

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Immunotherapeutic Approaches for Endometrial Cancer

Thursday, May 14, 2026

6:00 AM – 7:30 AM

Faculty

Sarah Karpen, MPAS, PA-C

J Alejandro Rauh-Hain, MD, MPH

Jaclyn Shaver, MS, APRN, CNP, WHNP

Moderator

Dana M Chase, MD

Faculty



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Moderator
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Los Angeles, California

Ms Karpen — Disclosures

Speakers Bureaus	Amgen Inc
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Dr Rauh-Hain — Disclosures

No relevant financial relationships to disclose.

Ms Shaver — Disclosures

No relevant financial relationships to disclose.

Dr Chase — Disclosures

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Contracted Research	GSK, Merck
Speakers Bureaus	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Eisai Inc, GSK, Pfizer Inc
Nonrelevant Financial Relationships	NRG Oncology

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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

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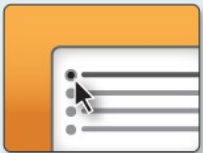
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Clinicians in the Meeting Room

Networked iPads are available.



Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.



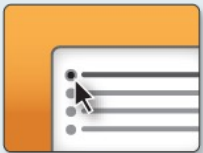
Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

Clinicians Attending via Zoom



Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.



Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.



Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, www.ResearchToPractice.com



NONMELANOMA SKIN CANCERS

Check out our recent program with Dr Nikhil I Khushalni from Moffitt Cancer Center in Tampa, Florida. Published May 7, 2026.



Overview of nonmelanoma skin cancers (12 min)



Systemic therapy for nonmelanoma skin cancers (8 min)

Immune checkpoint inhibitors for special patient populations (12 min)



Hedgehog inhibitors for basal cell carcinoma (6 min)

New developments in therapy for nonmelanoma skin cancers (5 min)



CASE: A man in his early 70s with cutaneous squamous cell carcinoma receives cemiplimab (8 min)

CASE: A man in his mid 70s with a history of basal cell carcinoma presents with disease of the ocular surface and receives immunotherapy (6 min)



CASE: A man in his early 70s with recurrent metastatic basal cell carcinoma receives vismodegib followed by cemiplimab on disease progression (6 min)

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Feedback (Please!)



“Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse”

Eighteenth Annual RTP-ONS NCPD Symposium Series

Wednesday
May 13

Antibody-Drug Conjugates

11:15 AM – 12:45 PM CT

Ovarian Cancer

6:00 PM – 7:30 PM CT

Thursday
May 14

Immunotherapeutic Approaches for Endometrial Cancer

6:00 AM – 7:30 AM CT

Prostate Cancer

12:15 PM – 1:45 PM CT

Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

6:00 PM – 7:30 PM CT

Friday
May 15

Pancreatic Cancer

6:00 AM – 7:30 AM CT

Targeting the PI3K/AKT/mTOR Pathway in HR-Positive Metastatic BC

12:15 PM – 1:45 PM CT

Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia

6:00 PM – 8:00 PM CT

Saturday
May 16

CDK4/6 Inhibitors for HR-Positive Breast Cancer

6:00 AM – 7:30 AM CT

Relapsed/Refractory Multiple Myeloma

12:15 PM – 1:45 PM CT

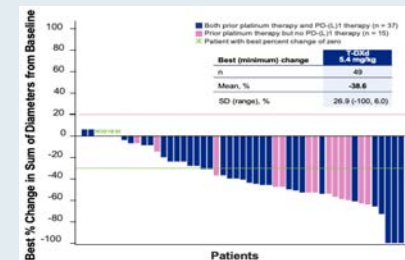
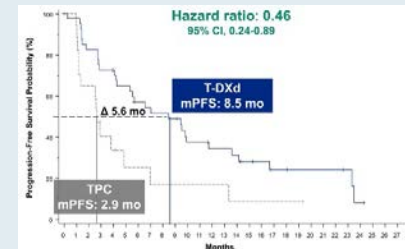
Oral SERDs for Breast Cancer

6:00 PM – 7:30 PM CT

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

New Agents, Therapies and Regimens

- When should it be used, for whom and why?
- How to prevent and manage side effects:
 - dose holds and reductions
 - Kaplan Meier curves — HR and absolute benefit
- Waterfall plots



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Moderator

Dana M Chase, MD

Agenda

Introduction: Biology of Endometrial Cancer (EC)

Module 1: First-Line Therapy for Advanced or Recurrent EC

Module 2: Potential Benefits of PARP Inhibition Combined with Immunotherapy in Advanced EC

Module 3: Role of Lenvatinib/Pembrolizumab in the Management of Progressive Advanced EC

Module 4: Other Nursing Considerations in the Care of Patients with Advanced EC

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Biology of Endometrial Cancer; Rationale for the Use of Immune Checkpoint Inhibitors in This Disease

J. Alejandro Rauh-Hain, MD, MPH
MD Anderson Cancer Center

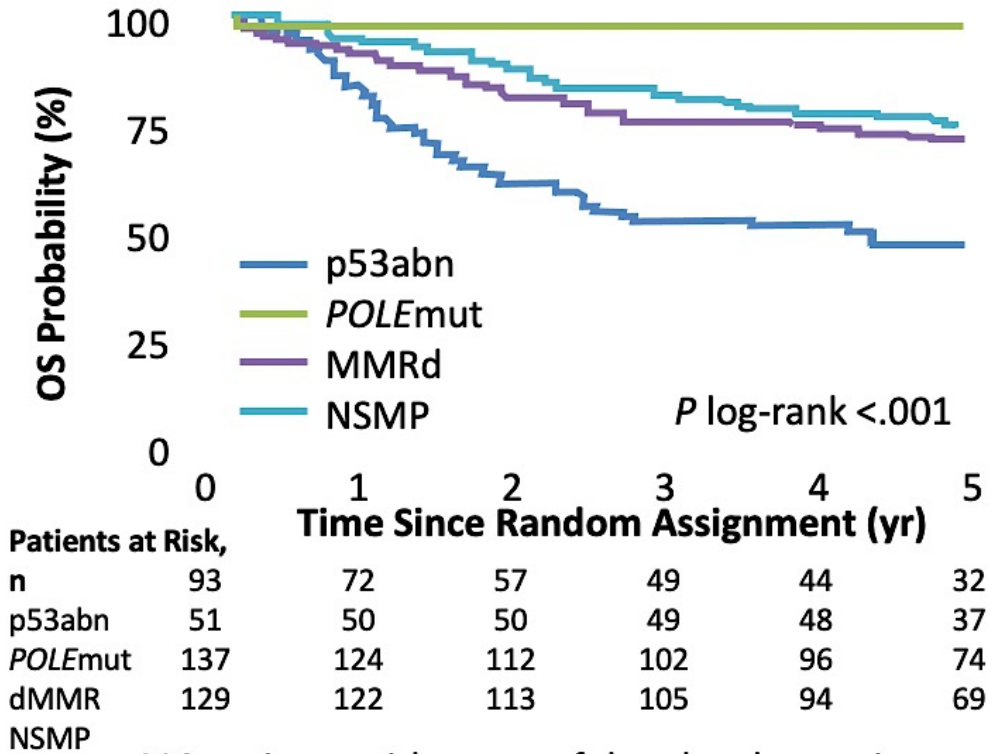
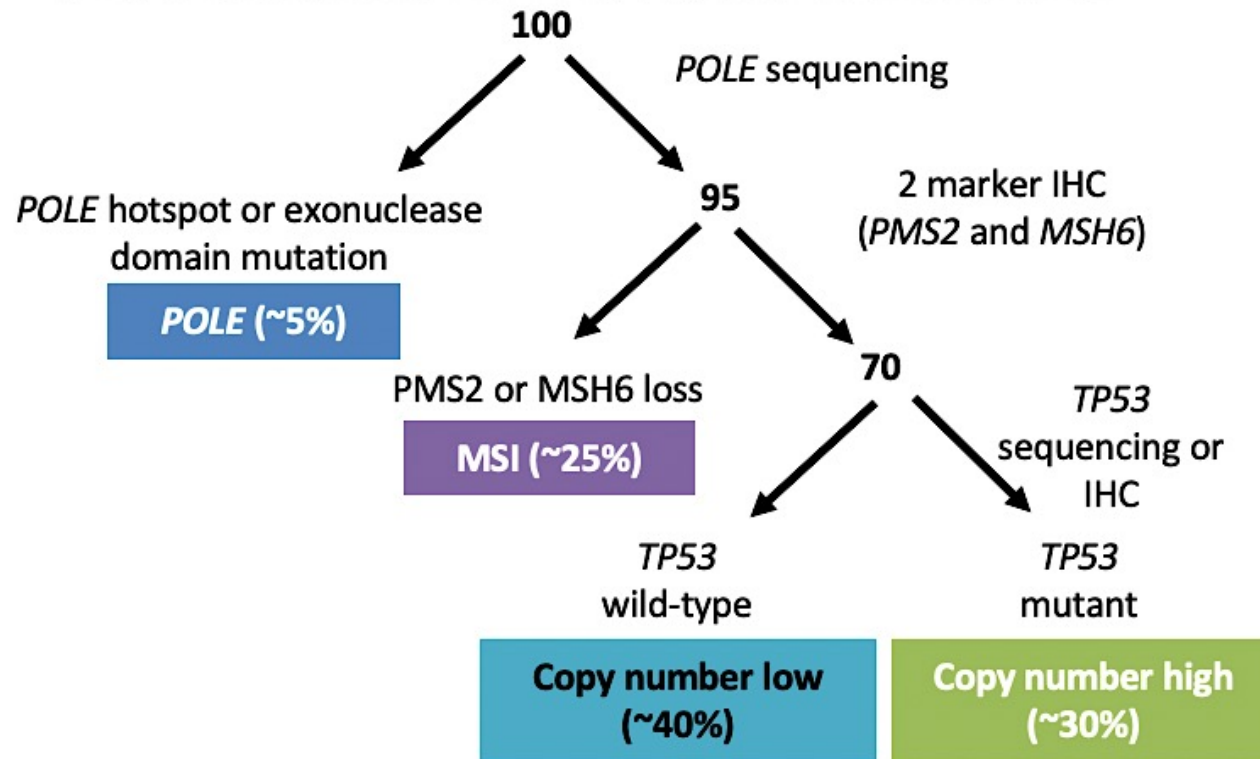
TCGA Molecular Subgroups

<i>POLE</i> ultramutated	• Ultra-high somatic mutation frequency; MSS; frequent mutations in the exonuclease domain of <i>POLE</i>; high <i>ASNS</i> and <i>CCNB1</i> expression • Represents ~4% of endometrioid tumors* • Best prognosis
MSI hypermuted	• High mutation rate and few copy number alterations; high rate of <i>MLH1</i> promoter methylation; high phospho-AKT; low <i>PTEN</i> expression; frequent <i>PIK3CA</i> and <i>PIK3R1</i> mutations co-occurring with <i>PTEN</i> mutations • Represents ~39% of endometrioid tumors*†
Copy-number low‡	• High frequency of mutations in <i>CTNNB1</i>, <i>KRAS</i>, <i>SOX17</i>; frequent <i>PIK3CA</i> and <i>PIK3R1</i> mutations co-occurring with <i>PTEN</i> mutations; elevated levels of progesterone receptor and <i>RAD50</i> expression • Represents ~49% of endometrioid tumors*
Copy-number high‡	• Greatest transcriptional activity; frequent <i>TP53</i> mutations; decreased levels of phospho-AKT; mutually exclusive <i>PIK3CA</i>, <i>PIK3R1</i>, and <i>PTEN</i> mutations • Represents ~9% of endometrioid tumors* • Worst prognosis

TCGA Molecular Classification and Outcomes

Patients Divided Into TCGA subgroups

100 hypothetical patients with newly diagnosed endometrial cancer

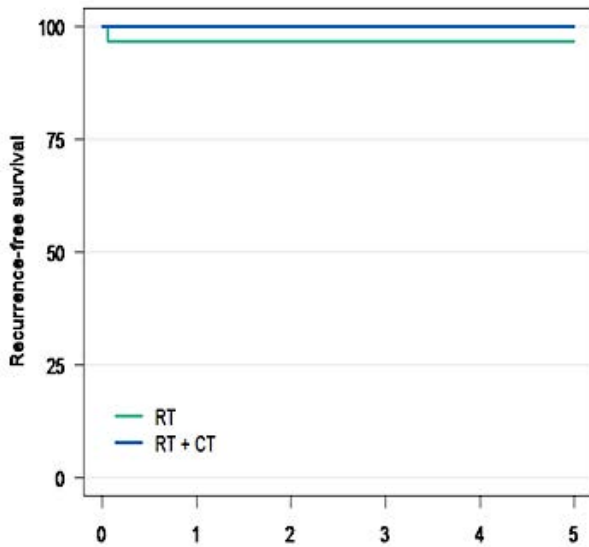


410 patients with successful molecular testing

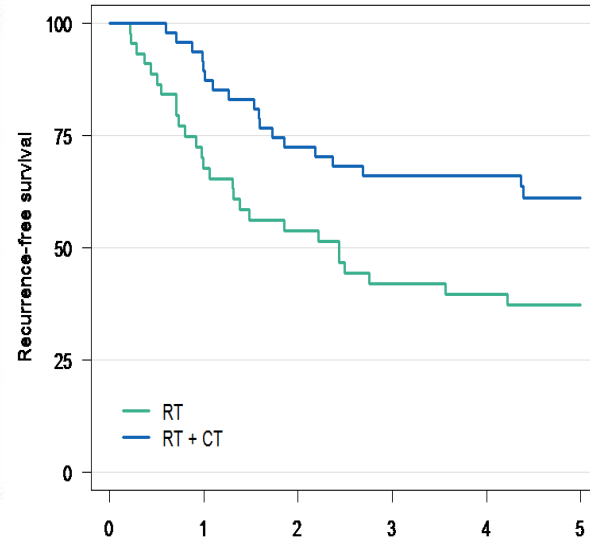
- 23% p53abn: p53 abnormal
- 12% POLEmut: POLE ultramutated
- 33% dMMR: mismatch repair deficient
- 32% NSMP: no specific molecular profile

Molecular Classification and Benefit from Adjuvant Chemotherapy

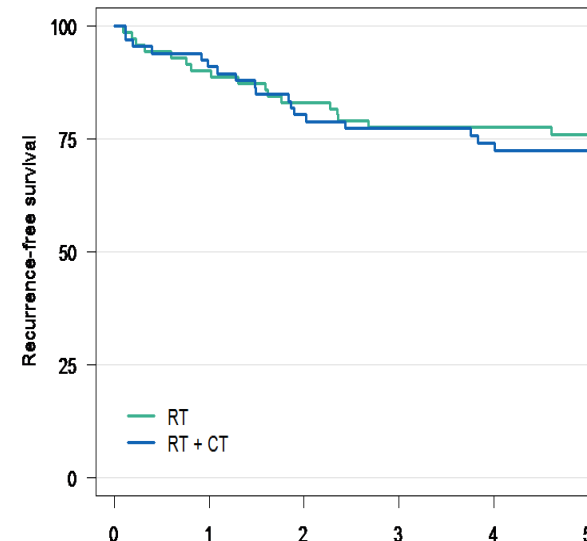
POLEmut
N=51



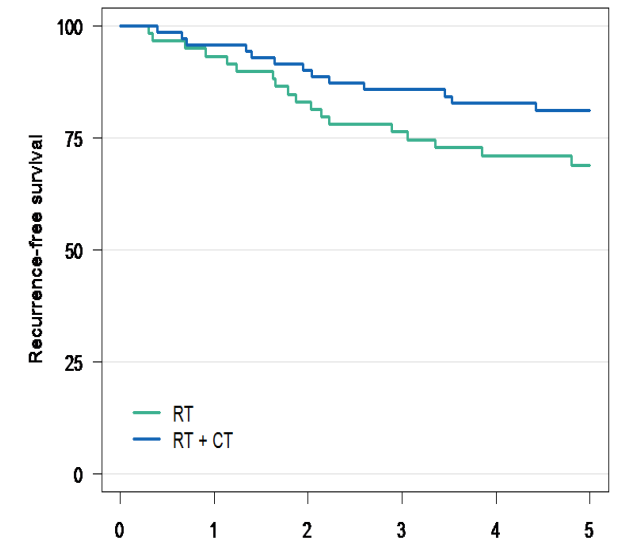
P53abn
N=93



MMRd
N=137



NSMP
N=129



$p=0.015$, HR 0.50 (95%CI 0,28-0,88)

- P53abn: worst prognosis but greatest benefit from adj Ctx
- POLEmut: does not relapse regardless of tx
- MSI and NSMP: intermediate prognosis , but little benefit from Adj Ctx



GOG 209: Design

- Adenocarcinoma
- Stage III/IV or recurrent
- No prior chemotherapy
- Measurable disease
- Primary Endpoint: Equiv OS
- ER/PR status recorded



I	Doxorubicin 45 mg/m ²	x7
	Cisplatin 50 mg/m ²	
	Paclitaxel 160 mg/m ² (d2,3h)	
	Every 21 days	
	With G-CSF support	

II	Carboplatin AUC 6	x7
	Paclitaxel 175 mg/m ² (3 h)	
	every 21 days	

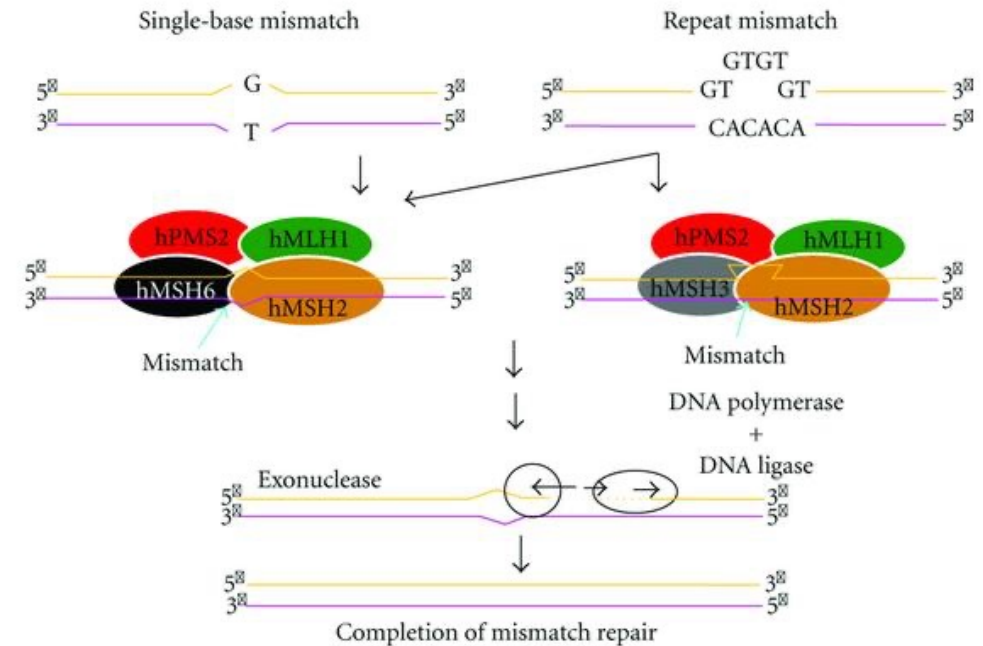
Open: 25-Aug-03
Closed: 20-Apr-09
Accrual: 1316 (eligible)

GOG 209: Survival

Outcome Measure	TAP	TC	HR
Median PFS	14 mos	14 mos	1.03
Median OS	38 mos	37 mos	1.01
OS (90% CI, Test for Non-inferiority)		1.16	P>0.1

Microsatellite Instability (MSI)

- MSI is a condition of genetic hypermutability that is the result of defective DNA mismatch repair (MMR)¹
- The MMR pathway corrects DNA replication errors that lead to incorporation of the wrong nucleotides and/or nucleotide insertions or deletions²
- Deficient MMR (dMMR) causes accumulations of mutations and can lead to an MSI-high (MSI-H) phenotype²
 - A tumor is considered dMMR when ≥ 1 MMR protein is inactivated
 - Germline mutations in MMR genes cause Lynch syndrome²
 - Accounts for ~2% of endometrial cancers³
- MSI-H/dMMR status is predictive of clinical benefit from checkpoint inhibitor therapy⁴

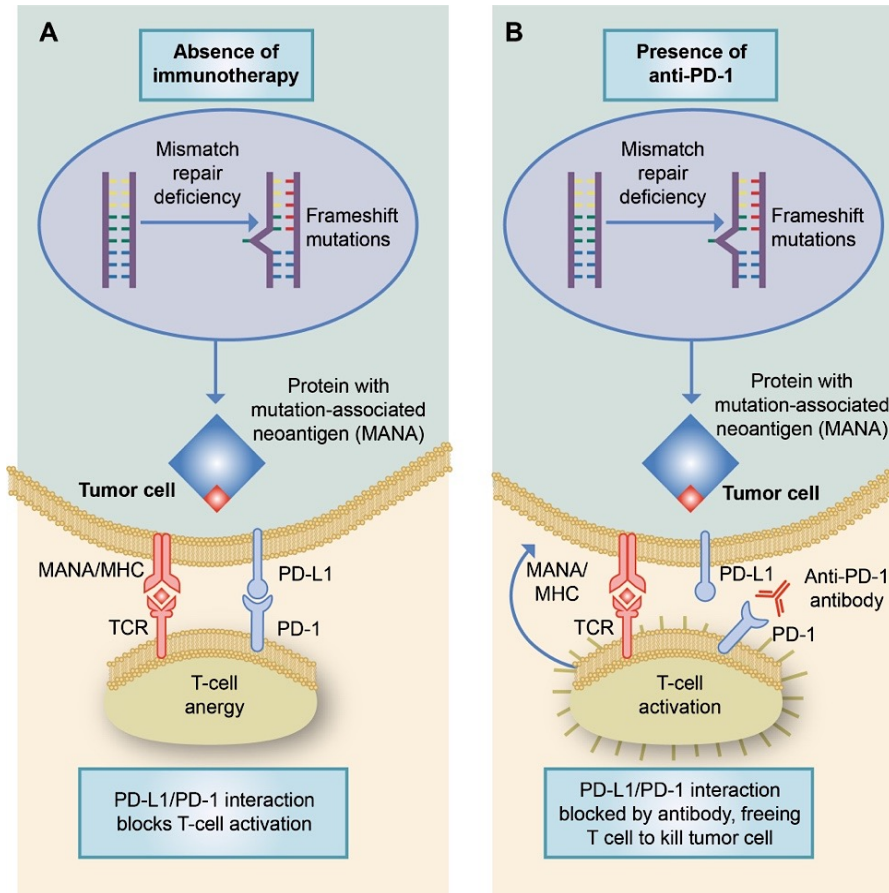


MMR, mismatch repair; MSI, microsatellite instability; MSI-H, microsatellite instability-high.

