Cancer Conference Update: ESMO Congress 2025 Review — Gynecologic Cancers

A CME/MOC-Accredited Live Webinar

Thursday, January 22, 2026
5:00 PM – 6:00 PM ET

Faculty

Ritu Salani, MD, MBA

Moderator

Neil Love, MD

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Faculty

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

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, GSK, and Merck.

Dr Love — Disclosures

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

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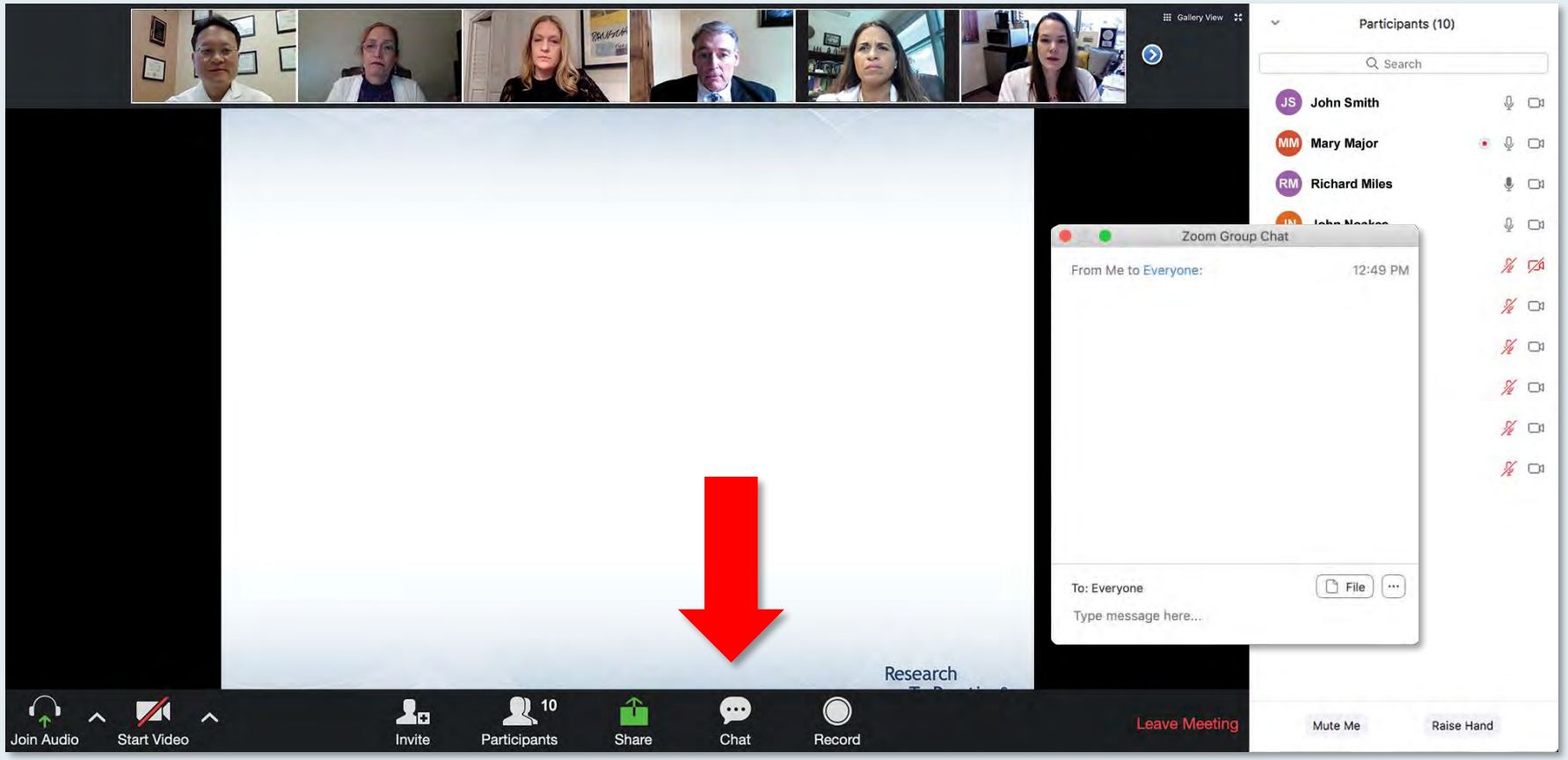
We Encourage Clinicians in Practice to Submit Questions



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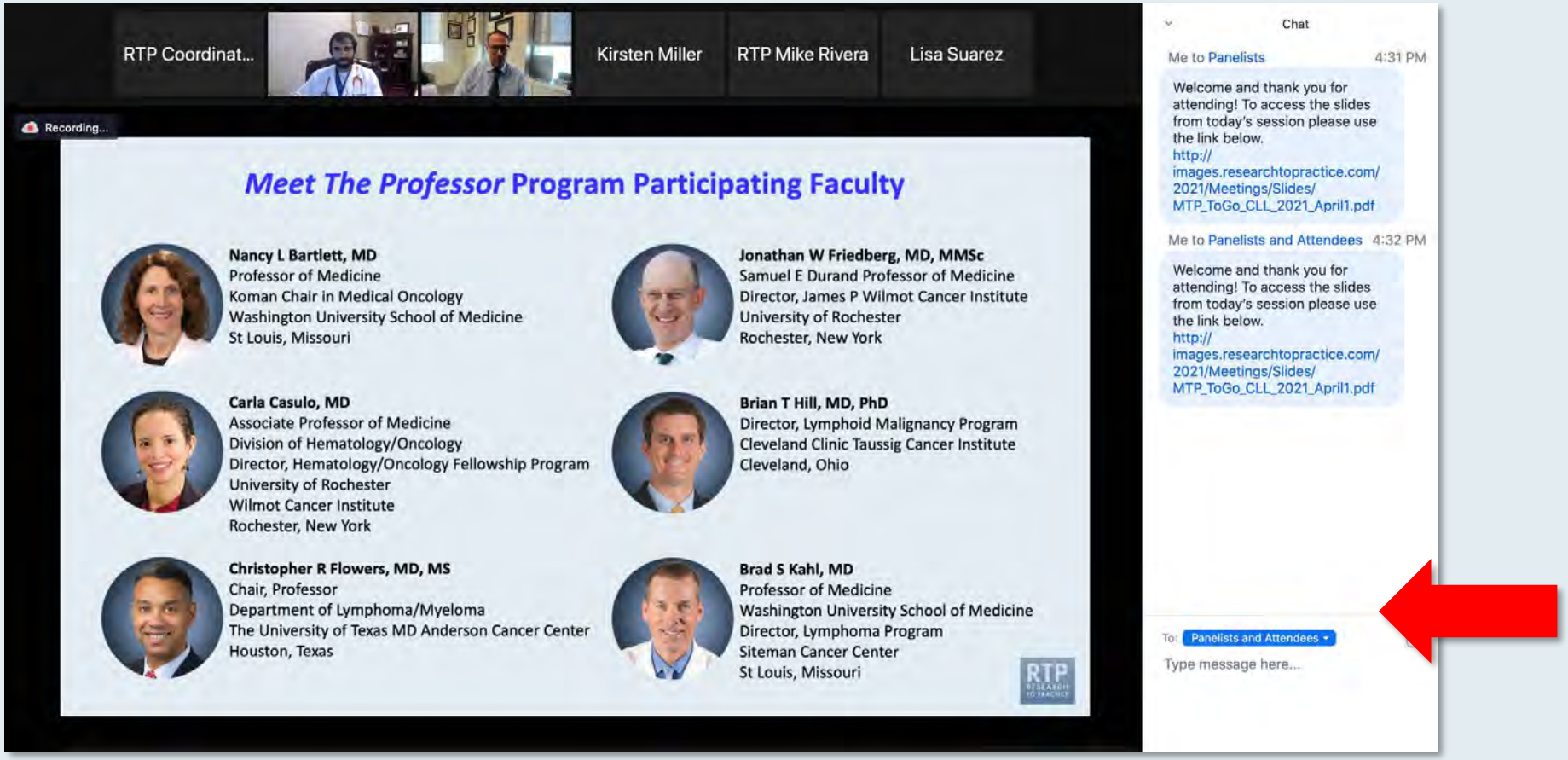

