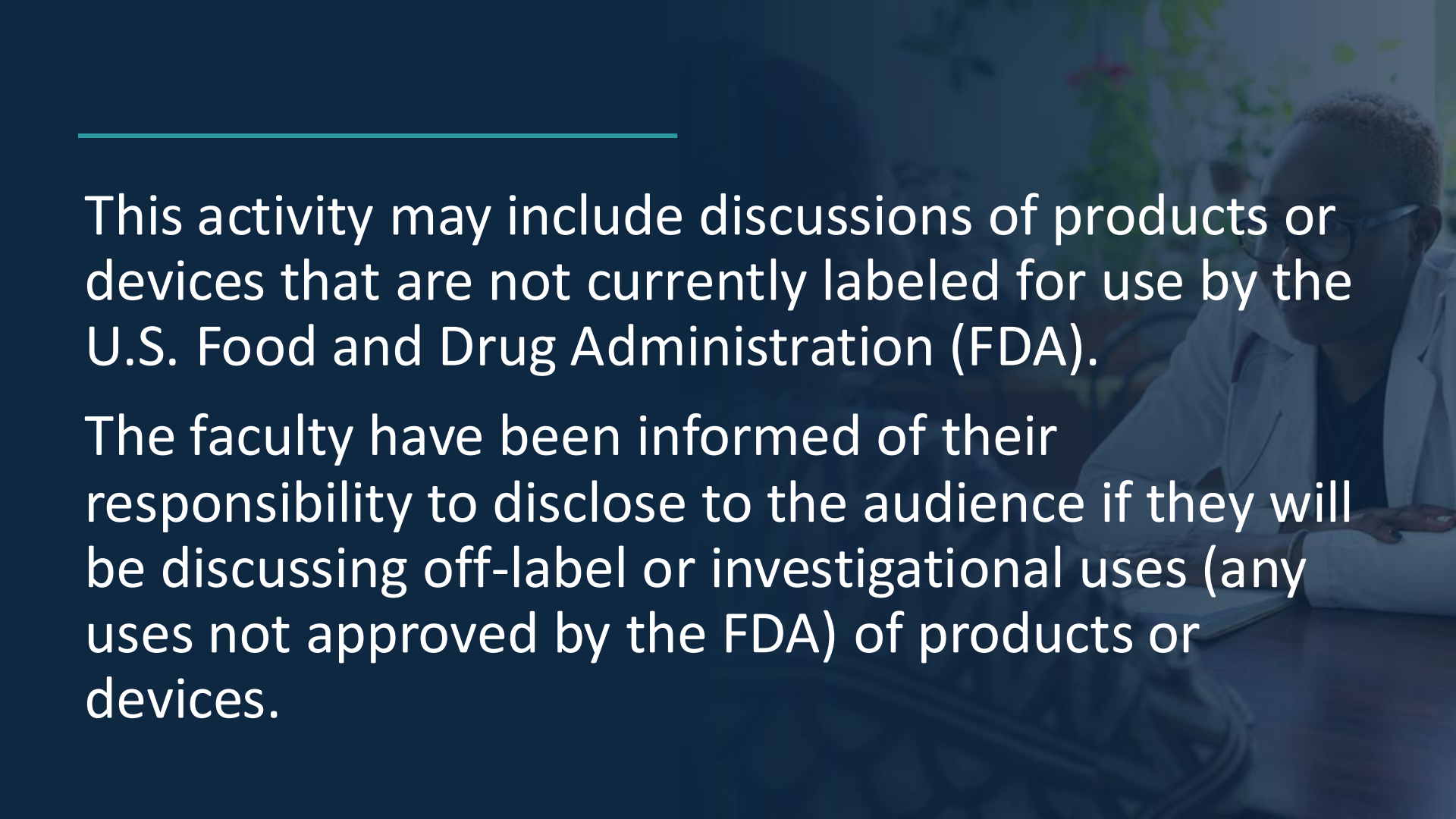
cec ONCOLOGY

EXPLORING THE HORIZONS IN ADVANCED OR RECURRENT ENDOMETRIAL CANCER

Practical Considerations and Future Directions for New Treatment Strategies

This activity is supported by an educational grant from Merck & Co., Inc., Rahway, NJ, USA



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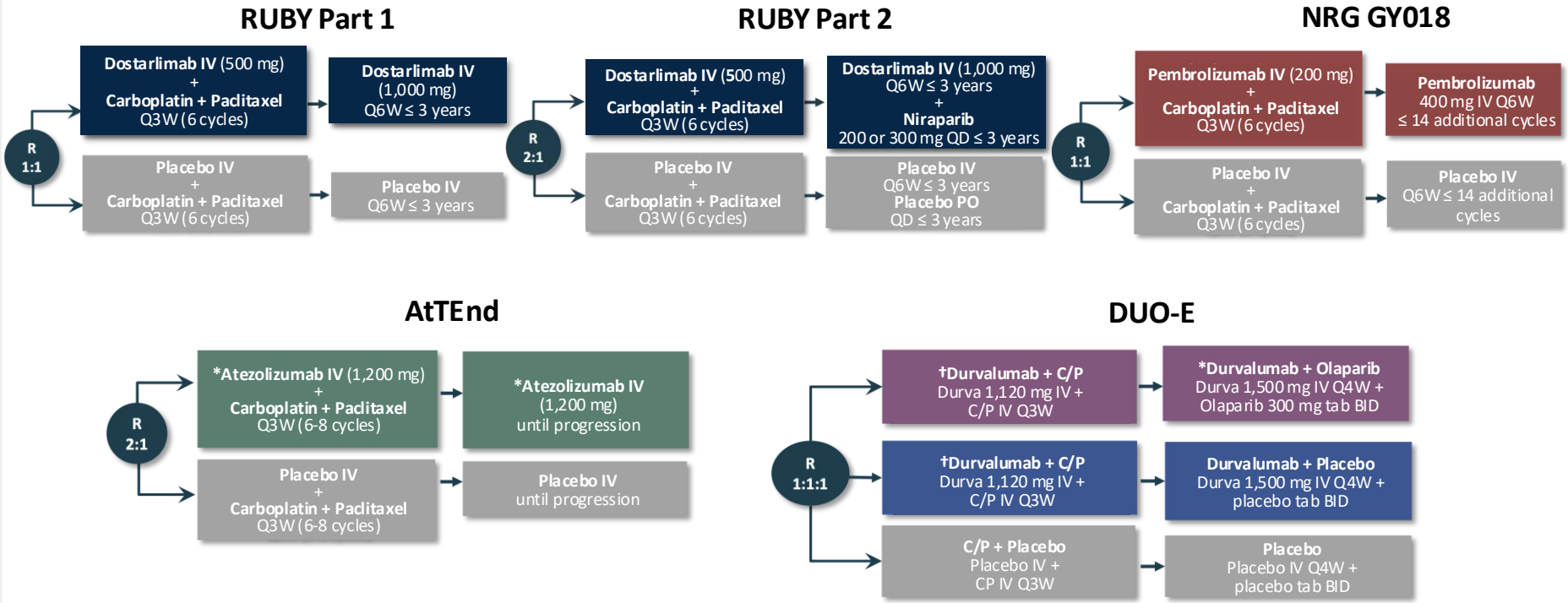
LEARNING OBJECTIVES

1. Interpret clinical evidence on new and emerging therapies to define their role in current and evolving treatment paradigms for advanced or recurrent endometrial cancer
2. Manage treatment-related adverse effects using evidence-based strategies to maintain treatment continuity and ensure patient safety
3. Implement multidisciplinary and patient-centered strategies to overcome access barriers, address disparities, and incorporate patient education and patient-reported outcomes into the care of patients with advanced or recurrent endometrial cancer

Evolving Treatment Landscape in Advanced or Recurrent Endometrial Cancer

Chemoimmunotherapy for Advanced or Recurrent EC



*Not FDA approved for the management of endometrial cancer;
†FDA approved only for the management of advanced mismatch repair deficient endometrial cancer.

BID = twice a day; C/P = carboplatin/paclitaxel; EC = endometrial cancer; IV = intravenous; QD = once a day.

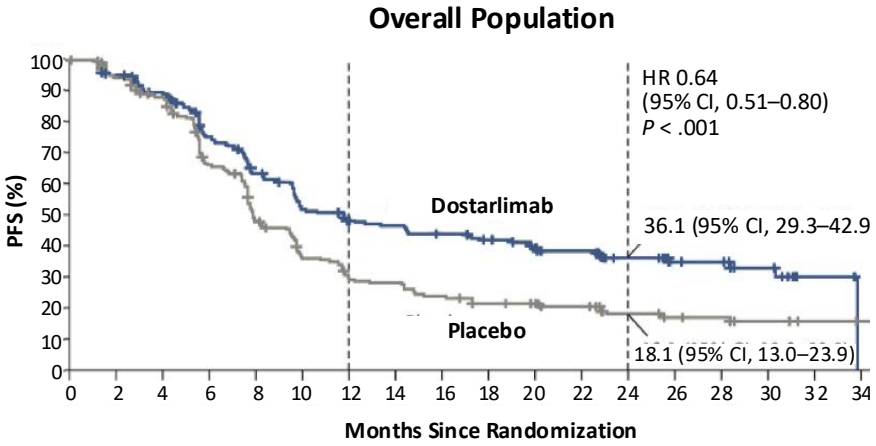
Mirza MR, et al. *N Engl J Med*. 2023;388(23):2145-2158. Eskander RN, et al. *N Engl J Med*. 2023;388(23):2159-2170.
Colombo N, et al. *Lancet Oncol*. 2024;25(9):1135-1146. Westin SN, et al. *J Clin Oncol*. 2024;42(3):283-299.