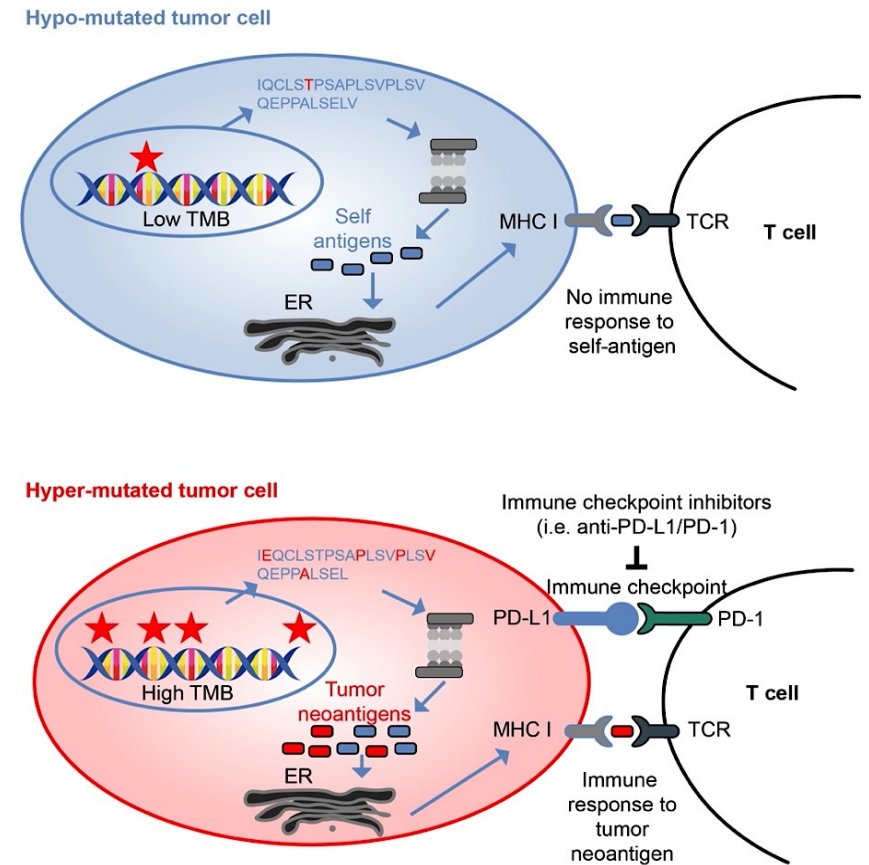
1. Luchini C et al. *Ann Oncol*. 2019;30:1232-1243. 2. Kristeleit RS et al. *Am Soc Clin Oncol Educ Book*. 2016;35:e259-e268. 3. Hampel H et al. *Cancer Res*. 2006;66:7810-7817. 4. Le DT et al. *Science*. 2017;357:409-413.

MSI-H/dMMR or TMB-H Tumors and Response to Checkpoint Blockade

MSI-H/dMMR Tumors¹



TMB-H Tumors²



Single Agent IO in “biomarker” Selected Endometrial Cancer Populations (dMMR)

- Response to single agent IO in dMMR or MSI-high endometrial

Study & Drug	Patient Population	Outcome
Keynote 158: Pembrolizumab (N=49)	Advanced stage or metastatic dMMR endometrial cancer	ORR: 57.1%
PHAEDRA trial: Durvalumab (N=35 dMMR)	Advanced stage or metastatic endometrial cancer	ORR in dMMR: 43%
GARNET study: Dostarlimab (N=70)	Previously treated, recurrent advanced stage endometrial cancer	ORR in dMMR: 45%
Ph II Avelumab study (N= 15 dMMR)	Advanced stage or metastatic endometrial cancer	ORR: 26.7%

Case 1

67-year-old new diagnosis of grade 3 endometrial cancer

Initial Workup

- Endometrial biopsy: Grade 3 endometrioid endometrial adenocarcinoma
- CT imaging: Concern for adrenal metastasis, diffuse lymphadenopathy
- Biopsy confirmed adrenal metastasis

Molecular Testing: dMMR tumor

Biopsychosocial Context

Social Context

- Husband died from cancer 1 year ago
- Lives >2 hours from cancer center

Emotional Concerns

- Fear of losing independence
- Anxiety regarding chemotherapy toxicity
- Concern about burdening family

Medical Comorbidities

- Hypertension

Treatment Decision

CT scan 6 months later (Pt declined treatment): Adrenal gland metastasis, bone metastasis, diffuse lymphadenopathy

Treatment Selected

- Carboplatin + paclitaxel + pembrolizumab

Rationale

- Advanced/recurrent EC
- dMMR/MSI-H tumor with high likelihood of response to PD-1 inhibition

Supportive Interventions

- Nutrition referral
- Early symptom-management planning

Clinical Course

Treatment Course

- Significant improvement in pelvic pain after Cycle 3 and excellent response
- CT after 6 cycles: Partial response, only area of disease adrenal metastasis

Toxicities: Fatigue, Immune-related hypothyroidism

Management: Levothyroxine initiated, zoledronic acid, dose adjustments and supportive care

Current Status: Continuing maintenance pembrolizumab, Surgery with Endocrine Surg Onc pending

Key Lessons From This Case

Molecular Testing Matters

- dMMR/MSI-H status directly influenced frontline therapy selection
- Biomarker testing should be performed at diagnosis

Immunotherapy Has Changed the Treatment Landscape

- Chemoimmunotherapy can produce meaningful and durable responses
- Particularly impactful in dMMR EC

Cancer Care Extends Beyond Tumor Biology

- Transportation barriers
- Caregiver responsibilities
- Emotional distress

Discussion Questions

What is the optimal approach to biomarker assessment for patients with newly diagnosed advanced EC?

Given that first-line chemoimmunotherapy regimens are available regardless of MSI/MMR status, are you still assessing this in all patients?

Do you test for other potential biomarkers of response to immune checkpoint inhibition (eg, POLE mutations, tumor mutational burden, PD-L1 status)? What about other biomarkers, such as BRCA, TP53 and HER2 status?

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First-Line Therapy for Advanced or Recurrent Endometrial Cancer

Dana M. Chase, MD

Professor and Fellowship Program Director

Division of Gynecologic Oncology

David Geffen School of Medicine at UCLA

Objectives

- Key efficacy findings with dostarlimab, pembrolizumab and durvalumab, respectively, in combination with chemotherapy as first-line treatment for advanced or recurrent EC
- Impact of MSI/MMR status on outcomes with the addition of anti-PD-1/PD-L1 antibodies to chemotherapy
- FDA-approved indications for dostarlimab, pembrolizumab and durvalumab for patients with advanced or recurrent EC; optimal incorporation into up-front therapy

Treatment Options for Metastatic and/or Recurrent Endometrial Cancer—FDA approved

Trials	RUBY	GY018	DUO-E
Population Included	• dMMR and pMMR • Advanced metastatic or Recurrent • Includes carcinosarcoma • Some patients with non-measurable disease • 6+ months from last treatment	• dMMR and pMMR • Advanced metastatic or Recurrent • Measurable only • 12+ months from last treatment • Includes performance status 2	• dMMR only • Advanced metastatic or Recurrent • 12+ months from last treatment • Includes carcinosarcoma
Treatment	Carboplatin AUC5 Paclitaxel 175 mg/m ² Dostarlimab 500 mg + Dostarlimab 1000 mg q6 weeks for up to 3 years	Carboplatin AUC5 Paclitaxel 175 mg/m ² Pembrolizumab 200 mg + Pembrolizumab 400 mg q6 weeks for up to 14 cycles	Carboplatin AUC5 Paclitaxel 175 mg/m ² Durvalumab 1,120 mg + Durvalumab 1500 mg q4weeks until progression

1. Powell MA, et al. *Ann Oncol*. 2024;35(8):728-738; 2. Mirza MR, et al. *N Engl J Med*. 2023;388(23):2145-2158; 3. Eskander RN, et al. *Nat Med*. 2025;31(5):1539-1546; 4. Westin SN, et al. *J Clin Oncol*. 2024;42(2):283-299.

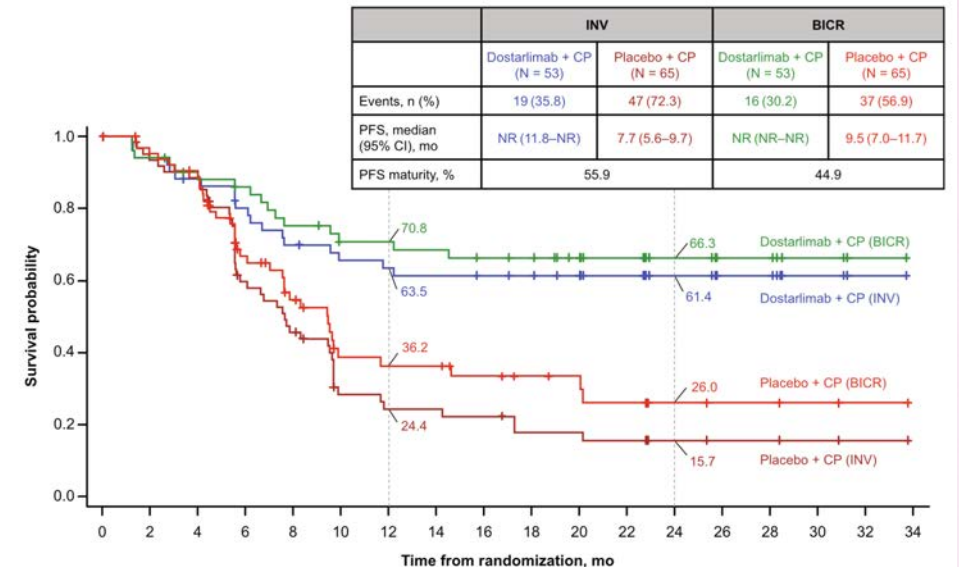
RUBY Trial

July 31, 2023: Initial FDA Approval

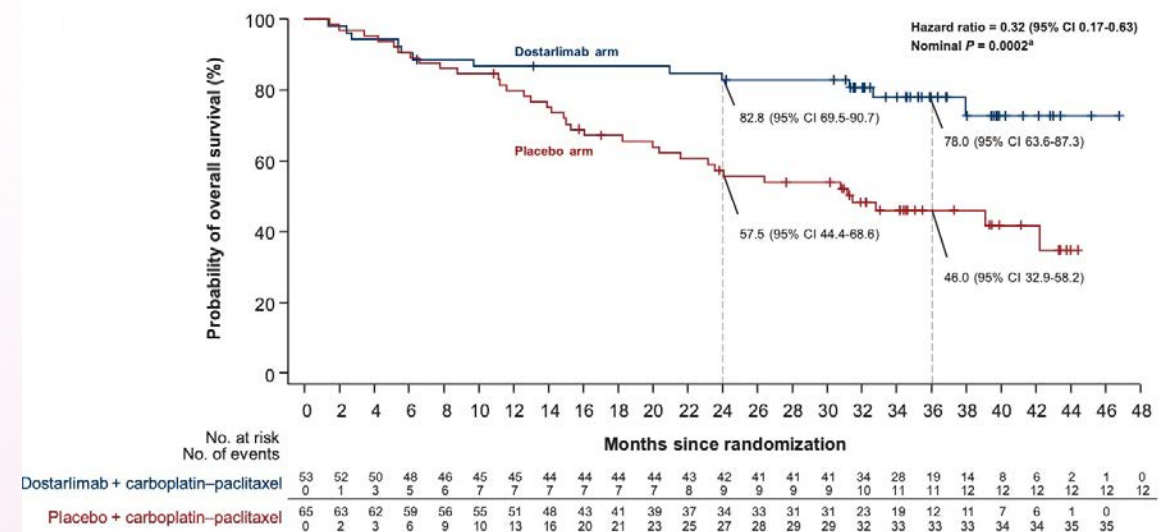
Dostarlimab + chemo followed by single-agent dostarlimab for patients with **dMMR** endometrial carcinoma

Powell MA et al. *Gyn Oncol* 2025;192:40-49;
Powell MA et al. *Ann Oncol* 2024;35(8);728-38.

Substantial PFS Benefit in dMMR/MSI-H Population

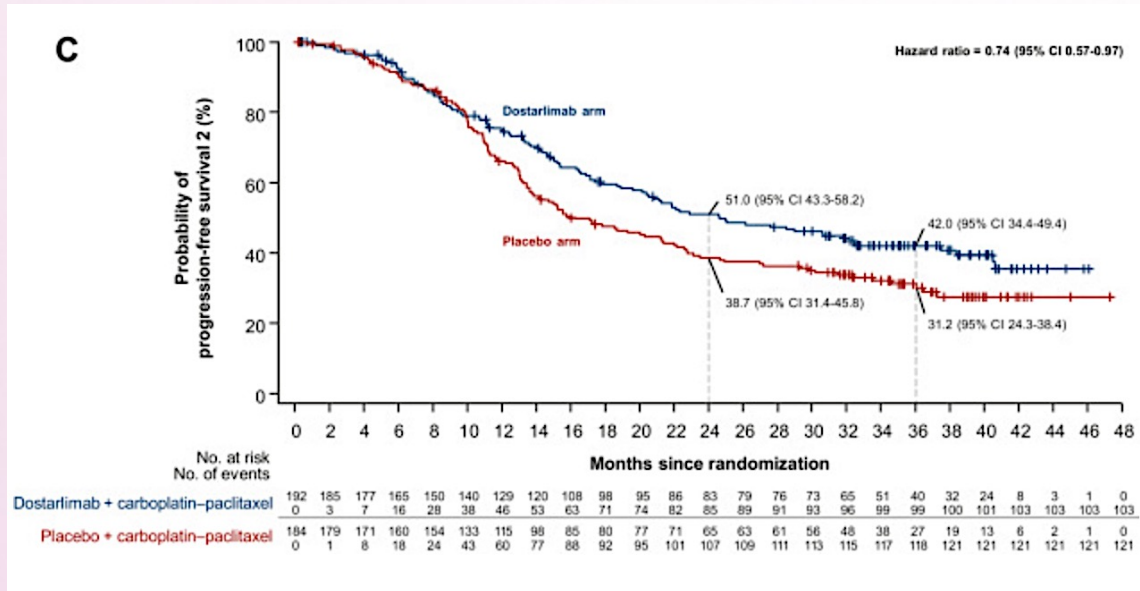


Substantial OS Benefit in dMMR/MSI-H Population

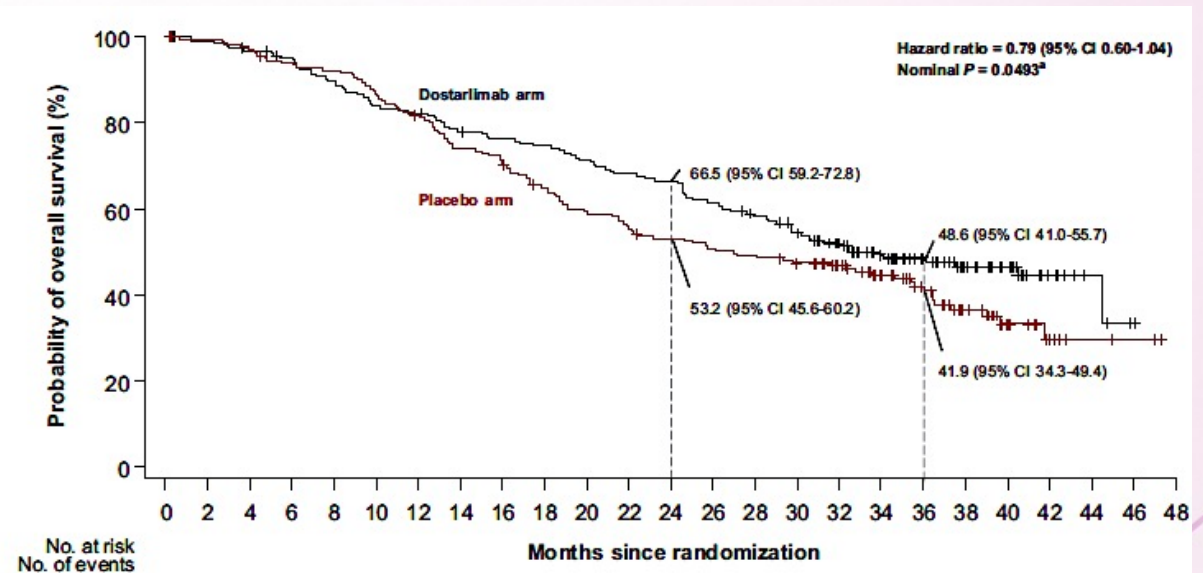


RUBY Trial- pMMR patients

PFS2 Benefit in pMMR/MSS Population



OS Benefit in pMMR/MSS Population



August 1, 2024: Expanded FDA Approval

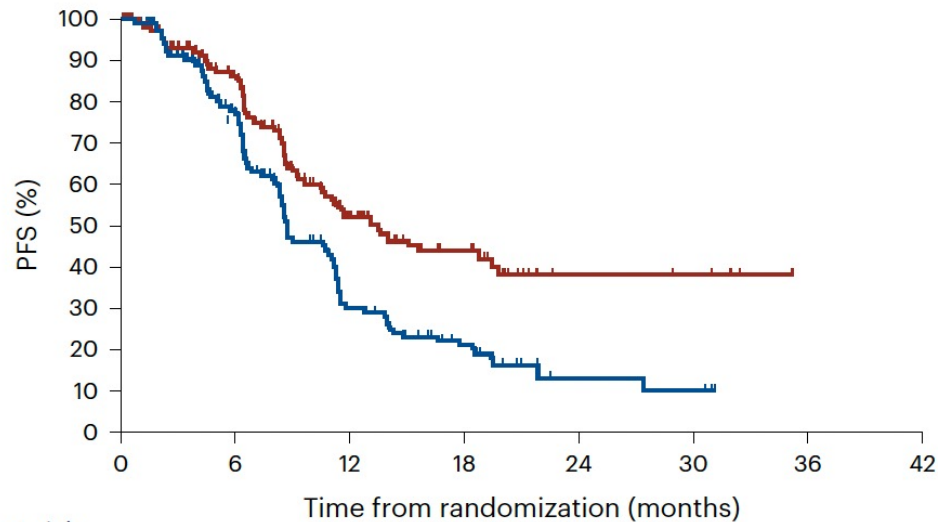
Dostarlimab + chemo followed by single-agent dostarlimab for patients with **either dMMR or pMMR** endometrial carcinoma

GY018

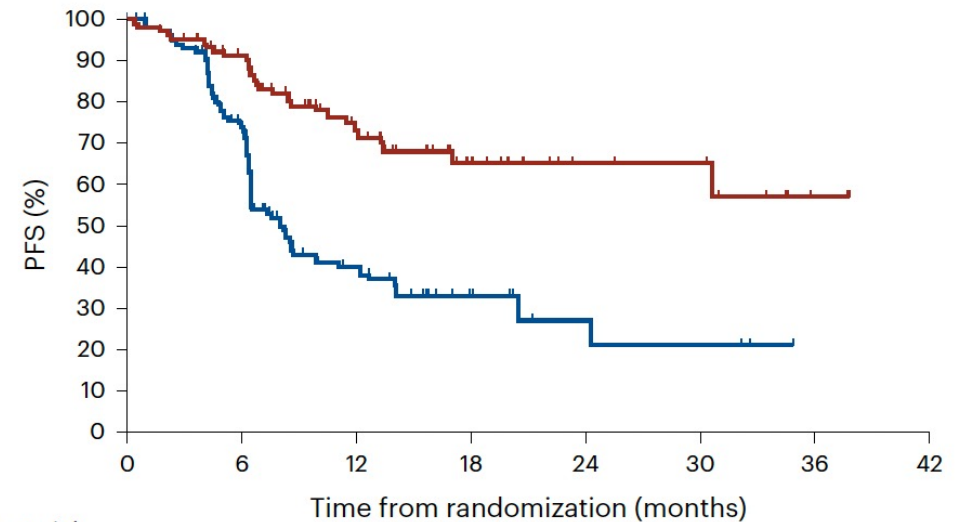
PFS in pMMR

and dMMR

	Events, n/N	Median PFS (95% CI), months	HR (95% CI) ^a , P value ^b
Pembrolizumab + CT	95/294	13.1 (10.6–19.5)	0.57 (0.44–0.74) P < 0.0001
Placebo + CT	138/294	8.7 (8.4–11.0)	



