Year in Review:
Management of Gynecologic Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, June 17, 2025
5:00 PM – 6:00 PM ET

Faculty

Susana Banerjee, MBBS, MA, PhD
Ursula Matulonis, MD

Moderator

Neil Love, MD

RTP Year in Review 2025

Faculty

Susana Banerjee, MBBS, MA, PhD
Consultant Medical Oncologist
The Royal Marsden NHS Foundation Trust
Professor in Women's Cancers
The Institute of Cancer Research, London
President
Royal Society of Medicine, Oncology Section
London, United Kingdom

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

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, GSK, and Natera Inc.

Dr Love — Disclosures

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Prof Banerjee — Disclosures

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, BioNTech SE, Eisai Inc, Epsilogen, Genmab US Inc, Gilead Sciences Inc, GSK, Greywolf Therapeutics, ImmunoGen Inc, Incyte Corporation, ITM Oncologics GmbH, Lilly, Mersana Therapeutics Inc, MSD, Myriad Genetic Laboratories Inc, OncXerna Therapeutics Inc, pharmaand GmbH, Seagen Inc, TORL BioTherapeutics, Verastem Inc, Zymeworks Inc
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Nonrelevant Financial Relationships	Perci Health

Dr Matulonis — Disclosures

Advisory Committees	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Day One Biopharmaceuticals, GSK, NextCure, Novartis, Tango Therapeutics
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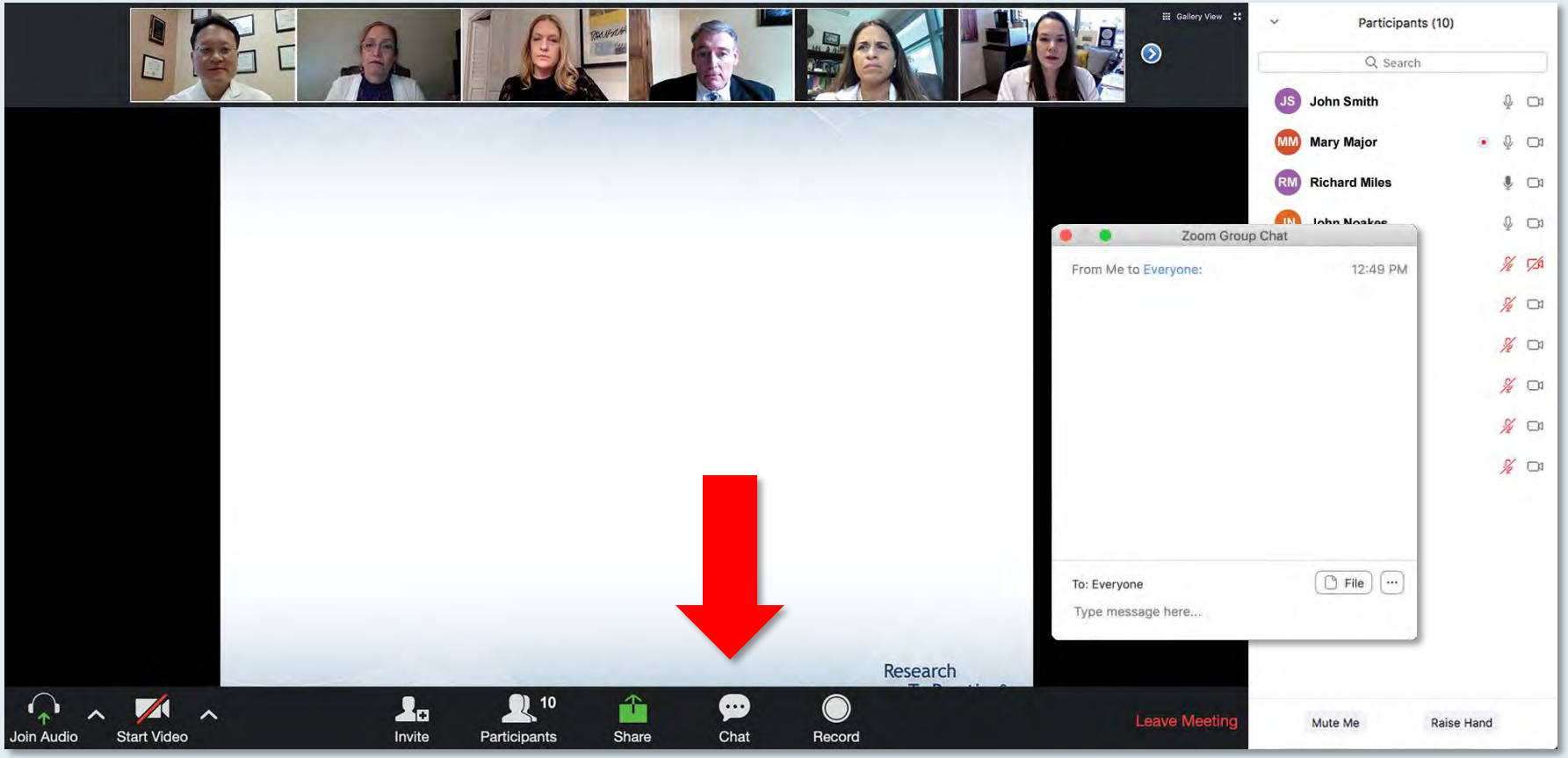
We Encourage Clinicians in Practice to Submit Questions



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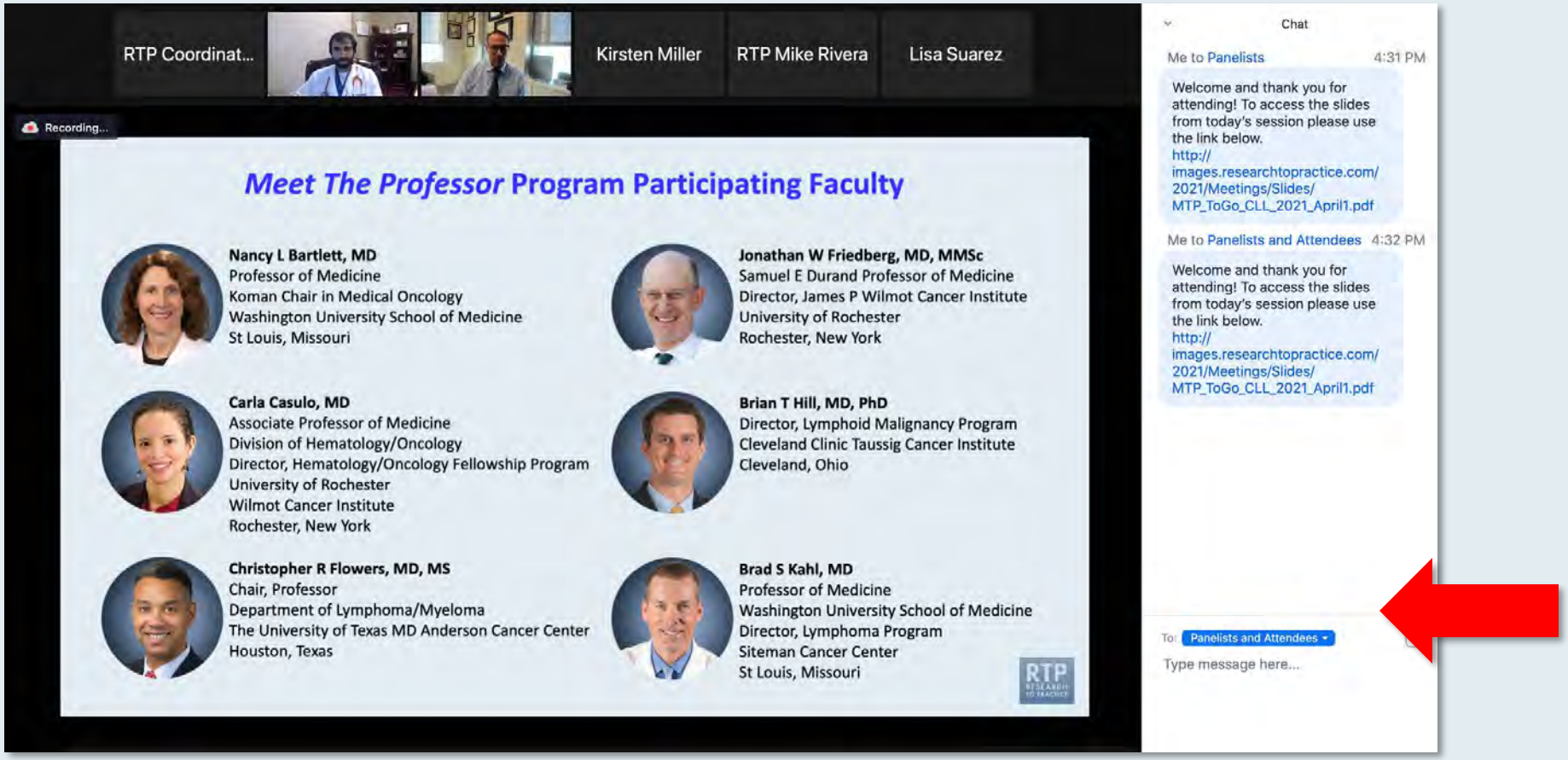

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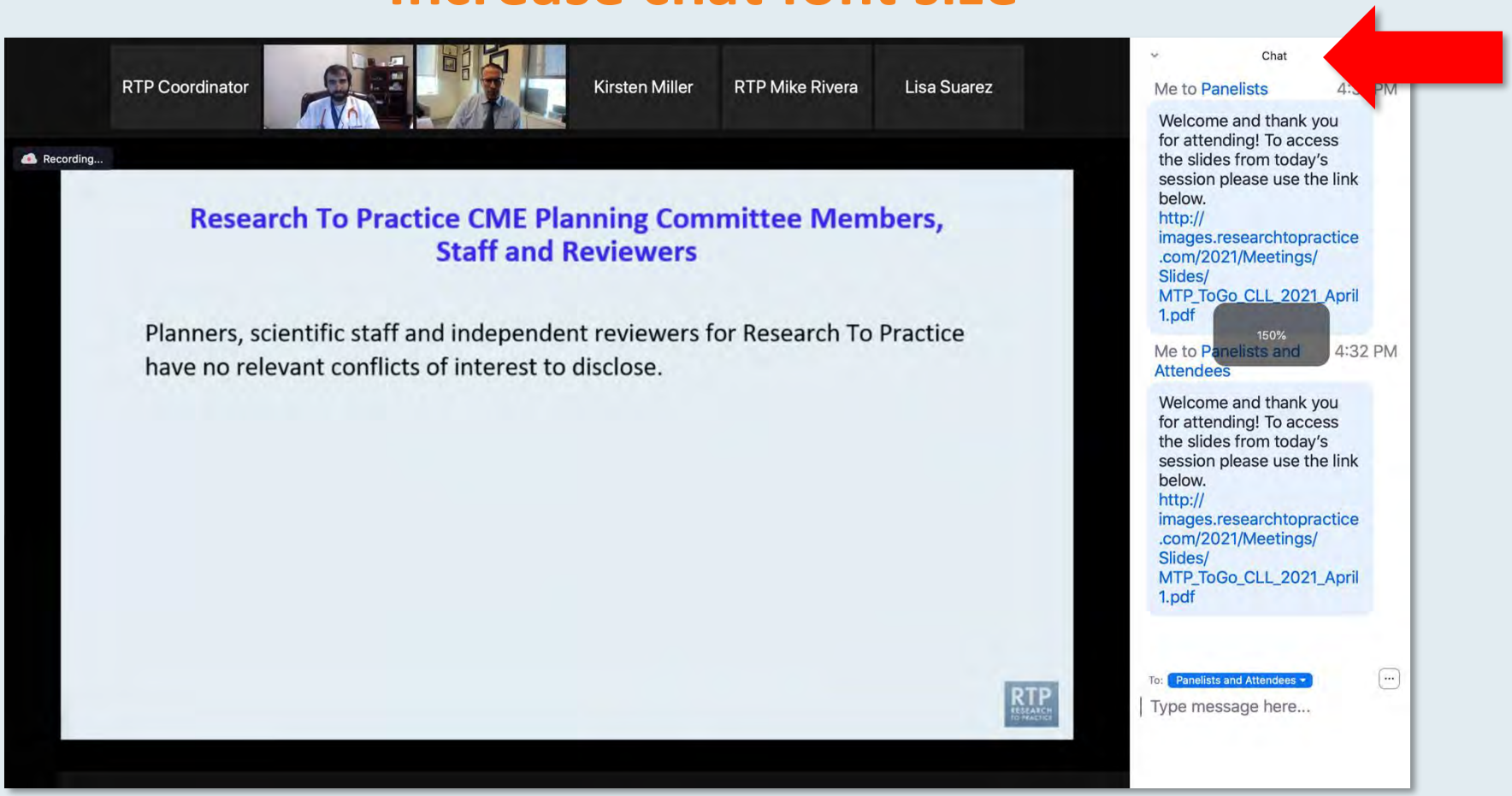

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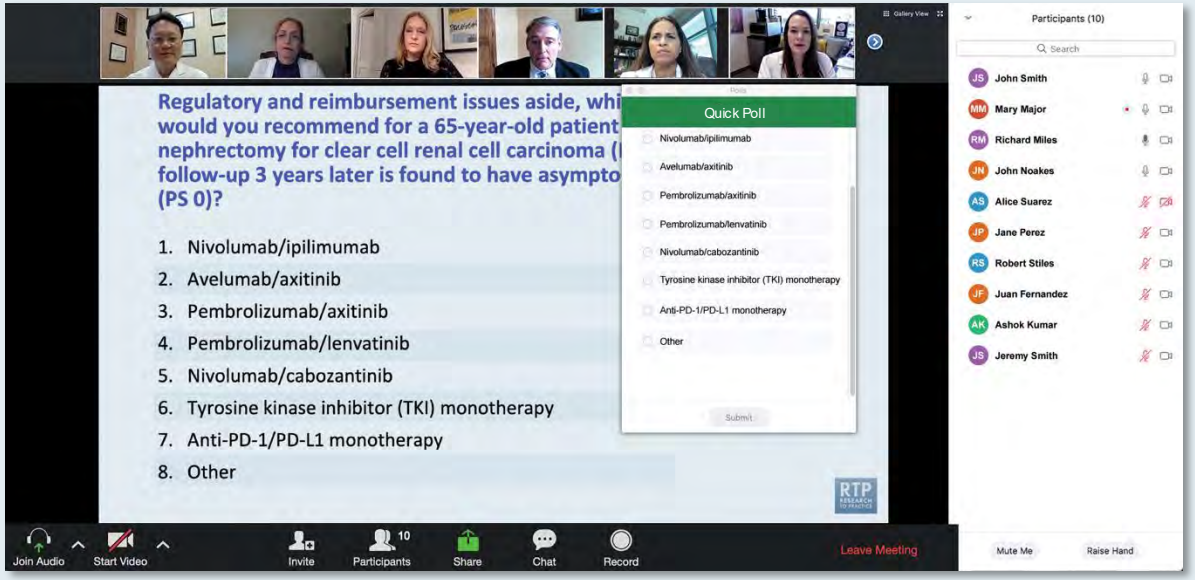

Gynecologic Cancers — Fourth Annual National General Medical Oncology Summit

DR DAVID M O'MALLEY
THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER

DR BRIAN M SLOMOVITZ
MOUNT SINAI MEDICAL CENTER

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

Nontargeted Approaches for Lung Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, June 24, 2025
5:00 PM – 6:00 PM ET

Faculty

Benjamin Levy, MD

Moderator

Neil Love, MD

RTP Year in Review 2025

Optimizing the Selection of First-Line Therapy for Patients with Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Tuesday, July 1, 2025
5:00 PM – 6:00 PM ET

Faculty

Xavier Leleu, MD, PhD
Peter Voorhees, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

A Webinar Series for Clinicians and Patients,
Developed in Partnership with Cancer*Care*®

Tuesday, July 8, 2025
6:00 PM – 7:00 PM ET

Wednesday, July 23, 2025
5:00 PM – 6:00 PM ET

Faculty

Natalie S Callander, MD
Sagar Lonial, MD, FACP

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Practical Perspectives: Experts Review Actual Cases of Patients with Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 16, 2025
5:00 PM – 6:00 PM ET

Faculty

Stephen V Liu, MD
Charles Rudin, MD, PhD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Year in Review:
Management of Gynecologic Cancers

INTRODUCTION: Tale of Two Cities — ASCO 2025

MODULE 1: Ovarian Cancer

MODULE 2: HER2-Positive Gynecologic Cancers

MODULE 3: Endometrial Cancer

MODULE 4: Cervical Cancer

RTP Year in Review 2025

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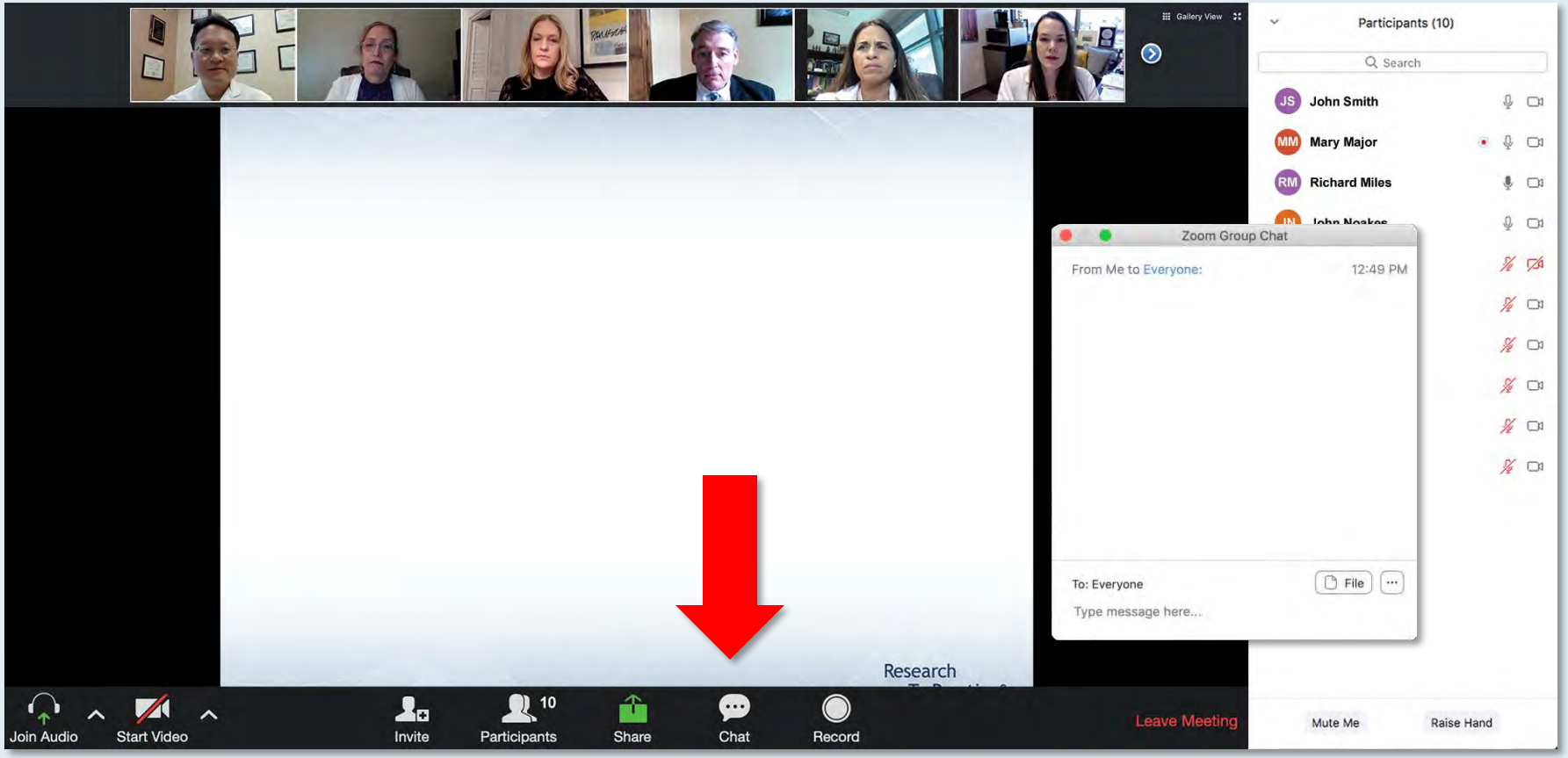

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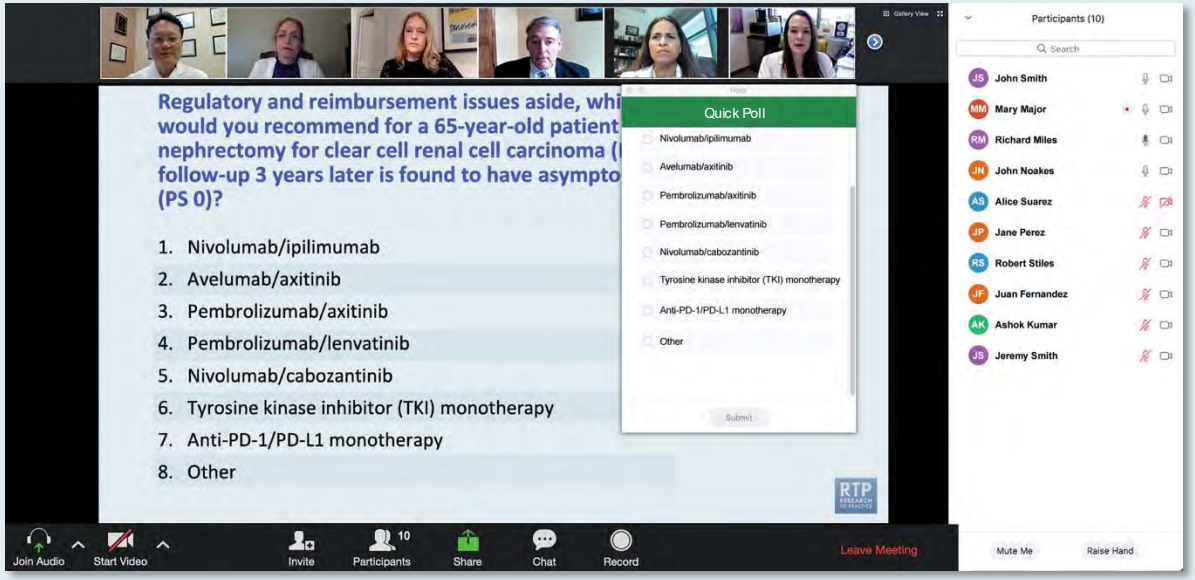

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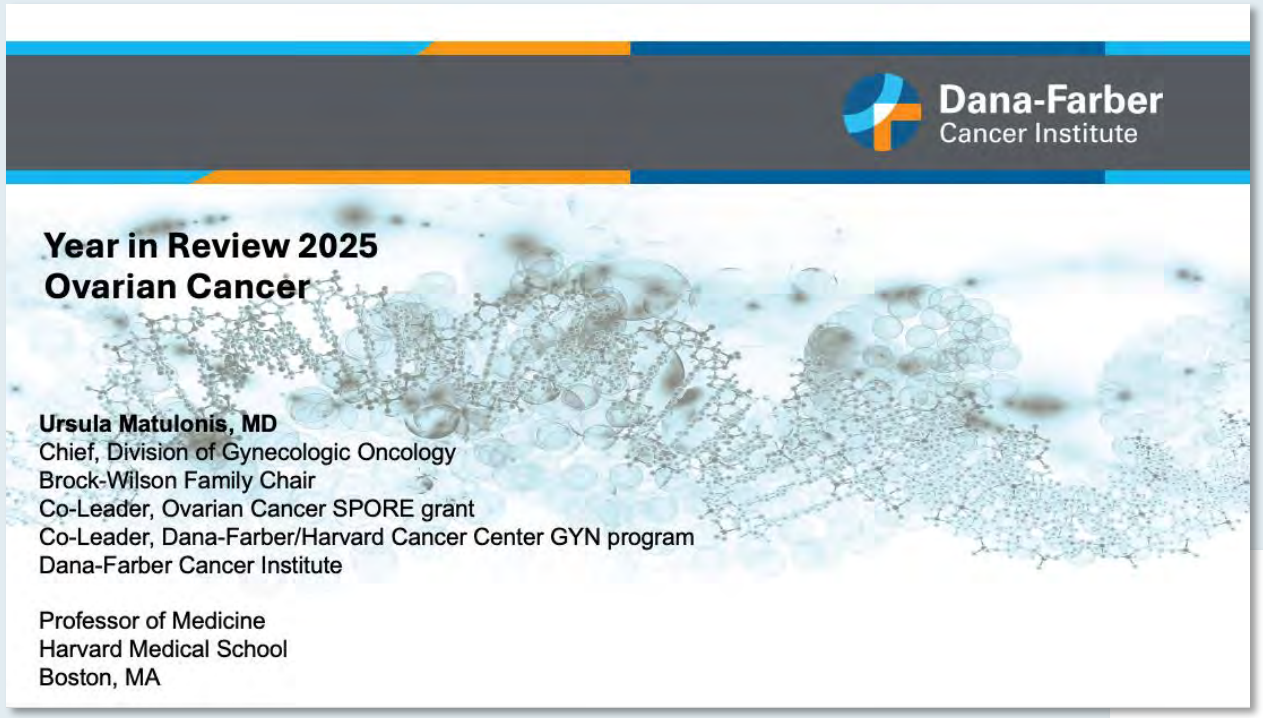

Endometrial and Cervical Cancer Year in Review 2025

Prof Susana Banerjee
The Royal Marsden NHS Foundation Trust
London, United Kingdom

RTP Year in Review 2025

Key Datasets

Ursula Matulonis, MD

- Lorusso D et al. Updated progression-free survival and final overall survival with **maintenance olaparib plus bevacizumab according to clinical risk** in patients with **newly diagnosed advanced ovarian cancer** in the phase III **PAOLA-1/ENGOT-ov25** trial. *Int J Gynecol Cancer* 2024;34(4):550-8.
- Monk BJ et al. **Niraparib first-line maintenance therapy** in patients with **newly diagnosed advanced ovarian cancer**: **Final overall survival results from the PRIMA/ENGOT-OV26/GOG-3012** trial. *Ann Oncol* 2024;35(11):981-92.
- Graybill WS et al. **Predictors of long-term progression-free survival** in patients with **ovarian cancer** treated with **niraparib** in the **PRIMA/ENGOT-OV26/GOG-3012 study**. *Int J Gynecol Cancer* 2024;34(7):1041-50.
- Trillsch F et al. **Durvalumab (D) + carboplatin/paclitaxel (CP) + bevacizumab (B) followed by D, B + olaparib (O) maintenance** (mtx) for **newly diagnosed advanced ovarian cancer (AOC) without a tumour BRCA1/BRCA2 mutation (non-tBRCAm)**: **Updated results from DUO-O**. ESMO Gynaecological Cancers Congress 2024;Abstract 43O.
- Vergote I et al. **Chemotherapy with or without pembrolizumab followed by maintenance with olaparib** or placebo for first-line treatment of advanced **BRCA non-mutated** epithelial ovarian cancer: Results from the randomized **phase 3 ENGOT-OV43/GOG-3036/KEYLYNK-001 study**. ESGO 2025;Abstract 128.
- Hardy-Bessard AC et al. **FIRST/ENGOT-OV44**: A phase 3 clinical trial of **dostarlimab (dost) and niraparib (nira)** in first-line (1L) **advanced ovarian cancer** (aOC). ASCO 2025;Abstract LBA5506.

Key Datasets

Ursula Matulonis, MD (continued)

- Van Gorp T et al**. Final overall survival analysis** among patients with **FRα-positive, platinum-resistant ovarian cancer** (PROC) treated with **mirvetuximab soravtansine** (MIRV) vs investigator's choice chemotherapy (ICC) in the **phase 3 MIRASOL (GOG 3045/ENGOT-ov55) study**. SGO 2025;Abstract 939696.
- Olawaiye AB et al. **Relacorilant and nab-paclitaxel** in patients with **platinum resistant ovarian cancer (ROSELLA)**: an open-label, randomised, controlled, phase 3 trial. *Lancet* 2025; June 2 [epub ahead of print].
- Phase 3 **KEYNOTE-B96** trial **met primary endpoint of progression-free survival** (PFS) in **patients with platinum-resistant recurrent ovarian cancer** whose tumors expressed PD-L1 and in all comers [press release]. May 15, 2025. https://www.merck.com/news/merck-announces-phase-3-keynote-b96-trial-met-primary-endpoint-of-progression-free-survival-pfs-in-patients-with-platinum-resistant-recurrent-ovarian-cancer-whose-tumors-expressed-pd-l1-and-in-all-c/.
- Moore KN et al. **Raludotatug deruxtecan** monotherapy among patients with **previously treated ovarian cancer:** Subgroup analysis of a **first-in-human phase I study**. *Gynecol Oncol* 2024;190(Suppl 1):6-7.
- Grisham R et al. **Avutometinib + defactinib** in **recurrent low-grade serous ovarian cancer** (ENGOT-ov60/GOG-3052/RAMP 201): Dose intensity and subgroup analysis. SGO 2025;Abstract 814605.

Key Datasets

Susana Banerjee, MBBS, MA, PhD

- Powell MA et al. **Overall survival** in patients with **endometrial cancer** treated with **dostarlimab plus carboplatin-paclitaxel** in the randomized **ENGOT-EN6/GOG-3031/RUBY** trial. *Ann Oncol* 2024;35(8):728-38.
- Eskander RN et al. **Pembrolizumab plus chemotherapy** in **advanced or recurrent endometrial cancer**: Overall survival and exploratory analyses of the **NRG GY018** phase 3 randomized trial. *Nat Med* 2025 May;31(5):1539-46.
- Westin et al. **Durvalumab plus carboplatin/paclitaxel followed by durvalumab with or without olaparib** as **first-line treatment** for **endometrial cancer**: longitudinal changes in circulating tumor DNA. ASCO 2025 Abstract 5512.
- Mirza MR et al. **Progression-free survival (PFS)** in **primary advanced or recurrent endometrial cancer** (pA/rEC) in the **overall and mismatch repair proficient (MMR/MSS) populations** and in histological and molecular subgroups: **Results from part 2 of the RUBY trial**. ESMO Gynaecological Cancers Congress 2024;Abstract 38MO.
- Makker V et al. **Long-term follow-up** of efficacy and safety of selinexor maintenance treatment in patients with **TP53wt advanced or recurrent endometrial cancer**: A subgroup analysis of the **ENGOT-EN5/GOG-3055/SIENDO** study. *Gynecol Oncol* 2024;185:202-11.

Key Datasets

Susana Banerjee, MBBS, MA, PhD (continued)

- Recio F et al. **Post-surgical ctDNA-based molecular residual disease** detection in patients with **stage I uterine malignancies**. *Gynecol Oncol* 2024;182:63-9.
- Duska LR et al. **Pembrolizumab with chemoradiotherapy** in patients with **high-risk locally advanced cervical cancer: Final analysis** results of the phase 3, randomized, double-blind **ENGOT-cx11/GOG-3047/KEYNOTE-A18 study**. ASCO 2025;Abstract LBA5504.
- Mayadev J et al. Ultrasensitive detection and tracking of **circulating tumor DNA (ctDNA) and association with relapse and survival** in **locally advanced cervical cancer** (LACC): **Phase 3 CALLA trial analyses**. ASCO 2025;Abstract 5502.
- Lorusso D et al. **Pembrolizumab plus chemotherapy** for **advanced and recurrent cervical cancer**: **Final analysis according to bevacizumab use** in the randomized **KEYNOTE-826** study. *Ann Oncol* 2025;36(1):65-75.
- Vergote I et al. **Tisotumab vedotin** as second- or third-line therapy for **recurrent cervical cancer**. *N Engl J Med* 2024;391(1):44-55.
- Oaknin A et al. Efficacy of **trastuzumab deruxtecan** in HER2-expressing solid tumors by enrollment HER2 IHC status: **Post hoc analysis of DESTINY-PanTumor02**. *Adv Ther* 2024;41(11):4125-39.

