Expert Second Opinion: Investigators Provide Perspectives on the Best-Practice Use of Immunotherapy for Endometrial Cancer

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Saturday, April 11, 2026

12:45 PM – 2:15 PM AST

Faculty

Floor J Backes, MD

Matthew A Powell, MD

Moderator

Ritu Salani, MD, MBA

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Faculty

Floor J Backes, MD
Professor
Larry J Copeland Professorship
in Gynecologic Oncology
Director of Clinical Research
Associate Fellowship Director
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
The Ohio State University College of Medicine
The James Cancer Hospital and Solove
Research Institute
Columbus, Ohio

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

Moderator

Ritu Salani, MD, MBA
Director, Division of Gynecologic Oncology
Professor, Department of Obstetrics and Gynecology
David Geffen School of Medicine at UCLA
Los Angeles, California

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Dr Backes — Disclosures
Faculty

Advisory Committees	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BioNTech SE, Daiichi Sankyo Inc, Eisai Inc, Genmab US Inc, GSK, ImmunoGen Inc, Merck
Contracted Research	AbbVie Inc, ImmunoGen Inc, Merck, Natera Inc
Data and Safety Monitoring Boards/Committees	MacroGenics Inc

Dr Powell — Disclosures
Faculty

Consulting Agreements	Eisai Inc, GSK, Merck
Contracted Research	GSK

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Dr Salani — Disclosures
Moderator

Advisory Committees	AbbVie Inc, Corcept Therapeutics Inc, Daiichi Sankyo Inc, Eisai Inc, Genmab US Inc, GSK, Merck, Pfizer Inc, Whitehawk Therapeutics
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Prof Ledermann — Disclosures
Consulting Clinical Investigator

Financial-relationship disclosures have been requested.

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Dr Matulonis — Disclosures
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Dr Secord — Disclosures
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Stock Options/Stock — Public Companies	Stock in Amgen Inc and Johnson & Johnson, divested in June 2024

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Expert Second Opinion: Investigators Provide Perspectives on the Best-Practice Management of Ovarian Cancer

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Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Nicoletta Colombo, MD

Gottfried E Konecny, MD

Alexander B Olawaiye, MD

Moderator

Shannon N Westin, MD, MPH, FASCO, FACOG

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Data + Perspectives: The Potential Role of TROP2- and CDH6-Directed Antibody-Drug Conjugates in Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Ramez N Eskander, MD

Bradley J Monk, MD

Moderator

Kathleen N Moore, MD, MS

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Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Clinicians in the Meeting Room

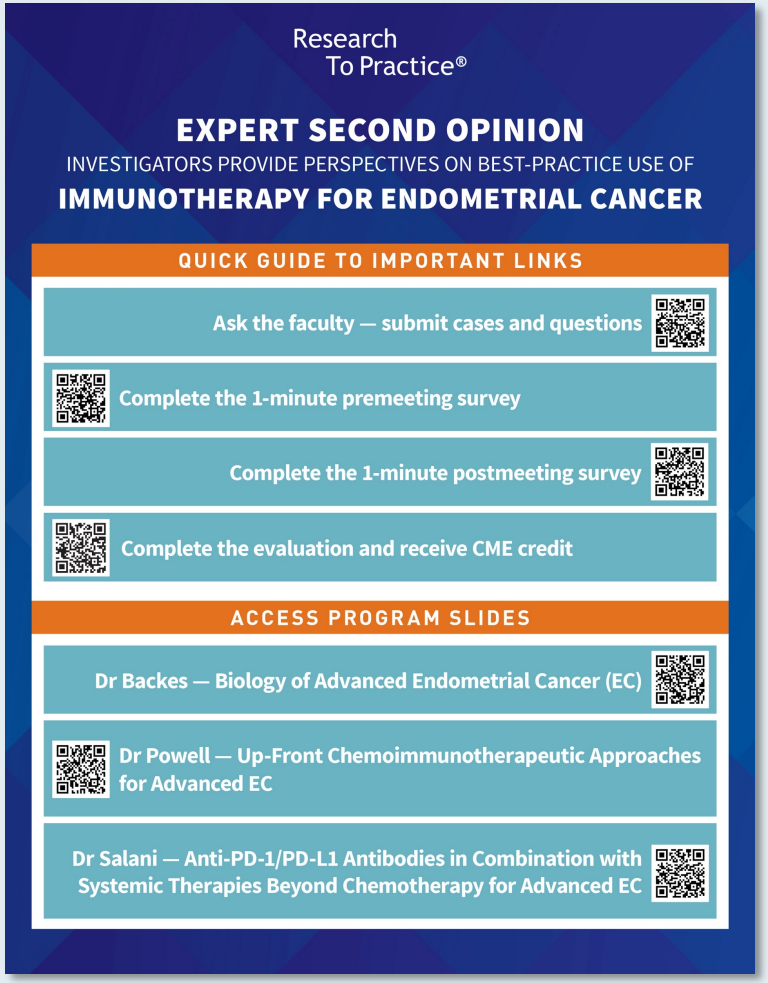
Please refer to the printed handout provided with your meeting syllabus, and scan the corresponding QR code to

Review and Download Program Slides.

Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: We will aim to address as many questions as possible during the program.

Get CME Credit: Complete the course evaluation.



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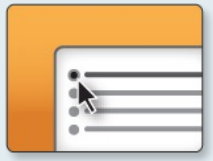
Clinicians Attending via Zoom

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.

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

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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.
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Second Opinion

Professor Jonathan A Ledermann
Professor of Medical Oncology
UCL Cancer Institute
London, United Kingdom

Angeles Alvarez Secord, MD, MHSc
Director of Gynecologic Oncology Clinical Trials
Associate Director, Clinical Research, Gynecologic Oncology Program
Duke Cancer Institute
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
Duke University School of Medicine
Durham, North Carolina

Ursula Matulonis, MD
Chief, Division of Gynecologic Oncology
Brock-Wilson Family Chair
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Neil Love, MD
Research To Practice
Miami, Florida

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Agenda

Module 1: Biology of Advanced Endometrial Cancer (EC); Optimal Approach to Biomarker Assessment in Patients with Newly Diagnosed Disease — Dr Backes

Module 2: Current Up-Front Chemoimmunotherapeutic Approaches for Advanced EC — Dr Powell

Module 3: Current and Future Role of Anti-PD-1/PD-L1 Antibodies in Combination with Systemic Therapies Beyond Chemotherapy in Advanced EC — Dr Salani

Agenda

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Biology of Advanced Endometrial Cancer

Optimal Approach to Biomarker Assessment in Patients with Newly Diagnosed Disease

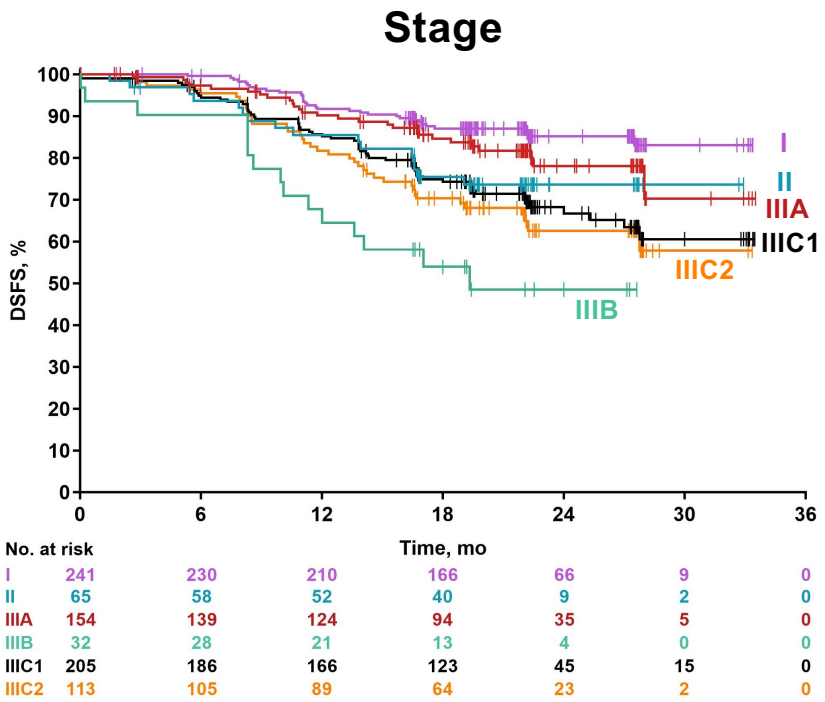
Floor Backes, MD
Professor
Division of Gynecologic Oncology
The Ohio State University
Columbus, OH, USA

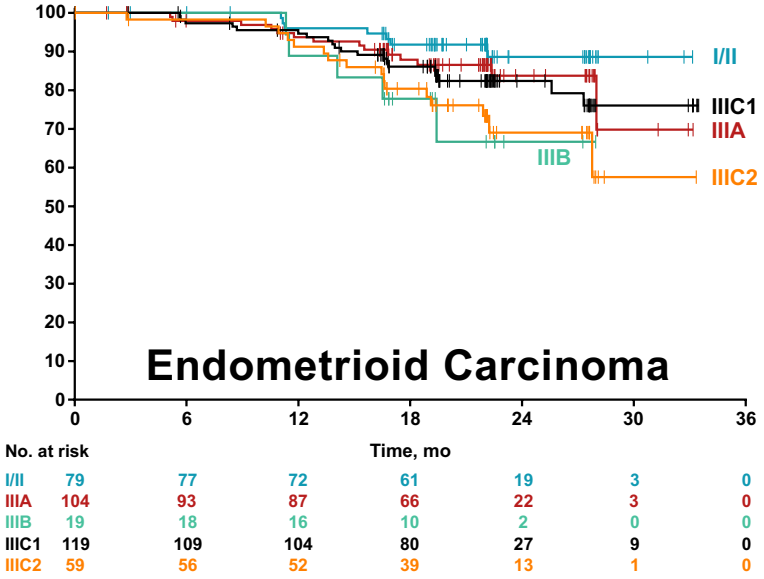
The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

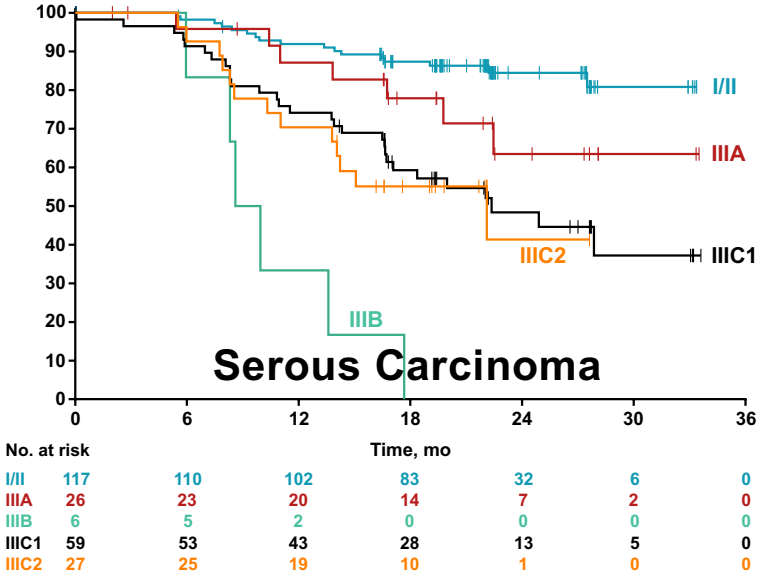
Objectives

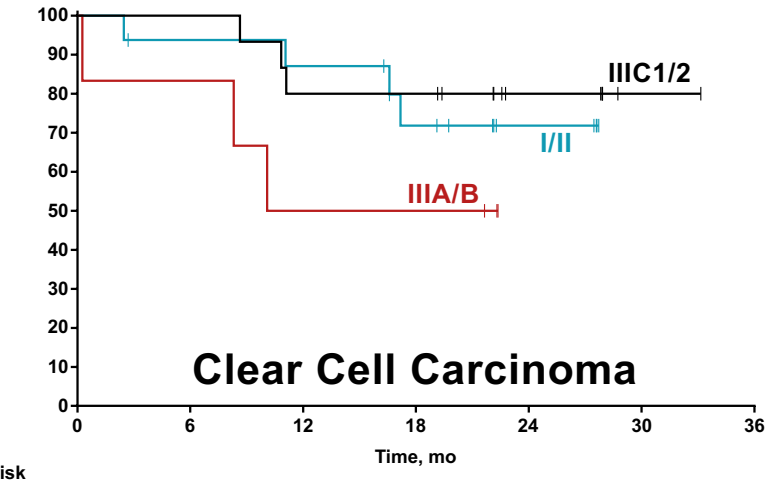
- Discuss endometrial cancer molecular subtypes
- Review implications for prognosis and therapeutic decision-making
- Review potential biomarkers of response to immune checkpoint inhibition
- BRCA1/2 and other HRR/HRD in endometrial cancer
- Guideline-endorsed approach to assessment of other clinically relevant biomarkers

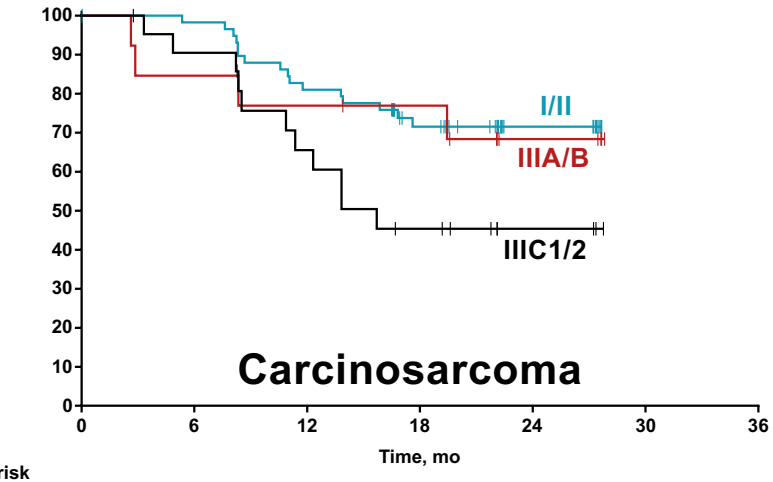
Prognosis by Stage (FIGO 2009) and Histology in pMMR EC (Keynote-B21 Treatment Arms Combined)





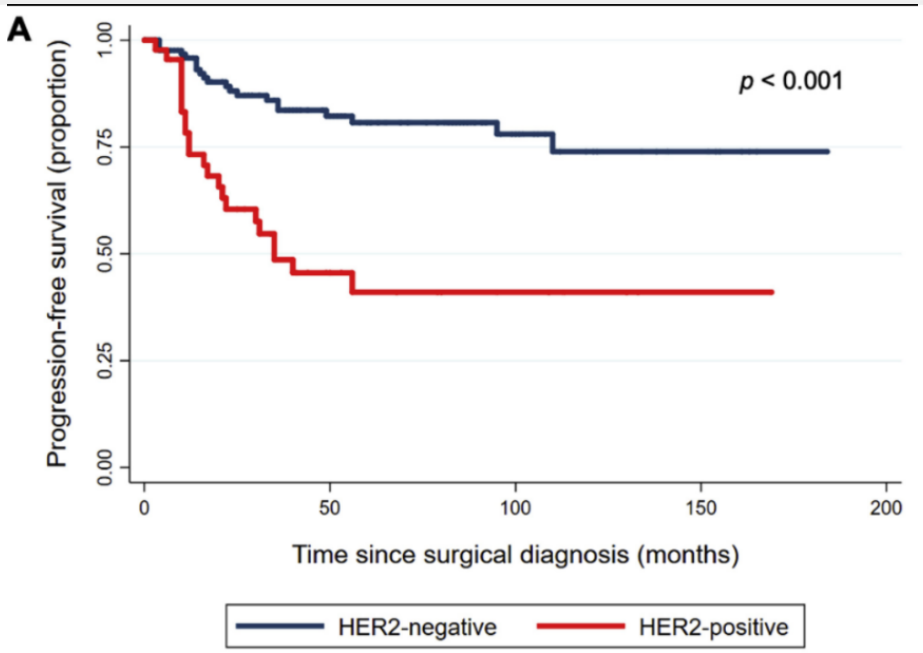






Halaskala, ESGO 2024

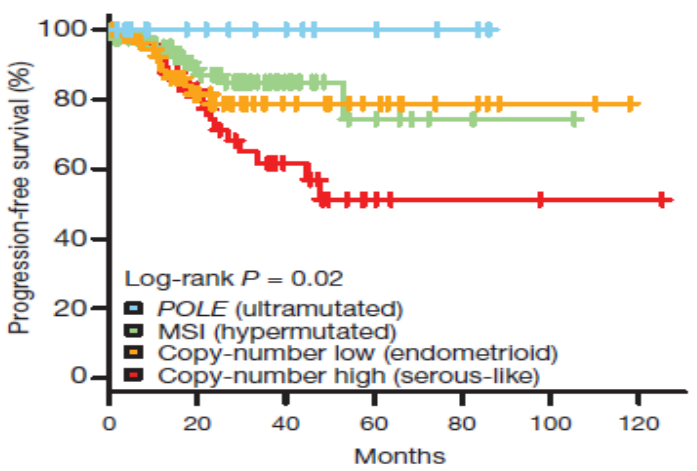
Uterine Serous Carcinoma

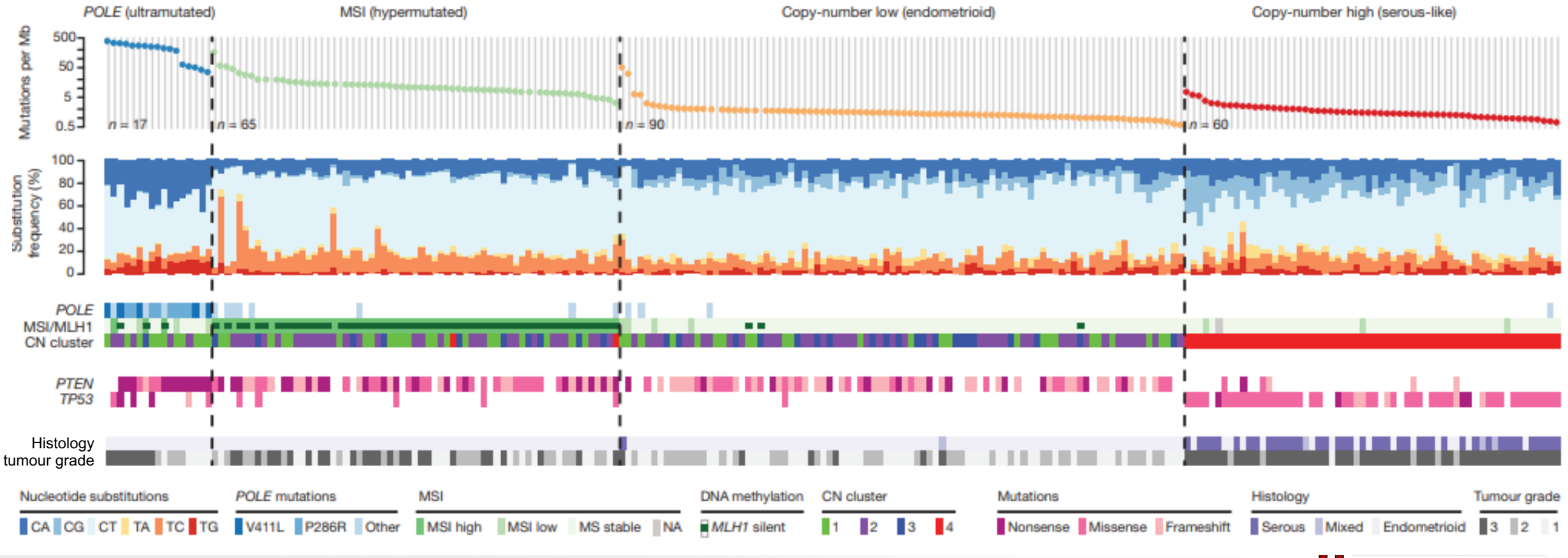


- 10% of all endometrial cancers, but 40% of deaths
- 75% have TP53 alteration
- HER2 overexpression and/or amplification ERBB2
  - 18-42%
- Stage I uterine serous uterine cancer:
  - 26% were HER2 positive (by IHC and/or FISH).
  - Recurrence for HER2 positive 50.0% vs 16.8%, p<0.001 (despite 70% of patients receiving chemotherapy)
- HER2 associated with worse PFS and OS
- Trastuzumab and Pertuzumab are humanized monoclonal antibodies against HER2
- Trastuzumab-Deruxtecan and Trastuzumab-Pamirtecan are HER2 targeting ADCs

Erickson, Gynecol Oncol 2020; Curr Opin Obstet Gynecol 2020

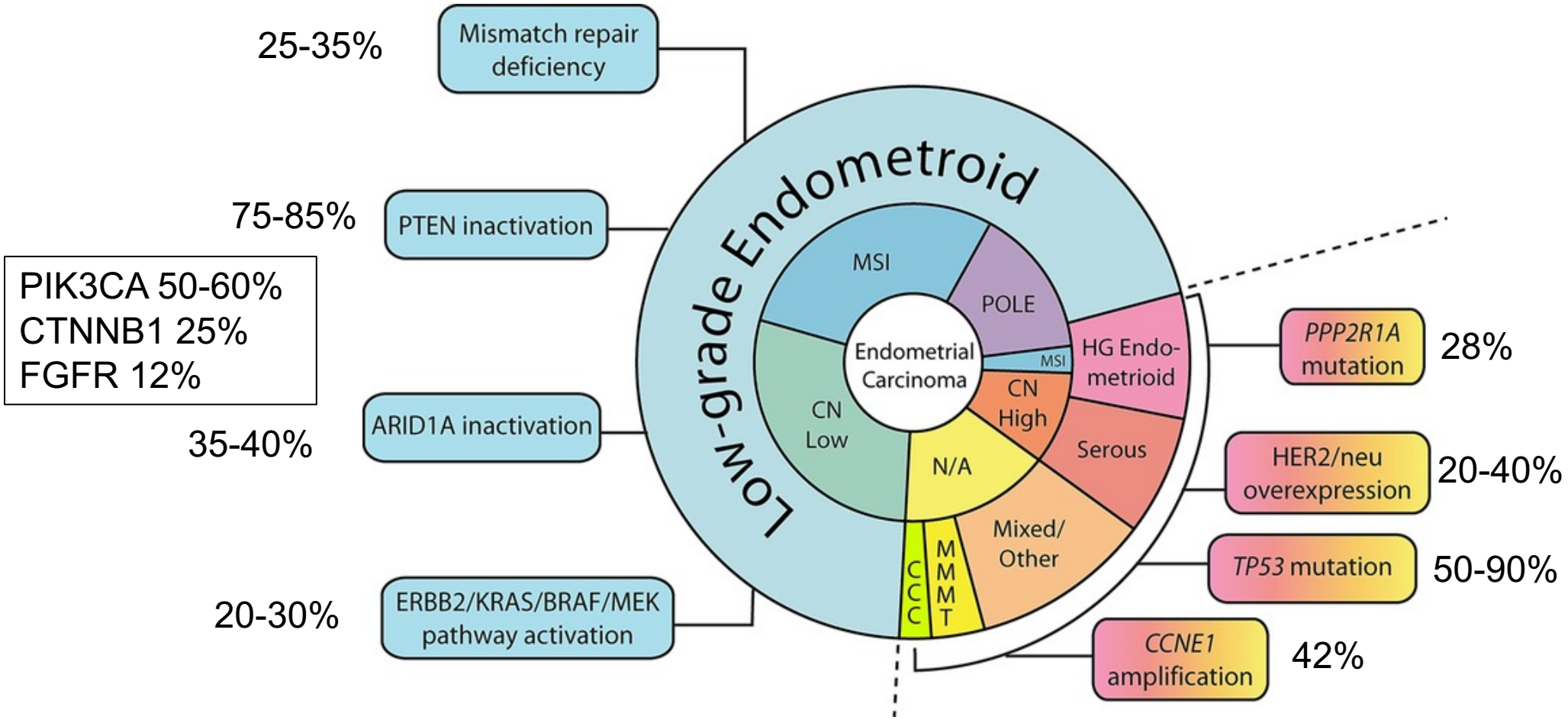
Molecular Profiling





Cancer Genome Atlas Research Network., Kandoth C, Nature 2013

Changing Molecular Landscape



Other Factors
p53
PD-L1
HER2 IHC/FISH
TROP2 (>90%)
FRα (64%)
B7H4 (80%)
HRD/HRR (22%)

Yen TT, et al. *Int J Gynecol Pathol*. 2020;39(1):26-35.

Molecular subgroups and treatment decision making

PORTEC-3: TCGA Subgroups

TCGA group	n	Treatment	5-yr RFS	HR (95% CI)	5-year OS	HR (95% CI)
p53abn	93 (23%)	EBRT versus CisRT + chemo	36.2% 58.6%	1 0.52 (0.30-0.91)	41.8% 64.9%	1 0.55 (0.30-1.00)
POLEmut	51 (12%)	EBRT versus CisRT + chemo	96.6% 100%	1 0.02 (<0.01->10^5)	96.6% 100%	1 0.02 (<0.01->10^5)
MMRd	137 (33%)	EBRT versus CisRT + chemo	75.5% 68%	1 1.29 (0.68-2.45)	84% 78.6%	1 1.33 (0.64-2.75)
NSMP	129 (32%)	EBRT versus CisRT + chemo	67.7% 79.7%	1 0.68 (0.36-1.3)	87.6% 89.3%	1 0.68 (0.26-1.77)

- TCGA = The Cancer Genome Atlas; NSMP = no specific molecular profile; EBRT = external beam radiation; CisRT = cisplatin/radiotherapy.
- Leon-Castillo, 2020.

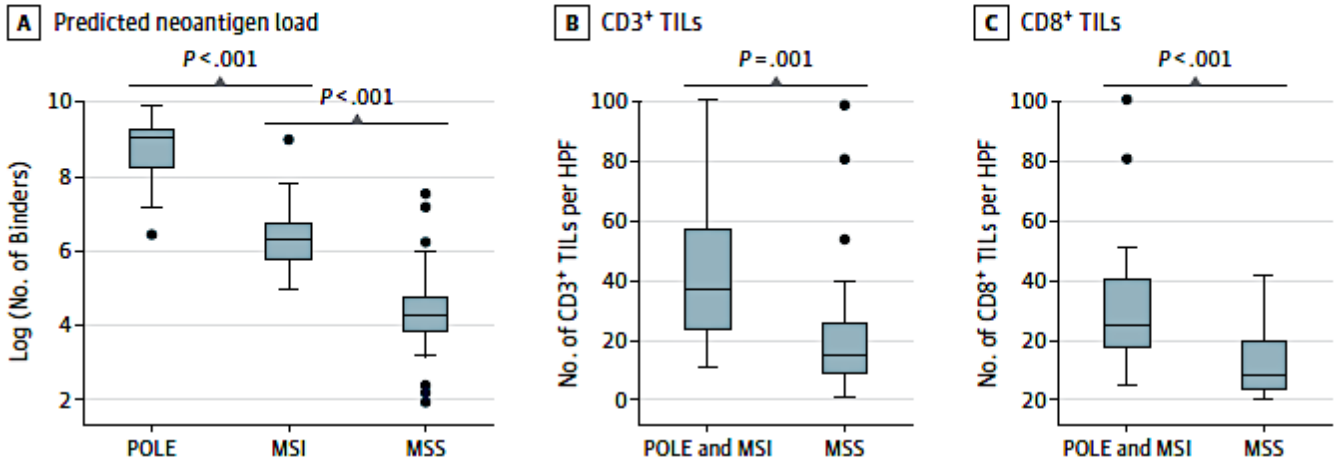
Hyper-mutated/Microsatellite Instable Group: Responses to IO in the 2nd Line Setting as compared to MSS/MMRp

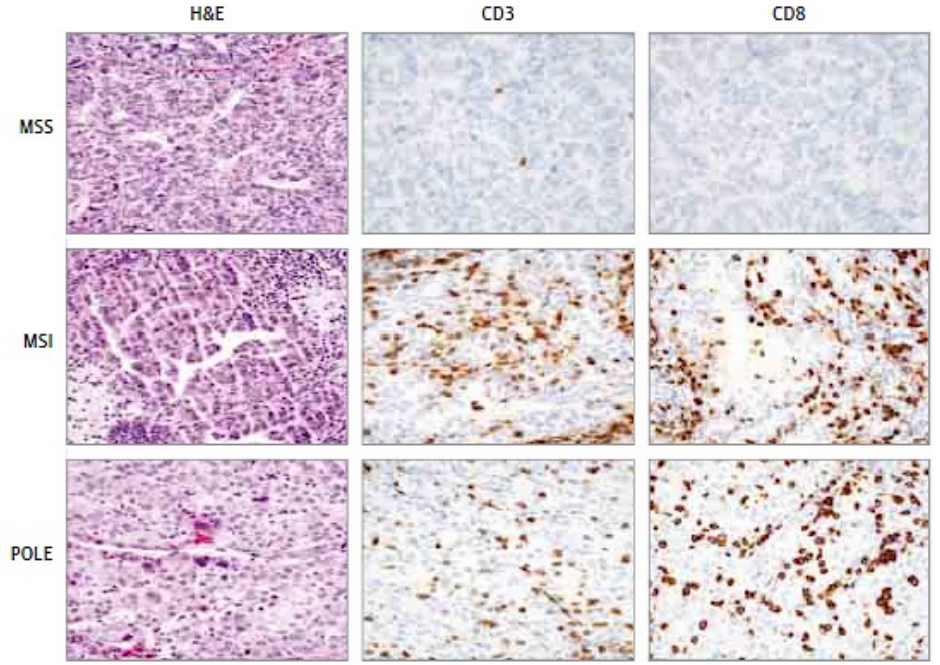
	Keynote-158[1]	GARNET[2]	KEYNOTE-028[3]	NCT01375842[3]	GARNET[2]
Phase / type	2	2	1b	1a	2
Population	Previously treated MSI-H	Previously treated MSI-H/dMMR	Previously treated PD-L1+ MSS/pMMR	Recurrent EC MSS/pMMR	Recurrent MSS/pMMR
Patients, n	90	108	24	15	156
Treatment	Pembrolizumab	Dostarlimab	Pembrolizumab	Atezolizumab	Dostarlimab
Prior lines	0 - >5	1-3			1-3
ORR, %	48%*	43.5%	13%	13	14.1%
DCR, %	66%	56%	26%	27%	35%
DOR	NR (3-50+)	NR	—	—	NR
mPFS	13.1 mo	Immature	1.8 mo	1.7 mo	
mOS	12-mo OS= 69%	NR	NR	9.6 mo	
Safety summary (TRAE grade ≥3)	12%	13%	16.7%	Any TRAE: 47%	19%

1. O'Malley D et al. JCO 2022 ; *in efficacy population n=79 (patients who received 1 or more doses of pembro and were enrolled >26 weeks before data cut off. 2.. Oaknin A et al. J Immunother 2022; 3. Ott PA et al. *J Clin Oncol*. 2017;35(22):2535-2341; 4. Fleming GF et al. 2017 ASCO Annual Meeting. Abstract 5585;

Tumor Microenvironment in Endometrial Cancer

Figure 1. Neoantigen load and CD3⁺ and CD8⁺ Tumor-Infiltrating Lymphocytes (TILs) in Polymerase e (POLE), Microsatellite-Instable (MSI), and Microsatellite-Stable (MSS) Tumors





CD = cluster of differentiation; PD-1 = programmed cell death protein 1; TILs = tumor-infiltrating lymphocytes; MSS = microsatellite stable.

Howitt et al, 2015.

- Both POLE and MSI are associated with significantly increased predicted neoepitopes and numbers of CD3-positive and CD8-positive TILs compared with MSS tumors
- In addition, hypermutated tumors harbor higher neoantigen loads and are associated with increased tumor infiltration by cytotoxic T lymphocytes
- POLE and MSI tumors are excellent candidates for immunotherapies targeting the PD-1 pathway

Chemotherapy +/- IO: Benefit in PFS

Study	Chemotherapy + Drug	Hazard ratio dMMR (vs chemo alone)	Hazard ratio pMMR (vs chemo alone)
GY018	Pembrolizumab	0.30	0.54
RUBY	Dostarlimab	0.28	0.76
AtTEnd	Atezolizumab		0.92
MITO END-3		0.46	1.17
DUO-E	Durvalumab +olaparib	0.42 0.41	0.77 0.57
RUBY Part 2	Dostarlimab +Niraparib	0.48	0.63

Chemotherapy and Immunotherapy for all???