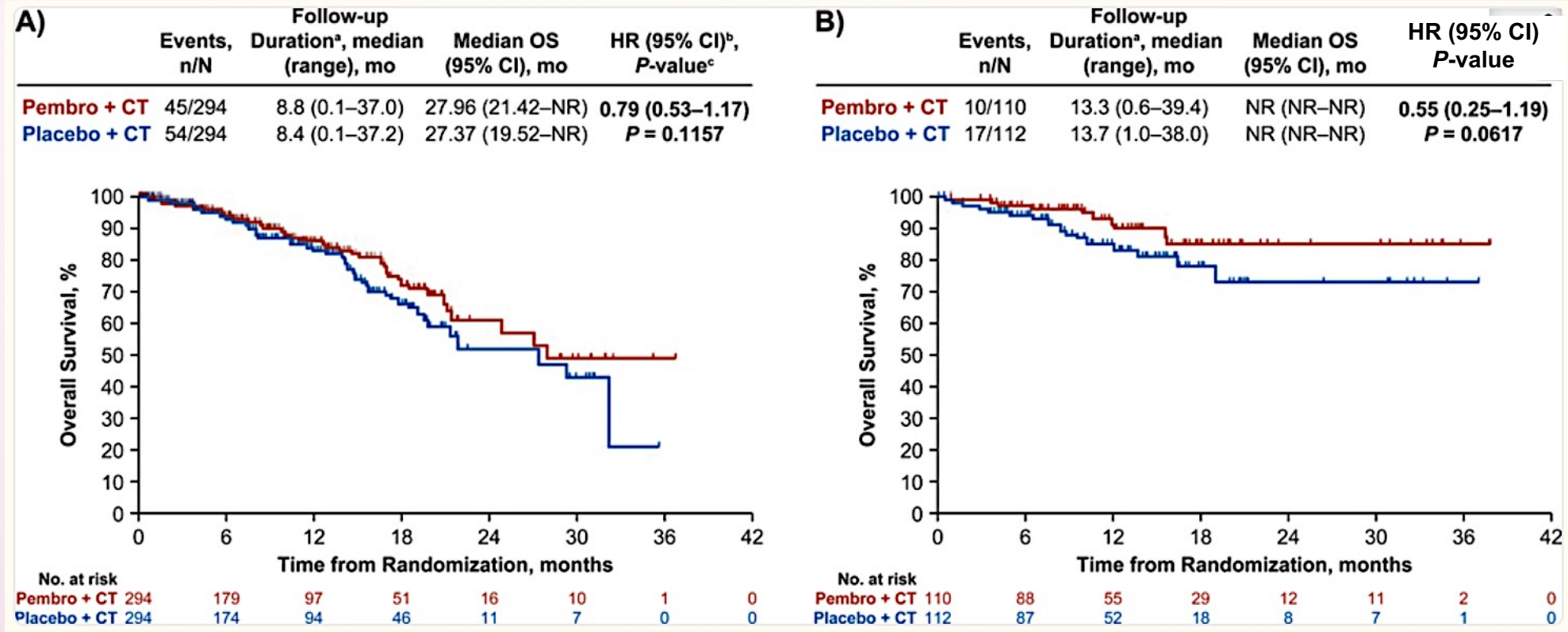
	Events, n/N	Median PFS (95% CI), months	HR (95% CI) ^a , P value ^b
Pembrolizumab + CT	29/110	NR (30.7–NR)	0.34 (0.22–0.53) P < 0.0001
Placebo + CT	60/112	8.3 (6.5–12.3)	



GY018

OS in pMMR

and dMMR



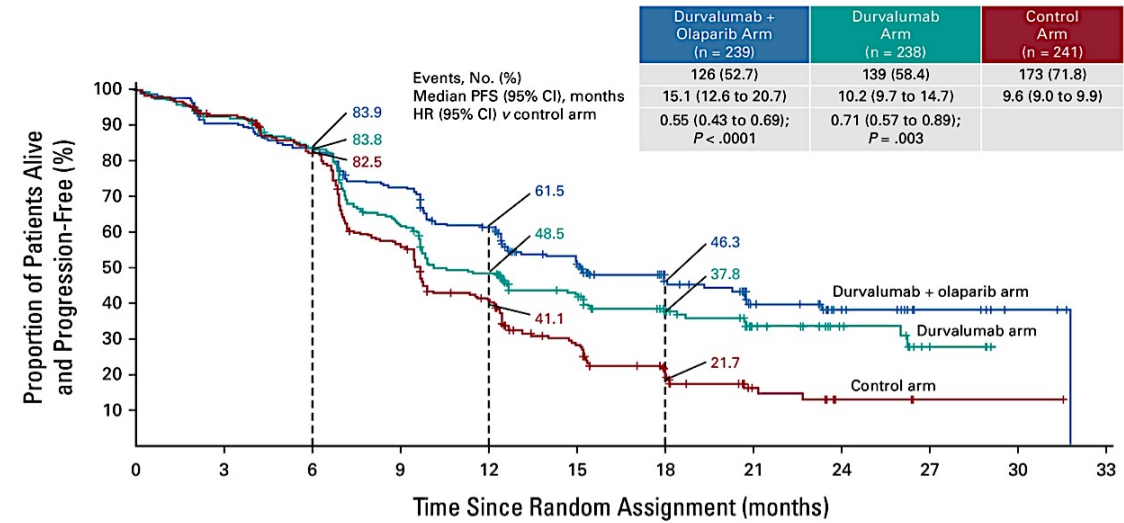
June 17, 2024: FDA Approval

Pembrolizumab + chemo followed by single-agent pembrolizumab
for patients with **either dMMR or pMMR** endometrial carcinoma

DUO-E

- June 14, 2024: FDA Approval
- Durvalumab + chemotherapy followed by single-agent durvalumab for patients with dMMR endometrial carcinoma

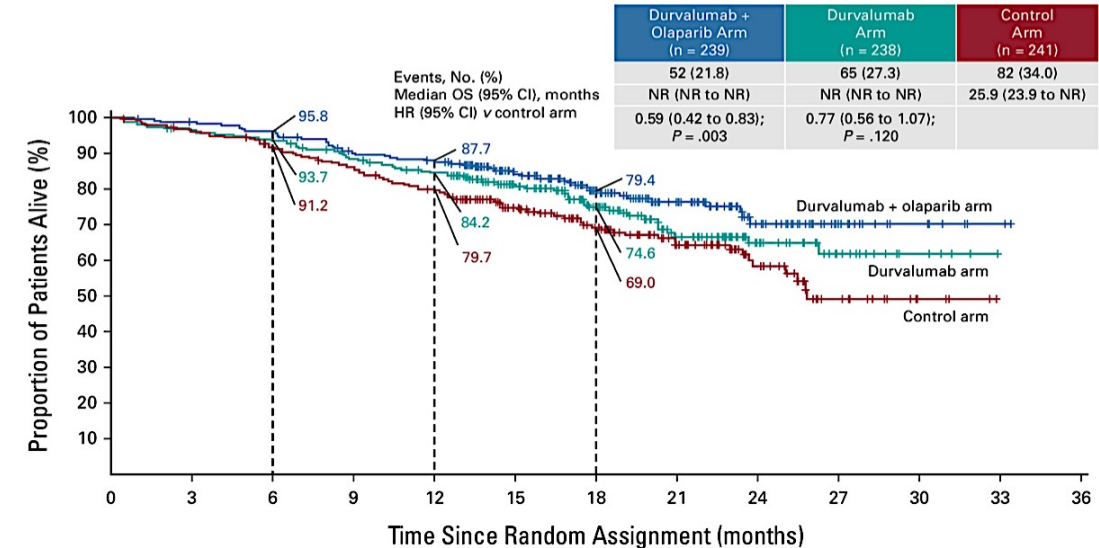
A



No. at risk:

Durvalumab + olaparib arm	239	214	198	169	139	95	51	30	16	7	3	0
Durvalumab arm	238	211	188	138	105	69	45	26	13	5	0	0
Control arm	241	213	184	125	86	45	26	10	3	1	1	0

B



No. at risk:

Durvalumab + olaparib arm	239	233	227	208	202	152	109	77	38	18	8	2	0
Durvalumab arm	238	227	221	205	192	147	105	64	34	17	6	0	0
Control arm	241	229	215	201	185	136	104	69	35	15	4	0	0

Patient Case

64 y.o. female had TLHBSO, BSLN 9/30/2024 at outside hospital, Stage IB G2 endometrioid adenocarcinoma, + LVSI, 71% myometrial invasion, MLH1+PMS2 loss, +MLH1 promoter methylation. **Completed brachytherapy in December 2024**

- **Presents 1/20/2026 with abdominal discomfort, worsens with position changes, subsides with passing gas and walking. Occasional rectal bleeding, described as red blood not mixed with stool**
- PMH: back pain, GERD, Pseudogout
- PSH: cholecystectomy, laparoscopic USO, TLHUSO, BSLN 9/2024
- SH: divorced, has a baking business, retired case manager, former smoker
- POBGYNHX: G3P3, children live nearby
- FH: mother with breast cancer in her 50s

Physical Exam

BP 147/77 | Pulse 87 | Temp 37.1 ° C (98.7 ° F) (Forehead) | Ht 5' 2" (1.575 m) | Wt 190 lb 9.6 oz (86.5 kg) | SpO2 97% | BMI 34.86 kg/m²

ECOG performance status: 0

General: Pleasant female in no apparent distress. AAOx3

HEENT: Mucous membranes: pink and moist. No scleral icterus

Lymph: No supraclavicular or anterior cervical lymphadenopathy.

Pulmonary: Speaks in full sentences, no labored breathing

Abdomen: soft, non tender, slightly distended, no fluid wave, no masses, no hepatosplenomegaly

Pelvic:

EGWNL

Vaginal atrophy and shortening noticed

No palp masses, NT

Rectum: no masses, NT

Extremities: no lower extremity edema, no calf tenderness

Neuro: Grossly intact, no focal deficits

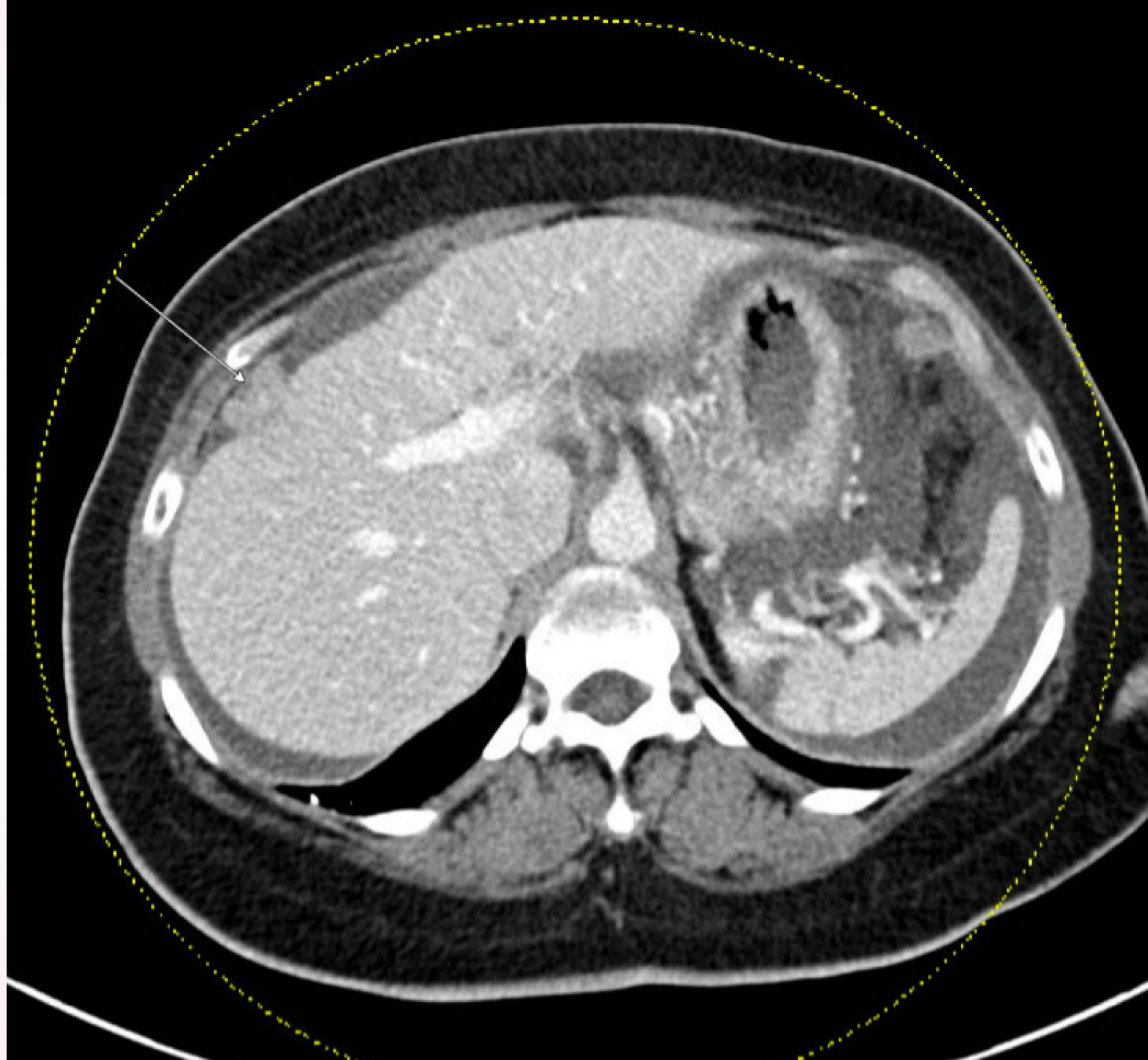
Psych: Appropriate mood and affect, good judgement

CT 1/27/2026

ONCOLOGIC FINDINGS:

History of endometrial adenocarcinoma status post hysterectomy, bilateral salpingo-oophorectomy, and sentinel lymph node dissection with:

- New moderate volume ascites and multifocal new enhancing peritoneal nodules/masses in the pelvis and right perihepatic space, the largest one measuring up to 6.6 cm along the left pelvic sidewall (3-121), compatible with peritoneal carcinomatosis



- Started on carboplatin, paclitaxel, dostarlimab
- Now s/p cycle 6 of carboplatin, paclitaxel, dostarlimab on C1 of dostarlimab maintenance
- C2 of chemo developed lower extremity rash
 - Tried topical Benadryl and hydrocortisone without relief
 - Methylprednisolone dose pack with resolution

Discussion Questions

How do you choose among dostarlimab, pembrolizumab and durvalumab in combination with first-line chemotherapy for individual patients with MSI-H/dMMR EC? What about for those with MSS/pMMR disease?

Do you believe these regimens are essentially equivalent in terms of efficacy and tolerability?

Are there any patients with newly diagnosed advanced EC for whom you wouldn't currently add an anti-PD-1/PD-L1 antibody to up-front chemotherapy?

Tolerability and Other Practical Considerations with the Use of Anti-PD-1/PD-L1 Antibodies in Advanced Endometrial Cancer

Sarah Karpen PA-C
UC San Diego Health
Division of Gynecologic Oncology

Agenda

01

Incidence and spectrum of immune-mediated adverse events (AEs) with anti-PD-1/PD-L1 antibodies

02

Recommended monitoring and management paradigms for immune-related AEs with immune checkpoint inhibitors

03

Strategies to discern whether toxicities stem from anti-PD-1/PD-L1 antibodies or their therapeutic partners when administered in combination

04

Relative and absolute contraindications to anti-PD-1/PD-L1 antibody therapy; role in patients with preexisting autoimmune conditions or a history of solid organ transplant

Incidence & Spectrum of Immune-Related Adverse Events

40-45%

of patients have any AE

92%

AEs are mild to moderate (Grade 1-2)

<1%

fatal irAE rate with monotherapy (~0.36-0.38%)

Most Common irAEs

- Rash / Pruritus (~10% each)
- Diarrhea (9.5%)
- Hypothyroidism (6.1%)
- AST/ALT increase (3.1-3.4%)
- Vitiligo (3.3%)
- Hyperthyroidism (2.8%)
- Pneumonitis (2.8%)

High Severity irAEs (Grade ≥3 risk)

- Hepatitis — ~50% of cases are Grade ≥3
- Colitis — ~38% of cases are Grade ≥3
- Pneumonitis — ~24% of cases are Grade ≥3; most common irAE-related death
- Myocarditis, Myasthenia Gravis, GBS — rare but potentially fatal
- Stevens-Johnson Syndrome / TEN — rare

Incidence substantially lower with monotherapy vs combination therapy

irAE Incidence by Organ System

Organ System / irAE	All-Grade Incidence	Grade ≥3 Incidence
ENDOCRINE		
Hypothyroidism	6.1%	0.08%
Hyperthyroidism	2.8%	—
Adrenal Insufficiency	0.69%	0.18%
Type 1 Diabetes	Uncommon	0.18%
GASTROINTESTINAL		
Diarrhea	9.5%	0.59%
Colitis	1.2%	0.47% (~38% of all colitis)
HEPATIC		
Hepatitis (AST/ALT elevation)	3.1–3.4%	~50% of cases
PULMONARY		
Pneumonitis	2.8%	0.67% (~24% of all pneumonitis)
DERMATOLOGIC		
Rash / Pruritus	~10% each	Low
Vitiligo	3.3%	—

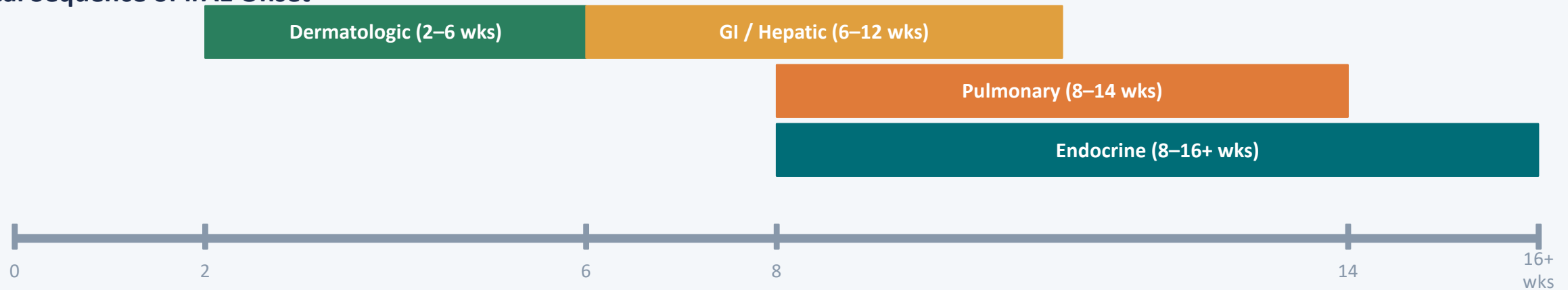
Source: Wang Y et al. JAMA Oncol. 2019

Timing of Immune-Related Adverse Events

Most irAEs occur within the first 10 weeks of therapy

Late-onset events (>1 year) occur in ~30% of patients on long-term therapy

Typical Sequence of irAE Onset



Dostarlimab Clinical Trial Data — Endometrial Cancer

RUBY trial (dostarlimab + carboplatin/paclitaxel): Hypothyroidism in 11.2% of patients

GARNET trial (dostarlimab monotherapy): Hypothyroidism and diarrhea most common at 5.8% | *Endocrinopathies predominate — manageable with hormone replacement, rarely leads to discontinuation*

Recommended Monitoring for irAEs (NCCN)

Pre-Therapy Assessment

- Physical exam
- Patient/family history of autoimmune disease
- Infectious disease screening: HIV, hepatitis A/B/C
- CBC with differential
- Complete metabolic panel (CMP)
- TSH / free T4
- Baseline ECG + high-sensitivity troponin + NT-proBNP (consider)
- PFTs for high-risk pulmonary patients (prior COPD or lung toxicity)

Routine Monitoring During Therapy

- CBC + CMP prior to each treatment cycle
- TSH + free T4 every 4–6 weeks
- Serum cortisol every 4–6 weeks
- High-risk CV patients: troponin every cycle × 3, then every 3 months
- Monitor oxygen saturation at each visit

Clinical Pearl: Endocrinopathies often asymptomatic — routine thyroid and cortisol monitoring is essential for early detection

Management of irAEs — Grade-Based Framework (ASCO/NCCN)

Grade 1 Continue ICI	Grade 2 Hold ICI	Grade 3 Hold ICI	Grade 4 Discontinue ICI
• Close monitoring • Symptomatic/supportive care • Exceptions: myocarditis, some neurologic & hematologic toxicities → hold	• Resume when symptoms resolve to ≤Grade 1 • Prednisone 1–2 mg/kg/day (oral) • Exception: myocarditis → permanent discontinuation	• High-dose corticosteroids (IV methylprednisolone 1–2 mg/kg/day) • Consider permanent discontinuation (organ-dependent) • Specialist consultation often required	• Permanently discontinue ICI • IV high-dose corticosteroids • Exception: endocrinopathies controlled by hormone replacement may continue

Steroid Tapers: 6–8 weeks (or longer) for pneumonitis, hepatitis, or neuromuscular toxicities | **Preferred agents:** Prednisone (oral) · Methylprednisolone (IV) | Prophylactic steroids: **NOT indicated**

Management Example: ICI-Mediated Colitis / Diarrhea

Grade 1

- Continue ICI
- Hydration
- Dietary modification
- Consider loperamide
- Consider holding ICI

Grade 2

- Hold ICI
- Prednisone 1–2 mg/kg/day
- Colonoscopy with biopsy
- If no response in 3 days → IV steroids

Grade 3

- Hold ICI
- IV methylprednisolone 1–2 mg/kg/day
- Inpatient care
- GI consultation

Grade 4

- Discontinue ICI permanently
- IV steroids
- Inpatient care
- Urgent GI consultation

Steroid-Refractory Options

First-line: Infliximab 5 mg/kg or Vedolizumab

If still refractory: Tofacitinib or Ustekinumab | Fecal microbiota transplant may be considered in selected cases

Supportive care: Blood glucose monitoring, PPI/H2 blocker (gastritis prevention), antimicrobial/antifungal prophylaxis, vitamin D/calcium supplementation