Year in Review:
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INTRODUCTION: Tale of Two Cities — ASCO 2025

MODULE 1: Ovarian Cancer

MODULE 2: HER2-Positive Gynecologic Cancers

MODULE 3: Endometrial Cancer

MODULE 4: Cervical Cancer

RTP Year in Review 2025

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RTP Year in Review 2025

Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Clinical Care of Patients with EGFR Mutation-Positive Non-Small Cell Lung Cancer

Friday, May 30, 2025
6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)

Faculty

Nicolas Girard, MD, PhD
Jonathan Goldman, MD
Pasi A Jänne, MD, PhD, FASCO
Suresh S Ramalingam, MD
Joshua K Sabari, MD

Moderator

Helena Yu, MD

RTP RESEARCH TO PRACTICE

Faculty

Nicolas Girard, MD, PhD
Head of Medical Oncology, Institut Curie
Full Professor
UVSQ, Paris-Saclay University
Paris, France

Jonathan Goldman, MD
Professor of Medicine
UCLA Hematology and Oncology
Director of Clinical Trials in Thoracic Oncology
Associate Director of Drug Development
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Santa Monica, California

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Lowe Center for Thoracic Oncology
Professor of Medicine
Harvard Medical School
David M Livingston, MD, Chair
Director, Robert and Renée Belfer Center for Applied Cancer Science
Director, Chen-Huang Center for EGFR-Mutant Lung Cancers
Dana-Farber Cancer Institute
Boston, Massachusetts

Suresh S Ramalingam, MD
Executive Director, Winship Cancer Institute
Roberto C Goizueta Chair for Cancer Research
Emory University School of Medicine
Atlanta, Georgia

Joshua K Sabari, MD
Attending Physician
Thoracic Medical Oncology
Assistant Professor of Medicine
NYU Langone Health
Perlmutter Cancer Center
New York, New York

Moderator
Helena Yu, MD
Medical Oncologist
Associate Attending
Memorial Sloan Kettering Cancer Center
New York, New York

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RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Colorectal Cancer

Friday, May 30, 2025
6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)

Faculty

Andrea Cercek, MD
Arvind Dasari, MD, MS
Pashtoon Kasi, MD, MS
Eric Van Cutsem, MD, PhD

Moderator

J Randolph Hecht, MD

RTP
RESEARCH TO PRACTICE

Faculty

Andrea Cercek, MD
Section Head, Colorectal Cancer
Co-Director, Center for Young Onset Colorectal and Gastrointestinal Cancers
Attending, Gastrointestinal Oncology Service
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Arvind Dasari, MD, MS
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The University of Texas
MD Anderson Cancer Center
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Pashtoon Kasi, MD, MS
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Endowed Rad Family Chair in Gastrointestinal Oncology
Associate Professor
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Eric Van Cutsem, MD, PhD
Professor of Medicine
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University Hospitals Leuven
Leuven, Belgium

Moderator
J Randolph Hecht, MD
Professor of Clinical Medicine
Director, UCLA GI Oncology Program
Carol and Saul Rosenzweig Chair in Cancer Therapies Development
UCLA David Geffen School of Medicine
Santa Monica, California

RTP
RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Ovarian and Endometrial Cancer

Sunday, June 1, 2025

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Joyce F Liu, MD, MPH

David M O'Malley, MD

Ritu Salani, MD, MBA

Alessandro D Santin, MD

Moderator

Shannon N Westin, MD, MPH, FASCO, FACOG

RTP RESEARCH TO PRACTICE

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Joyce F Liu, MD, MPH
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Director and Professor
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John G Boutselis Chair in Gynecologic Oncology
The Ohio State University and The James Comprehensive Cancer Center
Columbus, Ohio

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

Alessandro D Santin, MD
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Co-Chief, Gynecologic Oncology
Yale University School of Medicine
New Haven, Connecticut

Moderator
Shannon N Westin, MD, MPH, FASCO, FACOG
Professor
Medical Director, Gynecologic Oncology Center
Director, Early Drug Development
Department of Gynecologic Oncology and Reproductive Medicine
The University of Texas
MD Anderson Cancer Center
Houston, Texas

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RESEARCH TO PRACTICE

Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Deficient DNA Mismatch Repair (dMMR) Colon Cancer (Alliance A021502; ATOMIC)

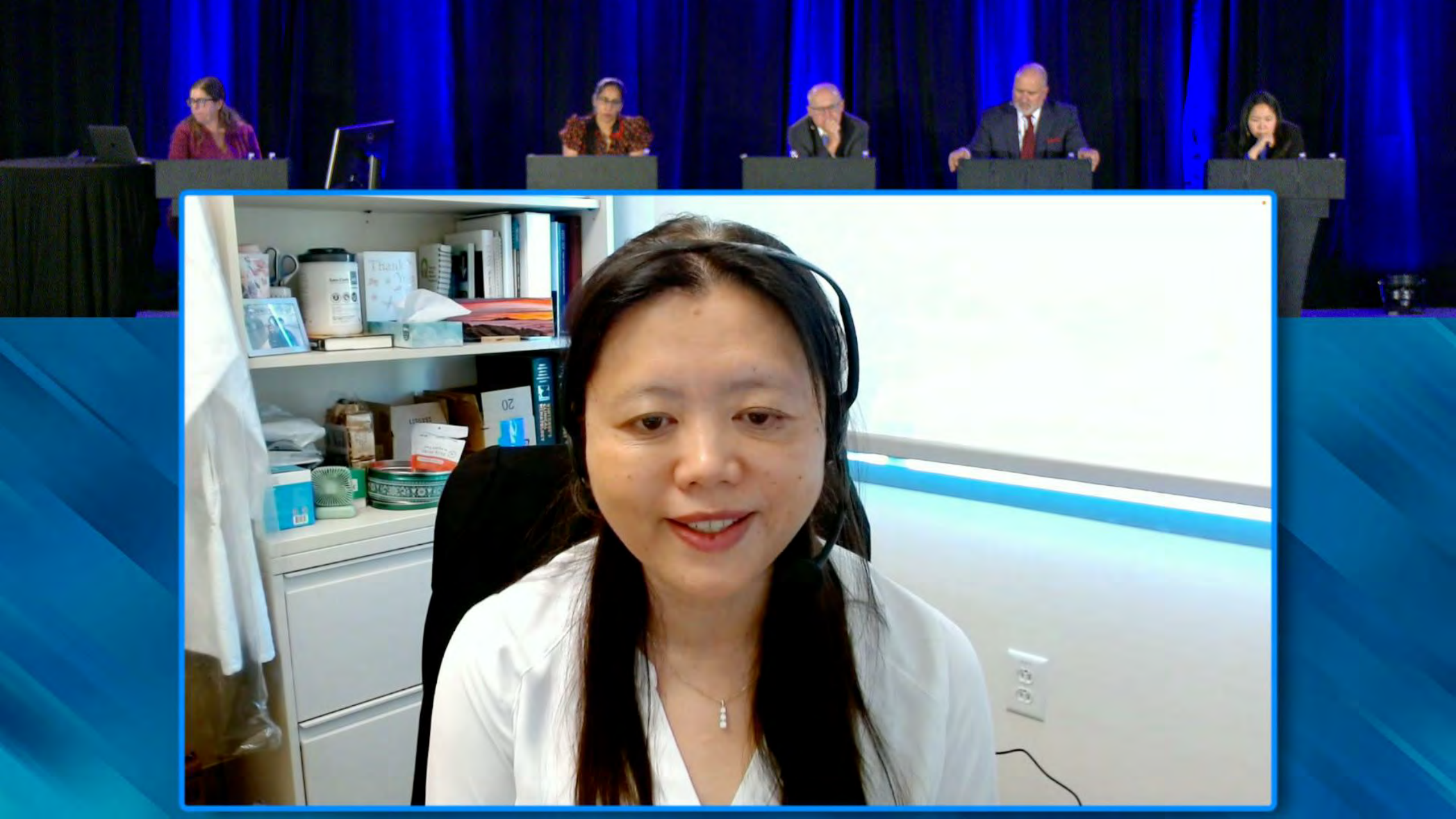
Sinicrope F et al.
ASCO 2025;Abstract LBA1.

Three-year disease-free survival:
Atezolizumab/mFOLFOX6 (n = 355), 86.4%
mFOLFOX6 (n = 357), 76.6%
(HR, 0.50; 95% CI, 0.35-0.72)

Case Presentation: 61-year-old woman with Stage IIIC dMMR endometrial cancer and Lynch syndrome undergoes debulking surgery and receives carboplatin/docetaxel/pembrolizumab followed by pembrolizumab maintenance

Dr Gigi Chen (Walnut Creek, California)

RTP RESEARCH TO PRACTICE



Clinical Trial Updates

Pembrolizumab or Placebo Plus Adjuvant Chemotherapy With or Without Radiotherapy for Newly Diagnosed, High-Risk Endometrial Cancer: Results in Mismatch Repair-Deficient Tumors

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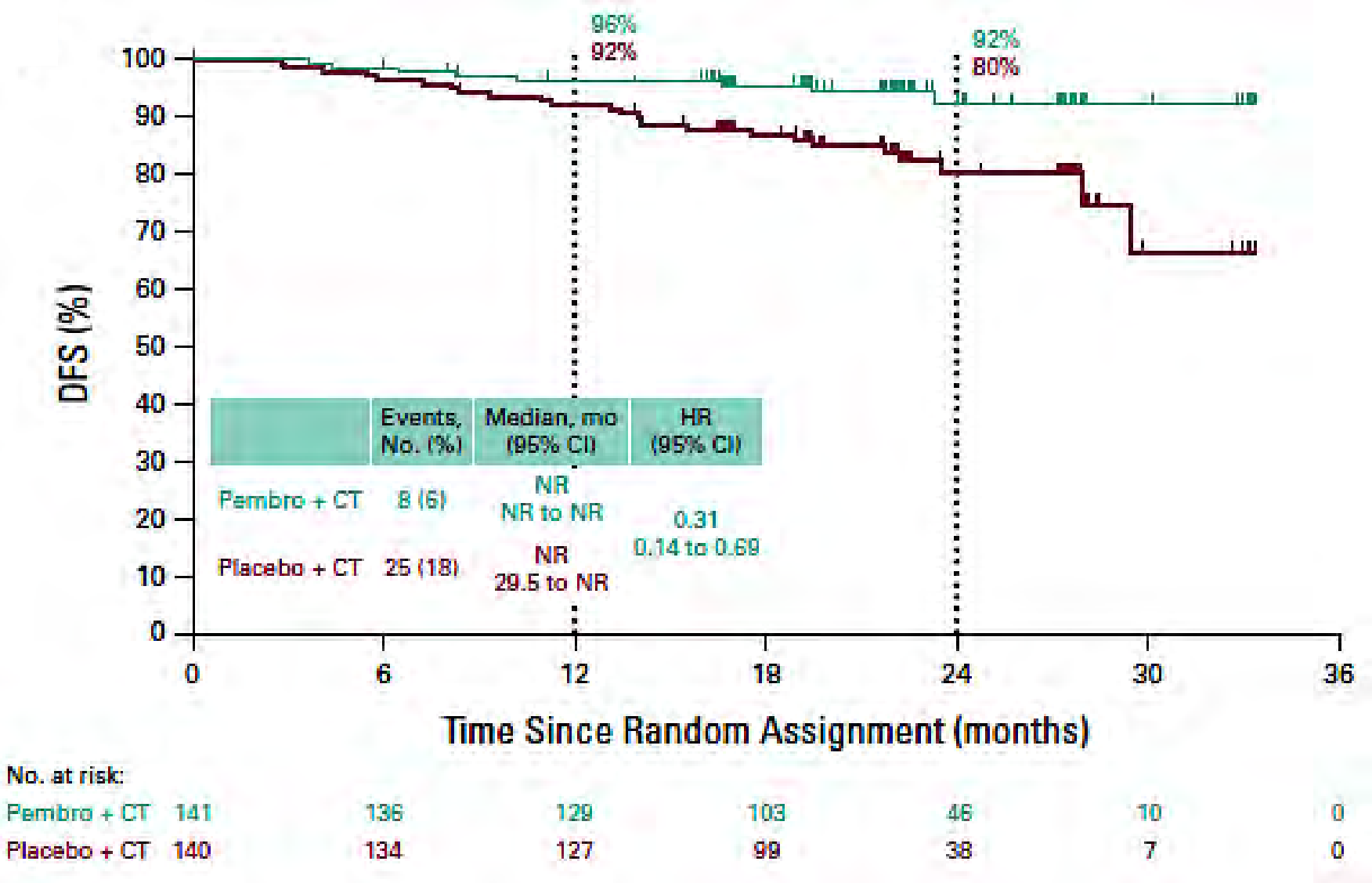
J Clin Oncol 2024;43(3):251-9.

KEYNOTE-B21: Disease-Free Survival with Pembrolizumab and Adjuvant Chemotherapy in Patients with High-Risk Endometrial Cancer and dMMR Tumors

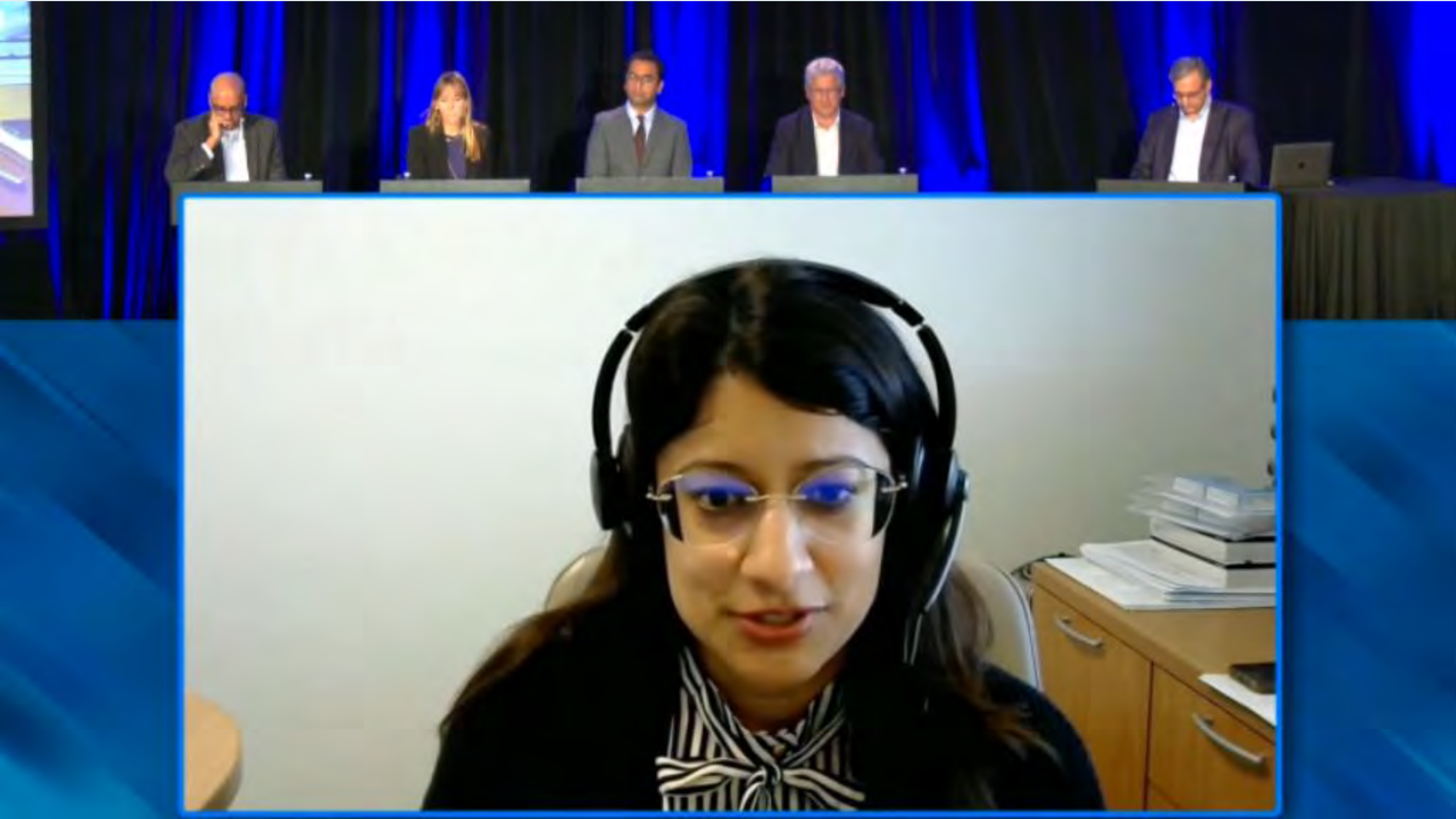


Slomovitz BM et al. *J Clin Oncol* 2024;43(3):251-9.

Case Presentation: 68-year-old man with T3N1 MSI-H rectal cancer receives neoadjuvant dostarlimab

Dr Henna Malik (Houston, Texas)

RTP
RESEARCH
TO PRACTICE



ASCO 2025: Select Abstracts

- Montagut C et al. A precision medicine trial leveraging tissue and blood-based tumor genomics to optimize treatment in resected stage III and high-risk stage II colon cancer (CC) patients (pts): The SAGITTARIUS Trial. ASCO 2025;Abstract TPS3647.
- Shen JPY et al. Development of a methylation-based, tissue-free test for the detection of molecular residual disease by circulating tumor DNA. ASCO 2025;Abstract 3048.
- Oki E et al. Impact of perioperative complications on ctDNA-based MRD detection and prognosis: Insights from the GALAXY study. ASCO 2025;Abstract 3600.*
- Osterlund E et al. Biologic correlates of circulating tumor DNA (ctDNA) shedding in the INTERCEPT colorectal cancer (CRC) study. ASCO 2025;Abstract 3591.*
- Malla M et al. ctDNA dynamics and targeted therapies associated with genetic mutations in patients with colorectal cancer. ASCO 2025;Abstract 3597.*
- Adnan N et al. Signatera ctDNA in stage II CRC: A retrospective comparison with traditional risk factors for survival and prognostic stratification. ASCO 2025;Abstract e15641.

* Includes Stage IV

Post-surgical ctDNA detection rates in patients with stage I endometrial malignancies

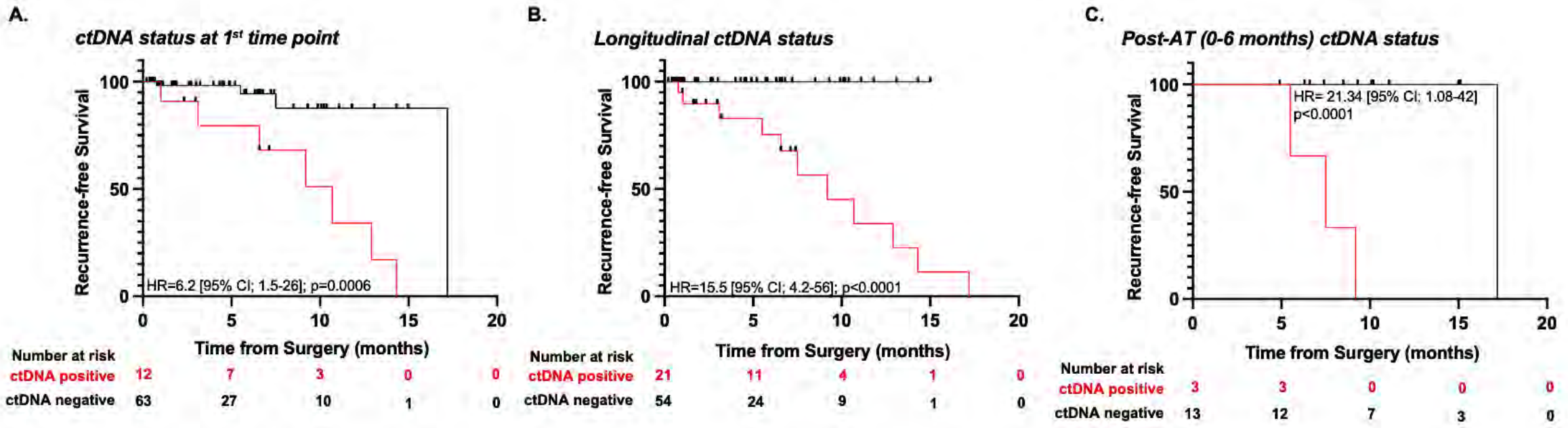


Fig. 1. Kaplan-Meier estimates represent the association of ctDNA status with RFS; A) at the first time point after surgery, B) longitudinally, and C) post-AT (The median time to relapse was 7.5 months for the ctDNA-positive patients and 10.2 months for the one ctDNA-negative patient who recurred). Abbreviations: AT, Adjuvant therapy; ctDNA, circulating tumor DNA, CI, Confidence interval; HR, Hazard ratio.

Recio F et al. *Gynecol Oncol* 2024:182:63-9.

Courtesy of Susana Banerjee, MBBS, MA, PhD

Post-surgical ctDNA detection rates in patients with stage I endometrial malignancies

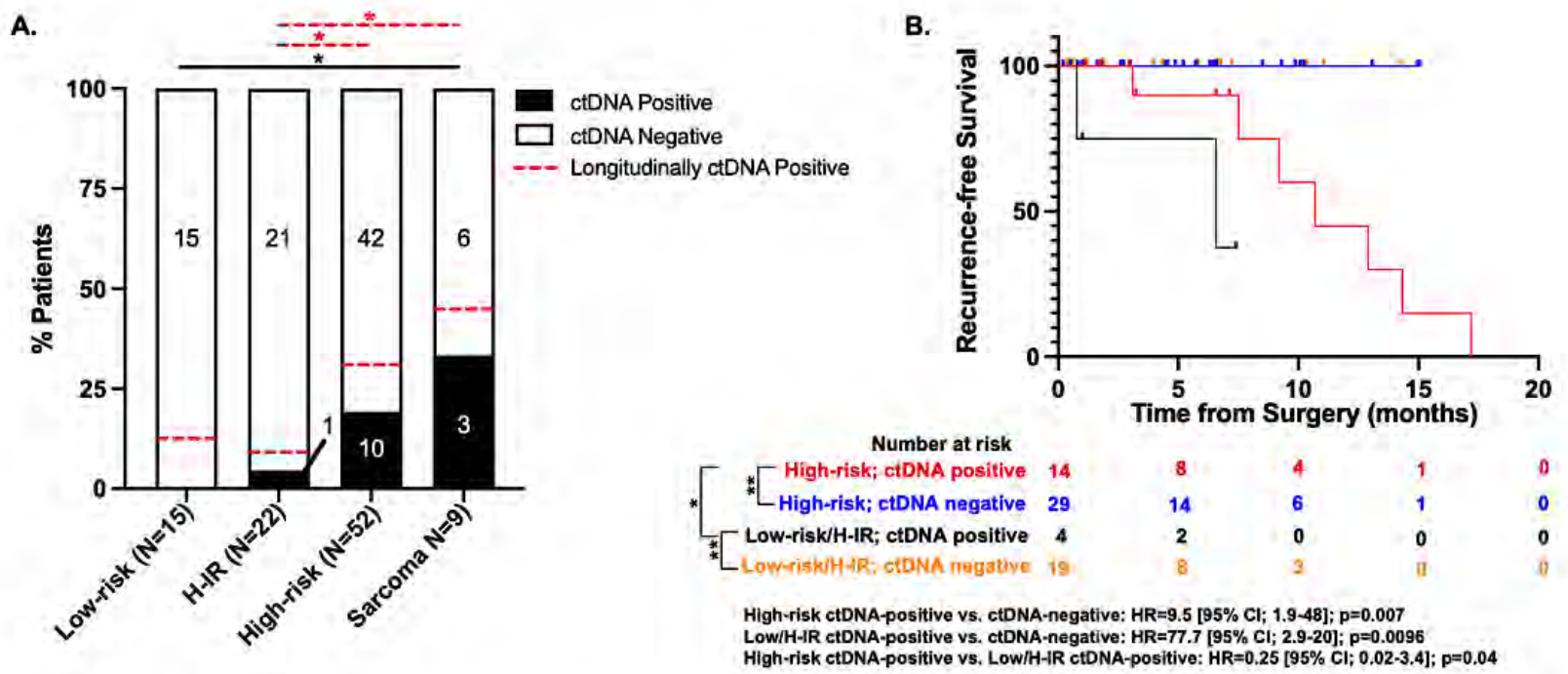


Fig. 3. A. Percentage of patients with ctDNA detection at the first post-surgical time point (black bars) and longitudinally (dotted red line). B. Kaplan-Meier estimates representing the association of ctDNA and risk groups with RFS. Abbreviations: ctDNA, circulating tumor DNA; CI, Confidence interval; HR, Hazard ratio; H-IR, High-intermediate risk.

Results suggest:

- patients who were ctDNA-positive at the first time point or at any time point post-surgery had significantly worse RFS ($p = 0.0006$; $p < 0.0001$) compared to patients who were either ctDNA-negative at the first time point or remained serially negative.

- Increase in ctDNA levels pre- and post-adjuvant therapy identified patients experiencing disease recurrence, while all patients with serially negative ctDNA status remained clinically NED.

Recio F et al. *Gynecol Oncol* 2024:182:63-9.

Courtesy of Susana Banerjee, MBBS, MA, PhD

Post-surgical ctDNA detection rates in patients with stage I endometrial malignancies

- Limitations- retrospective, real world, short follow up
- Prospective trials required for incorporation of post-surgical ctDNA status, together with longitudinal ctDNA to direct adjuvant therapy, escalation/ de-escalation, and maintenance therapy in patients with or without detectable ctDNA

Courtesy of Susana Banerjee, MBBS, MA, PhD

Year in Review:
Management of Gynecologic Cancers

INTRODUCTION: Tale of Two Cities — ASCO 2025

MODULE 1: Ovarian Cancer

MODULE 2: HER2-Positive Gynecologic Cancers

MODULE 3: Endometrial Cancer

MODULE 4: Cervical Cancer

RTP Year in Review 2025

Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

A Meet The Professor Series

August 20, 2020

Don S Dizon, MD
Professor of Medicine, Brown University
Director, Women's Cancers and Hematology-Oncology Outpatient Clinics
Lifespan Cancer Institute
Director, Medical Oncology and the Oncology Sexual Health Program
Rhode Island Hospital
Providence, Rhode Island

Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

A Meet The Professor Series

August 21, 2020

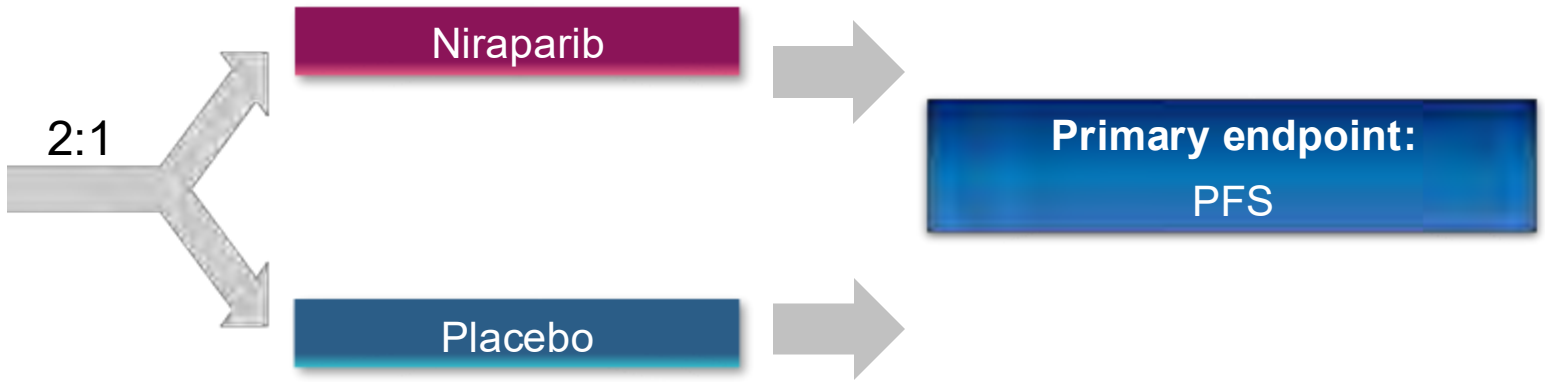
Brad S Kahl, MD
Professor of Medicine
Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
St Louis, Missouri

RTP
RESEARCH TO PRACTICE

PRIMA: Niraparib as upfront maintenance for advanced high grade ovarian cancer

Patients

- Newly diagnosed, stage III or IV
- CR or PR to most recent platinum therapy
- High grade ovarian cancer



After response to first-line chemotherapy, patients were randomized 2:1 to receive oral niraparib or placebo
733 pts enrolled

Subsequent PARPi therapy was received by:
Niraparib treated group:
11.7% overall population
15.8% of HRD pts

Placebo treated group:
37.8% in the overall population
48.4% of the HRD pts (in BRCAm group: 57% received a subsequent PARPi)

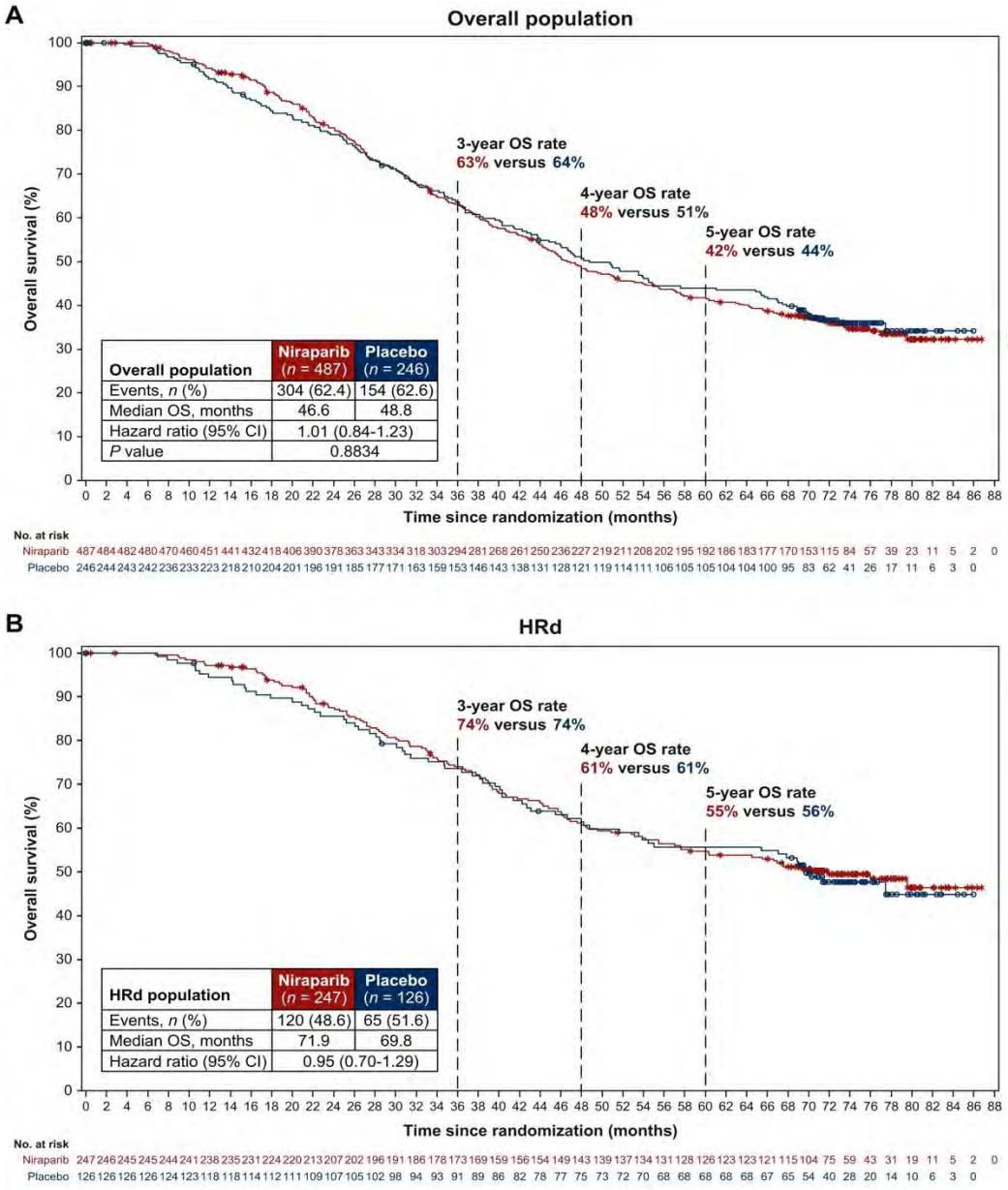
ESMO 2024, Monk et al, Annals of Oncology 2024
Graybill WS, et al. Int J Gynecol Cancer2024;34:1041–1050

Courtesy of Ursula Matulonis, MD

PRIMA OS results

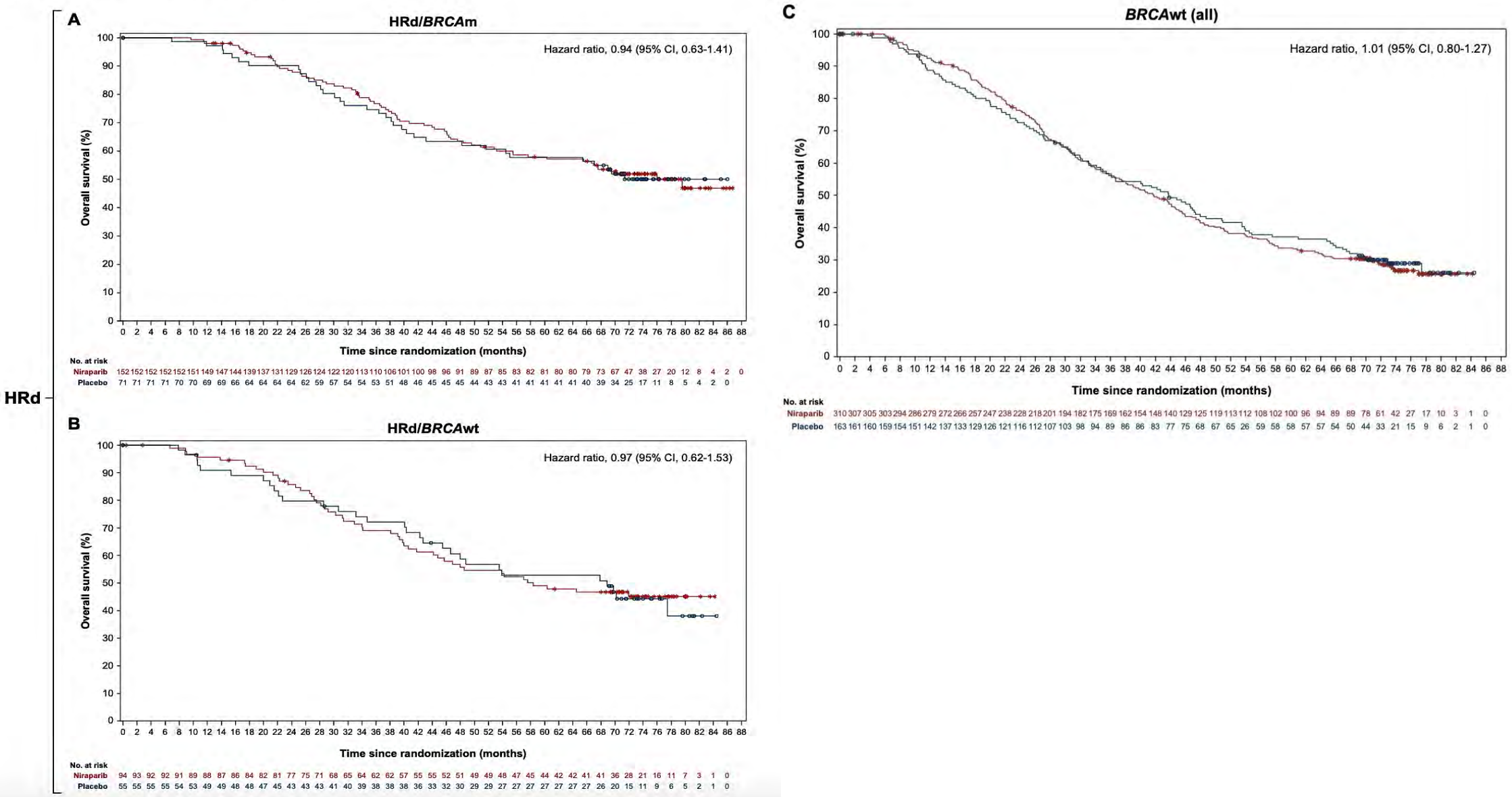
OS tested in the overall population: NS

So formal OS analysis of HRD population did not occur



PRIMA OS results

Figure S2. Overall survival by HRD/*BRCA* status.