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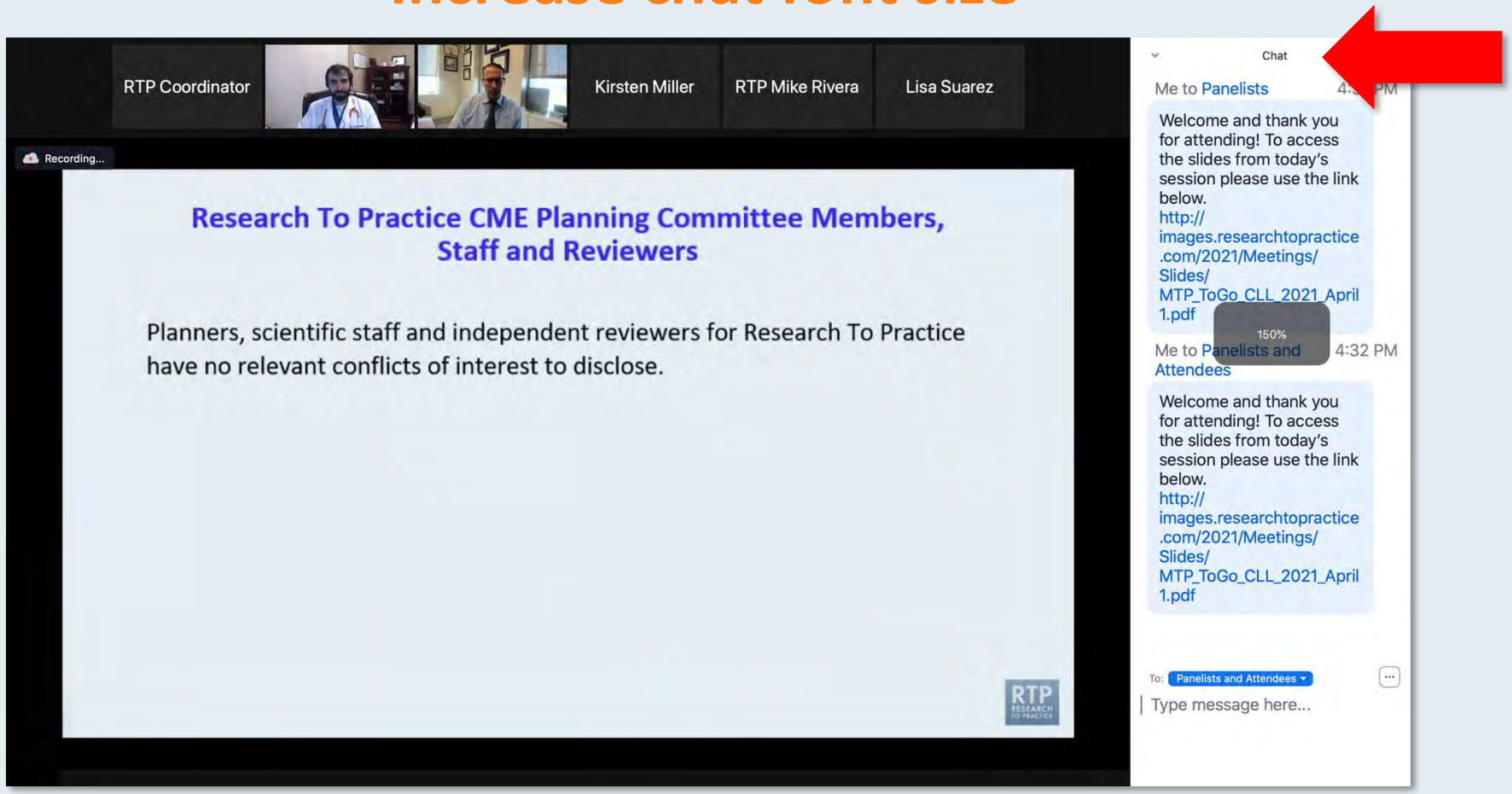

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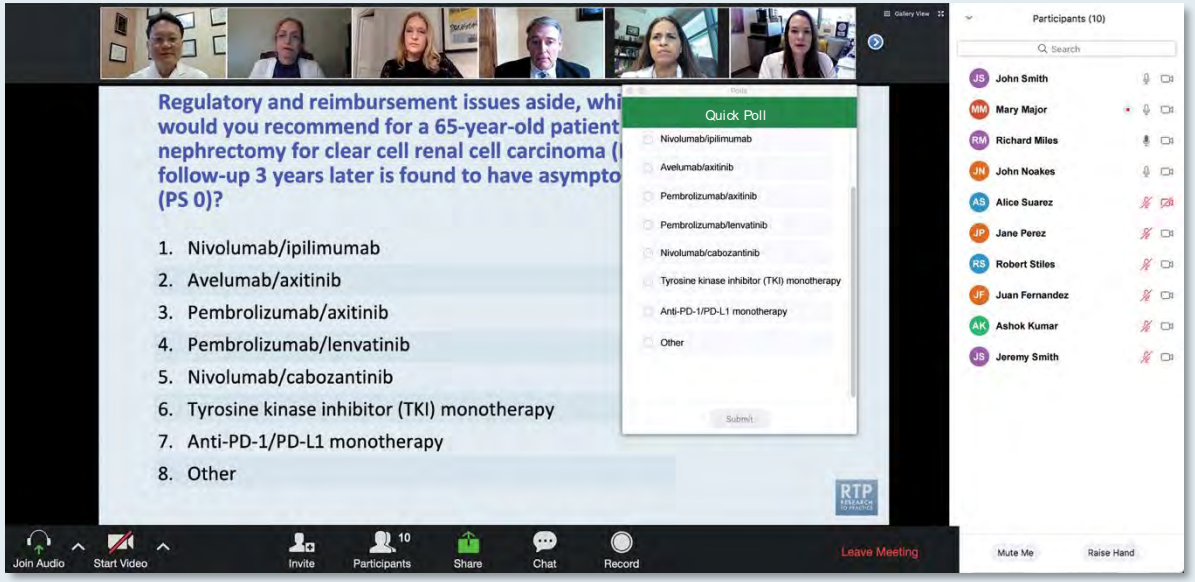

Gynecologic Cancers — Year in Review Series on Relevant New Datasets and Advances

PROF SUSANA BANERJEE
THE INSTITUTE OF CANCER RESEARCH

DR URSULA MATULONIS
DANA-FARBER CANCER INSTITUTE

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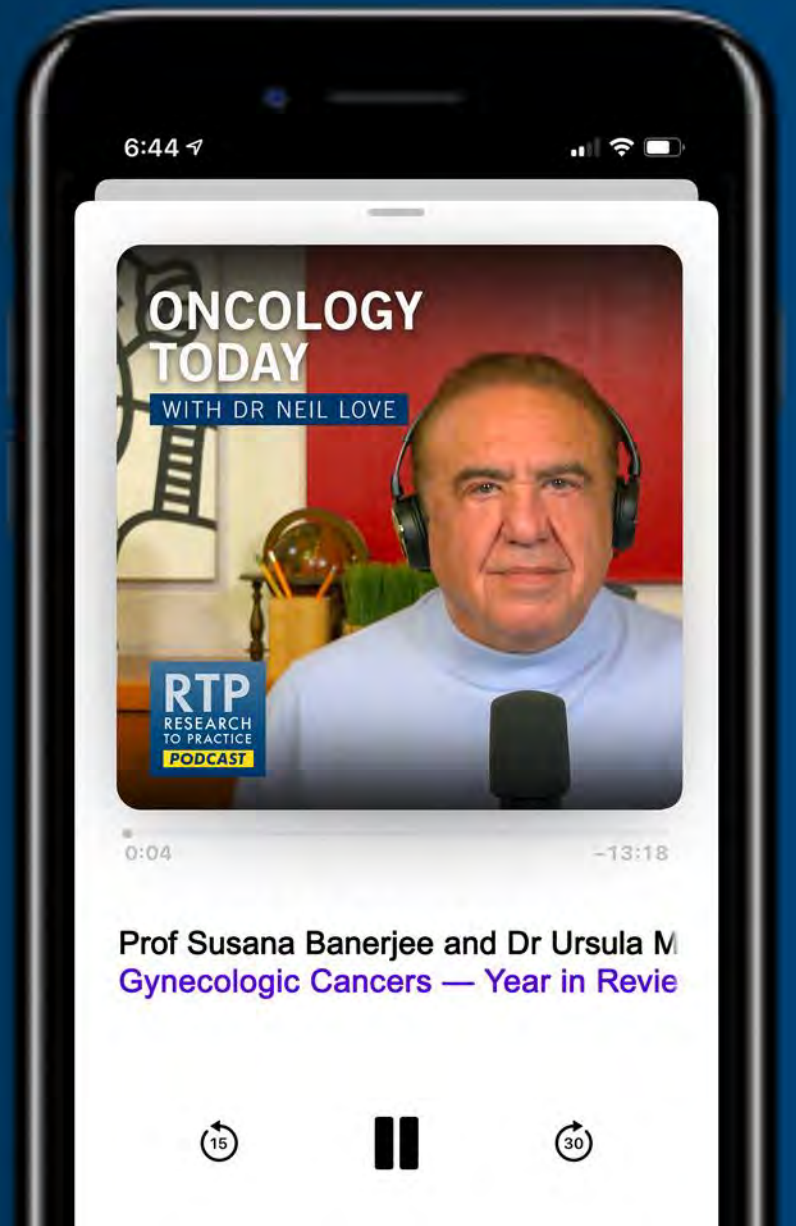