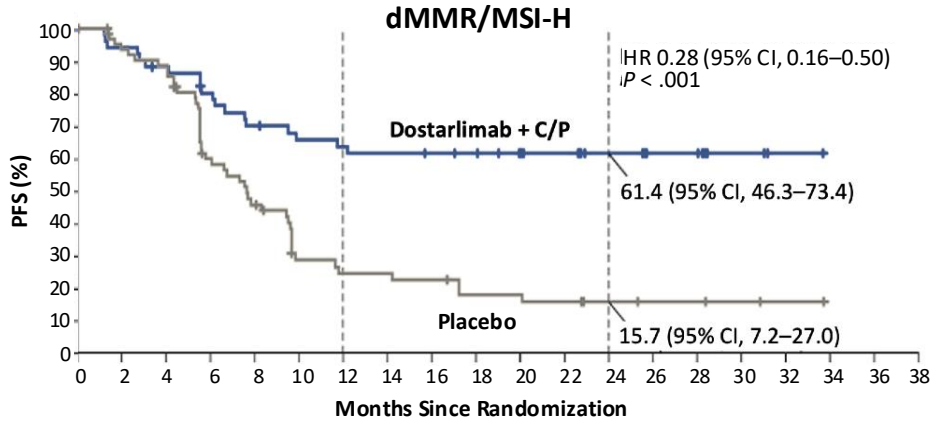
RUBY Part 1: Dostarlimab + Carboplatin/Paclitaxel

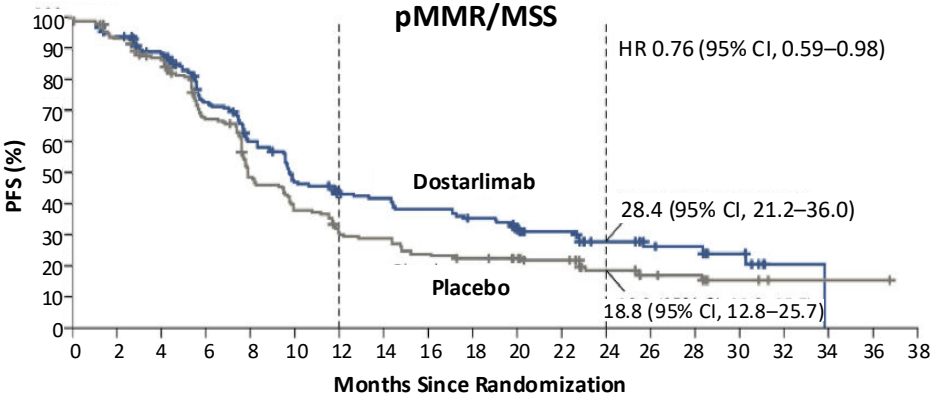
Randomized Phase III Trial

- 494 patients with primary advanced or first recurrent EC were randomized 1:1 to dostarlimab or placebo + carboplatin/paclitaxel

Primary Endpoints: PFS and OS





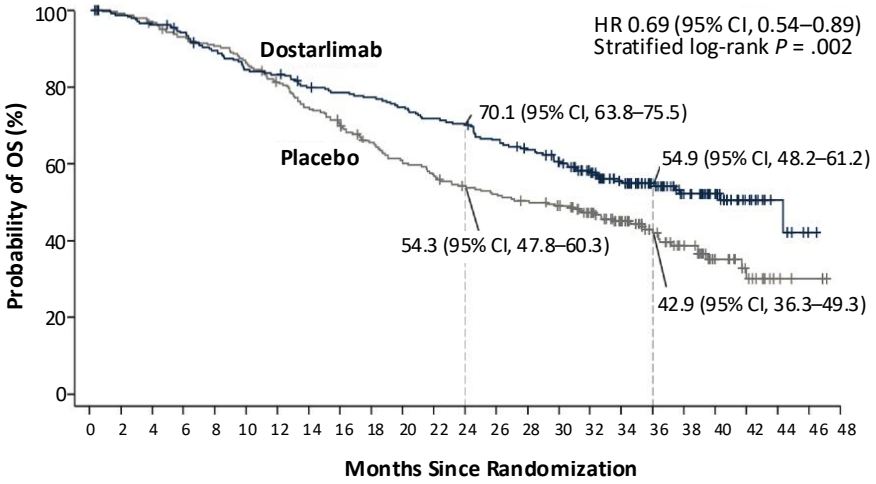


CI = confidence interval; dMMR = mismatch repair deficient; HR = hazard ratio; MSI-H = microsatellite instability-high; MSS = microsatellite stable; OS = overall survival; PFS = progression-free survival; pMMR = mismatch repair proficient.

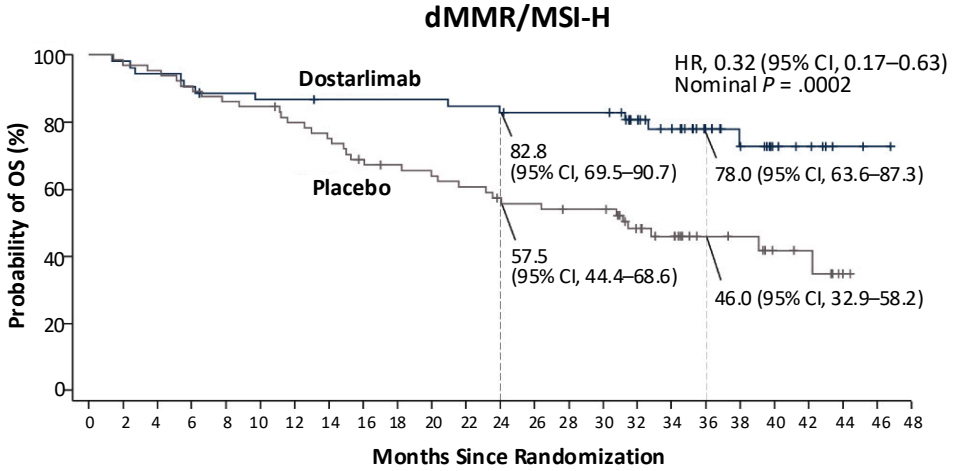
RUBY Part 1: Dostarlimab + Carboplatin/Paclitaxel

Overall Survival

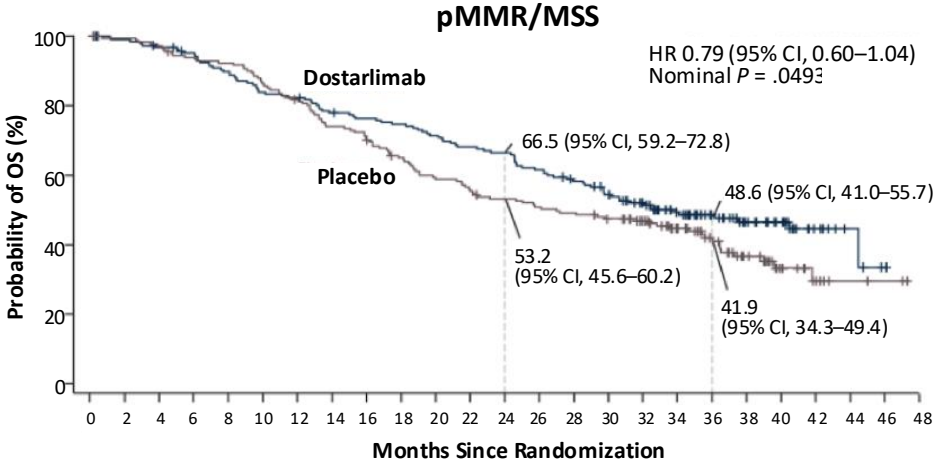
Overall Population



dMMR/MSI-H



pMMR/MSS



RUBY Part 2: Dostarlimab + Carboplatin/Paclitaxel

Randomized Phase III Trial

- 291 patients with primary advanced or recurrent EC were randomized 2:1 to dostarlimab + C/P followed by dostarlimab + niraparib vs. placebo + C/P followed by placebo

Primary Endpoint:

- PFS in overall and pMMR/MSS

	Dostarlimab + C/P → Dostarlimab + Niraparib	Placebo + C/P → Placebo	HR (95% CI)
Overall, n	192	99	0.60 (0.43–0.82) *P* = .0007
Median PFS, months (95% CI)	14.5 (11.8–17.4)	8.3 (7.6–9.8)	–
MMRp/MS, n	142	74	0.63 (0.44–0.91) *P* = .0060
Median PFS, months (95% CI)	14.3 (9.7–16.9)	8.3 (7.6–9.8)	–

Mirza MR, et al. *Ann Oncol*. 2024;35(suppl 5):103538.

NRG-GY018 (Pembrolizumab + Carboplatin/Paclitaxel)

Investigator-Assessed PFS by MMR Status

Randomized Phase III Trial

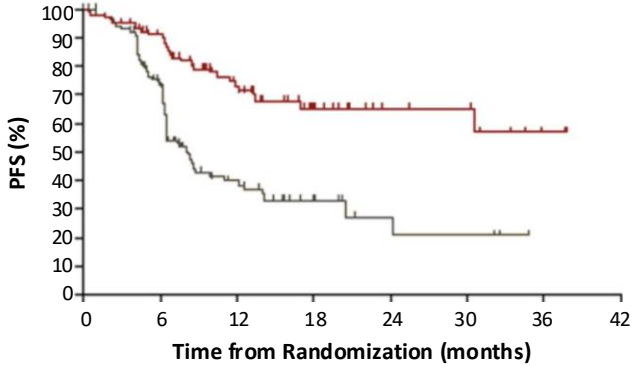
- 810 patients with primary advanced or recurrent EC were randomized 1:1 to receive pembrolizumab or placebo in combination with carboplatin + paclitaxel followed by single-agent maintenance therapy

Primary Endpoint: PFS in dMMR and pMMR cohorts

Key Secondary Endpoint: OS

dMMR

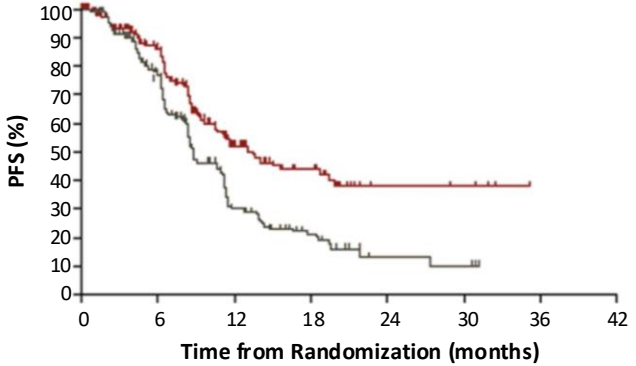
	Events, n/N	Median PFS, Months (95% CI)	HR (95%CI) *P* Value
Pembro + C/P	29/110	NR (30.7–NR)	0.34 (0.22–0.53) *P* < .0001
Placebo + C/P	60/112	8.3 (6.5–12.3)	



Benefit observed in both biomarker cohorts

pMMR

	Events, n/N	Median PFS, Months (95% CI)	HR (95%CI) *P* Value
Pembro + C/P	95/294	13.1 (10.6–19.5)	0.57 (0.44–0.74) *P* < .0001
Placebo + C/P	138/294	8.7 (8.4–11.0)	



NR = not reached.