Distinguishing ICI vs Chemotherapy/PARP Inhibitor Toxicities

Strongly Suggests ICI	Overlapping AEs	Strongly Suggests Chemo/PARP
• Hypothyroidism / Hyperthyroidism • Thyroiditis • Adrenal insufficiency • Pneumonitis • Myocarditis • Inflammatory arthritis • Clinical pearl: any "-itis" is more likely ICI-related	• Diarrhea • Hepatotoxicity (AST/ALT elevation) • Fatigue • Rash • Note: Timing and histopathology can help differentiate	• Neutropenia / Thrombocytopenia • Myelosuppression • Alopecia • Peripheral neuropathy • Cycle-dependent nausea/vomiting • Note: Chemo may suppress or delay irAEs

Dechallenge Approach

1. Low suspicion for irAE? Hold the non-ICI agent first and monitor before starting immunosuppression | **2. Toxicity resolves?** Non-ICI likely causative | **3. Toxicity persists?** Suspect irAE → hold ICI and initiate management | **4. Responds to steroids?** *Diagnostic clue for irAE*

Contraindications to Anti-PD-1/PD-L1 Therapy

ABSOLUTE CONTRAINDICATION

Severe hypersensitivity to the drug or its components — ICI is contraindicated regardless of clinical context

RELATIVE CONTRAINDICATIONS — Risk Stratification

Higher Risk

- Uncontrolled autoimmune disease on immunosuppression
- Solid organ transplant (rejection risk)
- Prior allogeneic HCT
- Active myasthenia gravis
- Multiple sclerosis

Moderate / Consider With Caution

- Any autoimmune disorder (even controlled)
- Chronic hepatitis B or C
- HIV infection
- Significant renal or hepatic insufficiency
- Preexisting autoimmune neurologic disorders

Risk-benefit assessment required; multidisciplinary consultation recommended for patients with autoimmune conditions or prior transplant history

Case Study: irAE in Advanced Endometrial Cancer

Patient Profile

70-year-old female | PMH: HTN, obesity

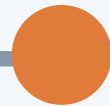
Stage IVB endometrial cancer — dMMR (MLH1/PMS2 loss), MSI-high, TP53 wild-type, HER2-negative, ER/PR-positive

Surgery: Robotic hysterectomy, BSO, omentectomy, lymph node sampling

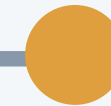
Treatment: Carboplatin + paclitaxel + pembrolizumab every 3 weeks



Cycles 1–4
Treatment



After Cycle 4
Symptoms



irAE Identified
& Managed



6-Week
Follow-Up

Presenting Symptoms & Labs (After Cycle 4)

Symptoms: Worsening fatigue, constipation, dry skin

TSH: 18.6 (markedly elevated)

Free T4: Low

Diagnosis: ICI-induced hypothyroidism (Grade 2)

Management & Outcome

Action: ICI continued; levothyroxine 50 mcg daily initiated

6-Week Follow-up TSH: 5.2 (normalized)

Free T4: Normal

Key Teaching: Endocrinopathies managed with hormone replacement — ICI does not need to be discontinued

Agenda

Introduction: Biology of Endometrial Cancer (EC)

Module 1: First-Line Therapy for Advanced or Recurrent EC

Module 2: Potential Benefits of PARP Inhibition Combined with Immunotherapy in Advanced EC

Module 3: Role of Lenvatinib/Pembrolizumab in the Management of Progressive Advanced EC

Module 4: Other Nursing Considerations in the Care of Patients with Advanced EC

Potential Benefits of PARP Inhibition Combined with Immunotherapy in Advanced Endometrial Cancer

J. Alejandro Rauh-Hain, MD, MPH
MD Anderson Cancer Center

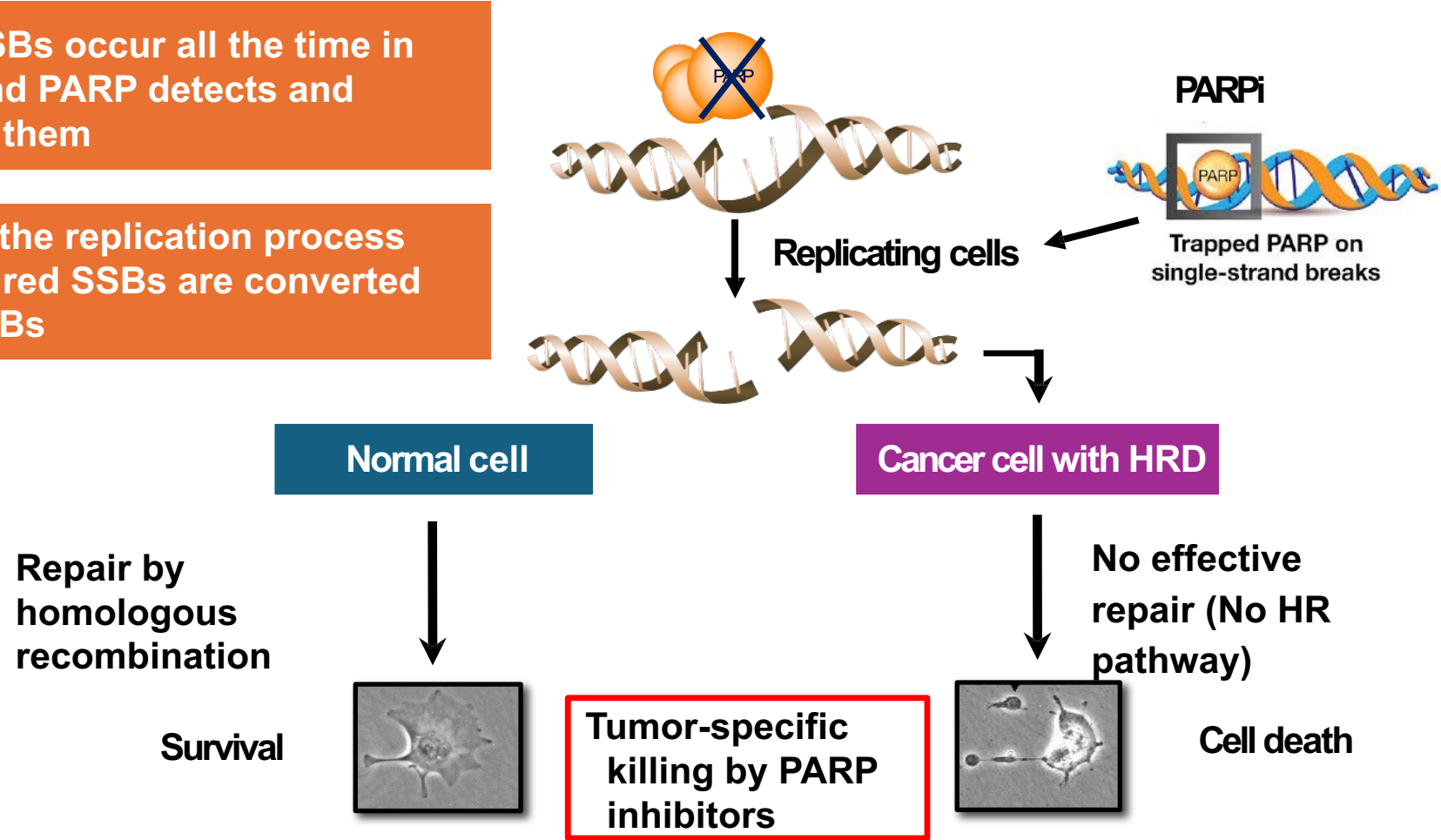
Landmark Immunotherapy Frontline Trials

	NRG-GY018	RUBY 1	AtTEnd	DUO-E	RUBY 2
dMMR Immuno	NR (31-NR)	NR (12-NR)	NR (12-NR)	NR (NR-NR)	
dMMR Control	8 (6-10)	8 (6-10)	7 (6-9)	7 (7-15)	8 (5-NR)
dMMR Imm + PARP				32 (12-NR)	NR (11.8-NR)
d Hazard Ratio	0.3 (0.2-0.5)	0.3 (0.2-0.5)	0.4 (0.2-0.6)	0.4 (0.2-0.8)	
d Hazard Ratio + PARP				0.4 (0.2-0.7)	0.5 (0.2-0.9)
pMMR Immuno	13 (10-19)	10 (9-13)	9 (9-10)	10 (9-12)	
pMMR Control	9 (8-11)	8 (8-10)	9 (8-10)	10 (9-10)	8 (8-10)
pMMR Imm + PARP				15 (12-18)	14 (10-17)
p Hazard Ratio	0.5 (0.4-0.7)	0.8 (0.6-1)	0.9 (0.7-1.2)	0.8 (0.6-1)	
p Hazard Ratio + PARP				0.6 (0.4-0.7)	0.6 (0.4-0.9)

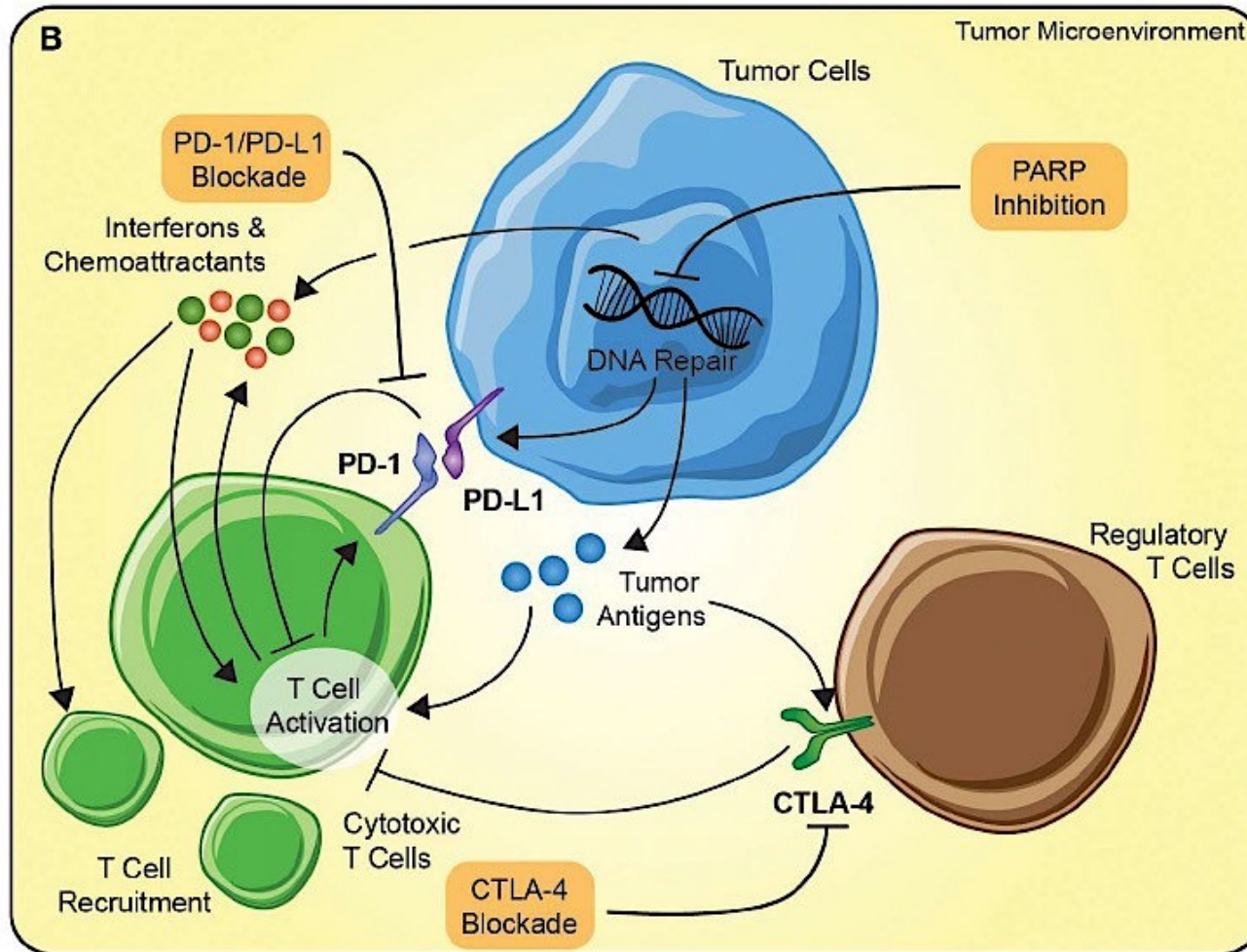
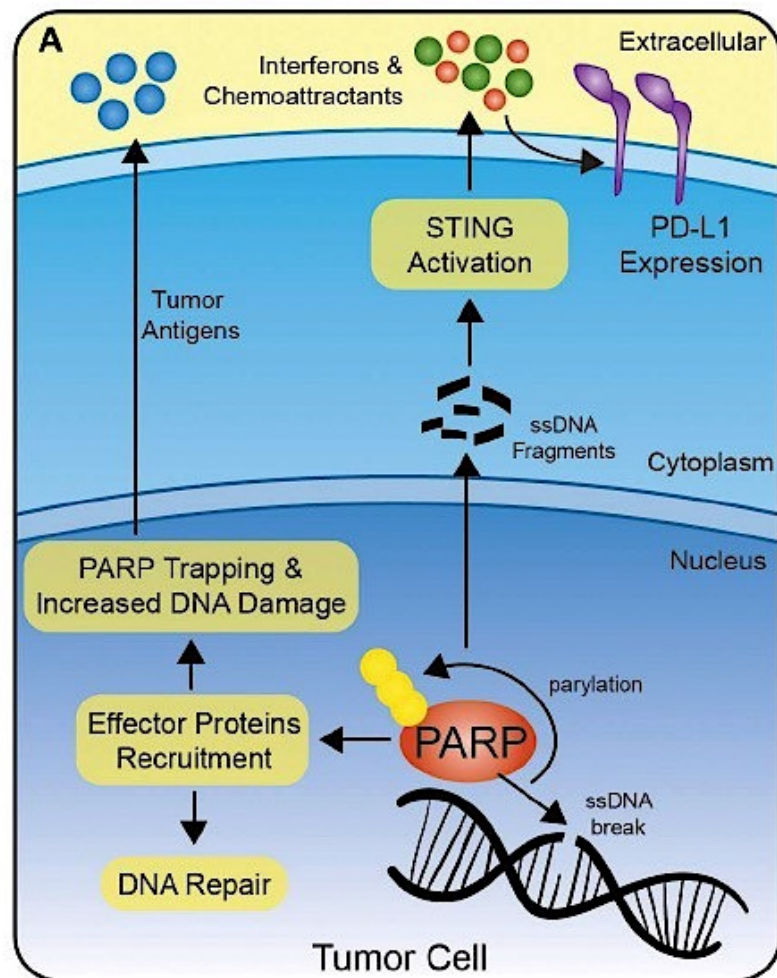
Mechanism of Action of PARP Inhibitors

DNA SSBs occur all the time in cells and PARP detects and repairs them

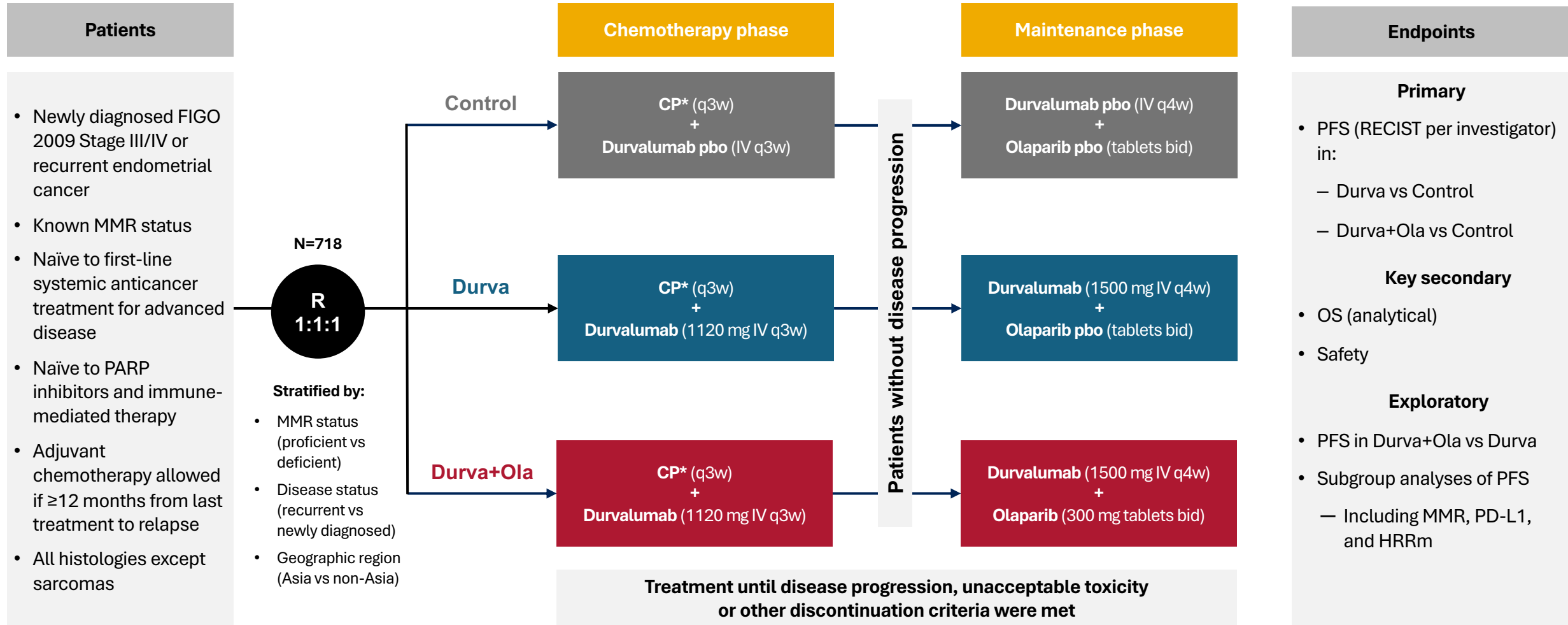
During the replication process unrepaired SSBs are converted into DSBs



The Potential Synergy Between PARP Inhibition and Immune Checkpoint Blockade



DUO-E study design



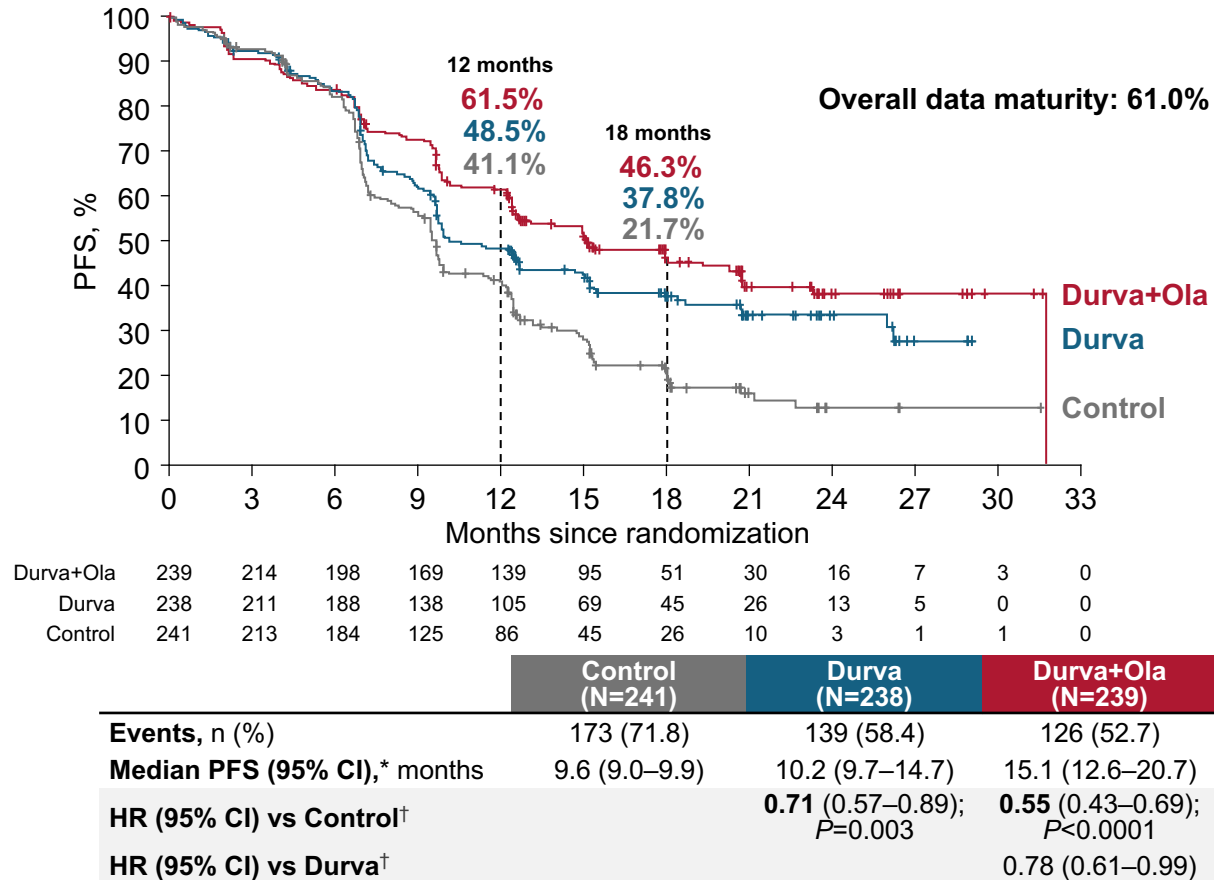
*Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg per mL/min and paclitaxel 175 mg/m².

bid, twice daily; CP, carboplatin/paclitaxel; Durva, durvalumab; FIGO, International Federation of Gynaecology and Obstetrics; HRRm, homologous recombination repair mutation; IV, intravenously; MMR, mismatch repair; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Ola, olaparib; OS, overall survival; PARP, poly(ADP-ribose) polymerase; pbo, placebo; q3(4)w, every 3(4) weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumours.