Inside the Issue: The Emerging Role of Cereblon E3 Ligase Modulators in Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Wednesday, January 28, 2026
5:00 PM – 6:00 PM ET

Faculty

Natalie S Callander, MD
Paul G Richardson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Exploring Current Patterns of Care in the Community: Selection of First-Line and Maintenance Therapy for Patients with Extensive-Stage Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 4, 2026
5:00 PM – 6:00 PM ET

Faculty

Hossein Borghaei, DO, MS
Anne Chiang, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

Antibody-Drug Conjugates for Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 18, 2026

5:00 PM – 6:00 PM ET

Faculty

Hope S Rugo, MD

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2026

Expert Second Opinion: Investigators Provide Perspectives on the Future Role of AKT Inhibition in the Management of Prostate Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Friday, February 27, 2026
6:00 PM – 7:30 PM PT (9:00 PM – 10:30 PM ET)

Faculty

Professor Karim Fizazi, MD, PhD
Daniel George, MD

Moderator

Elisabeth I Heath, MD

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Grand Rounds

CME/MOC-Accredited Interactive Series

Through April 2026

Three Series

Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

Host a 1-hour session at your institution:
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Save The Date

Fifth Annual
National General Medical Oncology Summit

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

Friday to Sunday, April 24 to 26, 2026

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

Moderated by Neil Love, MD

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us.

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

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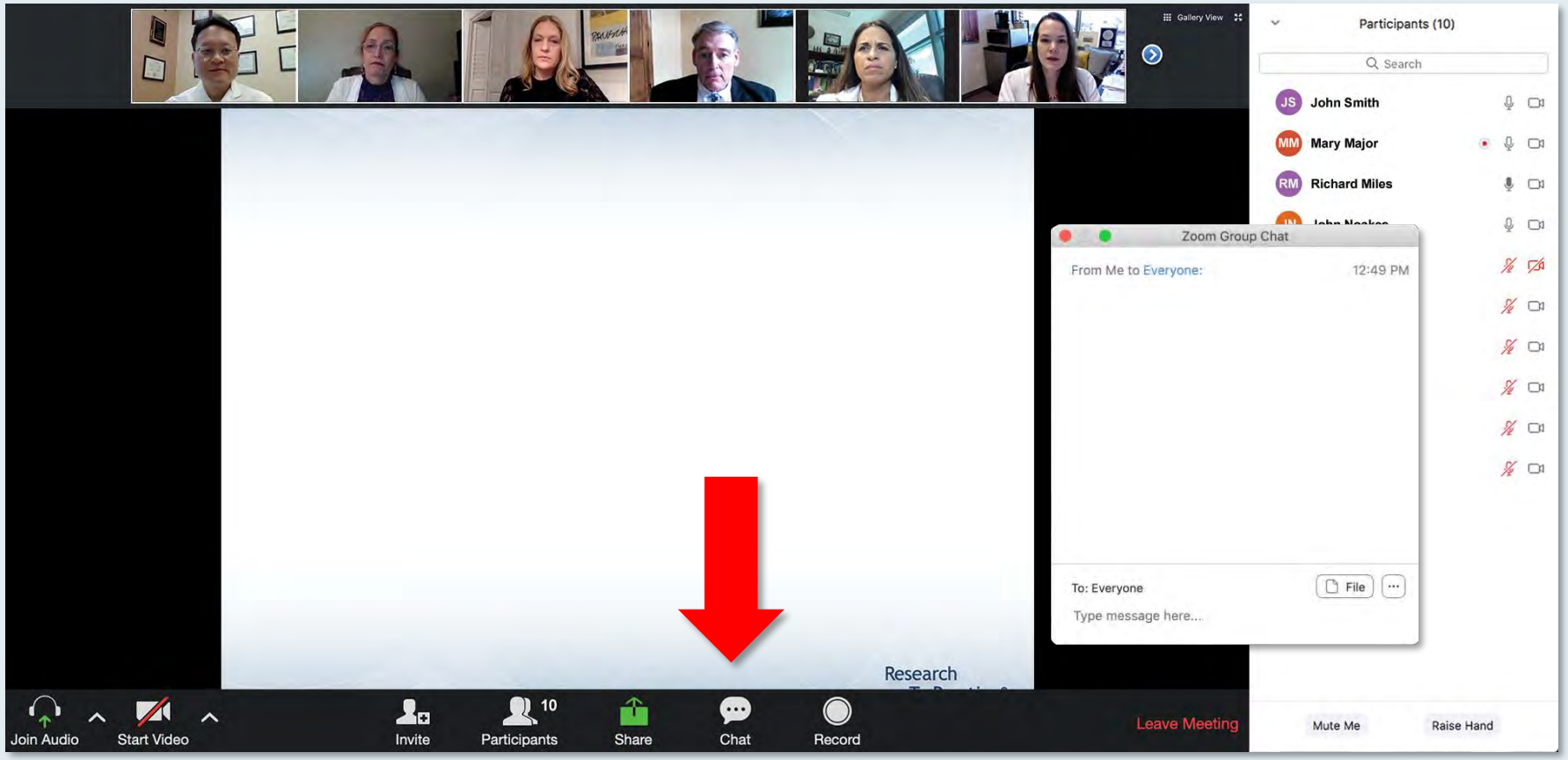

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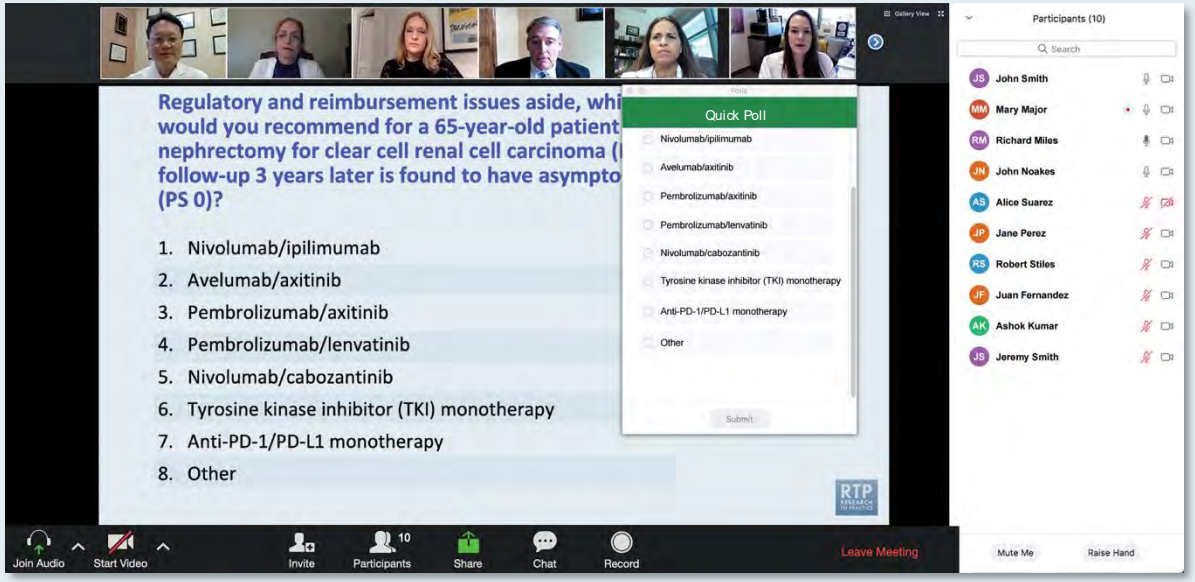