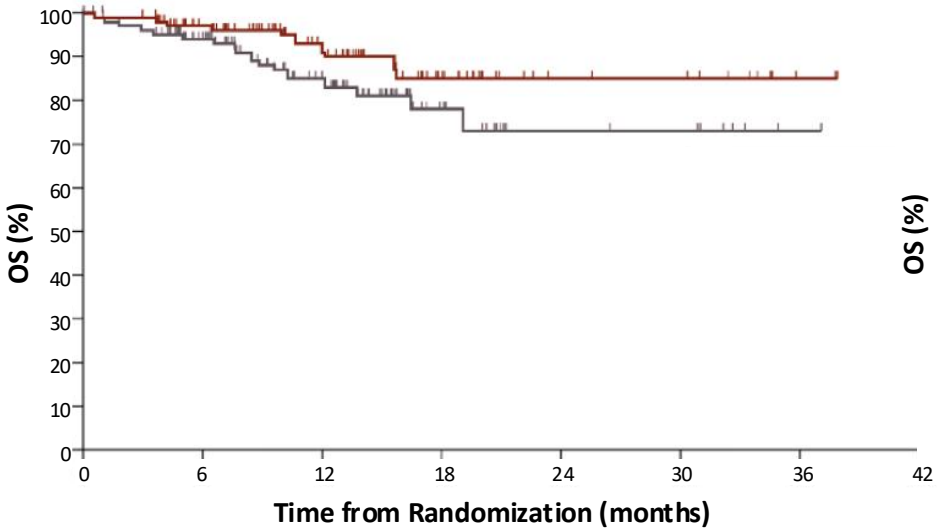
Eskander RN, et al. *Nat Med.* 2025;31(5):1539-1546. Eskander R, et al. *Gynecol Oncol.* 2024;190(suppl 1):S5.

NRG-GY018 (Pembrolizumab + Carboplatin/Paclitaxel)

Overall Survival

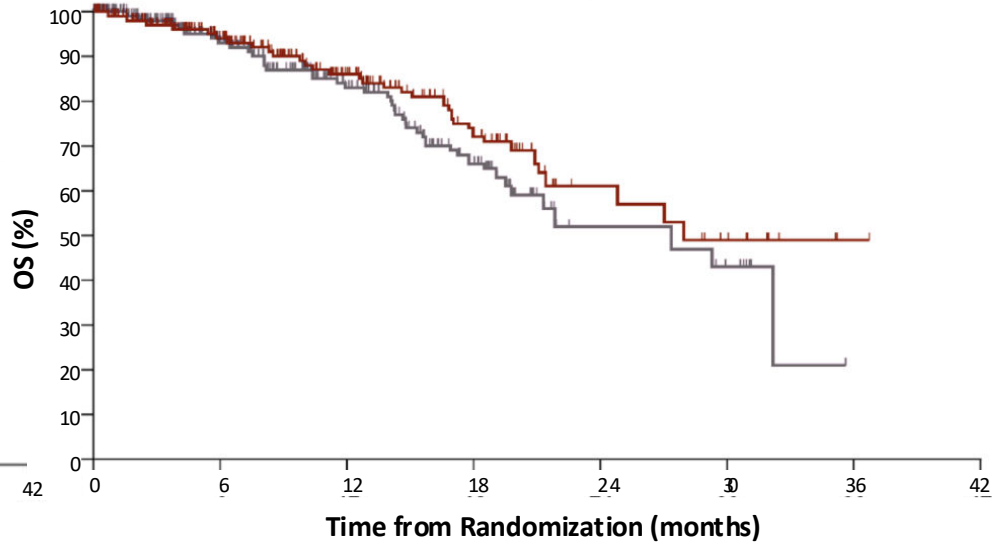
dMMR

	Events, n/N	Median OS (95% CI), Months	HR (95%CI) *P* Value
Pembro + C/T	10/110	NR (NR–NR)	0.55 (0.25–1.19) *P* = .0617
Placebo + C/T	17/112	NR (NR–NR)	



pMMR

	Events, n/N	Median OS (95% CI), Months	HR (95%CI) *P* Value
Pembro + C/T	45/294	27.96 (21.42–NR)	0.79 (0.53–1.17) *P* = .1157
Placebo + C/T	54/294	27.37 (19.52–NR)	



C/T = chemotherapy.

Eskander RN, et al. *Nat Med*. 2025;31(5):1539-1546. Eskander R, et al. *Gynecol Oncol*. 2024;190(suppl 1):S5.

AtTEnd (Atezolizumab* + Carboplatin/Paclitaxel)

Randomized Phase III Trial

- 549 patients with primary advanced or recurrent EC randomized 2:1 to atezolizumab or placebo combined with carboplatin + paclitaxel followed by maintenance monotherapy

Primary Endpoint: PFS in overall and dMMR populations

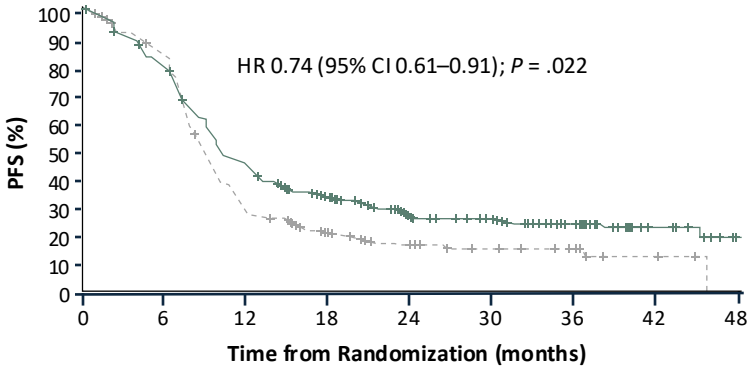
Key Secondary Endpoint: OS

Overall median OS: 36.0 vs. 30.5 months
(HR 0.87, 95% CI: 0.69–1.10; *P* = .0824)

dMMR median OS: NR vs. 31.8 months
(HR 0.49, 95% CI: 0.28–0.83; *P* = .0038)

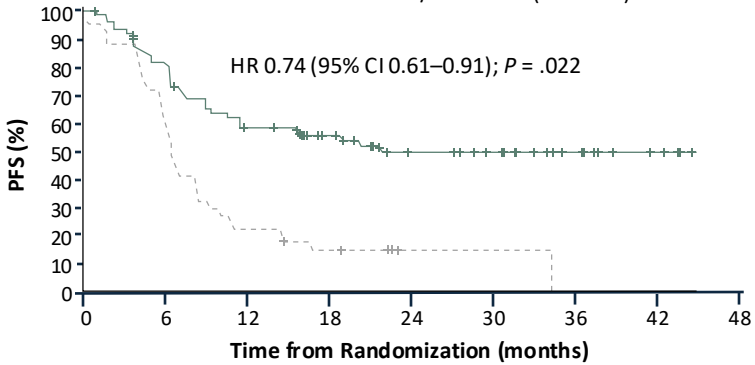
Overall Population

	Events/ N	Median, Months (95% CI)
Atezolizumab	253/360	10.1 (9.5–12.3)
Placebo	148/189	8.9 (8.1–9.6)



dMMR

	Events/ N	Median, Months (95% CI)
Atezolizumab	37/81	NE (12.4–NE)
Placebo	37/44	6.9 (6.3–10.1)



*Atezolizumab is not FDA-approved for the management of EC.
NE = not evaluable.

Colombo N, et al. *Lancet Oncol*. 2024;25(9):1135-1146. Barretina Ginestra MP, et al. *Ann Oncol*. 2025;36(suppl 2):S1583.