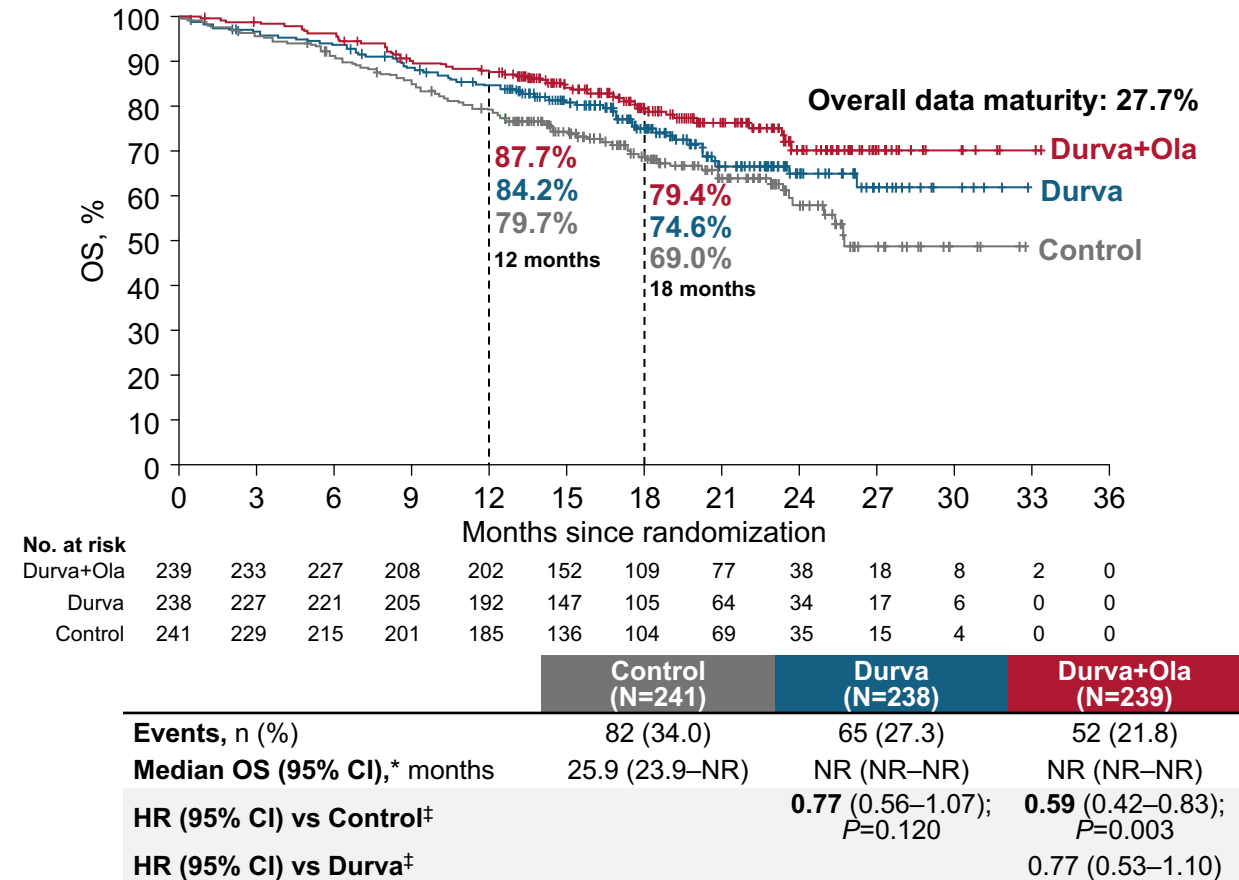
Westin SN et al. *J Clin Oncol* 2023;DOI:10.1200/JCO.23.02132.

DUO-E met its dual primary endpoints

PFS: dual primary endpoints



OS: secondary endpoint; interim analysis



The median (range) duration of follow-up for PFS was 12.6 (0.0–31.6), 15.4 (0.0–29.1), and 15.4 (0.0–31.7) months in censored patients for the Control, Durva, and Durva+Ola arms, respectively. The median (range) duration of follow-up for OS was 18.6 (0.5–32.9), 18.4 (2.1–33.0), and 18.7 (1.1–33.4) months in censored patients for the Control, Durva, and Durva+Ola arms, respectively. PFS and OS rates were estimated by the KM method.

*CI for median PFS and OS is derived based on the Brookmeyer–Crowley method; [†]The primary PFS analysis for each comparison was performed separately. The HR and CI were estimated from a Cox proportional hazards model stratified by MMR and disease status. The CI was calculated using a profile likelihood approach. The *P* value was calculated using a log-rank test stratified by MMR and disease status; [‡]The HRs were estimated from an unstratified Cox proportional hazards model. The CI was calculated using a profile likelihood approach. *P* values failed to reach statistical significance.

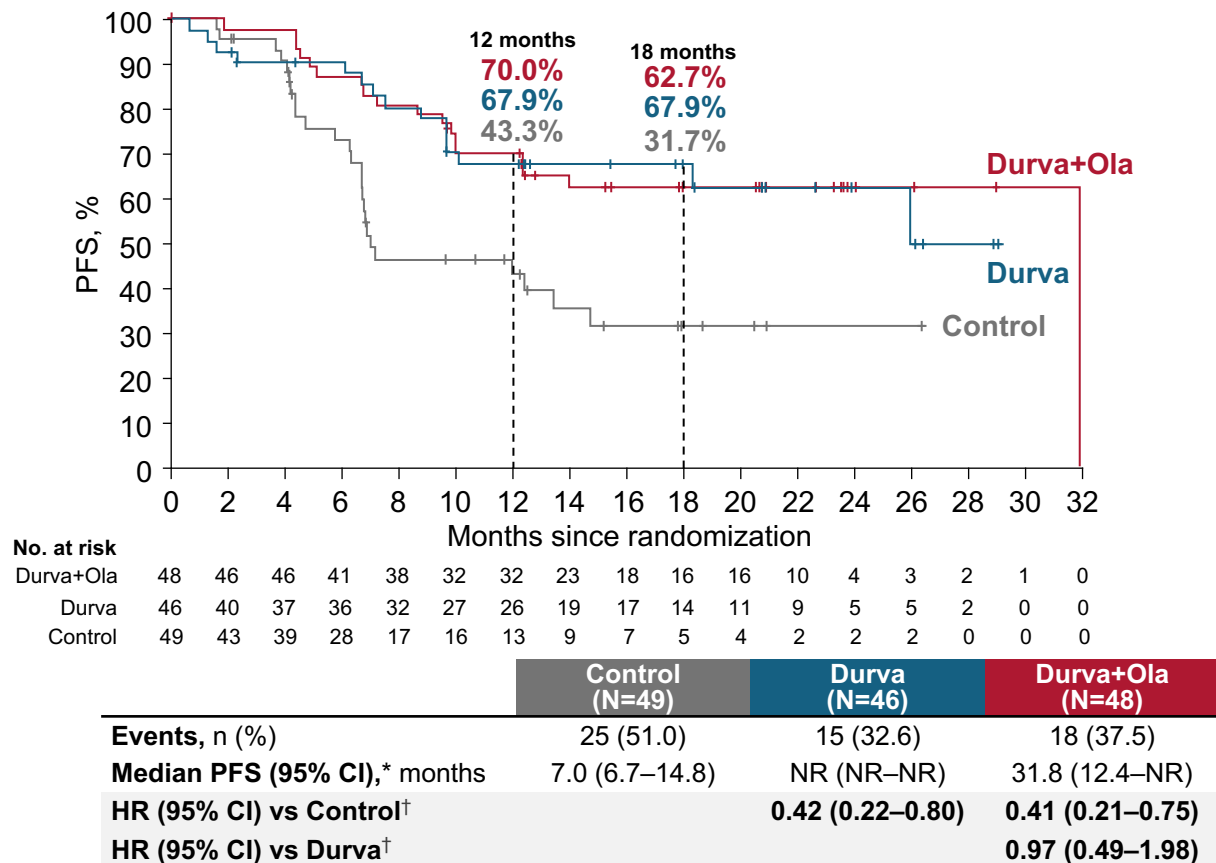
CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; KM, Kaplan–Meier; NR, not reached.

Figure borrowed with permission from Westin SN *et al. J Clin Oncol* 2023;DOI:10.1200/JCO.23.02132

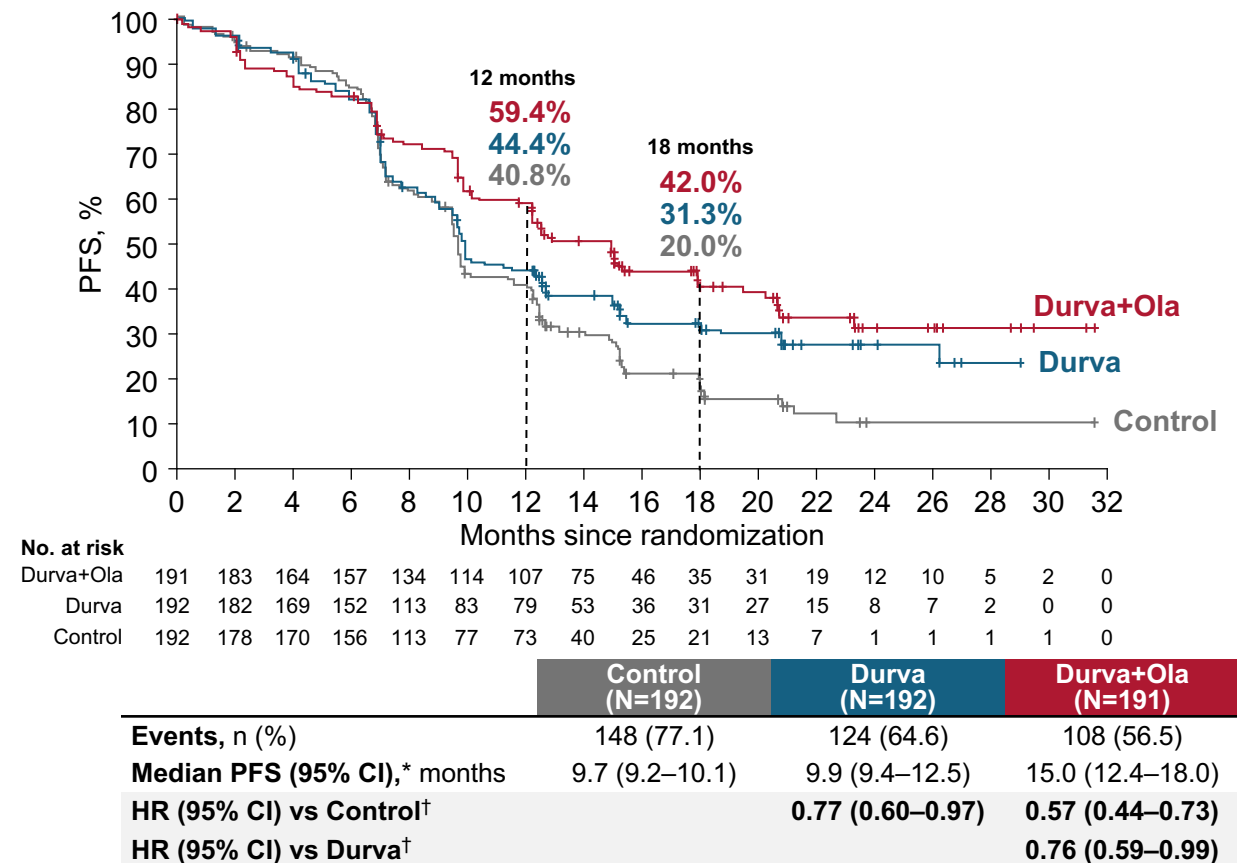
Subgroup analyses of PFS by MMR status

Prespecified exploratory analyses

dMMR (20% of population)



pMMR (80% of population)



Exploratory subgroup analysis. MMR status evaluated using the Ventana immunohistochemistry MMR panel. PFS rates were estimated by the KM method.

*CI for median PFS was derived based on the Brookmeyer–Crowley method; [†]The HR and CI were estimated from an unstratified Cox proportional hazards model.

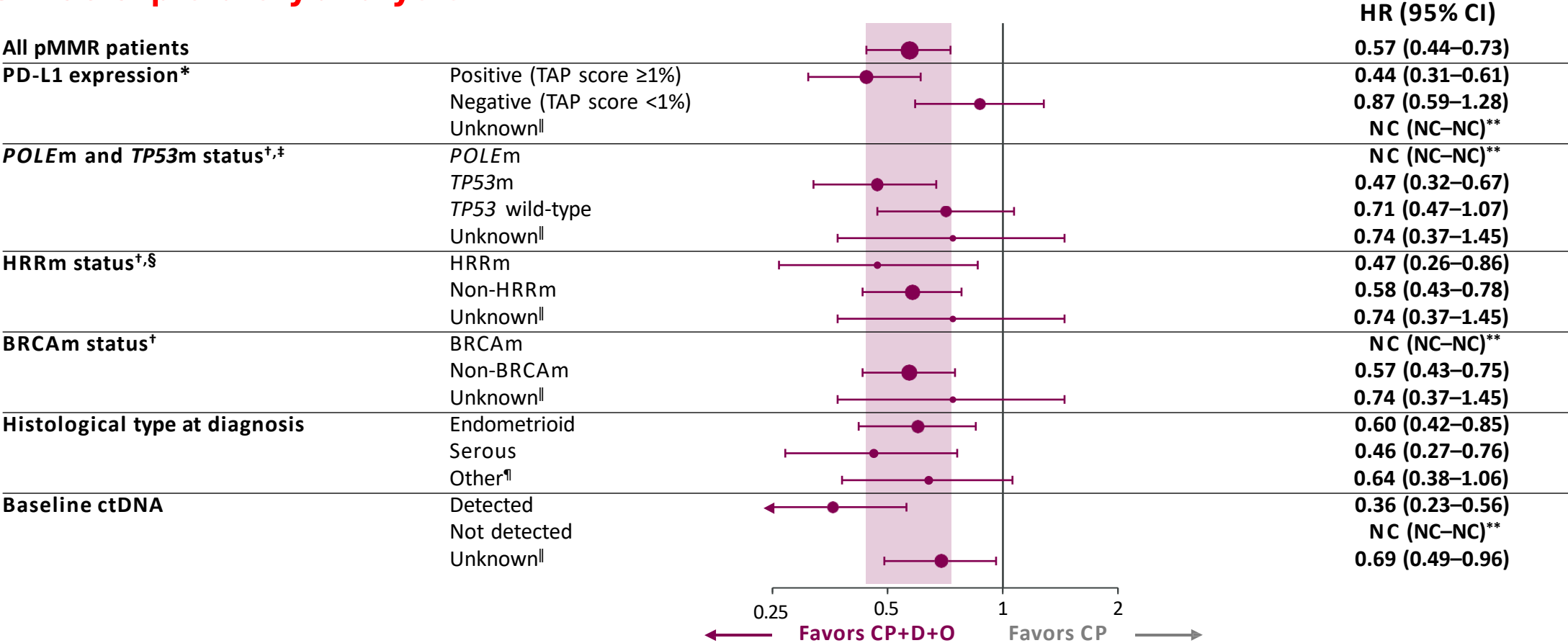
dMMR, mismatch repair deficient; pMMR, mismatch repair proficient.

Figure borrowed with permission from Westin SN et al. *J Clin Oncol* 2023;DOI:10.1200/JCO.23.02132

pMMR subpopulation: PFS by biomarker subgroup

CP + durvalumab + olaparib vs CP

Post hoc exploratory analysis



DCO: April 12, 2023. *PD-L1 expression was evaluated using the VENTANA PD-L1 (SP263) assay. PD-L1 positive defined as TAP ≥1%, PD-L1 negative defined as TAP <1%; [†]Status determined retrospectively in two ways: from tissue samples (FoundationOne[®]CDx assay; Foundation Medicine, Inc.), and by molecular profiling of ctDNA (FoundationOne[®]Liquid CDx; Foundation Medicine, Inc.) from blood samples; [‡]TP53m status defined as a sample with a deleterious or suspected deleterious mutation in TP53 excluding samples with a deleterious or suspected deleterious mutation in POLE; TP53 wild-type status defined as a sample with no deleterious or suspected deleterious mutation in TP53 excluding samples with a deleterious or suspected deleterious mutation in POLE; [§]Positive HRRm status defined as a sample with a deleterious or suspected deleterious mutation in any of the following prespecified genes: ATM, BRCA1, BRCA2, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L; negative HRRm status (non-HRRm) defined as a sample with no deleterious or suspected deleterious mutations in any of the prespecified genes; ^{||}‘Unknown’ status included patients recruited in China (where molecular testing was not performed) and/or patients who withdrew consent and/or those without available samples; *‘Other’ includes carcinosarcoma, mixed epithelial, clear cell, undifferentiated, mucinous, and other; **Not calculated due to low event numbers. NC, not calculable.