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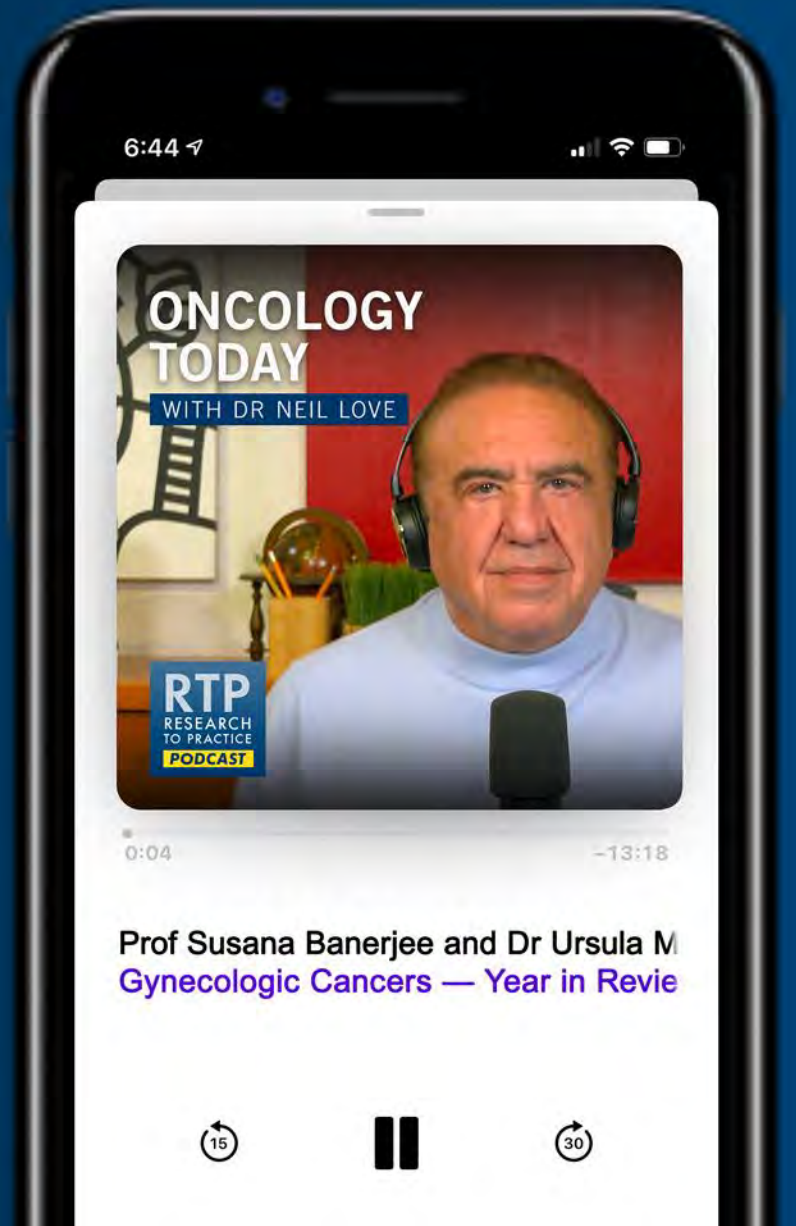

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Agenda

Module 1: Up-Front Treatment of Ovarian Cancer (OC)

Module 2: Management of Platinum-Resistant OC

Module 3: Up-Front Management of Metastatic Endometrial Cancer

Module 4: Management of HER2-Positive Gynecologic Cancers

Module 5: Management of Cervical Cancer

Agenda

Module 1: Up-Front Treatment of Ovarian Cancer (OC)

Module 2: Management of Platinum-Resistant OC

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Module 4: Management of HER2-Positive Gynecologic Cancers

Module 5: Management of Cervical Cancer

Case Presentation: Dr Salani

- 39-year-old patient.
- 1/16/24: CT chest/abdomen/pelvis: Moderate to large ascites, low density liver lesions and capsular attenuation, possible carcinomatosis/endometriosis/hemorrhagic clots. Small, shotty retroperitoneal lymph nodes; no groin adenopathy. Bilateral pleural effusions.
- 1/17/24: Pelvic ultrasound: Uterus measures 6.7 x 3.3 x 3.0 cm with a 0.7 cm endometrium and surrounded by ill-defined soft tissue concerning for extensive peritoneal or omental neoplasm. Right complex adnexal mass, 4.2 x 3.3 x 3.2 cm, with septations and nodularity. Pelvic ascites.
- 1/29/24: PET CT: Large hypermetabolic pelvic masses and extensive hypermetabolic peritoneal disease. There is diffuse ascites. There is peritoneal disease along the liver surface and liver hila. There are moderate bilateral pleural effusions with mildly increased FDG uptake. There are no hypermetabolic pulmonary mass lesions.
- 2/5/24: Diagnostic laparoscopy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, right pelvic lymph node debulking, omentectomy, appendectomy, splenectomy, cystotomy repair, and extensive tumor reductive surgery with optimal cytoreduction: High grade serous carcinoma (Stage IIIC).

Case Presentation: Dr Salani (Continued)

3/4/24 – 6/18/24: Carboplatin, paclitaxel and bevacizumab (added cycle 2) x 6 cycles.

3/5/24: Genomic tumor testing: P53m, TMB low, MSS, HRD positive (22.6% LOH).

7/8/24: CT chest/abdomen/pelvis: No intrathoracic disease. Thickening/scalloping (13 mm) at the right liver dome, no other evidence of disease.

7/9/24: Bevacizumab maintenance started.

8/2/24: Olaparib maintenance started.

1/22/25: CT chest/abdomen/pelvis: Resolution of nodules by liver; no evidence of disease.

7/9/25: CT chest/abdomen/pelvis: Decrease in perihepatic nodule; no new evidence of disease.

10/21/25: Bevacizumab cycle 22.

11/12/25: CT abdomen/pelvis: Stable perihepatic implant at the right hepatic dome measuring; no new metastatic disease in the abdomen or pelvis.

Current status: She is doing well, plans to continue olaparib maintenance until 8/2026 (2 years).

Tumor Markers

	CA-125
2/29/2024	349
3/22/2024	175
4/12/2024	105
5/3/2024	61
5/24/2024	29
6/17/2024	19
7/9/2024	14
7/30/2024	12
8/20/2024	10
9/10/2024	10
10/1/2024	8
10/22/2024	7
11/12/2024	6
12/4/2024	6

Tumor Markers (Continued)

	CA-125
12/27/2024	6
1/17/2025	6
2/7/2025	7
3/1/2025	17
3/12/2025	12
4/11/2025	9
5/2/2025	6
6/17/2025	5
7/8/2025	5
7/29/2025	6
8/19/2025	5
9/9/2025	7
10/1/2025	6
10/21/2025	6

Key Datasets

- Clamp A et al. ICON8B: GCIG phase III randomized trial comparing first-line weekly dose-dense chemotherapy + bevacizumab to three-weekly chemotherapy + bevacizumab in high-risk Stage III-IV epithelial ovarian cancer (EOC): Final overall survival (OS) analysis. ESMO 2025;Abstract 1064O.
- Li N et al. Fuzuloparib (FZPL) monotherapy or in combination with apatinib as first-line maintenance therapy in advanced ovarian cancer: Final analysis of the FZOCUS-1 trial. ESMO 2025;Abstract 1063O.
- Kim SI et al. First-line niraparib maintenance therapy in BRCA wild-type, low-risk advanced ovarian cancer: The POLO trial. ESMO 2025;Abstract 1084P.
- Denys H et al. Quality-adjusted progression-free survival (QA-PFS) and quality-adjusted time without symptoms of disease or toxicity (Q-TWIST) results from the PRIMA/ENGOT-OV26/GOG-3012 final analysis. ESMO 2025;Abstract 1070P.