DUO-E

(Durvalumab + C/P* Followed by Durvalumab ± Olaparib† Maintenance)

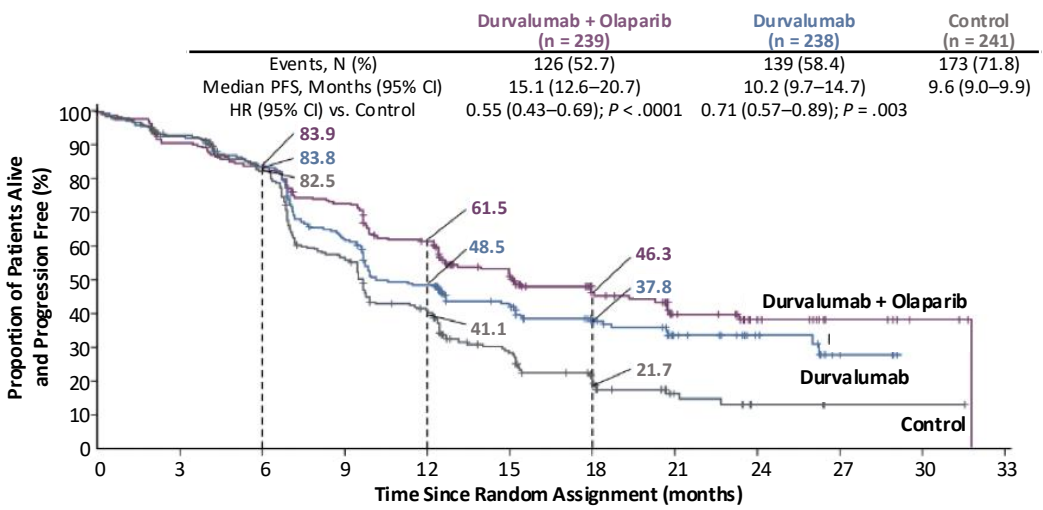
Phase III Randomized Trial

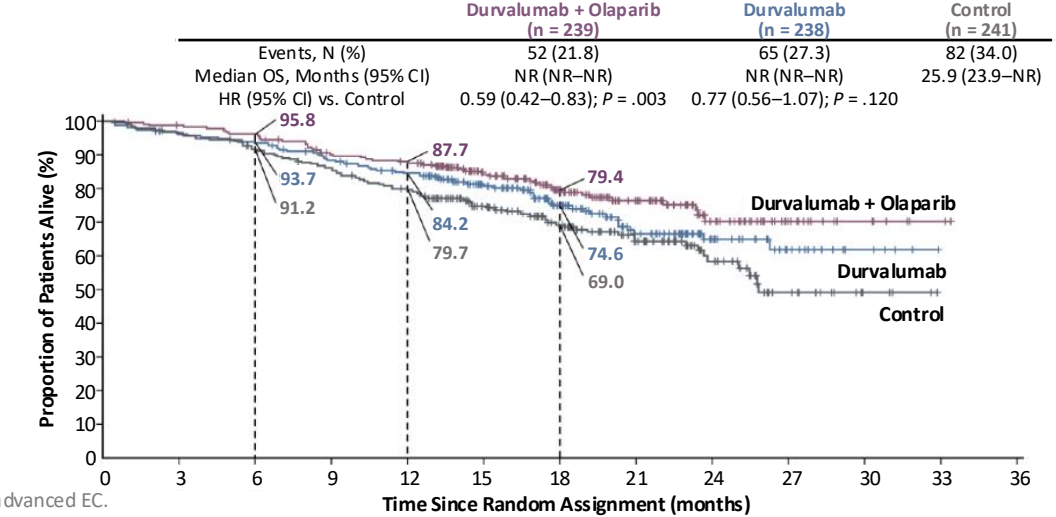
- 708 patients with newly diagnosed advanced or recurrent EC were randomized 1:1:1 to durvalumab + C/P followed by maintenance durvalumab +/- olaparib or placebo + C/P followed by placebo

Primary Endpoints:

- PFS in overall population
- Prespecified biomarker-stratified analyses (dMMR, pMMR)

Key Secondary Endpoint: OS





*Durvalumab + C/P is FDA-approved only for the management of advanced dMMR EC;
†Durvalumab in combination with olaparib is not FDA-approved for the management of advanced EC.

Westin SN, et al. *J Clin Oncol.* 2024;42(3):283-299.

Safety of First-Line Chemoimmunotherapy

Overall Tolerability

- Safety profile consistent with carboplatin/paclitaxel backbone
- Modest increase in grade ≥3 AEs with IO addition
- Discontinuation rates slightly higher but manageable

Common Adverse Events

- Hematologic: neutropenia, anemia
- Fatigue, nausea, alopecia
- Peripheral neuropathy (chemotherapy-related)

Immune-Related AEs

- Thyroid dysfunction most common
- Rash, hepatitis, colitis less frequent
- Grade ≥3 immune AEs uncommon

Maintenance Phase Considerations

- IO maintenance generally well tolerated
- PARP combinations (RUBY Part 2, DUO-E) increase anemia and fatigue

AEs = adverse events; IO = immunotherapy.

Mirza MR, et al. *N Engl J Med*. 2023;388(23):2145-2158. Mirza MR, et al. *Ann Oncol*. 2024;35(suppl 5):103538.
Eskander RN, et al. *N Engl J Med*. 2023;388(23):2159-2170. Colombo N, et al. *Lancet Oncol*. 2024;25(9):1135-1146.
Westin SN, et al. *J Clin Oncol*. 2024;42(3):283-299.

Safe Delivery of Chemoimmunotherapy Requires a Multidisciplinary Approach

Pathology/Molecular Diagnostics

- Timely MMR/MSI testing to guide frontline selection
- Clear communication of biomarker and histologic risk features

Gynecologic/Medical Oncology

- Biomarker-informed frontline treatment selection
- Adherence to evolving guideline-based systemic therapy
- Structured management of irAEs
- Coordinated strategy at recurrence

Infusion and Nursing Teams

- Patient education
- Ongoing symptom surveillance
- Early identification of immune-related events
- Care coordination

Supportive Care and Subspecialists

- Rapid referral for irAEs
- Genetic counseling and hereditary risk assessment
- Early palliative care involvement when appropriate

MDT involvement improves OS through more precise staging, guideline adherence, and coordinated relapse management

irAEs = immune-related adverse events; MDT = multidisciplinary team.

Mangone L, et al. *Healthcare (Basel)*. 2023;12(1):64.

Patient Case 1

A 63-year-old woman with newly diagnosed metastatic endometrial cancer; ECOG PS = 0

- dMMR/MSI-H
- PD-L1 TPS = 10%
- TP53 WT
- HER2-negative

What would you most likely recommend as first-line systemic therapy?

ECOG PS = Eastern Cooperative Oncology Group performance status; TPS = tumor proportion score; WT = wild-type.

A 63-year-old woman presents with newly diagnosed metastatic EC. Molecular testing shows dMMR/MSI-H disease. Her ECOG performance status is 0, PD-L1 TPS is 10%, p53 is wild-type, and HER2 is negative. What would you most likely recommend as first-line therapy?

A. Carboplatin/paclitaxel
B. Carboplatin/paclitaxel + dostarlimab
C. Carboplatin/paclitaxel + durvalumab
D. Carboplatin/paclitaxel + pembrolizumab
E. Pembrolizumab or dostarlimab monotherapy
F. Other
G. I don't know

A 63-year-old woman presents with newly diagnosed metastatic EC. Molecular testing shows dMMR/MSI-H disease. Her ECOG performance status is 0, PD-L1 TPS is 10%, p53 is wild-type, and HER2 is negative. What would you most likely recommend as first-line therapy?

A. Carboplatin/paclitaxel
B. Carboplatin/paclitaxel + dostarlimab
C. Carboplatin/paclitaxel + durvalumab
D. Carboplatin/paclitaxel + pembrolizumab
E. Pembrolizumab or dostarlimab monotherapy
F. Other
G. I don't know

Patient Case 2

A 71-year-old woman with newly diagnosed metastatic endometrial cancer; ECOG PS = 1

- pMMR/MSS
- PD-L1 TPS <1%
- p53 WT
- HER2-negative

What would you most likely recommend as first-line systemic therapy?

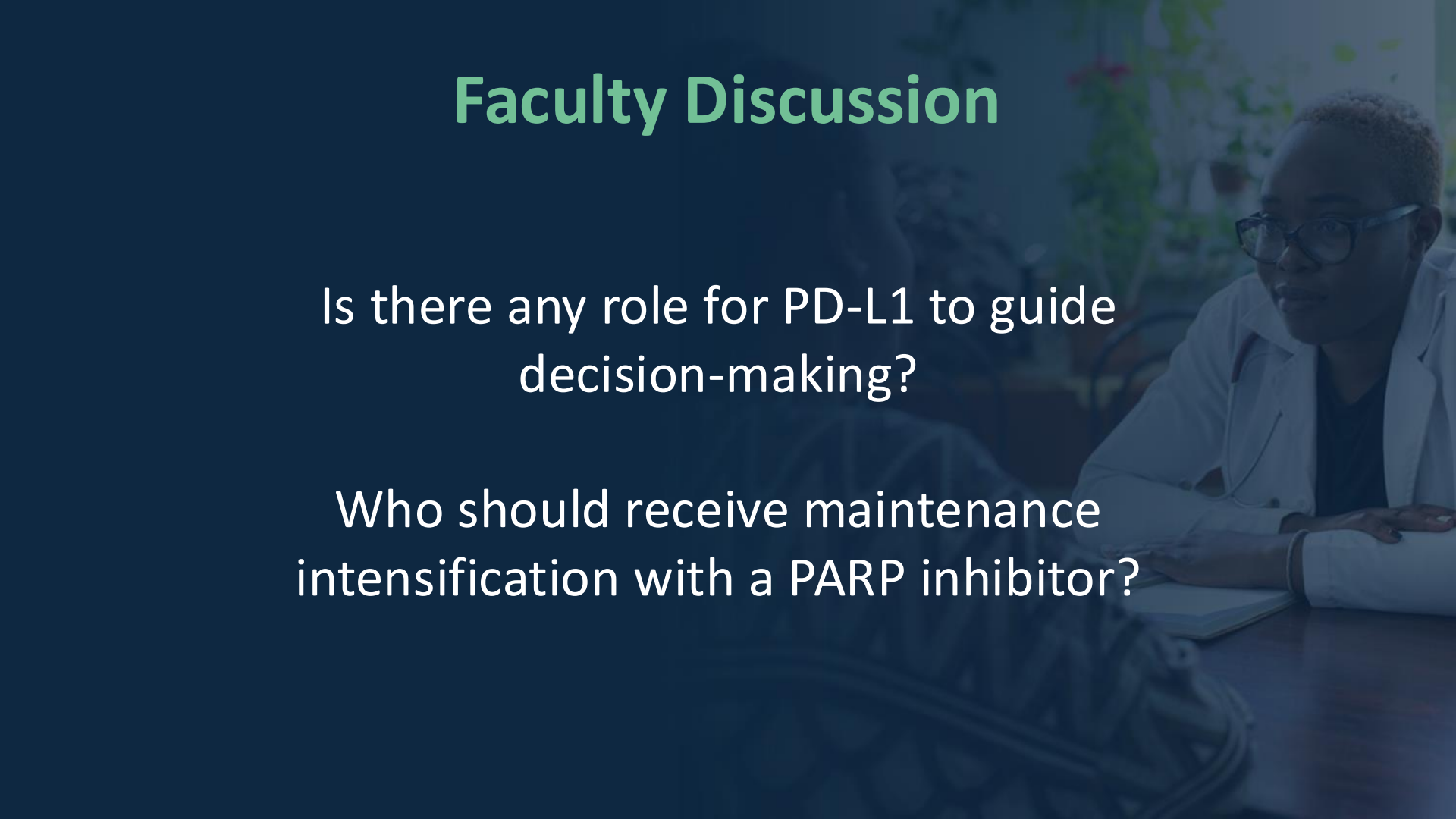
A 71-year-old woman presents with newly diagnosed metastatic EC. Her ECOG performance status is 1. Molecular testing shows pMMR/MSS disease. PD-L1 tumor proportion score is <1%, p53 is wild-type, and HER2 is negative. Which first-line systemic therapy would you most likely recommend for this patient?