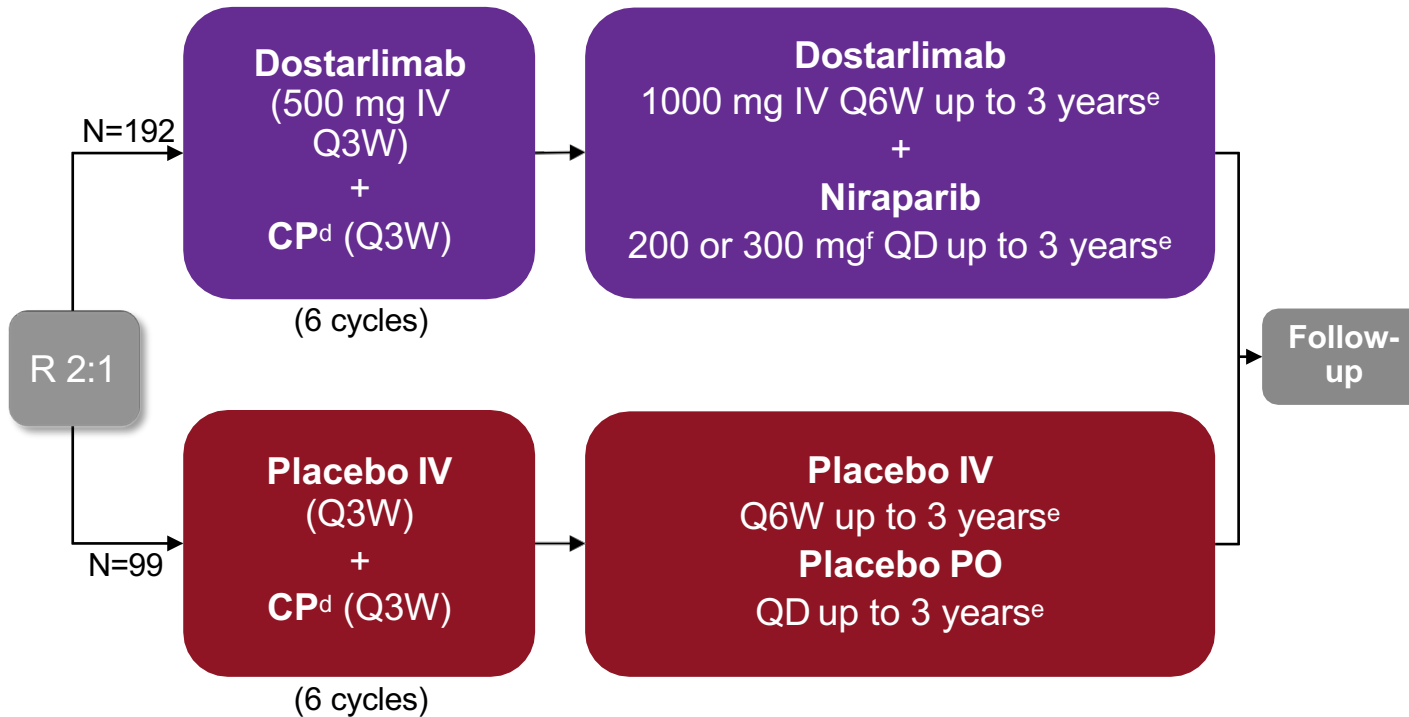
ENGOT-EN6-NSGO/GOG-3031/RUBY Part 2

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



Primary endpoint

- PFS by INV per RECIST v1.1
 - Overall
 - MMRp/MSS

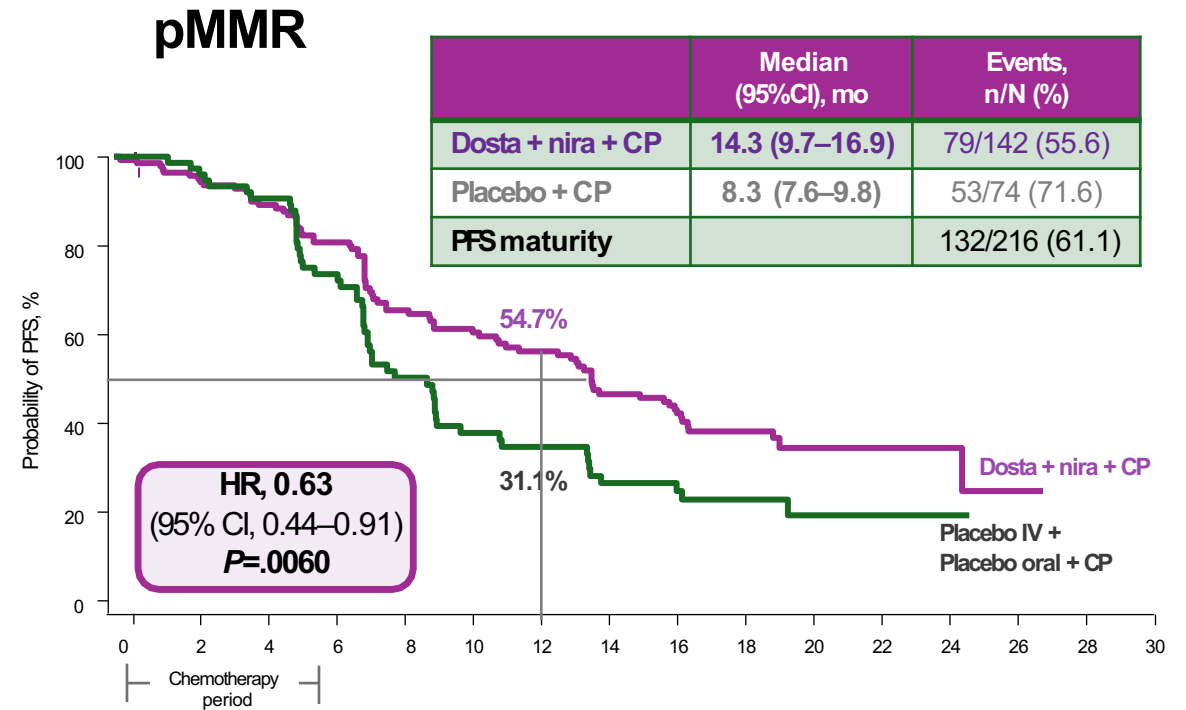
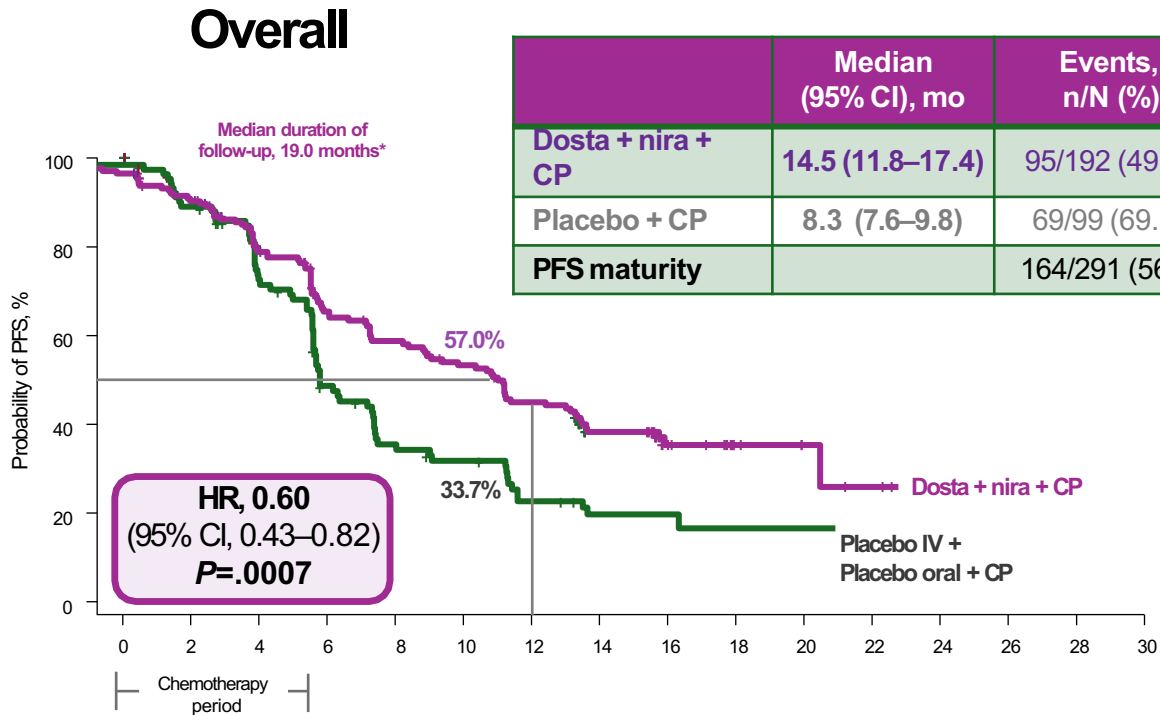
Secondary endpoints

- OS
- PFS by BICR
- ORR
- DOR
- DCR (BOR of CR, PR, or SD)
- PFS2
- HRQOL/PRO
- PK
- Safety

On-study imaging assessments were performed Q6W (±7 days) from the randomization date until week 25 (cycle 8), followed by Q9W (±7 days) until week 52. Subsequent tumor imaging was performed every 12 weeks (±7 days) until radiographic PD was documented by investigator assessment per RECIST v1.1 followed by 1 additional imaging 4–6 weeks later, or subsequent anticancer therapy was started, whichever occurred first. Thereafter, scans were performed per standard of care.

^aHistologically/cytologically proven advanced or recurrent EC; stage III/IV disease or first recurrent EC with low potential for cure by radiation therapy or surgery alone or in combination. ^bCarcinosarcoma, clear cell, serous, or mixed histology permitted (mixed histology containing ≥10% carcinosarcoma, clear cell, or serous histology). ^cPatients were randomized based on either local or central MMR/MSI testing results. Central testing was used with local results were not available. For local determination of MMR/MSI status, IHC, next-generation sequencing, and polymerase chain reaction assays were accepted. For central determination of MMR/MSI status IHC per Ventana MMR RxDx panel was used. ^dCarboplatin AUC 5 mg/mL/min and paclitaxel 175 mg/m². ^eTreatment ends after 3 years, PD, 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. ^fDose of 300 mg in patients with body weight ≥77 kg and platelet count ≥150,000/μL and 200 mg in patients with body weight <77 kg or platelet count <150,000/μL or both. AUC, area under the plasma or serum concentration-time curve; BICR, blinded independent central review; BOR, best overall response; CP, carboplatin-paclitaxel; CR, complete response; DCR, disease control rate; dMMR, MMR deficient; DOR, duration of response; EC, endometrial cancer; HRQOL, health-related quality of life; IHC, immunohistochemistry; INV, investigator assessment; MMR, mismatch repair; MMRp, MMR proficient; MSI, microsatellite instability; MSI-H, MSI high; MSS, microsatellite stable; ORR, objective response rate; OS, overall survival; PARP, poly(ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetic; PO, by mouth; PR, partial response; PRO, patient-reported outcome; Q3W, every 3 weeks; Q6W, every 6 weeks; Q9W, every 9 weeks; QD, once daily; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

RUBY Part 2: Maintenance Dostarlimab ± Niraparib on PFS in Overall and pMMR Populations



Maintenance dostarlimab + niraparib resulted in a statistically significant improvement in PFS in the overall and pMMR populations

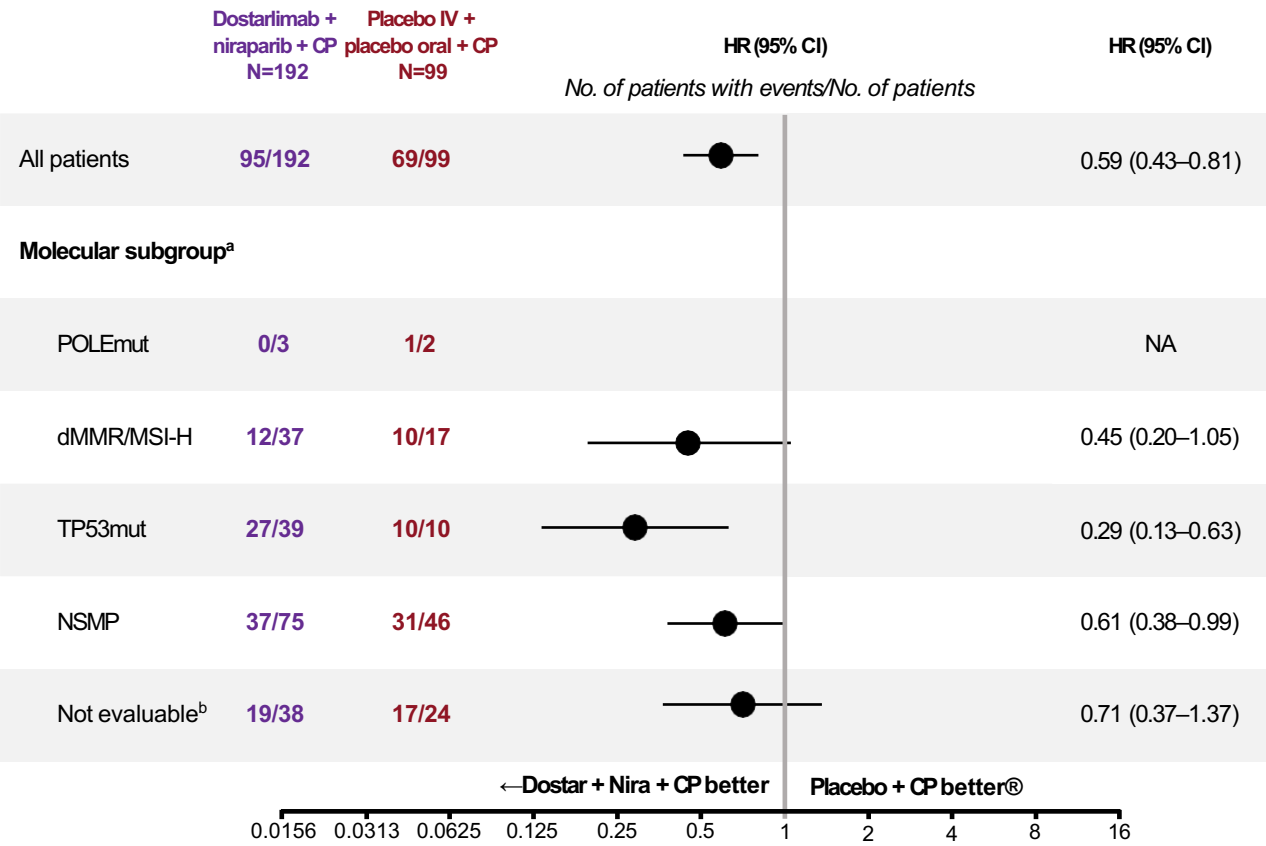
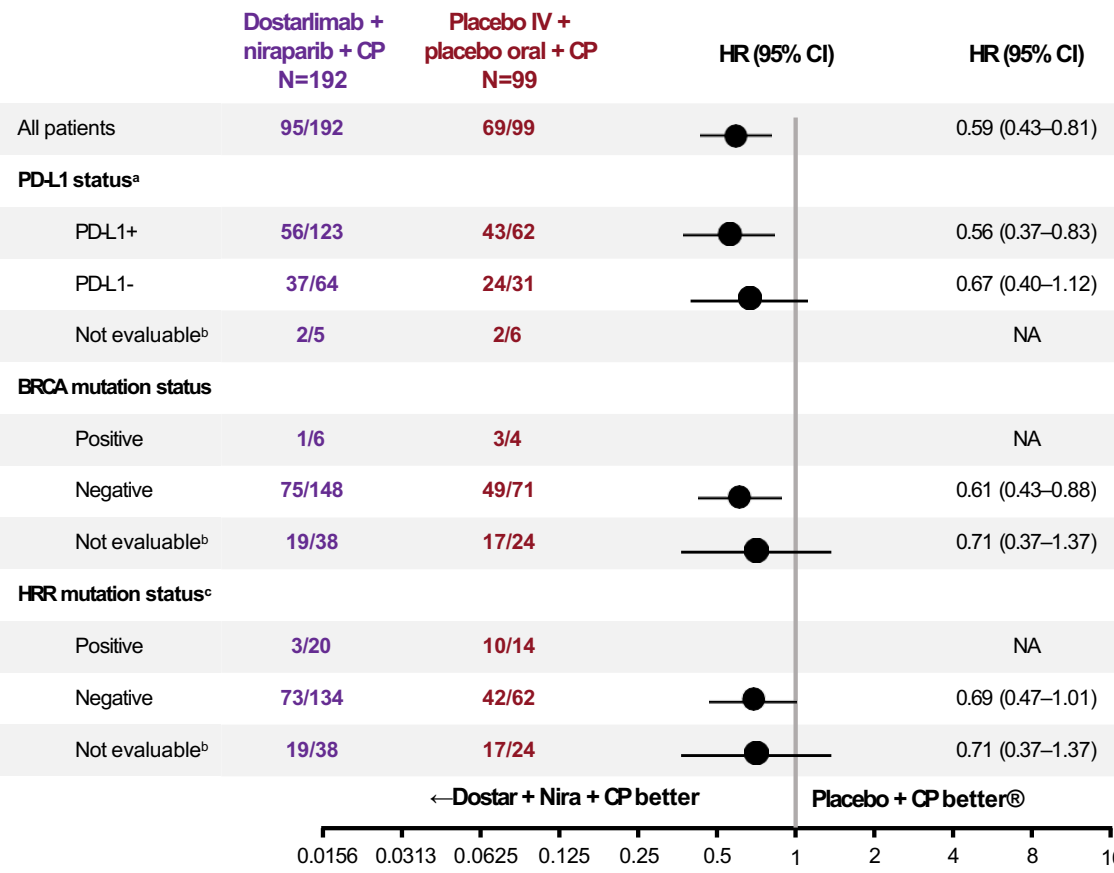
*Median expected duration of follow-up.

Nira, niraparib.

Mirza MR, et al. Presented at: 2024 ESMO Gynecological Cancers Congress; June 20-22, 2024; Florence, Italy. Oral abstract 38M0.

Selecting Which Patient May Benefit From Addition of PARPi

RUBY Part 2 ITT



Results should be interpreted with caution as the study was not powered to detect a treatment difference in any subgroup, and there were small numbers and low data maturity in some subgroups. Where there were less than 20 events in the subgroup, the HR estimation and 95% CI were not analyzed as there were too few events (“not applicable”). ^aBased on available whole exome sequencing results; ^bSample not available. ^cDefined by a mutation in 1 or more genes included in the FMI14 panel: BRCA1, BRCA2, ATM, BARD1, BRIP1, PALB2, RAD51B, RAD51C, RAD51D, RAD54L, CDK12, CHEK1, CHEK2, and FANCL. BRCA, breast cancer gene; CI, confidence interval; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; dostar, dostarlimab; HR, hazard ratio; HRR, homologous recombination repair; ITT, intention to treat; IV, intravenous; MSI-H, microsatellite instability high; mut, mutation; nira, niraparib; NSMP, no specific molecular profile; PARPi, poly (ADP-ribose) polymerase inhibitor; PD-L1, protein death ligand-1; POLE, polymerase epsilon.

Mirza MR, et al. Presented at the Society of Gynecologic Oncology Annual Meeting 2024. Presentation #LBA2.

Case Presentation

- 72-year-old postmenopausal woman presented with progressive vaginal bleeding, pelvic pressure, fatigue, early satiety, and unintentional 18-lb weight loss over 3 months
- PMH: hypertension, obesity, type 2 diabetes, and chronic anemia
- ECOG performance status: 1
- CT chest/abdomen/pelvis demonstrated a large uterine mass, bulky pelvic and para-aortic adenopathy, omental nodularity, and multiple bilateral pulmonary metastases
- Endometrial biopsy confirmed high-grade uterine carcinosarcoma
- Final stage: FIGO Stage IVB disease

Pathology and Molecular Profile

- Pathology: Biphasic malignant epithelial and sarcomatous components consistent with uterine carcinosarcoma
- Immunohistochemistry showed abnormal diffuse p53 staining pattern
- Mismatch repair proteins intact (MLH1, PMS2, MSH2, MSH6 retained) consistent with pMMR/MSS disease
- HER2 testing negative

Why Consider Frontline Dostarlimab?

- RUBY Part 1 and NRG-GY018 established chemoimmunotherapy as a frontline standard in advanced/recurrent EC
- RUBY Part 2 further suggested that combining PD-1 blockade with PARP inhibitor maintenance may enhance benefit in pMMR disease
- Carcinosarcomas frequently harbor genomic instability, TP53 abnormalities, and high replication stress, potentially increasing sensitivity to combination strategies

Treatment Plan

- Initiated carboplatin/paclitaxel plus dostarlimab every 3 weeks
- Planned maintenance dostarlimab following completion of chemotherapy
- Niraparib maintenance was discussed but deferred because of baseline anemia, frailty concerns, and limited carcinosarcoma-specific prospective data
- Supportive interventions included early palliative care involvement, nutrition consultation, neuropathy monitoring, and transportation assistance

Clinical Course and Response

- Patient experienced rapid improvement in bleeding, pelvic pain, appetite, and functional status after 2 cycles
- Restaging imaging after 3 cycles demonstrated partial response with marked reduction in pulmonary metastases, nodal disease, and omental implants
- Toxicities included Grade 1 fatigue, mild sensory neuropathy, and transient neutropenia
- No significant immune-related adverse events observed
- Patient remained highly motivated to continue therapy because of substantial improvement in quality of life and symptom burden

Educational Discussion Points

- Uterine carcinosarcoma remains one of the highest-risk endometrial cancer histologies with historically poor survival outcomes
- Molecular classification is increasingly important even in aggressive histologies such as carcinosarcoma
- Checkpoint inhibitors combined with chemotherapy are now changing frontline management of advanced EC
- Maintenance strategies should be individualized based on patient comorbidities, marrow reserve, toxicity risk, and goals of care

Discussion Questions

Would you like to be able to administer up-front chemoimmunotherapy followed by combined anti-PD-1/PD-L1 antibody and PARP inhibitor maintenance to any of your patients with newly diagnosed advanced EC? If so, which ones?

Would you be more likely to do so for certain patient subsets (eg, those with MSS/pMMR disease, those with documented HRR mutations) than others?

Side Effects and Other Practical Considerations with PARP Inhibitors

Jaclyn Shaver, MS, APRN, CNP, WHNP

Section of Gynecologic Oncology

Stephenson Cancer Center

OU Health

Oklahoma City, Oklahoma

Side Effects and Other Practical Considerations with PARP Inhibitors

- Combining PARP inhibitors with immunotherapy frequently results in manageable safety profile, but with increased toxicity compared to monotherapy
- Common adverse events include – Fatigue, nausea, diarrhea and hematologic toxicities

Specific Combinations

- Niraparib + immunotherapy
 - Increased Nausea and HTN
- Olaparib + immunotherapy
 - Increased associated diarrhea
- Rucaparib + immunotherapy
 - GI effects, fatigue, anemia, and liver enzymes elevations

Key Side Effect Profile with combined PARP and Immunotherapy

- Hematologic Toxicity
 - Anemia is the most common – 15-41% incidence of grade ≥ 3
 - Thrombocytopenia
 - Neutropenia
- Gastrointestinal Effects
 - Nausea, vomiting, diarrhea, constipation
- Fatigue
- Immune- Related Adverse Events
 - Higher incidence of rash, pneumonitis, colitis

Key Monitoring – PARP Inhibitors

- Hematologic Monitoring
 - Frequent CBC's, CMP's
 - Niraparib –weekly for the first month then monthly
 - Olaparib/Rucaparib – Monthly monitoring
 - Can space out to every 3M once dosage is tolerated
- Cardiovascular Monitoring
 - Niraparib – Home BP/HR monitoring
- Duration
 - Most side effects occur shortly after starting treatment, especially in first 3 months
- Dose modifications
 - Hold vs dose reduce as indicated
- Long term safety
 - Monitor for MDS/AML – look for persistent cytopenia

Common Side Effects

- Olaparib
 - **Nausea, fatigue**, vomiting, anemia, neutropenia, thrombocytopenia
- Niraparib (dose based on weight/platelet count and hepatic impairment)
 - **Thrombocytopenia**, anemia, Neutropenia, nausea, vomiting, constipation, fatigue, joint pain, loss of appetite, **HTN**, headaches, insomnia, dizziness, cough
- Rucaparib
 - Nausea, vomiting, constipation, **diarrhea**, abd pain, fatigue, dysgeusia, **rash**, **increased sensitivity to sunlight**, **increased ALT/AST**, **creatinine**, anemia, and thrombocytopenia

Patient Education

- First 3M – side effects are the worse, then improve
- Oral medication compliance
- Frequency of labs value monitoring and office visits
- Anti-emetics prior to taking PARP inhibitor
- Home BP/HR monitoring
- Reporting symptoms- ie hypertension, uncontrolled nausea/vomiting, worsening fatigue, bruising, abd pain, HTN, fever, diarrhea

Patient Resources

- Pill Organizers
- Alarms on Phones/Calendars
- Ensuring they have clinic phone numbers - day/night to report symptoms
 - Adequate clinic staff with triage experience
- Ensuring patients have refills on supportive care medication
- Blood pressure monitor
- Social needs are met
 - Transportation, finances, mental health, nutritional
 - Refer when appropriate

Case Study – 57 y/o with Recurrent EMCA

- 57 y/o CF G2P2 Recurrent Stage IIIC1 grade 2 EMCA
- Comorbidities: Obesity - BMI 45, Seasonal Allergies
 - Initially thought to be endometrioid endometrial cancer vs possible endocervical origin - s/p MRI & PET/CT with 4.8cm lower uterine segment mass invading into cervix with left parametrial involvement
 - AUB – IUD was in place 2 years after due to be removed
 - MRI/PET CT 4.8cm lower uterine segment tumor with invasion into cervix with parametrial involvement
 - AGUS pap, + HPV 18, + ECC adenocarcinoma
- Underwent Cisplatin x 6 cycles with external beam pelvic RT and brachy completed 5/18/2019
- Robotic hyst, BSO, B/L PALND on 6/24/2019 followed by Carbo/Taxol x4 cycles completed 9/26/2019
- Recurrent
 - Splenic lesion 7/2021 2.3cm, placed on DUO-E Carbo/Taxol/Durva x 6 cycles completed 12/2021
 - CT 1/2022 Splenic lesion 1.2cm
 - Completed DUO-E maintenance with Durva/placebo + Olaparib/placebo x 45 cycles 12/2024
 - Overall tolerated well with persistent nausea that was controlled with anti-emetics
 - CT 1/2025 – splenic lesion 1cm
 - PET/CT – Not FGD avid
 - Molecular residual disease test - negative

Case Study – 57 y/o with Recurrent EMCA

- Currently in surveillance doing well – NED on exam
- CT scan 4/17/26 – Stable splenic lesion 0.6cm
- 5 years from initial diagnosis of recurrence

Discussion Questions

Are there any unexpected side effects when anti-PD-1/ PD-L1 antibodies are administered in combination with PARP inhibitors?