Key Datasets (Continued)

- Moore KN et al. FIRST/ENGOT-OV44 trial: Does the addition of dostarlimab impact niraparib tolerability, exposure, or dose modification? ESMO 2025;Abstract 1101P.
- Aghajanian C et al. Durvalumab + paclitaxel/carboplatin + bevacizumab followed by durvalumab, bevacizumab + olaparib maintenance in patients with newly diagnosed non-tBRCA-mutated advanced ovarian cancer: Final overall survival from DUO-O/ENGOT-ov46/GOG-3025. ESMO 2025;Abstract LBA44.
- Cibula D et al. Phase 3, randomized, double-blind, placebo (Pbo)-controlled ENGOT-ov43/GOG-3036/KEYLYNK-001 study of 1L chemotherapy (CT) ± pembrolizumab (Pembro) then maintenance (Maint) pembro ± olaparib (Ola) for advanced BRCA-nonmutated epithelial ovarian cancer (EOC): Analysis by HRD status. ESMO 2025; Abstract 1071P.

GCIG GYNECOLOGIC CANCER INTERGROUP | ENGOT European Network of Gynaecological Oncological Trial groups | CANCER RESEARCH UK

UKRI MRC Clinical Trials Unit | UCL | ICON8B

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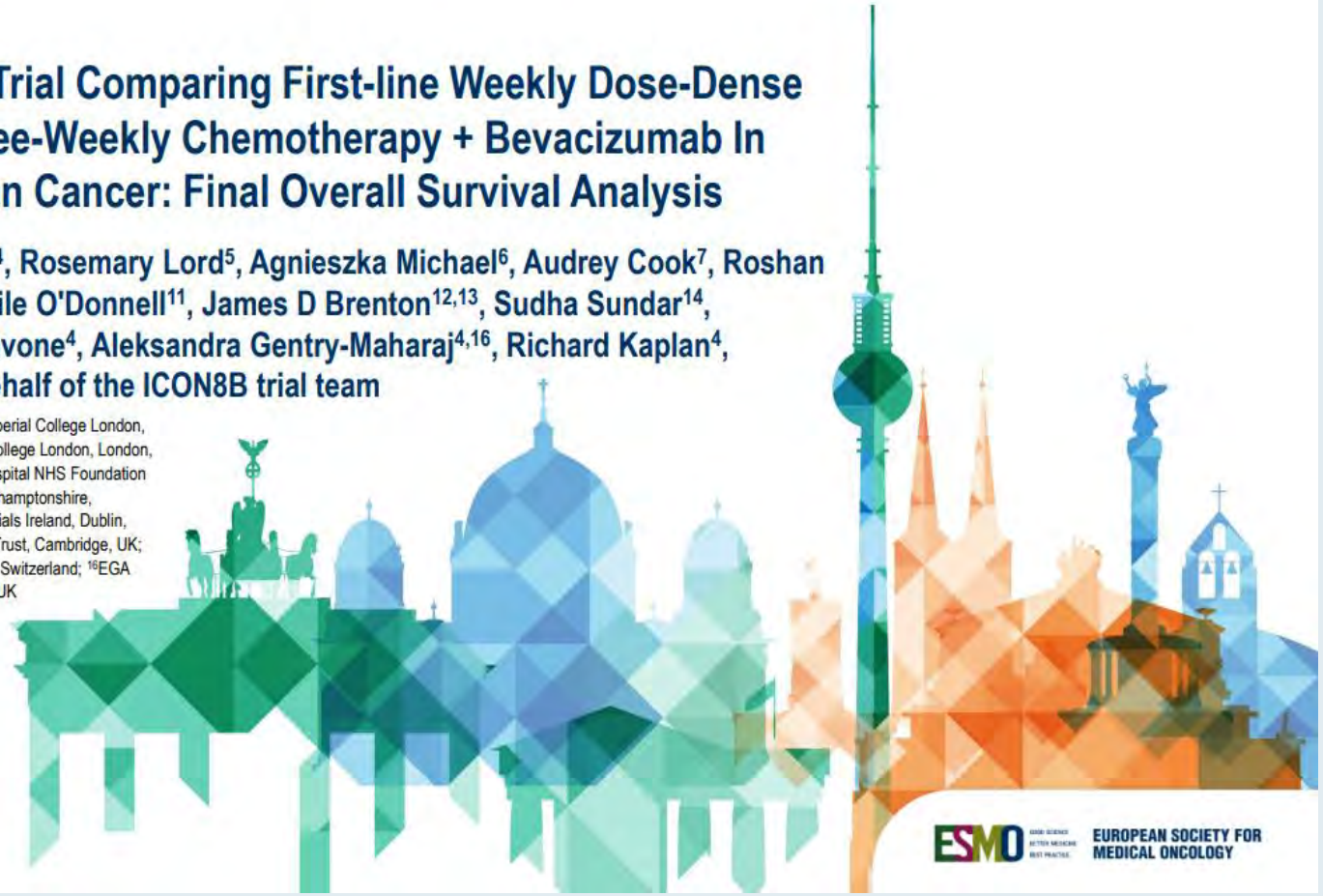
Abstract 1064O

ICON8B: GCIG Phase III Randomised Trial Comparing First-line Weekly Dose-Dense Chemotherapy + Bevacizumab To Three-Weekly Chemotherapy + Bevacizumab In High-Risk Stage III-IV Epithelial Ovarian Cancer: Final Overall Survival Analysis

Andrew Clamp[1,2], Iain McNeish[3], Domenico Radice[4], Rosemary Lord[5], Agnieszka Michael[6], Audrey Cook[7], Roshan Agarwal[8], Axel Walther[9], Sarah Blagden[10], Dearbhaile O'Donnell[11], James D Brenton[12,13], Sudha Sundar[14], Cristiana Sessa[15], Laura Murphy[4], Francesca Schiavone[4], Aleksandra Gentry-Maharaj[4,16], Richard Kaplan[4], Mahesh KB Parmar[4], Jonathan Ledermann[17]; on behalf of the ICON8B trial team

[1]The Christie NHS Foundation Trust, Manchester, UK; [2]University of Manchester, Manchester, UK; [3]Imperial College London, London, UK; [4]MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology, University College London, London, UK; [5]The Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool, UK; [6]Royal Surrey County Hospital NHS Foundation Trust, Guildford, UK; [7]Gloucestershire Oncology Centre, Cheltenham, UK; [8]University Hospitals of Northamptonshire, Northampton, UK; [9] Bristol Cancer Institute, Bristol, UK; [10]University of Oxford, Oxford, UK; [11]Cancer Trials Ireland, Dublin, Ireland; [12]University of Cambridge, Cambridge, UK; [13]Cambridge University Hospital NHS Foundation Trust, Cambridge, UK; [14]University of Birmingham, Birmingham, UK; [15]Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; [16]EGA Institute for Women's Health, UCL, London, UK;[17]University College London Cancer Institute, London, UK



Dr Andrew Clamp

19 October 2025

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ICON8B Study Conclusions

Bevacizumab in combination with 3-weekly carboplatin and weekly dose-dense paclitaxel compared to bevacizumab and 3-weekly chemotherapy in patients with high-risk stage III and stage IV Epithelial Ovarian Cancer

- Increased median Progression-Free Survival by 4.9 months (16.5 months to 21.4 months; HR 0.72)
- Improved median Overall Survival by 10.2 months (39.6 months to 49.8 months; HR 0.79)

Bevacizumab in combination with 3-weekly carboplatin and weekly dose-dense paclitaxel should be considered a standard-of-care option for patients with high-risk stage III and IV Epithelial Ovarian Cancer

- Translational work programme will determine interaction between intrinsic tumour chemosensitivity (KELIM) and Homologous recombination deficiency and efficacy of dose-dense chemotherapy

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Clamp A et al. ESMO 2025;Abstract 1064O.

