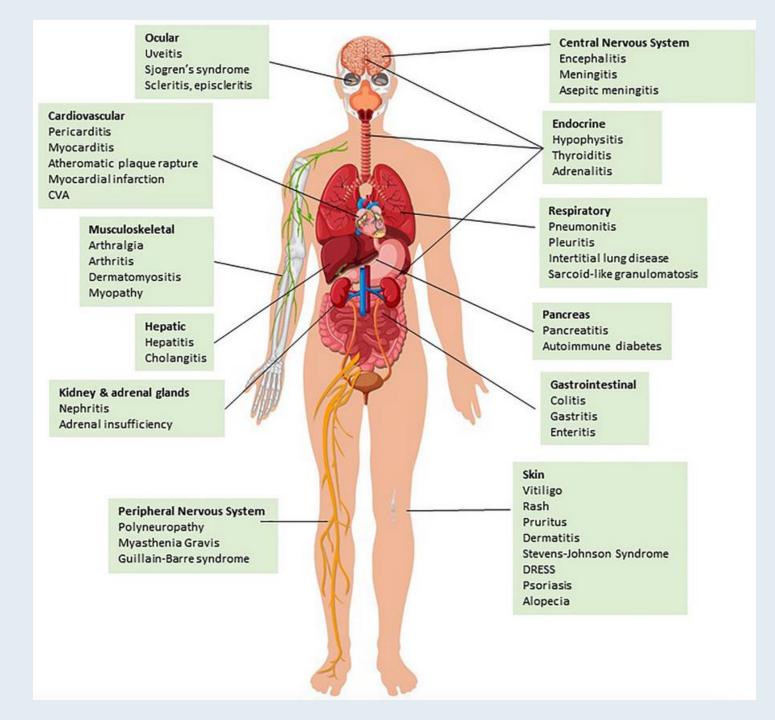
Case 6: Dr Giffi – 73-year-old woman

Case 7: Dr ElSahwi – 68-year-old woman

Data Review: Autoimmune Toxicity with Immunotherapy

■ Data Review: Novel Antibody-Drug Conjugates





Immune-Related AEs Associated with Checkpoint Inhibitors



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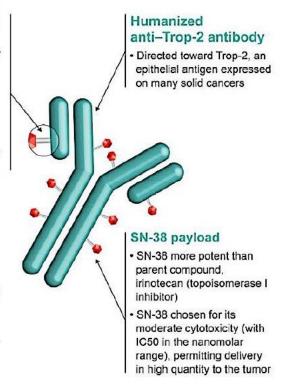
Targeting TROP2

Sacituzumab govitecan

Linker for SN-38

- · pH-sensitive. hydrolyzable linker for SN-38 release in targeted tumor cells and tumor microenvironment. allowing bystander effect
- High drug-to-antibody ratio (7.6:1)

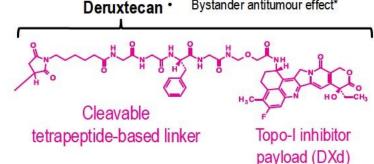
Internalization and enzymatic cleavage by tumor cell not required for SN-38 liberation from antibody



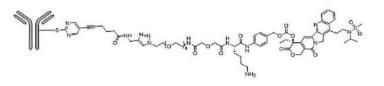
Datopotamab deruxtecan



- Payload mechanism of action: Topo-I inhibitor*
- High potency payload*
- Optimised drug to antibody ratio ≈4*†
- Payload with short systemic half-life*†
- Stable linker-payload*
- Tumour-selective cleavable linker*
 - Bystander antitumour effect*



Sacituzumab tirumotecan (SKB264/MK-2870)



- anti-TROP2 ADC
- Sulfonyl pyrimidine-CL2Acarbonate linker
- Payload: belotecan-derivative topoisomerase I inhibitor
- DAR: 7.4

KL264-01 Phase II Study Design: Endometrial and Ovarian Cohorts

Sacituzumab Tirumotecan (sac-TMT) for Locally Advanced, Refractory Metastatic Solid Tumors

Cohort 8: Advanced EC (N=44)

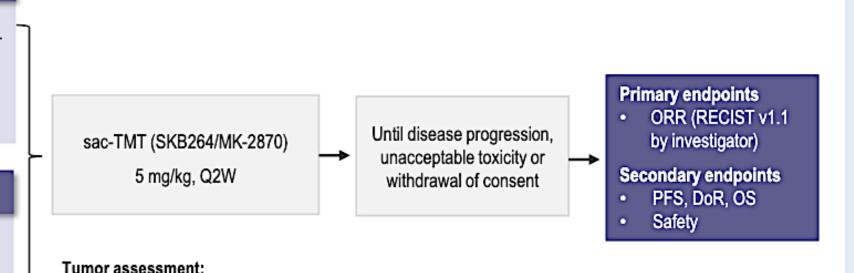
Key inclusion criteria

- Received at least 1 prior line of platinumbased therapy
- Prior anti-PD-1/L1 therapy required for MSI-H/dMMR patients
- ECOG PS 0 or 1

Cohort 2: Advanced OC (N=40)

Key inclusion criteria

- Received at least 1 prior line of platinumbased therapy
- Pts with platinum-sensitive disease must have received at least 2 prior lines of platinum-based therapy
- ECOG PS 0 or 1



ADC, antibody-drug conjugate; dMMR, deficient mismatch repair; DoR, duration of response; EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; MSI-H, microsatellite instability high; OC, ovarian cancer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; pts, patients; Q2W, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Once every 8 weeks for the first 12 months, and every 12 weeks thereafter.