SOLO-1 and PRIMA Trials: Progression-Free and Overall Survival

SOLO-1	Olaparib (n = 260)	Placebo (n = 131)
Median PFS	56 mo	13.8 mo
PFS HR (*p*-value)	0.33 (not reported)	
Median OS	Not reached	75.2 mo
OS HR (*p*-value)	0.55 (0.0004)	

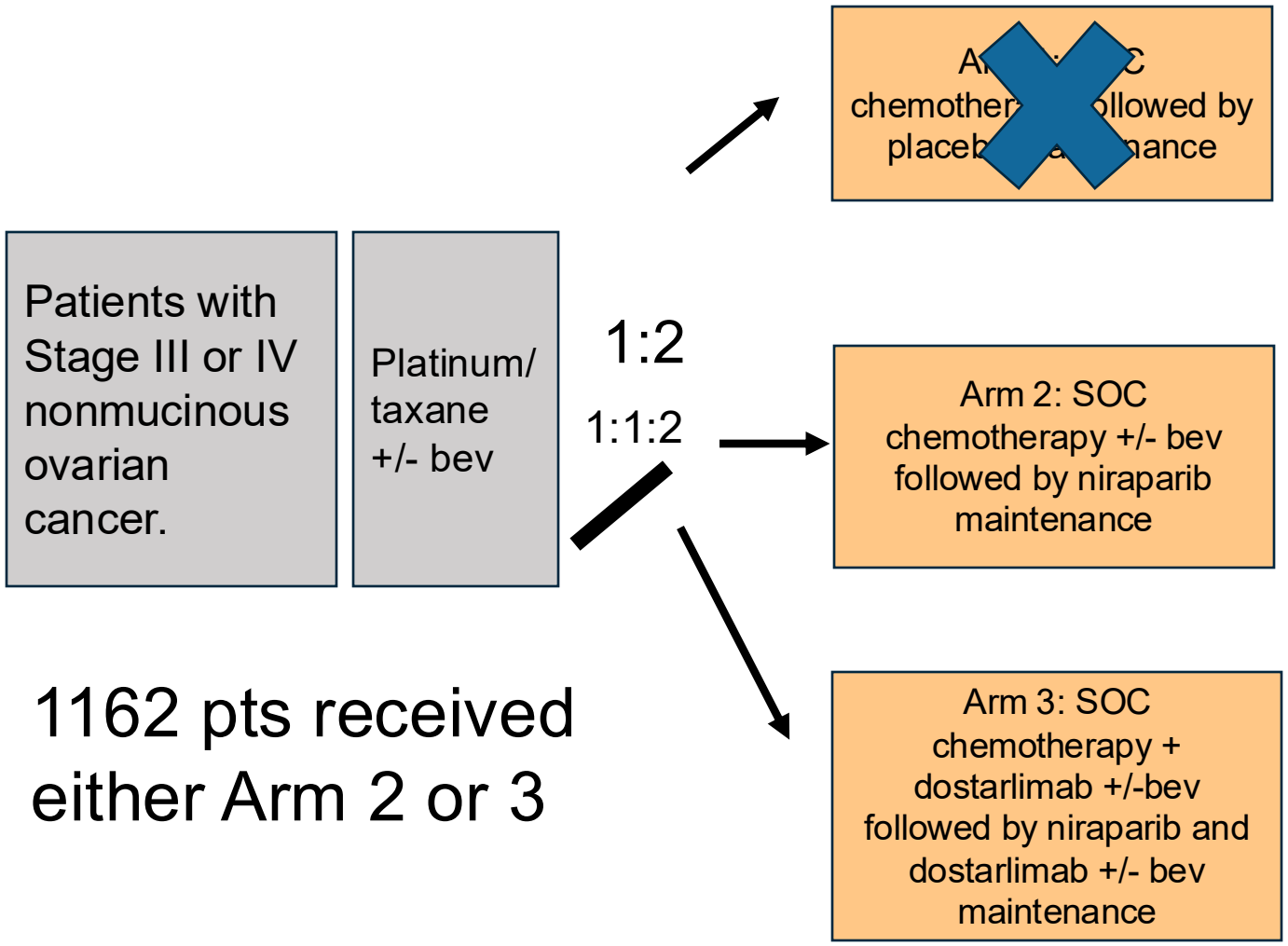
PFS = progression-free survival; OS = overall survival; HR = hazard ratio; HRd = homologous recombination deficient; BRCAm = BRCA mutated

PRIMA	Niraparib	Placebo	HR (*p*-value)
Median PFS – Overall* (n = 487, 246)	13.8 mo	8.2 mo	0.66 (NR)
Median PFS – HRd* (n = 247, 146)	24.5 mo	11.2 mo	0.51 (NR)
Median PFS – HRd/BRCAm* (n = 152, 71)	30.1 mo	11.5 mo	0.43 (NR)
Median OS – Overall (n = 487, 246)	46.6 mo	48.8 mo	1.01 (0.8834)

* Investigator assessed; NR = not reported

DiSilvestro P et al. ESMO 2022;Abstract 5170; *J Clin Oncol* 2023;41(3):609-17; Monk BJ et al. *Ann Oncol* 2024;35(11):981-92; González-Martín A et al ESMO 2024;Abstract LBA29 .

FIRST study



1162 pts received either Arm 2 or 3

Due to the approvals of PARP inhibitors in the first-line setting, Arm 1 (n=193) was closed and participants were subsequently randomized 1:2 to Arms 2 (n= 385) and 3 (n= 753) only.

Primary endpoint: investigator-assessed PFS in Arms 2 and 3. If PFS results were significant, then OS testing would continue

Secondary endpoints: OS, PFS2, time to first and second subsequent therapy.

Pts with PD-L1+ or HRD+ and those with concurrent bevacizumab were identified a priori as clinically "plausible" groups to have differentiated results

FIRST take away points

Essentially the same PFS benefit of adding dostarlimab:
1.4 months difference in median PFS

No overall survival benefit of adding dostarlimab to niraparib maintenance

PD-L1 biomarker did not predict impact of dostarlimab

~50% of patients received bevacizumab; how does receipt of bevacizumab influence therapy outcomes?

Courtesy of Ursula Matulonis, MD

ENGOT 0V43/GOG3036/KEYLYNK-001

ESGO 2025, SGO 2025
Patient population: Advanced non-BRCA mutated newly diagnosed ovarian cancer

Treatment arms:

I) Carboplatin/Paclitaxel

II) Carboplatin/Paclitaxel/Pembrolizumab, followed by Pembrolizumab maintenance

III) Carboplatin/Paclitaxel/Pembrolizumab followed by Pembrolizumab/Olaparib

All arms with or without bevacizumab; no PARPi maintenance alone arm

ENGOT 0V43/GOG3036/KEYLYNK-001: findings

PFS benefit for pembrolizumab/olaparib arm compared to chemotherapy alone

No OS benefit

Significance threshold of pembrolizumab versus control in the CPS10 population was not met: thus, formal testing of PFS in the overall population and OS was not performed

Table. Summary of PFS in ENGOT-OV43/GOG-3036/KEYLYNK-001

Population	Interim Analysis 1		Final Analysis	
	Median PFS, months	HR (95% CI)	Median PFS, months	HR (95% CI)
Pembrolizumab–olaparib vs Control				
CPS ≥10	23.7 vs 15.2	0.63 (0.49-0.80); *P* <0.0001[a]	23.9 vs 15.2	0.66 (0.53-0.83)
Overall	22.1 vs 14.6	0.68 (0.58-0.81); *P* <0.0001[a]	22.2 vs 14.6	0.71 (0.61-0.84)
Pembrolizumab vs Control				
CPS ≥10	17.1 vs 15.2	0.93 (0.74-1.18)	17.3 vs 15.2	0.95 (0.77-1.19); *P* = 0.3339[b]

[a]Statistical significance demonstrated. [b]Statistical significance not demonstrated.

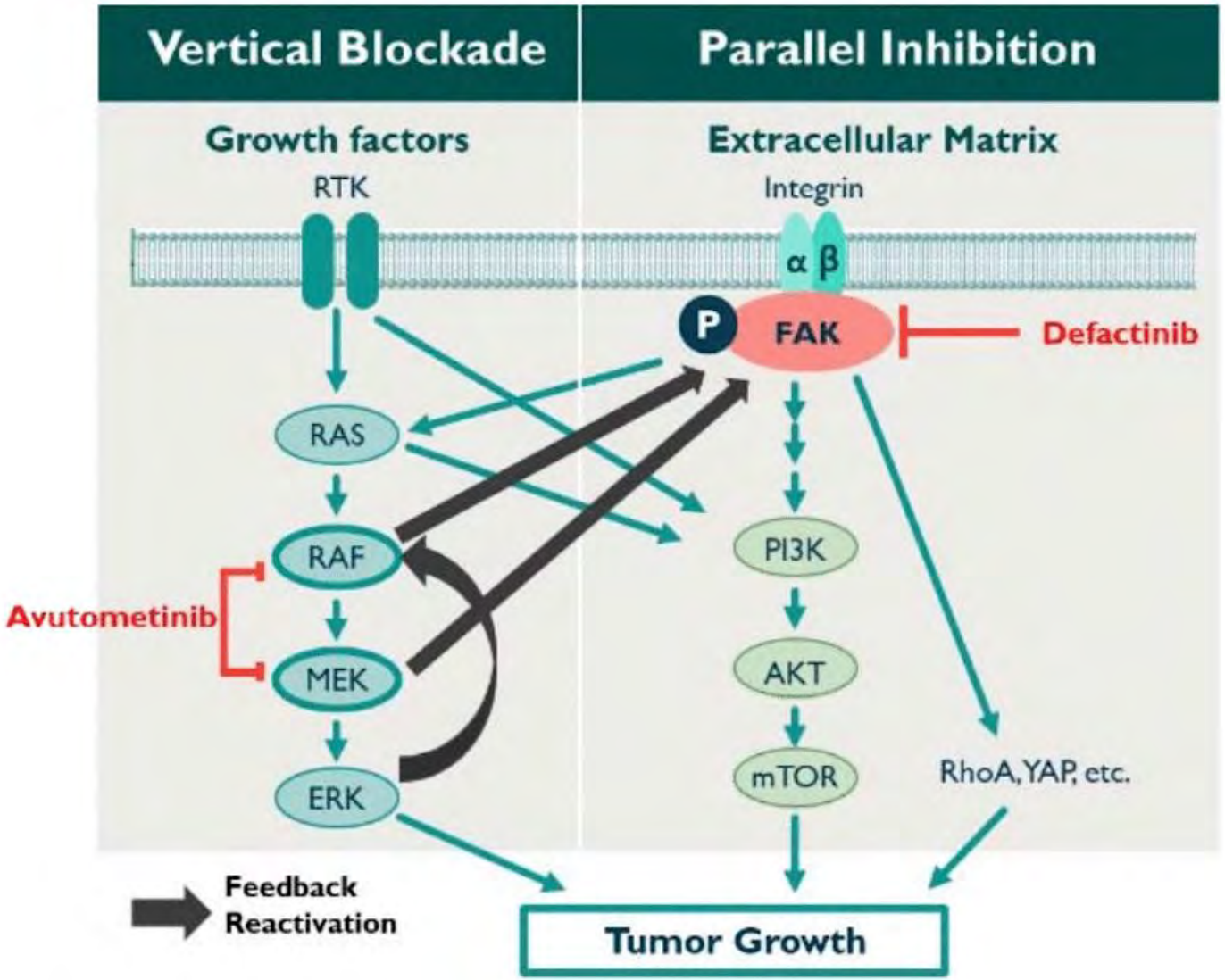
DUO-O and KEYLYNK studies

Both trials have no PARPi (+/- bev) arms as maintenance and cannot compare the experimental PARP/IO (+/-bev) to SOC PARPi maintenance

Based on these 3 studies – FIRST, DUO-O and KEYLYNK – data does not support adding an IO agent to a PARPi as maintenance nor justification for using an IO in the upfront setting

Courtesy of Ursula Matulonis, MD

Avutometinib and defactinib for recurrent low grade serous cancer

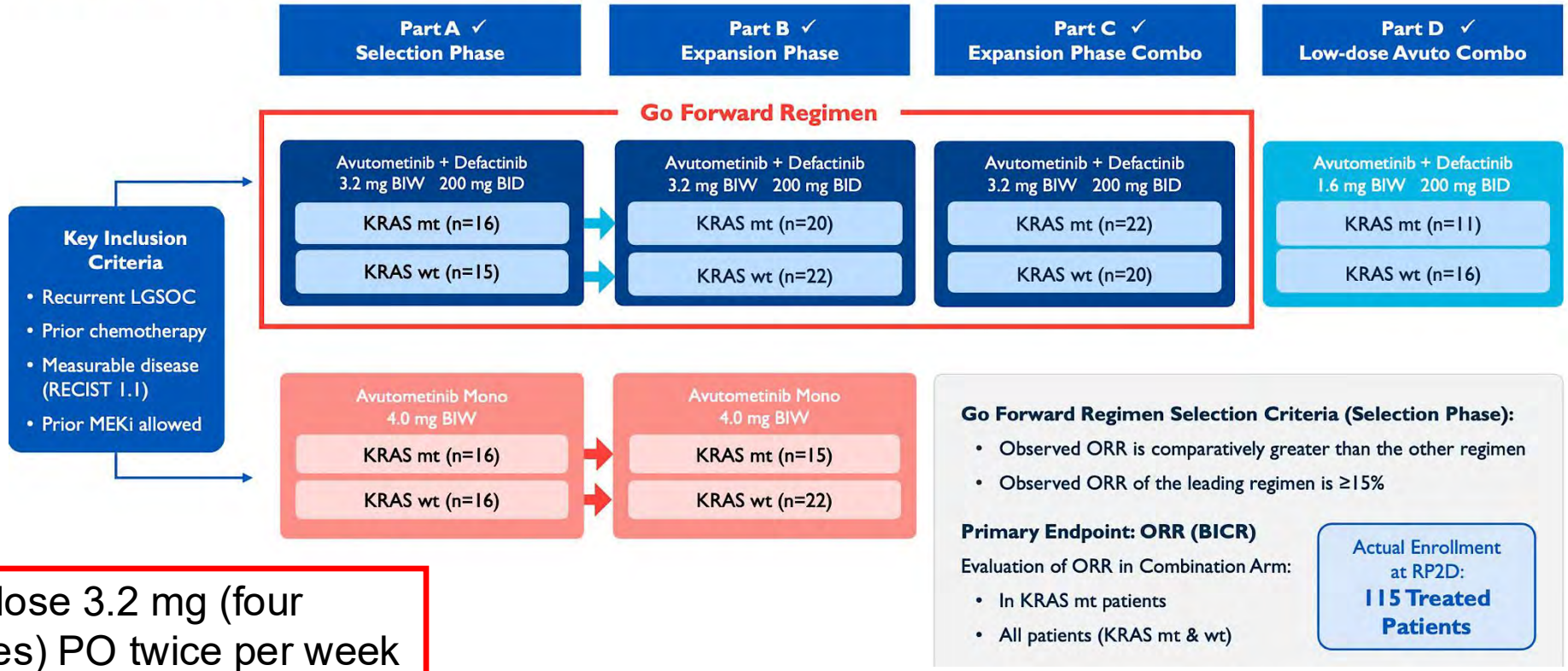


Combination was granted FDA accelerated approval on May 7, 2025 for recurrent KRAS mutated LGSC based on RAMP201

Courtesy of Ursula Matulonis, MD

RAMP 201: Registration-Directed Phase 2 Trial of Avutometinib ± Defactinib in Patients with Recurrent LGSOC

RAMP 201 (ENGOT-ov60/GOG-3052)



Avutometinib dose 3.2 mg (four 0.8 mg capsules) PO twice per week (d 1,4). for the first 3 weeks of each 4 week cycle

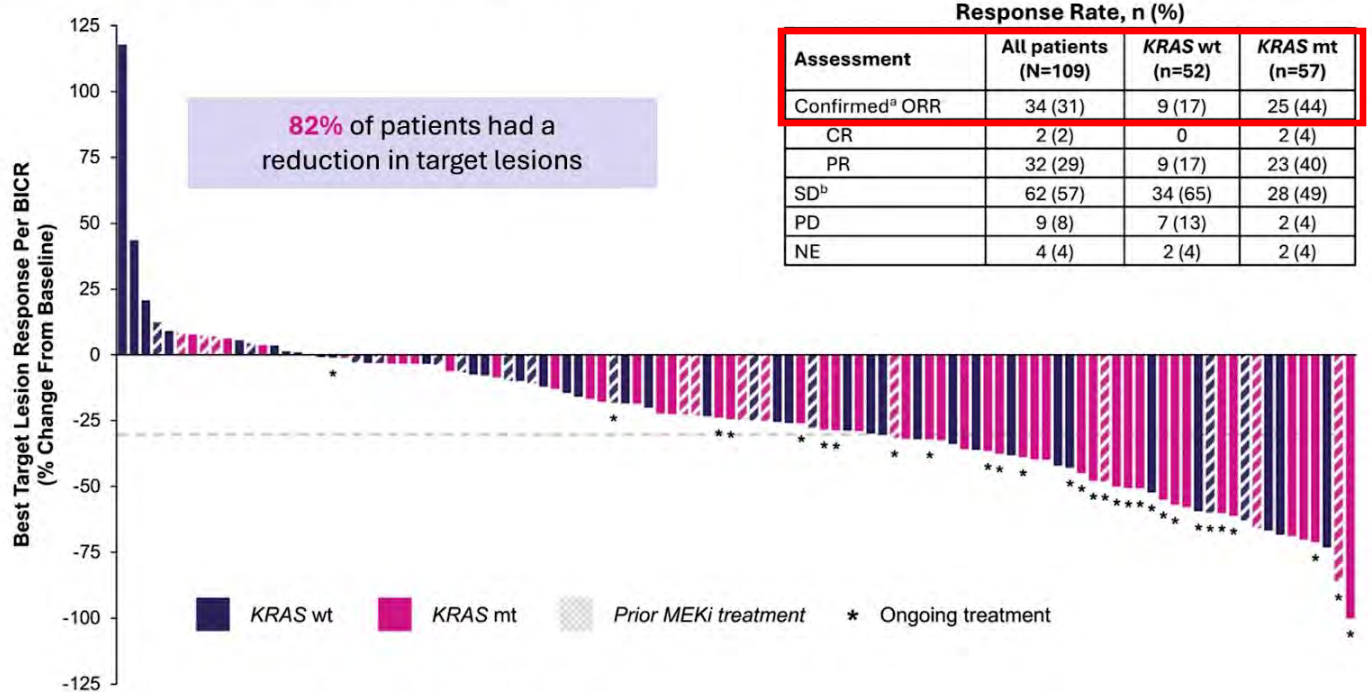
Defactinib 200 BID PO for 3 weeks out of 4 weeks

Phase 3 RAMP 301 trial is ongoing (NCT06072781) which is evaluating avutometinib plus defactinib vs investigator's choice of treatment in patients with recurrent low-grade serous ovarian cancer

RAMP 201

Best Percentage Change From Baseline in Target Lesions

Avutometinib 3.2 mg BIW and Defactinib 200 mg BID



Response Rate, n (%)

Assessment	All patients (N=109)	*KRAS* wt (n=52)	*KRAS* mt (n=57)
Confirmed[a] ORR	34 (31)	9 (17)	25 (44)
CR	2 (2)	0	2 (4)
PR	32 (29)	9 (17)	23 (40)
SD[b]	62 (57)	34 (65)	28 (49)
PD	9 (8)	7 (13)	2 (4)
NE	4 (4)	2 (4)	2 (4)

DOR, median (95% CI)

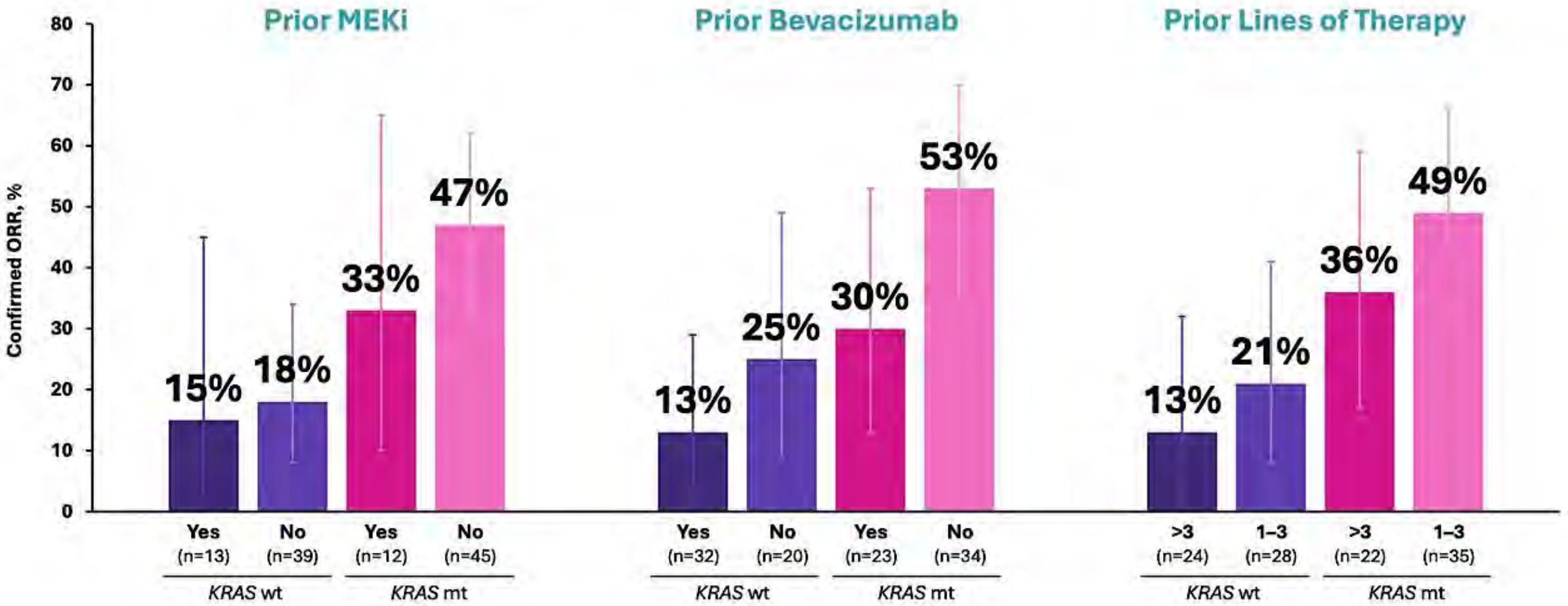
All patients (N=109)	*KRAS* wt (n=52)	*KRAS* mt (n=57)
31.1 mo (14.8, 31.1)	9.2 mo (5.5, NE)	31.1 mo (14.8, 31.1)

PFS, median (95% CI)

All patients (N=109)	*KRAS* wt (n=52)	*KRAS* mt (n=57)
12.9 mo (10.9, 20.2)	12.8 mo (7.4, 18.4)	22.0 mo (11.1, 36.6)

Confirmed ORR in Subgroups by Prior Therapies and *KRAS* Status

Avutometinib 3.2 mg BIW and Defactinib 200 mg BID



Grisham et al, SGO 2025

Courtesy of Ursula Matulonis, MD

Toxicities

80% of pts had AE's that led to dose interruption

37% of pts had AE's that led to dose reduction

10% of pts discontinued treatment because of AE's
--most common reason was for elevated CPK

Grisham et al, SGO 2025

Courtesy of Ursula Matulonis, MD

ROSELLA study (ASCO 2025, Lancet 2025)

The glucocorticoid receptor (GR) is a nuclear hormone receptor and transcription factor activated by cortisol and glucocorticoid treatment.

Increased glucocorticoid receptor (GR) expression is associated with decreased overall survival in ovarian cancer patients (Veneris et al, 2017, 2019)

In vitro, GR activation inhibits chemotherapy-induced ovarian cancer cell killing in association – thought to occur because of transcriptional upregulation of anti-apoptotic genes.

Hypothesis: modulating/inhibiting GR activity in combination with chemotherapy may improve pt outcomes.

Relacorilant: selective GR modulator

RP2 study (JCO 2023):
Patients were randomly assigned 1:1:1 to:

(1) nab-paclitaxel (80 mg/m^2) + intermittent relacorilant (150 mg the day before, of, and after nab-paclitaxel)
(2) nab-paclitaxel (80 mg/m^2) + continuous relacorilant (100 mg once daily)
(3) nab-paclitaxel monotherapy (100 mg/m^2)

Courtesy of Ursula Matulonis, MD

ROSELLA: PFS

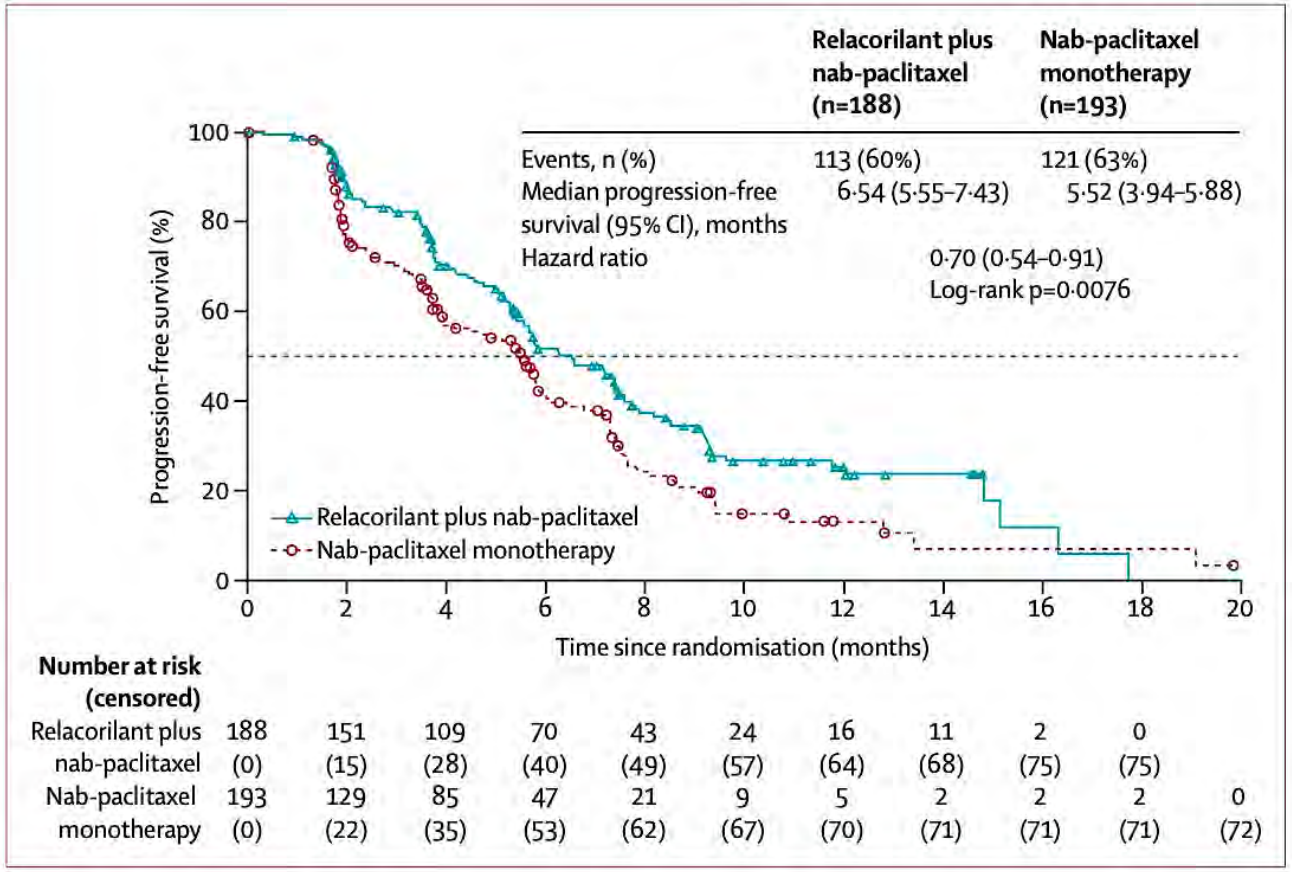


***Figure 2*: Efficacy findings comparing relacorilant plus nab-paclitaxel with nab-paclitaxel monotherapy for progression-free survival**

Kaplan–Meier estimates of the dual primary endpoint progression-free survival assessed by blinded independent central review in the relacorilant plus nab-paclitaxel group and the nab-paclitaxel monotherapy group are shown. Analyses were performed in the intent-to-treat population.