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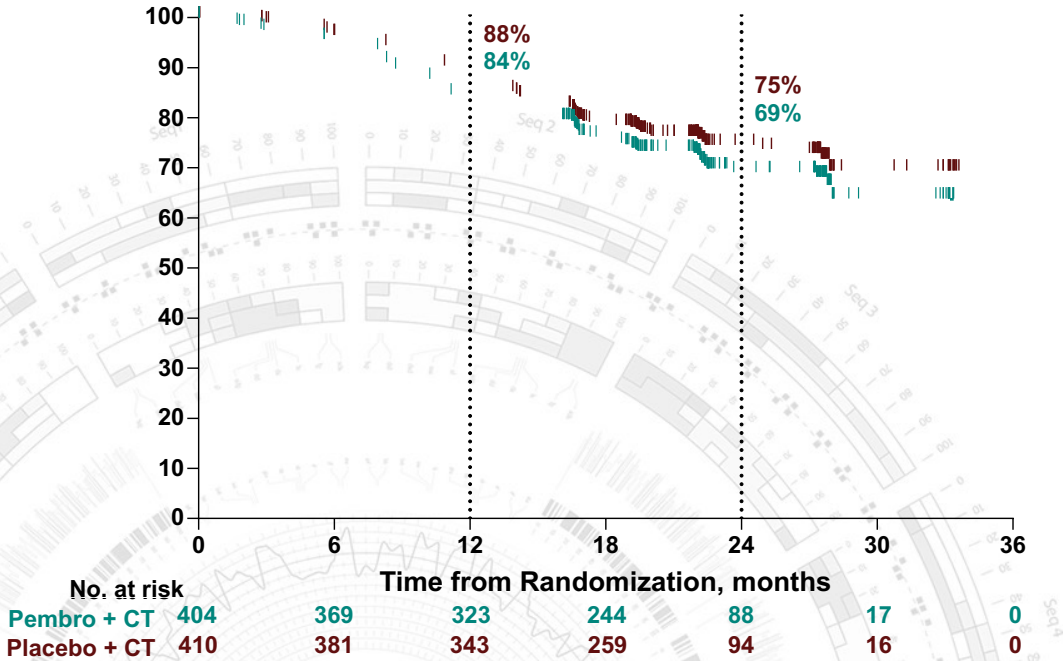
The Ohio State University
Comprehensive Cancer Center

Keynote-B21: Pembrolizumab plus Chemotherapy Improved DFS in dMMR Subgroup, but not in pMMR

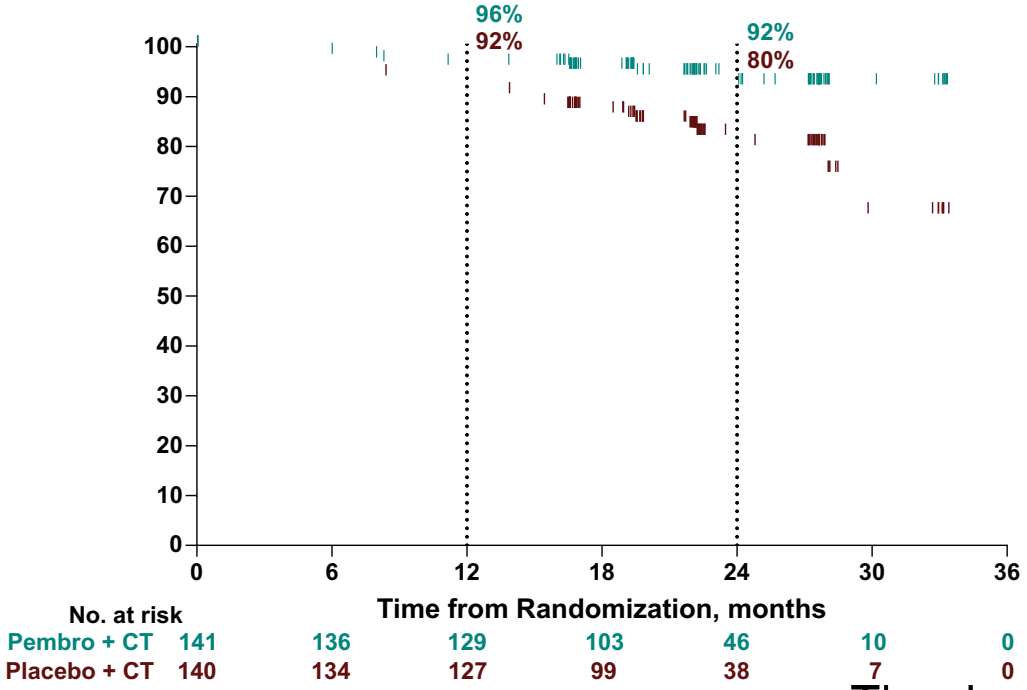
pMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	111 (27)	NR (NR-NR)	1.20 (0.91–1.57)
Placebo + CT	96 (23)	NR (NR-NR)	



dMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	8 (6)	NR (NR-NR)	0.31 (0.14-0.69)
Placebo + CT	25 (18)	NR (29.5-NR)	



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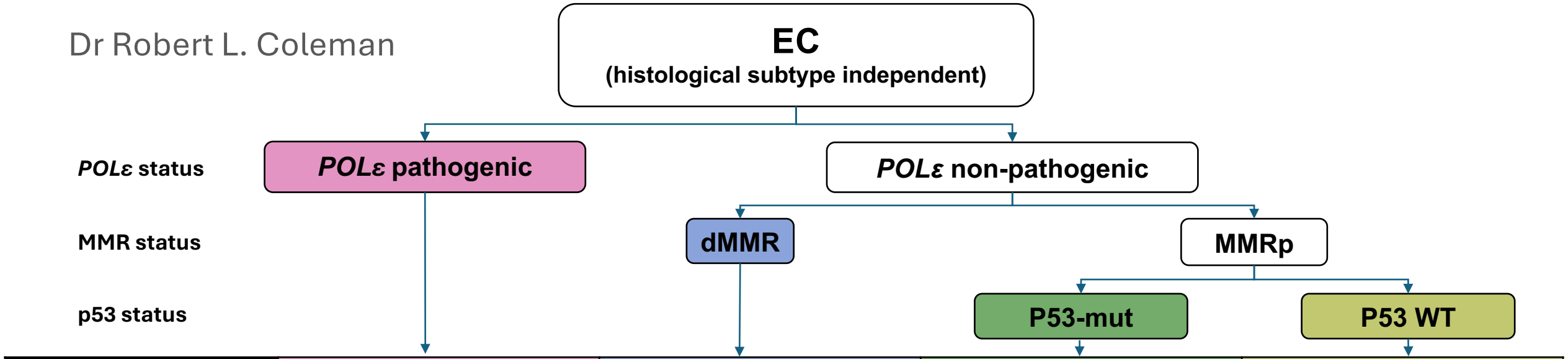
The Ohio State University Comprehensive Cancer Center

Van Gorp, Annals Oncol 2024

RUBY MOLECULAR CLASSIFICATION ALGORITHM

In RUBY Part 1, molecular classification was performed for all participants with WES results – 400 of 494 patients

Dr Robert L. Coleman

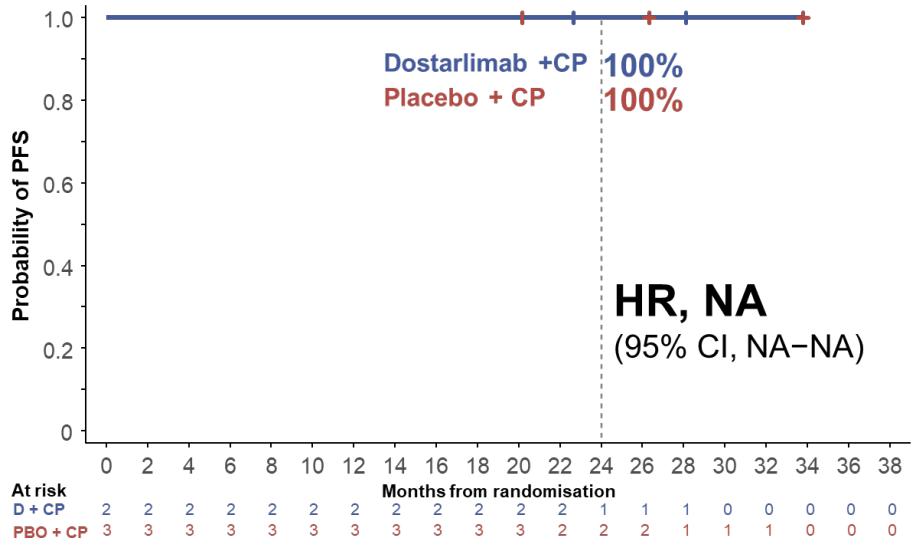


Integrated diagnosis	*POLε*mut (EDM)	dMMR (or MSI-H)	TP53 aberrant[a]	NSMP
Prevalence in RUBY, % (n/N)	**1.25%** (5/400)	**22.75%** (91/400)	**22%** (88/400)	**54%** (216/400)
Diagnostic test	WES	Results of local (IHC, NGS, PCR) or central test (IHC) provided for RUBY at randomization	WES	—

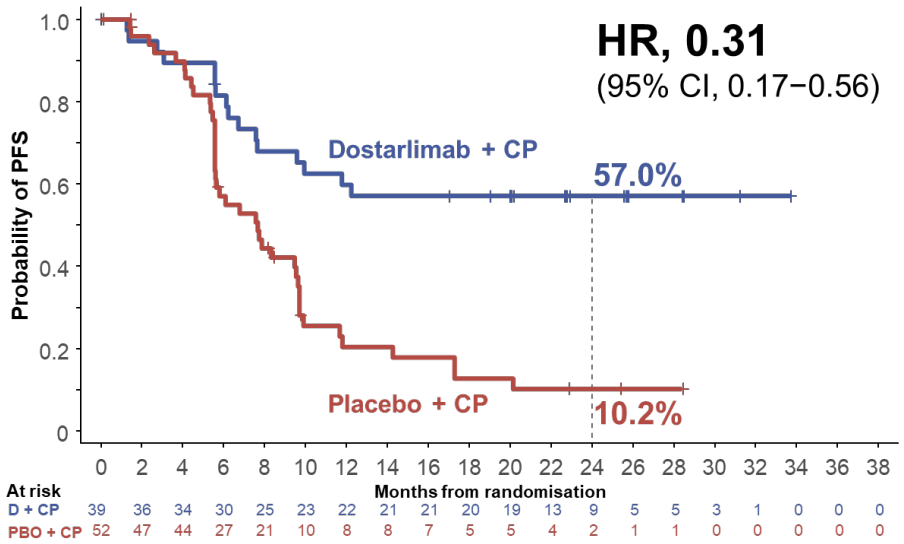
R. Coleman, ESMO GYN 2024. Mirza, ESMO 2023

RUBY: PFS According to Molecular Subgroup

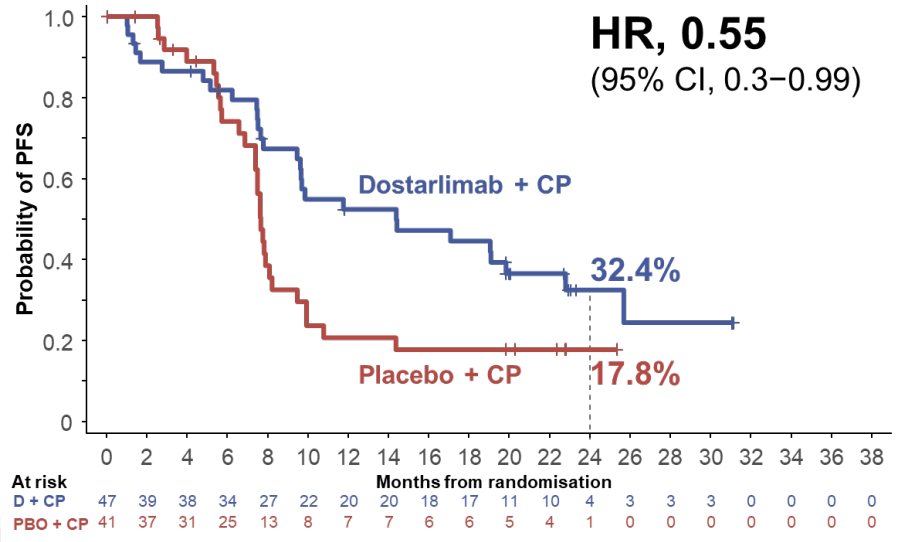
POLε mut



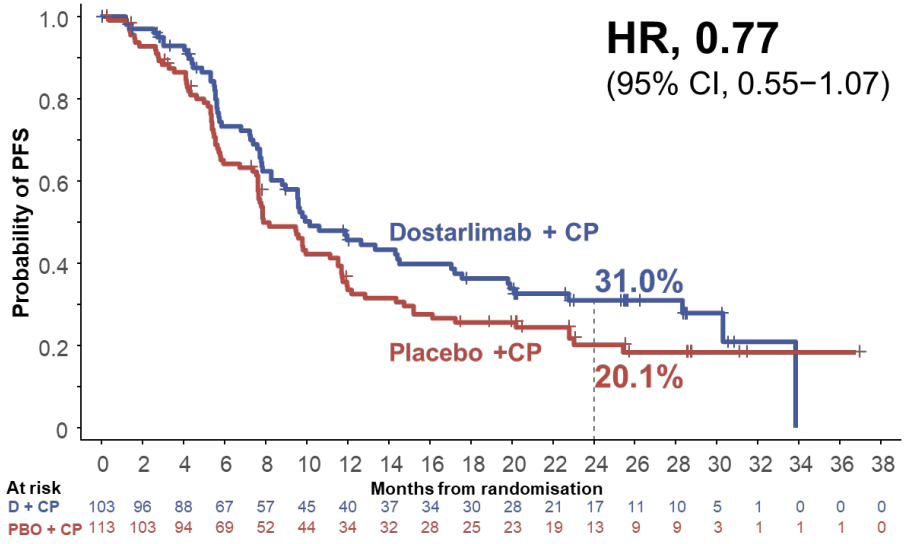
dMMR/MSI-H



TP53 mut



NSMP



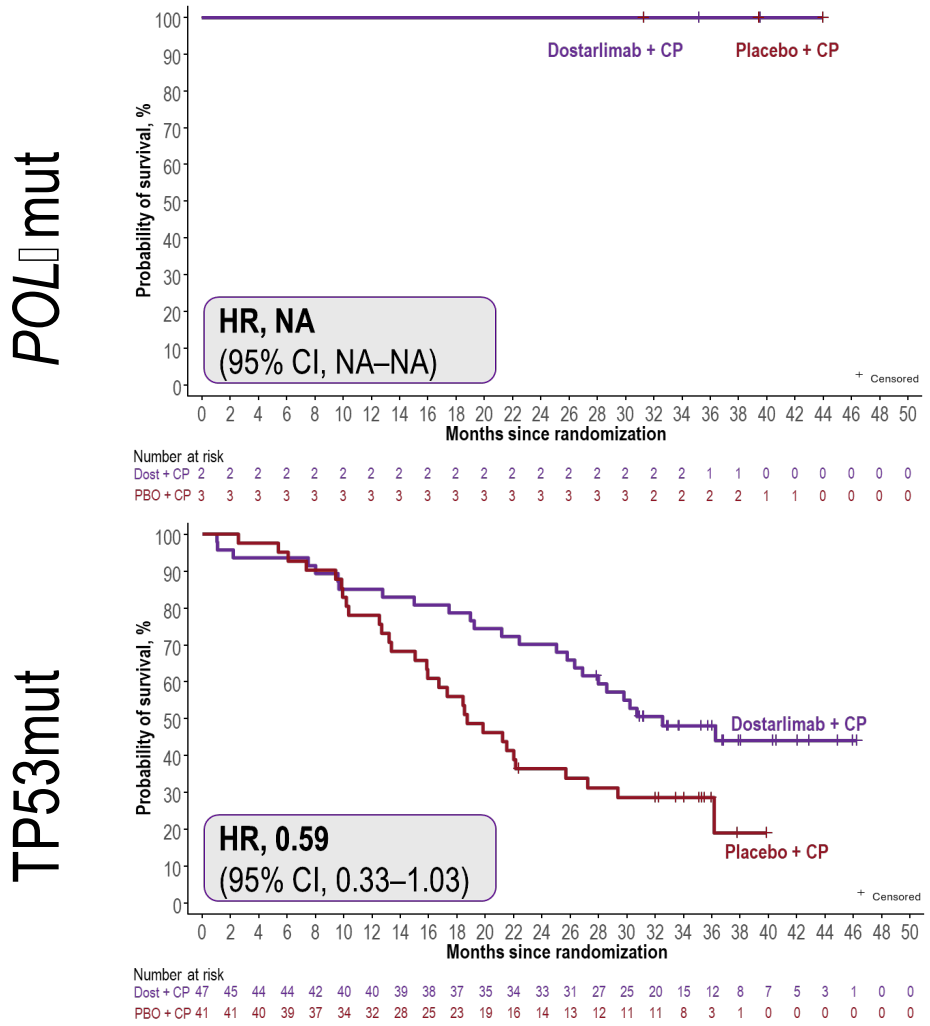
mes

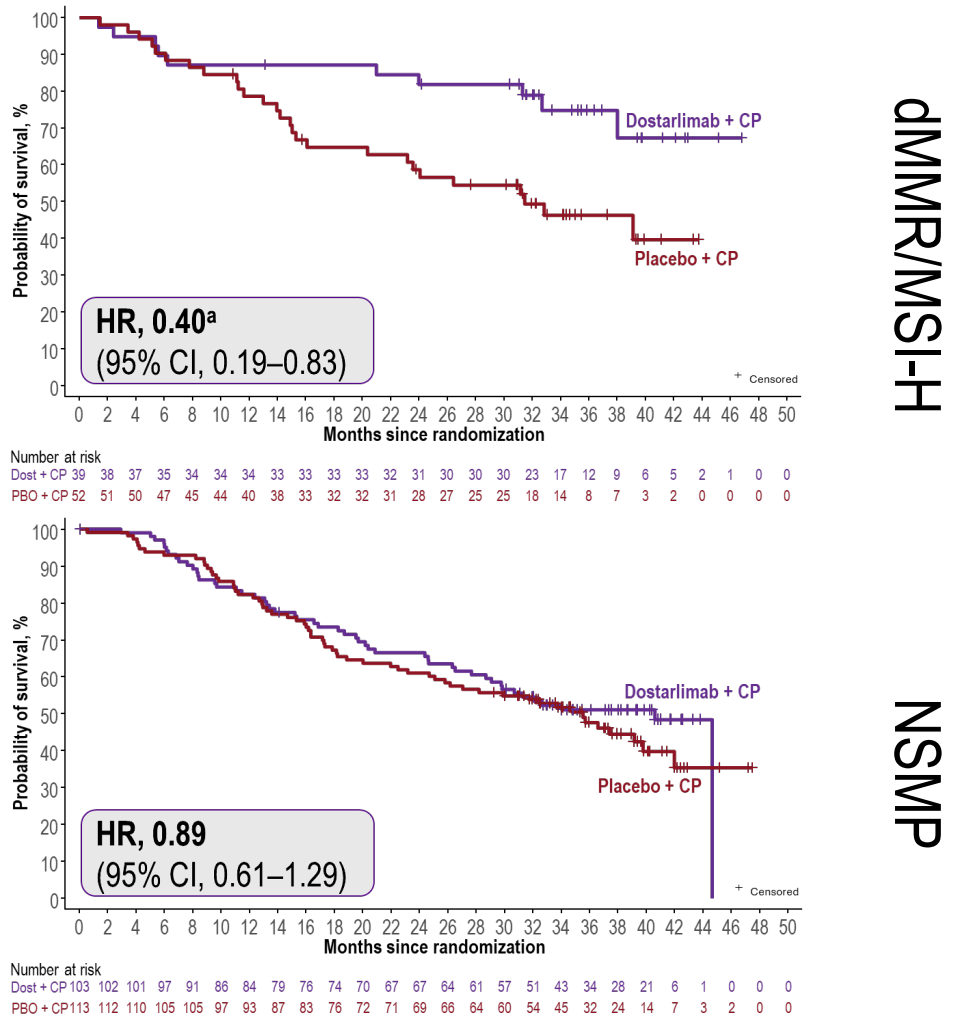
- Dr Mansoor Raza Mirza, ESMO 2023

Data based on exploratory analysis based on 400 patients from the RUBY trial with known molecular classification with whole exome sequencing. CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NR, not reached; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε , polymerase epsilon; TP53, tumor protein 53.

Exploratory analysis of OS per molecular subgroup

- Based on 400/494 patients with known molecular classification per WES



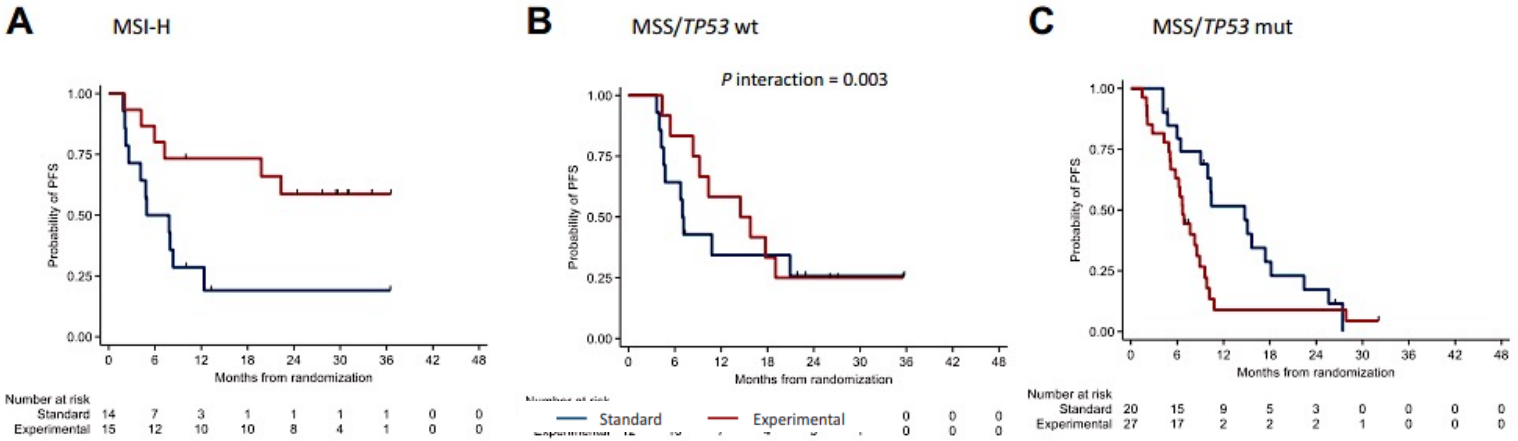


Median expected duration of follow-up in the overall population: 37.2 months (range, 31.0–49.5 months).

[a]Analysis shown on this slide is post hoc exploratory analysis of 91 patients with dMMR/MSI-H EC and WES results. In the prespecified OS analysis of the dMMR/MSI-H population (n=118), shown earlier, HR was 0.32. CP, carboplatin-paclitaxel; Dost, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability-high; mut, mutated; NA, not applicable; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε, polymerase epsilon; TP53, tumor protein 53; WES, whole-exome sequencing.

Are all pMMR/MSS/p53mut the same?

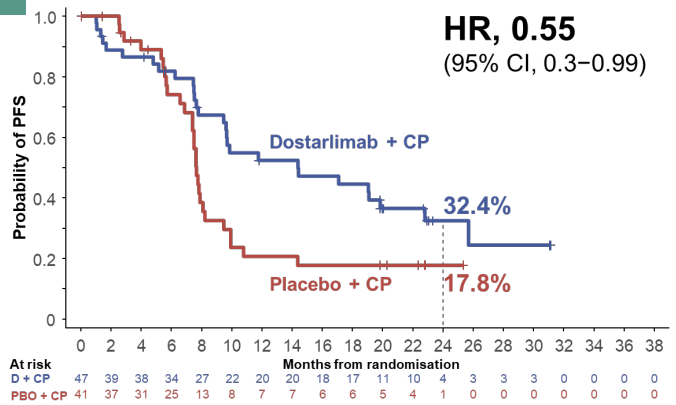
MITO END-3 (Avelumab)



TP53 mutation is associated with a poor effect of avelumab, while mutations of PTEN and ARID1A are related to a positive effect of the drug in patients with advanced EC.

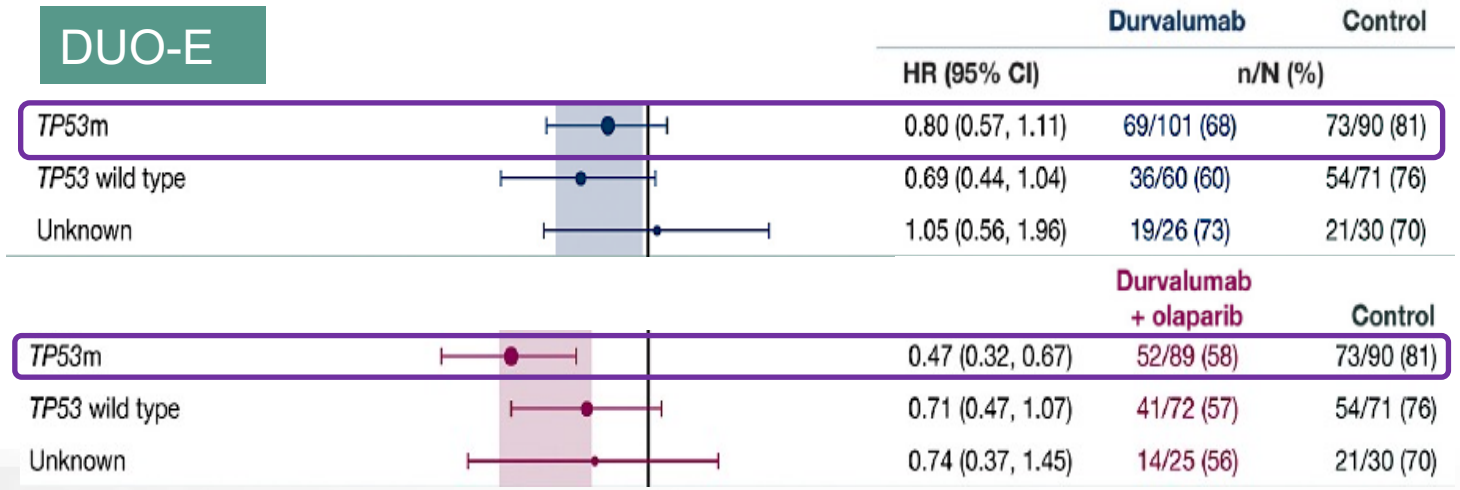
RUBY

TP53 mut



MADRID 2023 ESMO congress

DUO-E



THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER

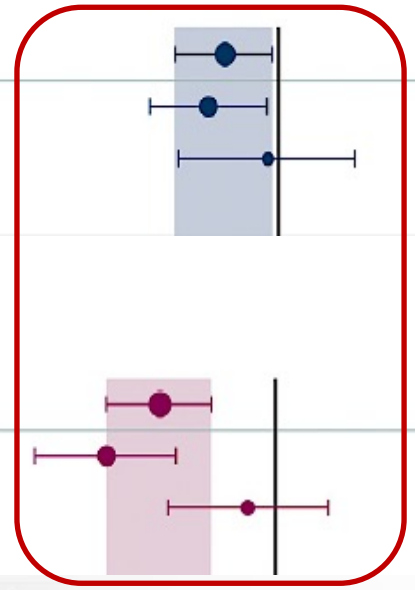
Pignata, Ann Oncol 2024; Mirza, ESMO 2023; Westin Gynecol Oncol 2026

PD-L1 in pMMR

- PD-L1 not predictive of IO activity in GY018
- PD-L1 predictive of IO activity in DUO-E

PD-L1 CPS ≥1	Events, n/N	Median PFS (95% CI), months	HR (95% CI)
Pembrolizumab + CT	71/208	13.1 (9.1–19.8)	0.59 (0.43–0.80)
Placebo + CT	100/205	8.5 (8.0–10.7)	

PD-L1 CPS <1	Events, n/N	Median PFS (95% CI), months	HR (95% CI)
Pembrolizumab + CT	21/80	15.1 (11.1–NR)	0.44 (0.26–0.75)
Placebo + CT	37/83	11.0 (8.3–11.4)	



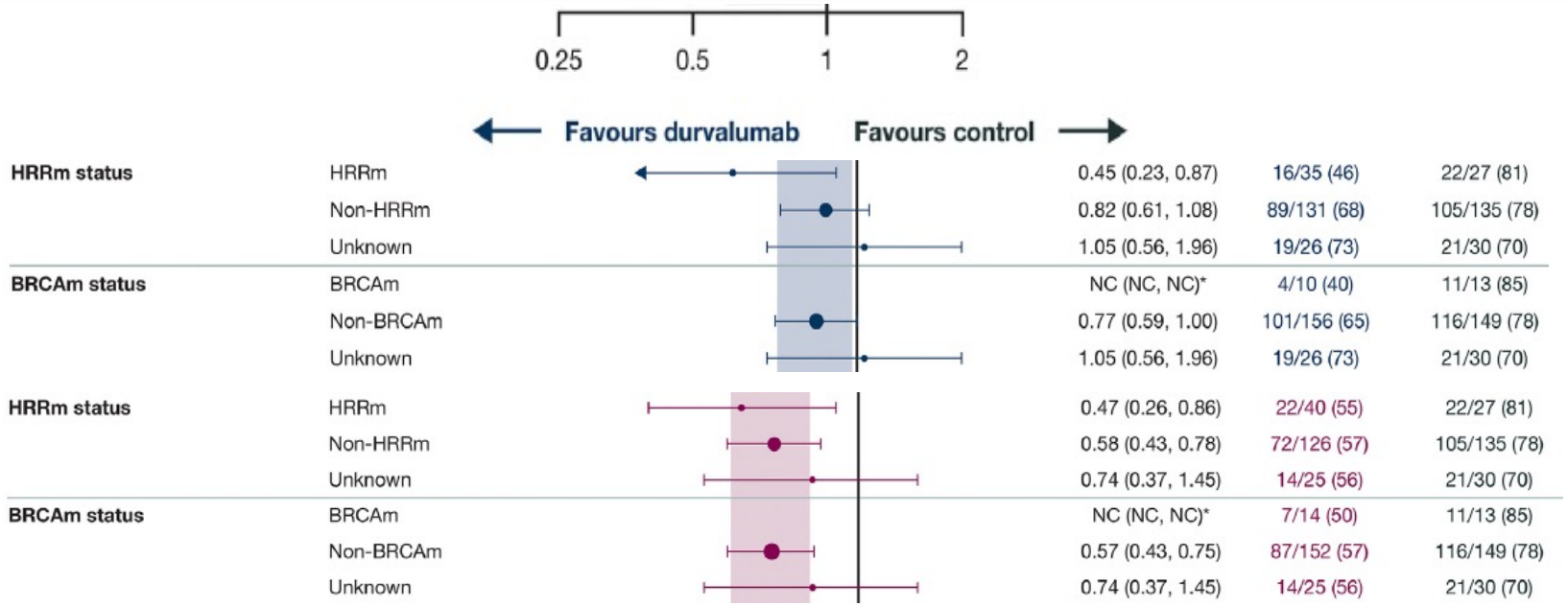
		Durvalumab	Control
		HR (95% CI)	n/N (%)
All pMMR patients		0.77 (0.60, 0.97)	124/192 (65)	148/192 (77)
PD-L1 expression	Positive (TAP score ≥1%)	0.71 (0.53, 0.95)	85/133 (64)	94/124 (76)
	Negative (TAP score <1%)	0.95 (0.61, 1.45)	35/53 (66)	53/67 (79)
	Unknown	NC (NC, NC)*	4/6 (67)	1/1 (100)

		Durvalumab + olaparib	Control
		HR (95% CI)	n/N (%)
All pMMR patients		0.57 (0.44, 0.73)	108/191 (57)	148/192 (77)
PD-L1 expression	Positive (TAP score ≥1%)	0.44 (0.31, 0.61)	54/112 (48)	94/124 (76)
	Negative (TAP score <1%)	0.87 (0.59, 1.28)	52/73 (71)	53/67 (79)
	Unknown	NC (NC, NC)*	2/6 (33)	1/1 (100)