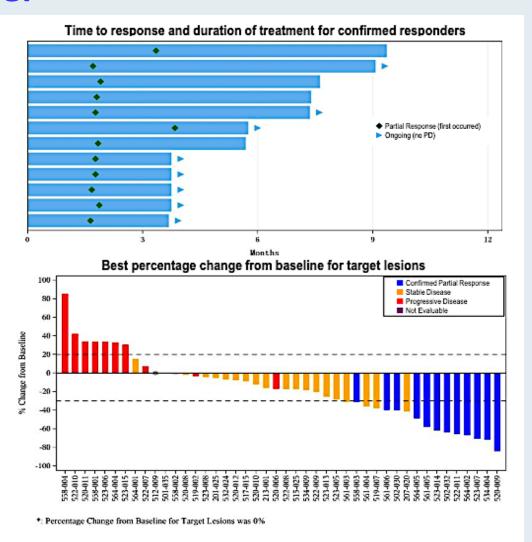


KL264-01 Phase II: Preliminary Efficacy with Sacituzumab Tirumotecan for Endometrial Cancer

	EC (N = 44)a
ORR, % (n/N)	34.1 (15/44) ^b
Confirmed ORR	27.3 (12/44)
Subgroups	
TROP2 H-score >200	41.7 (5/12)
Prior IO	37.5 (6/16)
DCR, % (n/N)	75.0 (33/44)
PR	34.1 (15/44)
SD	40.9 (18/44)
DoR	
Median (range), months	5.7 (3.8, 7.4+)
PFS	
Median (95% CI), months	5.7 (3.7, 9.4)

Responses assessed per RECIST v1.1 by investigator.

CI, confidential interval; DCR, disease control rate; DoR, duration of response; EC, endometrial cancer; IO, immunotherapy; ORR, objective response rate; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TROP2, trophoblast cell surface antigen 2.







b. Two patients with unconfirmed response were still receiving treatment at the data cutoff date.

KL264-01 Phase II: Preliminary Safety with Sacituzumab Tirumotecan for Endometrial Cancer

% (n)	EC (N = 44) ^a		OC (N = 40) ^a	
TRAEs	100% (44)		100% (40)	
Grade ≥3 TRAEs	72.7% (32)		67.5% (27)	
Serious TRAEs	20.5% (9)		37.5% (15)	
TRAEs leading to discontinuation ^b	2.3% (1)		12.5% (5)	
TRAE preferred term	All grades	Grade ≥3°	All grades	Grade ≥3°
Anemia	88.6% (39)	29.5% (13)	85.0% (34)	35.0% (14)
WBC decreased	81.8% (36)	40.9% (18)	60.0% (24)	22.5% (9)
Neutrophil count decreased	65.9% (29)	43.2% (19)	57.5% (23)	30.0% (12)
Stomatitis	38.6% (17)	13.6% (6)	57.5% (23)	15.0% (6)
Vomiting	36.4% (16)	0	40.0% (16)	0
Alopecia	34.1% (15)	0	45.0% (18)	0
Nausea	27.3% (12)	0	42.5% (17)	2.5% (1)
Platelet count decreased	25.0% (11)	6.8% (3)	42.5% (17)	7.5% (3)
Rash	15.9% (7)	2.3% (1)	32.5% (13)	2.5% (1)

The most common hematologic toxicities were anemia, WBC decreased and neutrophil count decreased.

- The most common gastrointestinal toxicities were stomatitis, vomiting and nausea. Incidence rates diarrhea among TRAEs were 2.3% and 10.0% in EC and OC cohorts.
- No TRAEs led to death.
- No drug-related ILD/pneumonitis.

EC, endometrial cancer; ILD, interstitial lung disease; OC, ovarian cancer; TRAE, treatment-related adverse event; WBC, white blood cell.



a. Both cohorts received sac-TMT treatment at a dosage of 5 mg/kg (Q2W).

TRAEs leading to discontinuation: EC cohort - neutrophil count decreased. OC cohort (n=1 each): myocardial infarction, mucosal inflammation, hypokalemia, hypersensitivity and hematologic toxicity.

c. Additional grade ≥3 TRAES with incidence ≥5%: EC cohort - none. OC cohort- neutropenia (10.0%), malaise (5.0%), mucosal inflammation (5.0%), amylase increased (5.0%), lymphocyte count decreased (5.0%) and hypokalemia (5.0%).

Sacituzumab Tirumotecan (Sac-TMT) Monotherapy in Advanced/Metastatic Endometrial Carcinoma (EC): Results from a Phase 1/2 Study (MK-2870-001/KL264-01)

Wang K et al.