ROSELLA: OS

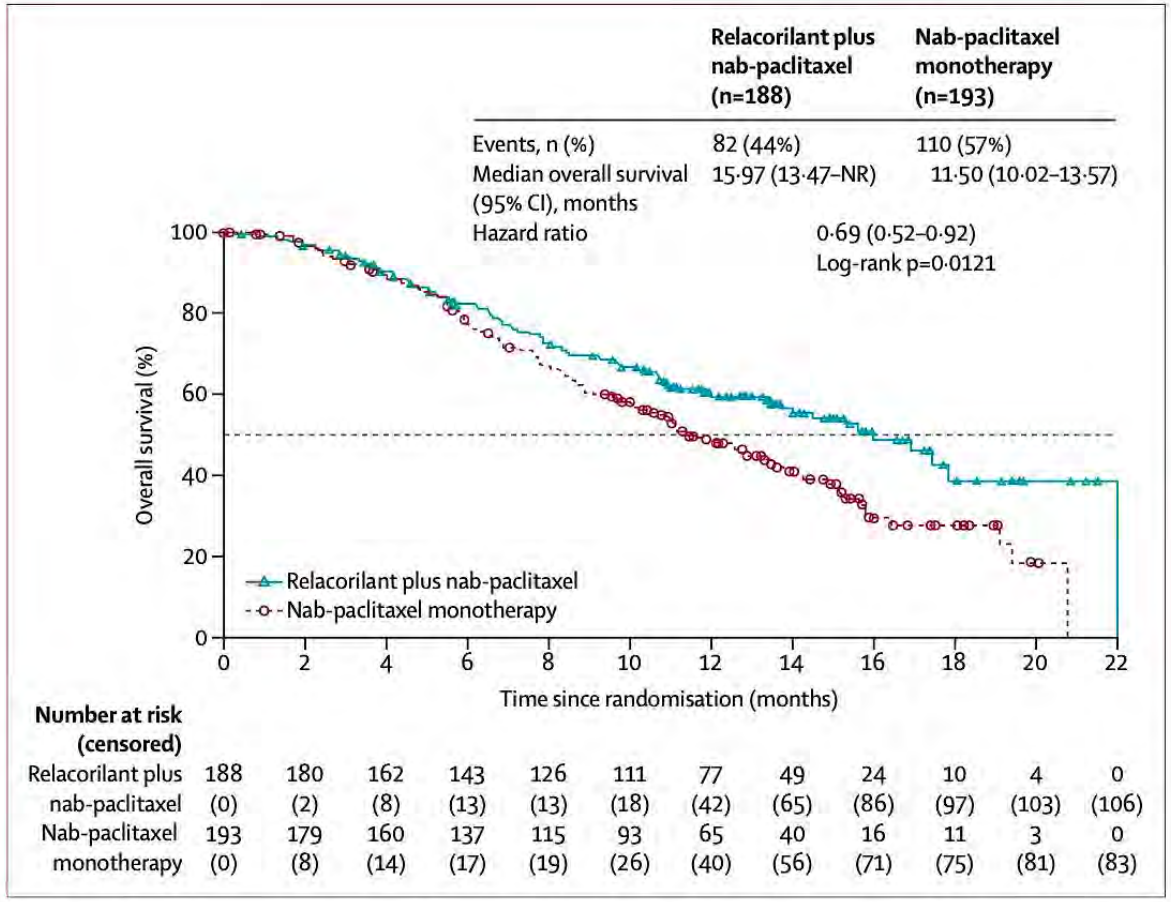


***Figure 3*: Efficacy findings comparing relacorilant plus nab-paclitaxel with nab-paclitaxel monotherapy for the interim overall survival analysis**

ROSELLA: Toxicities

	Relacorilant plus nab-paclitaxel (n=188)		Nab-paclitaxel monotherapy (n=190)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse events	188 (100%)	140 (74%)	189 (99%)	113 (59%)
Treatment-related adverse events*				
Related to relacorilant	146 (78%)	74 (39%)	..	..
Related to nab-paclitaxel	177 (94%)	113 (60%)	172 (91%)	78 (41%)
Related to both relacorilant and nab-paclitaxel	138 (73%)	69 (37%)	..	..
Serious adverse events	66 (35%)	60 (32%)	45 (24%)	39 (21%)
Treatment interruptions due to adverse events				
Nab-paclitaxel (plus relacorilant)†	137 (73%)	..	104 (55%)	..
Dose reductions due to adverse events				
Relacorilant‡	13 (7%)	..	..	..
Nab-paclitaxel	91 (48%)	..	60 (32%)	..
Discontinuations due to adverse events				
Relacorilant	18 (10%)	..	..	..
Nab-paclitaxel (plus relacorilant)†	17 (9%)	..	15 (8%)	..
Adverse events leading to death	4 (2%)	..	0	..

Higher rate of ≥ grade 3 neutropenia and anemia in the combination arm

Lancet 2025

Courtesy of Ursula Matulonis, MD

Reservations about the ROSELLA study

Lancet paper and ASCO 2025 data represent an interim analysis:
- OS benefit is not statistically significant
- Very minimal PFS benefit for the experimental arm

Non-blinded study

Nab-paclitaxel is not used standardly

No control over what patients received post treatment

Mix of ovarian cancer histologies enrolled

No quantification of the glucocorticoid receptor

Higher rate of grade 3 or higher neutropenia and anemia in the combination arm

Phase 3, randomized, double-blind study of pembrolizumab versus placebo plus paclitaxel with optional bevacizumab for platinum-resistant recurrent ovarian KEYNOTE-B96

Study design:
Pembrolizumab + weekly paclitaxel ± bev vs placebo + weekly paclitaxel ± bev in pts with platinum resistant ovarian cancer

Eligibility:
Histologically confirmed recurrent platinum resistant epithelial ovarian cancer
Up to 1-2 prior lines of systemic therapy, including ≥1 prior platinum-based therapy with ≥4 cycles in first line

Randomization was stratified by:
Planned bev use (yes vs no)
Region (US vs Europe vs rest of world),
PD-L1 status (combined positive score [CPS] <1 vs CPS 1-<10 vs CPS ≥10).

Primary endpoint is PFS by investigator in pts with tumor PD-L1 CPS ≥1 and in all pts.

Secondary endpoints are OS in pts with tumor PD-L1 CPS ≥1 and in all pts, PFS per RECIST v1.1 by BICR in pts with tumor PD-L1 CPS ≥1 and in all pts,
safety and PROs

Courtesy of Ursula Matulonis, MD

KEYNOTE-B96

Planned accrual was 643 pts
Pembro dose: 400 mg IV every 6 weeks
Paclitaxel dose/schedule: 80 mg/m2 per week on a 3 weekly schedule

Press release May 15th 2025:
Trial met its primary endpoint of PFS for platinum-resistant recurrent ovarian cancer whose tumors expressed PD-L1 and in all comers.

The study also met a secondary endpoint of OS in patients whose tumors express PD-L1.

KN100 (Ann Onc 2019)
Pembro alone in plat resistant ovarian cancer:
ORR based on CPS: 4.1% for CPS <1, 5.7% CPS ≥1, and 10.0% for CPS ≥10.
No additional molecular determinants identified for prediction of response (Gyn Onc 2023)

Courtesy of Ursula Matulonis, MD

https://www.merck.com/news/merck-announces-phase-3-keynote-b96-trial-met-primary-endpoint-of-progression-free-survival-pfs-in-patients-with-platinum-resistant-recurrent-ovarian-cancer-whose-tumors-expressed-pd-l1-and-in-all-c/.

Final OS results of MIRASOL

Phase 3 randomized trial of mirvetuximab versus IC's chemotherapy (weekly paclitaxel, PLD or topotecan)
Eligibility: PROC/high grade serous, FOLR1+, prior bev not mandated, up to 3 prior lines of treatment

Primary platinum refractory ovarian cancer excluded (Primary PFI < 3 months)

Pts randomized 1:1 to mirvetuximab vs IC chemotherapy

Primary endpoint: PFS by investigator
Key secondary endpoint: OS, ORR, mDOR, safety

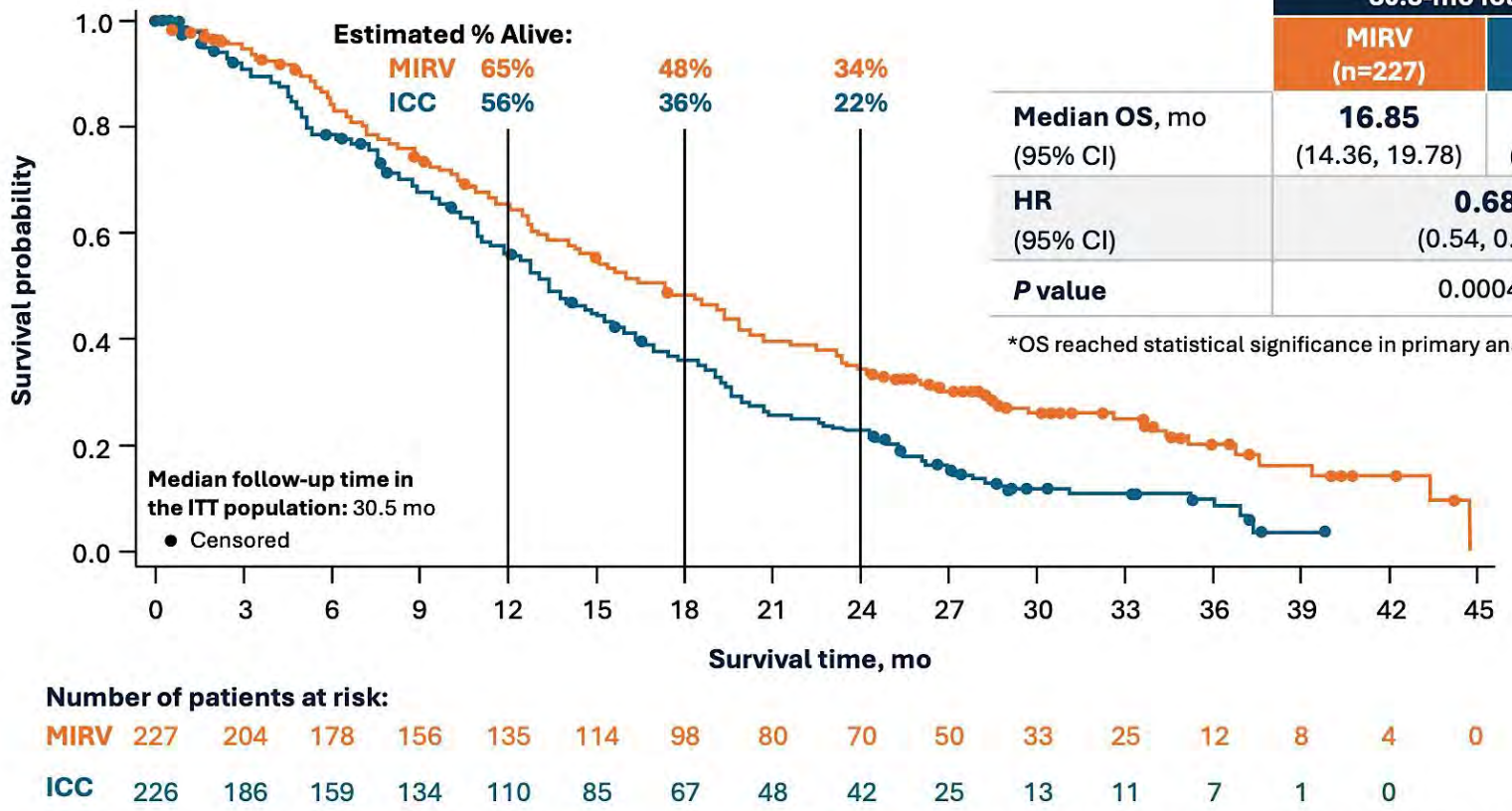
Van Gorp et al, SGO 2024

Courtesy of Ursula Matulonis, MD

Final OS: First trial in platinum resistant OC to show an OS benefit

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

Final Overall Survival



	Final analysis[a] 30.5-mo follow-up		Primary analysis[b] 13.1-mo follow-up	
	MIRV (n=227)	ICC (n=226)	MIRV (n=227)	ICC (n=226)
Median OS, mo (95% CI)	**16.85** (14.36, 19.78)	**13.34** (11.37, 15.15)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
HR (95% CI)	**0.68** (0.54, 0.84)		0.67 (0.50, 0.89)	
***P* value**	0.0004*		0.0046	

*OS reached statistical significance in primary analysis. The *P* value at the final analysis is descriptive.

At the final analysis, the HR for OS (0.68) **continued to favor MIRV** over ICC, with patients treated with MIRV exhibiting a **32% reduction in risk of death**

HR, hazard ratio; ICC, investigator's choice chemotherapy; ITT, intent-to-treat; MIRV, mirvetuximab soravtansine-gynx; OS, overall survival; PFS, progression-free survival.

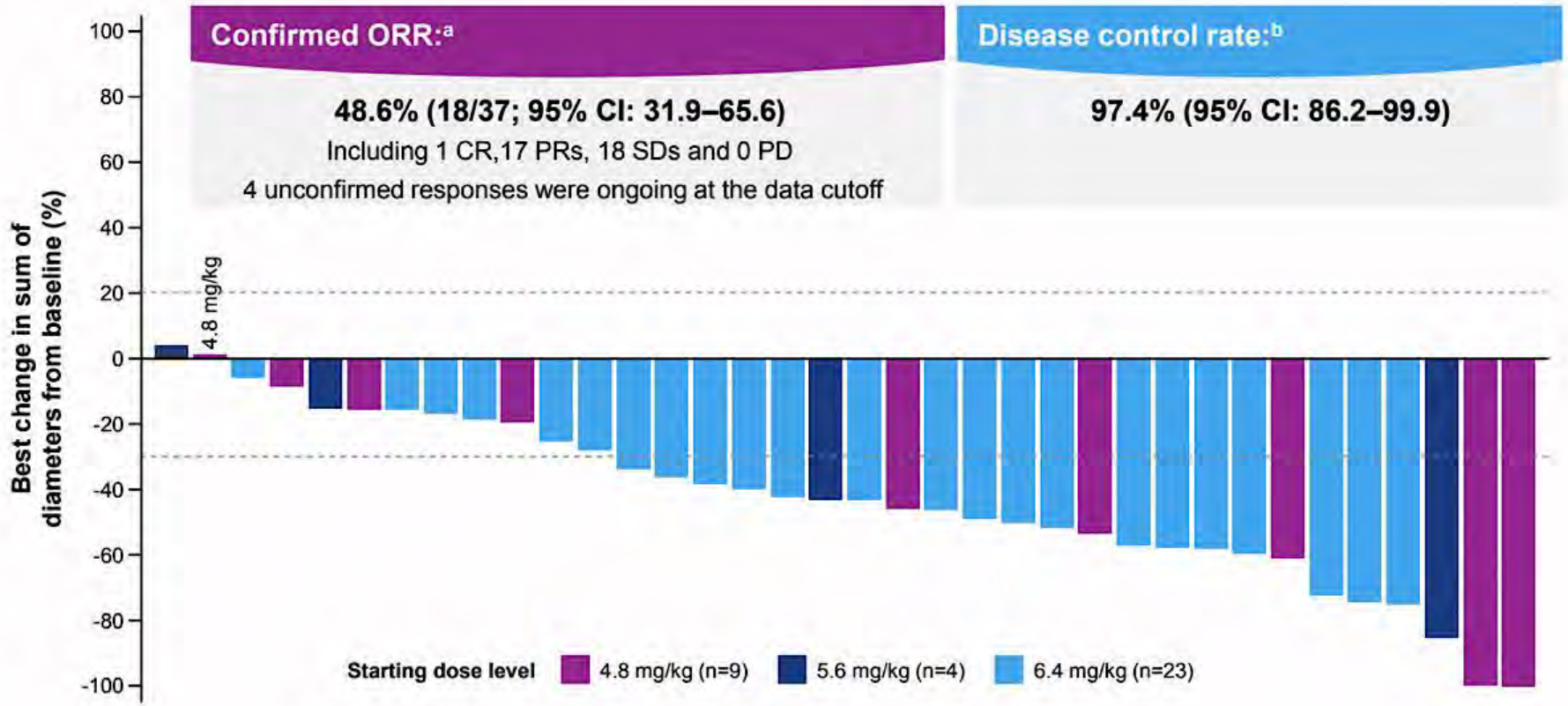
[a]Data cutoff: September 26, 2024. [b]Data cutoff: March 6, 2023.

Raludotatug deruxtecan

DAR ~8

Anti-CDH6 ADC

Preliminary antitumor activity of R-DXd is promising in heavily pretreated patients with OVC receiving doses of 4.8–6.4 mg/kg

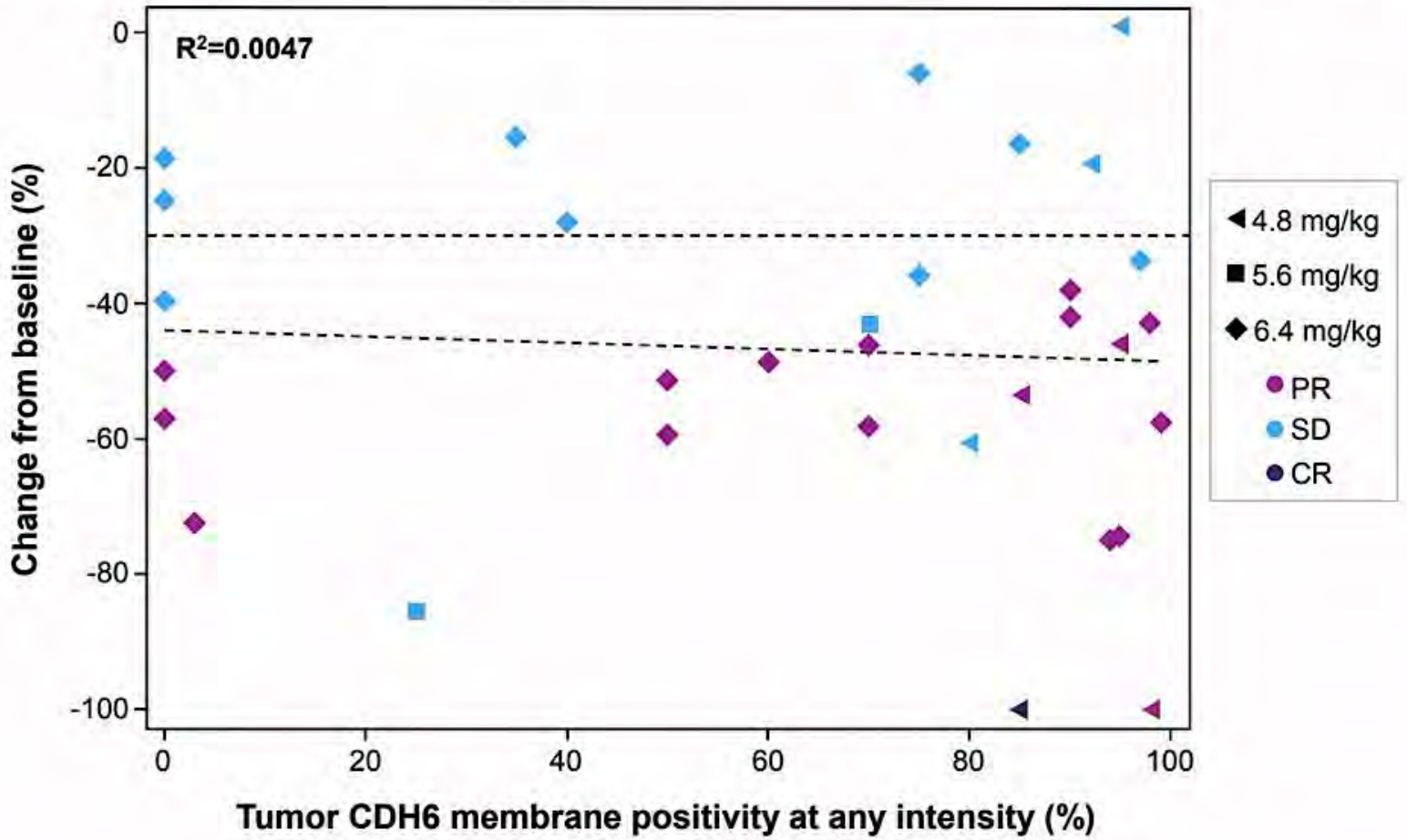


Moore et al, SGO 2024

Courtesy of Ursula Matulonis, MD

Preliminary biomarker assessment: Patients with a wide range of CDH6 expression show antitumor activity

CDH6 level by percent change from baseline for evaluable patients (n=32)[a,b]



Best overall response

CR: 1
PR: 17
SD: 14

Tumor samples from patients at baseline

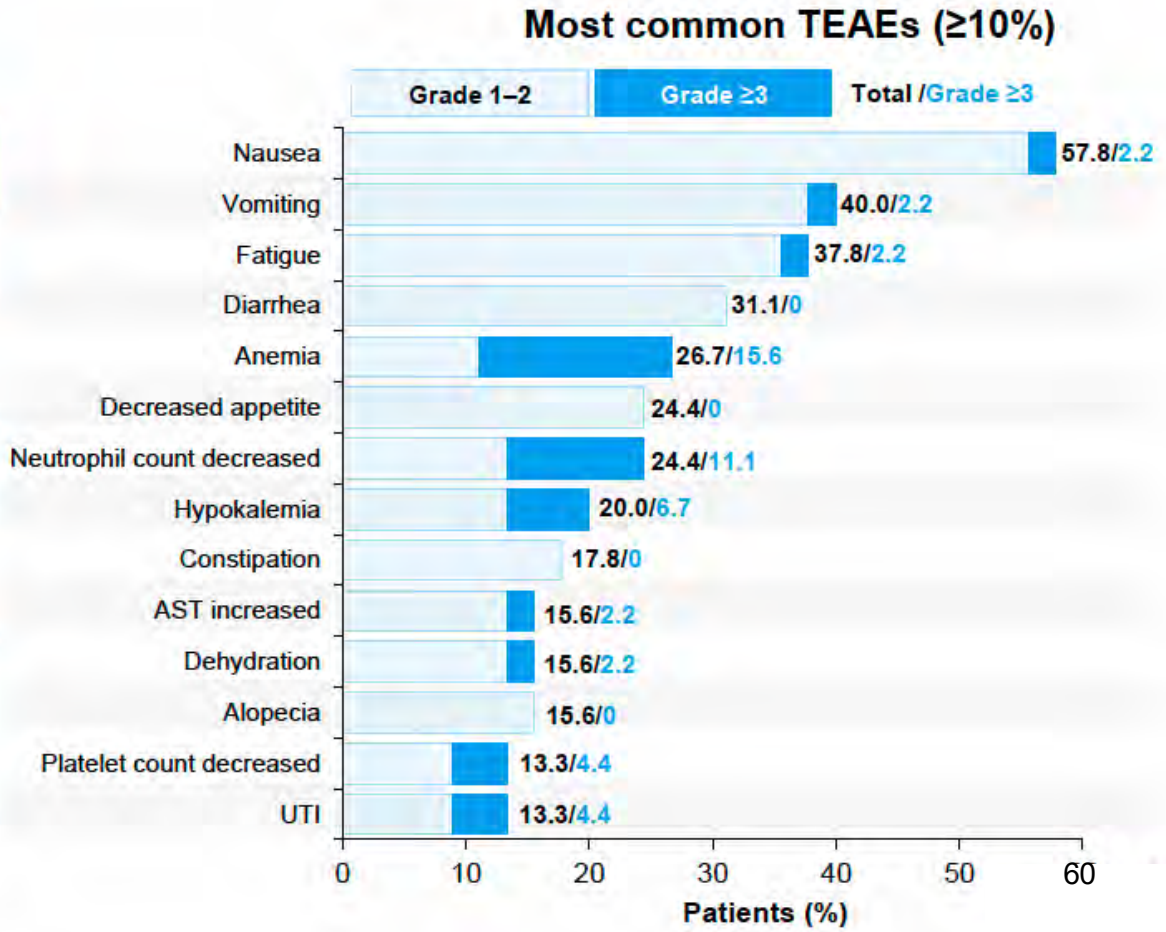
Archival samples: 18
Freshly collected biopsies: 14

Safety summary: The AE profile of R-DXd appears to be manageable

Overall safety summary

	4.8–6.4 mg/kg R-DXd N=45
Any TEAE, n (%)	42 (93.3)
Grade ≥3	20 (44.4)
Treatment-related TEAE, n (%)	41 (91.1)
Grade ≥3	12 (26.7)
Grade 5	0
Any SAE, n (%)	11 (24.4)
Grade ≥3	10 (22.2)
Treatment-related SAE, n (%)	4 (8.9)
Grade ≥3	3 (6.7)
Grade 5	0
Dose modifications,[a] n (%)	
Drug discontinuation	5 (11.1)
Dose interruption	14 (31.1)
Dose reduction	7 (15.6)

- Drug-related ILD/pneumonitis was reported in 2 patients, who received a starting dose of 6.4 mg/kg. Both cases were Grade 2



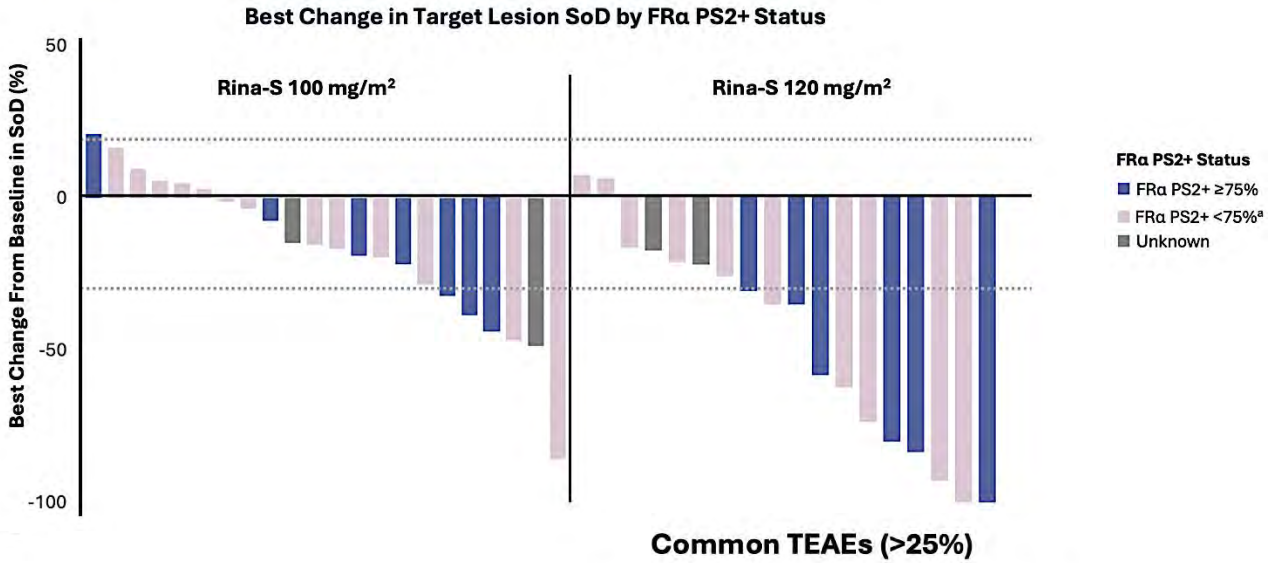
Data cutoff: July 14, 2023.
[a]Dose modifications associated with TEAE.
Patients received R-DXd at doses of 4.8 mg/kg (n=13), 5.4 mg/kg (n=8) and 6.4 mg/kg (n=24).
AE, adverse event; AST, aspartate aminotransferase; ILD, interstitial lung disease; SAE, serious adverse event; TEAE, treatment-emergent adverse event; UTI, urinary tract infection.

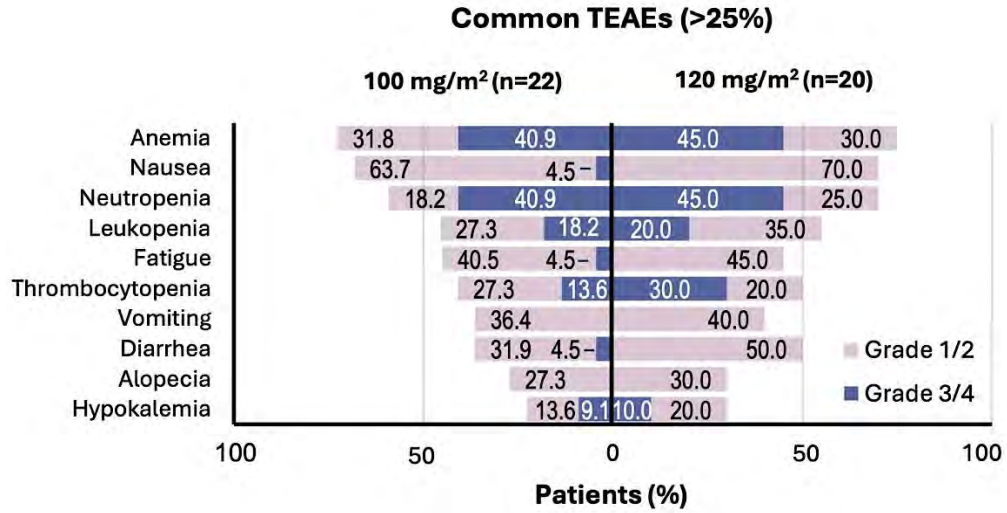
Rinatabart sesutecan

Antitumor Activity

	Rina-S 100 mg/m² (n=22)[a]	Rina-S 120 mg/m² (n=18)[a]
Median on-study follow-up, weeks (range)	46.4 (6.6, 65.3)	48.1 (10.9-65.9)
Confirmed ORR[b], % (95% CI)	22.7 (7.8-45.4)	55.6 (30.8-78.5)
Confirmed response, n (%)		
CR	1 (4.5)	2 (11.1)
PR	4 (18.2)	8 (44.4)
SD	14 (63.6)	6 (33.3)
NE	0	1 (5.6)
Disease control rate, % (95% CI)	86.4 (65.1-97.1)	88.9 (65.3-98.6)

Response by FRα Expression





RAINFOL™-01, Part C (NCT05579366, enrolling): single-arm phase 2 study of single-agent Rina-S 120 mg/m² in patients with PROC after 1-3 prior lines of therapy (or up to 4 prior lines if patient received prior MIRV) [SGO Abstract #827857]

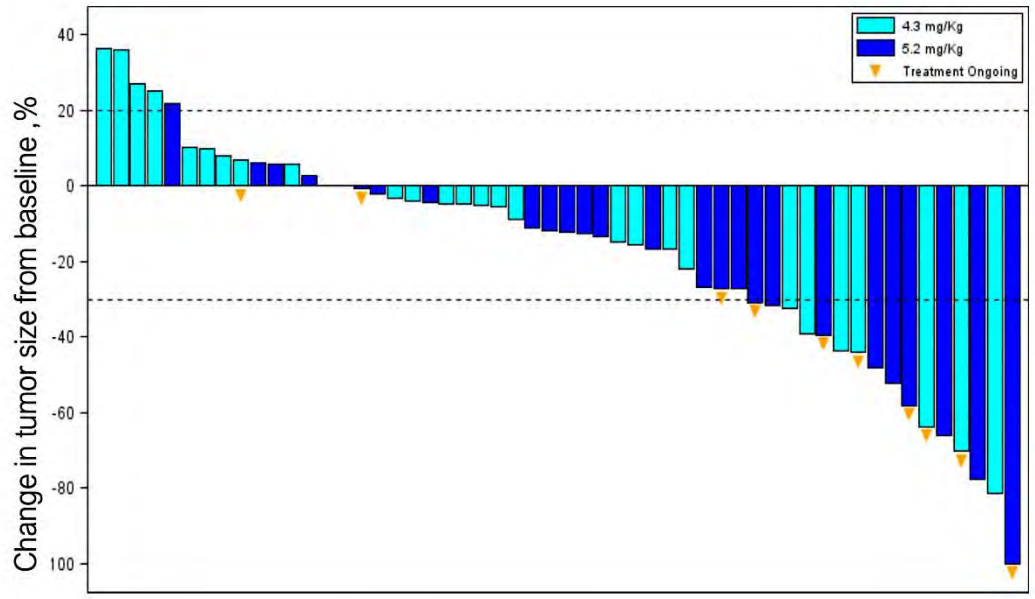
RAINFOL™-02 (NCT06619236, enrolling): open-label, randomized, phase 3 study of single-agent Rina-S 120 mg/m² vs investigator's choice chemotherapy in patients with PROC after 1-4 prior lines of therapy [SGO Abstract #809034]

Luveltamab tazevibulin

March 13, 2025 press release:

-The pharmaceutical company will continue to advance exatecan and dual-payload ADC programs; luveltamab tazevibulin development will be deprioritized

March 15, 2025 SGO presentation



Tumor response (efficacy evaluable)*	Starting Dose 5.2 mg/kg N=25*	Starting Dose 4.3 mg/kg N=29
Best response, n (%)		
CR	1(4.0)	0
PR	7 (28.0)**	4 (13.8)
SD	17 (68.0)	16 (55.2)
PD	1 (4.0)	9 (31.0)
ORR (95% CI)	32% (17,50)**	13.8% (3.9, 32)
DCR (95% CI)	96% (80,99.9)**	69% (49,85)
Time to response, (range)	6.0 wk (4.7–11)	6.4 wk (5.4-11.9)

*Three patients were not efficacy evaluable; **After data extraction, one additional patient experienced a confirmed PR and is included in the analysis.