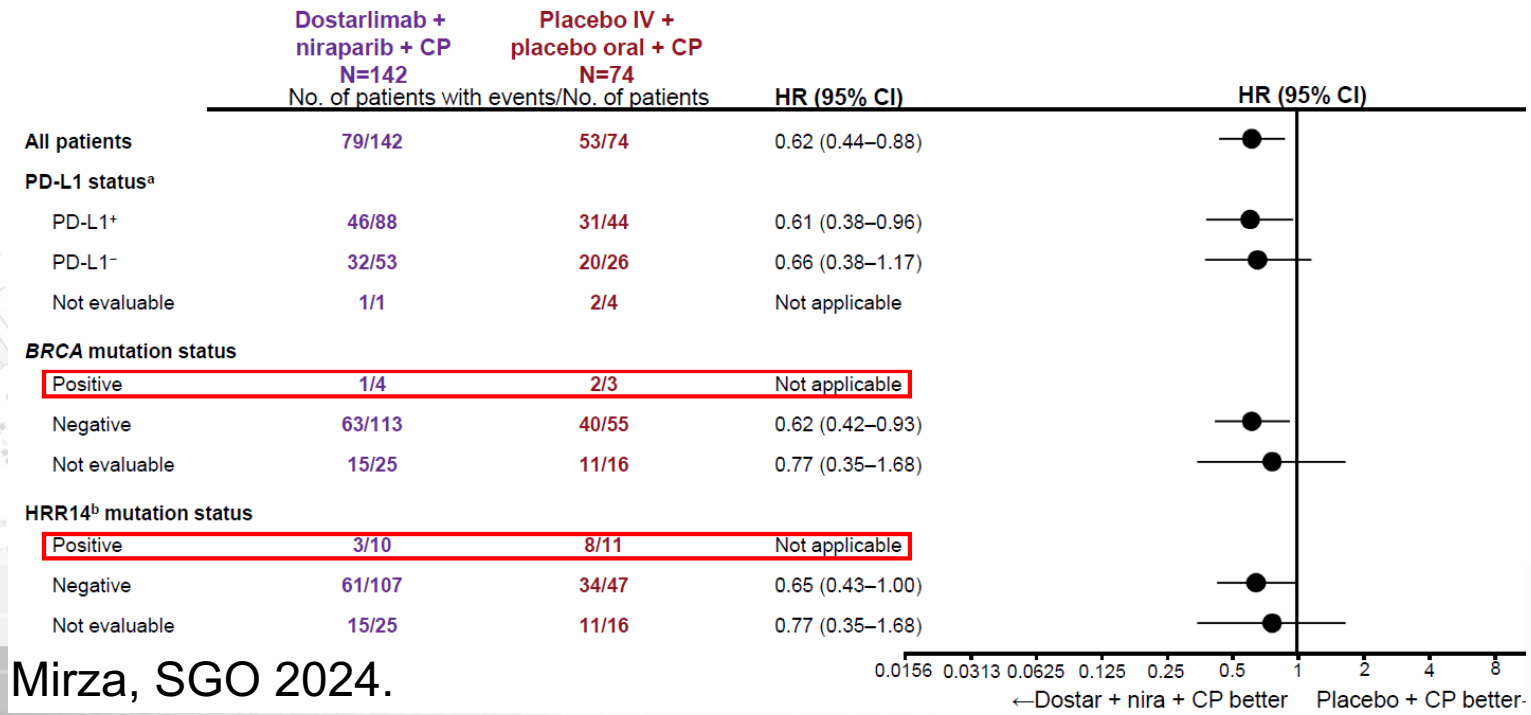
Eskander, Nat Medicine 2024; Westin, Gynecol Oncol 2026

HRR/HRD in pMMR

- DUO-E:
  - HRR ↑ benefit
  - HRR +/- both benefit
  - BRCAwt benefits



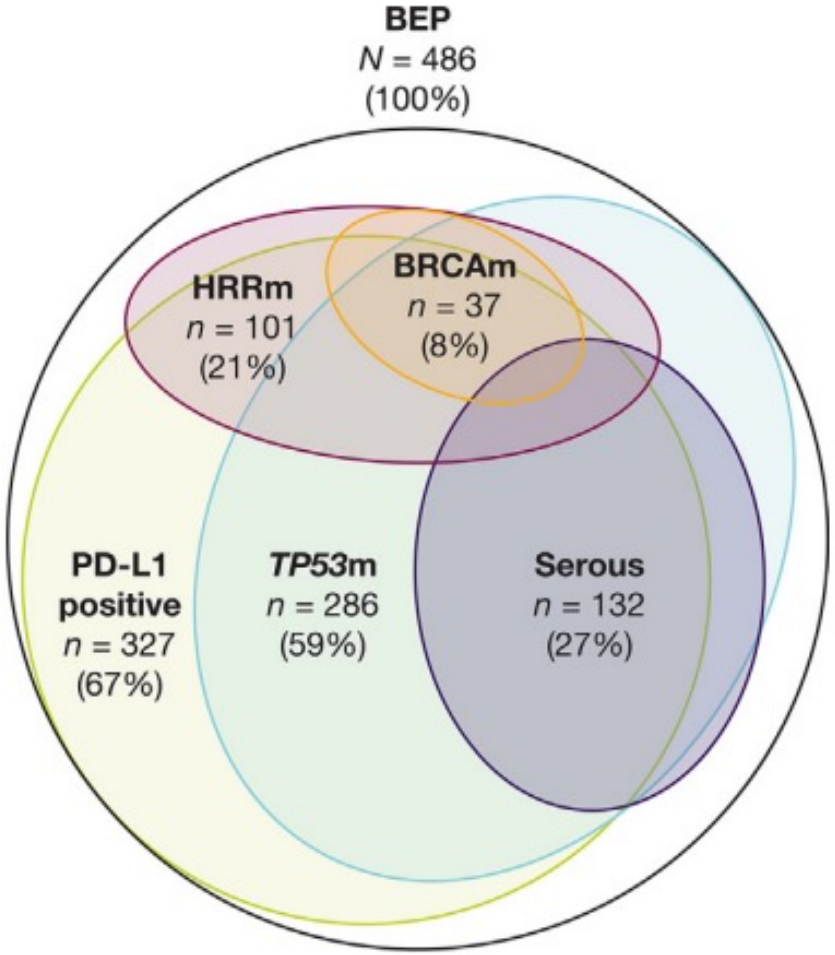
- RUBY Part 2
  - HRR - benefit
  - BRCA - benefits



Westin, Gynecol Oncol 2026; Mirza, SGO 2024.

DUO-E Biomarker Evaluable Population (BEP) in pMMR

	PD-L1 positive	*TP53*m	HRRm	BRCAm	*POLE*m	Serous
PD-L1 positive	327 (67)	215 (44)	78 (16)	28 (6)	11 (2)	99 (20)
*TP53*m	215 (44)	286 (59)	66 (14)	30 (6)	10 (2)	119 (24)
HRRm	78 (16)	66 (14)	101 (21)	37 (8)	10 (2)	31 (6)
BRCAm	28 (6)	30 (6)	37 (8)	37 (8)	7 (1)	13 (3)
*POLE*m	11 (2)	10 (2)	10 (2)	7 (1)	11 (2)	0 (0)
Serous	99 (20)	119 (24)	31 (6)	13 (3)	0 (0)	132 (27)



8.6% of pMMR tumors were TMB high

13% of dMMR tumors were TMB low

10% of dMMR tumors were not MSI-H

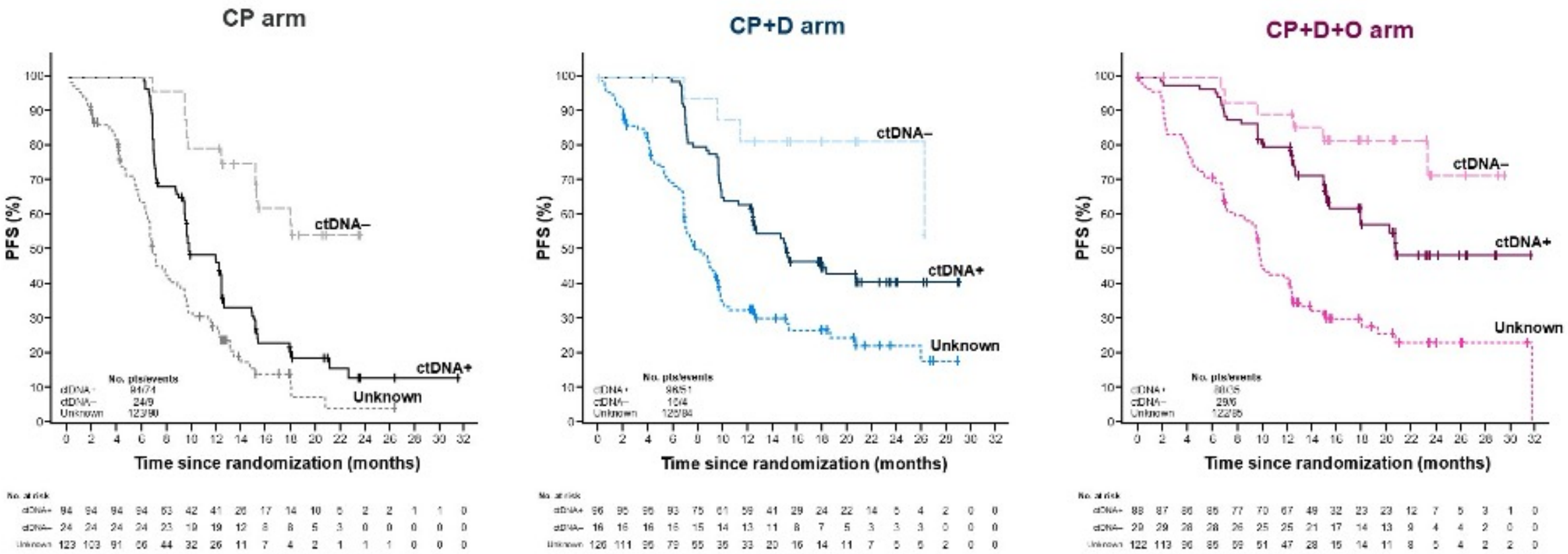
pMMR | PD-L1 positive | *TP53*m | HRRm | BRCAm | Serous

Variability in Biomarker Assessment in pMMR

Parameter	NRG-GY018	RUBY	AtTEnd	DUO-E
ICI Agent	Pembrolizumab (anti-PD-1)	Dostarlimab (anti-PD-1)	Atezolizumab (anti-PD-L1)	Durvalumab (anti-PD-L1)
MMR Testing	Central IHC (Agilent)	Central IHC (VENTANA)	Central IHC (Agilent)	Central IHC (VENTANA)
PD-L1 Antibody	22C3 pharmDx	22C3 pharmDx	SP142 (Ventana)	SP263 (Ventana)
PD-L1 Scoring System	CPS ≥1%	Not specified	TAP	TAP ≥1%
PD-L1 positivity	71.7%	RUBY-2: 61%	-	67%
p53 Assessment	Not reported (yet)	WES	Not reported	NGS*
TP53 prevalence	Not reported (yet)	29% (RUBY part 1)	Not reported	59%
POLE Assessment	Not reported	WES	Not reported	NGS* (2%)
HRD/HRR Testing	Not reported	FMI14 panel RUBY 2 : HRRm 9.7%; BRCAm 3.2%	Not reported	NGS* (FoundationOne CDx + ctDNA) HRRm 21%, BRCAm 8%
HRR Genes Assessed	N/A	*BRCA1, BRCA2, ATM, BARD1, BRIP1, PALB2, RAD51B, RAD51C, RAD51D, RAD54L, CDK12, CHEK1, CHEK2, FANCL*	N/A	ATM, BRCA1, BRCA2, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L
ARID1A Testing	Not reported	Not reported	Central IHC (Abcam EPR13501-73)	Not reported
Asian Population	5% of pMMR	None	20%	28%

DUO-E: ctDNA as a prognostic biomarker for PFS in ITT population

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



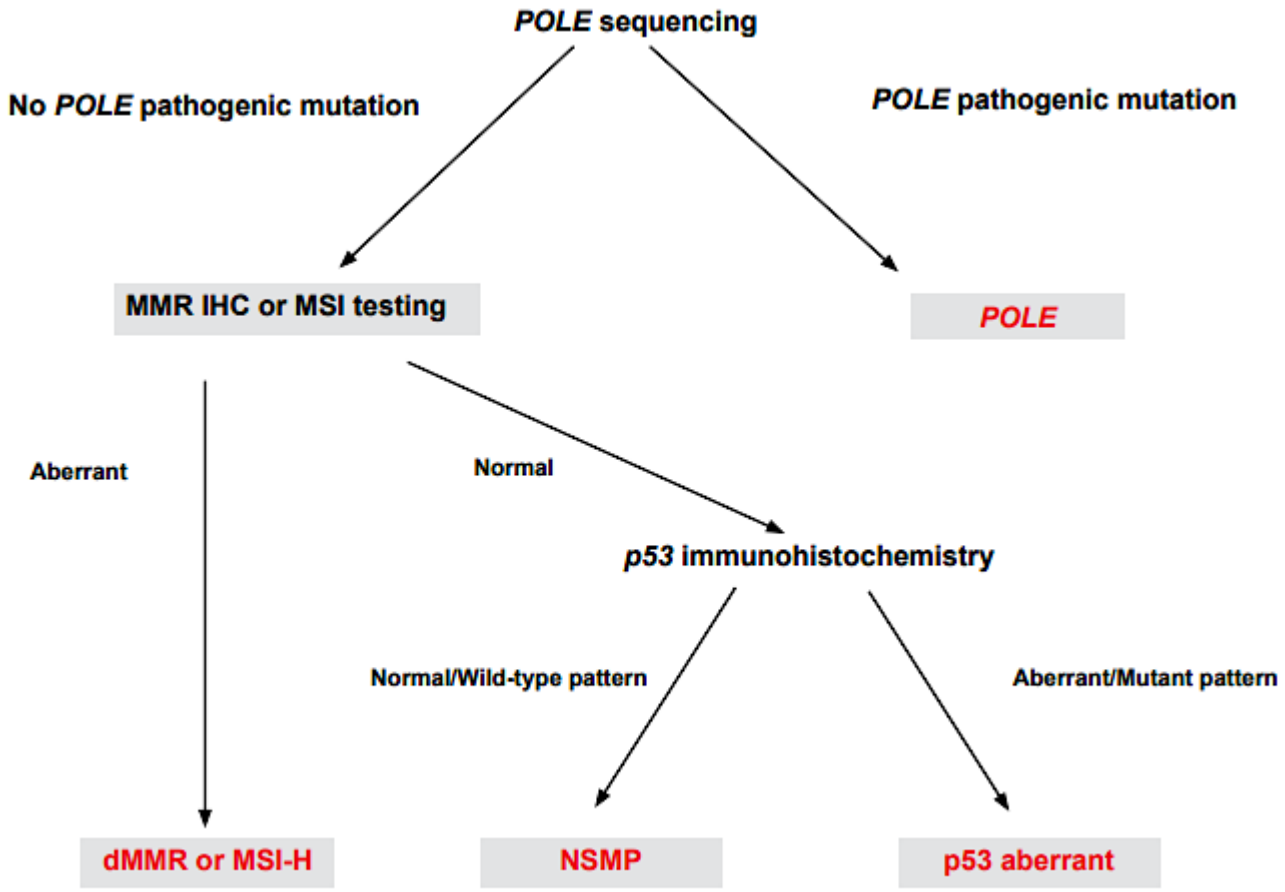
NOTE: 49% of the ITT population has known ctDNA status → biomarker evaluable population .

Westin S et al. ASCO 2025;Abstract 5512.

The James

The Ohio State University Comprehensive Cancer Center

Guideline-endorsed approach to assessment of clinically relevant biomarkers



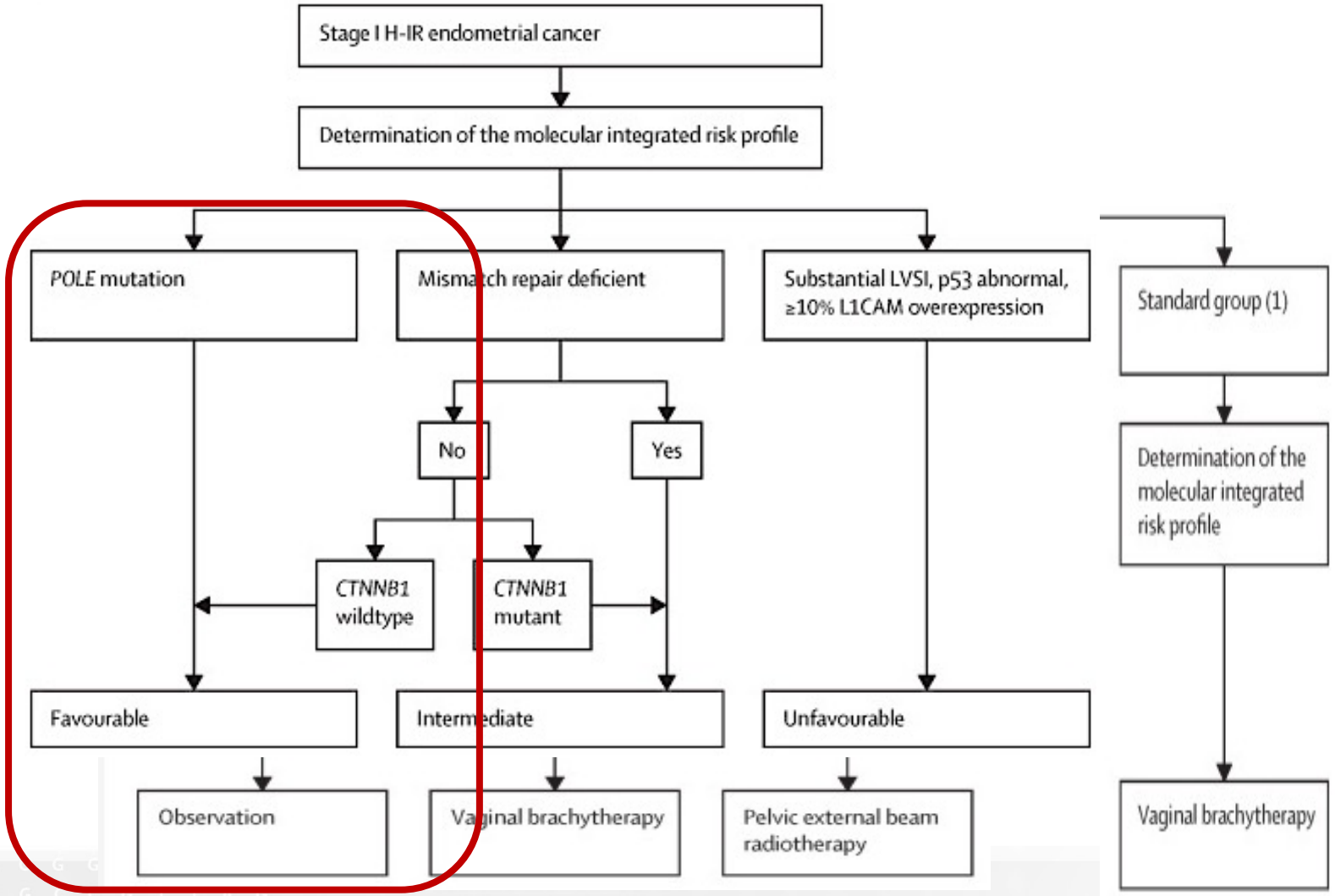
- Molecular profiling via validated and/or FDA-approved assay in initial evaluation to help facilitate cancer diagnosis
- POLE, MMR/MSI, p53
- NTRK gene fusion
- TMB
- HER2 IHC/FISH for all p53 aberrant
- ER/PR
- Genetic counseling and germline testing

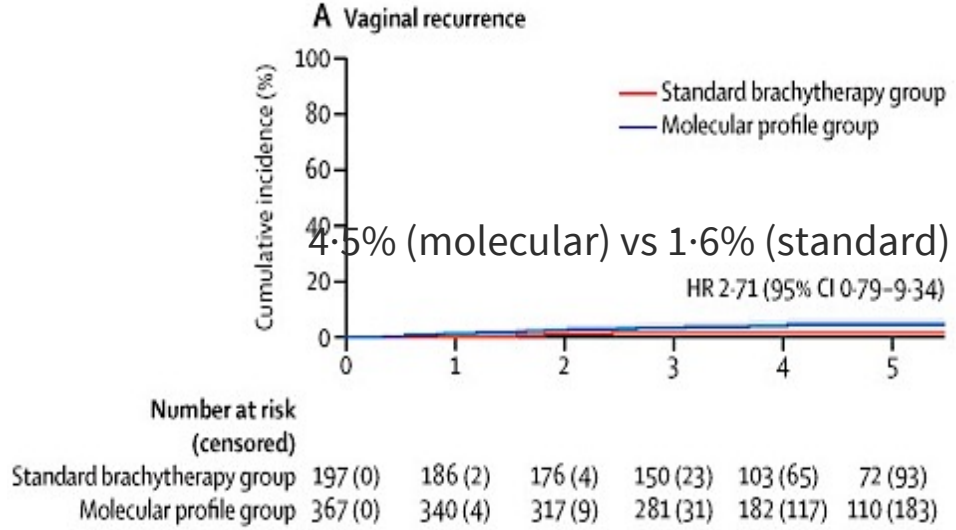
NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2026
Endometrial Carcinoma

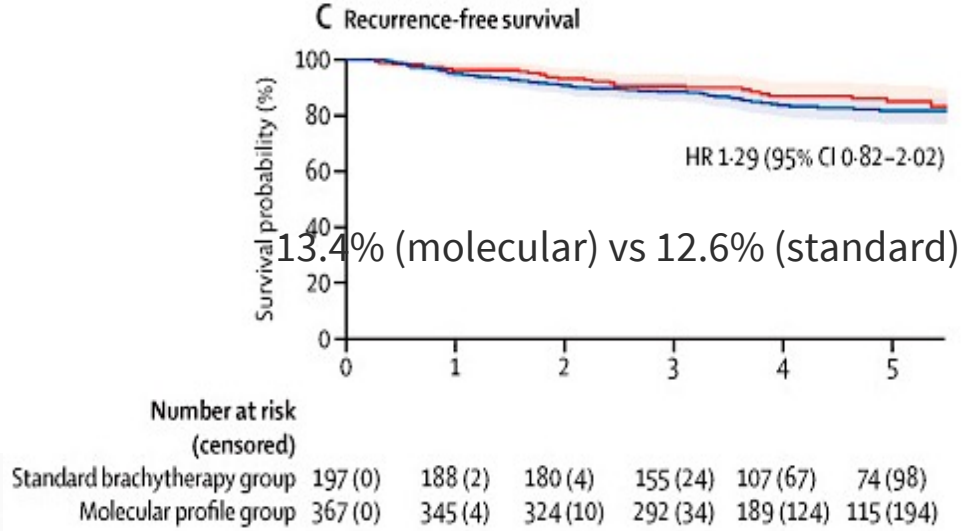
The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

PORTEC 4a: No adjuvant treatment is non-inferior to brachytherapy for vaginal control in H-I-R EC *POLE*^{mut} and NSMP-*CTNNB1* wildtype





4·5% (molecular) vs 1·6% (standard)



13.4% (molecular) vs 12.6% (standard)

Conclusions

- Molecular profiling has prognostic and predictive implications
- Across most subsets there is a benefit of IO in addition to chemotherapy
- Lack of strong predictive biomarker, other than MMR/MSI status
- Challenges
  - Small subsets
  - Variable methods of assessment
- We need:
  - Broader access to clinical trial specimens
  - Support for new biomarker discovery

Second Opinion

Ursula Matulonis, MD

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How would you treat this 78-year-old patient with MSS/pMMR, ER-negative, HER2-negative metastatic endometrial cancer (EC) with TP53, PIK3R1 and PTEN mutations if she presented today?

What is the optimal approach to biomarker assessment for patients with advanced EC (eg, TP53, BRCA, HRR, HER2)? How important is it to biopsy from the metastatic site versus the primary tumor? Is there a value in evaluating both?

What role, if any, does liquid biopsy have in this setting?

QUESTIONS FOR THE FACULTY

At the current time, are you conducting molecular analysis for all patients with EC? Are you altering your treatment approach in any way based on molecular subgroup?

In general, how would you respond to a fellow who asks you to estimate the long-term chance of survival for patients with advanced EC who receive chemotherapy alone versus chemotherapy/IO? Does your response differ between MSI-H/dMMR and MSS/pMMR disease? Do you believe that some patients in this setting are “cured”?

Agenda

Module 1: Biology of Advanced Endometrial Cancer (EC); Optimal Approach to Biomarker Assessment in Patients with Newly Diagnosed Disease — Dr Backes

Module 2: Current Up-Front Chemoimmunotherapeutic Approaches for Advanced EC — Dr Powell

Module 3: Current and Future Role of Anti-PD-1/PD-L1 Antibodies in Combination with Systemic Therapies Beyond Chemotherapy in Advanced EC — Dr Salani

Research To Practice
Current Up-Front Chemoimmunotherapeutic Approaches for Advanced EC — Dr Powell

Matthew A. Powell, MD

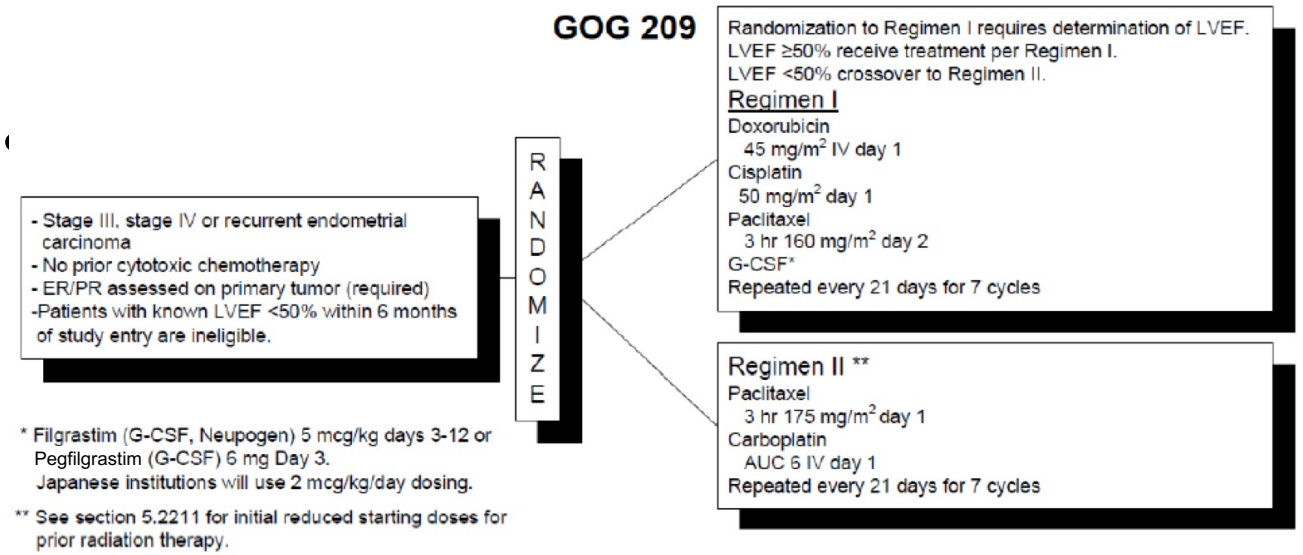
Ira C. and Judith Gall Professor

Division Gyn Oncology

Chair Uterine Corpus Committee, NRG Oncology

Washington University School of Medicine, St Louis, Missouri USA

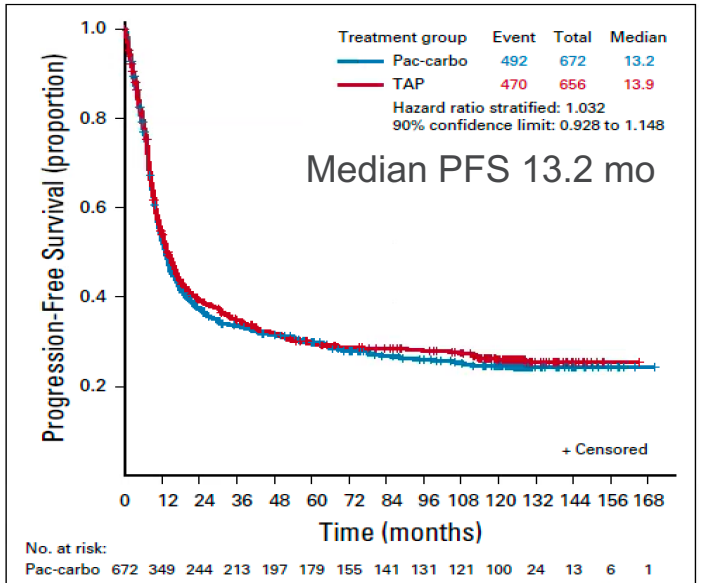
GOG 209: Chemotherapy Comparison in Advanced or Recurrent Endometrial Cancer



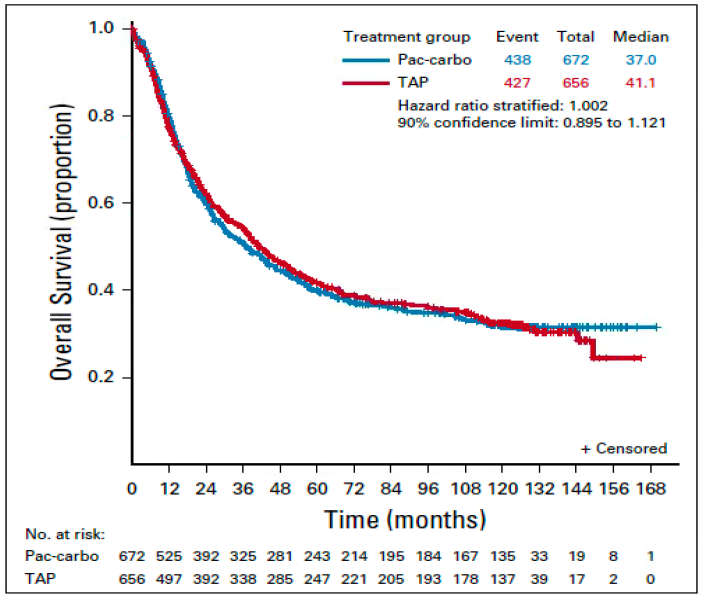
Key eligibility criteria

- **Stage III, Stage IV or recurrent endometrial carcinoma. No mandate for measurable disease**
- **NO prior cytotoxic chemotherapy**, including chemotherapy used for radiation sensitization
- GOG PS 0,1 or 2

Progression Free Survival



Overall Survival



Miller DS, et al. J Clin Oncol. 2020 Nov 20;38(33):3841-3850.

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=90)	Advanced stage or metastatic dMMR endometrial cancer	ORR: 48%
PHAEDRA trial: Durvalumab (N=35 dMMR)	Advanced stage or metastatic endometrial cancer	ORR in dMMR: 47%
GARNET study: Dostarlimab (N=129)	Previously treated, recurrent advanced stage endometrial cancer	ORR in dMMR: 43.5%
Ph II Avelumab study (N= 15 dMMR)	Advanced stage or metastatic endometrial cancer	ORR: 26.7%

O’Malley D, et al. J Clin Oncol, 2022
Antill PSK et al. J Clin Oncol 2019
Oaknin A et al. Journal for ImmunoTherapy of Cancer 2022
Konstantinopoulos PA et al. J Clin Oncol 2019

Note: Cross-trial data should be interpreted with caution.

Pivotal Phase III Trials of Immunotherapy in Advanced Endometrial Cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer

M.R. Mirza, D.M. Chase, B.M. Slomovitz, R. dePont Christensen, Z. Novák, D. Black, L. Gilbert, S. Sharma, G. Valabrega, L.M. Landrum, L.C. Hanker, A. Stuckey, I. Boere, M.A. Gold, A. Auranen, B. Pothuri, D. Cibula, C. McCourt, F. Raspagliesi, M.S. Shahin, S.E. Gill, B.J. Monk, J. Buscema, T.J. Herzog, L.J. Copeland, M. Tian, Z. He, S. Stevens, E. Zografos, R.L. Coleman, and M.A. Powell, for the RUBY Investigators*

ORIGINAL ARTICLE

Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer

Ramez N. Eskander, M.D., Michael W. Sill, Ph.D., Lindsey Beffa, M.D., Richard G. Moore, M.D., Joanie M. Hope, M.D., Fernanda B. Musa, M.D., Robert Mannel, M.D., Mark S. Shahin, M.D., Guilherme H. Cantuaria, M.D., Eugenia Girda, M.D., Cara Mathews, M.D., Juraj Kavecansky, M.D., Charles A. Leath III, M.D., M.S.P.H., Lilian T. Gien, M.D., Emily M. Hinchcliff, M.D., M.P.H., Shashikant B. Lele, M.D., Lisa M. Landrum, M.D., Floor Backes, M.D., Roisin E. O'Cearbhaill, M.D., Tareq Al Baghdadi, M.D., Emily K. Hill, M.D., Premal H. Thaker, M.D., Veena S. John, M.D., Stephen Welch, M.D., Amanda N. Fader, M.D., Matthew A. Powell, M.D., and Carol Aghajanian, M.D.