ESMO 2025; Abstract 1111P.

POSTER SESSION 1 | SATURDAY, OCTOBER 18

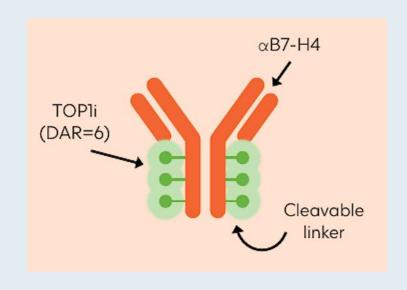


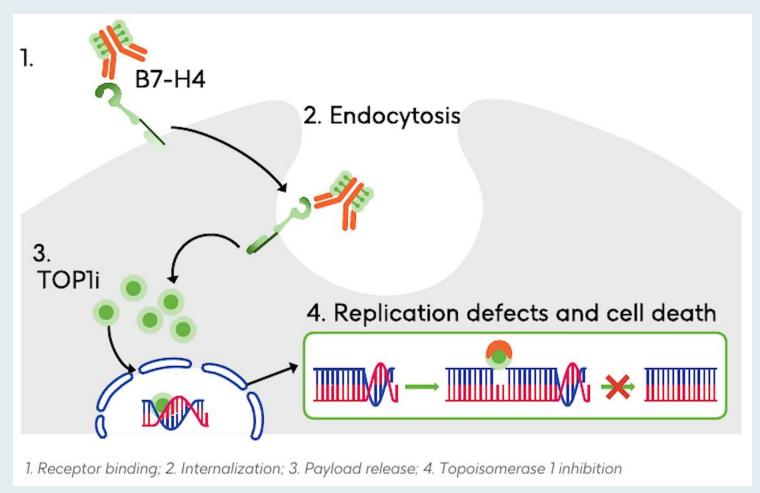
Ongoing Phase III Trials of Sacituzumab Tirumotecan for Endometrial Cancer

Trial identifier	Study population	Treatment arms	Estimated primary completion date
TroFuse-005 (NCT06132958)	After platinum and immunotherapy	Sacituzumab tirumotecanChemotherapy	January 2028
TroFuse-033 (NCT06952504)	MMR proficient, first line	Pembrolizumab + chemotherapy followed by maintenance: • Sacituzumab tirumotecan + pembrolizumab • Pembrolizumab	May 2032



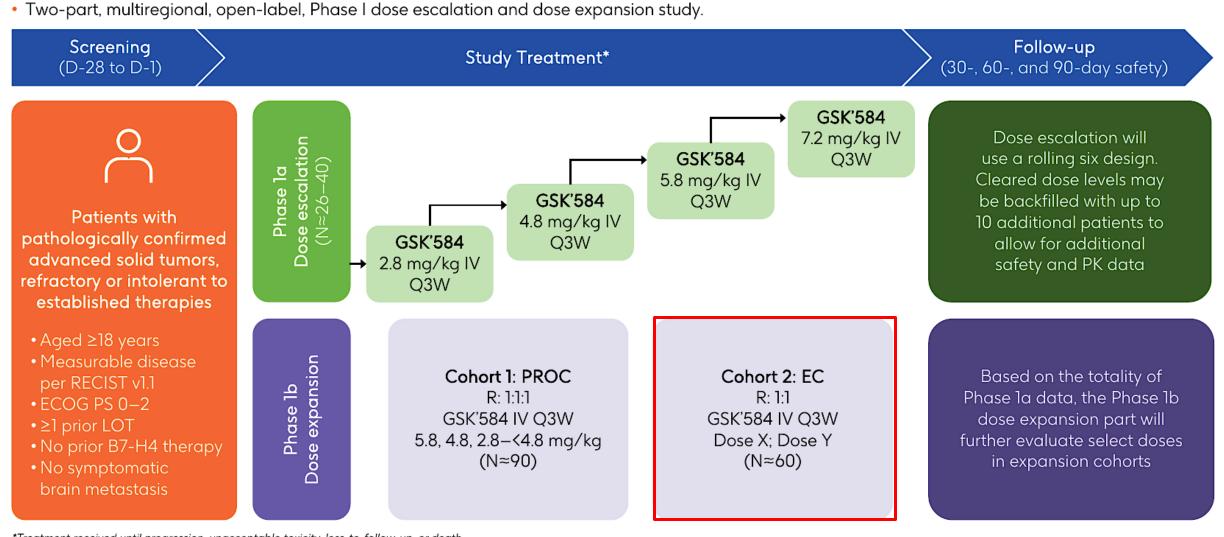
GSK5733584: A B7-H4-Targeted Antibody-Drug Conjugate







GSK5733584: Phase I Study Design



^{*}Treatment received until progression, unacceptable toxicity, loss-to-follow-up, or death.



Contributing General Medical Oncologists



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& Research Institute
Lake Worth, Florida



Practical Perspectives: Experts Review Actual Cases of Patients with HER2-Positive Gastrointestinal Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, October 21, 2025 5:00 PM - 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD Kristen K Ciombor, MD, MSCI

Moderator Neil Love, MD



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