Abstract 1063O

BERLIN 2025 ESMO congress

Fuzuloparib monotherapy or in combination with apatinib as first-line maintenance therapy in advanced ovarian cancer

Final analysis of the FZOCUS-1 trial

Presenter: Ning Li, MD
Leading PI: Lingying Wu, MD, PhD

National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

19 October 2025

ESMO EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

FZOCUS-1 Study Conclusions

- **This trial was the first to compare the efficacy of PARPi plus antiangiogenic agents and PARPi alone in the first-line maintenance setting for advanced OC.**
- **Fuzuloparib combined with apatinib or fuzuloparib alone as first-line maintenance therapy prolonged PFS in patients with newly diagnosed advanced OC, regardless of *BRCA1/2* mutation status.**
  - Overall, median PFS by BIRC was 26.9 months (HR, 0.57 [95% CI, 0.44-0.75]) in fuzuloparib + apatinib and 29.9 months (HR, 0.58 [95% CI, 0.44-0.75]) in fuzuloparib, compared with 11.1 months in placebo.
  - In patients with g*BRCA1/2* mutation, median PFS was 45.1 months (HR, 0.50 [95% CI, 0.30-0.84]) in fuzuloparib + apatinib and 47.8 months (HR, 0.51 [95% CI, 0.30-0.86]) in fuzuloparib, compared with 16.6 months in placebo.
- **Adding apatinib to fuzuloparib did not further improve PFS in the overall population or among *BRCA1/2*–mutated/HRD patients, but the combination therapy showed a PFS benefit trend over fuzuloparib monotherapy among HRP patients.**
  - In HRP patients, median PFS was 16.6 months in fuzuloparib + apatinib vs. 11.0 months in fuzuloparib (HR, 0.73 [95% CI, 0.45-1.19]).
- **Fuzuloparib + apatinib and fuzuloparib showed manageable safety in patients with advanced OC.**
  - The safety profile was consistent with previous reports of fuzuloparib and apatinib.
  - Most grade ≥3 TRAEs were hematological toxicities; the incidence of hypertension was higher in the combination group than monotherapy.

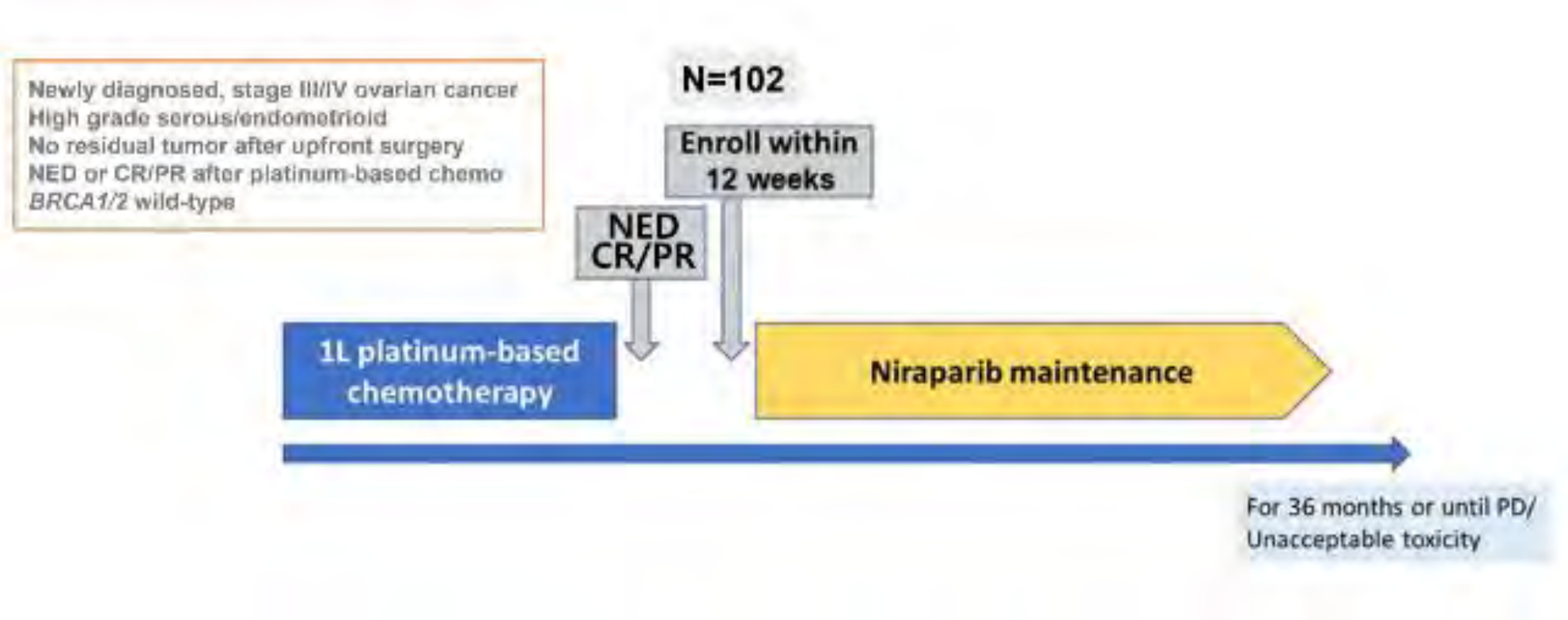
PARPi = PARP inhibitor; PFS = progression-free survival; BIRC = blinded independent central review; OC = ovarian cancer; TRAE = treatment-related adverse event

Li N et al. ESMO 2025;Abstract 1063O.

First-Line Niraparib Maintenance Therapy in BRCA Wild-Type, Low-Risk Advanced Ovarian Cancer: The POLO Trial

Kim SI et al.
ESMO 2025;Abstract 1084P.

The POLO Trial Study Design

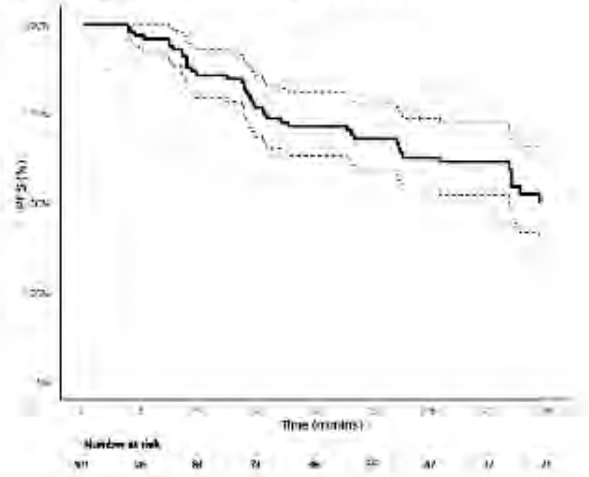


NED = no evidence of disease; CR = complete response; PR = partial response

Kim SI et al. ESMO 2025;Abstract 1084P.

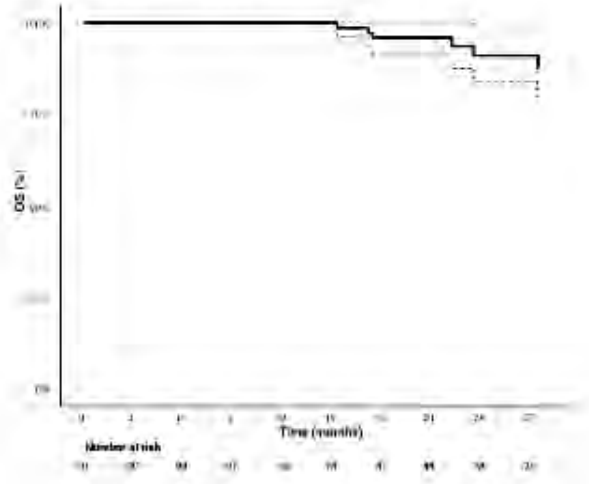
The POLO Trial: PFS and Overall Survival (OS) in the Intent-to-Treat Population

(A) Progression-free survival



	Event	Rate	95% CI Lower	95% CI Upper
3 mon	3	97.00%	83.34%	99.49%
6 mon	14	85.86%	70.52%	93.57%
9 mon	23	76.65%	60.13%	87.02%
12 mon	28	71.47%	54.59%	83.00%
15 mon	31	67.93%	50.70%	80.24%
18 mon	35	62.82%	45.17%	76.19%
24 mon	41	50.06%	29.91%	67.26%

(B) Overall survival



	Event	Rate	95% CI Lower	95% CI Upper
3 mon	0	100.00%	-	-
6 mon	0	100.00%	-	-
9 mon	0	100.00%	-	-
12 mon	0	100.00%	-	-
15 mon	0	100.00%	-	-
18 mon	3	95.88%	79.48%	99.23%
24 mon	5	91.25%	69.88%	97.69%

Kim SI et al. ESMO 2025;Abstract 1084P.