ASCO Journal of Clinical Oncology®

Durvalumab Plus Carboplatin/Paclitaxel Followed by Maintenance Durvalumab With or Without Olaparib as First-Line Treatment for Advanced Endometrial Cancer: The Phase III DUO-E Trial

Shannon N. Westin, MD, MPH[1]; Kathleen Moore, MD[2]; Hye Sook Chon, MD[3]; Jung-Yun Lee, MD[4]; Jessica Thomes Pepin, MD[5]; Michael Sundborg, MD[6]; Ayelet Shai, MD, PhD[7]; Joseph de la Garza, MD[8]; Shin Nishio, MD[9]; Michael A. Gold, MD[10]; Ke Wang, MD[11]; Kristi McIntyre, MD[12]; Todd D. Tillmanns, MD[13]; Stephanie V. Blank, MD[14]; Ji-Hong Liu, MD[15]; Michael McCollum, MD[16]; Fernando Contreras Mejia, MD[17]; Tadaaki Nishikawa, MD[18]; Kathryn Pennington, MD[19]; Zoltan Novak, MD, PhD[20]; Andreia Cristina De Melo, MD[21]; Jalid Sehouli, MD[22]; Dagmara Klasa-Mazurkiewicz, MD[23]; Christos Papadimitriou, MD[24]; Marta Gil-Martin, MD[25]; Birute Brasiuniene, MD, PhD[26]; Conor Donnelly, PhD[27]; Paula Michelle del Rosario, MD[28]; Xiaochun Liu, MD, PhD[29]; and Els Van Nieuwenhuysen, MD[30]; on behalf of the DUO-E Investigators

DOI https://doi.org/10.1200/JCO.23.02132

Atezolizumab and chemotherapy for advanced or recurrent endometrial cancer (AtTEnd): a randomised, double-blind, placebo-controlled, phase 3 trial

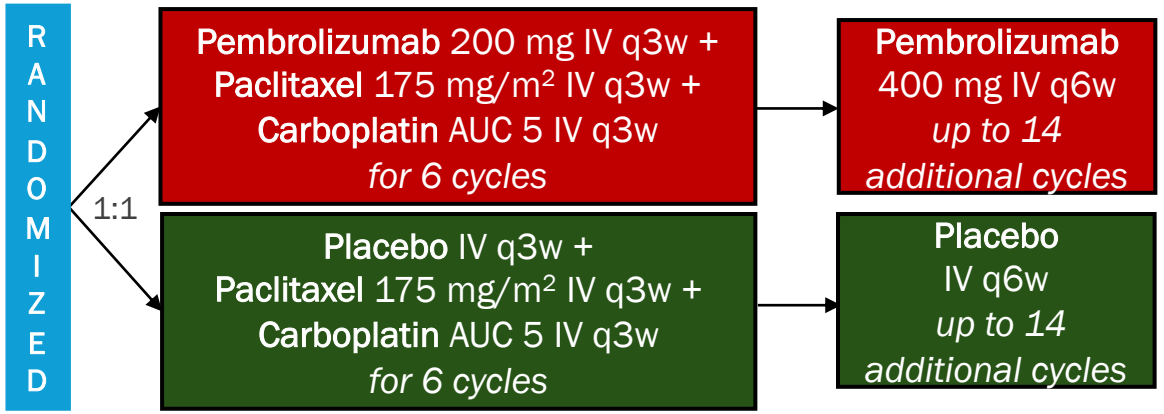
*Nicoletta Colombo, Elena Biagioli, Kenichi Harano, Francesca Galli, Emma Hudson, Yoland Antill, Chel Hun Choi, Manuela Rabaglio, Frederic Marmé, Christian Marth, Gabriella Parma, Lorena Fariñas-Madrid, Shin Nishio, Karen Allan, Yeh Chen Lee, Elisa Piovano, Beatriz Pardo, Satoshi Nakagawa, John McQueen, Claudio Zamagni, Luis Manso, Kazuhiro Takehara, Giulia Tasca, Annamaria Ferrero, Germana Tognon, Andrea Alberto Lissoni, Mariacristina Petrella, Maria Elena Laudani, Eliana Rulli, Sara Uggeri, M Pilar Barretina Ginesta, and AtTEnd study group**

THE LANCET

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

Key Eligibility Criteria

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



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

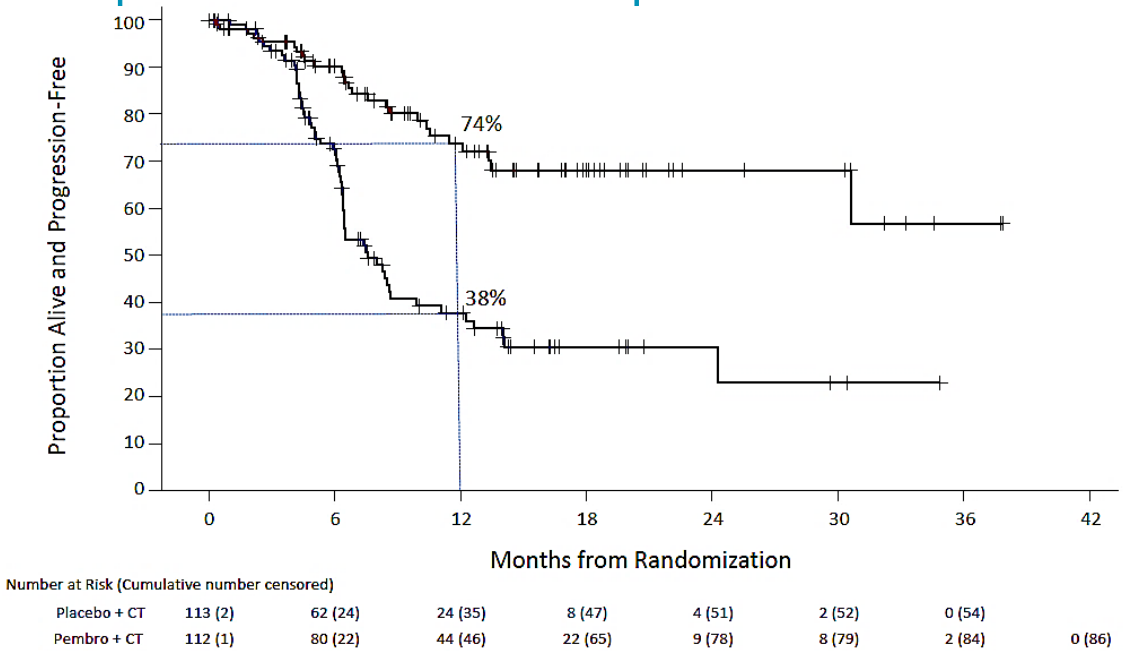
Primary endpoints: PFS per RECIST v1.1 by INV in pMMR and dMMR cohorts
Secondary endpoints: Safety, ORR/DOR, OS, PRO/QoL, concordance of MMR testing results

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

Data cutoff: December 16, 2022 for dMMR; December 6, 2022 for pMMR.
Eskander R, et al. SGO 2023. Abstract 264. Eskander RN et al. NEJM 2023

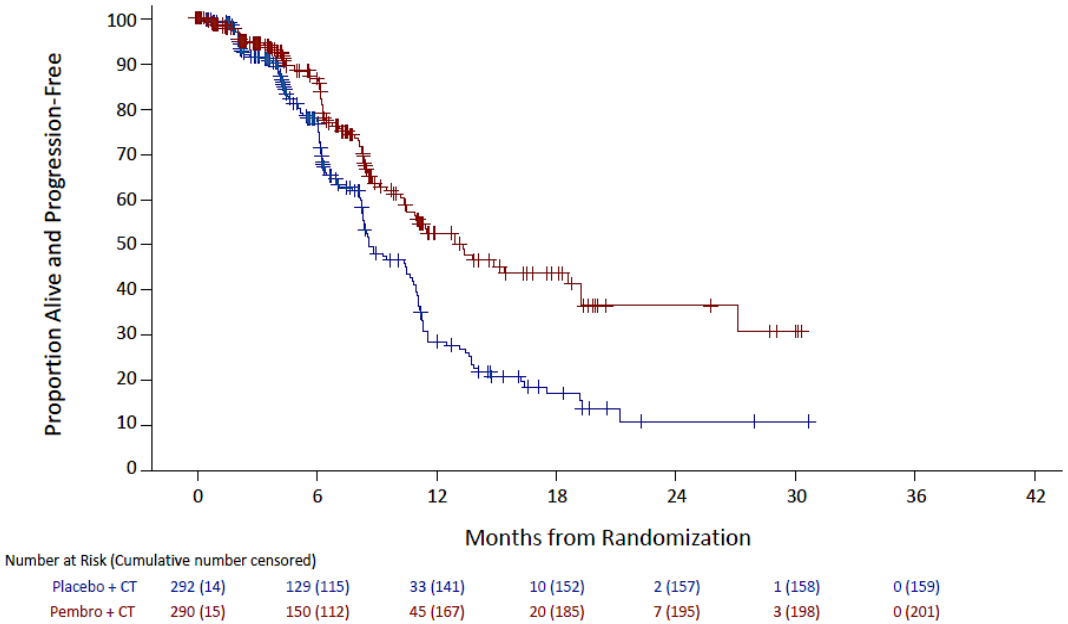
NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC – PFS

PFS per RECIST v1.1 in dMMR Population



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

PFS per RECIST v1.1 in pMMR Population



	Events, n/N	Median (95% CI), mo	HR (stratified; 95% CI)
Pembro + CT	89/290	13.1 (10.5-18.8)	**0.54 (0.41-0.71)** ***P*<0.00001**
Placebo + CT	133/292	8.7 (8.4-10.7)	

- Median follow-up: 12 months for dMMR, 7.9 months for pMMR

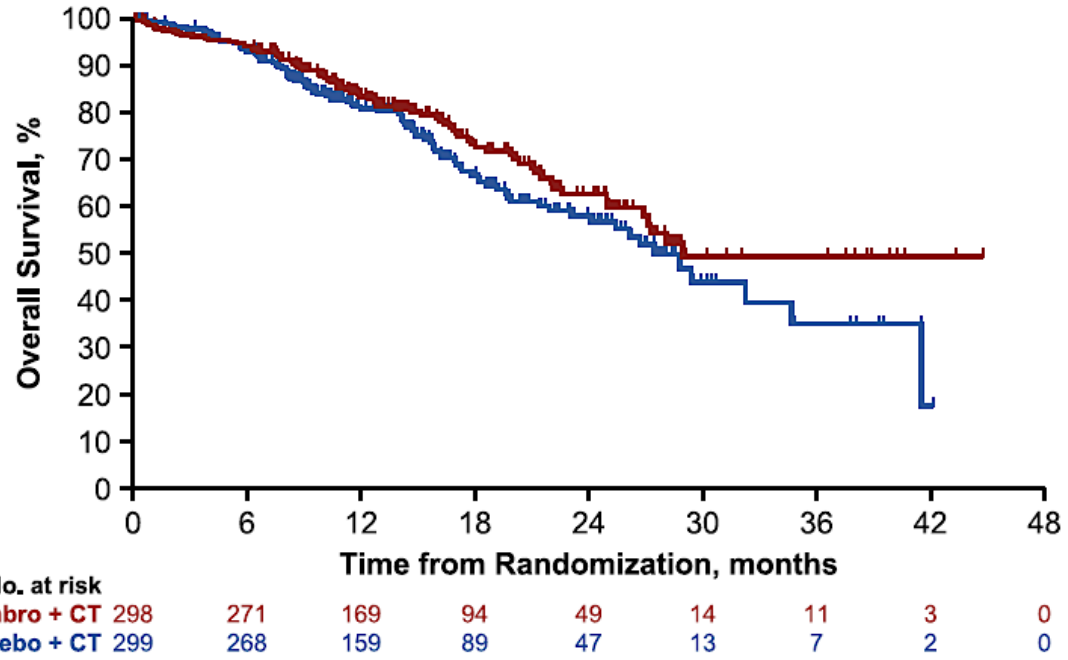
Data cutoff: December 16, 2022 for dMMR; December 6, 2022 for pMMR.
Eskander R, et al. N Eng J Med. March 2023

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

OS in pMMR Population

A)

	Events, n/N	Follow-up Duration[a], median (range), mo	Median OS (95% CI), mo	HR (95% CI)[b], *P*-value[c]
Pembro + CT	77/298	15.7 (0.5–45.4)	28.9 (26.8–NR)	**0.80 (0.59–1.08)**
Placebo + CT	92/299	15.0 (0.9–45.6)	28.7 (24.0–34.6)	***P* = 0.0683**

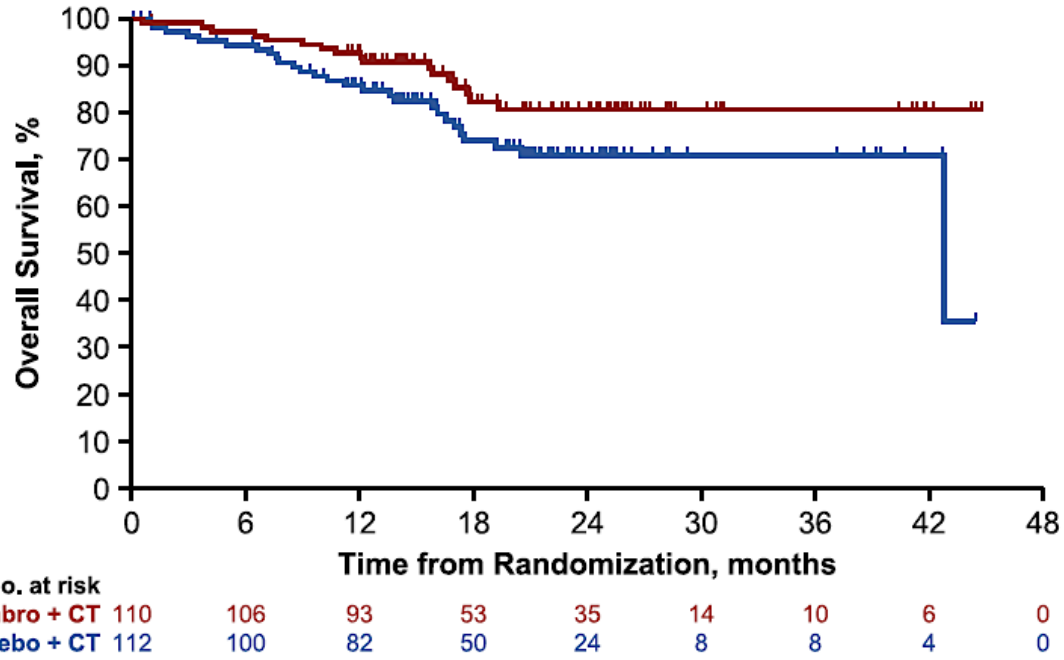


No. at risk									
Pembro + CT	298	271	169	94	49	14	11	3	0
Placebo + CT	299	268	159	89	47	13	7	2	0

OS in dMMR Population

B)

	Events, n/N	Follow-up Duration[a], median (range), mo	Median OS (95% CI), mo	HR (95% CI)[b], *P*-value[c]
Pembro + CT	17/110	19.3 (0.6–47.4)	NR (NR–NR)	**0.57 (0.31–1.04)**
Placebo + CT	27/112	19.0 (1.0–44.8)	42.7 (42.7–NR)	***P* = 0.0323**



No. at risk									
Pembro + CT	110	106	93	53	35	14	10	6	0
Placebo + CT	112	100	82	50	24	8	8	4	0

- **Ad-hoc analysis** with DCO on Aug 18, 2023
- OS data immature: 46.4% information fraction pMMR and 29.3% dMMR

Eskander RN, et al. Nat Med. 2025 Mar 5. doi: 10.1038/s41591-025-03566-1. Epub ahead of print.

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

nature medicine

Article https://doi.org/10.1038/s41591-025-03566-1

Pembrolizumab plus chemotherapy in advanced or recurrent endometrial cancer: overall survival and exploratory analyses of the NRG GY018 phase 3 randomized trial

Received: 23 September 2024

Accepted: 5 February 2025

Published online: 05 March 2025

Check for updates

A list of authors and their affiliations appears at the end of the paper

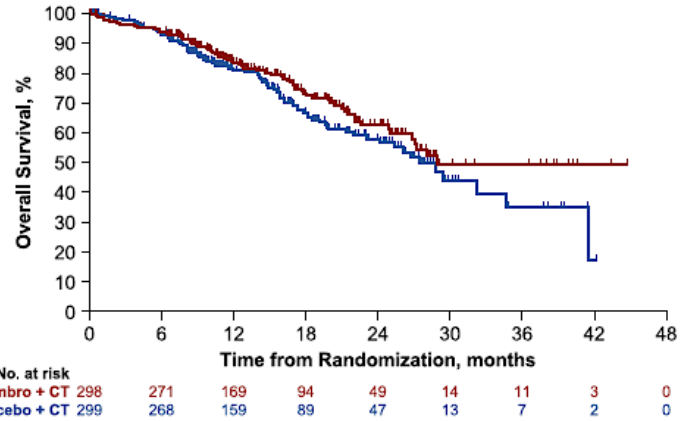
Historically, the treatment of patients with advanced stage or recurrent endometrial cancer included paclitaxel plus carboplatin. Immunotherapy in combination with chemotherapy resulted in improved clinical outcomes in several solid tumors. In the phase 3 NRG GY018 study, pembrolizumab

Among those who discontinued treatment, more patients in the placebo versus pembrolizumab group received subsequent PD-1/PD-L1 inhibitors in the pMMR (42.9% (118 of 275) versus 21.9% (47 of 215)) and dMMR (51.0% (53 of 104) versus 17.9% (10 of 56)) populations (Supplementary Information and Supplementary Table 3). Results of the sensitivity analysis demonstrated a lower HR for OS in the pMMR population (HR, 0.70; 95% CI, 0.50–0.98) when accounting for post-study immunotherapy use (Extended Data Fig. 4c). Due to

OS in pMMR Population

A)

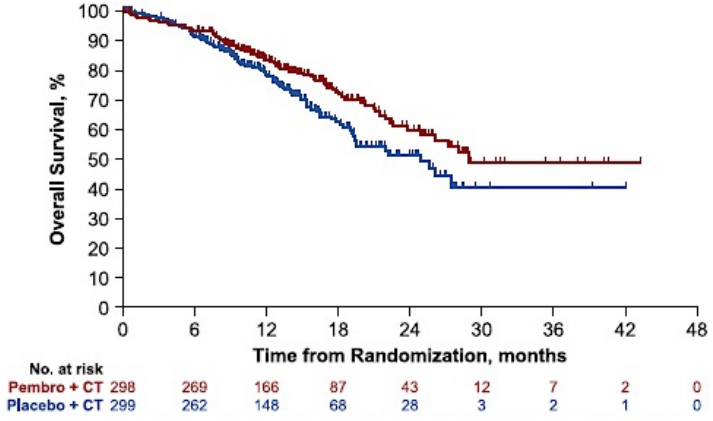
	Events, n/N	Follow-up Duration[a], median (range), mo	Median OS (95% CI), mo	HR (95% CI)[b], *P*-value[c]
Pembro + CT	77/298	15.7 (0.5–45.4)	28.9 (26.8–NR)	0.80 (0.59–1.08)
Placebo + CT	92/299	15.0 (0.9–45.6)	28.7 (24.0–34.6)	*P* = 0.0683



OS in pMMR Population after Adjusting for Post-study IO Use

C)

	Events, n/N	Median OS (95% CI), mo	HR (95% CI)[b]
Pembro + CT	77/298	28.9 (24.9–NR)	0.70 (0.50–0.98)
Placebo + CT	92/299	24.8 (19.3–NR)	



Extended Data Fig. 4 | Kaplan-Meier–estimated OS in the (A) pMMR and (B) dMMR populations and (C) sensitivity analysis in the pMMR population at ad hoc analysis. OS data were immature (46.4% information fraction for pMMR population [169/364 events needed for final analysis had occurred] and 29.3% information fraction for dMMR population [44/150 events needed for final analysis had occurred]). Data cutoff date: August 18, 2023. [a]Follow-up duration is the time from randomization to the date of death or the database cutoff date if the participant is still alive; follow-up duration was not calculated for the sensitivity analysis (panel C) owing to the nature of the bootstrap analysis. [b]Based on a Cox regression model with the Efron method of tie handling with treatment as a covariate stratified by prior chemotherapy. [c]One-sided *P* value based on log-rank test stratified by prior chemotherapy. CT, chemotherapy; dMMR, mismatch repair-deficient; HR, hazard ratio; NR, not reached; OS, overall survival; pembro, pembrolizumab; pMMR, mismatch repair-proficient.

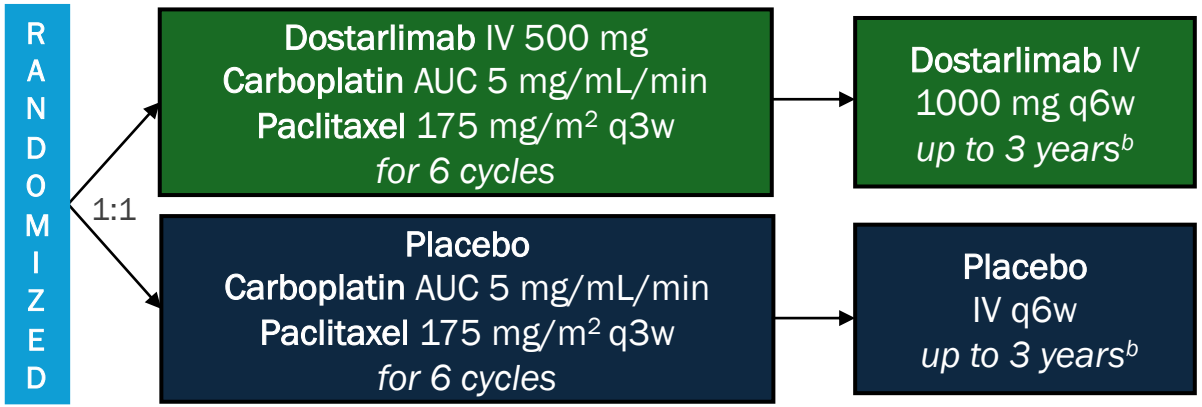
- **Ad-hoc analysis** with DCO on Aug 18, 2023
- OS data immature: 46.4% information fraction pMMR and 29.3% dMMR

Eskander RN, et al. Nat Med. 2025 Mar 5. doi: 10.1038/s41591-025-03566-1. Epub ahead of print.

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

Key Eligibility Criteria

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



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

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

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

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

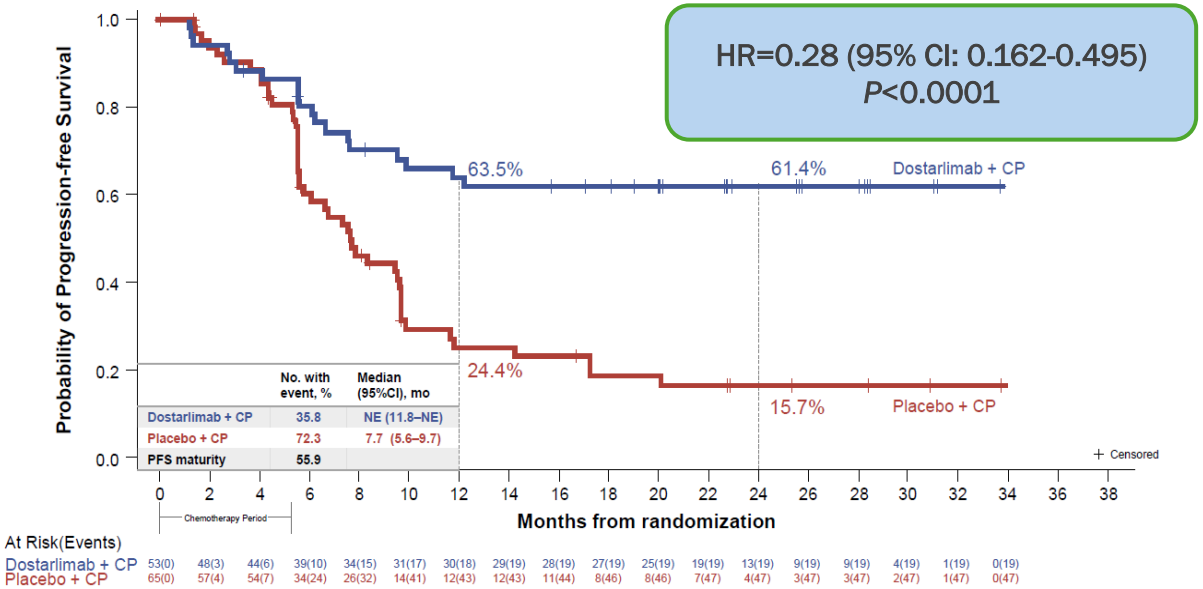
•Mirza MR, et al. SGO 2023. Abstract 265. Powell M et al. ASCO 2023. Abstract 5503.

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

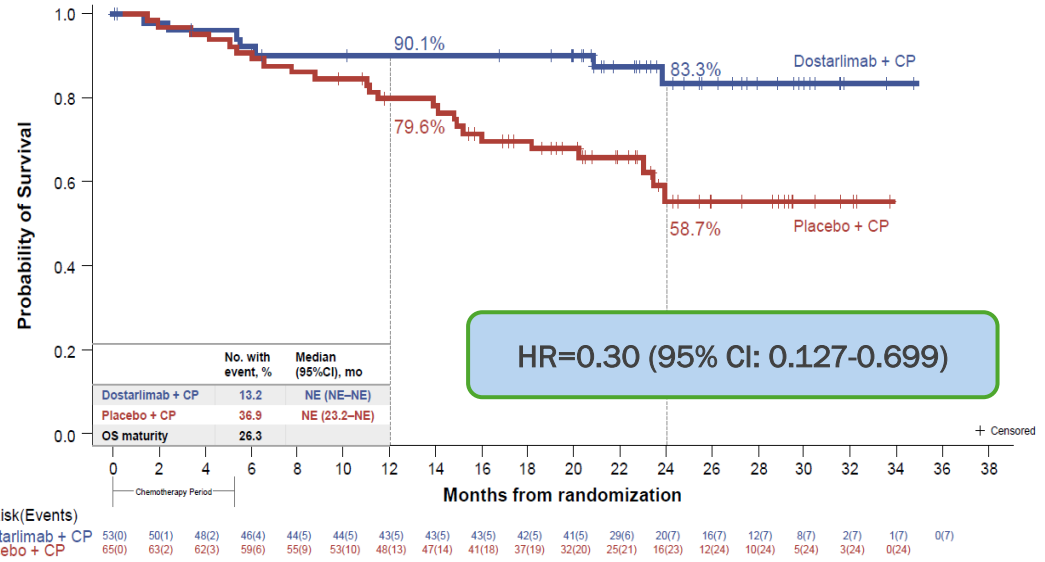
GOG-3031/RUBY

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

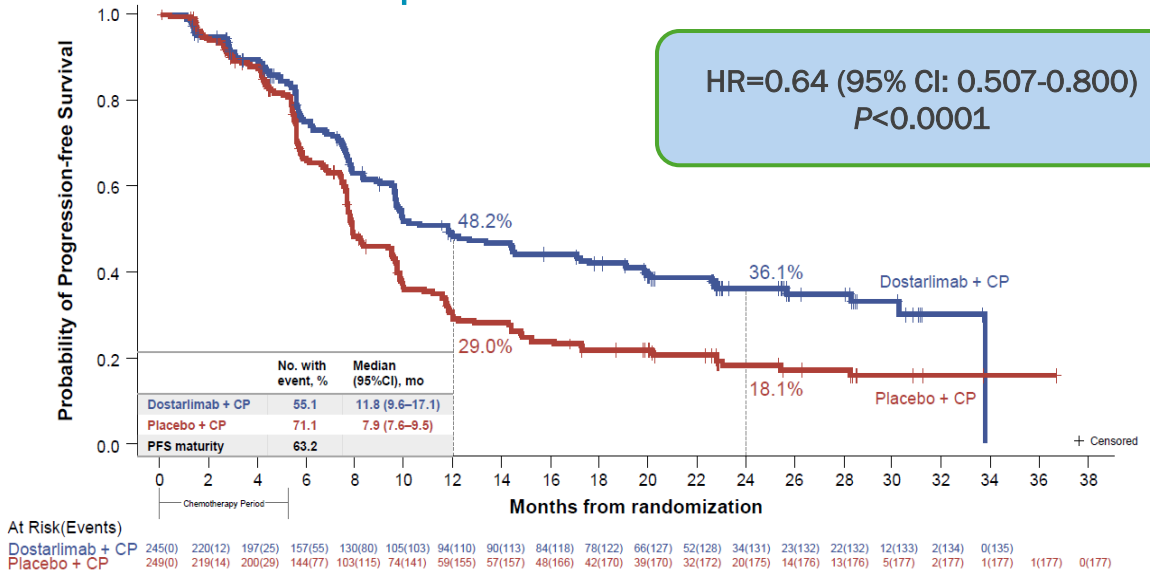
PFS in dMMR/MSI-H Population



OS in dMMR/MSI-H

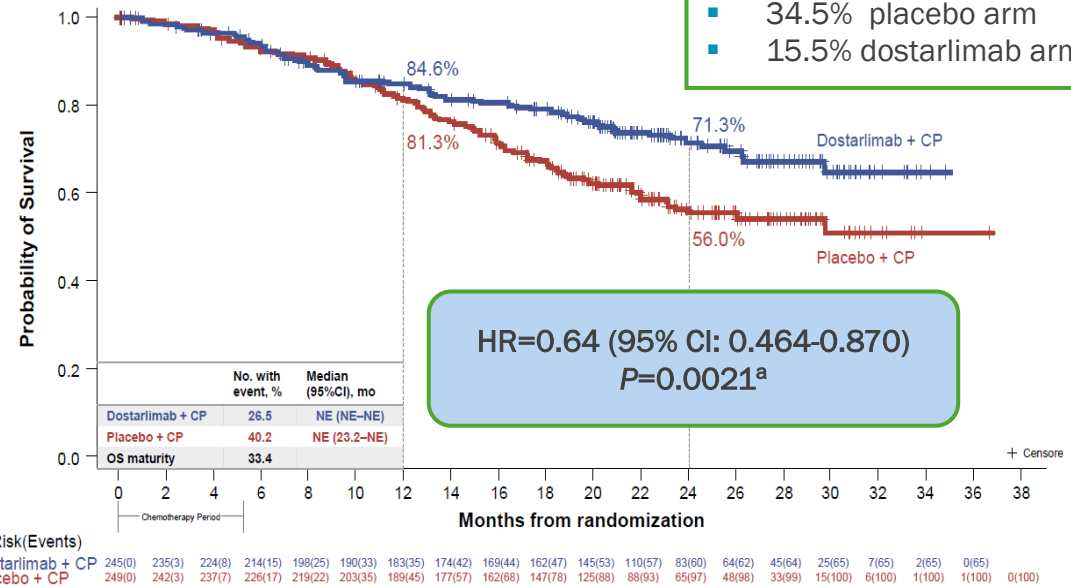


PFS in Overall Population



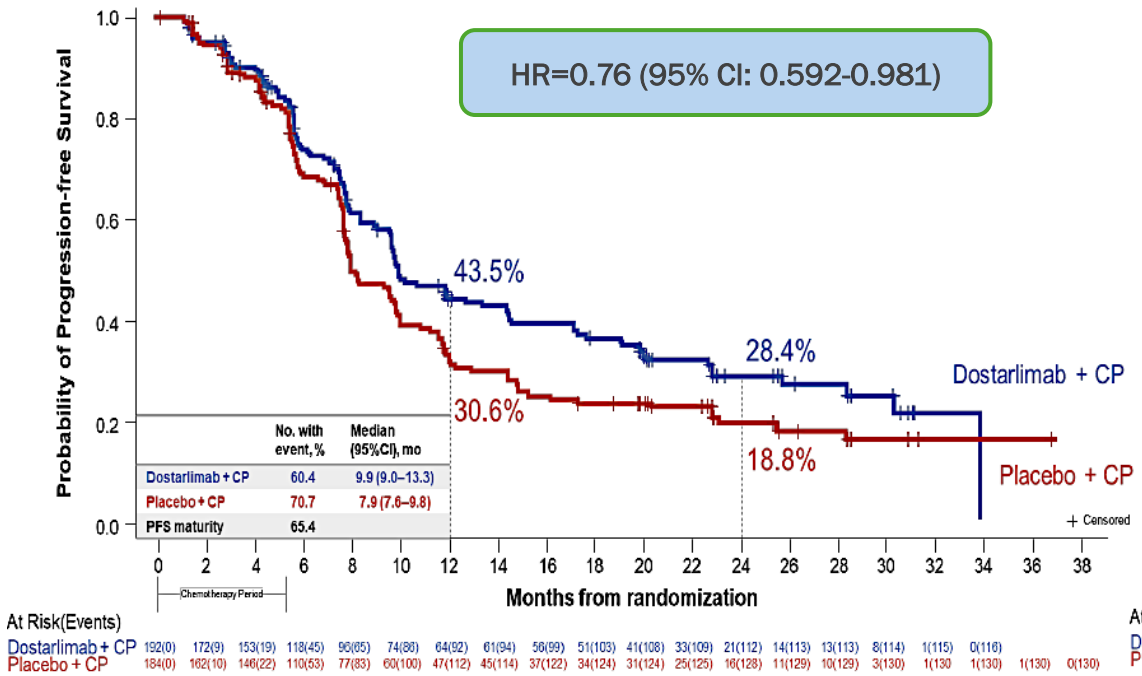
OS in Overall Population

Received subsequent IO:
- 34.5% placebo arm
- 15.5% dostarlimab arm

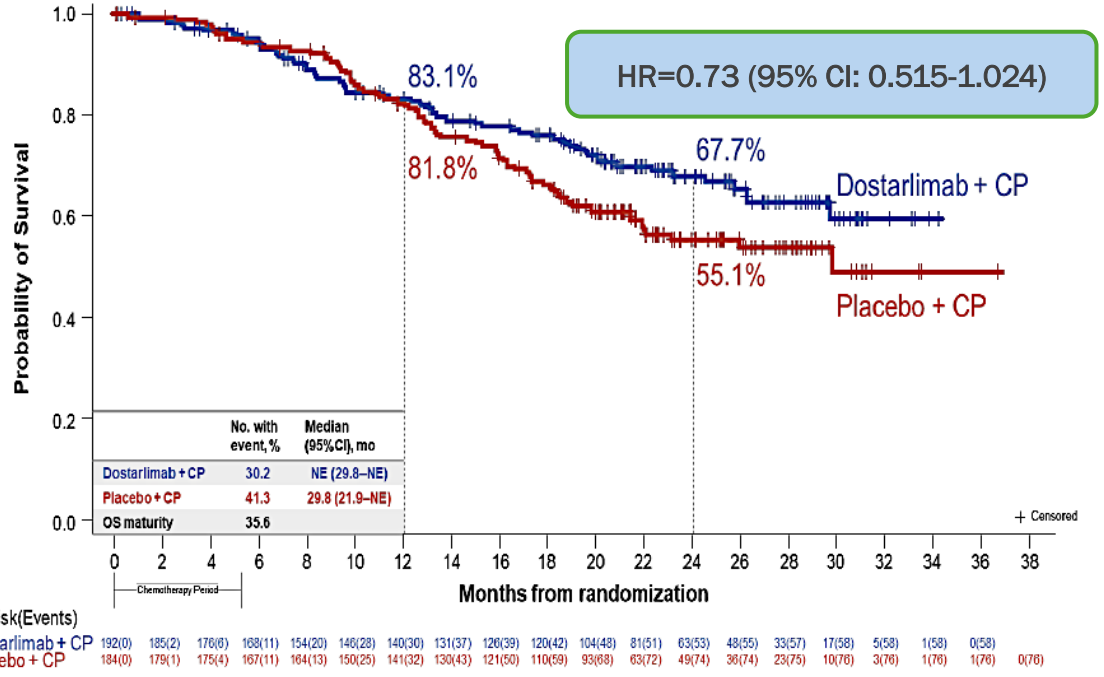


GOG-3031/RUBY: Efficacy in pMMR/MSS Population

PFS in pMMR/MSS Population



OS in pMMR/MSS Population



Received subsequent immunotherapy:

- 33.2% of patients on placebo arm
- 15.6% of patients on dostarlimab arm

Data cutoff: September 28, 2022.