A. Carboplatin/paclitaxel
B. Carboplatin/paclitaxel + dostarlimab
C. Carboplatin/paclitaxel + pembrolizumab
D. Other
E. I don't know

A 71-year-old woman presents with newly diagnosed metastatic EC. Her ECOG performance status is 1. Molecular testing shows pMMR/MSS disease. PD-L1 tumor proportion score is <1%, p53 is wild-type, and HER2 is negative. Which first-line systemic therapy would you most likely recommend for this patient?

A. Carboplatin/paclitaxel
B. Carboplatin/paclitaxel + dostarlimab
C. Carboplatin/paclitaxel + pembrolizumab
D. Other
E. I don't know

Faculty Discussion



Is there any role for PD-L1 to guide decision-making?

Who should receive maintenance intensification with a PARP inhibitor?

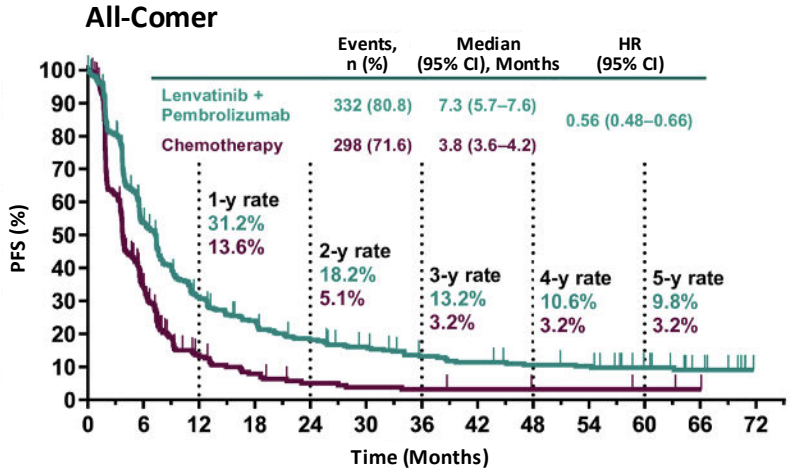
Post–Platinum Treatment Strategies in Advanced or Recurrent Endometrial Cancer

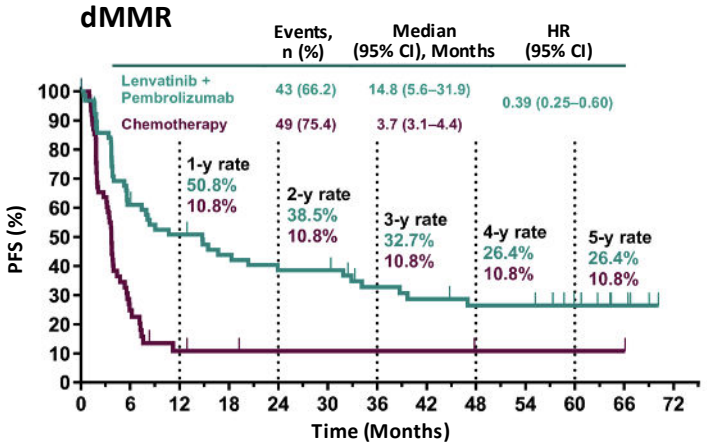
KEYNOTE-775: Lenvatinib + Pembrolizumab

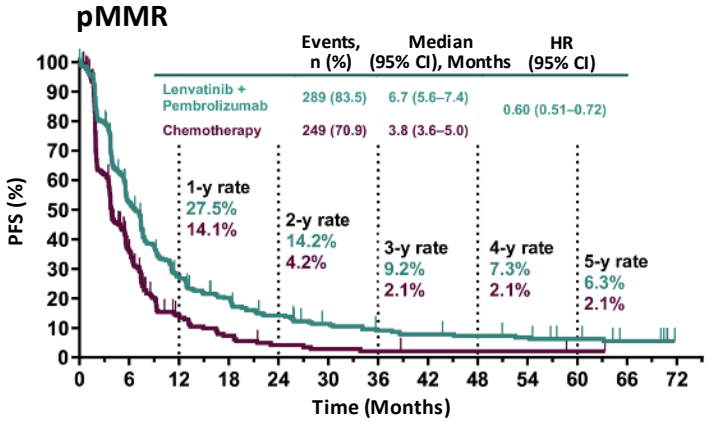
Phase III Randomized Trial

- 827 patients with advanced/recurrent EC after one prior platinum-based regimen were randomized 1:1 to receive lenvatinib + pembrolizumab vs. chemotherapy