Lee et al, SGO 2025

Courtesy of Ursula Matulonis, MD

Phase 2/3 ongoing or planned ADC studies in ovarian cancer

Line of therapy	Phase of trial	Year launched	ADC	Payload	Trial name	Trial design	NCT#
1st line	III	2025	Trastuzumab Deruxtecan (HER2)	Topo 1	ENGOT-ov89/DESTINY-OV-01	Maintenance HER2+	NCT06819007
2nd line platinum sensitive	III	not yet	Sacituzumab-tirumotecan (Sac-TMT) (TROP-2)	Topo 1	ENGOT-ov-84/GEICO141/MK-2870-022	2nd line Platinum sens Sac-TMT/bev vs SOC (no biomarker)	NCT06824467
	III	2022	Mirvetuximab (FOLR1)	DM4	GLORIOSA	Mirvetuximab/bev vs bev alone, as maintenance	NCT05445778
Platinum resistant	II/III	2023	Luveltamab tazevibulin (FOLR1)	Topo 1	ENGOTov79/GEICO134-O/STRO-002-GM3 (REFRaME-01)	up to 4 previous lines, FRα+	NCT05870748
	II/III	2024	Raludotatug-DXd (CDH6)	Topo 1	REJOICE-Ovarian01	up to 3 previous lines, high grade	NCT06161025
	III	2024	Rinatabart sesutecan (FOLR1)	Topo 1	ENGOT-ov86/GEICO152-O/RAINFOL-OV2	up to 4 lines high grade	NCT06619236

Courtesy of Ursula Matulonis, MD

Year in Review:
Management of Gynecologic Cancers

INTRODUCTION: Tale of Two Cities — ASCO 2025

MODULE 1: Ovarian Cancer

MODULE 2: HER2-Positive Gynecologic Cancers

MODULE 3: Endometrial Cancer

MODULE 4: Cervical Cancer

RTP Year in Review 2025

HER2 Overexpression and Amplification Rates in Gynecologic Cancer

Site	Histotype	HER2 Overexpression/Amplification
Endometrium	Serous	8–49 % [6,8–10,12,19,32–36]
	Carcinosarcoma	7–25 % [6,7,13,23,33,35,37]
	Endometrioid	0–12 % [6,12,32–34,36]
	Clear cell	6–30 % [6,12,32–34,36,38]
	Undifferentiated carcinoma	0–15 % [6,33]
Ovary	Mucinous	18–38 % [5,11,25,39–41]
	High grade serous	2 % [18]
	Clear cell carcinoma	1 % [38]
	Carcinosarcoma	7 % [7]
	All histotypes (pooled)	6 % [42]
Cervix	Gastric-type adenocarcinoma	15 % [16,24,43]
	HPV-associated adenocarcinoma	5 % [16]
	All adenocarcinoma	31 % [44]
	Squamous cell carcinoma	18 % [44]
Vulva	Paget's disease	12–80 % [45–47]

Lee EK et al. *Gynecol Oncol* 2025;195:152-64.

Select Trials of HER2-Targeted Therapies in Gynecologic Cancers

Trial	Agent	Drug Class	Study Population	HER2 Requirement	Results
GOG-170G [49]	Lapatinib	Reversible EGFR/HER1 & HER2 TKI	Ovarian	HER2 expression not required	ORR 0 %
GOG-0229D [50]	Lapatinib	Reversible EGFR/HER1 & HER2 TKI	Endometrial	HER2 expression not required	ORR 3 % (1/30)
SUMMIT trial [52] (NCT01953926)	Neratinib	Irreversible EGFR/HER1, HER2, & HER4 TKI	Ovarian, endometrial, cervical	HER2 or EGFR exon 18 mutation	Cervical cancer: ORR 25 % (3/12), mPFS 7.0 mo, mOS 16.8mo
NCT01367002 [27,28]	Trastuzumab (with carboplatin & paclitaxel)	Anti-HER2 Ab (monospecific, domain IV)	USC	HER2 IHC 3+, or 2+ with confirmatory FISH	Evaluable patients: mPFS 12.9 mo Primary stage III or IV: mPFS 17.7 mo, mOS 25.4 mo
NCT02892123 [53]	Zanidatamab	Anti-HER2 Ab (bispecific, domains II & IV)	Solid tumors, including ovarian, endometrial, vulvar	HER2 IHC ≥1+ or ≥ 2+ depending on cohort; HER2 IHC 3+ or 2+ with confirmatory FISH in dose expansion	Dose expansion non-biliary/non-CRC cohort: ORR 36 % (13/36), including 2 ovarian pts., 1 vulvar pt., 1 endometrial pt
NCT05150691 [54,55]	DB-1303	Anti-HER2 ADC, topoisomerase I-inhibiting payload	Solid tumors, including endometrial	HER2 IHC ≥1+ or ISH-positive	Endometrial: ORR 58.8 % (10/17) UCS ORR 87.5 % (7/8) USC ORR 50 % (1/2)
NCT02277717 [56]	Trastuzumab duocarmazine	Anti-HER2 ADC, DNA alkylating payload	Endometrial	HER2 IHC ≥1+ or ISH-positive	ORR 39 % (5/13), mPFS 4.3 mo
NCT04278144 [57]	BDC-1001 +/− nivolumab	Anti-HER2 ISAC, TLR7/8-agonist payload +/− anti-PD-1 Ab	Solid tumors, including ovarian, endometrial, cervical	HER2 IHC 3+ or amplified; or HER2 IHC 2+	6 PRs; including 1 ovarian pt. Prolonged SD in: 1 endometrial pt. (36 wks), 1 ovarian pt. (36 wks), 2 cervical pts. (24 and 60 wks)

Ab = antibody; ADC = antibody drug conjugate; CRC = colorectal cancer; FISH = fluorescence in-situ hybridization; ISH = in-situ hybridization; TKI = tyrosine kinase inhibitor; mo = months; mPFS = median PFS; mOS = median OS; ORR = objective response rate; UCS = uterine carcinosarcoma; USC = uterine serous carcinoma; wks = weeks.

Lee EK et al. *Gynecol Oncol* 2025;195:152-64.

DESTINY-PanTumor02: A Phase II Study of Trastuzumab Deruxtecan (T-DXd) for HER2-Expressing Tumors

An open-label, multicenter study (NCT04482309)

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

T-DXd
5.4 mg/kg
q3w

n≈40 per cohort planned

(Cohorts with no objective responses in the first 15 patients were to be closed)

- Cervical cancer
- Endometrial cancer
- Ovarian cancer
- Biliary tract cancer
- Pancreatic cancer
- Bladder cancer
- Other tumors[b]

Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

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

Data cut-off for analysis:

- Nov 16, 2022

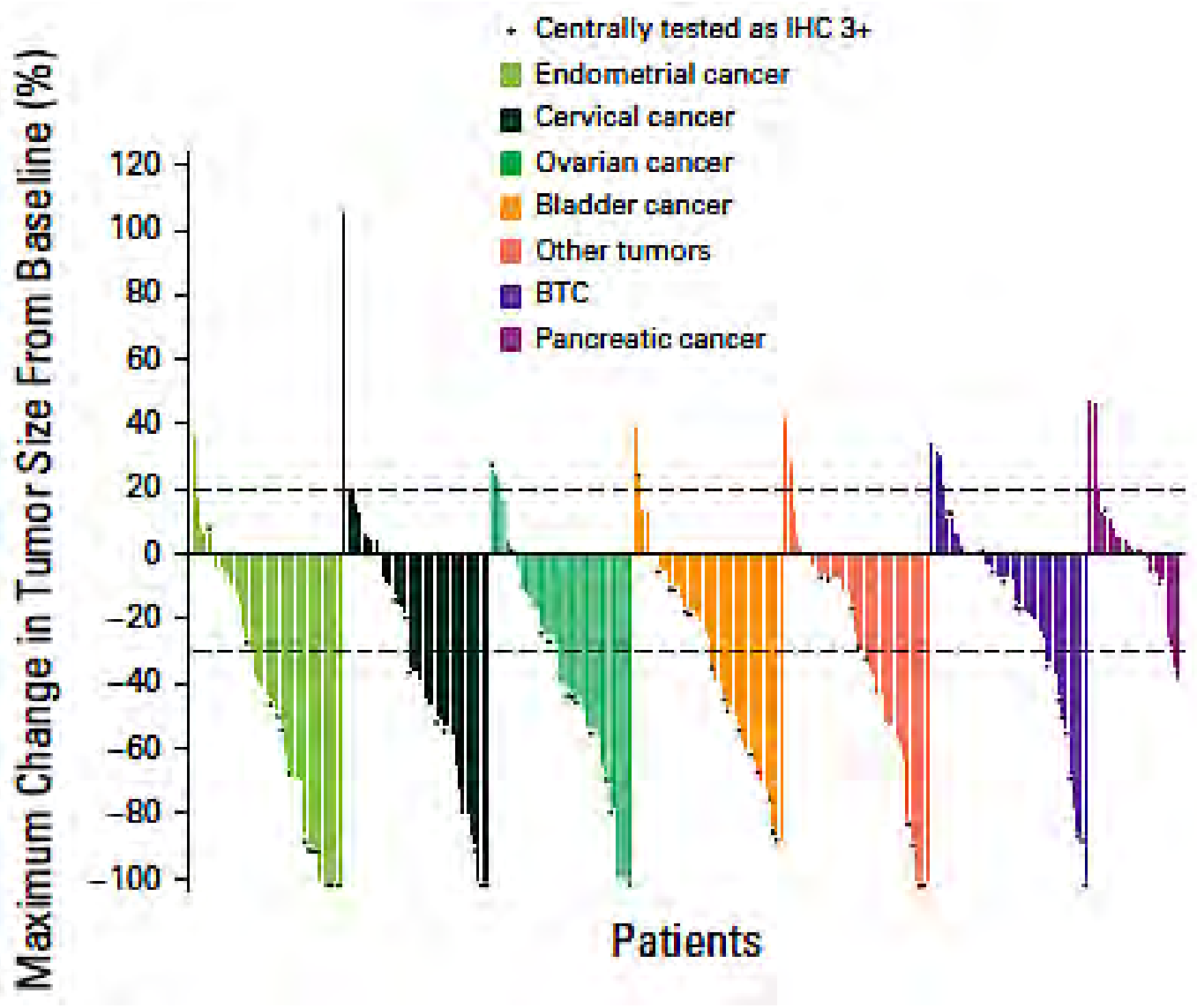
[a]Patients were eligible for either test. All patients were centrally confirmed. [b]Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer. [c]Investigator-assessed per Response Evaluation Criteria in Solid Tumors version 1.1.

2L, second-line; ASCO, American Society of Clinical Oncology; DCR, disease control rate; CAP, College of American Pathologists; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.

1. Hofmann M, et al. *Histopathology* 2008;52(7):797–805.

Meric-Bernstam F et al. ASCO 2023:Abstract LBA3000.

Efficacy of T-DXd: DESTINYPanTumor-02



FDA approval IHC3+ tumour agnostic

Primary endpoint (IHC3+/2+):
Investigator assessed ORR
37.1%

In patients central HER2 3+
RR 61% median DOR 22.1 months

*5 IHC1+ enrolled in cervical cancer

Meric-Bernstam F et al. J Clin Oncol 2024; 42(1):47-58.

Courtesy of Susana Banerjee, MBBS, MA, PhD

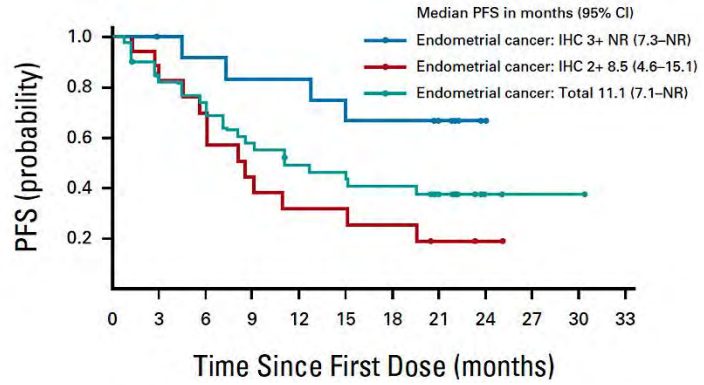
DESTINY-PanTumor02: Survival

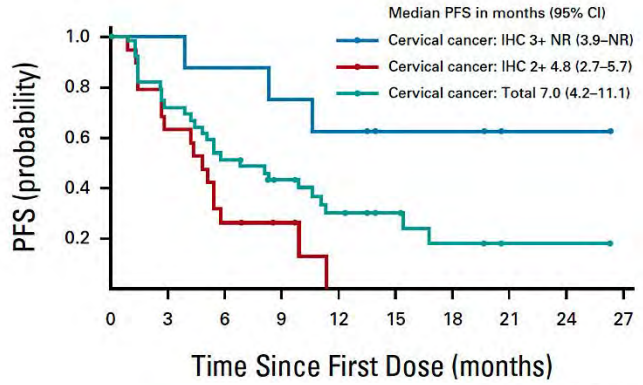
Endometrial

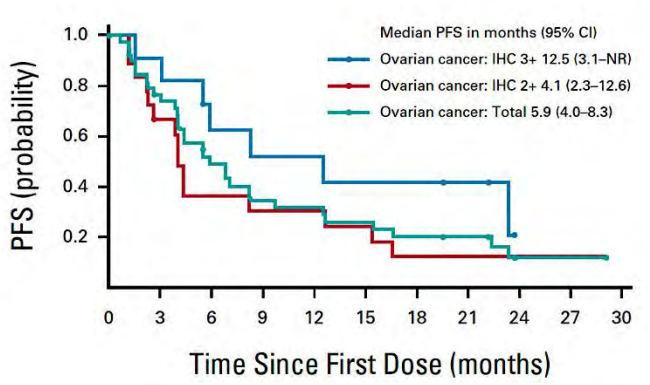
Cervical

Ovarian

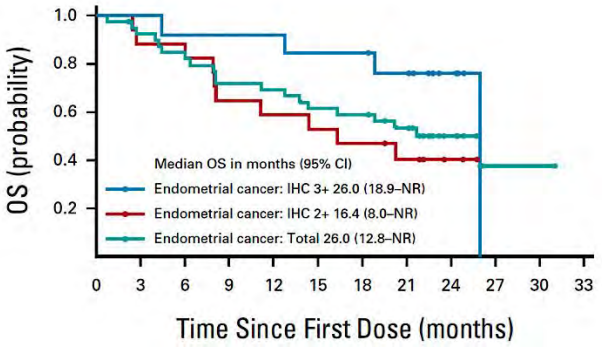
PFS

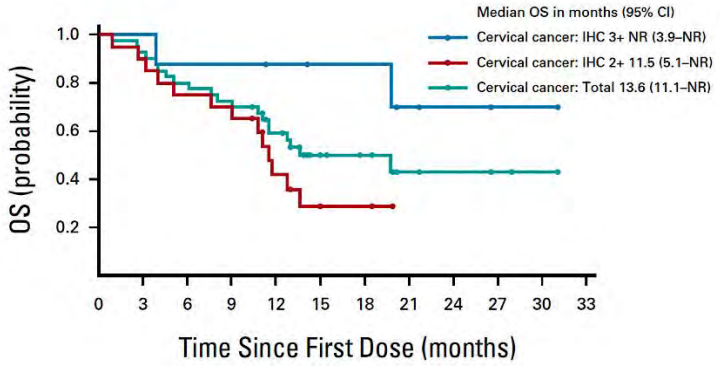


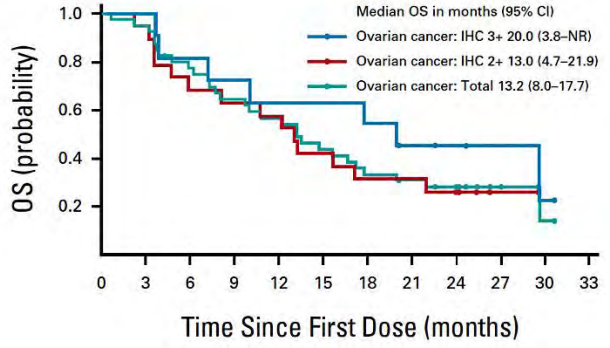




OS







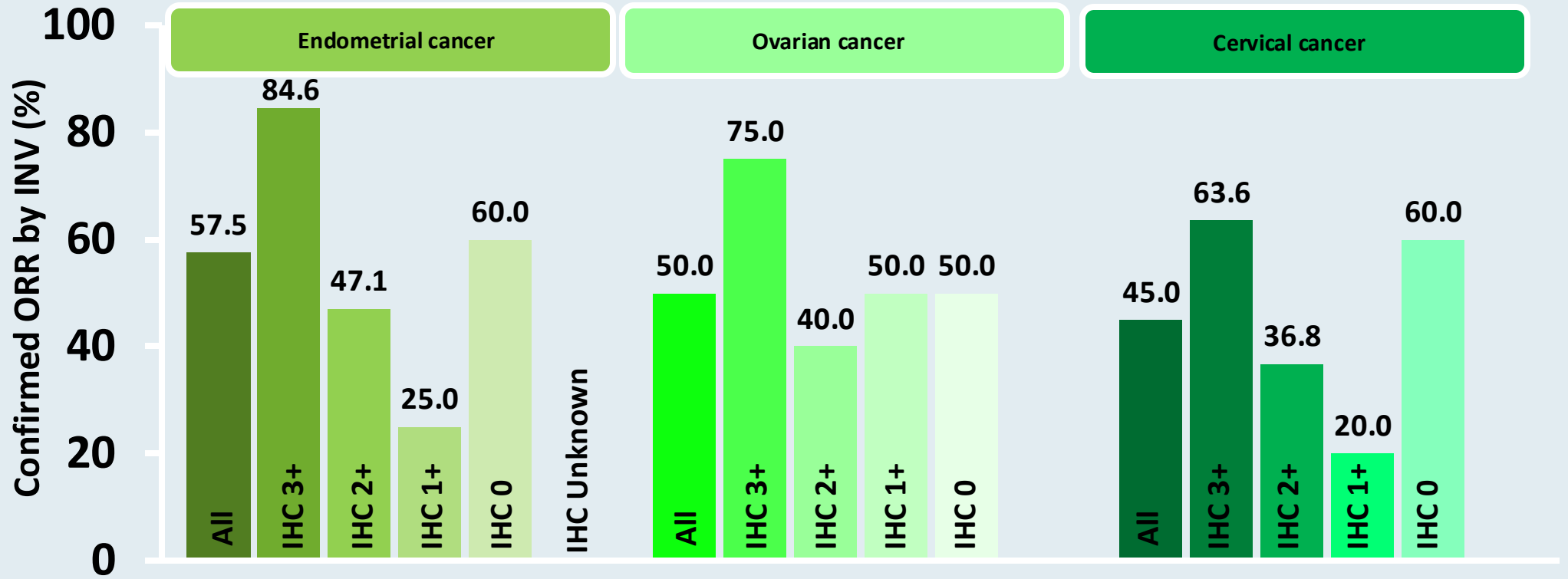
Meric-Bernstam F et al. *J Clin Oncol* 2024;42(1):47-58.

DESTINY-PanTumor02: Adverse Events

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

Meric-Bernstam F et al. *J Clin Oncol* 2024;42(1):47-58.

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

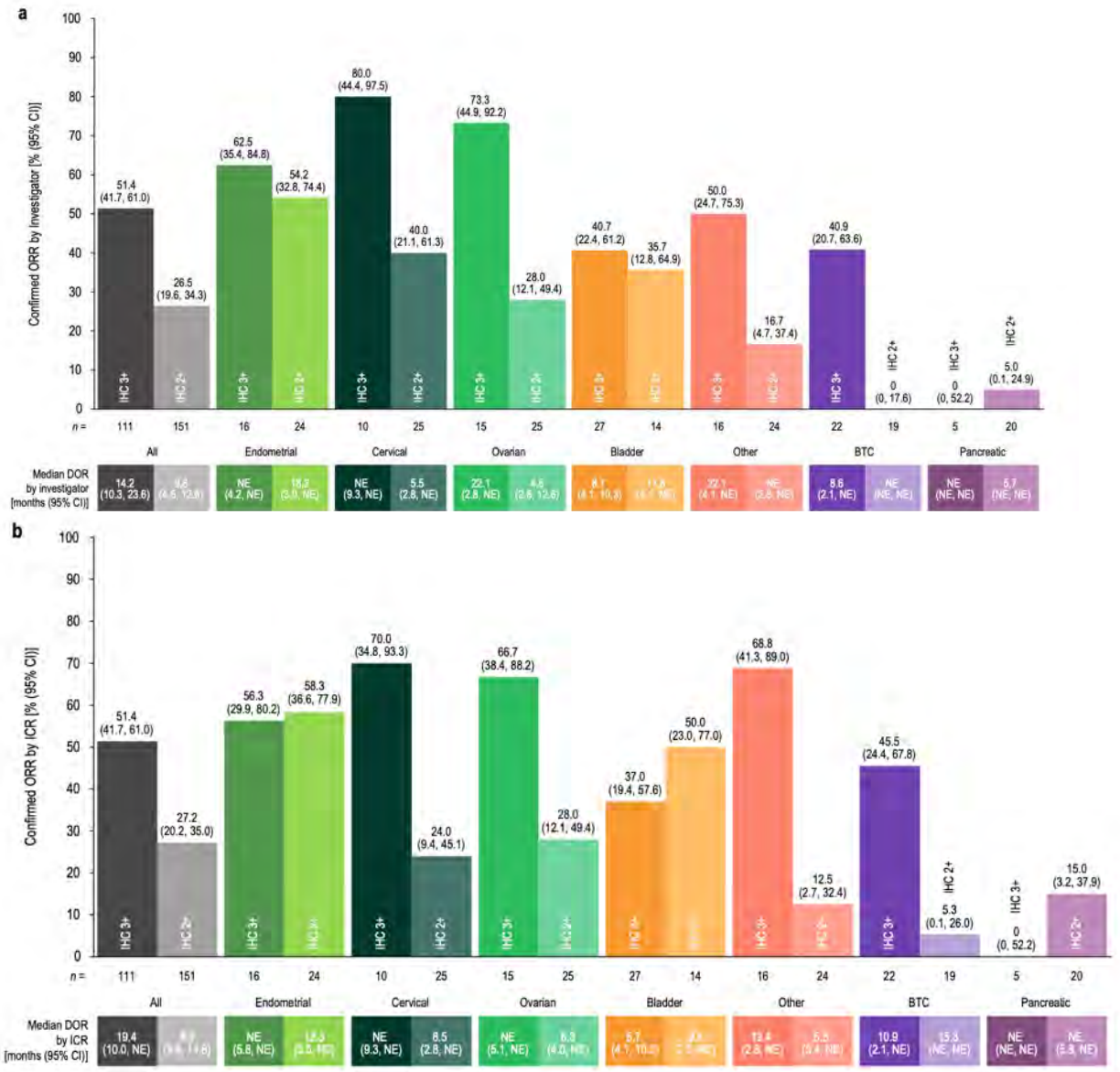


	Endometrial cancer						Ovarian cancer					Cervical cancer				
	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	IHC Unknown	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	All	IHC 3+	IHC 2+	IHC 1+	IHC 0
Total n in subgroup	40	13	7	4	5	1	40	8	20	8	4	40	11	19	5	5
n of responders	23	11	8	1	3	0	20	6	8	4	2	18	7	7	1	3
Median DOR, months	NR	NR	18.2	NR	9.9	–	14.2	NR	3.8	14.2	NR	11.3	22.1	11.3	8.3	4.5
95% CR	9.9, NE	9.6, NE	3.0, NE	–	2.8, NE	–	4.1, NE	9.3, NE	2.8, NE	8.3, NE	6.8, NE	4.4, 22.1	4.2, NE	2.8, NE	–	2.6, NE

ORR = objective response rate; INV = investigator; DOR = duration of response; CR = complete response; NR = not reached; NE = not estimable

Lee J-Y et al. International Gynecological Cancer Society (IGCS) 2023.

HER2 IHC Status: Efficacy T-DXd DESTINYPanTumor-02



Cervical

Local: IHC 3+ ORR 80%
IHC2+ ORR 40%

Central: IHC 3+ ORR 70%
IHC2+ ORR 24%

Single arm, relatively low numbers
Positive signals
Needs prospective trials/results

Oaknin A et al. *Adv Ther* 2024;41(11):4125-39.

Courtesy of Susana Banerjee, MBBS, MA, PhD

HER2/neu testing Guidelines for Gynecologic tumors

Clinicians should request **HER2 testing** on tumor tissue in the biopsy or resection specimens (primary or metastasis) prior to the initiation of trastuzumab/ADC therapy.

When HER2 status is being evaluated, laboratories/pathologists should perform/order IHC testing first, followed by ISH/FISH when IHC result is 2+ (equivocal). **Positive (3+) or negative (0 or 1+) HER2 IHC results do not require further ISH/FISH testing**.

Pathologists should identify and **mark areas with strongest intensity** of HER2 expression by IHC in the specimen for subsequent ISH/FISH scoring when required.

The prevalence of HER2 status may be discordant between the primary tumor and metastases in **approximately 25% of cases**, especially after treatment.

Per **NCCN guidelines** treating clinicians should offer **combination chemotherapy and HER2-targeted therapy** as the initial treatment for appropriate patients harboring HER2 positive advanced/recurrent USC and for any gynecologic cancer patient with recurrent tumors demonstrating HER2 2+/3+ expression by IHC.

Courtesy of Alessandro D Santin, MD

Year in Review:
Management of Gynecologic Cancers

INTRODUCTION: Tale of Two Cities — ASCO 2025

MODULE 1: Ovarian Cancer

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MODULE 3: Endometrial Cancer

MODULE 4: Cervical Cancer

RTP Year in Review 2025

ENGOT-EN6-NSGO/GOG-3031/RUBY (NCT03981796)

Phase 3, randomized, double-blind, multicenter study of dostarlimab plus carboplatin-paclitaxel versus placebo plus carboplatin/paclitaxel in patients with primary advanced or recurrent EC

Eligible patients

- Histologically/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
  - Carcinosarcoma, clear cell, serous, or mixed histology permitted
- Naïve to systemic anticancer therapy or had a recurrence or PD ≥6 months after completing systemic anticancer therapy
- ECOG PS 0-1
- Adequate organ function

Stratification

- MMR/MSI status
- Prior external pelvic radiotherapy
- Disease status

R1:1

Dostarlimab IV 500 mg
Carboplatin AUC 5 mg/mL/min
Paclitaxel 175 mg/m²
Q3W for 6 cycles

→ **Dostarlimab IV** 1000 mg Q6W up to 3 years[a]

Placebo IV
Carboplatin AUC 5 mg/mL/min
Paclitaxel 175 mg/m²
Q3W for 6 cycles

→ **Placebo IV** Q6W up to 3 years[a]

→ **Follow-up**

Primary endpoints

- PFS by INV per RECIST v1.1
- OS

Secondary endpoints

- PFS by BICR per RECIST v1.1
- PFS2
- ORR
- DOR
- DCR
- HRQOL/PRO
- Safety

Further study details can be found at Mirza MR, et al. N Engl J Med. 2023 Jun 8;388(23):2145-2158.

[a]Treatment 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. AUC, area under the plasma or serum concentration-time curve; BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response, EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQOL, health-related quality of life; INV, investigator assessment; MMR, mismatch repair; MSI, microsatellite instability; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, second progression-free survival; PRO, patient-reported outcome; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

MADRID 2023 ESMO congress

Dr Mansoor Raza Mirza

Courtesy of Susana Banerjee, MBBS, MA, PhD

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin–paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial

M. A. Powell[1], L. Bjørge[2,3], L. Willmott[4], Z. Novák[5], D. Black[6], L. Gilbert[7,8], S. Sharma[9], G. Valabrega[10], L. M. Landrum[11], M. Gropp-Meier[12,13], A. Stuckey[14], I. Boere[15], M. A. Gold[16], Y. Segev[17], S. E. Gill[18], C. Gennigens[19,20], A. Sebastianelli[21], M. S. Shahin[22], B. Pothuri[23,24], B. J. Monk[23,25], J. Buscema[26], R. L. Coleman[27], B. M. Slomovitz[28,29], K. L. Ring[30], T. J. Herzog[31], M. M. Balas[32], M. Grimshaw[33], S. Stevens[33], D. W. Lai[34], C. McCourt[35] & M. R. Mirza[36,37]*

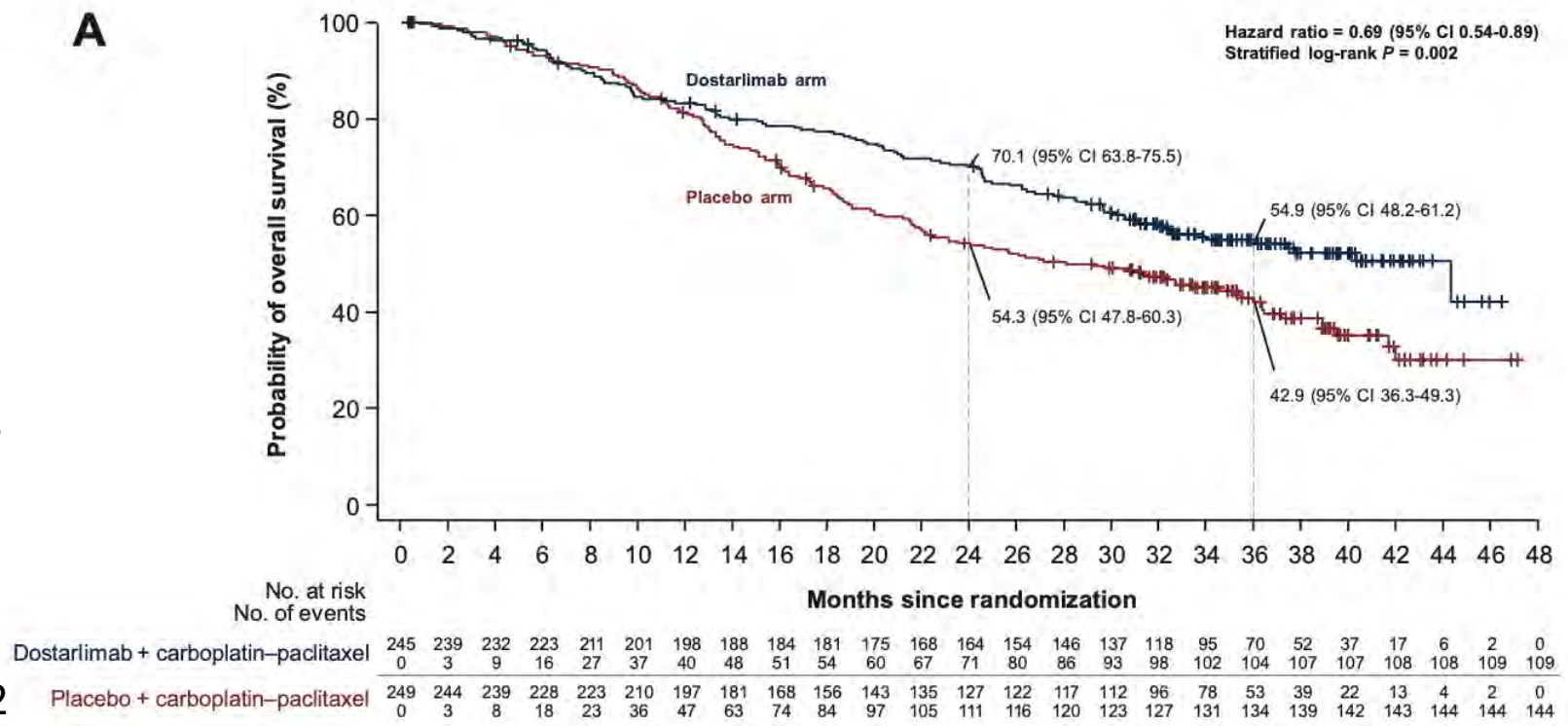
FDA approval (Aug 2024)
EMA approval (2025)
Dostarlimab with carboplatin and paclitaxel, followed by single-agent dostarlimab primary advanced or recurrent endometrial cancer
Regardless of MMR status

- 494 patients were randomized (245 in the dostarlimab arm; 249 in the placebo arm)