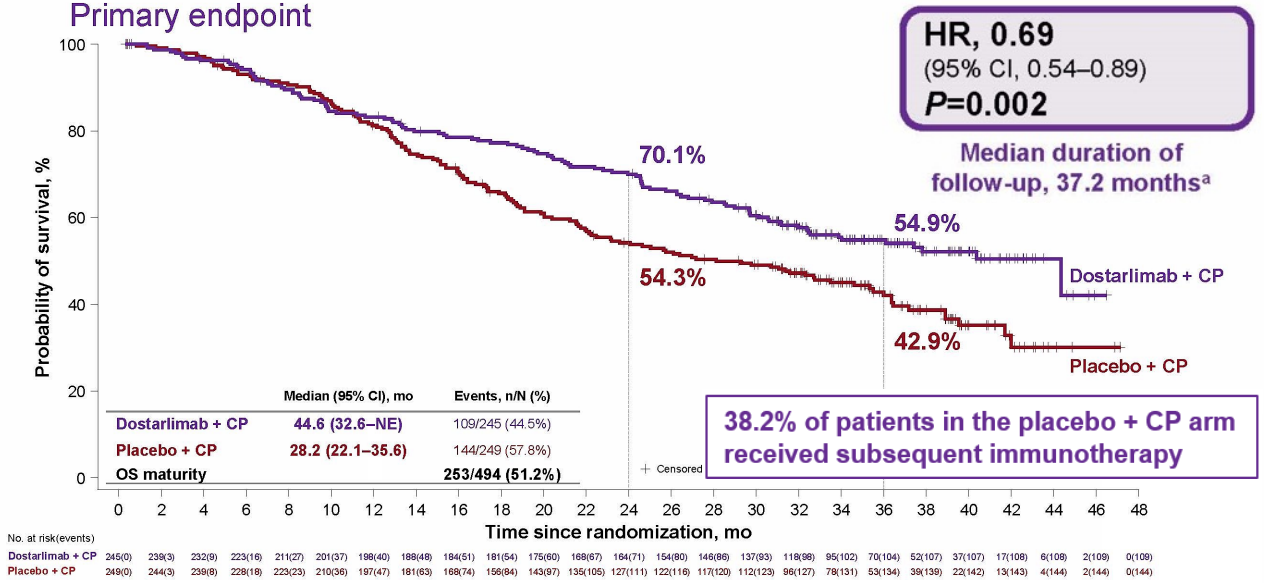
Mirza MR, et al. SGO 2023. Abstract 265.

GOG-3031/RUBY: Longer Follow-Up of OS (IA2)

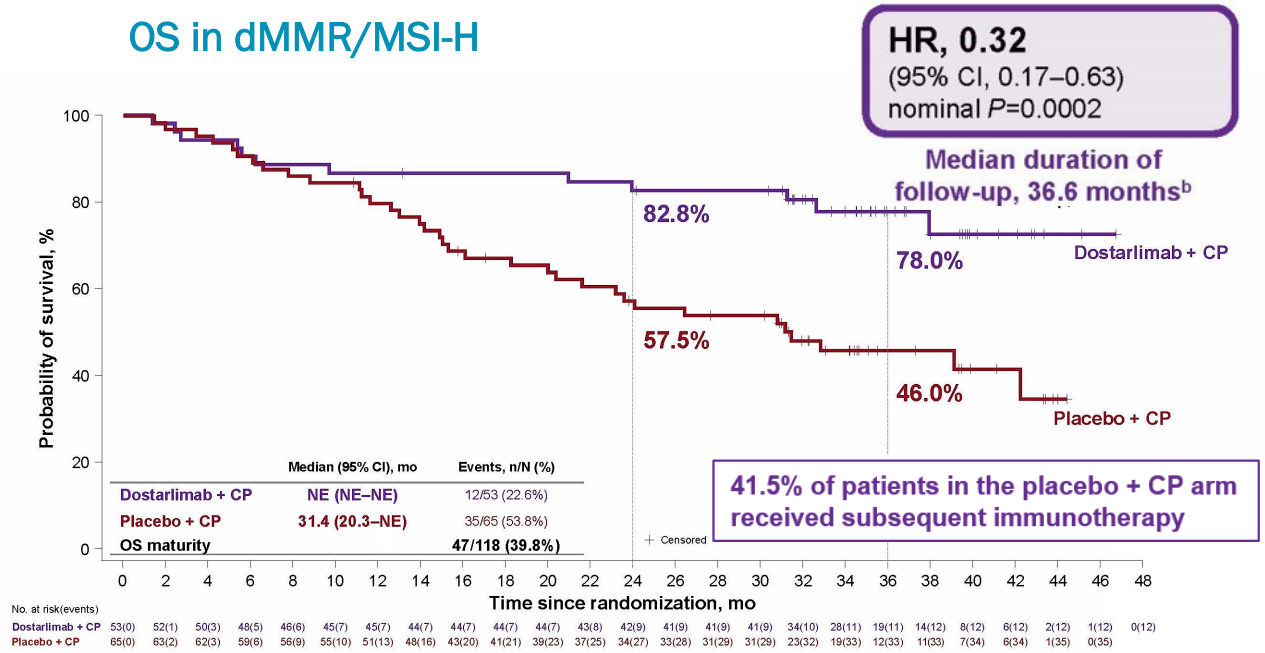
OS in Overall Population (Primary endpoint)

Statistically Significant OS Benefit in Overall Population

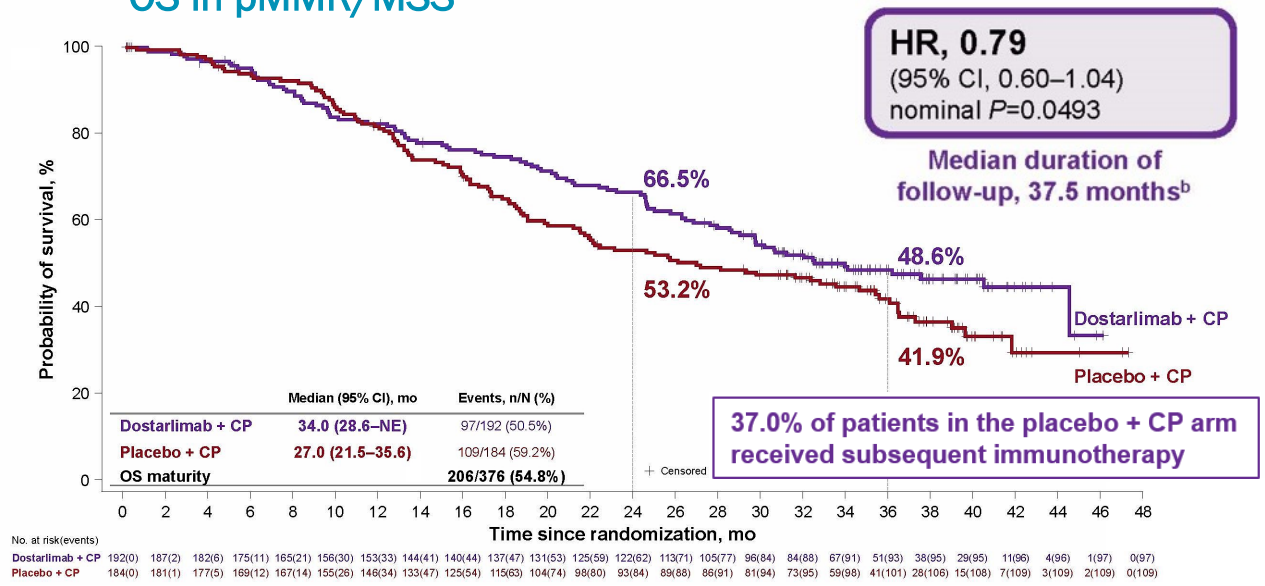
Primary endpoint



OS in dMMR/MSI-H



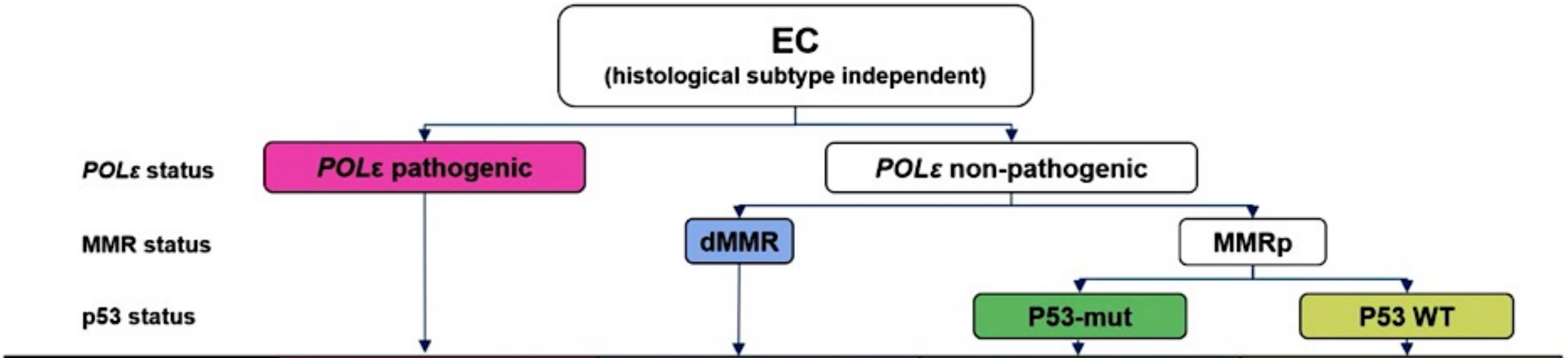
OS in pMMR/MSS



Powell MA, et al. SGO 2024.

RUBY Molecular Classification Algorithm

- In RUBY Part 1, molecular classification was performed for all participants with WES results – 400 of 494 patients



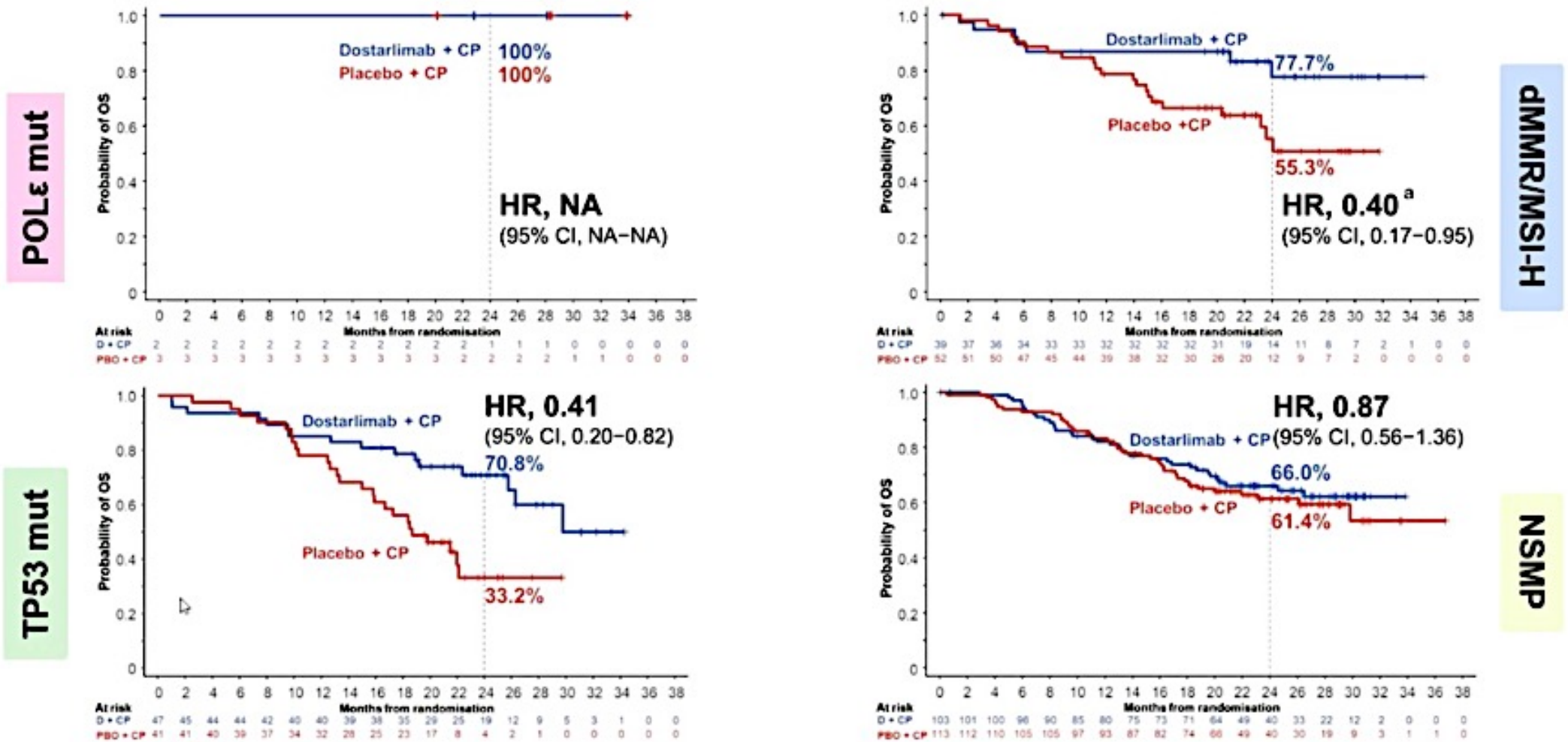
Integrated diagnosis	POLεmut (EDM)	dMMR (or MSI-H)	TP53 aberrant	NSMP
Prevalence in RUBY, % (n/N)	**1.25%** (5/400)	**22.75%** (91/400)	**22%** (88/400)	**54%** (216/400)
Diagnostic test	WES	Results of local (IHC, NGS, PCR) or central test (IHC) provided for RUBY at randomization	WES	

Efficacy per molecular classification was an exploratory analysis.
dMMR, mismatch repair deficient; EC, endometrial cancer; EDM, exonuclease domain; IHC, immunohistochemistry; MMRp, mismatch repair proficient; MSI-H, microsatellite instability-high; mut, mutated; NGS, next generation sequencing; NSMP, no specific molecular profile; PCR, polymerase chain reaction; POLε, polymerase epsilon; TP53, tumor protein 53; WES, whole exome DNA sequencing; WT, wild type.

Mirza MR. ESMO 2023

OS According to Molecular Subgroup

Based on 400/494 patients with known molecular classification per whole exome sequencing



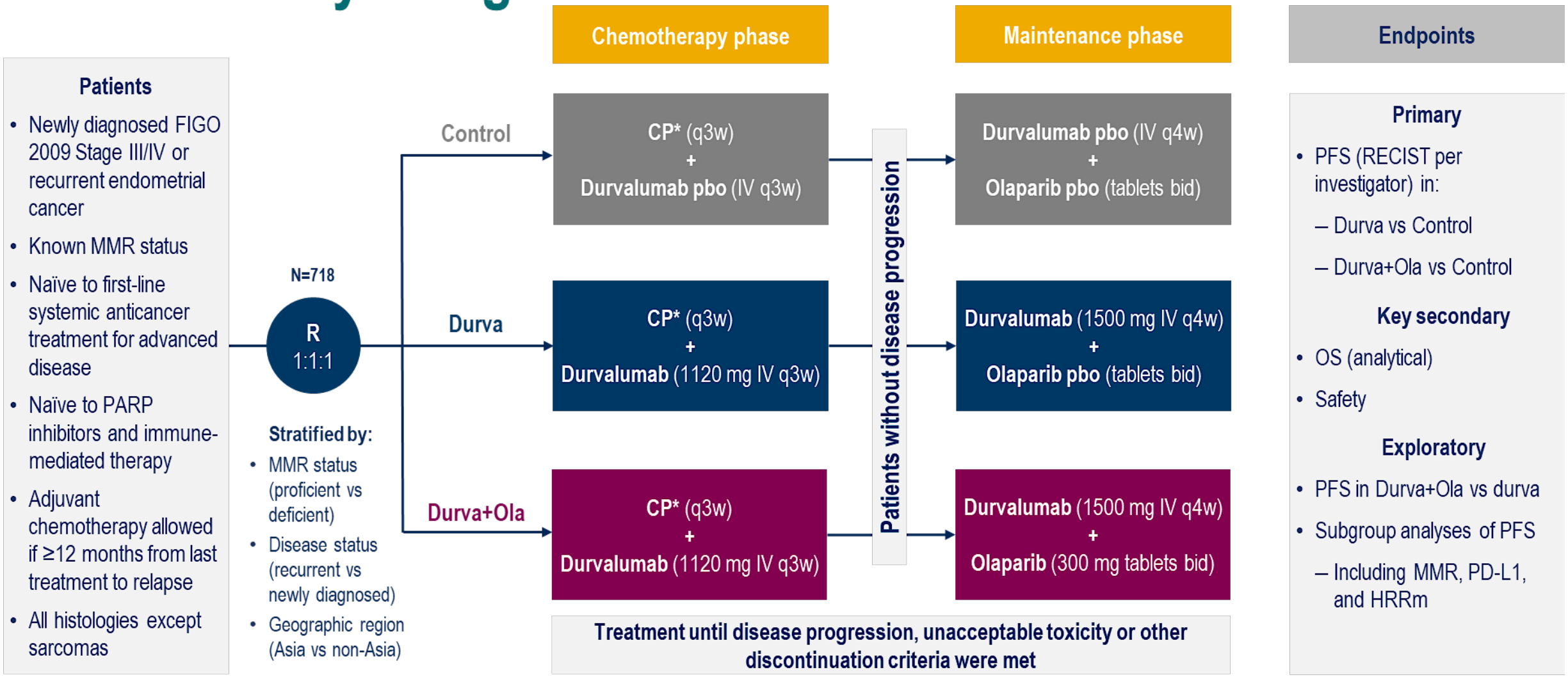
MADRID 2023 ESMO congress

[a]Prespecified OS analysis in dMMR/MSI-H patients (n=118) showed HR, 0.30.

CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NA, not applicable; NR, not reached; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε , polymerase epsilon; TP53, tumor protein 53.

Mirza MR. ESMO 2023

DUO-E study design

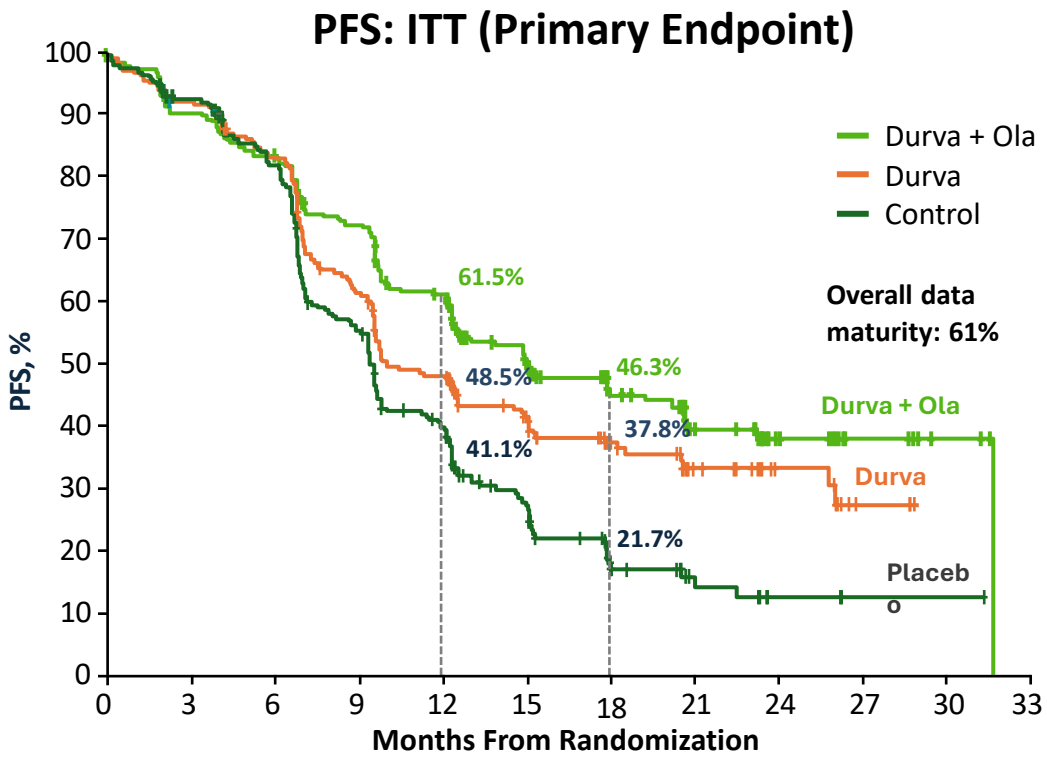


*Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg per mL/min and paclitaxel 175 mg/m^2.
bid, twice daily; CP, carboplatin/paclitaxel; durva, durvalumab; FIGO, International Federation of Gynaecology and Obstetrics; HRRm, homologous recombination repair mutation; IV, intravenously; ola, olaparib; pbo, placebo; q3(4)w, every 3(4) weeks; R, randomisation; RECIST, Response Evaluation Criteria for Solid Tumours.

Shannon N. Westin

Westin SN. ESMO 2023

DUO-E: Maintenance Durvalumab ± Olaparib on PFS in ITT Population

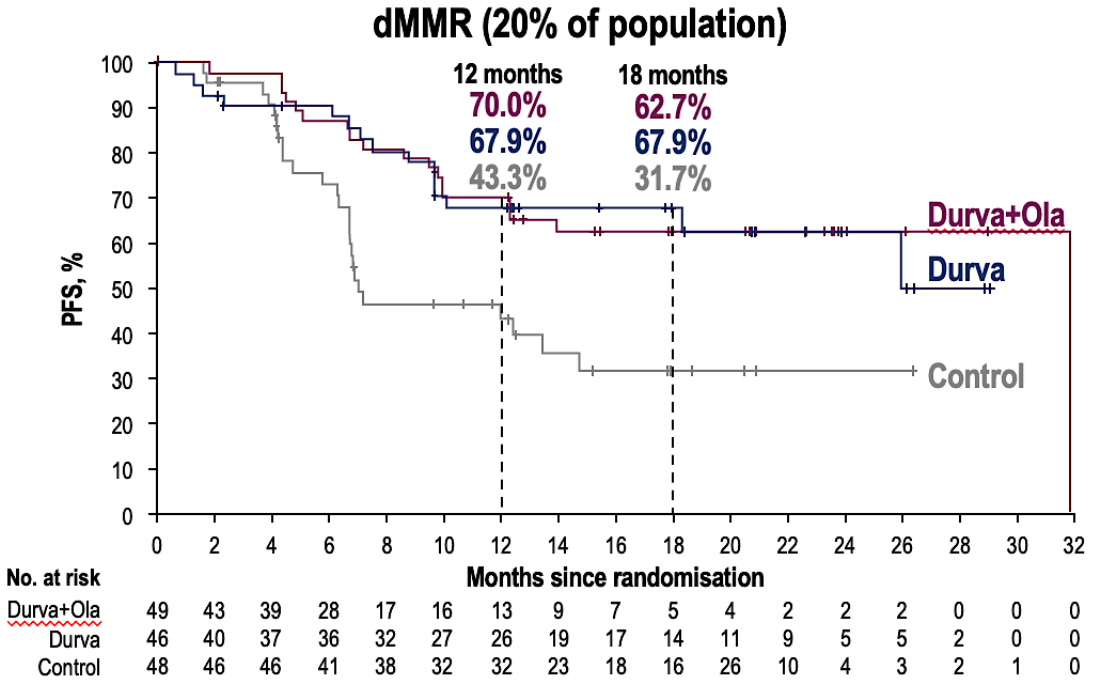


	Control (n = 241)	Durva (n = 238)	Durva + Ola (n = 239)
Events, n (%)	173 (71.8)	139 (58.4)	126 (52.7)
Median PFS, mo (95% CI)	9.6 (9.0-9.9)	10.2 (9.7-14.7)	15.1 (12.6-20.7)
HR (95% CI) vs control		**0.71 (0.57-0.89); *P* = .003**	**0.55 (0.43-0.69); *P* < .0001**
HR (95% CI) vs durva			**0.78 (0.61-0.99)**

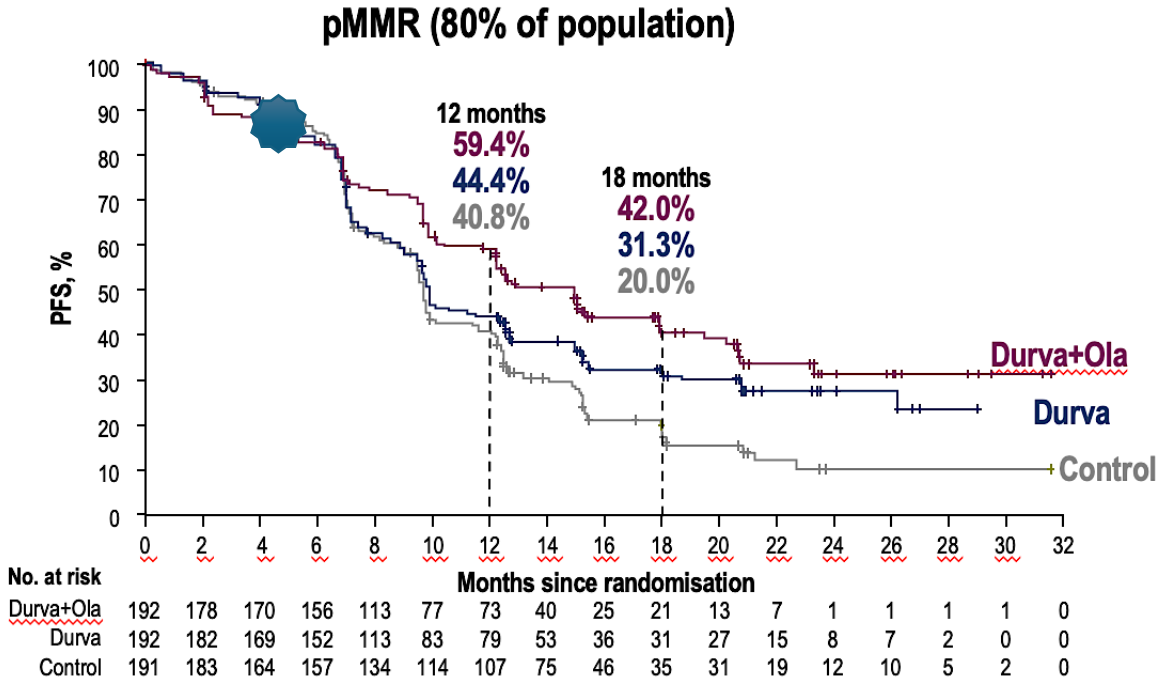
In pMMR (n = 575), 84% were positive for at least one biomarker: PD-L1 positivity (67%), *TP53* mutations (59%), homologous recombination repair mutations (21%) and *BRCA* mutations (8%) Westin SGO 2025.