How would you determine the root cause of tolerability issues (eg, gastrointestinal effects, fatigue) that could be attributable to either agent?

Agenda

Introduction: Biology of Endometrial Cancer (EC)

Module 1: First-Line Therapy for Advanced or Recurrent EC

Module 2: Potential Benefits of PARP Inhibition Combined with Immunotherapy in Advanced EC

Module 3: Role of Lenvatinib/Pembrolizumab in the Management of Progressive Advanced EC

Module 4: Other Nursing Considerations in the Care of Patients with Advanced EC

The Role of Lenvatinib/Pembrolizumab in the Management of Progressive Advanced EC

Dana M. Chase, MD

Professor and Fellowship Program Director

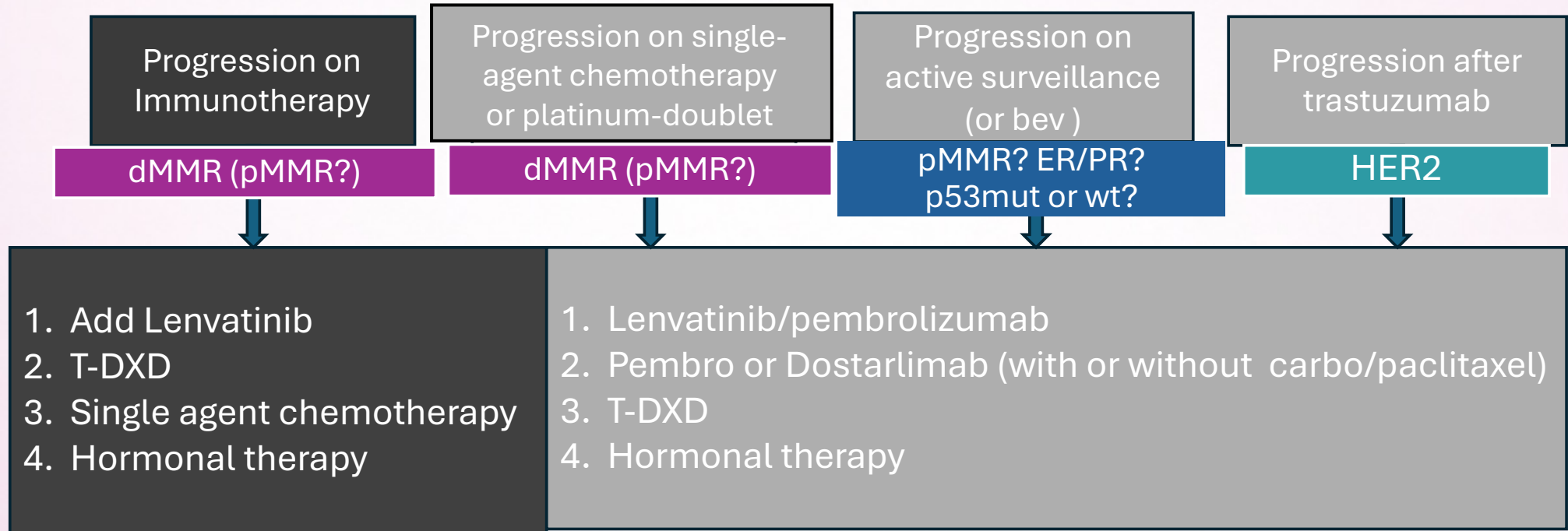
Division of Gynecologic Oncology

David Geffen School of Medicine at UCLA

Objectives

- Mechanism of action of Lenvatinib
- Rationale for combining immune checkpoint inhibitors with agents targeting the VEGF pathway in EC
- Long-term findings, including overall survival data, supporting the use of lenvatinib in combination with pembrolizumab for patients with pMMR advanced EC with disease progression after prior systemic therapy
- Optimal integration of lenvatinib/pembrolizumab into current EC management algorithms
- **Case Presentation:** A patient with progressive advanced EC who received Lenvatinib/pembrolizumab

Treatment of Recurrent Endometrial Cancer



Checkpoint Inhibitor Regimens for Endometrial Cancer in the Second-Line Setting

2021:

**Full FDA approval for
2L pembrolizumab +
lenvatanib (pMMR)**

2022:

**Full FDA approval for
2L pembrolizumab
monotherapy (dMMR)**

2023:

**Full FDA approval for
2L dostarlimab
monotherapy (dMMR)**

1. Keytruda (pembrolizumab) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/125514Orig1s186lbl.pdf.
2. Lenvima (lenvatanib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/206947s033lbl.pdf.
3. Jemperli (dostarlimab) Prescribing Information.
https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Jemperli/pdf/JEMPERLI-PI-MG.PDF.

Option: Lenvatinib + Pembrolizumab?

Phase III trial Keynote 775

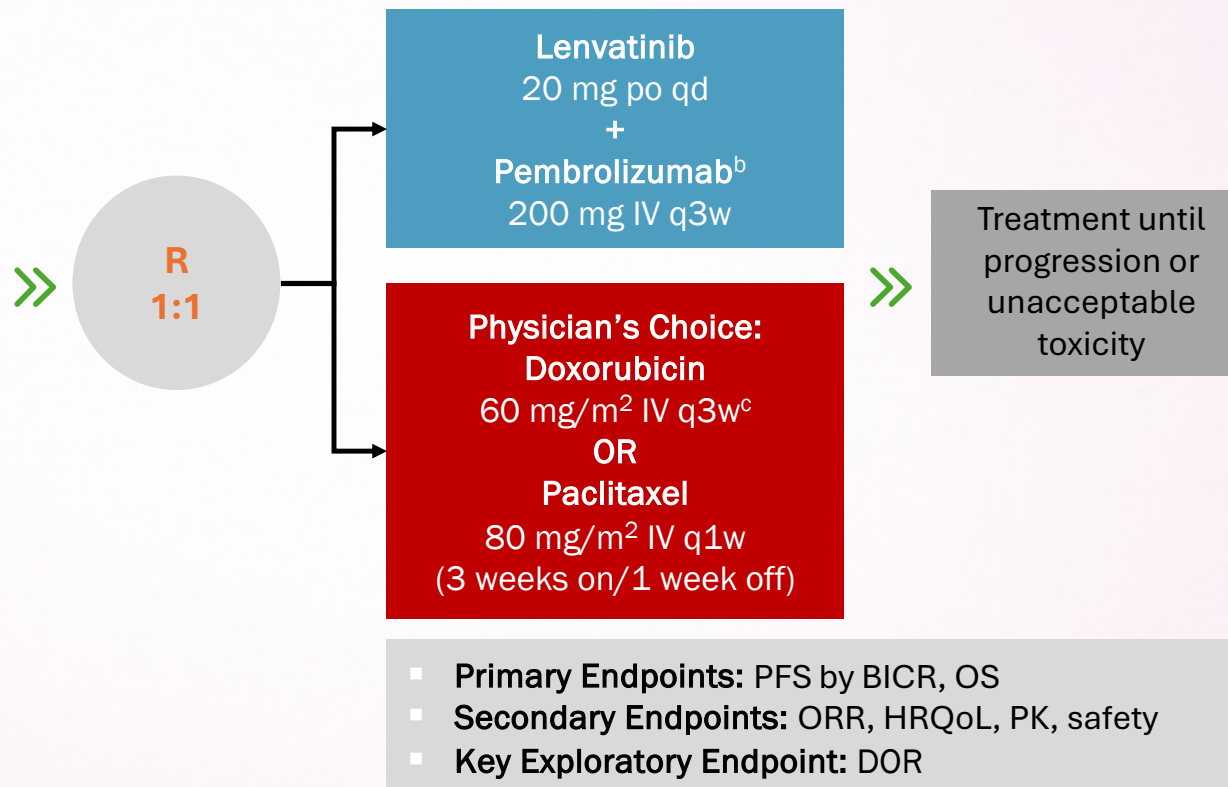
Key Eligibility Criteria

- Advanced, metastatic, or recurrent EC
- Measurable disease by BICR
- 1 prior platinum-based chemotherapy regimen^a
- ECOG PS 0-1
- Tissue available for MMR testing

Immunotherapy naïve!

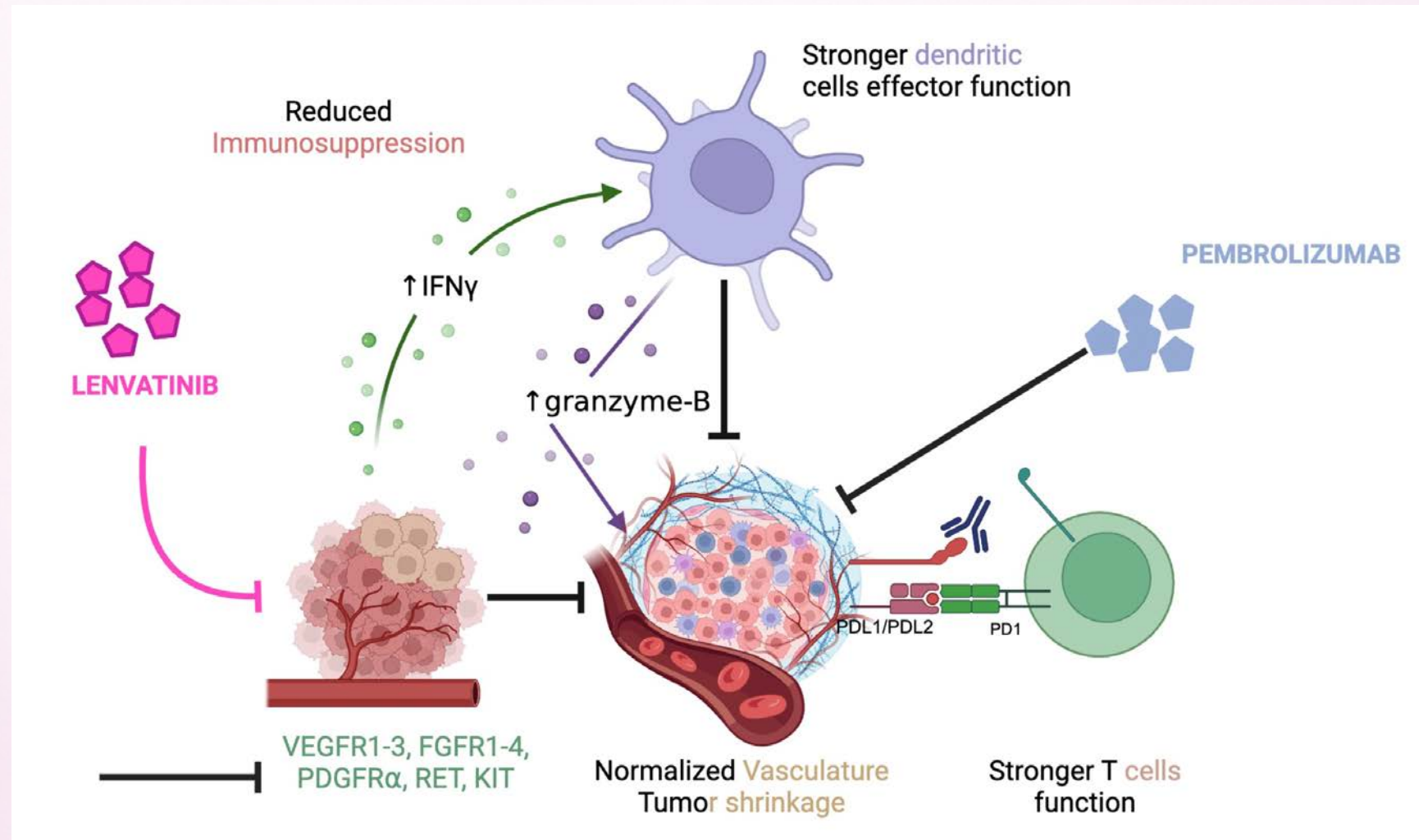
Stratification Factors

- MMR status (dMMR vs pMMR)
- pMMR by ECOG PS, geographic region, prior pelvic radiation



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

Mechanism of Action of Lenvatinib and Pembrolizumab



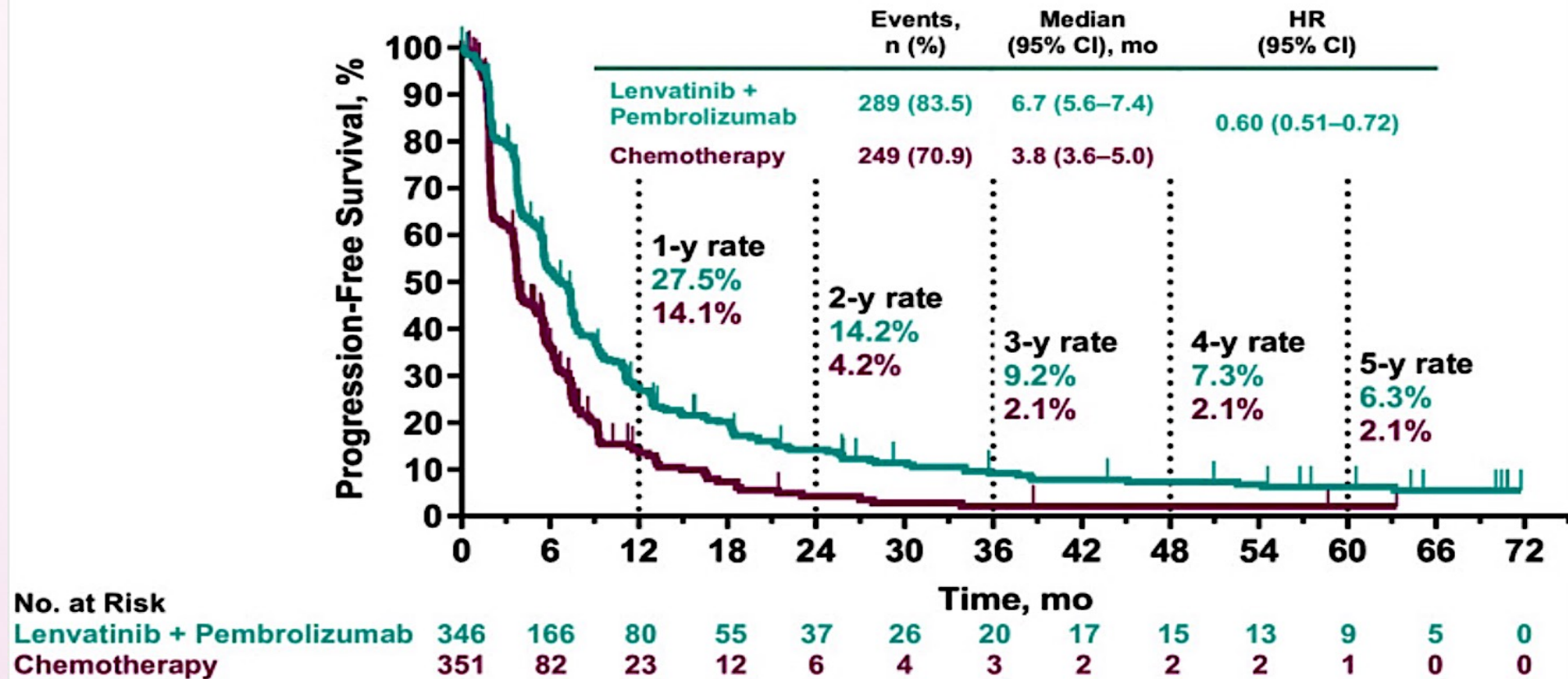
Lenvatinib + Pembrolizumab

Patient Characteristics:

Characteristic	pMMR population	
	Lenvatinib plus pembrolizumab (n=346)	Chemotherapy (n=351)
Median age (range), years	65 (30–82)	66 (35–86)
Age <65 years	171 (49.4)	165 (47.0)
Race		
White	220 (63.6)	212 (60.4)
Asian	74 (21.4)	80 (22.8)
Black or African American	15 (4.3)	9 (2.6)
Other	8 (2.3)	15 (4.3)
Missing	29 (8.4)	35 (10.0)
Geographic region [*]		
Region 1	202 (58.4)	204 (58.1)
Region 2	144 (41.6)	147 (41.9)
ECOG performance status		
0	212 (61.3)	207 (59.0)
1	133 (38.4)	144 (41.0)
3	1 (0.3) [†]	0
History of pelvic irradiation	144 (41.6)	149 (42.5)
Histology		
Endometrioid carcinoma	189 (54.6)	198 (56.4)
High-grade	73 (21.1)	77 (21.9)
Low-grade	50 (14.5)	41 (11.7)
Not specified [‡]	66 (19.1)	80 (22.8)
Serous carcinoma	99 (28.6)	112 (31.9)
Clear cell carcinoma	29 (8.4)	17 (4.8)
Mixed features	18 (5.2)	13 (3.7)
Other [§]	11 (3.2)	11 (3.1)

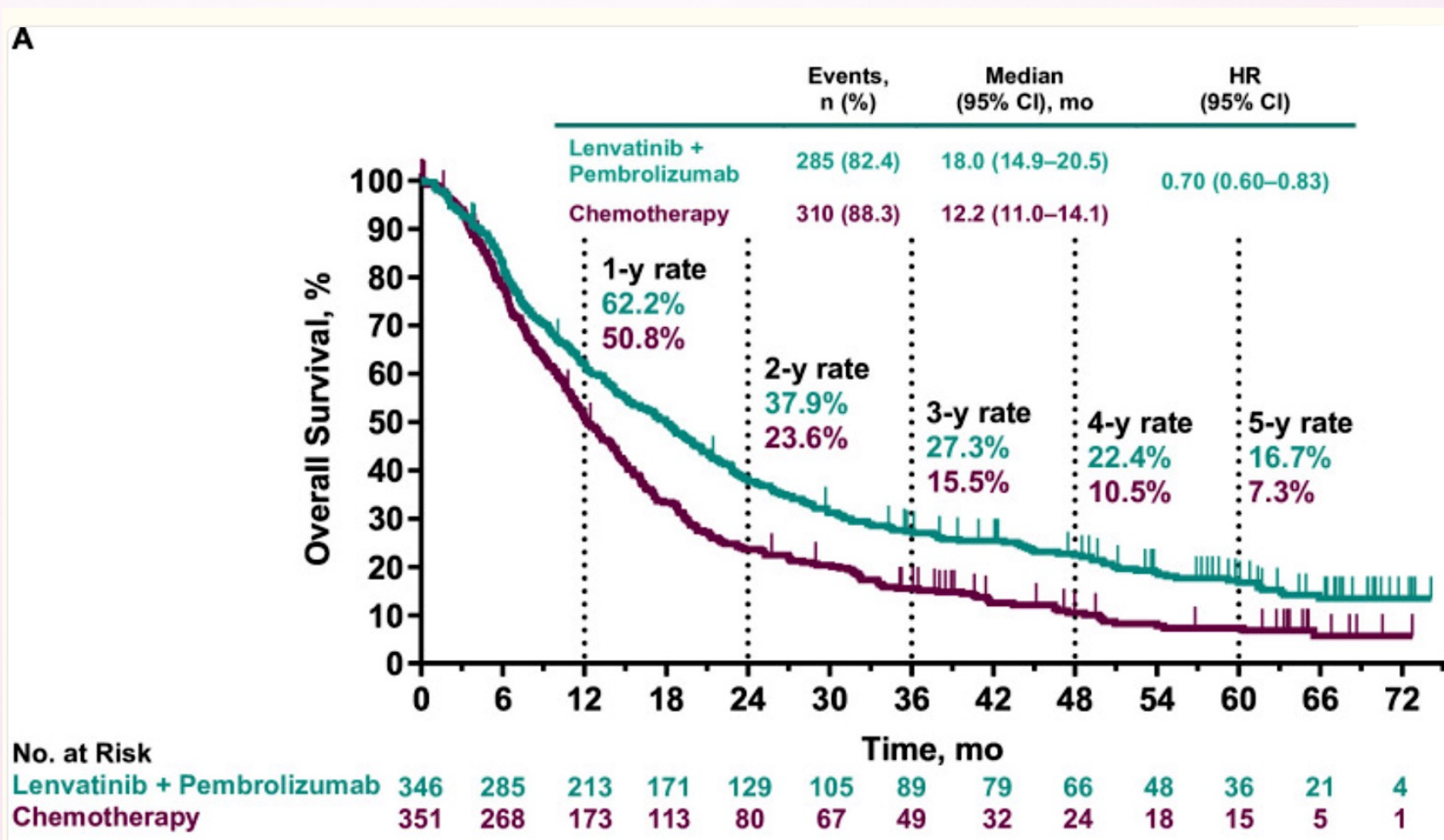
Lenvatinib + Pembrolizumab: pMMR population

A



Makker V, Colombo N, Casado A, Santin AD, Colomba E, Miller DS, Fujiwara K, Pignata S, Yonemori K, Kim YM, Baron-Hay S, Ray-Coquard I, Shapira-Frommer R, Kristeleit R, Nishio S, Suzuki S, Guerra Alía EM, Sanli UA, Selle F, Shikama A, Martínez Rodríguez JL, Arik Z, Arican A, Sebastianelli A, Yu Z, McKenzie J, Kruger S, Meng R, Okpara CE, Lorusso D. Lenvatinib plus pembrolizumab in previously treated advanced endometrial cancer: 5-year outcomes from the randomized, phase 3 Study 309/KEYNOTE-775. J Immunother Cancer. 2026 Feb 19;14(2):e013713. doi: 10.1136/jitc-2025-013713. PMID: 41714113; PMCID: PMC12927346.