The POLO Trial: Conclusions

- First-line niraparib maintenance was effective and safe in patients with *BRCA* wild-type, low-risk advanced ovarian cancer.
- The POLO trial met the primary endpoint and further long-term survival analyses and biomarker studies are scheduled.

Kim SI et al. ESMO 2025;Abstract 1084P.

Quality-Adjusted Progression-Free Survival (QA-PFS) and Quality-Adjusted Time without Symptoms of Disease or Toxicity (Q-TWiST) Results from the PRIMA/ENGOT-OV26/GOG-3012 Final Analysis

Denys H et al.

ESMO 2025;Abstract 1070P.

PRIMA Study Conclusions

- In the PRIMA final analysis, niraparib first-line maintenance treatment was associated with significant gains in restricted mean QA-PFS and Q-TWiST durations vs placebo in the overall, HRd, and HRp populations
- Niraparib treatment gains for restricted mean duration of QA-PFS and Q-TWiST were extended from the primary to final analysis, likely because PFS gains were sustained with longer follow-up while the majority of treatment-emergent AEs occur within the first 3 months of niraparib treatment
- By integrating the quantity and quality of progression-free time, these findings further support the clinical benefit of niraparib versus placebo for the maintenance treatment of patients with newly diagnosed advanced OC that responded to first-line platinum-based chemotherapy

QA-PFS = quality-adjusted progression-free survival; Q-TWiST = quality-adjusted time without symptoms of disease or toxicity; HRd = homologous recominbation-deficient; HRp = homologous recombination-proficient; AEs = adverse events

Denys H et al. ESMO 2025;Abstract 1070P.

FIRST/ENGOT-OV44 Trial: Does the Addition of Dostarlimab Impact Niraparib Tolerability, Exposure, or Dose Modification?

Moore KN et al.
ESMO 2025;Abstract 1101P.

FIRST/ENGOT-OV44 Study Conclusions

- In the FIRST trial, in which all patients received an individualized starting dose of first-line maintenance niraparib, exposure duration and dose modifications of niraparib in arm 2 were generally consistent with the observations of first-line maintenance niraparib in the PRIMA trial[1,2]
- The addition of dostarlimab did not significantly impact the tolerability of niraparib, as measured by duration of niraparib exposure and TEAEs leading to niraparib dose reductions, interruptions, and discontinuations

Moore KN et al. ESMO 2025;Abstract 1101P.

Abstract LBA44

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Durvalumab + paclitaxel/carboplatin + bevacizumab followed by durvalumab, bevacizumab + olaparib maintenance in patients with newly diagnosed non-tBRCA-mutated advanced ovarian cancer: final overall survival from DUO-O/ENGOT-ov46/GOG-3025

Carol Aghajanian,[1] Fabian Trillsch,[2] Shin Nishio,[3] Alexander Reuss,[4] Jung-Yun Lee,[5] Maria Jesús Rubio,[6] Mehmet Ali Vardar,[7] Vanda Salutari,[8] Frédéric Selle,[9] Sakari Hietanen,[10] Mariateresa Lapresa,[11] Anita Chudecka-Głaz,[12] Stephan Polterauer,[13] Stephanie Lheureux,[14] Stephanie Henry,[15] Fabienne Schochter,[16] Robert M. Wenham,[17] Aikou Okamoto,[18] Andrea Correa,[19] Philipp Harter[20]

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19 October 2025

DUO-O Study Conclusions

- DUO-O met both primary endpoints at DCO1 demonstrating statistically significant and clinically meaningful PFS improvement with B + D + O (Arm 3) vs control (Arm 1) in non-tBRCAm HRD-positive and ITT populations and this benefit was maintained at DCO3 with a ~56-month median follow-up
  - In the non-tBRCAm HRD-positive population, mPFS for Arm 3 vs Arm 1 was 45.1 vs 23.3 months, with 47% vs 27% of patients progression-free at 48 months
- At this final OS analysis (DCO3), the observed PFS benefits did not translate into a statistically significant OS improvement in the non-tBRCAm ITT population
  - Median OS was not reached for B + D (Arm 2) or B + D + O (Arm 3) in the non-tBRCAm HRD-positive population
- Safety continues to be generally consistent with the known profiles of each agent

tBRCAm = tumor BRCA mutation/mutated

Aghajanian C et al. ESMO 2025;Abstract LBA44.

Phase 3, Randomized, Double-Blind, Placebo (Pbo)-Controlled ENGOT-ov43/GOG-3036/KEYLYNK-001 Study of 1L Chemotherapy (CT) ± Pembrolizumab (Pembro) Then Maintenance (Maint) Pembro ± Olaparib (Ola) for Advanced BRCA-Nonmutated Epithelial Ovarian Cancer (EOC): Analysis by HRD Status

Cibula D et al.

ESMO 2025;Abstract 1071P.

ENGOT-ov43/GOG-3036/KEYLYNK-001 Study Conclusions

- In this post hoc exploratory analysis of participants with advanced *BRCA1*/*BRCA2*-nonmutated EOC, treatment with pembro plus chemo followed by maintenance pembro plus olaparib with or without bev prolonged PFS in the ITT and PD-L1 CPS ≥10 populations compared with chemo with or without bev, regardless of HRD status
- Treatment with pembro plus chemo followed by maintenance pembro plus placebo with or without bev did not prolong PFS or OS in the ITT and PD-L1 CPS ≥10 populations compared with chemo with or without bev, regardless of HRD status
- Results presented herein based on the Myriad assay were consistent with those previously reported based on the Foundation Medicine Inc. assay[7]
- Overall, in participants with HRD- disease who did not receive bev, the findings from this analysis suggest
  - PFS benefits with maintenance pembro irrespective of olaparib administration or PD-L1 status
  - OS benefits with maintenance pembro alone irrespective of PD-L1 status

Cibula D et al. ESMO 2025;Abstract 1071P.

Agenda

Module 1: Up-Front Treatment of Ovarian Cancer (OC)

Module 2: Management of Platinum-Resistant OC

Module 3: Up-Front Management of Metastatic Endometrial Cancer

Module 4: Management of HER2-Positive Gynecologic Cancers

Module 5: Management of Cervical Cancer

Case Presentation: Dr Salani

- 61 year old (diagnosed at age 58); healthy patient; musician.
- 11/21/22: CT abdomen/pelvis: Subcapsular liver and splenic deposits; numerous mesenteric nodules throughout the abdomen and pelvis (largest measuring 4.0 x 3.0 cm and invades the spleen). Right adnexal mass measuring 4.9 x 4.2 cm. Mild ascites and enlarged bilateral groin nodes.
- 11/23/22: Inguinal lymph node biopsy: Metastatic high grade serous carcinoma, favors tubo-ovarian origin consistent with stage IVb high grade serous ovarian cancer.
- Testing: HRD positive, FOLR1 positive, TP53 (exon 4 p.P87fs); MSS, TMB 9 muts/MB.
- 12/1/22 – 1/12/23: Neoadjuvant carboplatin and paclitaxel (1L) x 3 cycles.
- 2/15/23: Total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, tumor reductive surgery with complete cytoreduction: Microscopic high grade serous carcinoma (CRS3).
- 3/16/23 – 4/27/23: Carboplatin and paclitaxel resumed (1L); bevacizumab (cycle 5 and 6) x 6 cycles; olaparib/bevacizumab maintenance started 5/30/23.