Westin SN. JCO 2023

DUO-E: Subgroup analysis of PFS by MMR status



	Control (N=49)	Durva (N=46)	Durva+Ola (N=48)
Events, n (%)	25 (51.0)	15 (32.6)	18 (37.5)
Median PFS (95% CI),* months	7.0 (6.7–14.8)	NR (NR–NR)	31.8 (12.4–NR)
HR (95% CI) vs Control†		**0.42 (0.22–0.80)**	**0.41 (0.21–0.75)**
HR (95% CI) vs Durva†			**0.97 (0.49–1.98)**



	Control (N=192)	Durva (N=192)	Durva+Ola (N=191)
Events, n (%)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS (95% CI),* months	9.7 (9.2–10.1)	9.9 (9.4–12.5)	15.0 (12.4–18.0)
HR (95% CI) vs Control†		**0.77 (0.60–0.97)**	**0.57 (0.44–0.73)**
HR (95% CI) vs Durva†			**0.76 (0.59–0.99)**

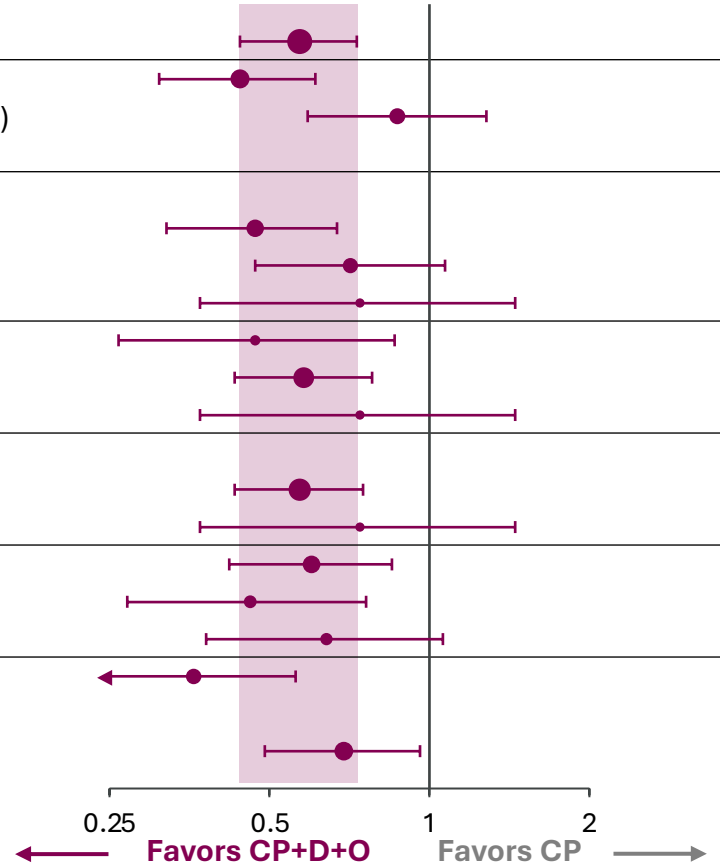
Westin, S et al. ESMO 2023.

pMMR subpopulation: PFS by biomarker subgroup

CP + durvalumab + olaparib vs CP

Post hoc exploratory analysis

		HR (95% CI)
All pMMR patients		**0.57 (0.44–0.73)**
PD-L1 expression*	Positive (TAP score ≥1%)	**0.44 (0.31–0.61)**
	Negative (TAP score <1%)	**0.87 (0.59–1.28)**
	Unknown[¶]	**NC (NC–NC)[††]**
***POLE*m and *TP53*m status[†,‡]**	*POLE*m	**NC (NC–NC)[††]**
	*TP53*m	**0.47 (0.32–0.67)**
	TP53 wild-type	**0.71 (0.47–1.07)**
	Unknown[¶]	**0.74 (0.37–1.45)**
HRRm status[†,§]	HRRm	**0.47 (0.26–0.86)**
	Non-HRRm	**0.58 (0.43–0.78)**
	Unknown[¶]	**0.74 (0.37–1.45)**
BRCAm status[†]	BRCAm	**NC (NC–NC)[††]**
	Non-BRCAm	**0.57 (0.43–0.75)**
	Unknown[¶]	**0.74 (0.37–1.45)**
Histological type at diagnosis	Endometrioid	**0.60 (0.42–0.85)**
	Serous	**0.46 (0.27–0.76)**
	Other[**]	**0.64 (0.38–1.06)**
Baseline ctDNA[‖]	Detected	**0.36 (0.23–0.56)**
	Not detected	**NC (NC–NC)[††]**
	Unknown[¶]	**0.69 (0.49–0.96)**



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; [‡]*TP53*m 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; [‖]ctDNA was analyzed using the methylation-based Guardant Infinity™ assay (Guardant Health, Palo Alto, CA); [¶]'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.

Moore K et al. SGO 2025.

Note: DUO-E duplet regimen is approved only for dMMR while DUO-E triplet regimen is not approved in Hong Kong yet.

This slide is for illustration only and not for cross-trial comparisons. Side-by-side data should be interpreted with great caution

Paradigm-Shifting Data in EC Management

Name	**EN6-RUBY** Part 1	**EN7 ATTEND**	**NRG- GY018**	**B21**	**EN6-RUBY** Part 2	**DUO-E**	**EN9 LEAP-001**	**EN15/C93**	**EN13 DOMENICA**
Lead group Study chair	NSGO-CTU Mirza/Powell	MaNGO Colombo	NRG Eskander/ Powell	BGOG Van Gorp	NSGO-CTU Mirza/Powell	GOG-P Westin	AGO-A Marth	GOG-P Slomowitz	GINECO Joly
Investigational agent	Dosta + Chemo	Atezo + Chemo	Pembro + Chemo	Pembro + Chemo	Dosta + Nira + Chemo	Durva + Ola + Chemo	Pembro + Lenva	Pembro	Dosta
N	494	551	816	990	291	718	842	350	260
Concomitant	+	+	+	+	+	+	Pembro + lenva vs chemo	Pembro vs chemo	Dosta vs chemo
Unique features	**Carcinosarc; 6 month interval; IIIC1 non-endo non-measurable all IIIC2**	+	**12 month interval; Stage III – measurable only**		+	**12 month interval; Stage III measurable only**			
Readout	**NEJM 2023**	**ESMO 2023**	**NEJM 2023**	**Negative *AnnOnc***	**SGO 2024**	**JCO 2023**	**“negative” SGO 2024**	?	?

This slide is for illustration only and not for cross-trial comparisons. Side-by-side data should be interpreted with great caution

Paradigm-Shifting Data in EC Management

Name	EN6 RUBY Part 1	EN7 ATTEND	NRG- GY018	EN11/B21	EN6 RUBY Part 2	DUO-E	EN9 LEAP-001	EN15/C93	EN13 DOMENICA
Lead group Study chair	NSGO-CTU Mirza Powell	MaNGO Colombo	NRG Eskander Powell	BGOG Van Gorp	NSGO-CTU Mirza Powell	GOG-P Westin	AGO-A Marth	GOG-P Slomowitz	GINECO Joly
Investigational agent	Dosta + chemo	Atezo + chemo	Pembro + chemo	Pembro + chemo	Dosta + nira + chemo	Durva + ola + chemo	Pembro + lenva	Pembro	Dosta
N	494	551	816	990	291	718	842	350	260
Concomitant	+	+	+	+	+	+	Pembro + lenva vs chemo	Pembro vs chemo	Dosta vs chemo
Maintenance	+	+	+		+	+			
Readout	**NEJM 2023**	**ESMO 2023**	**NEJM 2023**	**Negative**	**SGO 2024**	**JCO 2023**	**ESGO 2024**	?	?
The Good	**Statistically significant PFS dMMR and ITT, OS ITT**	**Statistically significant PFS dMMR and ITT**	**Statistically significant PFS dMMR and MMRp POWERED**	Large trial dMMR cohort active	**Statistically significant PFS ITT and PFS MMRp**	**Statistically significant PFS ITT for Durva and Durva + Ola**	**Important trial to evaluate concept**	?	?
The Bad	**Not powered for MMRp**	**OS immature**	**Not powered for OS**	Negative trial for pMMR	**Chemo + ICI arm is missing OS immature**	**Not powered for ICI+chemo +/- PARPi Not powered for MMRp or dMMR**	**Negative for both PFS and OS for MMRp and ITT**	**Chemo + ICI arm is missing**	**Chemo + ICI arm is missing**

PARPi = PARP inhibitor.

Mirza MR, et al. *N Engl J Med*. 2023;388(23):2145-2158. Colombo N, et al. Presented at: ESMO Congress; October 20-24, 2023; Madrid, Spain. Abstract LBA40. Eskander RN, et al. *N Engl J Med*. 2023;388(23):2159-2170. Van Gorp T, et al. *Ann Oncol*. 2024;35(11):968-980. Powell MA, et al. Presented at: Society for Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer; March 16-18, 2024; San Diego, California. Westin SN, et al. *J Clin Oncol*. 2024;42(3):283-299. Marth C, et al. *Int J Gynecol Cancer*. 2024;34:A570-A571. Slomovitz BM, et al. *J Clin Oncol*. 2022;40(16 suppl):TPS5623. Joly F, et al. *J Clin Oncol*. 2023;41(16 suppl):TPS5630. Author's slide

What about IO in early stage completely resected EC? ENGOT-EN11/GOG-3053/KEYNOTE-B21

Key Eligibility Criteria

- Newly diagnosed EC or carcinosarcoma
- Curative surgery with no residual disease
- At high risk for recurrence:
  - FIGO (2009) surgical stage I/II, non-endometrioid with myometrial invasion
  - FIGO (2009) surgical stage I/II of any histology with known aberrant p53 expression or *TP53* mutation with myometrial invasion
  - FIGO (2009) surgical stage III/IVA of any histology
- No prior radiation or systemic therapy (including neoadjuvant) for EC

Stratification Factors

- **MMR status (pMMR vs dMMR)**, and within pMMR stratum:
  - Planned radiation (chemo-EBRT vs EBRT vs no EBRT)
  - Histology (endometrioid vs non-endometrioid)
  - FIGO (2009) surgical stage (I/II vs III/IVA)

R 1:1
N=1095

	Stage 1	Stage 2
	Carboplatin (AUC 5 or 6) + paclitaxel 175 mg/m^2 (Q3W, 4 or 6 cycles)[a]	± radiotherapy ± cisplatin[b]
	Pembrolizumab 200 mg Q3W (6 cycles)	Pembrolizumab 400 mg Q6W (6 cycles)
	Carboplatin (AUC 5 or 6) + paclitaxel 175 mg/m^2 (Q3W, 4 or 6 cycles)[a]	± radiotherapy ± cisplatin[b]
	Placebo Q3W (6 cycles)	Placebo Q6W (6 cycles)

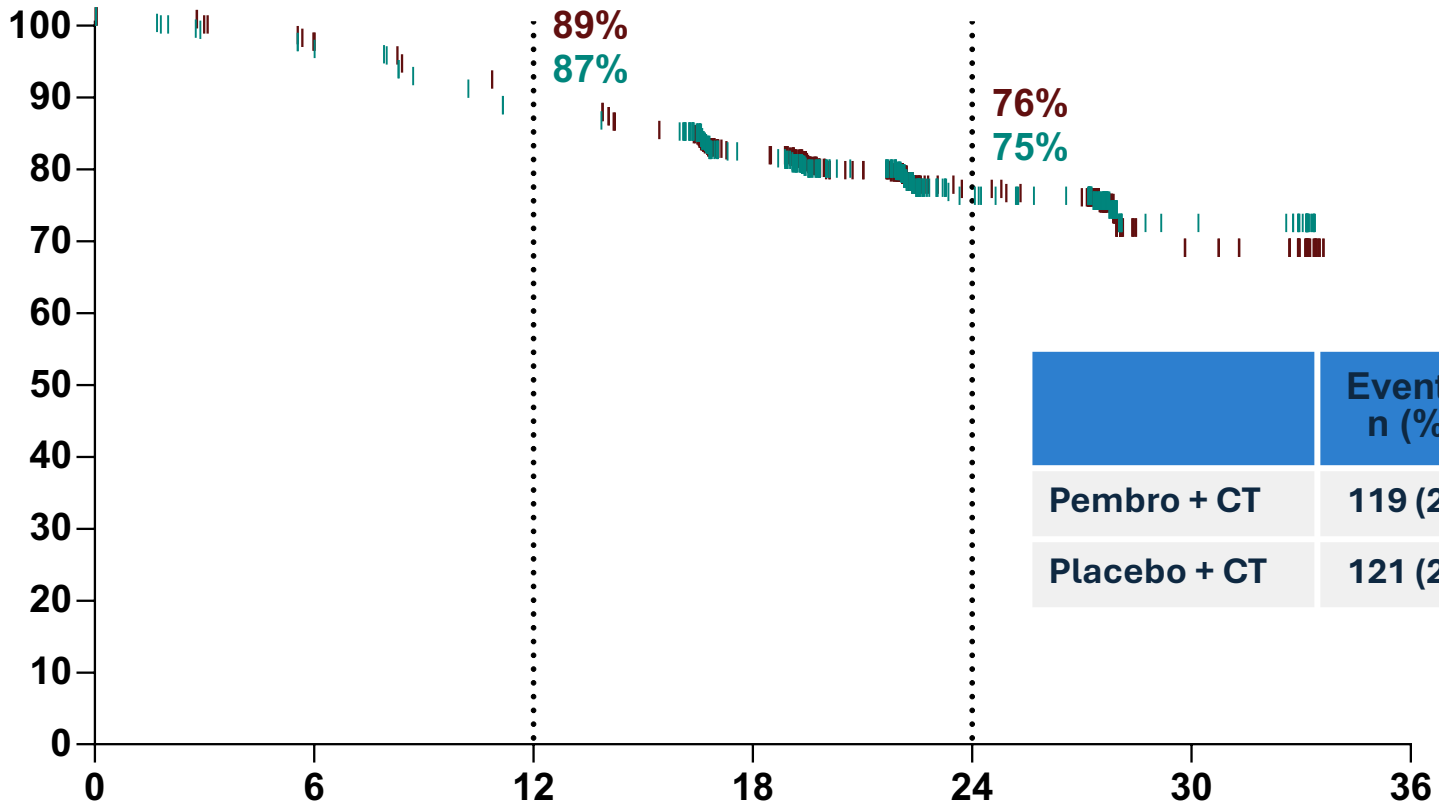
Dual primary endpoints

- DFS as assessed radiographically by the investigator or by histopathologic confirmation
- OS

Van Gorp et al. ESMO 2024

What about IO in early stage completely resected EC?

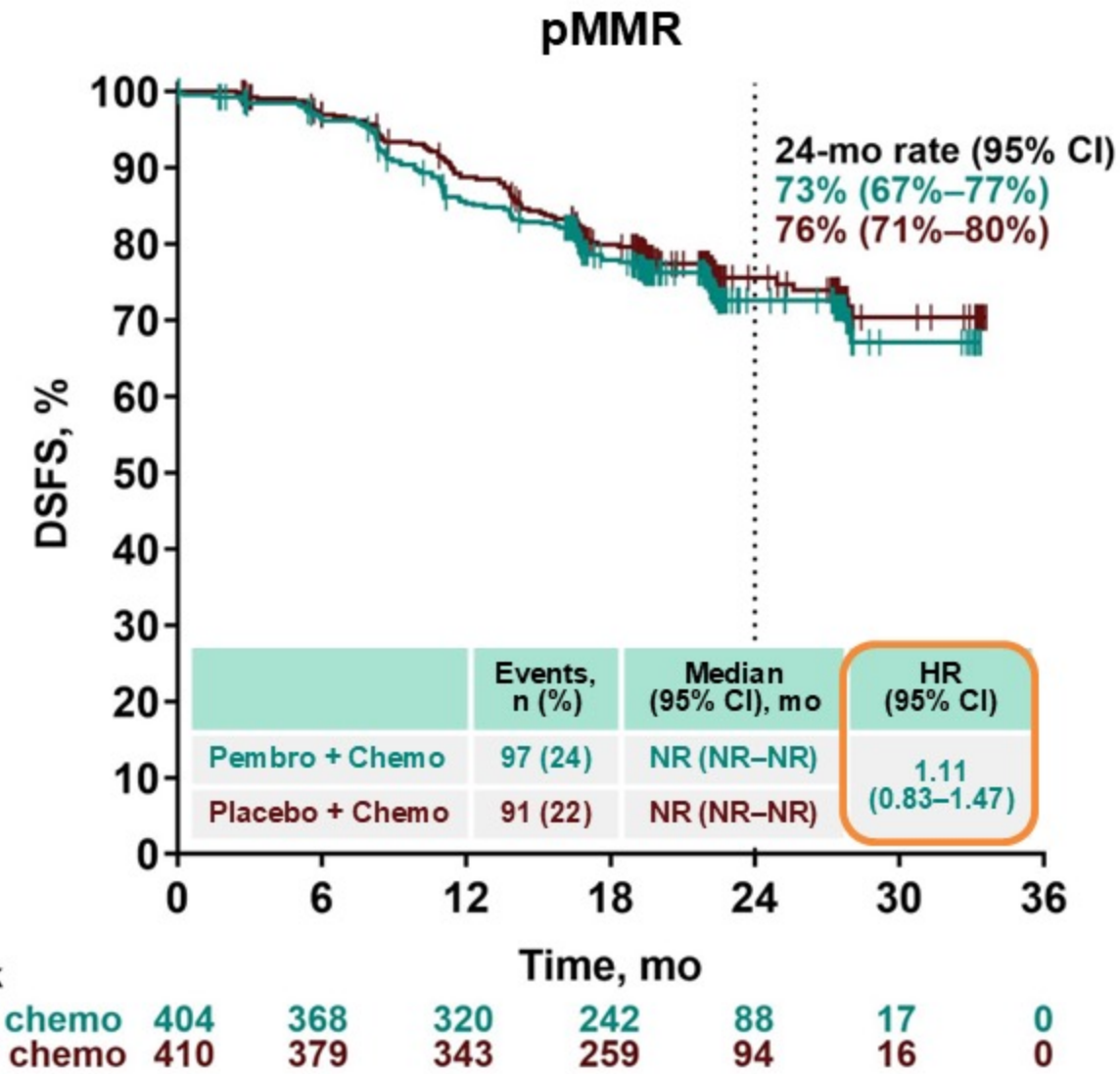
ENGOT-EN11/GOG-3053/KEYNOTE-B21: ITT

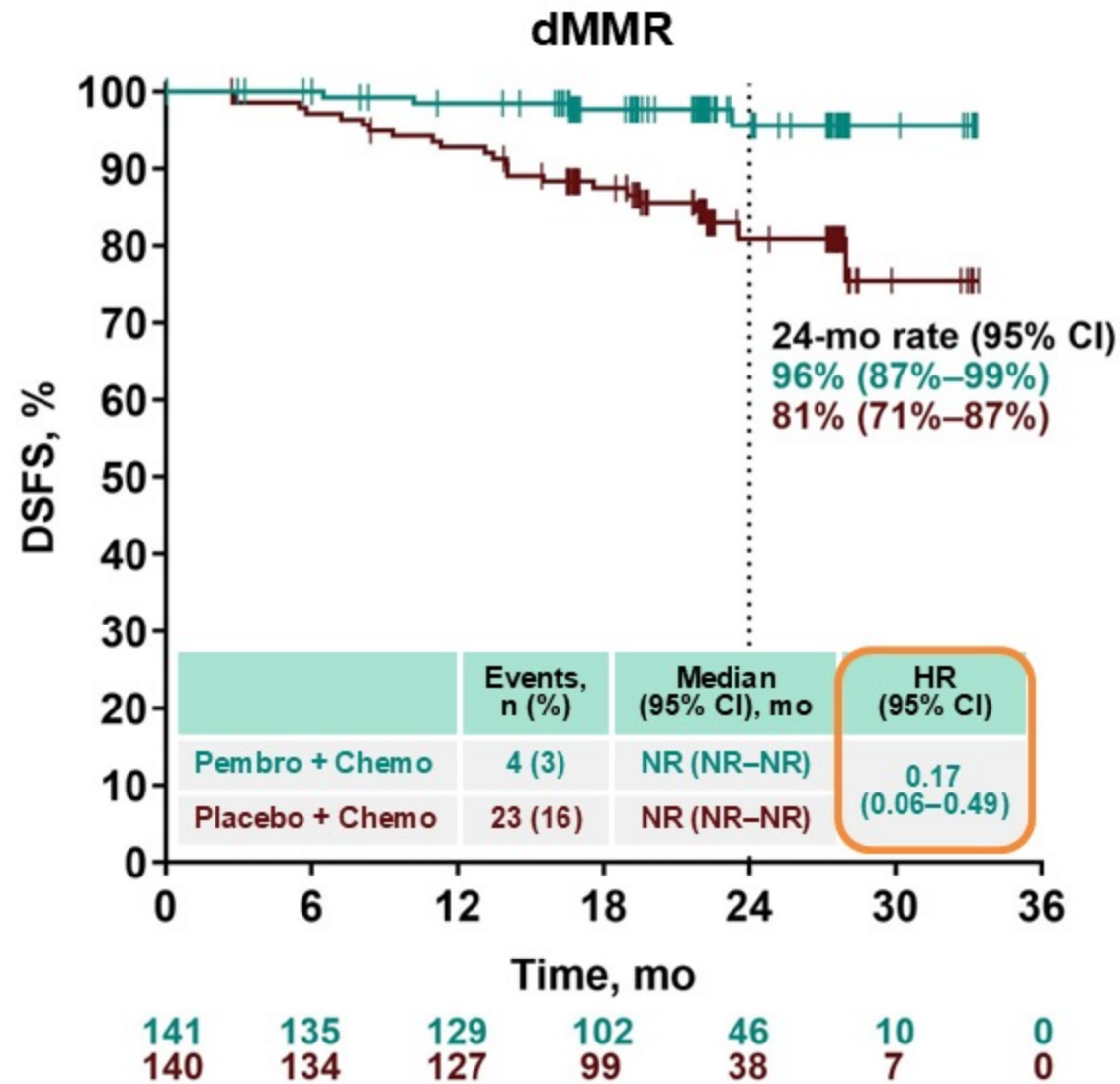


	Events, n (%)	Median (95% CI), mo	HR (95% CI)	*P* value
Pembro + CT	119 (22)	NR (NR–NR)	1.02 (0.79–1.32)	0.570
Placebo + CT	121 (22)	NR (NR–NR)		

Van Gorp et al. ESMO 2024

DSFS Was Not Improved With Pembrolizumab in pMMR EC, But Demonstrated Substantial Improvement in dMMR EC



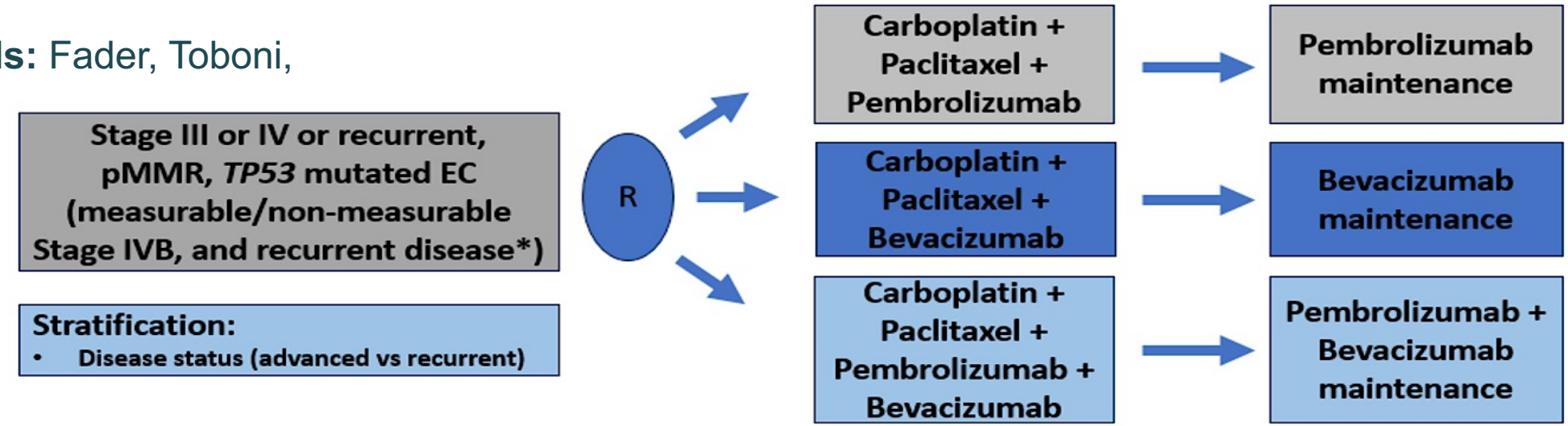


Data cutoff date: 4 March 2024.

GY035 (UC2323): Building on results of GY018 & 86P in *TP53* mutated Endometrial cancer patients: approved by GCSC

Randomized Phase II/III Study of Carboplatin + Paclitaxel + Pembrolizumab vs. Carboplatin + Paclitaxel + Bevacizumab vs. Carboplatin + Paclitaxel + Pembrolizumab + Bevacizumab in Patients with Advanced or Recurrent, pMMR and *TP53* mutated Endometrial Cancer

PIs: Fader, Toboni,

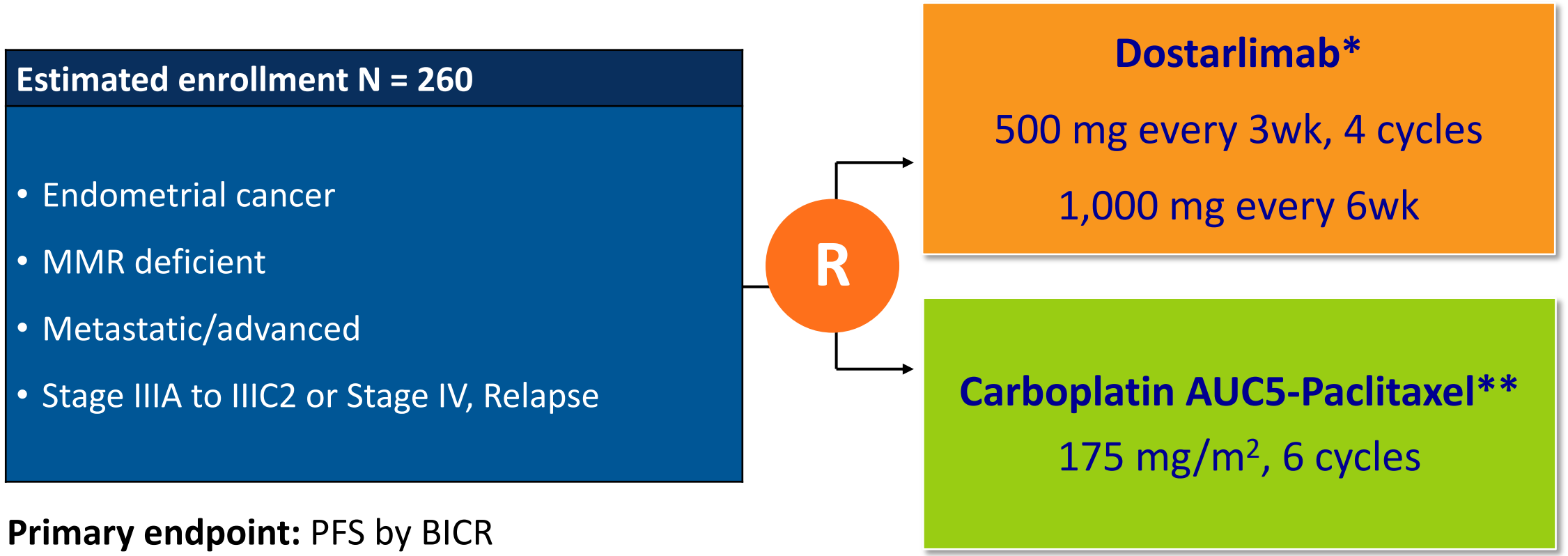


*Primary Phase II endpoint: PFS by RECIST V1.1
*Primary Phase III endpoint: OS

Treatment Plan:
Arm 1: IV carboplatin AUC 5 + IV paclitaxel 175 mg/m^2 + IV pembrolizumab 200 mg on day 1 every 3 weeks x 6-10 cycles followed by 14 additional cycles of pembrolizumab 400 mg IV maintenance every 6 weeks.
Arm 2: IV carboplatin AUC 5 + IV paclitaxel 175 mg/m^2 + bevacizumab 15 mg/kg on day 1 every 3 weeks x 6-10 cycles followed by 28 additional cycles of bevacizumab 15 mg/kg maintenance every 3 weeks.
Arm 3: IV carboplatin AUC 5 + IV paclitaxel 175 mg/m^2 + IV pembrolizumab 200 mg + bevacizumab 15 mg/kg on day 1 every 3 weeks x 6-10 cycles followed by 14 additional cycles of pembrolizumab 400 mg IV maintenance every 6 weeks and 28 additional cycles of bevacizumab 15 mg/kg IV maintenance every 3 weeks.
*Patients with recurrent disease who have received prior adjuvant therapy must have a platinum-free interval of >/=12 months.

Courtesy B. Monk

DOMENICA (GINECO-EN105b/ENGOT-en13): Study Design



Primary endpoint: PFS by BICR

Stratification factors: Prior adjuvant chemotherapy, previous pelvic irradiation, disease status (ND vs relapse)

*Up to 2 years or to disease progression

**Crossover to dostarlimab allowed at progression

PFS = progression-free survival; BICR = blinded independent central review; ND = newly diagnosed

Joly F et al. ASCO 2023.

KEYNOTE-C93/GOG-3064/ENGOT-en15: Study Design

Estimated enrollment N = 350

- ND Stage III/IV or recurrent EC that is not amenable to curative-intent surgery or radiation
- Radiographically evaluable disease
- Central confirmation of dMMR status
- No prior systemic therapy
- ECOG PS 0 or 1

R

Pembrolizumab 400 mg IV q6wk for up to 18 cycles (~2 years)

Carboplatin AUC 5 or 6 mg/mL/min IV q3wk

Paclitaxel 175 mg/m^2 IV q3wk for 6 cycles

Primary endpoint: PFS by BICR, overall survival

Stratification factors: Disease status (ND vs recurrent), histology (endometrioid vs nonendometrioid)

Slomovitz BM et al. ASCO 2022.

Four-Year Survival Outcomes with Dostarlimab plus Chemotherapy in dMMR/MSI-H Primary Advanced or Recurrent Endometrial Cancer in the ENGOT-EN6-NSGO/GOG-3031/RUBY Trial

Powell M et al.

SGO 2026.

FOCUSED FORUM VII: Beyond the Standard – Innovations in Endometrial Care

SUNDAY APRIL 12, 2026

Ballroom A

11:28 PM – 11:34 AM CST.

Efficacy and Safety of Cadonilimab Combined with Chemotherapy as the First-Line Treatment for Recurrent/Advanced Endometrial Carcinoma: A Multi-Center, Single-Arm Phase II Clinical Trial

Sun Y et al.

SGO 2026.

SCIENTIFIC PLENARY II: Transforming Endometrial Cancer Care

SATURDAY APRIL 11, 2026

Exhibit Hall A

7:54 AM – 8:01 AM CST.

Real-World Retrospective Analysis of First-Line Systemic Treatment with Dostarlimab plus Chemotherapy in Patients with Advanced or Recurrent Endometrial Cancer

Nakayama J et al.

SGO 2026. Abstract 1156 (Poster).

Key takeaways

- Molecular profiling of this disease has completely transformed our therapeutic approach
- **ICI + C/P is the new standard of care for patients with advanced/recurrent endometrial cancer**
- Sorting out: Asian patients, BMI, Asians from western countries, molecular subgroups

- **Unanswered Questions:**
  - Which dMMR patients do not benefit from ICI + chemotherapy?
  - Can we replace chemotherapy in dMMR patients in view of ICI-only treatment? And in which patients?
  - How to treat patients who experience relapse post-chemotherapy + immunotherapy?
  - How do we further validate the prognostic value of molecular subgroups for identifying those patients who will benefit the most?
  - What are the predictive biomarkers to understand which patients benefit most from PARPi addition to ICI in MMRp EC?

Second Opinion

Angeles Alvarez Secord, MD, MHSc

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

In general, what is your preferred initial treatment for metastatic EC? How, if at all, does it differ for patients with MSI-H/dMMR versus MSS/pMMR disease?

When using a checkpoint inhibitor as initial treatment for MSI-H/dMMR metastatic EC, do you have a preference among dostarlimab, pembrolizumab and durvalumab?

How, if at all, does histologic subtype factor into your choice of initial therapy? Would you be more likely to use dostarlimab for this patient with a carcinosarcoma?

QUESTIONS FOR THE FACULTY

How were the designs and eligibility criteria for the RUBY, NRG-GY018 and DUO-E trials similar and how were they different? Does this have any impact on how you interpret and apply the results in practice?

Based on available evidence, how would you indirectly compare the global efficacy of up-front dostarlimab, pembrolizumab and durvalumab in combination with chemotherapy for patients with EC? Do you believe these regimens are essentially equivalent in terms of efficacy, regardless of MMR status?

QUESTIONS FOR THE FACULTY

How do you think through first-line therapy for patients with HER2-positive advanced EC? How do you decide whether to add trastuzumab or an anti-PD-1/PD-L1 antibody to up-front chemotherapy? Do you ever add both?

How would you indirectly compare the global tolerability/toxicity profiles of the various approved chemoimmunotherapy regimens?

For patients who tolerate up-front chemoimmunotherapy well, how long do you continue treatment with each of the approved anti-PD-1/PD-L1 antibodies in the maintenance setting?

Second Opinion

Professor Jonathan A Ledermann

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Outside of a clinical trial, in what situations, if any, would you offer a neoadjuvant checkpoint inhibitor, without chemotherapy, to a patient with resectable MSI-H/dMMR EC?

If immunotherapy alone were to become available as neoadjuvant treatment for patients with EC, how would that impact later-line treatment? Would you have any hesitation about rechallenging with an immune checkpoint inhibitor for a patient who previously received it and tolerated it well?

QUESTIONS FOR THE FACULTY

Based on available data and ongoing trials, do you believe that chemotherapy in the neoadjuvant setting may become unnecessary in the future for patients with EC?