Lenvatinib + Pembrolizumab: pMMR population



Makker V, Colombo N, Casado A, Santin AD, Colomba E, Miller DS, Fujiwara K, Pignata S, Yonemori K, Kim YM, Baron-Hay S, Ray-Coquard I, Shapira-Frommer R, Kristeleit R, Nishio S, Suzuki S, Guerra Alía EM, Sanli UA, Selle F, Shikama A, Martínez Rodríguez JL, Arik Z, Arican A, Sebastianelli A, Yu Z, McKenzie J, Kruger S, Meng R, Okpara CE, Lorusso D. Lenvatinib plus pembrolizumab in previously treated advanced endometrial cancer: 5-year outcomes from the randomized, phase 3 Study 309/KEYNOTE-775. *J Immunother Cancer*. 2026 Feb 19;14(2):e013713. doi: 10.1136/jitc-2025-013713. PMID: 41714113; PMCID: PMC12927346.

Patient Case

87 yo with recurrent endometrial cancer

- 2013 Stage IB G2 endometrial cancer, +LVSI, pMMR
 - Adjuvant RT
 - 2015 hematemesis
 - Recurrent endometrial cancer to lung
 - 6/2022 Carbo/paclitaxel
 - Progression in lung
 - 10/2022 Lenvatinib+Pembrolizumab
 - Started at Lenvatinib 20 mg + Pembro → Dose reductions due to fatigue, weight loss, hypertension
 - 6/2023 on lenvatinib 8 mg + Pembro
- PMH: Meniere's disease, osteoporosis, hypertension
- FH: no history of cancer in the family
 - POBGYNHX: G2P2, no h/o abnormal pap tests
 - SH: Works as professional tennis photographer, still works

Tumor profiling and imaging

GENOMIC VARIANTS

Biologically Relevant	Variant Allele Fraction
ARID1A p.P1296fs Frameshift - LOF	21.3%
ERF1 p.Q110* Stop gain - LOF	19.1%
PTEN p.T319fs Frameshift - LOF	11.3%
PIK3R1 p.Y426* Stop gain - LOF	11.2%
PTEN c.1026+1G>T Splice region variant - LOF	11.0%
PIK3R1 p.N453del Inframe deletion - LOF	8.6%
PIK3R1 c.1426-2A>G Splice region variant - LOF	6.6%
CTCF p.K601fs Frameshift - LOF	5.6%

Germline - Pathogenic / Likely Pathogenic

No matched normal sample was received, therefore germline sequencing was not performed.

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

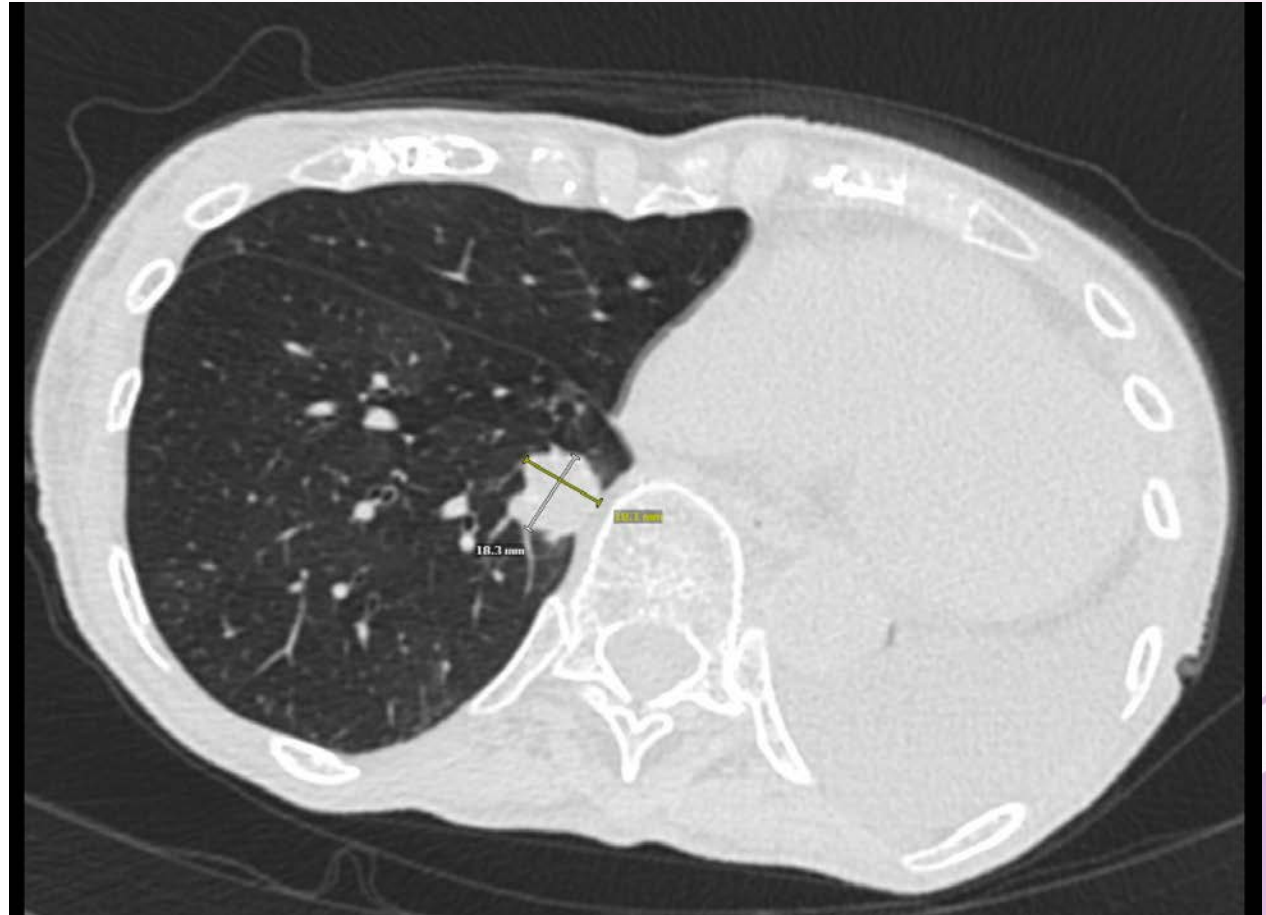
8.4 m/MB 83rd percentile

Microsatellite Instability Status

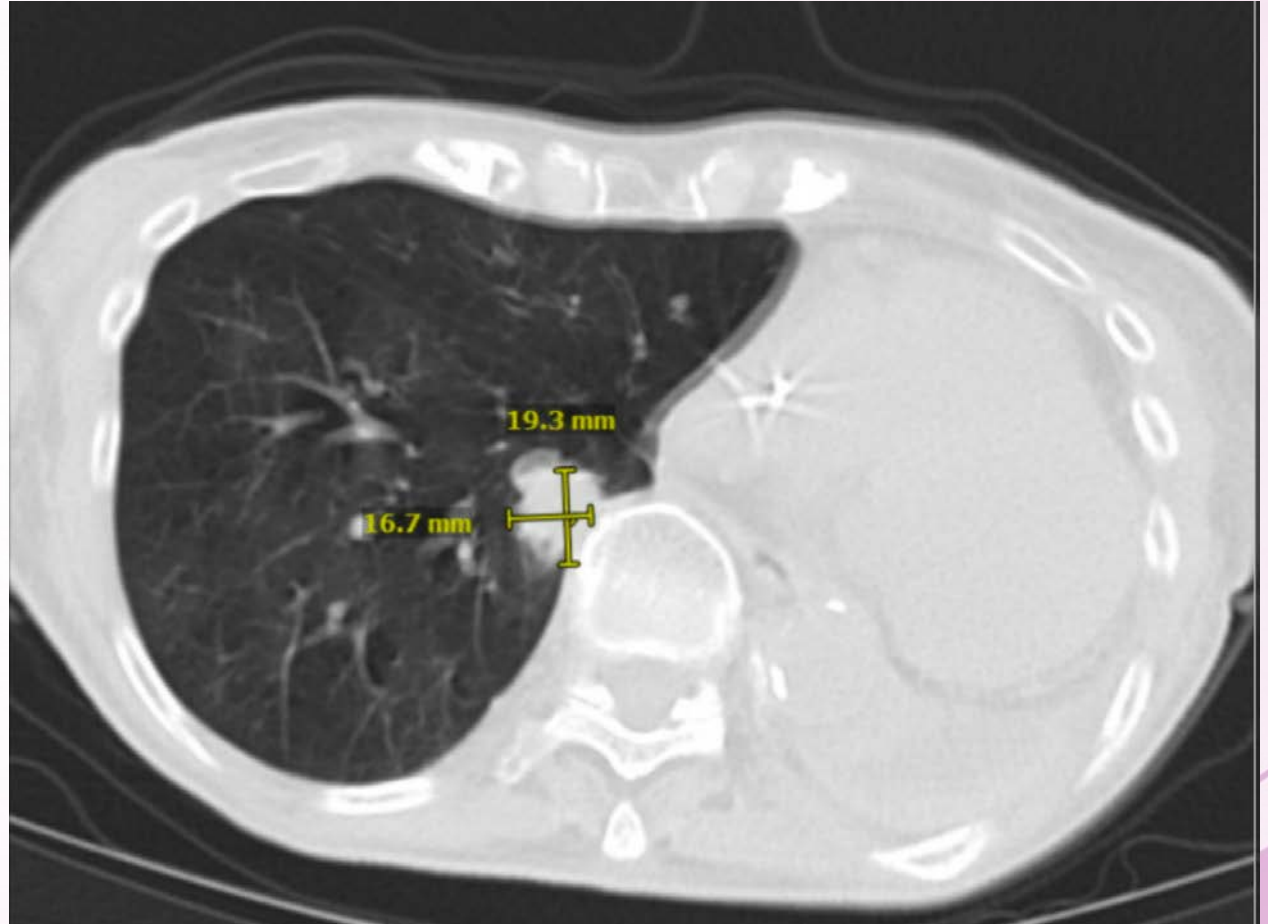
MSI can not be assessed because the tumor content is below 30%.

TREATMENT IMPLICATIONS

No reportable treatment options found.



- Progression of disease and discontinued Lenvatinib + Pembrolizumab in 1/2024 (1.5 years)
- Started on letrozole, transitioned to megestrol acetate/tamoxifen
- 9/2024 deceased



Discussion Questions

Is pembrolizumab/lenvatinib your preferred second-line regimen for most patients with relapsed/refractory (R/R) MSS/pMMR EC? Would you currently recommend this combination for patients with R/R MSI-H/dMMR EC under any circumstances?

Would you rechallenge with an immune checkpoint inhibitor-containing regimen, namely pembrolizumab/lenvatinib, in a patient who has received chemoimmunotherapy in the front-line setting?

Toxicities with Lenvatinib/Pembrolizumab

Sarah Karpen, PA-C

UC San Diego Health
Division of Gynecologic Oncology

Agenda

1

Incidence, severity, timing, and management of adverse events (AEs) observed in patients with endometrial cancer (EC) receiving lenvatinib/pembrolizumab

2

Approaches to encourage adequate nutrition among patients receiving lenvatinib/pembrolizumab

3

Initial dosing and dose-modification strategies for lenvatinib/pembrolizumab in EC; available data exploring the impact of lenvatinib dose reductions on antitumor activity

4

Strategies to determine the cause of toxicities that could stem from either lenvatinib or pembrolizumab in patients receiving the combination

Case Study

70-year-old female | PMH: HTN, HLD, aortic stenosis | Stage IIIC pMMR HER2 3+ papillary serous uterine cancer — platinum refractory

Surgical History

- Exploratory laparotomy
- Total abdominal hysterectomy
- Bilateral salpingo-oophorectomy
- Tumor debulking & omentectomy
- Pelvic and para-aortic lymphadenectomies

Molecular Profile

- p53 abnormal (overexpression)
- MMR status: pMMR — MLH1, PMS2, MSH2, MSH6 all intact
- Estrogen receptor positive
- HER2 positive (3+)

Treatment Course

- Carboplatin/paclitaxel/trastuzumab × 9 cycles
- Progression on imaging with new metastases to distant lymph nodes in the chest
- **Started lenvatinib 14 mg daily + pembrolizumab 200mg IV every 3 weeks**

Considerations for Starting Lenvatinib

This patient presented with progressive aortic stenosis (moderate → severe) identified on routine ECHO during trastuzumab therapy.

Cardiac Evaluation

Patient evaluated by cardiology prior to initiating lenvatinib. Dose pre-emptively reduced to **14 mg** daily given severe aortic stenosis.

Cardiovascular Risks

TKIs carry risk for rapid hypertension, which can precipitate cardiac stress, heart failure, pulmonary edema, myocardial infarction, and arrhythmias — particularly with pre-existing valvular disease.

Baseline Medications

Patient was already on atenolol and lisinopril (antihypertensives), atorvastatin, and aspirin — facilitating proactive blood pressure management.

CYP3A4 Considerations

Nondihydropyridine calcium channel blockers (verapamil, diltiazem) should be avoided due to CYP3A4 drug interactions with lenvatinib.

Incidence, Severity & Timing of Adverse Events (KEYNOTE-775)

~89%

had a grade ≥ 3 adverse event

1.9 mo

median time to lenvatinib
dose reduction

Nearly all patients experienced an adverse event, with most AEs occurring within the first 3 months of therapy.

Hypertension Management - most significant AE up to 64% of patients compared to 5.2% with chemo

- Monitor blood pressure proactively at baseline and throughout treatment
- First-line antihypertensives: ACE inhibitors or ARBs
- Avoid nondihydropyridine calcium channel blockers (verapamil, diltiazem) — CYP3A4 interactions

Gastrointestinal Toxicities: Within 1-4 Weeks

55% — Diarrhea

49% — Nausea

37% — Vomiting

Diarrhea Grading & Management

Grade	Definition	Management
Grade 1	<4 stools/day over baseline	Supportive care: hydration, bland/low-fiber diet, avoid greasy foods, caffeine, alcohol, dairy Loperamide: 4 mg initially, then 2 mg after each loose stool (max 16 mg/day)
Grade 2	4–6 stools/day	Continue loperamide; add diphenoxylate/atropine Lomotil (1–2 tabs q6h PRN, max 8/day); consider bulk-forming agents Hold lenvatinib if persistent; resume when resolved to grade 1
Grade 3	≥7 stools/day or hospitalization	Hospitalize; hold lenvatinib; resume at reduced dose once improved
Grade 4	Life-threatening	Discontinue lenvatinib

Nausea & Vomiting Management

Standard antiemetics:
ondansetron, prochlorperazine, metoclopramide

General GI Dietary Guidance

- BRAT-type foods (bland, low-fiber)
- Avoid greasy, spicy, or high-fiber foods
- Avoid caffeine, alcohol, and dairy if symptoms worsen
- Increase oral hydration and electrolyte intake

Nutritional Support & Management of Weight Loss

Prehabilitation

- Dietary counseling before therapy begins
- Dental evaluation
- Psychosocial support
- Referral to a registered dietitian

For Decreased Appetite

- Increase feeding frequency (smaller, more frequent meals)
- Limit fluids with food intake
- Encourage calorie-dense, nutrient-rich foods
- Avocados, nuts, nut butters, plant-based fat sources

For Stomatitis / Mucositis

- Avoid crunchy, spicy, acidic, or hot foods
- Encourage soft foods
- Gentle tooth brushing; bland rinses with salt water or baking soda
- Prescribe dexamethasone rinse or 'magic mouthwash'

Pharmacologic Appetite Stimulants (Severe Cases)

- Olanzapine
- Corticosteroids
- Megestrol acetate (Megace)

These agents may be considered when nutritional support and dietary modifications are insufficient to maintain adequate caloric intake.

Distinguishing Lenvatinib vs. Pembrolizumab Toxicities

TKI toxicities are managed with dose reduction/interruption and supportive care, while immune-mediated toxicities require immunosuppression (corticosteroids ± biologics).

Lenvatinib — Half-life: 1–3 days

Toxicities typically resolve quickly after dose hold

Pembrolizumab — Half-life: ~22 days

Toxicities may worsen even after pembrolizumab is discontinued

Clinical Pearls for Attribution

Symptom Pattern	Likely Lenvatinib	Likely Pembrolizumab
Resolution with hold	Resolves quickly after dose hold	Persists or worsens after hold
Diarrhea character	Without blood or mucus	May be associated with colitis (blood/mucus)
Fever	Not typically associated	Often associated
Rash	Less common	More common; immune-mediated
Hypertension	Yes — hallmark TKI toxicity	Not typical

Lenvatinib Dose Reductions

In the KEYNOTE-775 trial, 66.5% of patients required a dose reduction. Retrospective data (n=369) showed no significant difference in progression-free survival between patients receiving ≤ 20 mg vs. the standard 20 mg dose.

Standard Dose Reduction Sequence



Tablet Formulations Available

- Lenvatinib capsules are available in 10 mg and 4 mg strengths
- Dose reductions can be achieved using combinations of available capsule sizes
- Case patient began at 14 mg daily given pre-existing severe aortic stenosis

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Module 4: Other Nursing Considerations in the Care of Patients with Advanced EC

Other Nursing Considerations in the Care of Patients with Advanced Endometrial Cancer

Jaclyn Shaver, MS, APRN, CNP, WHNP

Section of Gynecologic Oncology

Stephenson Cancer Center

OU Health

Oklahoma City, Oklahoma

Assessing Symptom Burden

- Crucial for improving patient Quality of Life
- Guiding Supportive Care
- Optimizing Treatment
- Can Directly Impact
 - Prognosis
 - Functional status
 - Treatment Adherence

Importance of Assessment

- Improves Quality of Life
 - Systematic assessment allows clinicians to identify and manage symptoms such as fatigue, pain, sexual changes, and psychological distress
- Guides Treatment Decisions
 - Monitoring symptom burden allows for timely interventions, preventing premature treatment termination, and ensures better adherence to therapy
- Identifies Recurrence/Progression Early
 - Monitoring for and educating patient about signs and symptoms of disease
- Tailors Supportive Care
 - Enables referral to palliative care or other supportive services

Key Symptom Areas to Monitor

- Physical
 - Pain, fatigue, sleep disturbances, GI issues
- Emotional
 - Distress, depression, anxiety
- Functional
 - Impact on daily activities and overall lifestyle

Early Palliative Care - Advanced Endometrial Cancer

- Optimal timing: Within 8 weeks of diagnosis
- Particularly effective with high symptom burden at start of treatment
- Significantly improves quality of life
 - Manage Symptom Burden
 - Patients experience better coping skills, improved mood, and in some cases enhanced survival rates

Impact on Quality of Life and Clinical Outcomes

- Rapid Symptom Relief
- Enhanced Psychological Well-being
- Improved Patient Empowerment
- Lowered Care Intensity

Depression in Advanced Endometrial Cancer

- Prevalence is high exceeding 40%-50% in studies measuring emotional distress coupled with obesity and poor sleep
- Advanced disease increases the risk of major depressive episode up to 3.5 times compared to general population.
- Often peaking around diagnosis and treatment

Depression and Advanced Endometrial Cancer

- 47% of endometrial cancer survivors experienced depressed mood and 64% reported anxiety
- Risk of mental health disorders increased with stage of cancer
- Obesity – higher rates of depression and lower quality of life
- Associated with higher risk of mortality
- Highest rates occur within 2 months of diagnosis – indicating need for early screening
- Treatment disparities: Many patients do not receive appropriate mental health, counseling, or pharmaceutical treatment.
 - Referral to palliative/supportive care, social workers, local psychologist, psychiatrist, primary care providers

Clinical Trial Participation – Potential Advantages

- Access to cutting-edge therapies
- Treatments may be more effective
- Treatments may be less toxic
- Receive a higher level of personalized care
- Contribute to medical advancements that help future patients

Case Study – 66 y/o Woman

- 66 y/o CF G2P2
- Comorbidities: Obesity, HTN, DM
- Last seen gyn with birth of her last child
- Divorced, lives alone - on Medicare
- Reports PMB spotting/bleeding for the last 1-2 years. Reports symptoms to her PCP who referred her to gyn.
- TVUS showed an endometrial stripe of 53mm
- EMB – showed endometrial adenocarcinoma, high grade
- She referred to Gyn/Onc – CT scan revealed a 2.2 cm right pelvic lymph node.

Case Study – 66 y/o Woman

- She underwent RATLH/BSO/SLNB – Stage IIIC UPSC
- At her first post-op visit – She expressed worsening depression symptoms. She had stopped taking her anti-depressants several years ago. Denies SI/HI. She was restarted on paroxetine.
- She was started on chemotherapy – carboplatin/paclitaxel.
- At her pre-chemo visit s/p cycle #2 – she reported grade 2 fatigue, insomnia, loss of appetite with weight loss - wasn't sure if she wanted to continue therapy
 - Depression was assessed as possible cause of above symptoms and patient admits restarting paroxetine had not helped.
 - She was then referred to our supportive care team for counseling and medication adjustment
 - She underwent counseling and her anti-depressant was switched to mirtazapine
 - Subsequent cycles were better tolerated – her appetite improved and was now sleeping better. She had more energy and felt like she could complete her 6 cycles of chemotherapy.

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Management of Prostate Cancer

Thursday, May 14, 2026

12:15 PM – 1:45 PM

Faculty

Michael Lai, MSN, ARNP, FNP-C

Stacy E Walker, FNP-BC

Evan Y Yu, MD

Moderator

Scott T Tagawa, MD, MS

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.

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