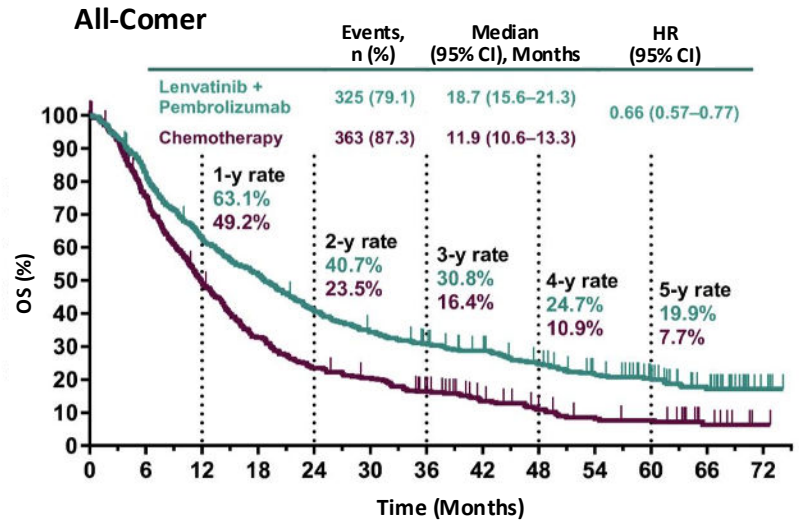
Primary endpoints: PFS and OS

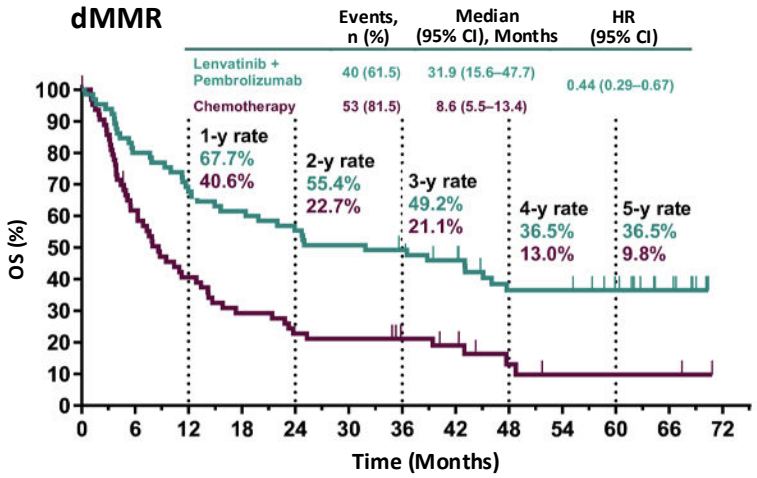


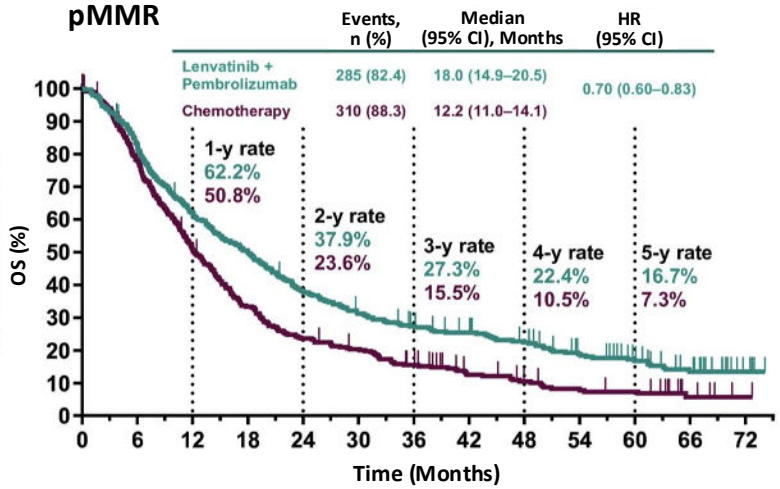




KEYNOTE-775: Lenvatinib + Pembrolizumab

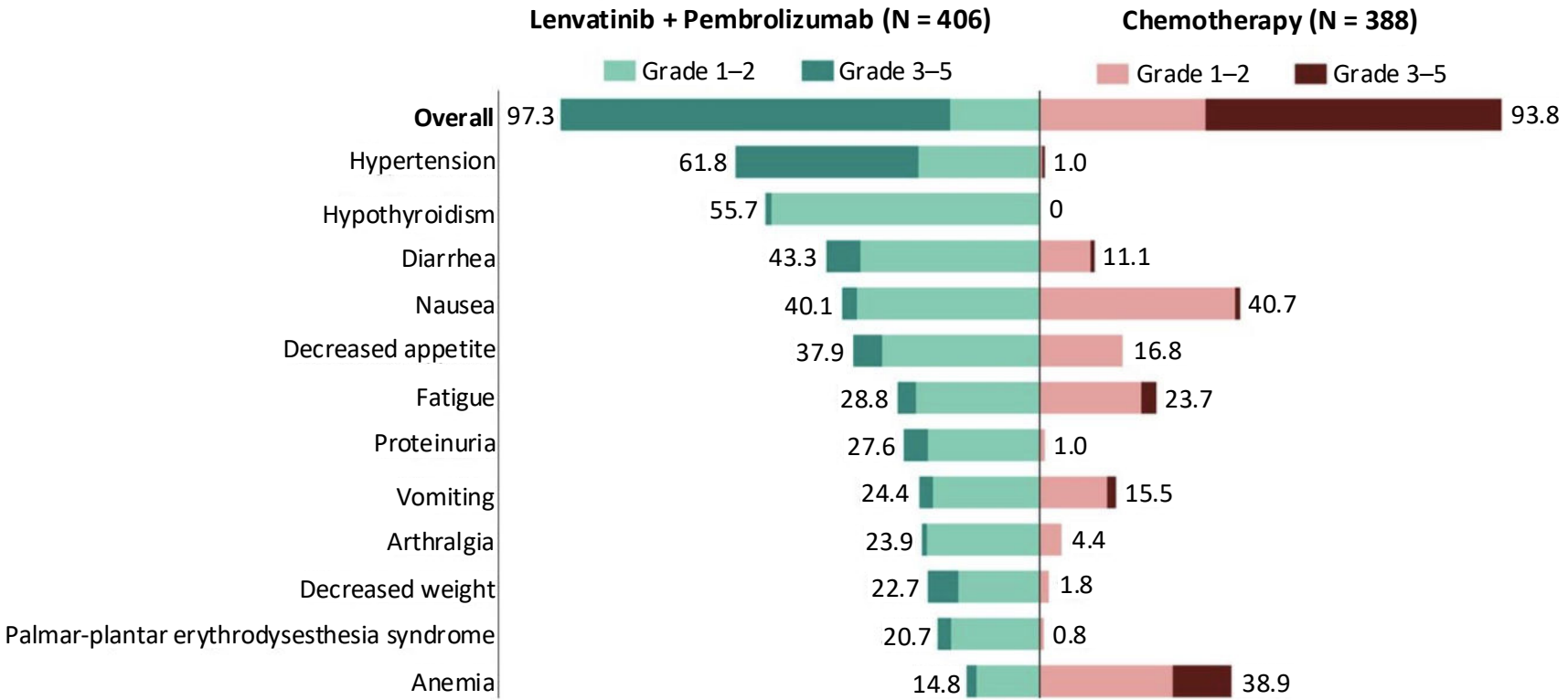






Makker V, et al. *J Immunother Cancer*. 2026;14(2):e013713.

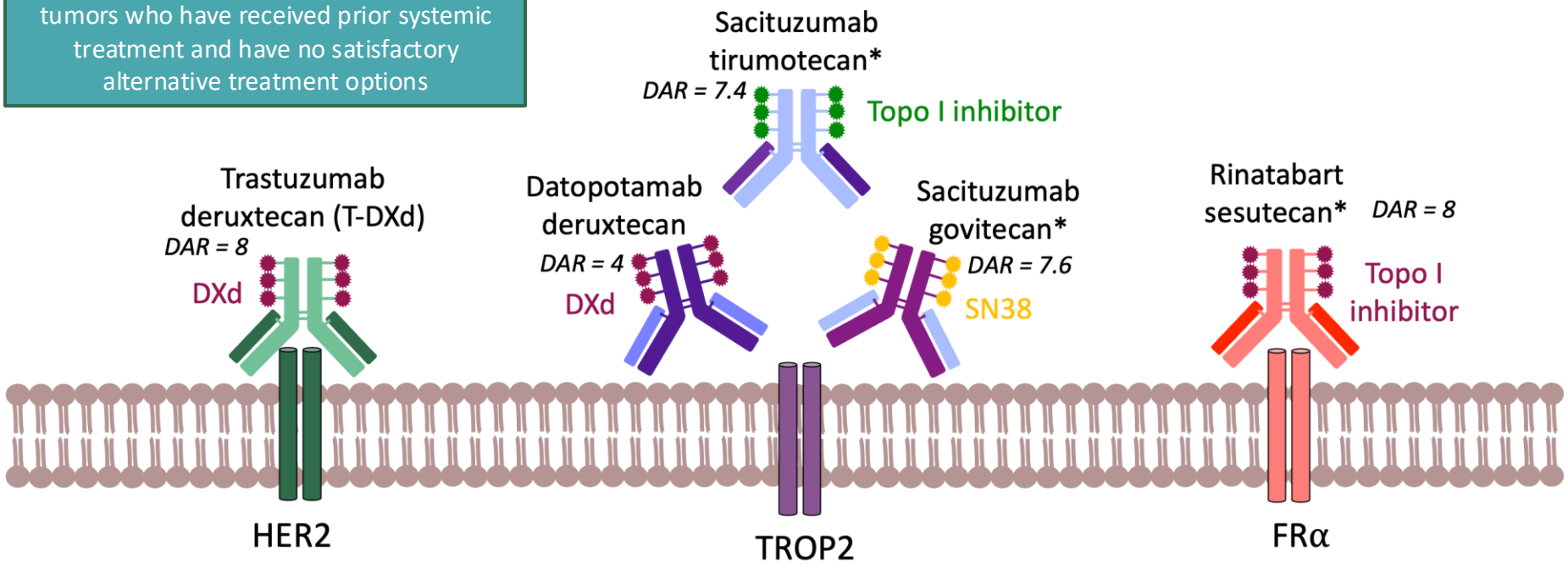
KEYNOTE-775: Lenvatinib + Pembrolizumab



Antibody-Drug Conjugates

ADCs in Endometrial Cancer

T-DXd is FDA-approved for patients with advanced HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options



*Not approved for the management of endometrial cancer.
ADC = antibody-drug conjugate; IHC = immunohistochemistry; T-DXd = trastuzumab deruxtecan.

Karpel HC, et al. *Am Soc Clin Oncol Educ Book*. 2023;43:e390772. Lorusso D, et al. *Ann Oncol*. 2024;35(suppl 2):S592. Winer IS, et al. *J Clin Oncol*. 2025;43(16_suppl):3039.

DESTINY-PanTumor02: T-DXd

Open-Label Phase II Trial

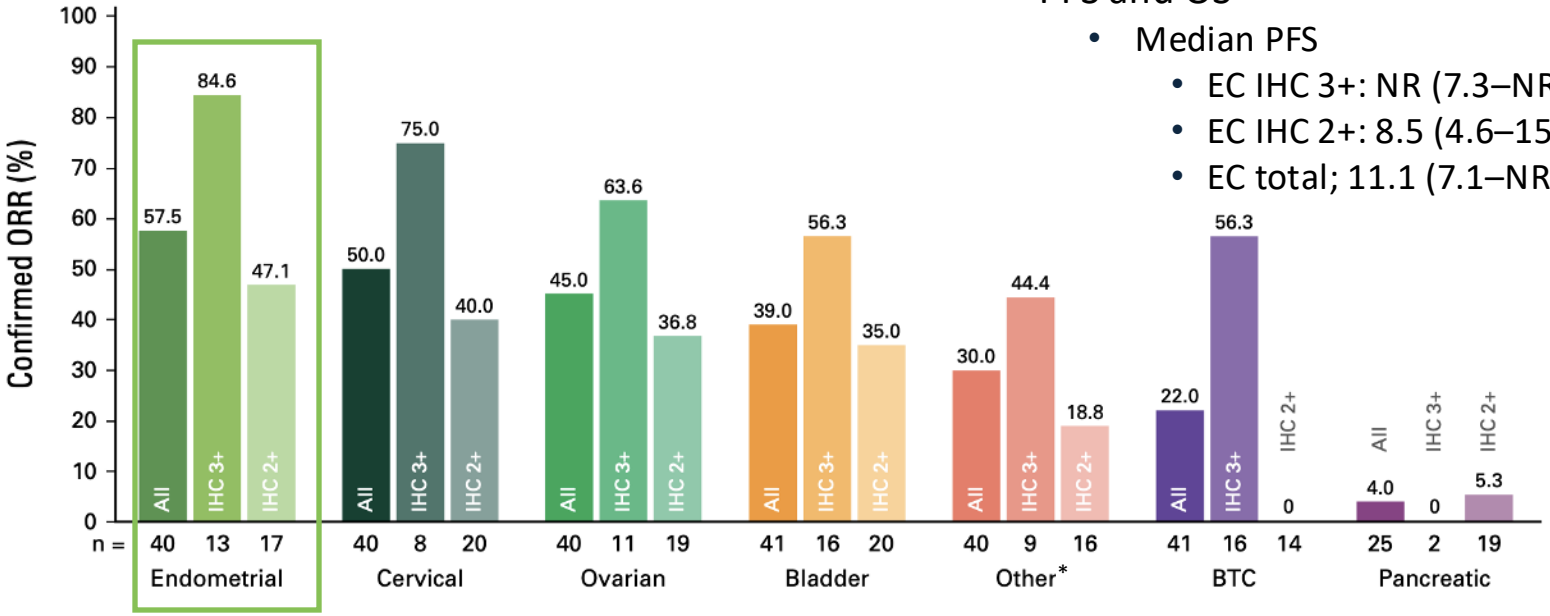
- 267 patients received T-DXd across 7 tumor cohorts including 40 patients with advanced EC

Primary Endpoint:

- Confirmed objective response rate

Key Secondary Endpoints:

- PFS and OS
  - Median PFS
    - EC IHC 3+: NR (7.3–NR)
    - EC IHC 2+: 8.5 (4.6–15.1)
    - EC total; 11.1 (7.1–NR)



*Other tumor cohorts include salivary gland cancer (n = 19), malignant neoplasm of unknown primary site (n = 5), extramammary Paget disease (n = 3), cutaneous melanoma (n = 2), oropharyngeal neoplasm (n = 2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n = 1).