Agenda

Module 1: Biology of Advanced Endometrial Cancer (EC); Optimal Approach to Biomarker Assessment in Patients with Newly Diagnosed Disease — Dr Backes

Module 2: Current Up-Front Chemoimmunotherapeutic Approaches for Advanced EC — Dr Powell

Module 3: Current and Future Role of Anti-PD-1/PD-L1 Antibodies in Combination with Systemic Therapies Beyond Chemotherapy in Advanced EC — Dr Salani

Current and Future Role of Anti-PD-1/PD-L1 Antibodies in Combination with Systemic Therapies Beyond Chemotherapy in Advanced EC

Ritu Salani, M.D., M.B.A.
Professor
Gynecologic Oncologist

UCLA Health

Objectives

- Review studies of PARP inhibition in advanced endometrial cancer
  - Synergy with PD1/PDL1 inhibitors
- Discuss the long-term findings with pembrolizumab/lenvatinib in the recurrent setting
- Explore the role of bevacizumab in TP53-mutant advanced EC

Leveraging Immune Checkpoint Activity

Radiotherapy

- Release of neo-antigens
- “Abscopal effect”

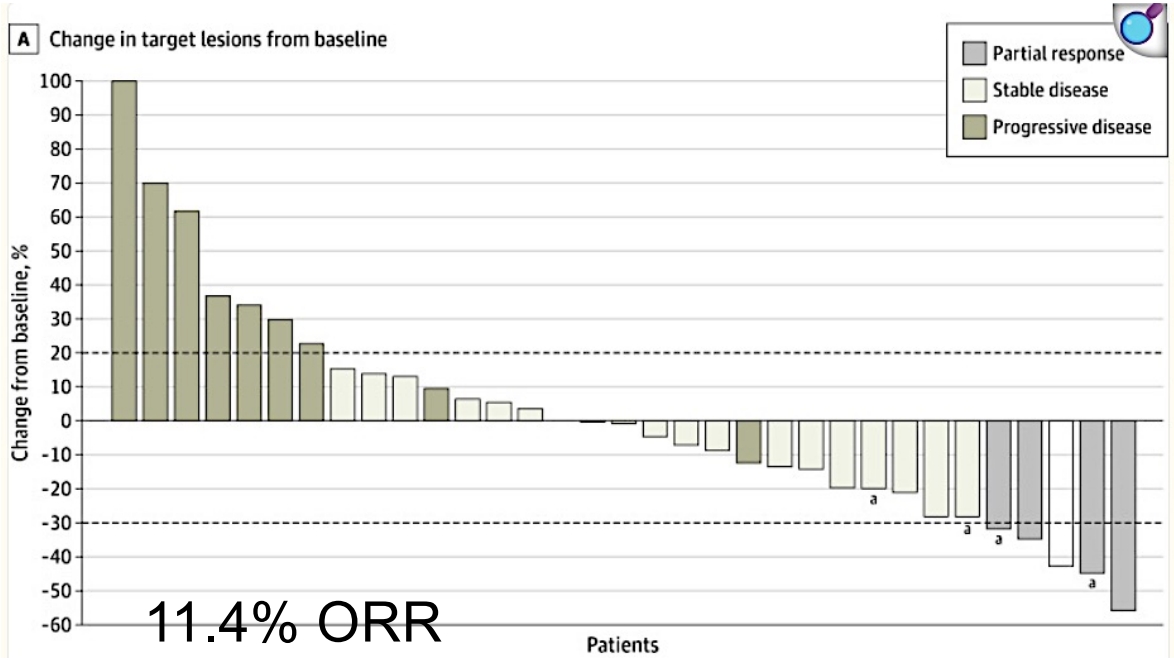
Chemotherapy

- Induces immunogenic cell death
- Release of neo-antigens

Phase 2: Checkpoint and PARP inhibitors

Talazoparib and Avelumab

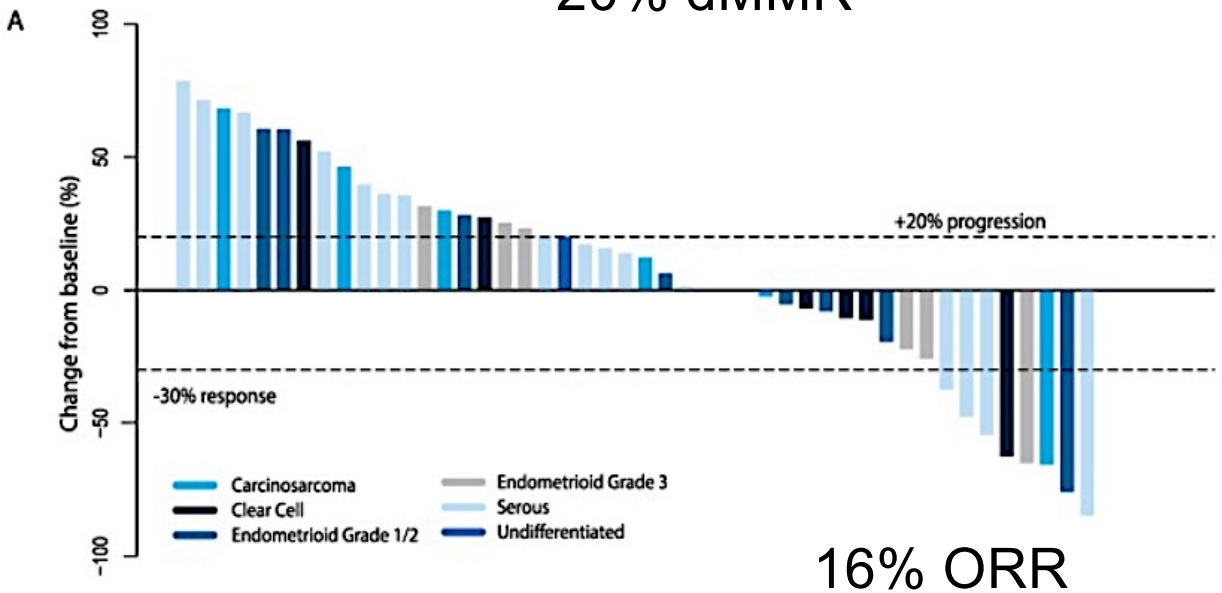
35 patients
MMRp



11.4% ORR

DOMEC: Durvalumab and Olaparib

55 patients
20% dMMR



16% ORR

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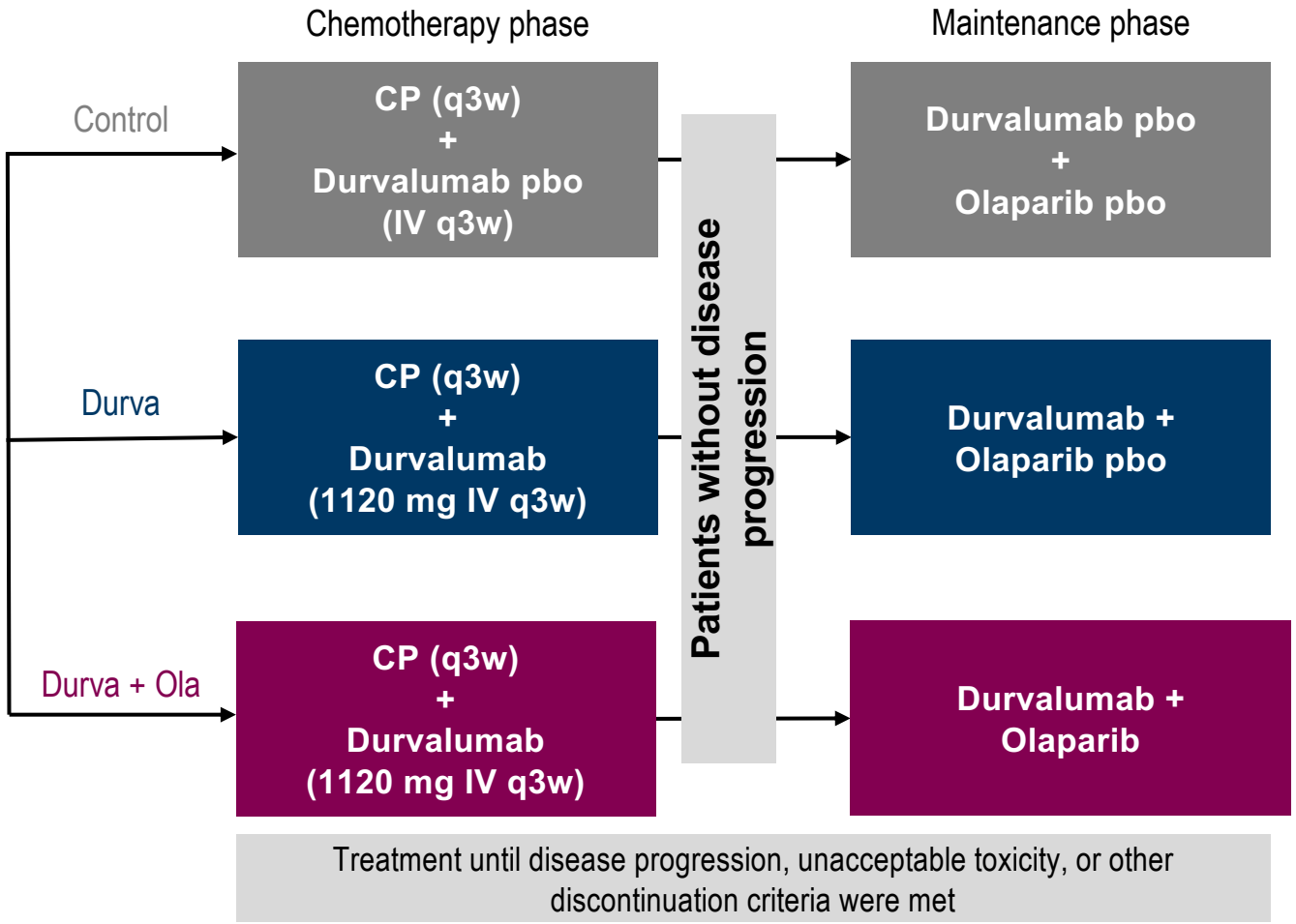
Konstantinopoulos P. JAMA Oncol 2022. Post CCB. Gynecol Oncol 2022.

DUO-E: Durvalumab and Olaparib

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

Stratified by:

- MMR status (proficient vs deficient)



Primary Endpoint:
PFS
-Durva vs Control
-Durva/Ola vs Control

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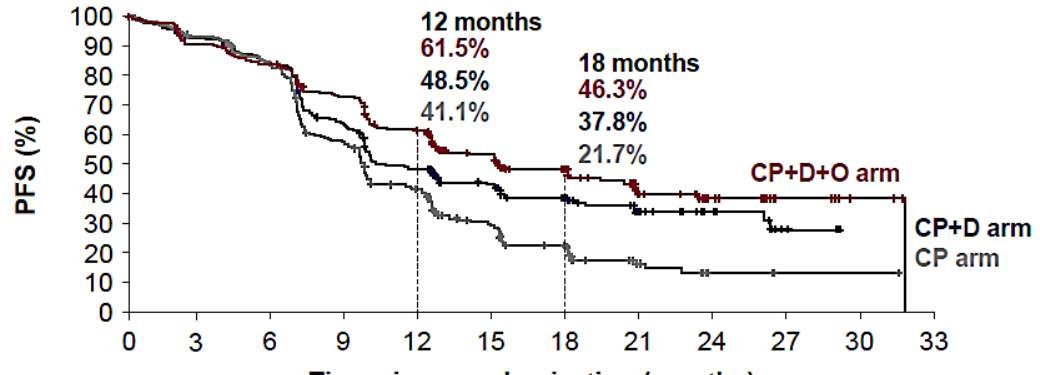
Westin SN. J Clin Oncol 2023.

DUO-E: ITT Survival Outcomes

Progression Free Survival



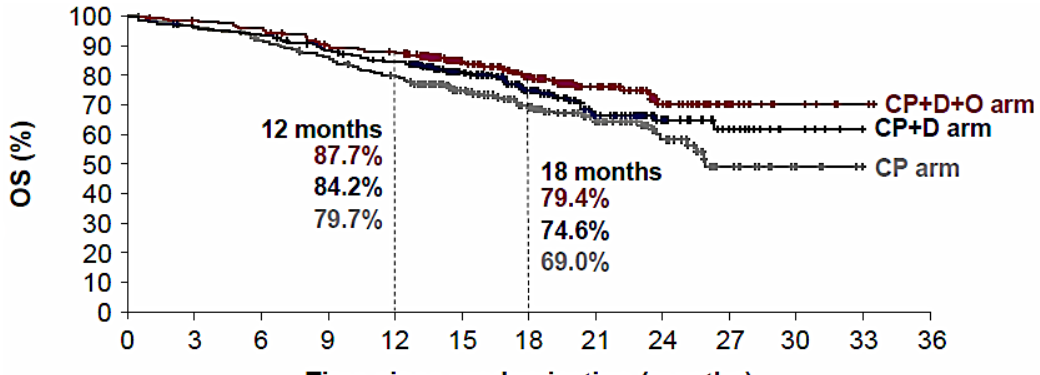
No. at risk

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

	CP arm (N=241)	CP+D arm (N=238)	CP+D+O arm (N=239)
Events, n (%)	173 (71.8)	139 (58.4)	126 (52.7)
Median PFS (95% CI), months	9.6 (9.0–9.9)	10.2 (9.7–14.7)	15.1 (12.6–20.7)
HR (95% CI) vs CP arm[a]		**0.71 (0.57–0.89); *P*=0.003**	**0.55 (0.43–0.69); *P*<0.0001**
HR (95% CI) vs CP+D arm[a]			0.78 (0.61–0.99)

Overall data maturity: 61.0%

Overall Survival



No. at risk

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

	CP arm (N=241)	CP+D arm (N=238)	CP+D+O arm (N=239)
Events, n (%)	82 (34.0)	65 (27.3)	52 (21.8)
Median OS (95% CI), months	25.9 (23.9–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm[b]		**0.77 (0.56–1.07); *P*=0.120**	**0.59 (0.42–0.83); *P*=0.003**
HR (95% CI) vs CP+D arm[b]			0.77 (0.53–1.10)

Overall data maturity: 27.7%

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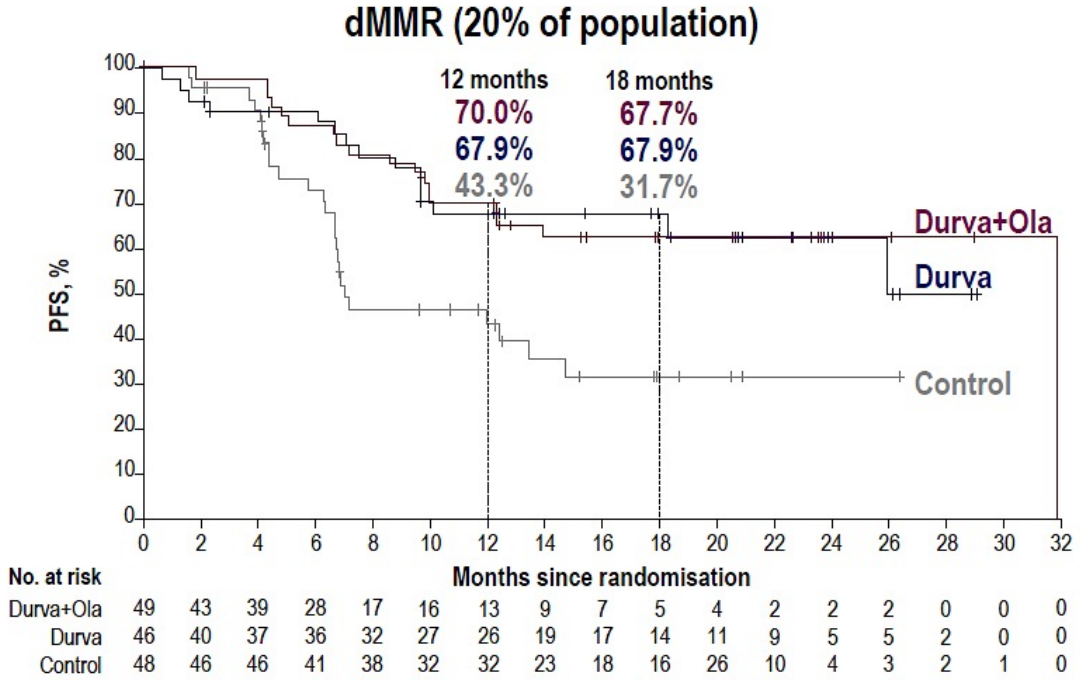
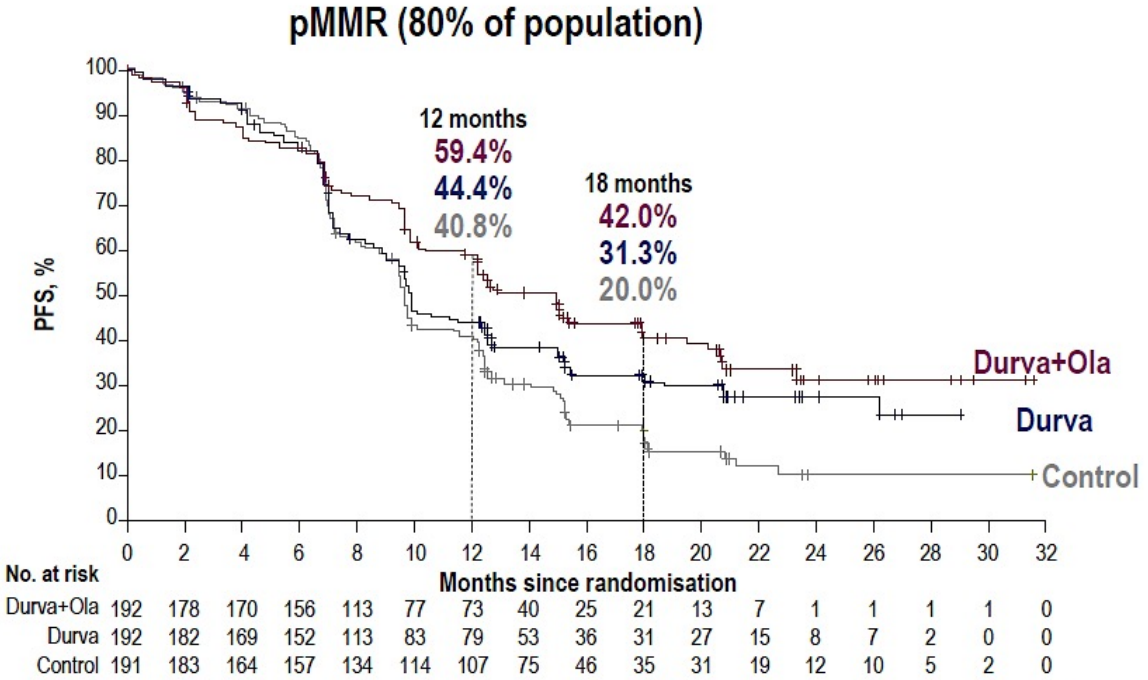
Westin SN. J Clin Oncol 2023. Baurain J-F, et al. SGO 2024.

DUO-E: Subgroup Analysis (Pre-specified)





	Control (N=49)	Durva (N=46)	Durva+Ola (N=48)
Events, n (%)	25 (51.0)	15 (32.6)	18 (37.5)
Median PFS (95% CI),* months	7.0 (6.7–14.8)	NR (NR–NR)	31.8 (12.4–NR)
HR (95% CI) vs Control†		**0.42 (0.22–0.80)**	**0.41 (0.21–0.75)**
HR (95% CI) vs Durva†			**0.97 (0.49–1.98)**

	Control (N=192)	Durva (N=192)	Durva+Ola (N=191)
Events, n (%)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS (95% CI),* months	9.7 (9.2–10.1)	9.9 (9.4–12.5)	15.0 (12.4–18.0)
HR (95% CI) vs Control†		**0.77 (0.60–0.97)**	**0.57 (0.44–0.73)**
HR (95% CI) vs Durva†			**0.76 (0.59–0.99)**

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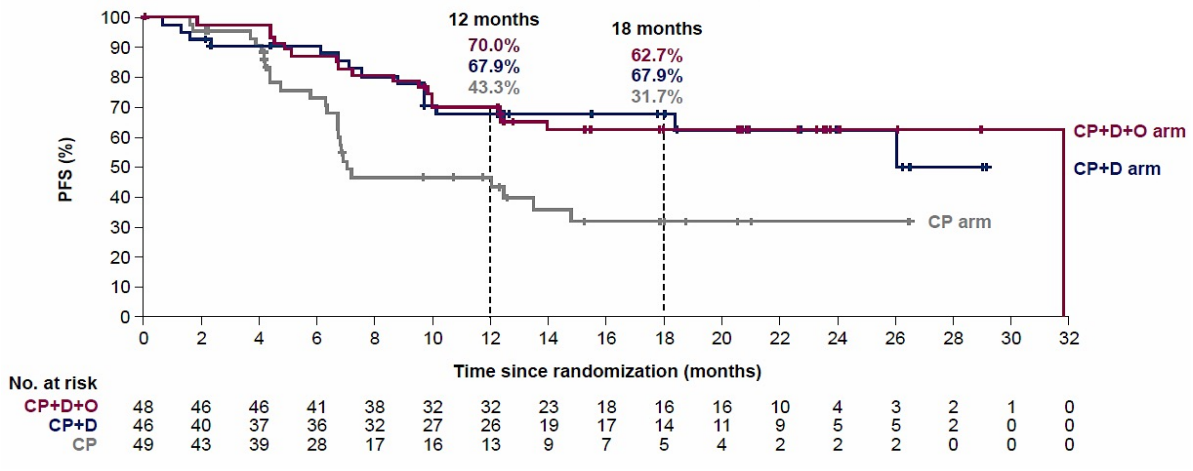
Westin SN. J Clin Oncol 2023.

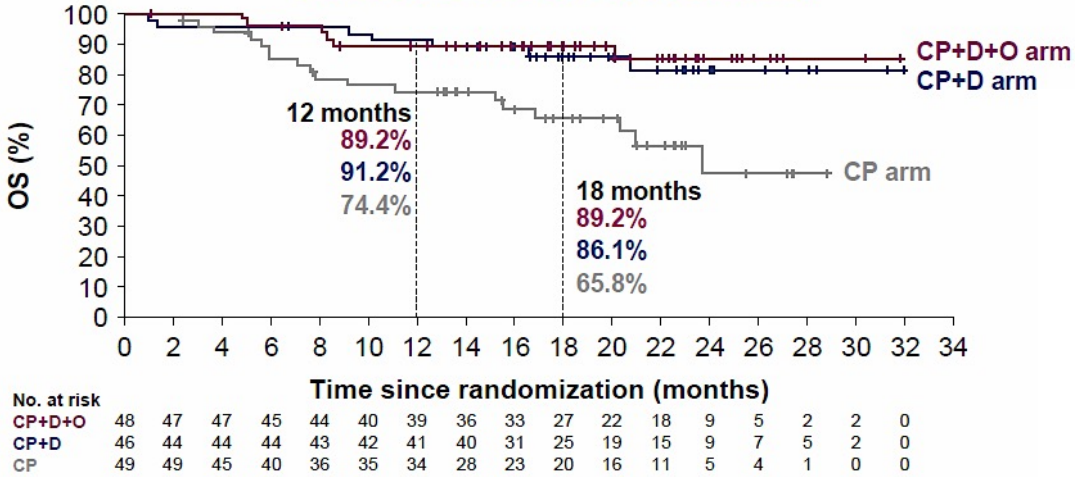
DUO-E: dMMR Survival Outcomes

Progression Free Survival



	CP arm (N=49)	CP+D arm (N=46)	CP+D+O arm (N=48)
Events, n (%)	25 (51.0)	15 (32.6)	18 (37.5)
Median PFS,[a] months (95% CI)	**7.0** (6.7–14.8)	**NR** (NR–NR)	**31.8** (12.4–NR)
HR (95% CI) vs CP arm[b]		**0.42 (0.22–0.80)**	**0.41 (0.21–0.75)**
HR (95% CI) vs CP+D arm[b]			0.97 (0.49–1.98)

Overall Survival



	CP arm (n=49)	CP+D arm (n=46)	CP+D+O arm (n=48)
Events, n (%)	18 (36.7)	7 (15.2)	6 (12.5)
Median OS (95% CI), months	23.7 (16.9–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm[b]		**0.34 (0.13–0.79)**	**0.28 (0.10–0.68)**
HR (95% CI) vs CP+D arm[b]			0.84 (0.27–2.52)

Overall data maturity: 21.7%

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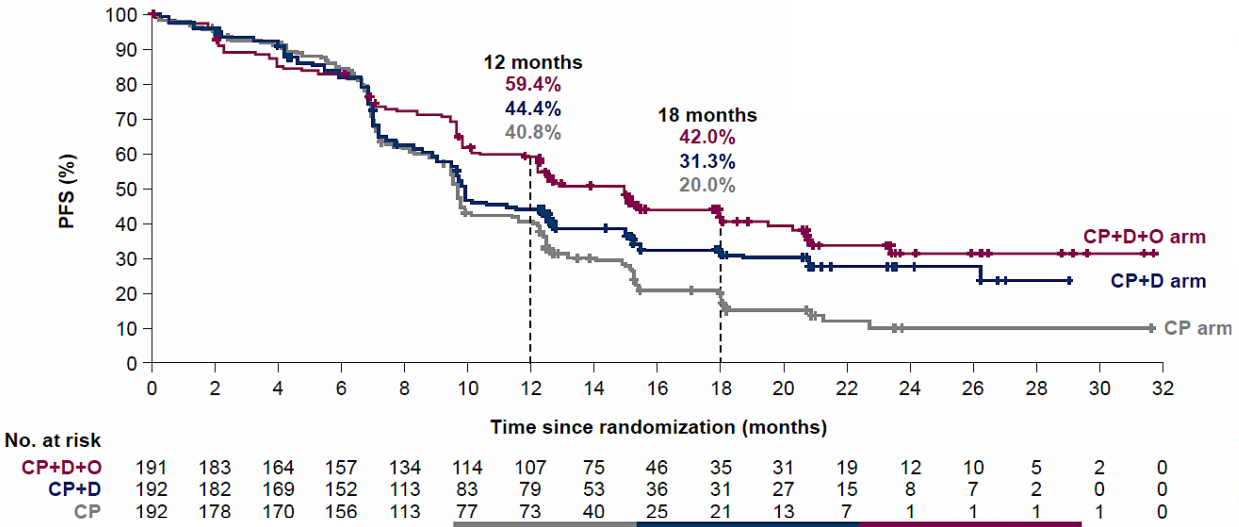
Baurain JF. SGO 2024; Westin SN. J Clin Oncol 2023.

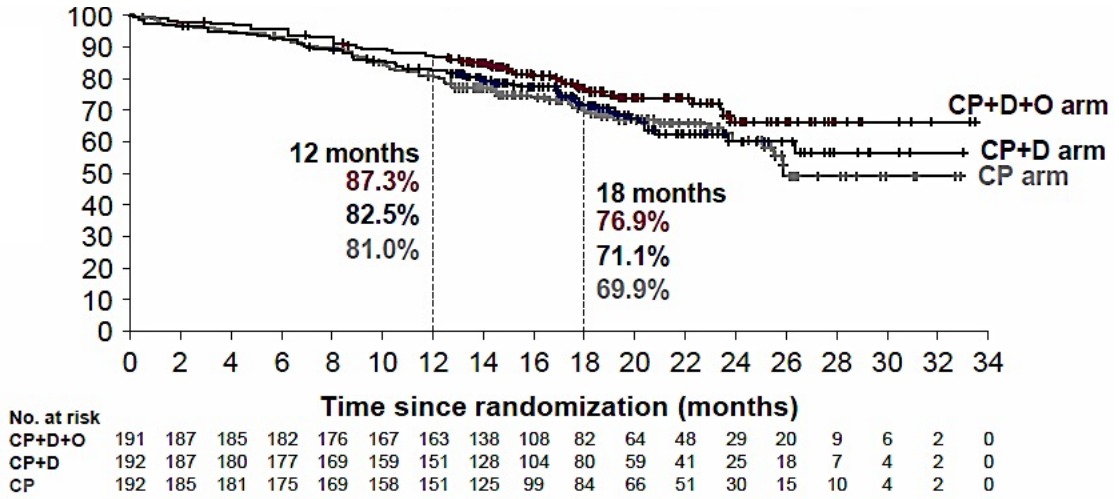
DUO-E: pMMR Survival Outcomes

Progression Free Survival



	CP arm (N=192)	CP+D arm (N=192)	CP+D+O arm (N=191)
Events, n (%)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS,[a] months (95% CI)	**9.7 (9.2–10.1)**	**9.9 (9.4–12.5)**	**15.0 (12.4–18.0)**
HR (95% CI) vs CP arm[b]		**0.77 (0.60–0.97)**	**0.57 (0.44–0.73)**
HR (95% CI) vs CP+D arm[b]			0.76 (0.59–0.99)

Overall Survival



	CP arm (n=192)	CP+D arm (n=192)	CP+D+O arm (n=191)
Events, n (%)	64 (33.3)	58 (30.2)	46 (24.1)
Median OS (95% CI), months	25.9 (25.1–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm[b]		**0.91 (0.64–1.30)**	**0.69 (0.47–1.00)**
HR (95% CI) vs CP+D arm[b]			0.75 (0.51–1.11)

Overall data maturity: 29.2%

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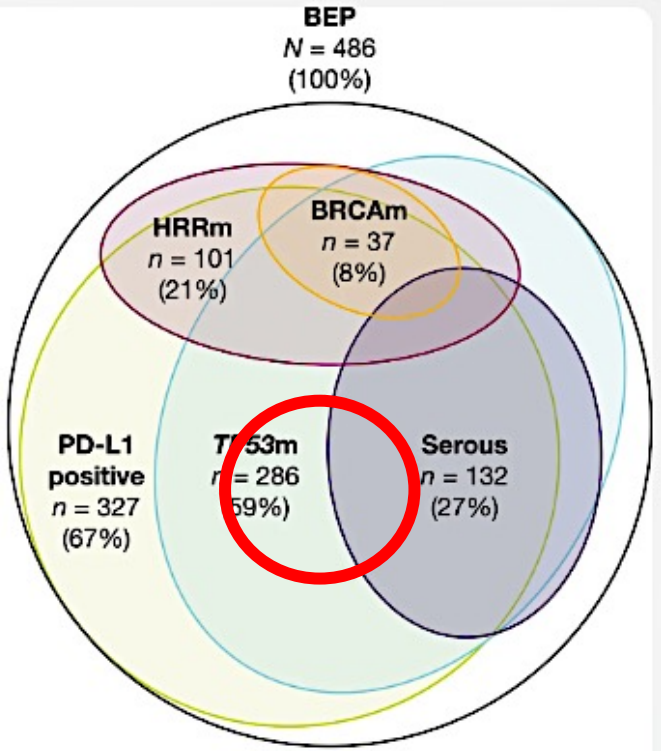
Baurain JF. SGO 2024; Westin SN. J Clin Oncol 2023.