- second interim analysis 51% maturity

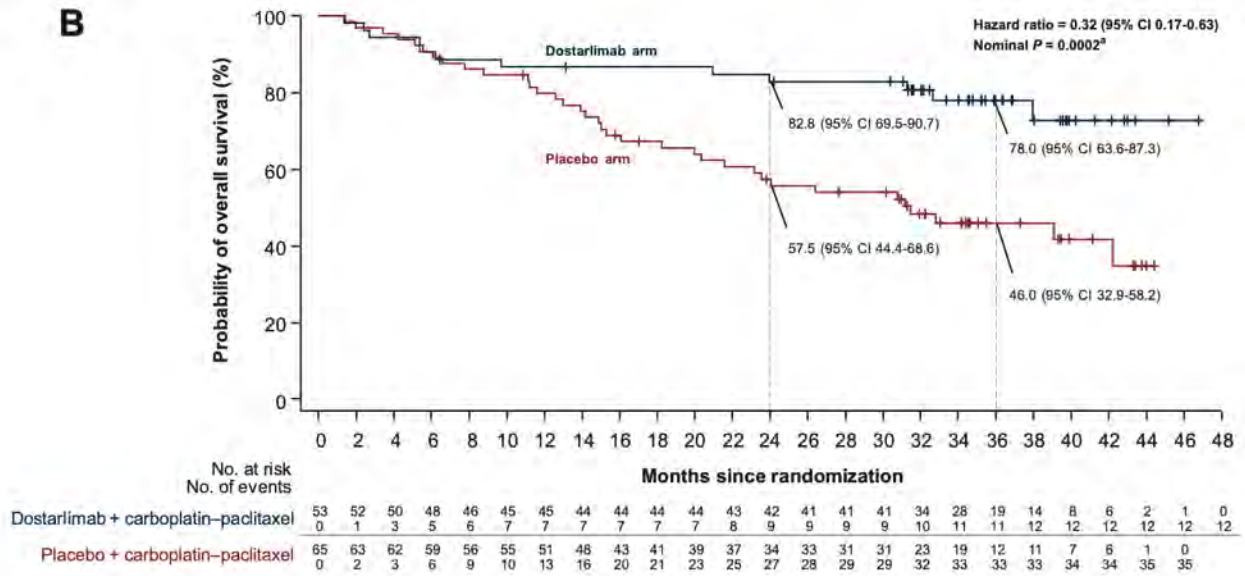
- Overall population statistically significant reduction in the risk of death HR 0.69, 95% (CI 0.54- 0.89, p= 0.0020) with addition of dostarlimab plus carboplatin/paclitaxel versus carboplatin/paclitaxel alone

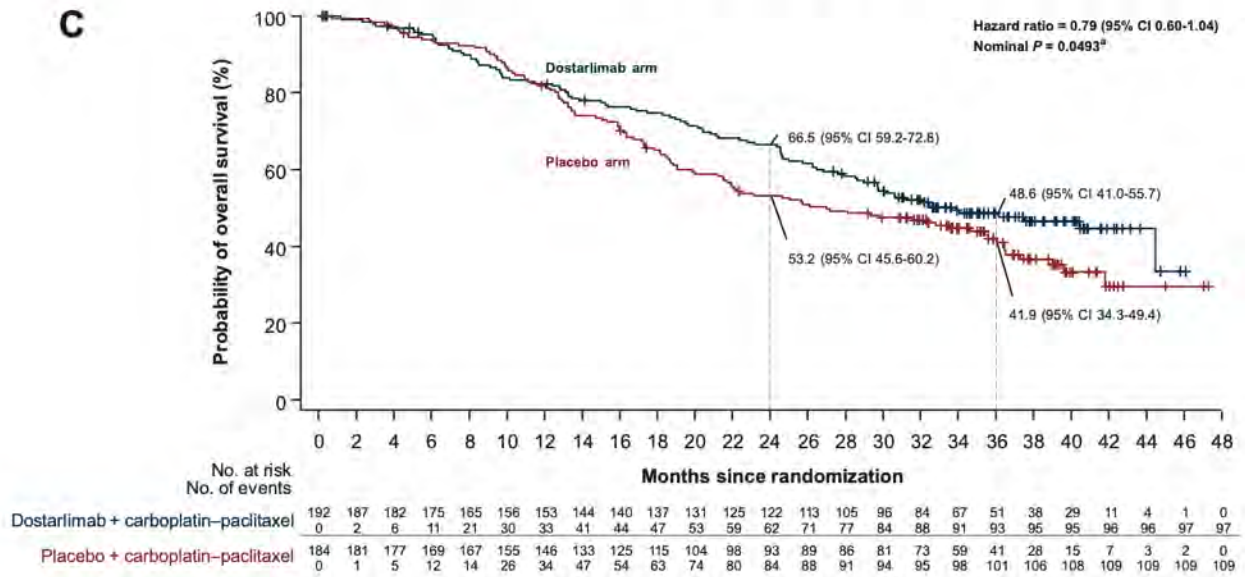
- median OS of 44.6 months versus 28.2 months



Courtesy of Susana Banerjee, MBBS, MA, PhD

Powell MA et al. *Ann Oncol* 2024;35(8):728-38.





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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin—paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial

M. A. Powell[1], L. Bjørge[2,3], L. Willmott[4], Z. Novák[5], D. Black[6], L. Gilbert[7,8], S. Sharma[9], G. Valabrega[10], L. M. Landrum[11], M. Gropp-Meier[12,13], A. Stuckey[14], I. Boere[15], M. A. Gold[16], Y. Segev[17], S. E. Gill[18], C. Gennigens[19,20], A. Sebastianelli[21], M. S. Shahin[22], B. Pothuri[23,24], B. J. Monk[23,25], J. Buscema[26], R. L. Coleman[27], B. M. Slomovitz[28,29], K. L. Ring[30], T. J. Herzog[31], M. M. Balas[32], M. Grimshaw[33], S. Stevens[33], D. W. Lai[34], C. McCourt[35] & M. R. Mirza[36,37]*

prespecified exploratory analysis.

- Risk of death was lower in the dMMR/MSI-H population (HR 0.32, 95% CI 0.17-0.63, nominal P = 0.0002)
- Median OS NR vs 31.4 months

- trend in favor of dostarlimab was seen in the MMRp/MSS (HR 0.79, 95% CI 0.60-1.04, nominal P=0.0493) median OS 34 vs 27 months

Powell MA et al. *Ann Oncol* 2024;35(8):728-38.

NRG-GY018 (NCT03914612)

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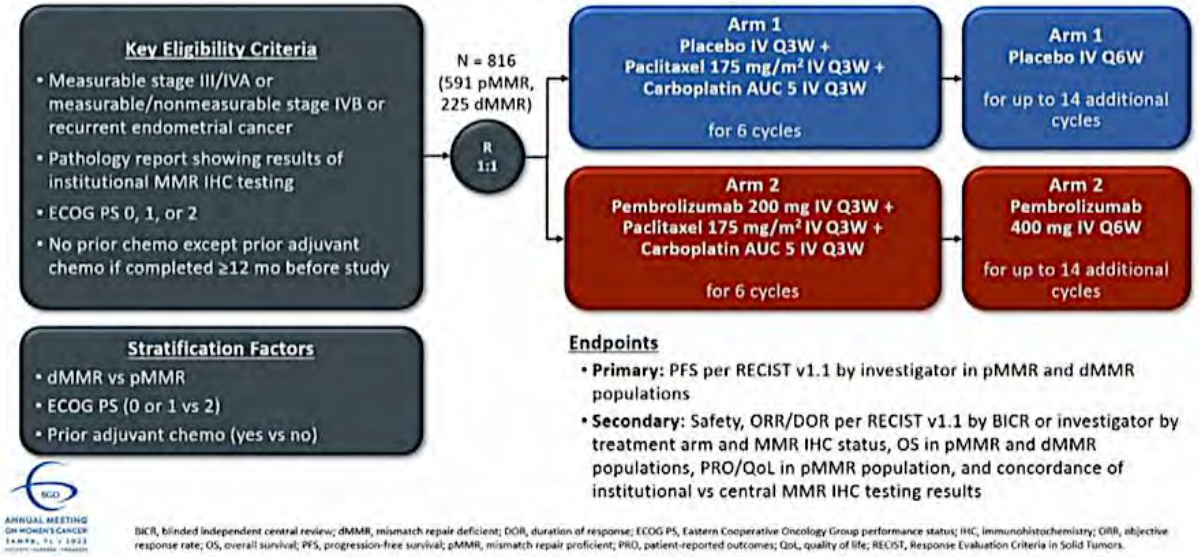


nature medicine

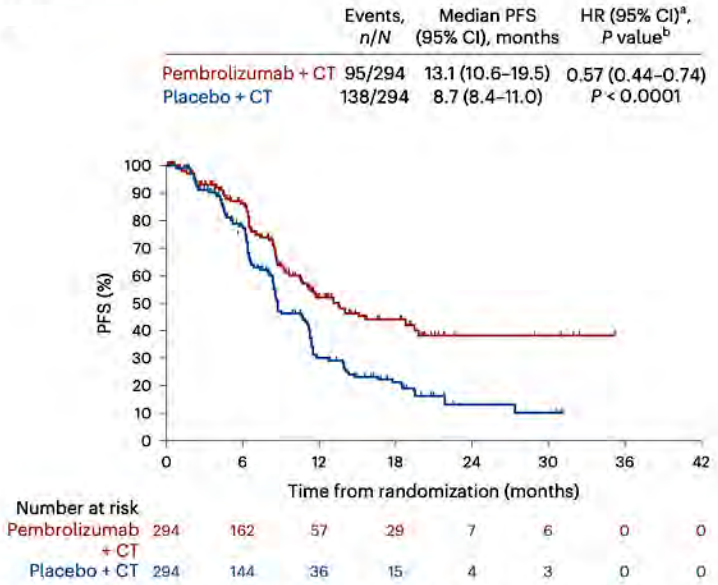
Article

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

Eskander RN et al. Nat Med 2025 May;31(5):1539-46.

Primary endpoint PFS investigator assessed
ITT
pMMR
Median PFS 13.1 (95% CI, 10.6–19.5) vs 8.7 (95% CI, 8.4– 11.0) months
HR pembrolizumab plus chemotherapy (0.57 (95% CI, 0.44– 0.74); P < 0.0001
dMMR
Median PFS NR vs 8.3 (95% CI, 6.5–12.3) months,
HR pembrolizumab plus chemotherapy (0.34 (95% CI, 0.22–0.53); P < 0.0001



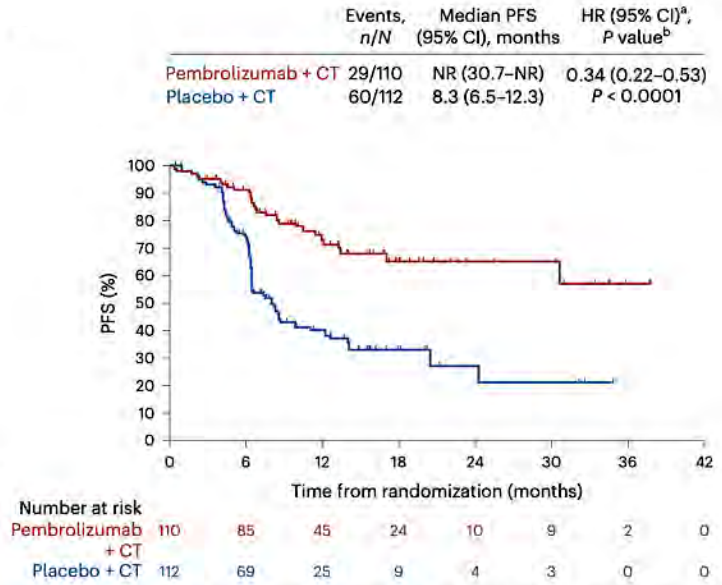


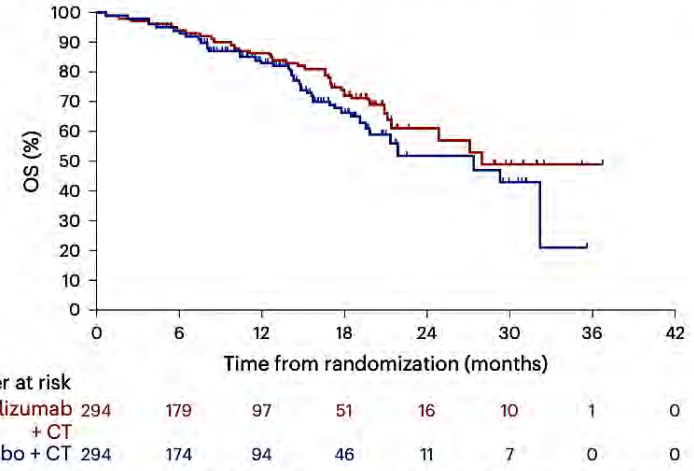
Fig. 2 | Kaplan–Meier-estimated PFS per RECIST v.1.1 as assessed by the investigators at IA. a,b, Kaplan–Meier-estimated PFS per RECIST v.1.1 at IA in the pMMR (**a**) and dMMR (**b**) populations. Tick marks indicate censored data. Data cutoff dates: 6 December 2022 (pMMR); 16 December 2022 (dMMR). [a]Based on a Cox regression model with the Efron method of tie handling with treatment as a covariate stratified by prior chemotherapy. [b]One-sided *P* value based on log-rank test stratified by prior chemotherapy. CT, chemotherapy; NR, not reached; pembro, pembrolizumab.

NRG GY018 OS secondary endpoint (immature)

- Ad hoc analyses (DCO August 2023)
- pMMR (46.8% information) HR 0.80 (95% CI, 0.59–1.08; 1-sided nominal P = 0.0683)
- dMMR (29.3% information) HR 0.57 (95% CI, 0.31–1.04; 1-sided nominal P = 0.0323)

a

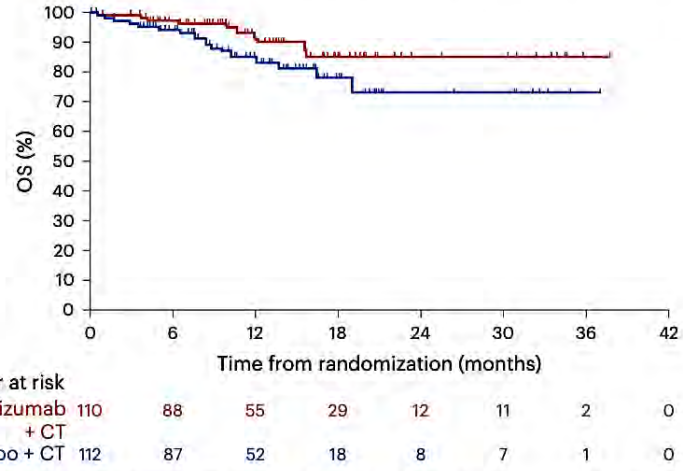
	Events, n/N	Follow-up Duration[a], median (range), months	Median OS (95% CI), months	HR (95% CI)[b], P value[c]
Pembrolizumab + CT	45/294	8.8 (0.1–37.0)	27.96 (21.42–NR)	0.79 (0.53–1.17)
Placebo + CT	54/294	8.4 (0.1–37.2)	27.37 (19.52–NR)	P = 0.1157



Number at risk								
Pembrolizumab + CT	294	179	97	51	16	10	1	0
Placebo + CT	294	174	94	46	11	7	0	0

b

	Events, n/N	Follow-up Duration[a], median (range), months	Median OS (95% CI), months	HR (95% CI)[b], P value[c]
Pembrolizumab + CT	10/110	13.3 (0.6–39.4)	NR (NR–NR)	0.55 (0.25–1.19)
Placebo + CT	17/112	13.7 (1.0–38.0)	NR (NR–NR)	P = 0.0617



Number at risk								
Pembrolizumab + CT	110	88	55	29	12	11	2	0
Placebo + CT	112	87	52	18	8	7	1	0

Fig. 3 | Kaplan–Meier-estimated OS at IA. a,b, Kaplan–Meier-estimated OS in the pMMR (**a**) and dMMR (**b**) populations at interim analysis. OS data were immature (27.2% information fraction for pMMR population (99 of the 364 events needed for final analysis had occurred) and 18.0% information fraction for dMMR population (27 of the 150 events needed for final analysis had occurred)). Tick marks indicate censored data. Data cutoff dates: 6 December 2022 (pMMR); 16 December 2022 (dMMR). [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. [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.

DCO of KM estimates Dec 2022

Eskander RN et al. *Nat Med* 2025 May;31(5):1539-46.

Courtesy of Susana Banerjee, MBBS, MA, PhD

2024 ESMO GYNAECOLOGICAL CANCERS
Annual Congress

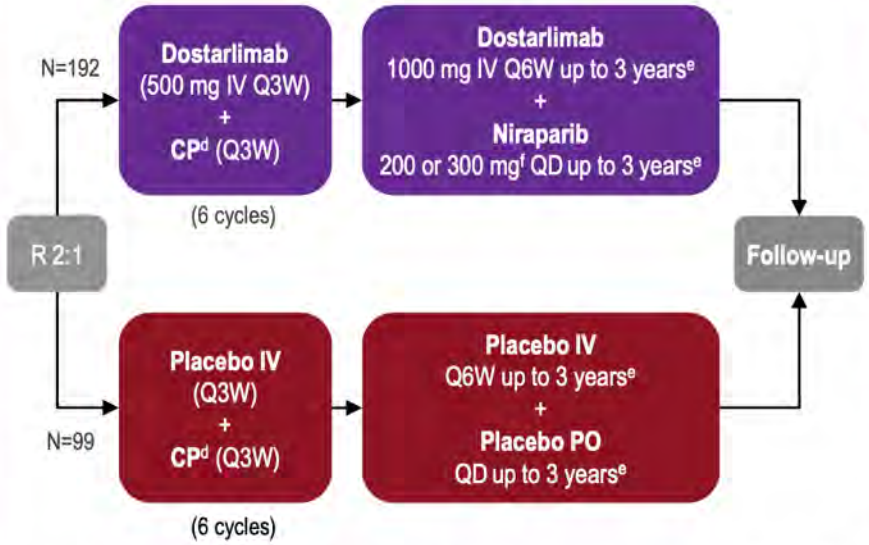
PROGRESSION-FREE SURVIVAL IN PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CANCER IN THE OVERALL AND MISMATCH REPAIR PROFICIENT POPULATIONS AND IN HISTOLOGICAL AND MOLECULAR SUBGROUPS: RESULTS FROM PART 2 OF THE RUBY TRIAL

Mansoor Raza Mirza,[1] Sharad Ghamande,[2] Lars Hanker,[3] Destin Black,[4] Nicoline Raaschou-Jensen,[5] Lucy Gilbert,[6] Ana Oaknin,[7] Angeles Alvarez Secord,[8] Antonella Savarese,[9] Robert Holloway,[10] Rebecca Kristeleit,[11] Joseph Buscema,[12] Ingrid Boere,[13] Sudarshan Sharma,[14] Christine Gennigens,[15] Prafull Ghatage,[16] Kaitlin Yablonski,[17] Shadi Stevens,[18] Hanna Trukhan,[19] Matthew A. Powell[20]

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 PARPi 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.
[a]Histologically/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. [b]Carcinosarcoma, clear cell, serous, or mixed histology permitted (mixed histology containing ≥10% carcinosarcoma, clear cell, or serous histology). [c]Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used when 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. [d]Carboplatin AUC 5 mg/mL/min and paclitaxel 175 mg/m^2. [e]Treatment 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. [f]Dose 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, mismatch repair deficient; DOR, duration of response; EC, endometrial cancer; HRQOL, health-related quality of life; IHC, immunohistochemistry; INV, investigator assessment; IV, intravenously; MMR, mismatch repair; MMRp, mismatch repair proficient; MSI, microsatellite instability, MSI-H, microsatellite instability-high; MSS, microsatellite stable; ORR, objective response rate; OS, overall survival; PARP, poly(ADP-ribose) polymerase inhibitor; 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.

Mirza MR et al. ESMO Gynaecological Cancers Congress 2024;Abstract 38MO.

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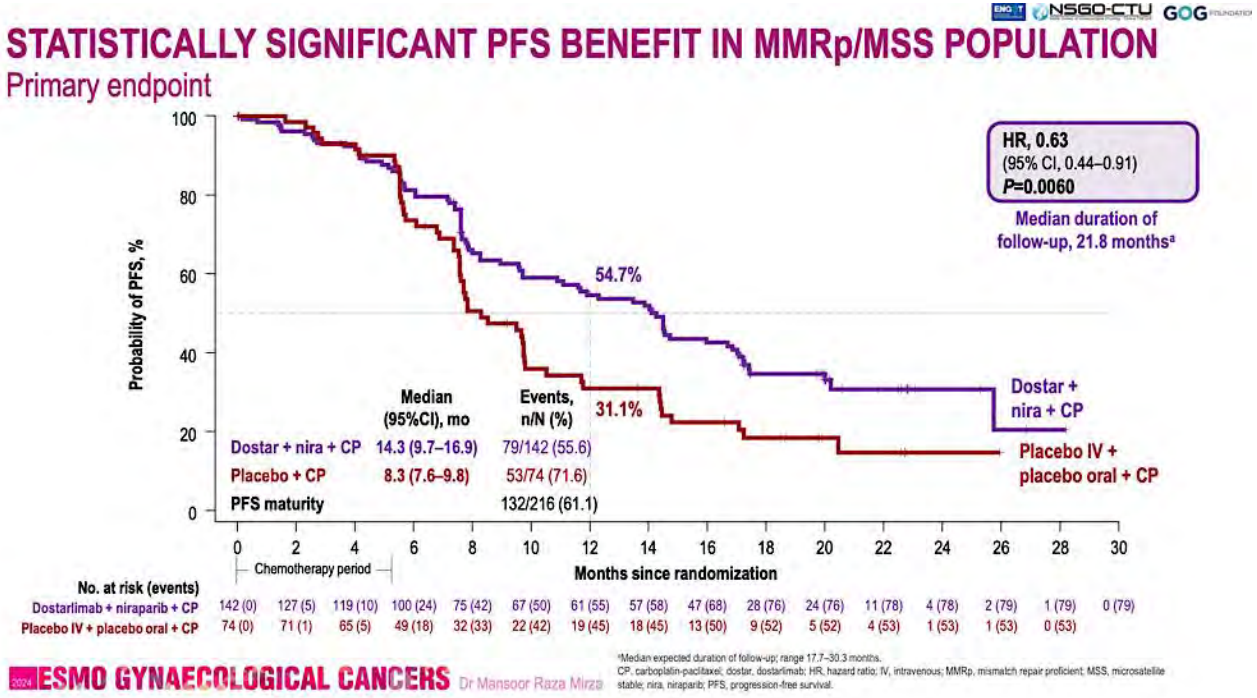
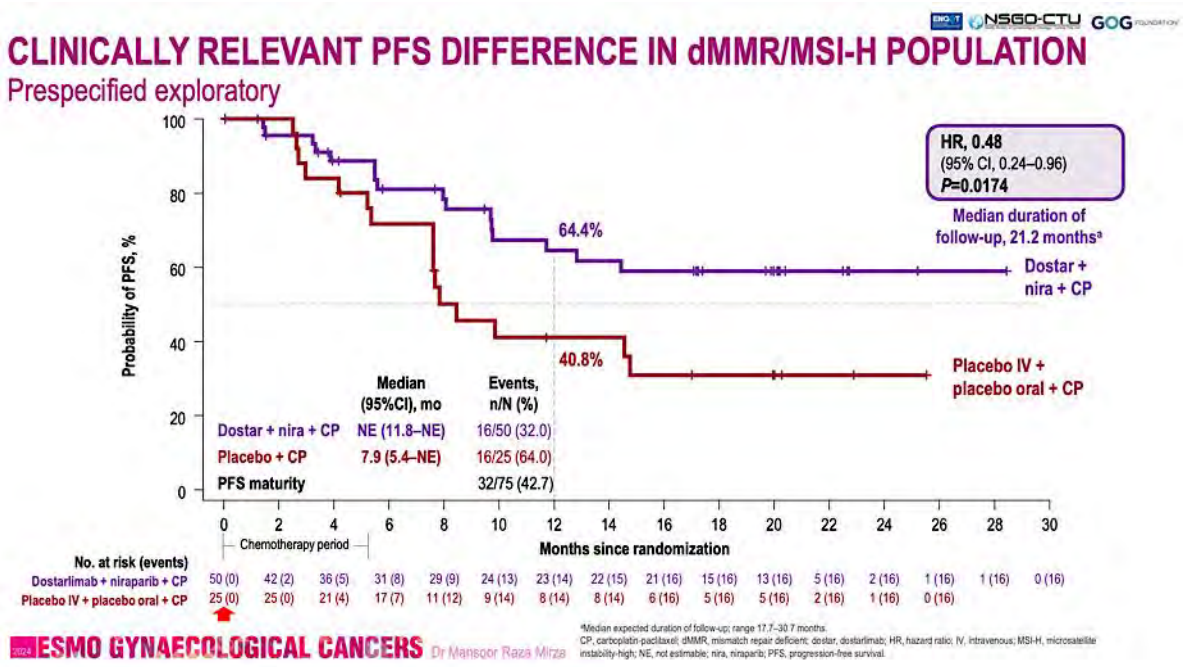
RUBY Trial Part 2: PFS Outcomes





Mirza MR et al. ESMO Gynaecological Cancers Congress 2024;Abstract 38MO.

Courtesy of Susana Banerjee, MBBS, MA, PhD

RUBY Part 2: Role for PARPi?

CONCLUSIONS

- RUBY Part 2 met its primary endpoint, showing significant and clinically meaningful improvement in PFS for dostarlimab + chemotherapy followed by dostarlimab + niraparib in the overall and MMRp/MSS populations
  - The trial is ongoing for OS follow-up
- Improvements in PFS were generally observed in patients treated with dostarlimab + chemotherapy followed by dostarlimab + niraparib across molecular and histology subgroups
- The safety profile observed was generally consistent with the known safety profiles of the individual agents
- These outcomes demonstrate a potential role for PARP inhibitor maintenance in patients receiving dostarlimab + chemotherapy, in particular for MMRp/MSS disease

MMRp, mismatch repair proficient; MSS, microsatellite stable; OS, overall survival; PARP, poly(ADP-ribose) polymerase; PFS, progression-free survival.

2024 ESMO GYNAECOLOGICAL CANCERS Dr Manoor Raza Mirza

No Dostarlimab alone arm
What is the magnitude of benefit with Addition of niraparib?

RUBY part 1 PFS HR (95% CI, 0.16–0.50) (NEJM 2023)
dMMR/MSI-H 0.28
Overall 0.64 (95% CI, 0.51–0.80)
pMMR/MSS 0.76 (95% CI (0.59-0.98)

Mirza MR et al. ESMO Gynaecological Cancers Congress 2024;Abstract 38MO.

Courtesy of Susana Banerjee, MBBS, MA, PhD

DUO-E met its dual primary endpoints

Randomized, placebo-controlled, double-blind study[1]

Patients

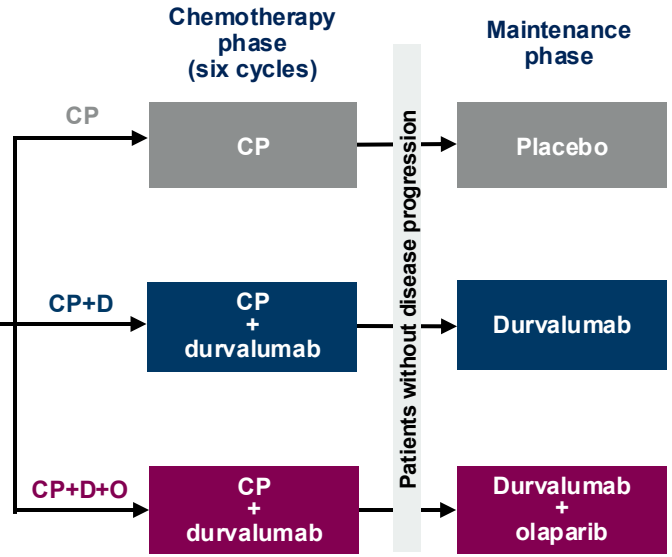
- Newly diagnosed Stage III/IV or recurrent endometrial cancer
- Known MMR status
- Naïve to first-line systemic anticancer treatment
- Naïve to PARP inhibitors and immune-mediated therapy
- All histologies except sarcomas

N=718

R 1:1:1

Stratified by:

- MMR status (proficient vs deficient)
- Disease status (recurrent vs newly diagnosed)
- Geographic region (Asia vs non-Asia)



Treatment until disease progression, unacceptable toxicity, or other discontinuation criteria were met

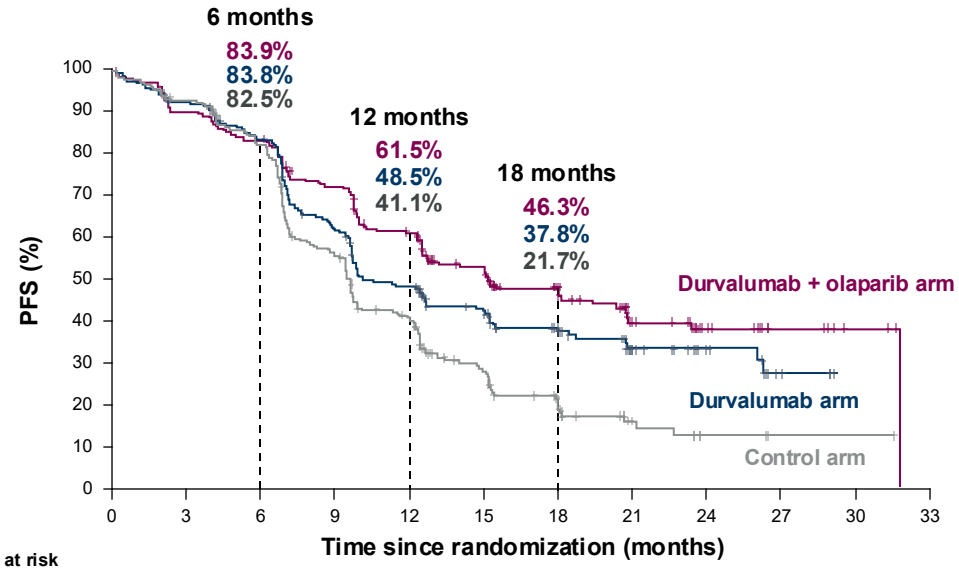
Endpoints

Primary (ITT): PFS (RECIST per investigator) in CP+D versus CP and CP+D+O versus CP

Secondary (ITT): OS (key secondary) and safety

Prespecified exploratory analyses: subpopulation analyses of PFS by MMR status

ITT population: PFS – primary endpoints



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

	Control arm (N=241)	Durvalumab arm (N=238)	Durvalumab + olaparib 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 control		**0.71** (0.57–0.89); **p=0.003**	**0.55** (0.43–0.69); **p<0.0001**

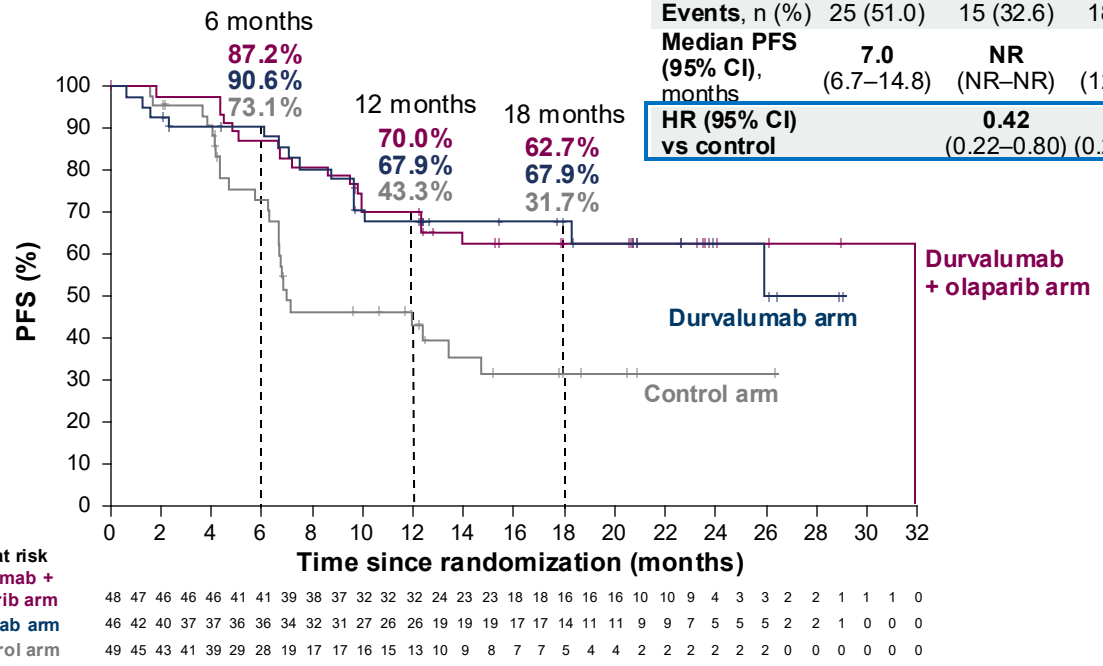
CI, confidence interval; CP, carboplatin + paclitaxel; D, durvalumab; HR, hazard ratio; ITT, intent to treat; MMR, mismatch repair; O, olaparib; OS, overall survival; PARP, poly(ADP-ribose) polymerase; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Westin SN, et al. *J Clin Oncol* 2024;42:283–99. Kaplan–Meier figure borrowed with permission from Westin SN, et al. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: the phase III DUO-E trial. *J Clin Oncol* 2024;42:283–99: https://ascopubs.org/doi/full/10.1200/JCO.23.02132.