TROPION Pan-Tumor03: Datopotamab Deruxtecan*

Phase II Open-Label Basket Study

- 40 patients with previously treated advanced EC

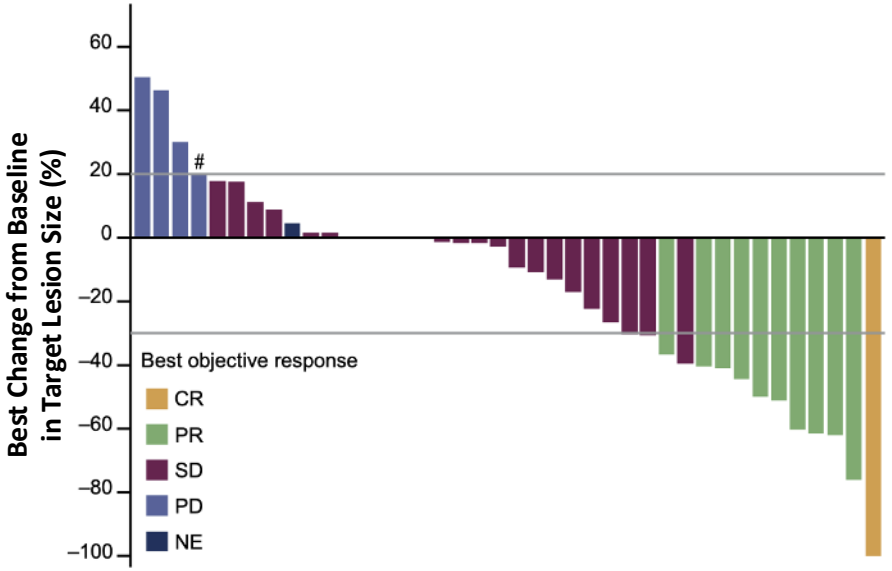
	Endometrial (N = 40)
Confirmed ORR, % (95% CI)	27.5 (14.6–43.9)
Best Overall Response, n (%)	
CR	1 (2.5)
PR	10 (25.0)
SD	23 (57.5)
PD	5 (12.5)
NE	1 (2.5)
Median Time to Response, Months (range)	2.8 (1.4–4.2)
Median DoR, Months (95% CI)	16.4 (7.1–NC)
DCR at 12 Weeks, % (80% CI)	57.5 (46.1–68.3)
Median PFS, Months (95% CI)	6.3 (2.8–NC)

Primary Endpoint:

- ORR

Key Secondary Endpoints:

- PFS, DoR, and DCR



*Datopotamab deruxtecan is not FDA-approved for the management of EC.

CR = complete response; DCR = disease control rate; DoR = duration of response; NC = not calculable; NE =not evaluable; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease.

Oaknin A, et al. *Ann Oncol*. 2024;35(suppl 2):S547-S548.

TROPiCS-03: Sacituzumab Govitecan*

Open-Label Phase II Basket Study

- 41 patients with previously treated advanced EC

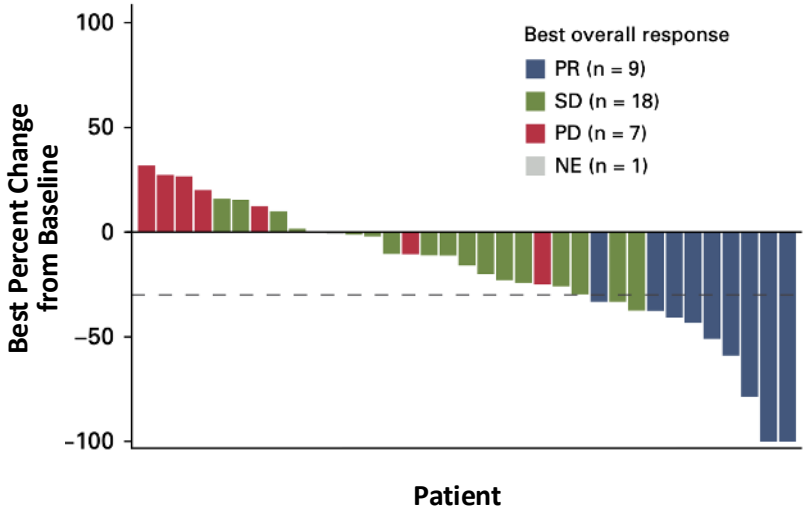
Variable	All Patients (N = 41)
ORR (confirmed CR + PR), N (%) 95% CI	9 (22) 11–38
Best overall response, N (%) Confirmed CR Confirmed PR SD PD NE Not assessed	 0 9 (22) 18 (44) 8 (20) 2 (5) 4 (10)
Clinical benefit rate (confirmed CR + PR + SD ≥6 months), N (%) 95% CI	13 (32) 18–48
Time to response, months Median (range)	2.8 (1.4–5.8)
DOR, months Median (95% CI)	8.8 (2.8–NE)

Primary Endpoint:

- ORR

Key Secondary Endpoints:

- PFS and OS



*Sacituzumab govitecan is not FDA-approved for the management of EC.

KL264-I-01: Sacituzumab Tirumotecan*

Open-Label Phase II Basket Study

- 44 patients with previously treated advanced EC

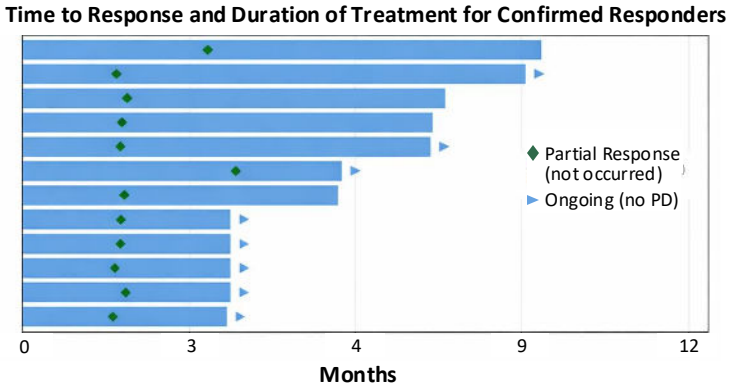
Primary Endpoint:

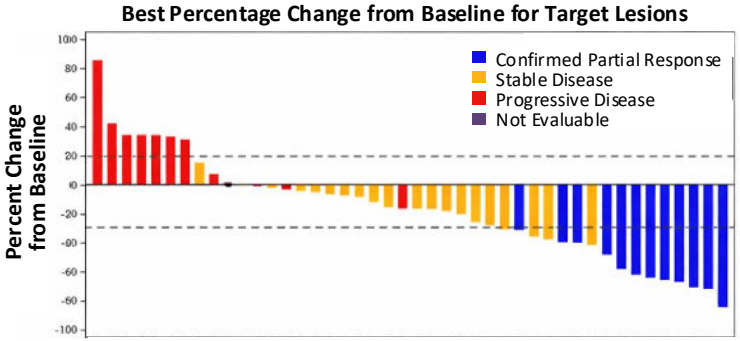
- ORR

Key Secondary Endpoints:

- PFS, DoR, and OS

	EC (N = 44)†
ORR, % (n/N)	**34.1 (15/44)‡**
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)





*Sacituzumab tirumotecan is not FDA-approved for the management of EC;
†Response assessed per RECIST v1.1 by investigator;
‡Two patients with unconfirmed response were still receiving treatment at the data cutoff date.

RAINFOL-01: Rinatabart Sesutecan*

Randomized Phase I/II study

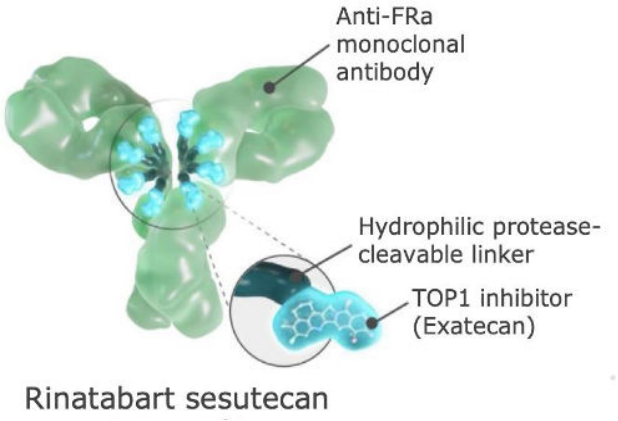
- 64 patients with advanced or recurrent EC after progression on platinum chemotherapy and a PD-(L)1 inhibitor

Primary Endpoint:

- Safety/tolerability

Key Secondary Endpoint:

- Antitumor activity



	100 mg/m² (n = 22)	120 mg/m² (n = 34)
Median On-Study Follow-up, Months (95% CI)	7.7 (7.2–8.4)	9.8 (7.9–11.8)
Confirmed ORR, % (95% CI)	50.0 (28.2–71.8)	47.1 (29.8–64.9)
Confirmed Response, n (%)		
CR	2 (9.1)	0
PR	9 (40.9)	16 (47.1)
SD	11 (50.0)	13 (38.2)
NE	0	1 (2.9)
DCR, % (95% CI)	10 (84.6–100.0)	85.3 (68.9–95.0)

*Rinatabart sesutecan is not FDA-approved for the management of EC.
FRa = folate receptor alpha.