DUO-E: Molecular Profile

	PD-L1 positive	*TP53*m	HRRm	BRCAm	*POLE*m	Serous
PD-L1 positive	327 (67)	215 (44)	78 (16)	28 (6)	11 (2)	99 (20)
***TP53*m**	215 (44)	286 (59)	66 (14)	30 (6)	10 (2)	119 (24)
HRRm	78 (16)	66 (14)	101 (21)	37 (8)	10 (2)	31 (6)
BRCAm	28 (6)	30 (6)	37 (8)	37 (8)	7 (1)	13 (3)
***POLE*m**	11 (2)	10 (2)	10 (2)	7 (1)	11 (2)	0 (0)
Serous	99 (20)	119 (24)	31 (6)	13 (3)	0 (0)	132 (27)



Westin SN. Gynecol Oncol. 2026

RUBY Part 2: Dostarlimab and Niraparib

Eligibility criteria

- Stage III/ or recurrent EC
- Naïve or >=6 months

Stratification: MMR/MSI status, prior external pelvic RT, and disease status

Maintenance

Dostarlimab + CP
Dostarlimab IV 500 mg +
Carbo AUC 5 mg/mL/min +
Pac 175 mg/m^2
q3w for 6 cycles

→ **Dostarlimab** IV 1000 mg q6w ≤3 years[a] +
Niraparib 200 or 300 mg tablets qd ≤3 years[a]

Placebo + CP
Carbo AUC 5 mg/mL/min +
Pac 175 mg/m^2 q3w
q3w for 6 cycles

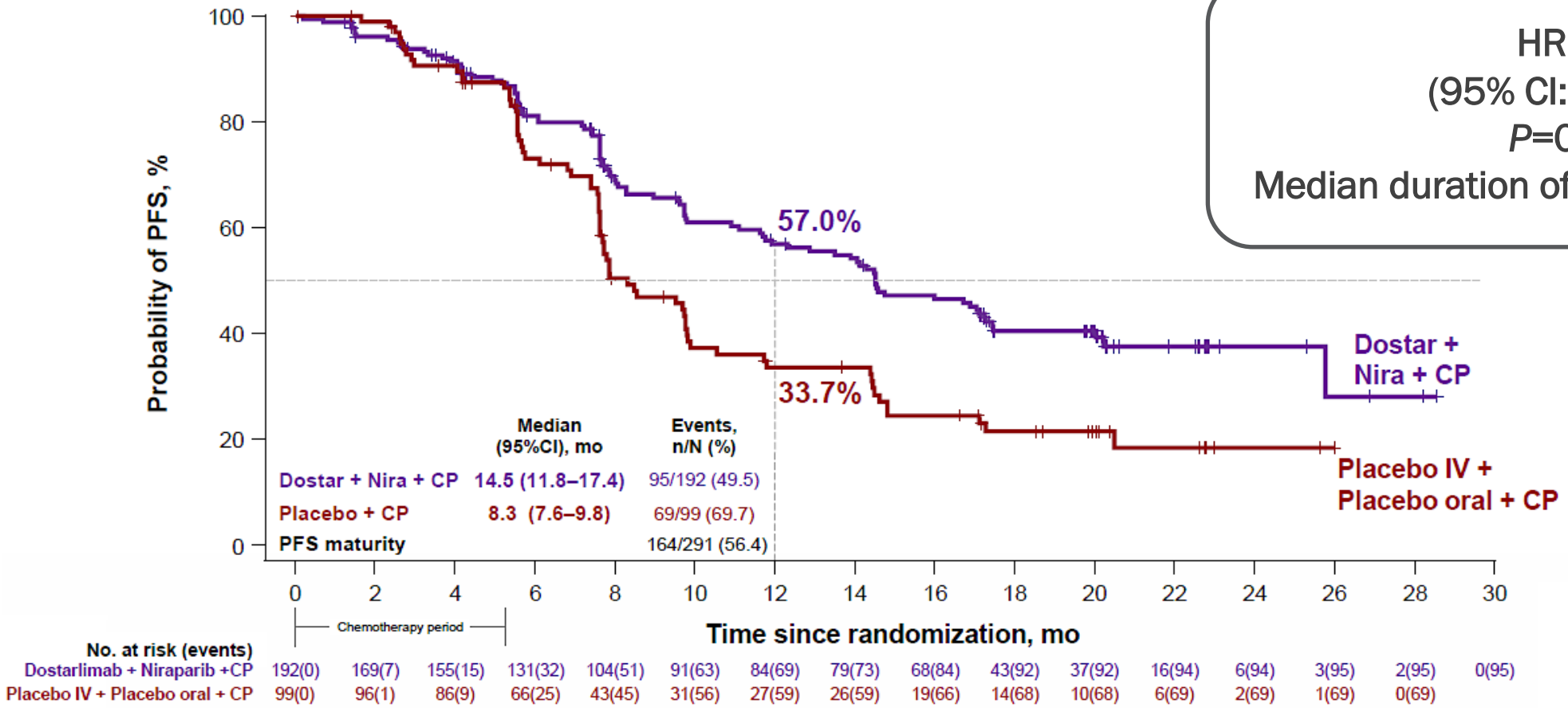
→ **Placebo** IV q6w ≤3 years[a] +
Placebo tablets qd ≤3 years[a]

Primary endpoints: PFS by INV in overall and pMMR/MSS cohorts
Secondary endpoints: OS, PFS by BICR, ORR, DOR, DCR (BOR of CR, PR, or SD), PFS2, HRQoL/PRO, PK, safety

UCLA Health

Mirza MR. SGO 2024.

RUBY Part 2: PFS in Overall Population



HR=0.60
(95% CI: 0.43-0.82)
P=0.0007
Median duration of follow up: 19 months

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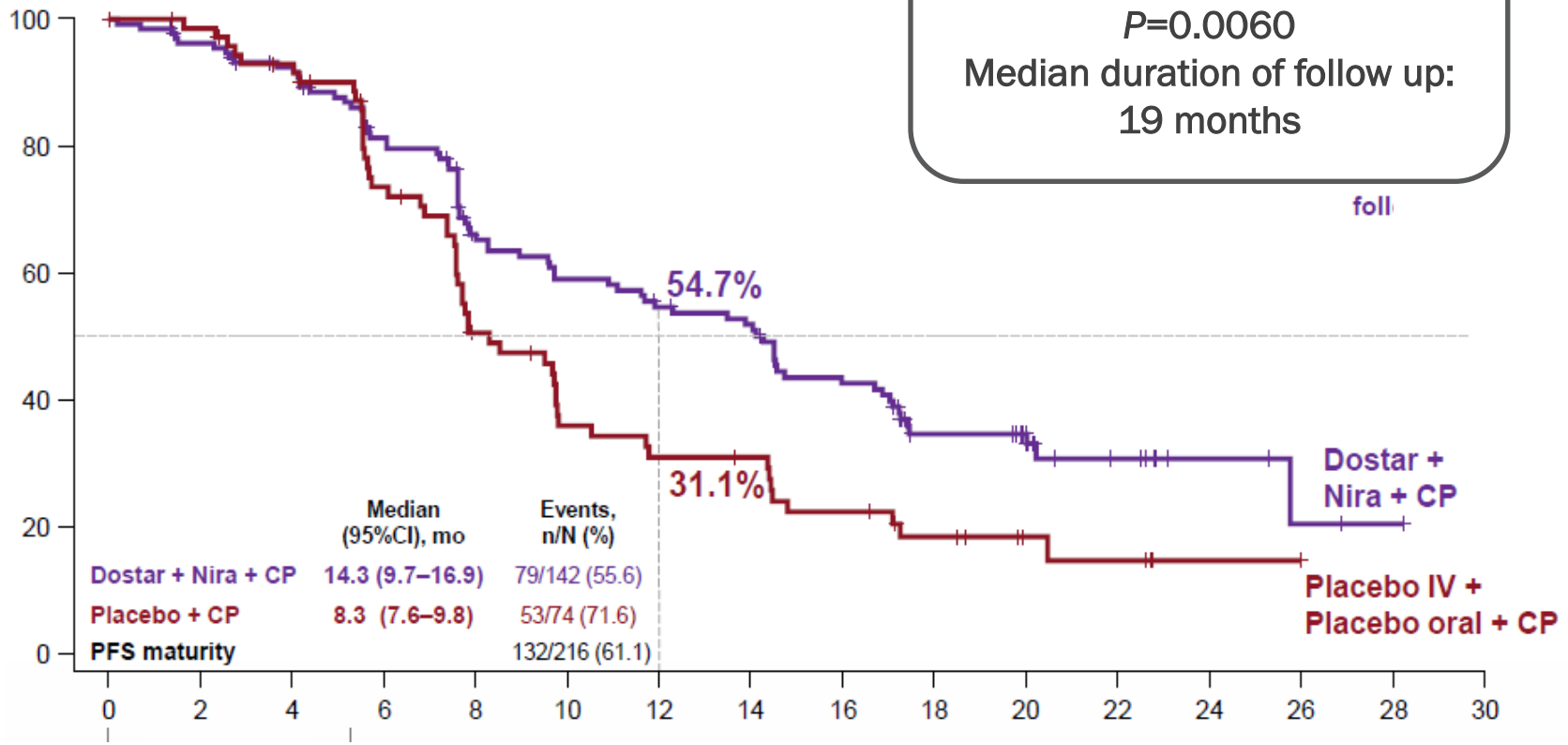
Mirza MR. SGO 2024.

RUBY Part 2: PFS by MMR status

pMMR



HR=0.63
(95% CI: 0.44-0.91)
P=0.0060
Median duration of follow up:
19 months

dMMR population
12-month PFS:
64.4% v 40.8%
PFS: 7.9 m v NE
HR=0.48
(95% CI: 0.24-0.96)
P=0.017

UCLA Health

Mirza MR. SGO 2024.

RUBY Part 2: Molecular Subgroups

MMRp/MSS population

	Dostarlimab + niraparib + CP N=142	Placebo IV + placebo oral + CP N=74	HR (95%CI)
	No. of patients with events/No. of patients		
All patients	79/142	53/74	0.62 (0.44–0.88)
PD-L1 Status[a]			
PD-L1+	46/88	31/44	0.61 (0.38–0.96)
PD-L1-	32/53	20/26	0.66 (0.38–1.17)
Not evaluable[b]	1/1	2/4	NA
BRCA mutation status			
Positive	1/4	2/3	NA
Negative	63/113	40/55	0.62 (0.42–0.93)
Not evaluable[b]	15/25	11/16	0.77 (0.35–1.68)
HRR mutation status[c]			
Positive	3/10	8/11	NA
Negative	61/107	34/47	0.65 (0.43–1.00)
Not evaluable[b]	15/25	11/16	0.77 (0.35–1.68)

HR (95%CI)

0.0156 0.0313 0.0625 0.125 0.25 0.5 1 2 4 8

←Dostar + nira + CP better Placebo + CP better→

	Dostarlimab + niraparib + CP N=192	Placebo IV + placebo oral + CP N=99	HR (95%CI)
	No. of patients with events/No. of patients		
All patients	95/192	69/99	0.59 (0.43–0.81)
Molecular subgroup[a]			
POLE	0/3	1/2	NA
dMMR/MSI-H	12/37	10/17	0.45 (0.20–1.05)
TP53mut	27/39	10/10	0.29 (0.13–0.63)
NSMP	37/75	31/46	0.61 (0.38–0.99)
Not evaluable[b]	19/38	17/24	0.71 (0.37–1.37)

HR (95%CI)

0.0150 0.0313 0.0625 0.125 0.25 0.5 1 2 4 8

←Dostar + nira + CP better Placebo + CP better→

UCLA Health

Mirza MR. SGO 2024.

KEYNOTE-775: Recurrent Endometrial Cancer

Key Eligibility Criteria

- Advanced, metastatic, or recurrent EC
- Measurable disease by BICR
- 1 prior platinum-based chemotherapy regimen
- ECOG PS 0–1

Stratification Factors

- MMR status (dMMR vs MMRp)
- ECOG PS
- Geographic region
- Prior pelvic radiation

Lenvatinib
20 mg po qd
+
Pembrolizumab
200 mg IV q3w

Physician's Choice:
Doxorubicin 60 mg/m^2 IV q3w
OR
Paclitaxel 80 mg IV mg/m^2 IV q1w

Primary Endpoints

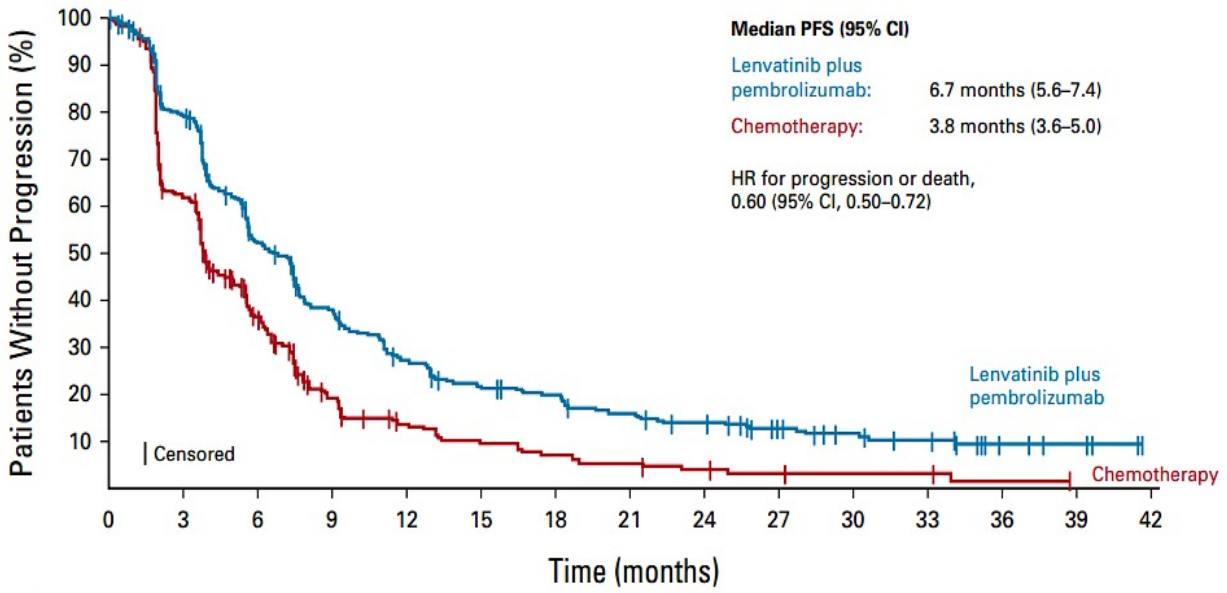
- PFS by BICR and OS

UCLA Health

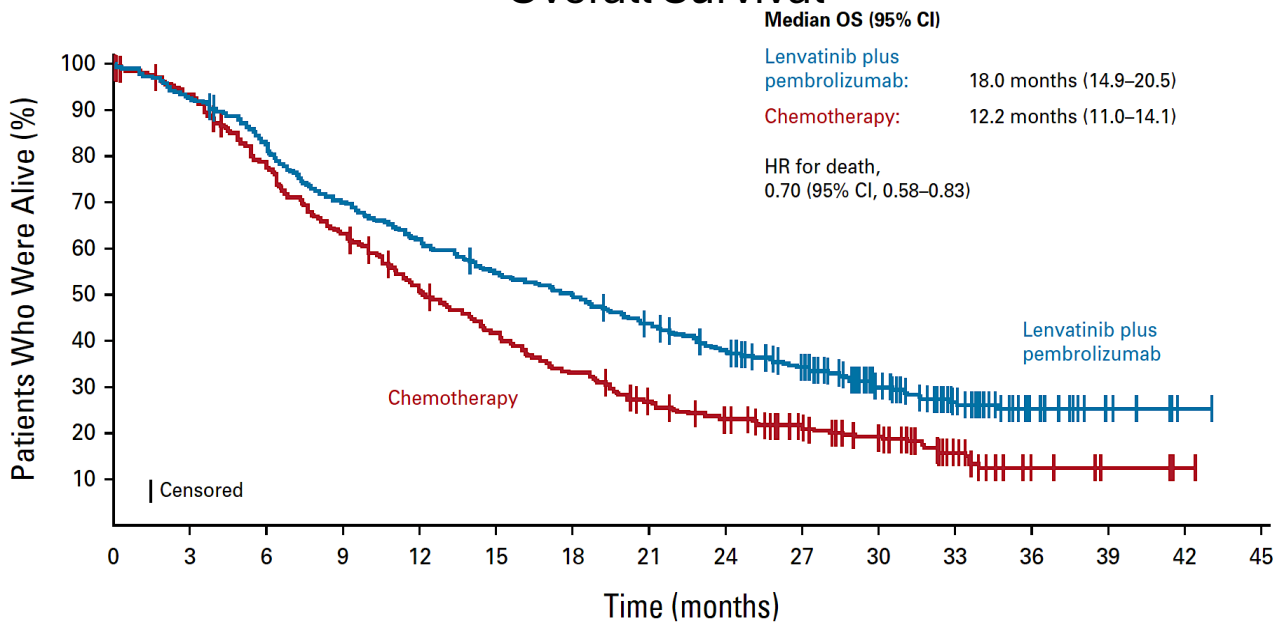
Makker V. *N Engl J Med*. 2022.

KEYNOTE-775 Survival Outcomes-pMMR

Progression Free Survival



Overall Survival



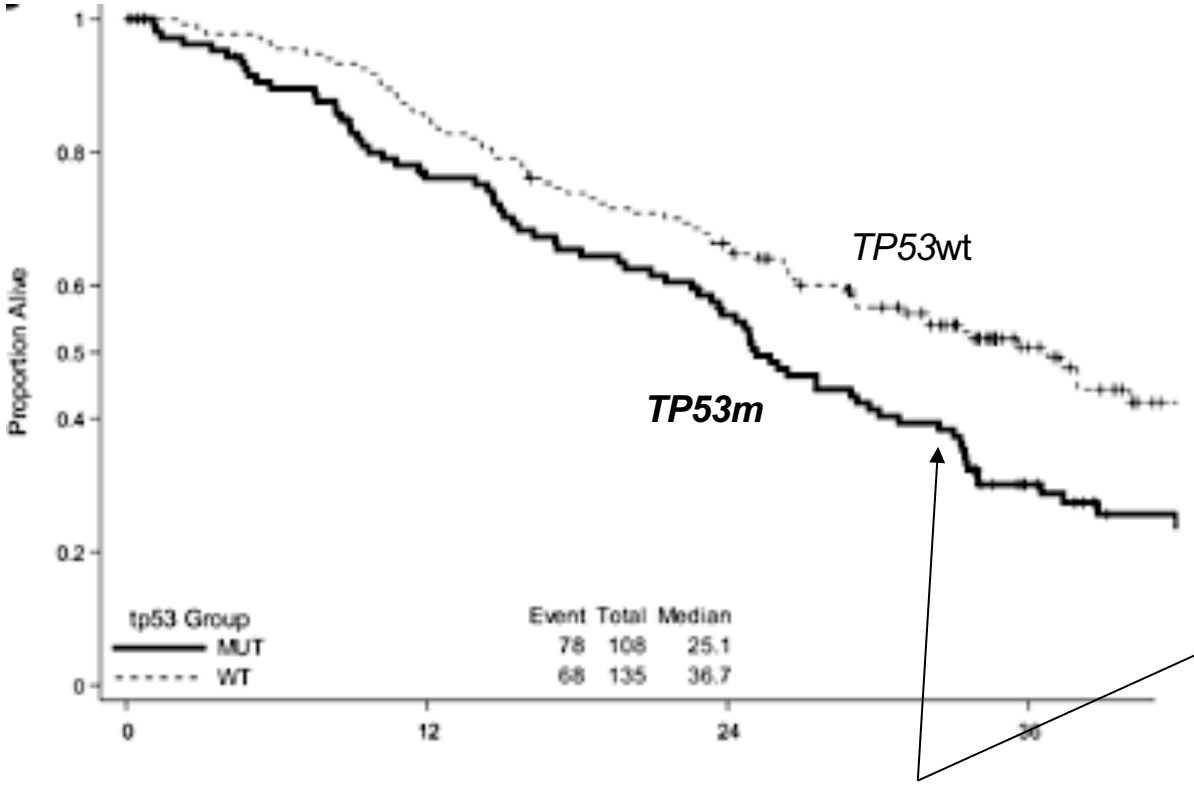
pMMR Population	ORR, % (95% CI)	mDOR, mo (range)	mOS, mo (95% CI)	HR
Len + Pem	32.4 (27.5–37.6)	9.3 (1.6+ to 39.5+)	18.0 (14.2–19.9)	0.70 (0.56–0.83)
Chemotherapy	15.1 (11.5–19.3)	5.7 (0.0+ to 37.1+)	12.2 (11.0–14.1)	

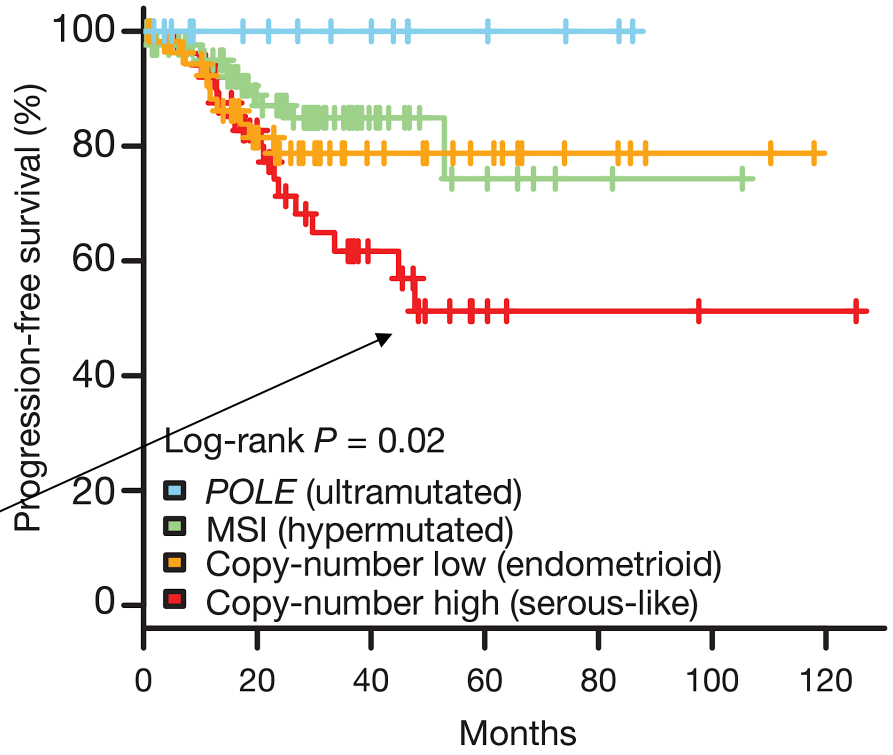
UCLA Health

Makker V. J Clin Oncol 2023.

Endometrial Cancer *TP53*: Biomarker for Prognosis

- Analysis of all patients from GOG 86P





TP53m associated with worse outcomes

UCLA Health

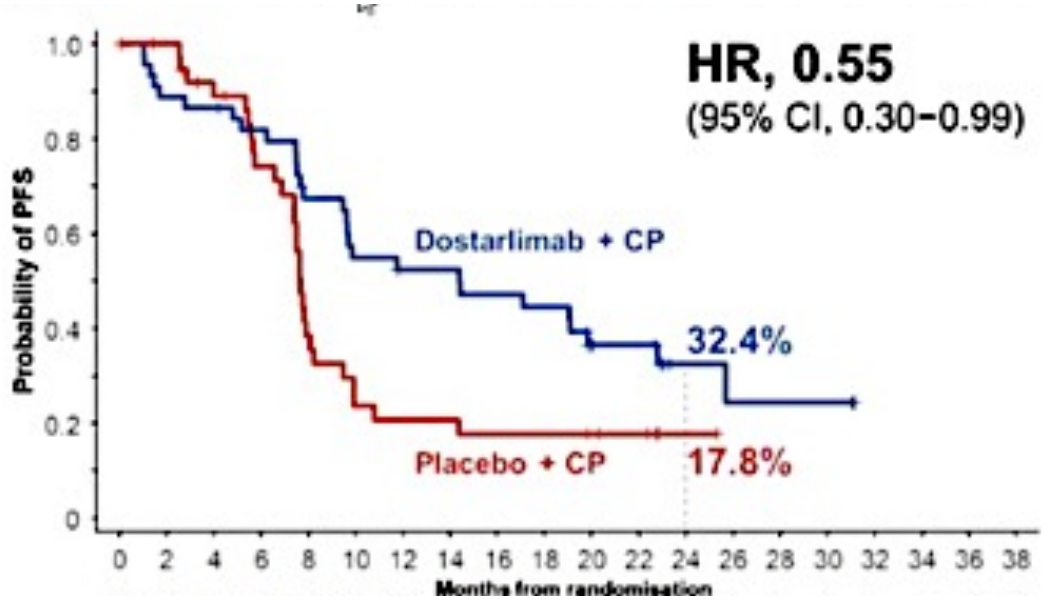
Aghajanian C. Gynecol Oncol 2018. Leslie KK. Gynecol Oncol. 2021. Levine DA. Nature 2013.

Endometrial Cancer *TP53*m

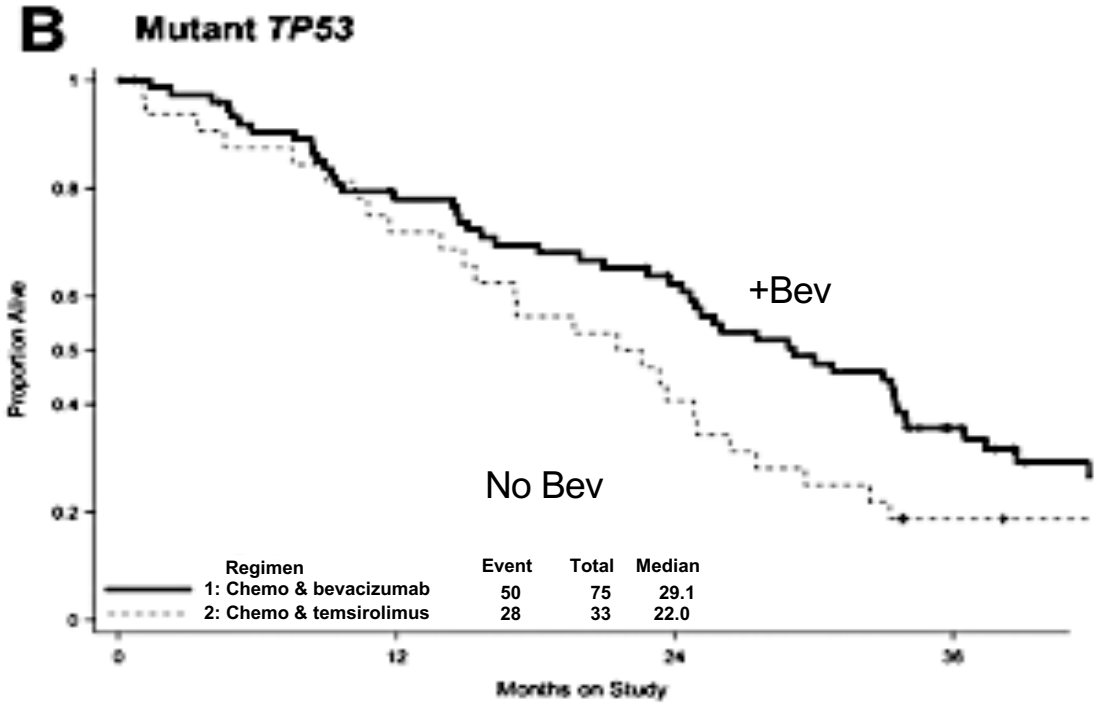
- Risk of recurrence is high; employment of new strategies

TP53 mut

Dostarlimab



Bevacizumab

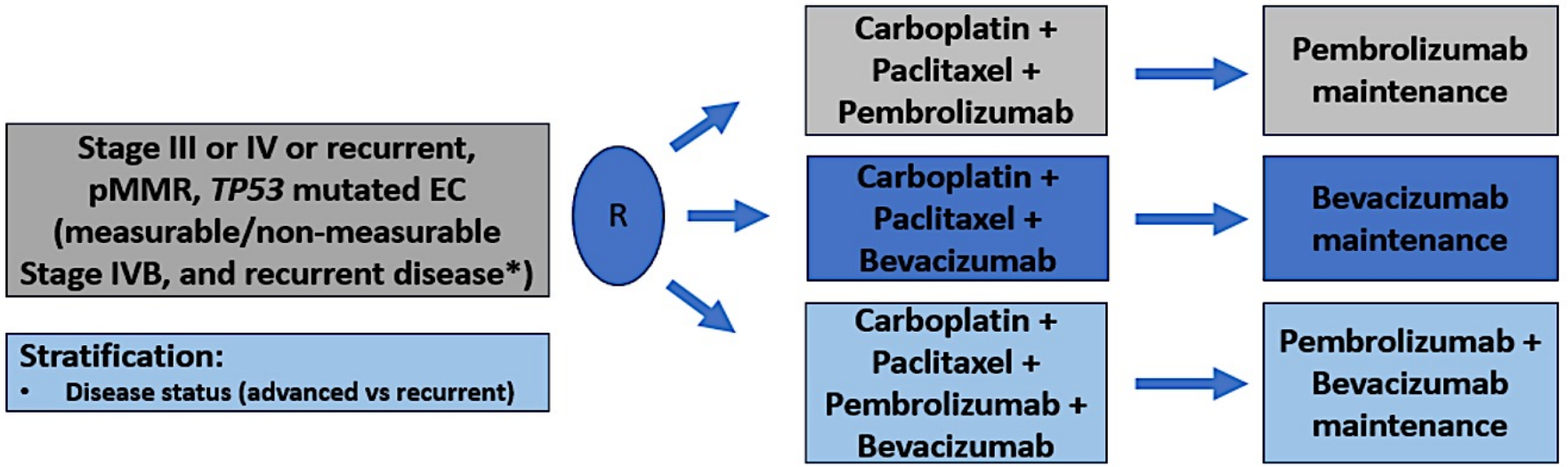


UCLA Health

Mirza M. ESMO 2023; Mirza M. NEJM 2023. Leslie KK. Gynecol Oncol 2021. Thiel KW. JCO 2022.

Endometrial Cancer *TP53*m: Future Trial GY035 (in development)

Randomized Phase II/III Study of Carboplatin + Paclitaxel + Pembrolizumab vs. Carboplatin + Paclitaxel + Bevacizumab vs. Carboplatin + Paclitaxel + Pembrolizumab + Bevacizumab in Patients with Advanced or Recurrent, pMMR and *TP53* mutated Endometrial Cancer



*Primary Phase II endpoint: PFS by RECIST V1.1
*Primary Phase III endpoint: OS

Treatment Plan:
Arm 1: IV carboplatin AUC 5 + IV paclitaxel 175 mg/m^2 + IV pembrolizumab 200 mg on day 1 every 3 weeks x 6-10 cycles followed by 14 additional cycles of pembrolizumab 400 mg IV maintenance every 6 weeks.
Arm 2: IV carboplatin AUC 5 + IV paclitaxel 175 mg/m^2 + bevacizumab 15 mg/kg on day 1 every 3 weeks x 6-10 cycles followed by 28 additional cycles of bevacizumab 15 mg/kg maintenance every 3 weeks.
Arm 3: IV carboplatin AUC 5 + IV paclitaxel 175 mg/m^2 + IV pembrolizumab 200 mg + bevacizumab 15 mg/kg on day 1 every 3 weeks x 6-10 cycles followed by 14 additional cycles of pembrolizumab 400 mg IV maintenance every 6 weeks and 28 additional cycles of bevacizumab 15 mg/kg IV maintenance every 3 weeks.
*Patients with recurrent disease who have received prior adjuvant therapy must have a platinum-free interval of >/=12 months.

Conclusions

- Molecular testing should be integrated into routine practice
  - Prognostic and therapeutic implications
  - Clear role of immunotherapy in dMMR
- Role of immunotherapy in pMMR setting less clear
  - Identifying which patients benefit from which therapies is key
    - PARPi? Bevacizumab?
- Future studies continue to exploit new targets!

Second Opinion

Ursula Matulonis, MD

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

What postsurgical adjuvant treatment, if any, would you recommend to a patient with Grade 1 MSS/pMMR EC? Does your approach differ for patients with MSI-H/dMMR disease? Would you include endocrine therapy as part of adjuvant treatment for a patient with ER-positive EC?

In what situations are you using endocrine therapy for patients with ER-positive EC? Beyond ER, do you evaluate other biomarkers such as ESR1 and PI3K/AKT/PTEN? Do you believe any of these are relevant and actionable for patients with ER-positive EC?

QUESTIONS FOR THE FACULTY

For a patient who receives carboplatin/paclitaxel/dostarlimab and progresses while on dostarlimab maintenance, would you consider immunotherapy rechallenge at any time point?

Do you believe there is a role for ctDNA for a patient with metastatic EC who achieves a complete response to treatment with no evidence of disease? Outside of a clinical trial setting, would you use ctDNA to inform whether or not to discontinue or de-escalate treatment?

Second Opinion

Professor Jonathan A Ledermann

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Do you believe there is a strong biologic rationale for the use of PARP inhibition in patients with EC? In your opinion, is there true therapeutic synergy between anti-PD-1/PD-L1 antibodies and PARP inhibitors in EC, or is the effect simply additive?

Based on the results of available trials, would you like to be able to administer up-front chemoimmunotherapy followed by combined anti-PD-1/PD-L1 antibody and PARP inhibitor maintenance for patients with newly diagnosed advanced or recurrent EC in your practice? In what situations, if any, have you used this approach outside of a clinical trial setting?

QUESTIONS FOR THE FACULTY

Do you believe the regimens evaluated in RUBY Part 2 and DUO-E are likely to obtain regulatory approval? If they were to become available, for which patients can you envision adding a PARP inhibitor in the maintenance setting? Would you be more likely to do so in certain patient subsets (eg, those with MSS/ pMMR disease, those with documented HRR mutations) than others?

Second Opinion

Professor Jonathan A Ledermann
Professor of Medical Oncology
UCL Cancer Institute
London, United Kingdom

Angeles Alvarez Secord, MD, MHSc
Director of Gynecologic Oncology Clinical Trials
Associate Director, Clinical Research, Gynecologic Oncology Program
Duke Cancer Institute
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
Duke University School of Medicine
Durham, North Carolina

Ursula Matulonis, MD
Chief, Division of Gynecologic Oncology
Brock-Wilson Family Chair
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Neil Love, MD
Research To Practice
Miami, Florida

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Expert Second Opinion: Investigators Provide Perspectives on the Best-Practice Management of Ovarian Cancer

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Nicoletta Colombo, MD

Gottfried E Konecny, MD

Alexander B Olawaiye, MD

Moderator

Shannon N Westin, MD, MPH, FASCO, FACOG

RTP RESEARCH TO PRACTICE

Data + Perspectives: The Potential Role of TROP2- and CDH6-Directed Antibody-Drug Conjugates in Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Ramez N Eskander, MD

Bradley J Monk, MD

Moderator

Kathleen N Moore, MD, MS

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