DUO-E: PFS based on mismatch repair status

PFS in the dMMR subpopulation

	Control (N=49)	D arm (N=46)	D+O arm (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)



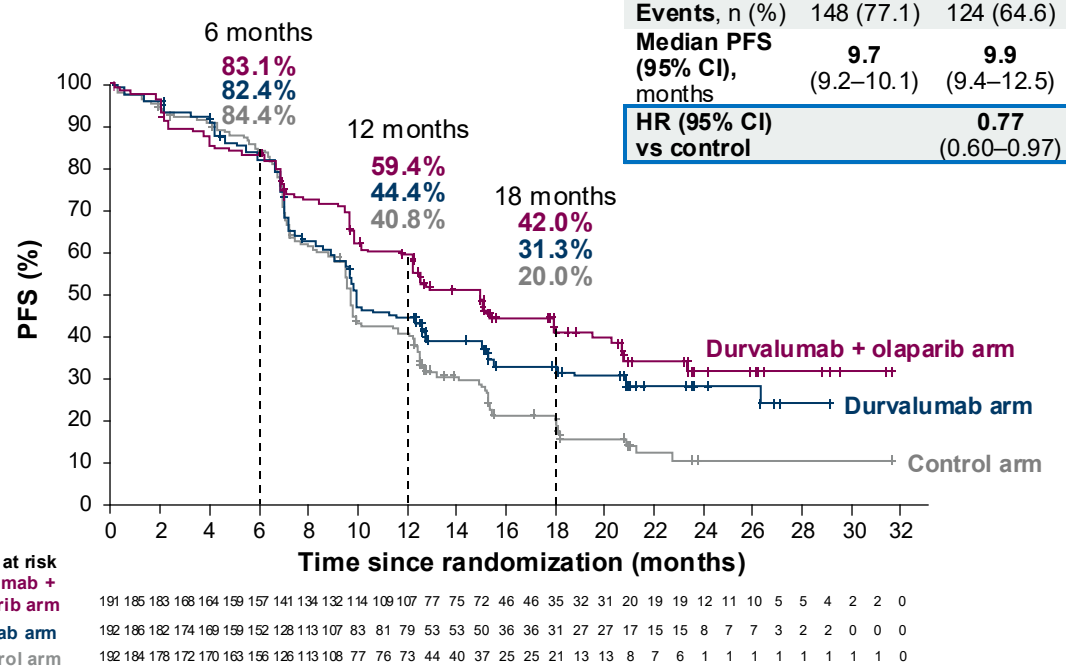
No. at risk

Durvalumab + olaparib arm	48	47	46	46	46	41	41	39	38	37	32	32	32	24	23	23	18	18	16	16	16	10	10	9	4	3	3	2	2	1	1	1	0
Durvalumab arm	46	42	40	37	37	36	36	34	32	31	27	26	26	19	19	19	17	17	14	11	11	9	9	7	5	5	5	2	2	1	0	0	0
Control arm	49	45	43	41	39	29	28	19	17	17	16	15	13	10	9	8	7	7	5	4	4	2	2	2	2	2	2	0	0	0	0	0	0

- The greatest benefit with CP + durvalumab versus CP was in the dMMR subpopulation[1]

PFS in the pMMR subpopulation

	Control (N=192)	D arm (N=192)	D+O arm (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)



No. at risk

Durvalumab + olaparib arm	191	185	183	168	164	159	157	141	134	132	114	109	107	77	75	72	46	46	35	32	31	20	19	19	12	11	10	5	5	4	2	2	0
Durvalumab arm	192	186	182	174	169	159	152	128	113	107	83	81	79	53	53	50	36	36	31	27	27	17	15	15	8	7	7	3	2	2	0	0	0
Control arm	192	184	178	172	170	163	156	126	113	108	77	76	73	44	40	37	25	25	21	13	13	8	7	6	1	1	1	1	1	1	1	1	0

- In the pMMR subpopulation, the addition of olaparib further enhanced the PFS benefit[1]

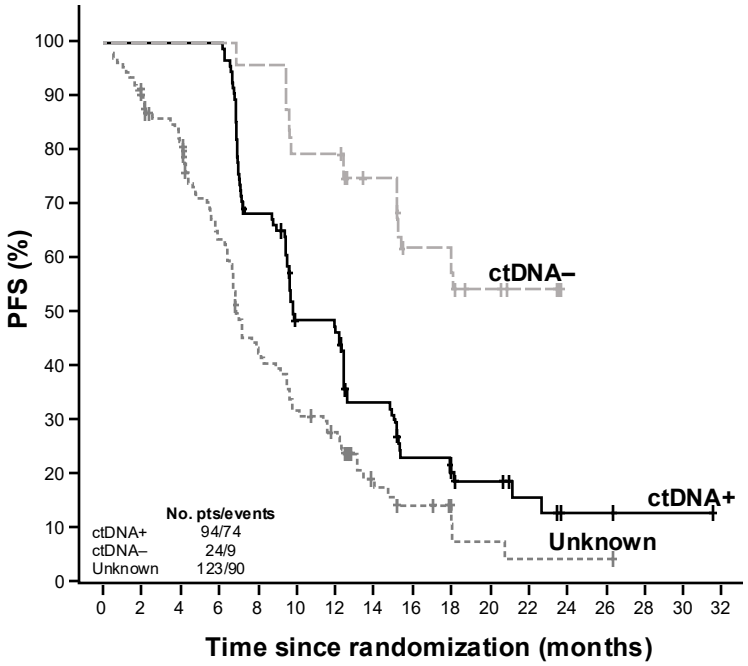
Here, we present post hoc exploratory longitudinal circulating tumor (ct)DNA analyses

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

DUO-E: PFS rate by treatment and baseline ctDNA status in the ITT population

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

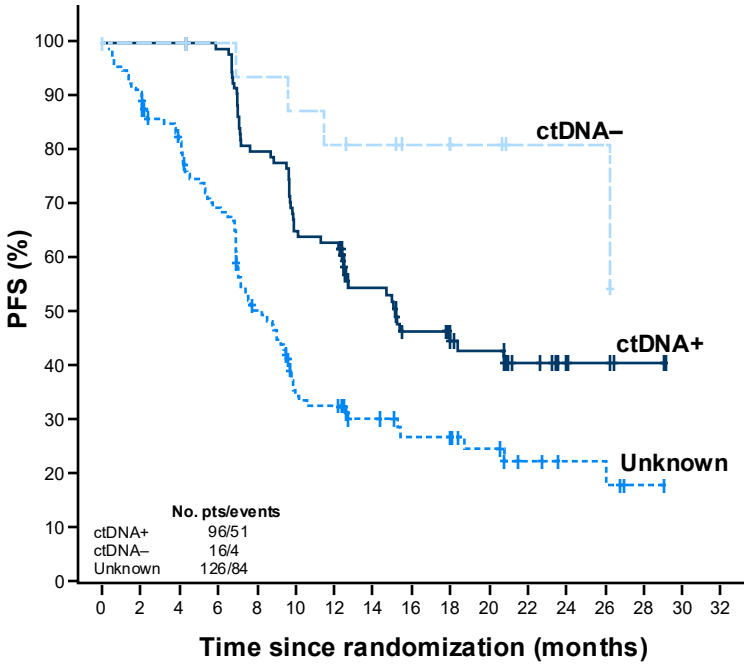
CP arm



No. at risk

ctDNA+	94	94	94	94	63	42	41	26	17	14	10	5	2	2	1	1	0
ctDNA–	24	24	24	24	23	19	19	12	8	8	5	3	0	0	0	0	0
Unknown	123	103	91	66	44	32	26	11	7	4	2	1	1	1	0	0	0

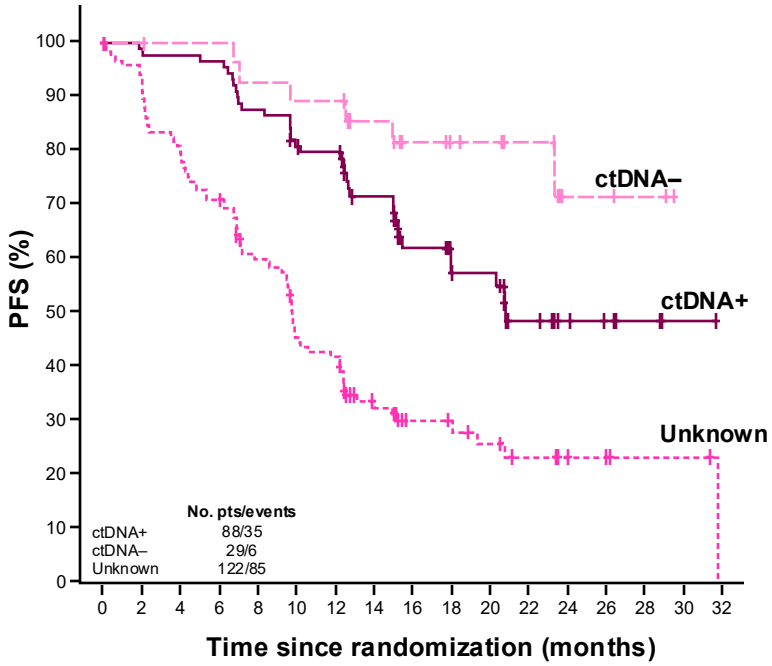
CP+D arm



No. at risk

ctDNA+	96	95	95	93	75	61	59	41	29	24	22	14	5	4	2	0	0
ctDNA–	16	16	16	16	15	14	13	11	8	7	5	3	3	3	0	0	0
Unknown	126	111	95	79	55	35	33	20	16	14	11	7	5	5	2	0	0

CP+D+O arm

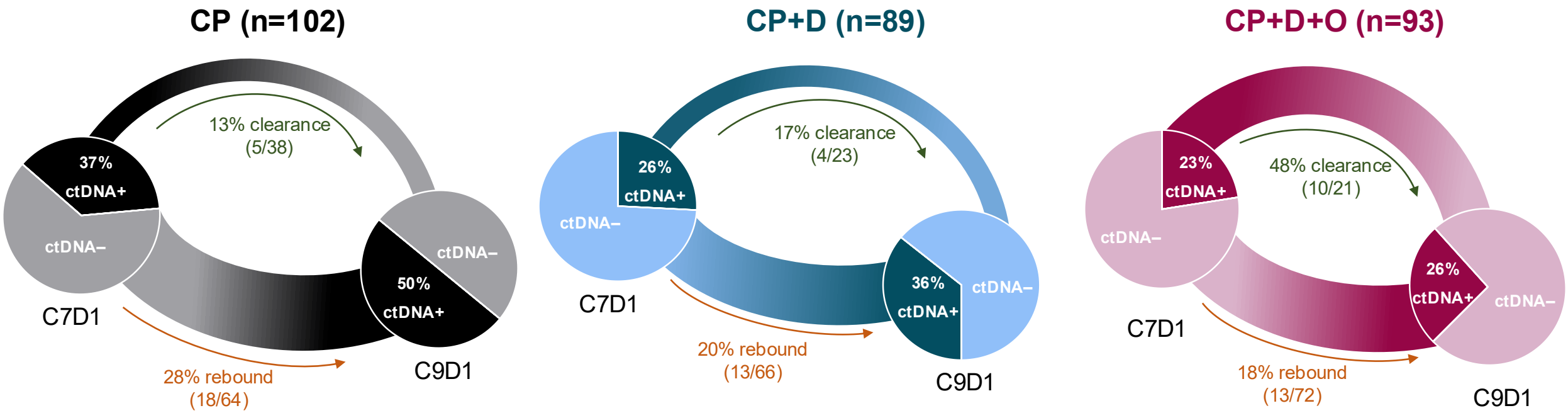


No. at risk

ctDNA+	88	87	86	85	77	70	67	49	32	23	23	12	7	5	3	1	0
ctDNA–	29	29	28	28	26	25	25	21	17	14	13	9	4	4	2	0	0
Unknown	122	113	96	85	69	51	47	28	15	14	11	8	5	4	2	2	0

DUO-E: durvalumab and olaparib mediated ctDNA changes during the maintenance phase (C7D1–C9D1) in pMMR patients

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



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

Key takeaway points

Baseline ctDNA positivity in DUO-E was associated with increased risk of progression in all treatment arms

Addition of durvalumab was associated with rapid reductions in ctDNA detection during chemotherapy phase and less rebound of ctDNA during maintenance phase compared with chemotherapy alone

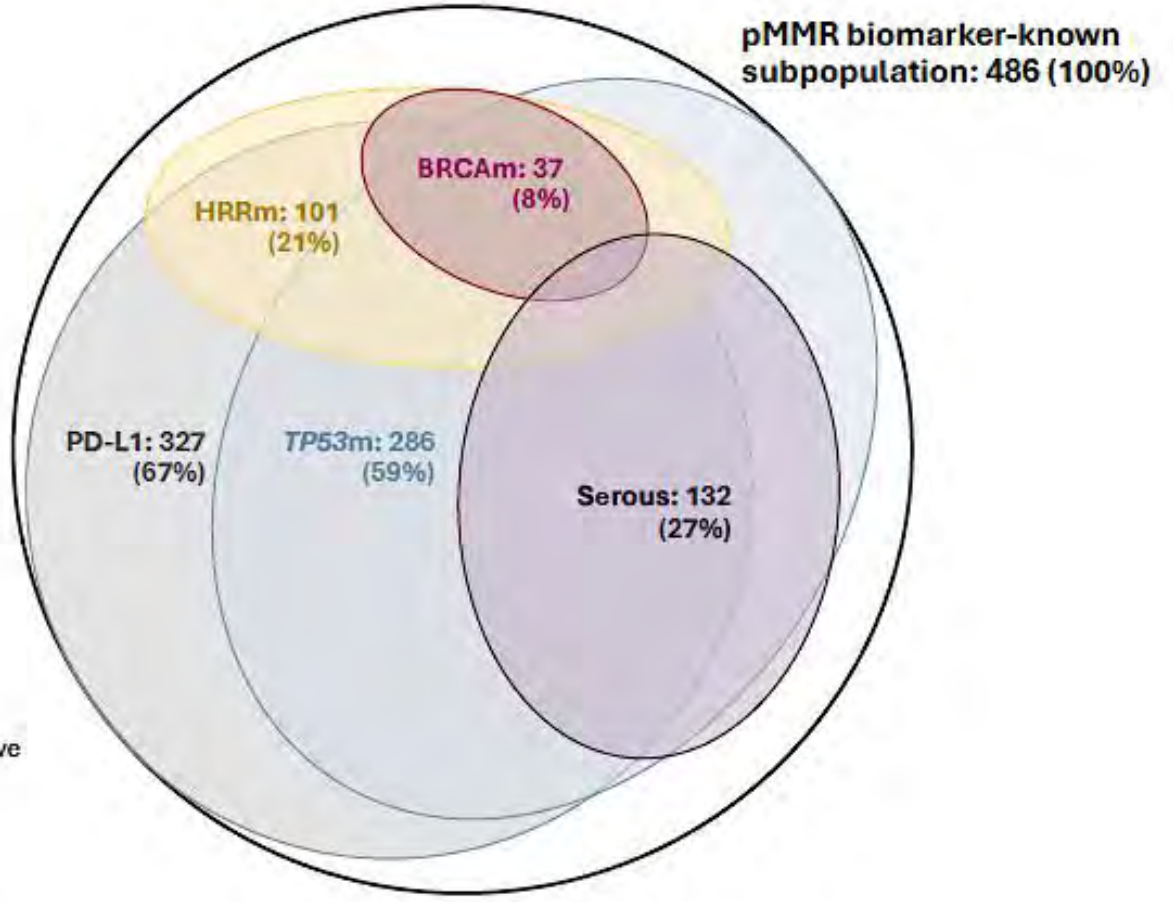
Addition of maintenance olaparib was associated with additional ctDNA clearance, resulting in a further reduction of detectable ctDNA in patients with pMMR tumors

DUO-E Mismatch Repair-Proficient (pMMR) Subpopulation: Coprevalence of Biomarkers

The pMMR biomarker-known (n=486) subpopulation was heterogeneous, with a frequent overlap of biomarkers:

- 84% of patients were positive for one or more biomarkers
- PD-L1 positive and *TP53*m were the most prevalent biomarkers

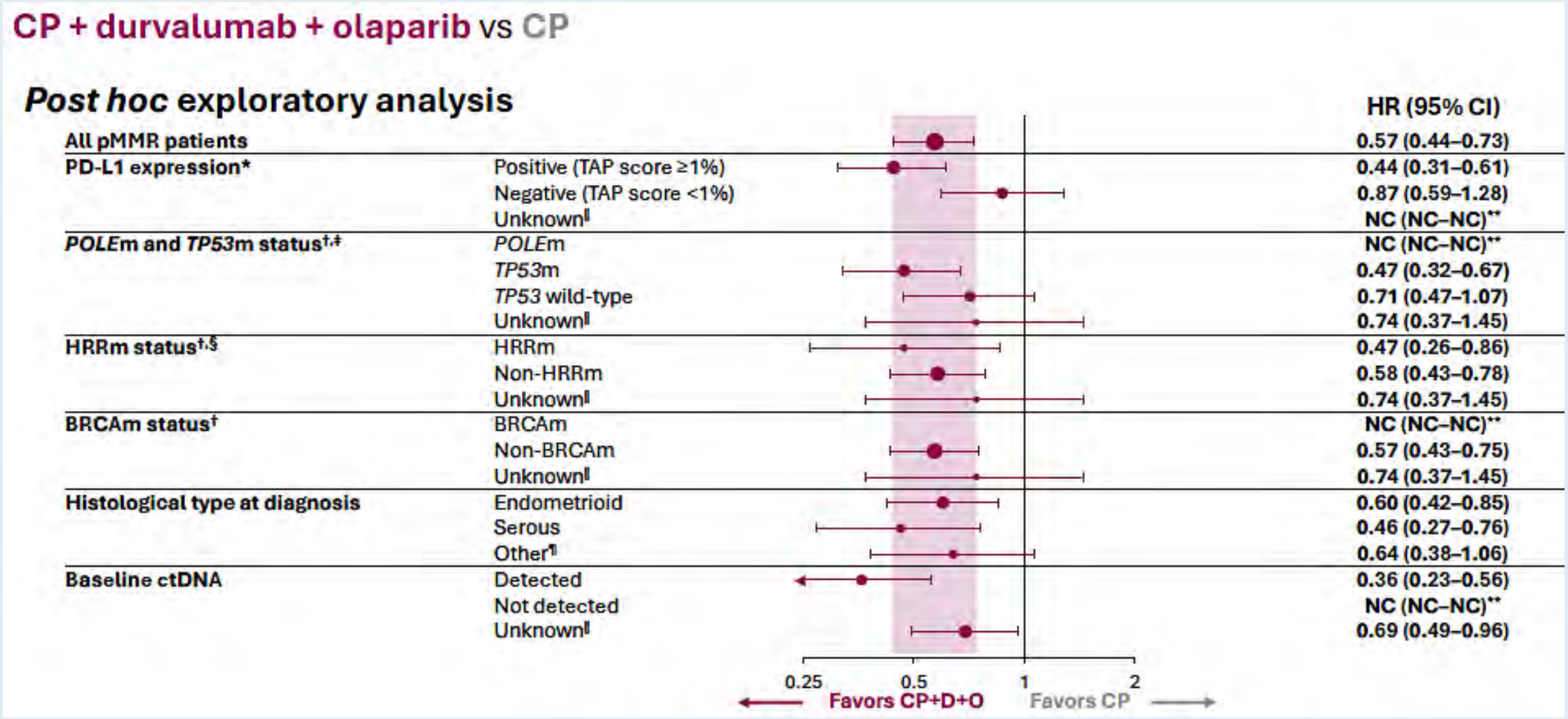
	PD-L1 positive	*TP53*m	HRRm	BRCAm	*POLE*m	Serous
PD-L1 positive	67%	44%	16%	6%	2%	20%
*TP53*m	44%	59%	14%	6%	2%	24%
HRRm	16%	14%	21%	8%	2%	6%
BRCAm	6%	6%	8%	8%	1%	3%
*POLE*m	2%	2%	2%	1%	2%	0%
Serous	20%	24%	6%	3%	0%	27%



Venn illustrates the overlap for key biomarker populations but does not show a complete set of all overlapping populations.
Venn includes 11 patients with a *POLE*m; biomarker overlap in this subgroup is not shown. Aggregate results (tissue + ctDNA) are used for HRRm, *TP53*m and BRCAm.

Moore K et al. SGO 2025;Abstract 922975.

DUO-E pMMR Subpopulation: PFS by Biomarker Subgroup



Moore K et al. SGO 2025;Abstract 922975.

Year in Review:
Management of Gynecologic Cancers

INTRODUCTION: Tale of Two Cities — ASCO 2025

MODULE 1: Ovarian Cancer

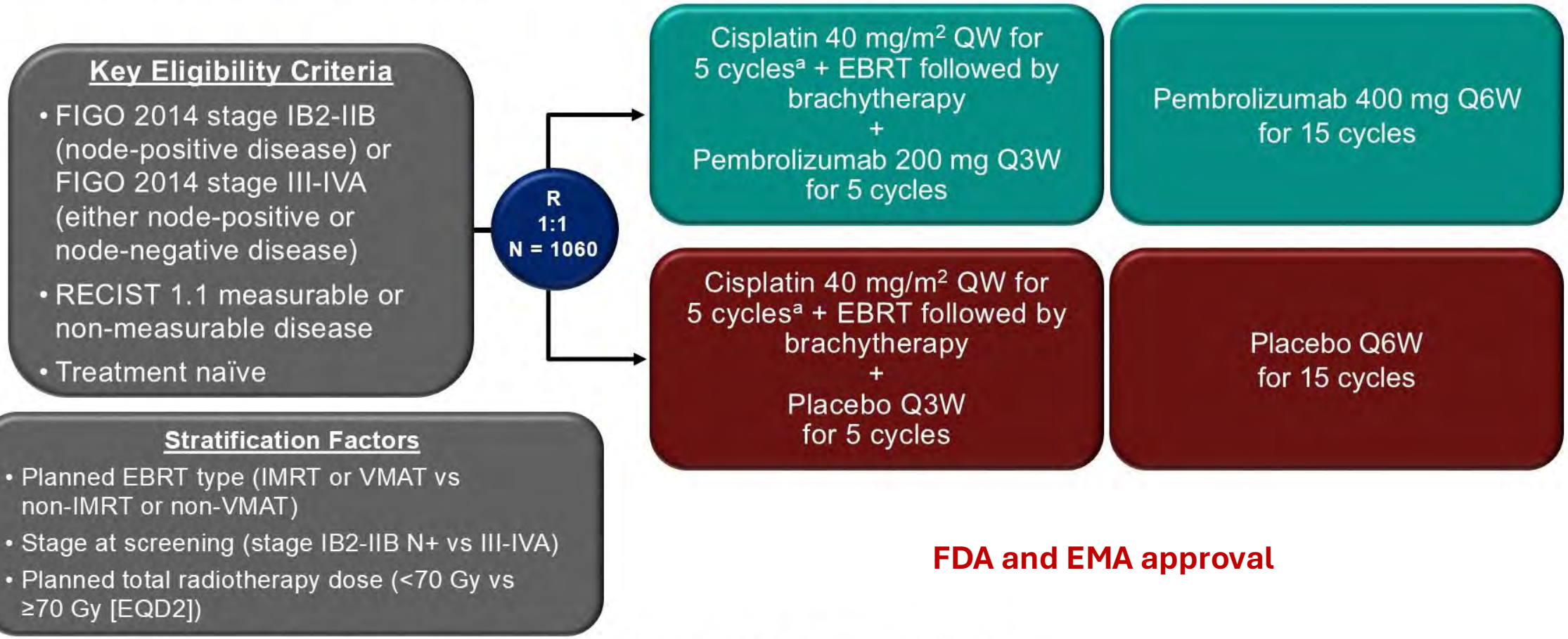
MODULE 2: HER2-Positive Gynecologic Cancers

MODULE 3: Endometrial Cancer

MODULE 4: Cervical Cancer

RTP Year in Review 2025

ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study



FDA and EMA approval

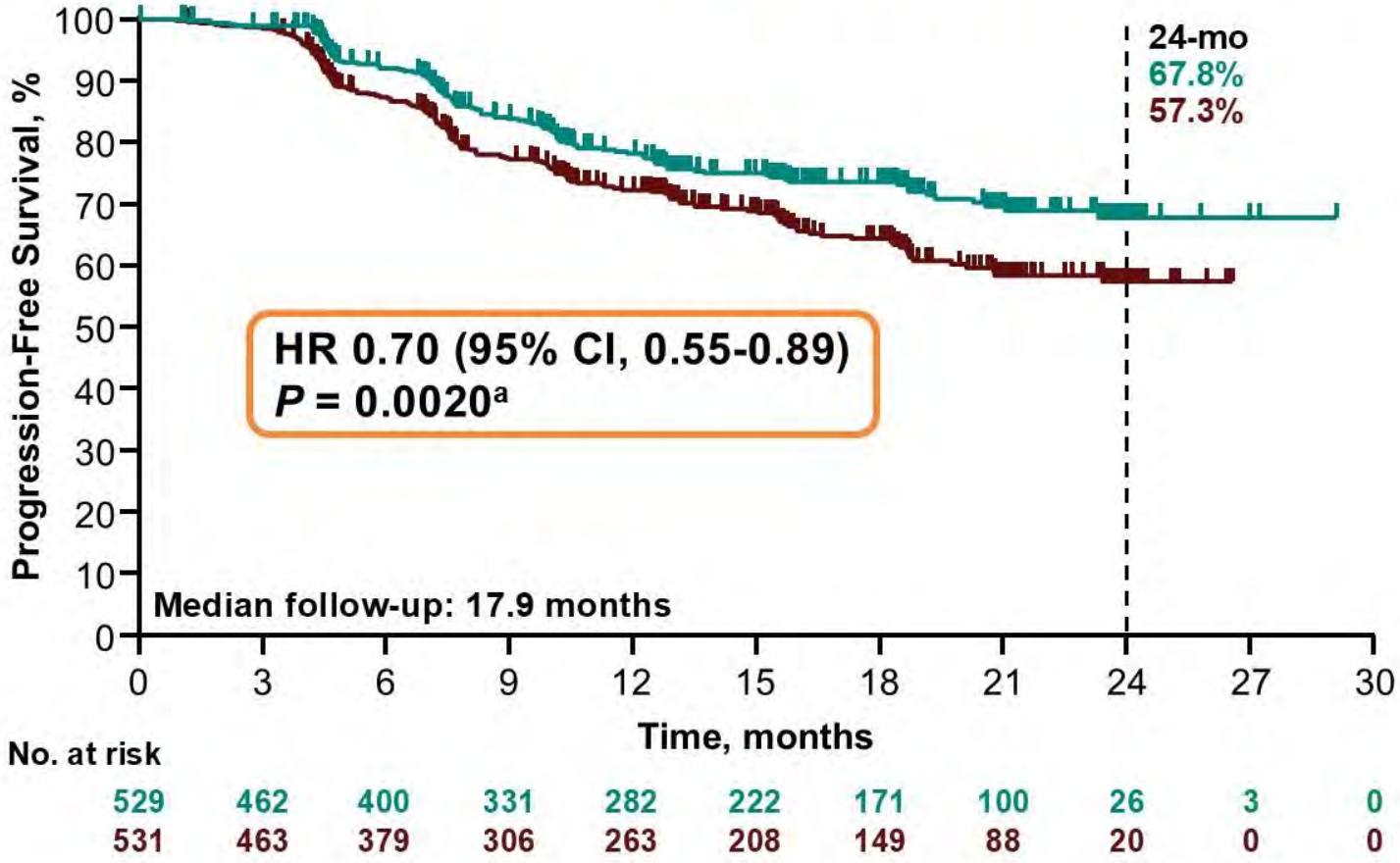
[a]A 6th cycle was allowed per investigator discretion. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

Duska LR et al. ASCO 2025;Abstract LBA5504.

Courtesy of Susana Banerjee, MBBS, MA, PhD

KEYNOTE-A18

Primary Endpoint: Progression-Free Survival at Interim Analysis 1



	Pts w/ Event	Pts Censored
Pembro Arm	21.7%	78.3%
Placebo Arm	29.0%	71.0%

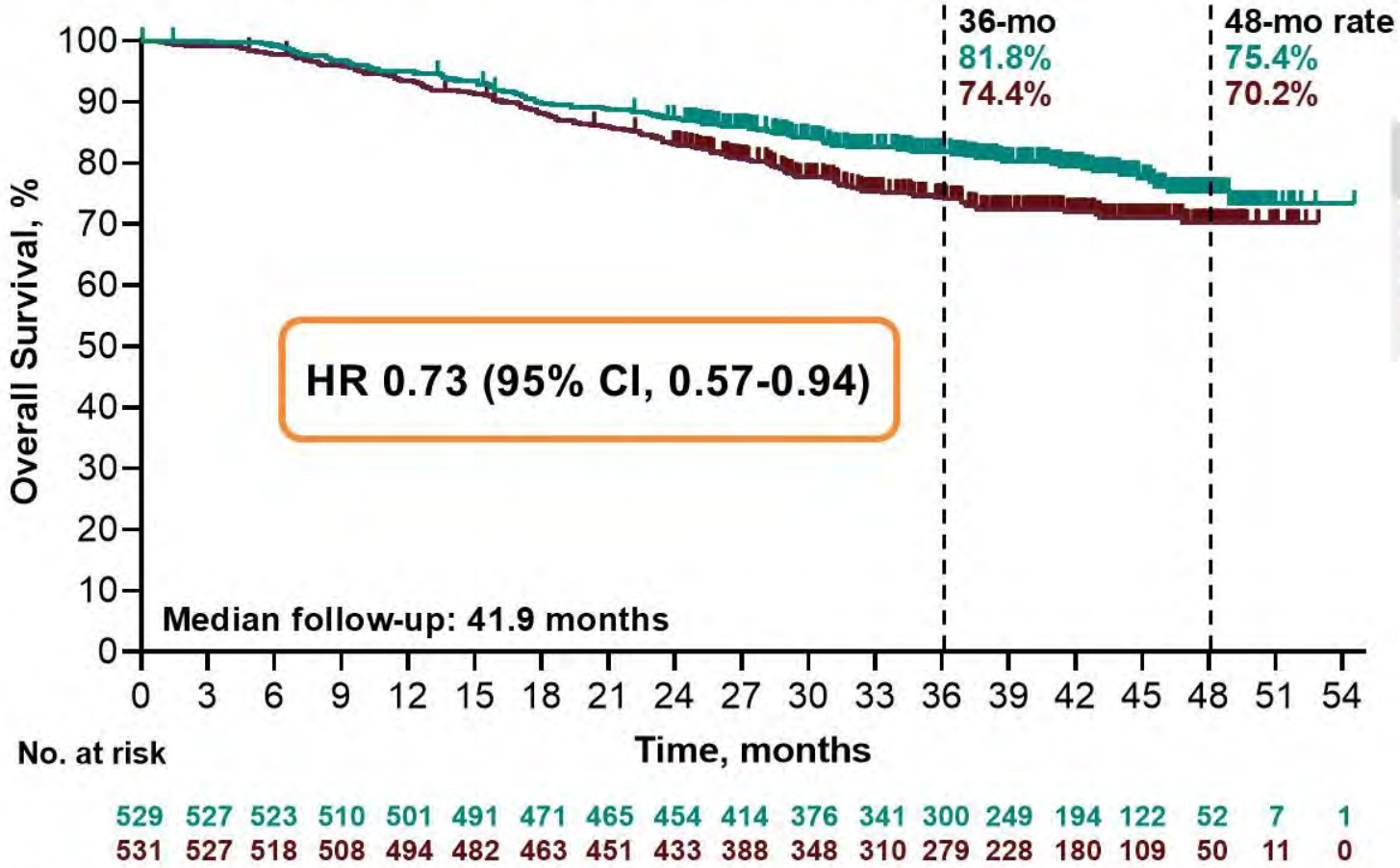
[a]With 269 events (88.5% information fraction), the observed *P* = 0.0020 (1-sided) crossed the prespecified nominal boundary of 0.0172 (1-sided) at this planned first interim analysis.