Safety of ADCs in Advanced EC

HER2

T-DXd

- Common AEs
- Nausea, vomiting, diarrhea
- Fatigue
- Mild-to-moderate anemia
- Predominantly gastrointestinal profile
- Moderate hematologic toxicity
- Monitor for interstitial lung disease (ILD)

TROP2

Datopotamab Deruxtecan

- Prominent stomatitis/mucositis
- Nausea common
- Mostly low-grade events
- Limited high-grade neutropenia
- Monitor for ILD

Sacituzumab Govitecan

- Neutropenia is the dominant high-grade toxicity
- Diarrhea frequently observed
- Anemia and fatigue common

Sacituzumab Tirumotecan

- Anemia and leukopenia prominent
- High rates of grade ≥3 hematologic toxicity
- Stomatitis observed
- Diarrhea not prominent

FRα

Rinatabart Sesutecan (Rina-S)

- Combination of hematologic + gastrointestinal toxicity
- Neutropenia and anemia common
- Fatigue and nausea frequently observed
- Myelosuppression more pronounced at higher dose levels

Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42(1):47-58.
Oaknin A, et al. *Ann Oncol*. 2024;35(suppl 2):S547-S548.
Santin AD, et al. *J Clin Oncol*. 2024;42(29):3421-3429.
Wang D, et al. *Ann Oncol*. 2024;35(suppl 2):S548.
Winer IS, et al. *J Clin Oncol*. 2025;43(16_suppl):3039.

Patient Case 3

A 66-year-old woman with metastatic endometrial cancer previously treated with first-line carboplatin/paclitaxel + pembrolizumab followed by second-line lenvatinib/ pembrolizumab; ECOG PS = 1

- pMMR/MSS
- HER2 IHC 1+
- No other actionable alterations

Assuming access is not a limiting factor, which systemic therapy would you most likely recommend next?

A 66-year-old woman with metastatic EC previously received first-line carboplatin/paclitaxel + pembrolizumab followed by second-line lenvatinib/pembrolizumab. Her ECOG performance status is 1. Molecular testing shows pMMR/MSS disease, HER2 IHC 1+, and no other actionable alterations. Assuming access is not a limiting factor, which systemic therapy would you most likely recommend next?

A. Axitinib + avelumab
B. Cabozantinib
C. Chemotherapy
D. FRa ADC
E. HER2 ADC
F. TROP2 ADC
G. I don't know

A 66-year-old woman with metastatic EC previously received first-line carboplatin/paclitaxel + pembrolizumab followed by second-line lenvatinib/pembrolizumab. Her ECOG performance status is 1. Molecular testing shows pMMR/MSS disease, HER2 IHC 1+, and no other actionable alterations. Assuming access is not a limiting factor, which systemic therapy would you most likely recommend next?

A. Axitinib + avelumab
B. Cabozantinib
C. Chemotherapy
D. FRa ADC
E. HER2 ADC
F. TROP2 ADC
G. I don't know

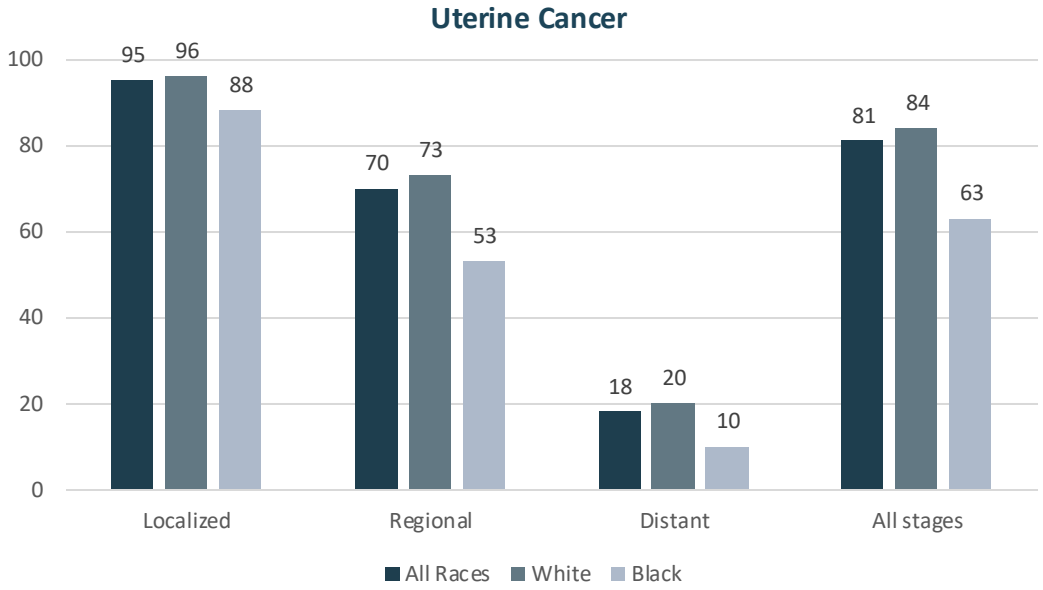
Improving Care in Advanced EC

Health Inequities in Advanced or Recurrent Endometrial Cancer

Documented Disparities in Care and Outcomes

- Higher incidence and mortality among Black patients
- Lower rates of timely diagnosis, guideline-concordant systemic therapy, and access to clinical trials
- Delays in molecular testing limit optimal treatment selection

Five-Year Relative Survival by Race and Stage at Diagnosis



NCCN Website. 2026. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.
ASCO Website. 2026. https://www.asco.org/practice-patients/cancer-care-standards. NIH Website. https://seer.cancer.gov/statfacts/.

Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- **Ensure MMR/MSI (and other relevant biomarker testing) results** are available within 14 days of diagnosis or documented recurrence in patients with advanced endometrial cancer.
- **Initiate guideline-concordant frontline chemotherapy–ICI** in 100% of eligible patients with advanced or recurrent endometrial cancer based on current phase III evidence.
- **At first progression, document biomarker status and treatment rationale** in 100% of cases before selecting next-line therapy.
- **Implement structured toxicity screening** at every visit with document management plans for grade ≥2 events.
- **Strengthen multidisciplinary coordination** (gynecologic oncology, pathology, supportive care) to ensure timely testing, equitable access, and comprehensive management.

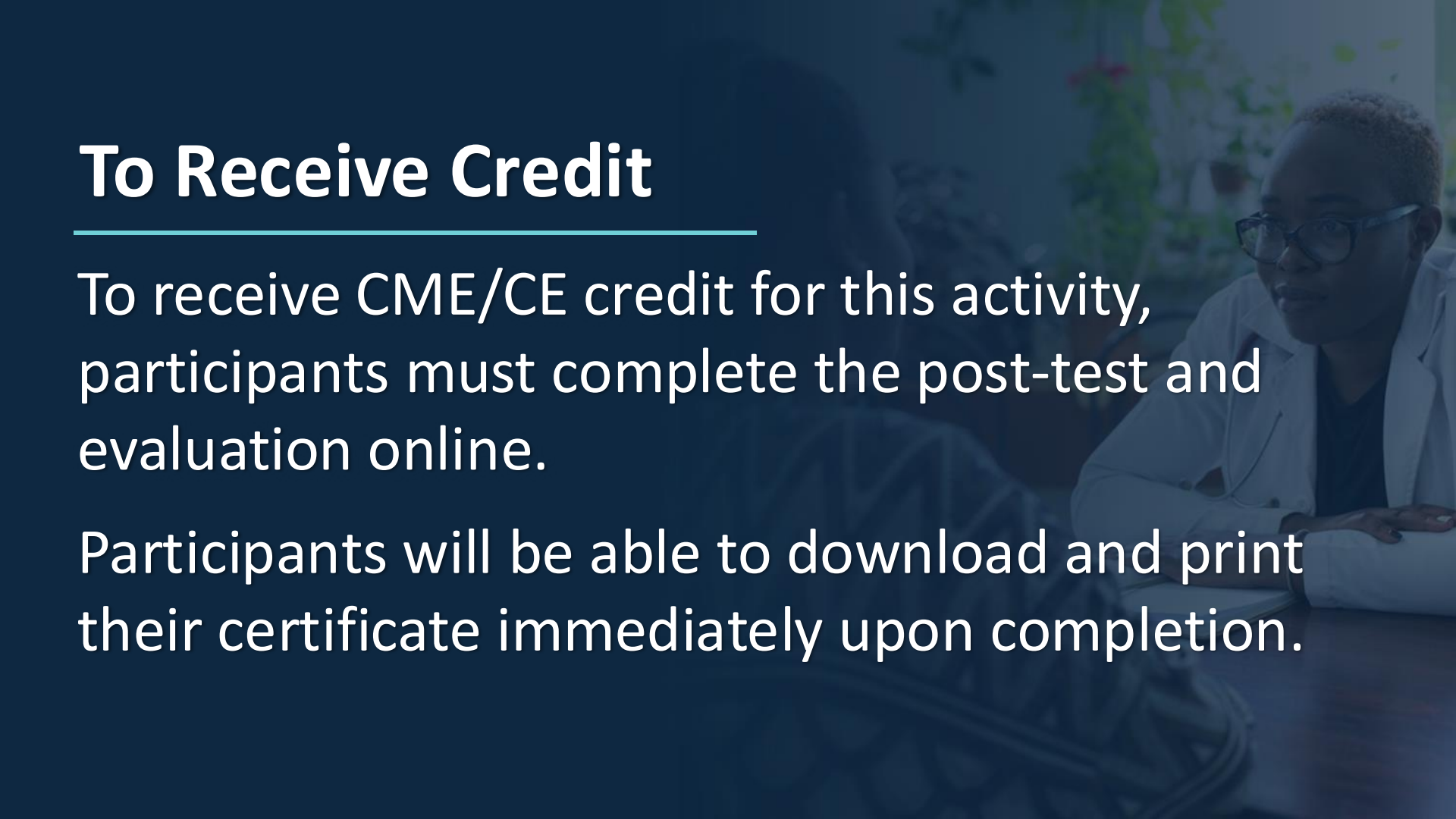
Additional Resources

Visit www.ceconcepts.com for clinical information and certified educational activities

To Receive Credit

To receive CME/CE credit for this activity, participants must complete the post-test and evaluation online.

Participants will be able to download and print their certificate immediately upon completion.



cec ONCOLOGY

EXPLORING THE HORIZONS IN ADVANCED OR RECURRENT ENDOMETRIAL CANCER

Practical Considerations and Future Directions for New Treatment Strategies

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