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. Data cutoff date: January 9, 2023.

Duska LR et al. ASCO 2025;Abstract LBA5504.

Courtesy of Susana Banerjee, MBBS, MA, PhD

KEYNOTE-A18
Descriptive Overall Survival at Final Analysis



	Pts w/ Event	Pts Censored
Pembro Arm	20.2%	79.8%
Placebo Arm	26.4%	73.6%

Data cutoff date: January 7, 2025.

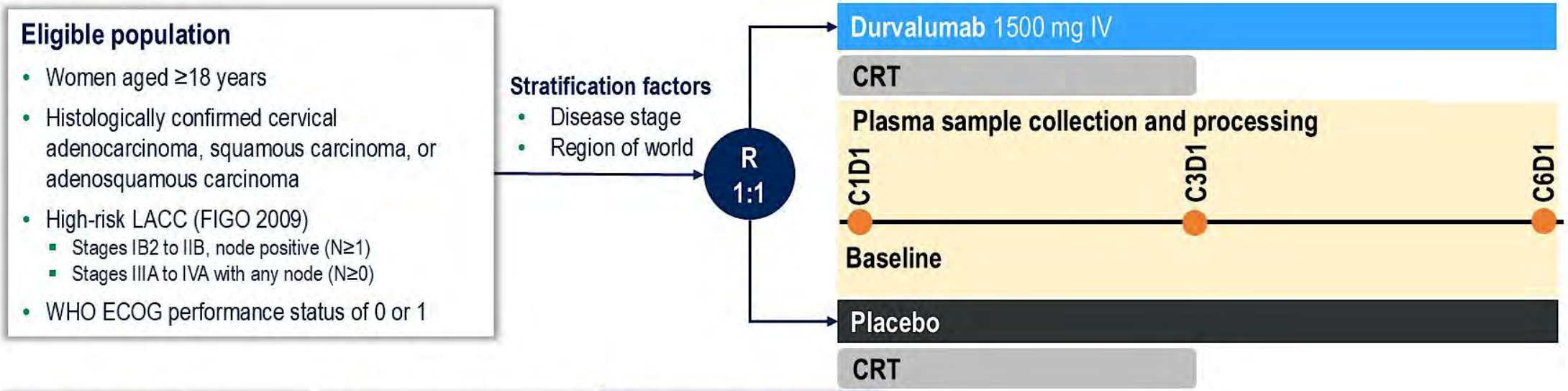
2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Linda R. Duska

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Duska LR et al. ASCO 2025;Abstract LBA5504.

Courtesy of Susana Banerjee, MBBS, MA, PhD

CALLA Study Design



Here, we present an analysis of the association of ultrasensitive ctDNA detection with relapse and survival

2025 ASCO ANNUAL MEETING #ASCO25

CALLA NCT03830866. C, cycle; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; ECOG, Eastern Cooperative Oncology Group; FIGO; Fédération Internationale de Gynécologie et d'Obstétrique; IV, intravenous; LACC, locally advanced cervical cancer; PD-L1, programmed death ligand-1; PFS, progression-free survival; R, randomization.

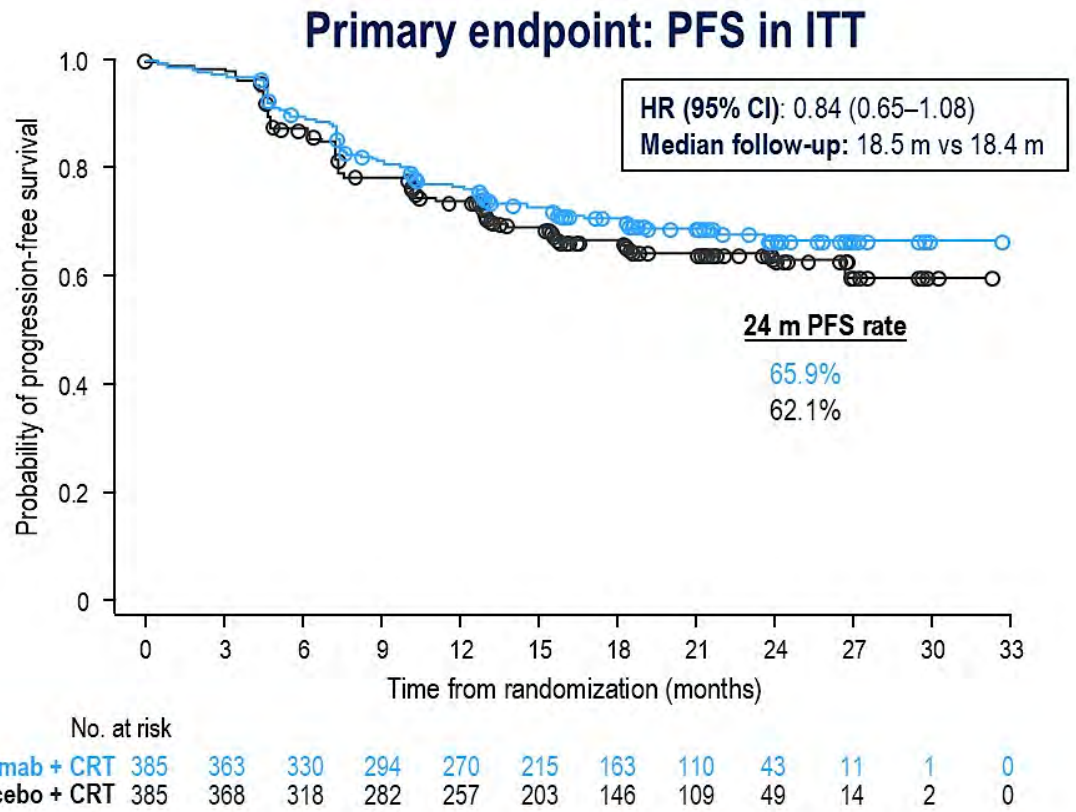
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Mayadev J et al. ASCO 2025;Abstract 5502.

Courtesy of Susana Banerjee, MBBS, MA, PhD

CALLA Study Background

- CALLA did not show a statistically significant improvement in PFS for durvalumab + CRT vs CRT alone in a biomarker unselected LACC population[1]
  - *Post hoc* analyses showed a PFS benefit with durvalumab + CRT vs CRT for patients with PD-L1 TAP ≥20%[1]
- 30–50% of patients with LACC have recurrent disease within 5 years after standard of care CRT[1]
  - ctDNA has shown promise as a prognostic marker of relapse in cervical cancer[2–5]



CALLA NCT03830866. Monk BJ, et al. *Lancet Oncol*. 2023;24:1334-1348. CI, confidence interval; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; HR, hazard ratio; ITT, intent to treat; LACC, locally advanced cervical cancer; m, months; PD-L1, programmed death ligand-1; PFS, progression-free survival; TAP, tumor area positivity.

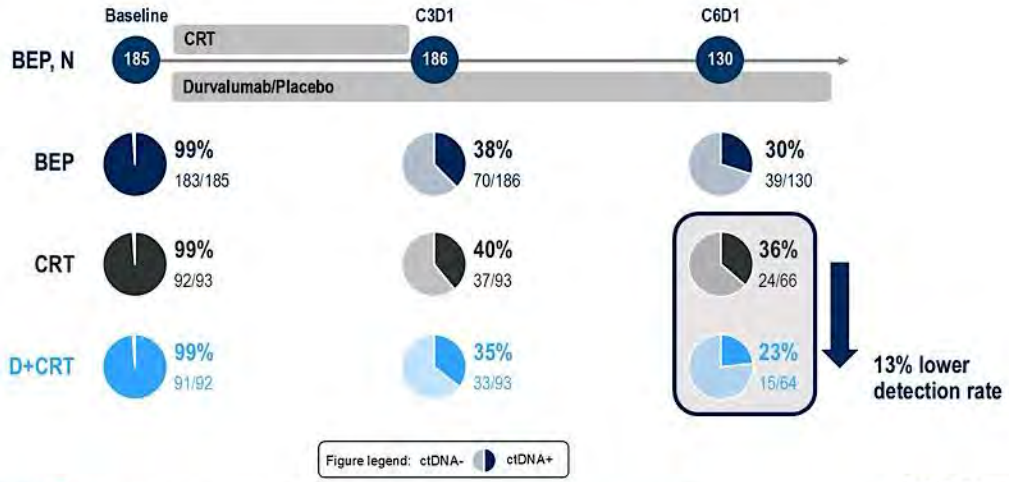
1. Monk BJ, et al. *Lancet Oncol*. 2023;24:1334-1348; 2. Han K, et al. *J Clin Oncol*. 2024;42:431-440; 3. Jeannot E, et al. *Clin Cancer Res*. 2021;27:5869-5877; 4. Li L, et al. *Cancer Cell Int*. 2023;23:329; 5. Williams JR, et al. *J Clin Oncol*. 2022;40(Suppl 16).

Mayadev J et al. ASCO 2025;Abstract 5502.

Courtesy of Susana Banerjee, MBBS, MA, PhD

CALLA: ctDNA Detection Rates

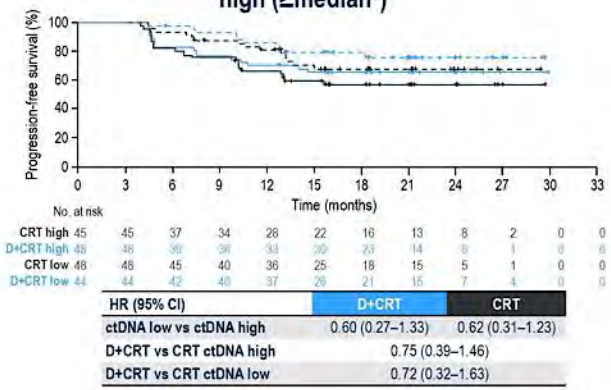
ctDNA+ rates decreased after treatment and appeared lower with D+CRT vs CRT at C6D1



BEP, biomarker evaluable population; C, cycle; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; D+CRT, durvalumab + chemoradiotherapy

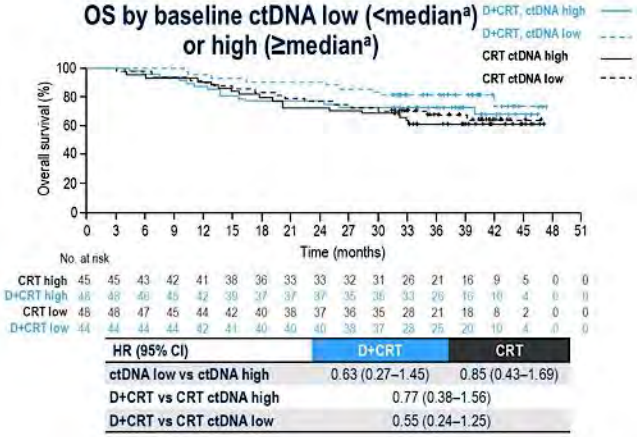
CALLA Baseline: Low ctDNA Was Associated With Reduced Risk of Progression and Death

PFS by baseline ctDNA low (<median[a]) or high (≥median[a])



HR (95% CI)	D+CRT	CRT
ctDNA low vs ctDNA high	0.60 (0.27–1.33)	0.62 (0.31–1.23)
D+CRT vs CRT ctDNA high	0.75 (0.39–1.46)	
D+CRT vs CRT ctDNA low	0.72 (0.32–1.63)	

OS by baseline ctDNA low (<median[a]) or high (≥median[a])



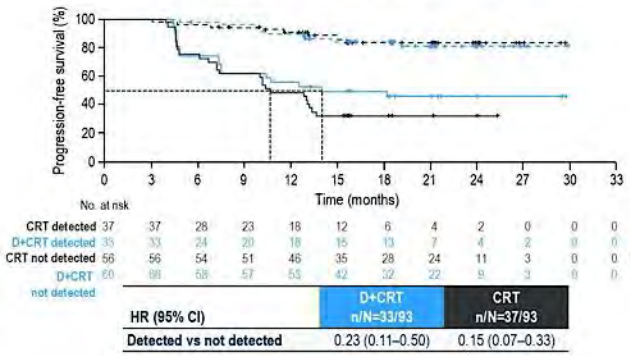
HR (95% CI)	D+CRT	CRT
ctDNA low vs ctDNA high	0.63 (0.27–1.45)	0.85 (0.43–1.69)
D+CRT vs CRT ctDNA high	0.77 (0.38–1.56)	
D+CRT vs CRT ctDNA low	0.55 (0.24–1.25)	

[a]Median was 5268.2 ppm. Median set globally based on parts per million values from all samples across arms. PFS data cutoff January 20, 2022. OS data cutoff July 3, 2023.
BEP, biomarker evaluable population; CI, confidence interval; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D+CRT, durvalumab + chemoradiotherapy; HR, hazard ratio; OS, overall survival; PFS, progression-free survival

CALLA Post-CRT: ctDNA+ Was a Negative Prognostic Factor for PFS and OS

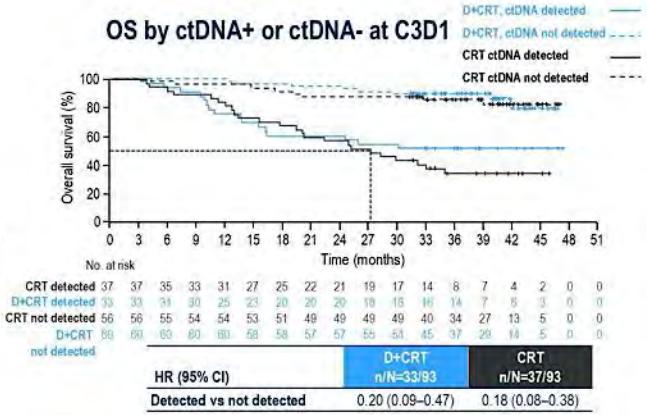
Risk was independent of treatment arm

PFS by ctDNA+ or ctDNA- at C3D1



HR (95% CI)	D+CRT n/N=33/93	CRT n/N=37/93
Detected vs not detected	0.23 (0.11–0.50)	0.15 (0.07–0.33)

OS by ctDNA+ or ctDNA- at C3D1



HR (95% CI)	D+CRT n/N=33/93	CRT n/N=37/93
Detected vs not detected	0.20 (0.09–0.47)	0.18 (0.08–0.38)

PFS data cutoff January 20, 2022. OS data cutoff July 3, 2023.
C, cycle; CI, confidence interval; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; D+CRT, durvalumab + chemoradiotherapy; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

Mayadev J et al. ASCO 2025;Abstract 5502.

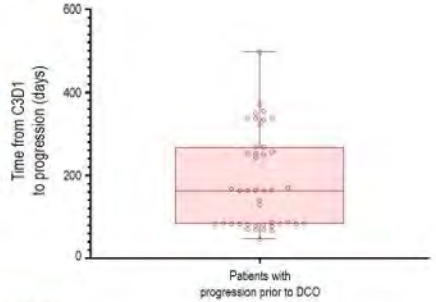
CALLA Post-CRT: 68% of Patients With ctDNA Detection at C3D1 Subsequently Progressed

ctDNA detection preceded progression by up to 497 days

Predictive value of ctDNA detection at C3D1[a]

	Progressed	Not progressed
ctDNA detected	43	27
ctDNA not detected	20	95

PPV = 61%
NPV = 83%
Sensitivity = 68%
Specificity = 78%



- 68% of patients with ctDNA detection at C3D1 progressed prior to DCO
- 83% of patients with no ctDNA detection at C3D1 had not progressed by the time of DCO
- Median (range) lead time between C3D1 ctDNA detection and progression was 164 (46–497) days

[a]Assessed in patients who had not progressed by, and were evaluable for ctDNA, at the given time point, and for whom subsequent progression status was available.
C, cycle; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; DCO, data cutoff; NPV, negative predictive value; PPV, positive predictive value

Courtesy of Susana Banerjee, MBBS, MA, PhD

Conclusions

- This preplanned exploratory ctDNA analysis of a large, global LACC population from CALLA demonstrates the high sensitivity of a personalized assay for ctDNA detection
- **Risk of progression and death were reduced by at least 95% in both treatment arms for patients with no ctDNA detected at C6D1**
  - Baseline high ctDNA level (≥ median) was associated with higher risk of progression and death
  - Continued detection of ctDNA following CRT was independently prognostic of outcome
  - Post-CRT ctDNA+ was associated with subsequent progression and was detected up to 497 days earlier than by scan
- Post-CRT, the difference in ctDNA detection between the durvalumab + CRT and CRT arms was greatest in the PD-L1 TAP ≥20% subgroup

This analysis supports the potential utility of ultrasensitive tumor-informed ctDNA analysis to help guide treatment decisions in LACC in the future

C, cycle; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; LACC, locally advanced cervical cancer; PD-L1, programmed death ligand-1; TAP, tumor area positivity.

High baseline ctDNA levels were associated with increased risk of progression and death

Undetectable ctDNA after treatment correlated with reduced risk of progression and death

Next steps:
Integrating prospectively in to clinical Trials?

Mayadev J et al. ASCO 2025;Abstract 5502.

Courtesy of Susana Banerjee, MBBS, MA, PhD

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

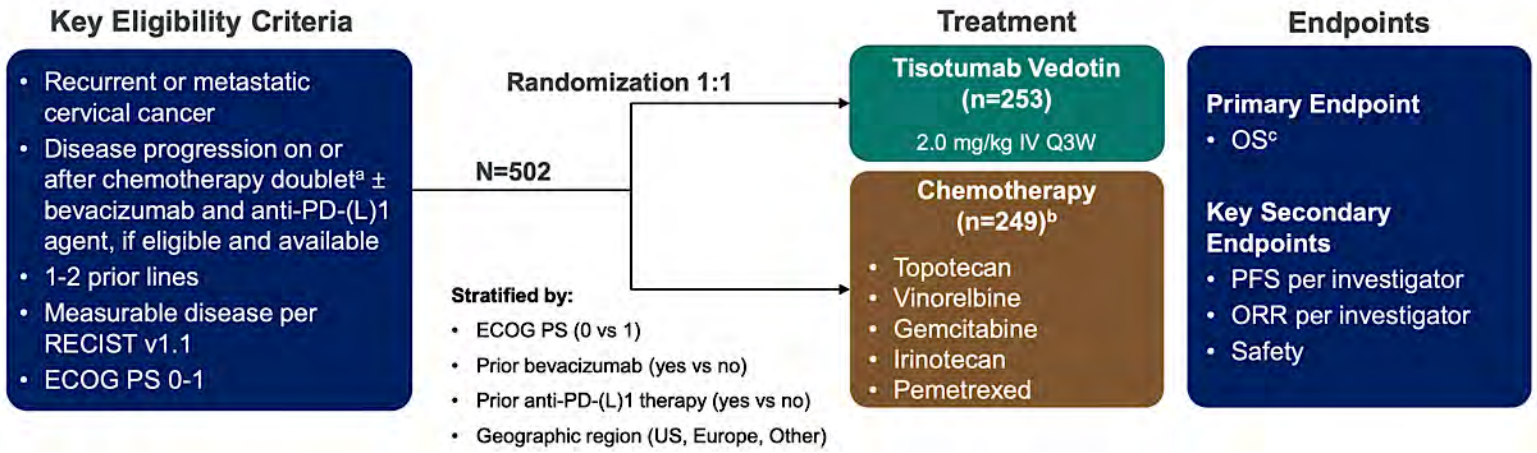
Tisotumab Vedotin as Second- or Third-Line Therapy for Recurrent Cervical Cancer

I. Vergote, A.G. Martín, K. Fujiwara, E. Kalbacher, A. Bagaméri, S. Ghamande, J.-Y. Lee, S. Banerjee, F.C. Maluf, D. Lorusso, K. Yonemori, E. Van Nieuwenhuysen, L. Manso, L. Woelber, A. Westermann, A. Covens, K. Hasegawa, B.-G. Kim, M. Raimondo, M. Bjurberg, F.M. Cruz, A. Angelergues, D. Cibula, L. Barraclough, A. Oaknin, C. Gennigens, L. Nicacio, M.S.L. Teng, E. Whalley, I. Soumaoro, and B.M. Slomovitz, for the innovaTV 301/ENGOT-cx12/GOG-3057 Collaborators*

1st ADC FDA approved in gynae cancers

innovaTV 301 Study Design[1,2]

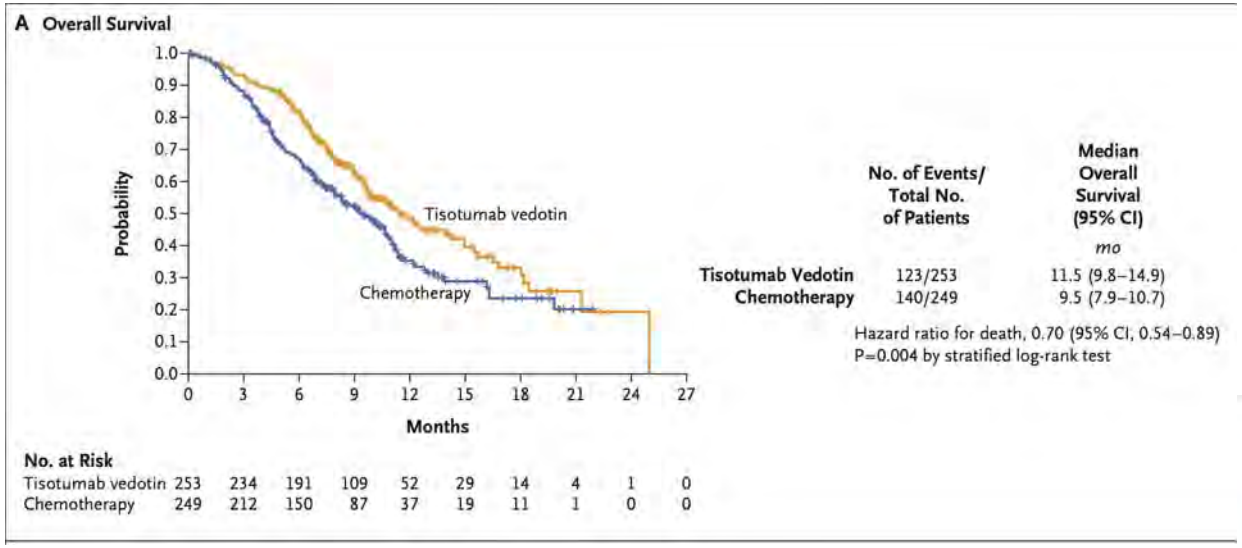
innovaTV 301 is a global, randomized, open-label, phase 3 trial of tisotumab vedotin vs chemotherapy in patients with 2L/3L r/m CC

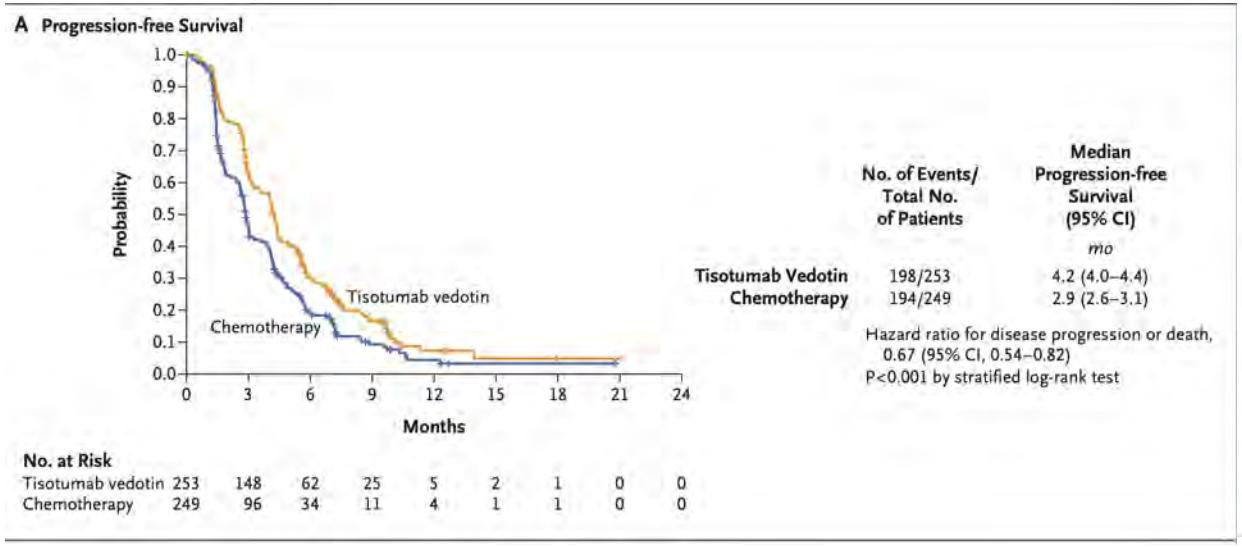


Vergote I et al. *N Engl J Med* 2024;391(1):44-55.

Courtesy of Susana Banerjee, MBBS, MA, PhD

innovaTV 301: Tisotumab Vedotin in recurrent Cervical Cancer

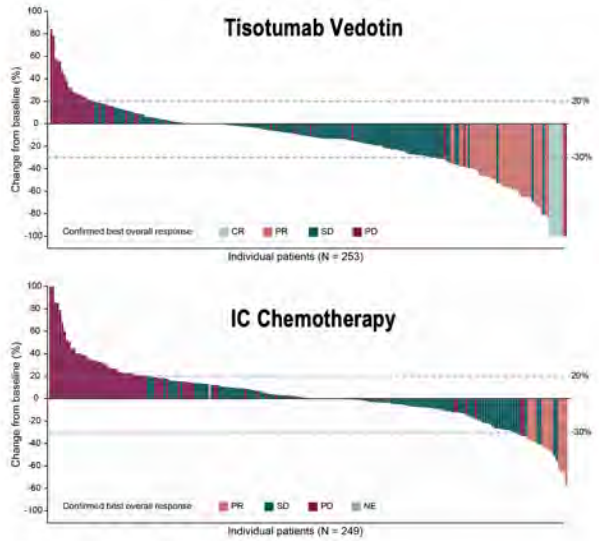




Antitumor Activity

	Tisotumab Vedotin (N=253)	IC Chemotherapy (N=249)
ORR, % (95% CI)	17.8 (13.3-23.1)	5.2 (2.8-8.8)
Odds ratio (95% CI) P value	4.0 (2.1-7.6) p<0.0001	
Best Overall Response, n (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
Not evaluable/Not available	15 (5.9)	30 (12.0)
DCR[a], % (95% CI)	75.9 (70.1-81.0)	58.2 (51.8-64.4)
Median DOR (95% CI)	5.3 (4.2-8.3)	5.7 (2.8-NR)

[a]DCR defined as CR+PR+SD; CR and PR were confirmed responses. The minimum criteria for SD duration was ≥5 weeks after the date of randomization.



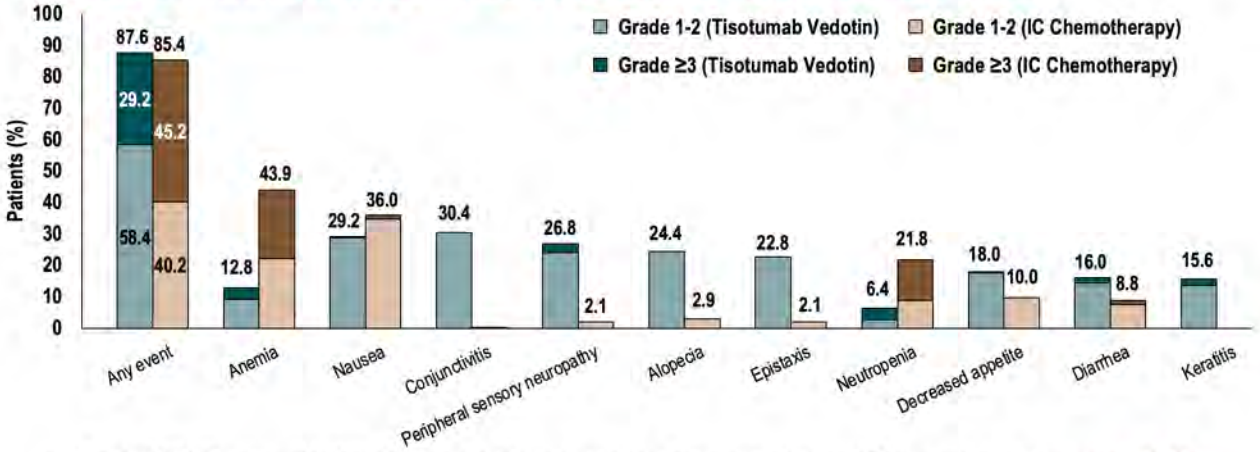
Prof. Ignace Vergote

Vergote I et al. *N Engl J Med* 2024;391(1):44-55; Vergote I et al. ESMO 2023. Abstract LBA9.

Courtesy of Susana Banerjee, MBBS, MA, PhD

innovaTV 301: Tisotumab Vedotin Adverse Events

Most Common Treatment-Related Adverse Events[a]

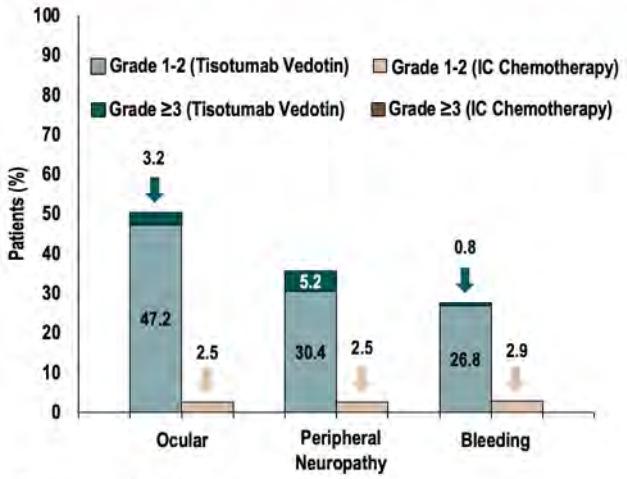


- Grade 5 TRAEs occurred in 2 (0.8%) and 1 (0.4%) patients in the tisotumab vedotin and IC chemotherapy arms, respectively[b]
- Median relative dose intensity was 96.1% and 90.0% in the tisotumab vedotin and IC chemotherapy arms, respectively

[a]TRAEs listed are those occurring in ≥15% of patients on either arm; [b]Grade 5 TRAEs included acute kidney injury (n=1) and Stevens-Johnson syndrome (n=1) in the tisotumab vedotin arm and pancytopenia (n=1) in the IC chemotherapy arm.

MADRID 2023 ESMO congress Prof. Ignace Vergote

Adverse Events of Special Interest for Tisotumab Vedotin[a]



- There were no grade 4 or 5 AESIs
- Dose discontinuation due to ocular and peripheral neuropathy events occurred in 5.6% of patients for each

Three most common preferred terms for each AESI	
Ocular	Conjunctivitis (30.4%), keratitis (15.6%), dry eye (13.2%)
Peripheral neuropathy	Peripheral sensory neuropathy (26.8%), paresthesia (2.8%), muscular weakness (2.4%), peripheral sensorimotor neuropathy (2.4%)
Bleeding	Epistaxis (22.8%), hematuria (3.2%), vaginal hemorrhage (3.2%)

AESI, adverse event of special interest
[a]Treatment-related AESIs

MADRID 2023 ESMO congress Prof. Ignace Vergote

Vergote I et al. ESMO 2023. Abstract LBA9.

Courtesy of Susana Banerjee, MBBS, MA, PhD

- Tisotumab vedotin showed a statistically significant and clinically meaningful improvement in OS

The hazard ratio for OS was 0.70, demonstrating a 30% reduction in the risk of death

- Adverse events – recognition of ocular toxicity
- Step forward – prognosis remains poor: need to further improve outcomes in recurrent cervical cancer

Courtesy of Susana Banerjee, MBBS, MA, PhD

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

Nontargeted Approaches for Lung Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, June 24, 2025
5:00 PM – 6:00 PM ET

Faculty

Benjamin Levy, MD

Moderator

Neil Love, MD

RTP Year in Review 2025

Thank you for joining us!

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Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2025