Case Presentation: Dr Salani (Continued)

- 12/17/23: CT chest/abdomen/pelvis: New left internal mammary artery chain lymph node measuring 5 x 9 mm; stable perisplenic deposit, no evidence of new metastatic disease.
- 1/16/24: Olaparib and bevacizumab maintenance discontinued (disease progression).
- 1/18/24: Mammary lymph node biopsy: Metastatic carcinoma consistent with clinical history. HER2 2+.
- 1/30/24 – 4/23/24: Carboplatin and liposomal doxorubicin (2L) x 4 cycles (liposomal doxorubicin held cycle 4).
- 5/6/24 – 5/13/24: SBRT to mammary node (4000 cGy).
- 7/11/24: PET CT: Decrease in size of left internal mammary lymph node (5 x 11 mm, no SUV uptake) and decrease in splenic deposits. Low pelvic mesenteric lymph node measuring 8 x 11 mm (SUV 3.2) and borderline enlarged left inguinal lymph node measuring 10 x 14 mm (SUV 3.6).
- 8/12/24 – 12/30/24: Mirvetuximab (3L) x 7 cycles; disease progression.
- 1/27/25 – 5/5/25: Cisplatin, gemcitabine and bevacizumab x 4 cycles (delays due to hematologic toxicities).

Case Presentation: Dr Salani (Continued)

- 6/3/25: PET CT: Increased FDG avid peritoneal disease (left upper quadrant, hepatic capsular nodule, right lower quadrant), new nodal disease in right common iliac, pericaval, cardiophrenic nodes; stable inguinal and mammary nodes. T11 FDG uptake without correlate.
- 6/17/25 – 9/26/25: Trastuzumab deruxtecan (5L) X 5 cycles.
- 10/4/25: CT chest/abdomen/pelvis: Increase size of right mammary node (5 mm), diaphragm and cardiophrenic nodes. Decrease in pulmonary nodule. Slightly increased burden of peritoneal disease, stable hepatic capsular implant and inguinal node, slight increased ascites. Increased size of a necrotic right common iliac node (13 x 17 mm, previously 9 x 10 mm). No new sites of metastatic disease in the abdomen or pelvis.
- 10/17/25: Pembrolizumab, bevacizumab, and cyclophosphamide (11/5/25) (6L) started.
- Current status: She has received 3 cycles and is tolerating therapy well. CA-125 started plateauing and clinically feeling better but has some GI symptoms. Scan with some slight increase, possible pseudoprogression. Plan is to continue with this regimen and rescan after 2-3 cycles; pre-screening for clinical trial options.

Tumor Markers

	CA-125
1/17/2025	539
2/10/2025	439
2/24/2025	318
3/11/2025	212
3/24/2025	162
4/7/2025	159
4/21/2025	176
5/5/2025	196
5/19/2025	198
6/5/2025	363
6/16/2025	446
7/7/2025	399

Tumor Markers (Continued)

	CA-125
7/7/2025	399
7/25/2025	500
8/15/2025	685
9/5/2025	1,318
9/26/2025	1,850
10/17/2025	2,651
11/6/2025	4,708
12/1/2025	4,704

Key Datasets

- Colombo N et al. Pembrolizumab vs placebo plus weekly paclitaxel ± bevacizumab in platinum-resistant recurrent ovarian cancer: Results from the randomized double-blind phase III ENGOT-ov65/KEYNOTE-B96 study. ESMO 2025;Abstract LBA3.
- 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;405(10496):2205-16.
- Ray-Coquard IL et al. Raludotatug deruxtecan (R-DXd) in patients (pts) with platinum-resistant ovarian cancer (PROC): Primary analysis of the phase II dose-optimization part of REJOICE-Ovarian01. ESMO 2025;Abstract LBA42.
- Oaknin A et al. First-in-human study of AZD5335, a folate receptor α (FRα)-targeted antibody-drug conjugate, in patients with platinum-resistant recurrent ovarian cancer. ESMO 2025;Abstract 1065MO.

Phase III KEYNOTE-B96 Trial Met Secondary Endpoint of Overall Survival in All-Comer Population of Patients with Platinum-Resistant Recurrent Ovarian Cancer

Press Release: October 16, 2025

"The Phase 3 KEYNOTE-B96 trial, also known as ENGOT-ov65, met its secondary endpoint of overall survival (OS) for the treatment of patients with platinum-resistant recurrent ovarian cancer in all comers. The trial studied pembrolizumab in combination with chemotherapy (paclitaxel) with or without bevacizumab for these patients.

As previously announced, KEYNOTE-B96 met its primary endpoint of progression-free survival PFS in patients with platinum-resistant recurrent ovarian cancer whose tumors express PD-L1 and in all comers, as well as its secondary endpoint of OS for patients whose tumors express PD-L1, at previous interim analyses.

Findings from these prior analyses will be presented in a Presidential Symposium at the upcoming European Society for Medical Oncology (ESMO) Congress 2025."

https://www.merck.com/news/merck-announces-phase-3-keynote-b96-trial-met-secondary-endpoint-of-overall-survival-os-in-all-comers-population-of-patients-with-platinum-resistant-recurrent-ovarian-cancer/

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Abstract LBA3

Pembrolizumab vs Placebo Plus Weekly Paclitaxel With or Without Bevacizumab for Platinum-Resistant Recurrent Ovarian Cancer: Results from the Randomized, Double-Blind Phase 3 ENGOT-ov65/KEYNOTE-B96 Study

Nicoletta Colombo[1,2], Emese Zsiros[3], Alexandra Sebastianelli[4], Mariusz Bidzinski[5], Carlos Gallardo[6], Emad Matanes[7], Kosei Hasegawa[8], Fatih Kose[9], Manuel Magallanes-Maciel[10], Rebecca Herbertson[11], Sumitra Ananda[12], Judith R. Kroep[13], Andreia Cristina de Melo[14], Philip R Debruyne[15], Jae-Weon Kim[16], Xuan Peng[17], Karin Yamada[17], Agata M. Bogusz[17], Thibault De La Motte Rouge[18], and Xiaohua Wu[19] on behalf of the ENGOT-ov65/KEYNOTE-B96 investigators

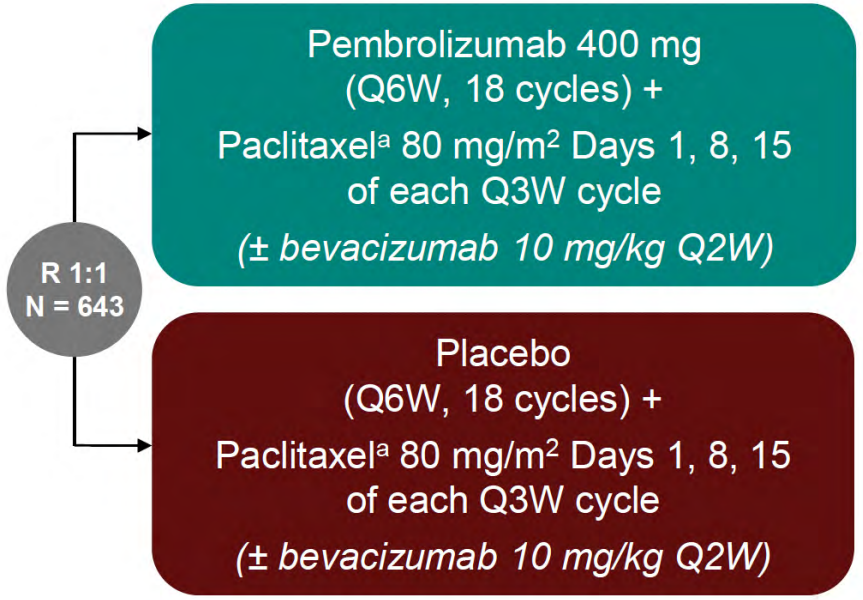
[1]Gynecologic Oncology Program, European Institute of Oncology, IRCCS, Milan, Italy; [2]Department of Medicine and Surgery, University of Milan-Bicocca, Italy; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [4]CHU de Québec-Université Laval, Québec, Canada; [5]Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie, Warsaw, Poland; [6]Bradford Hill Clinical Research Center, Santiago, Chile; [7]Rambam Health Care Campus and Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel; [8]Saitama Medical University International Medical Center, Hidaka, Japan; [9]Başkent University, Ankara, Turkey; [10]Centro Oncologico Internacional, Mexico City, Mexico; [11]University Hospitals Sussex NHS Foundation Trust, West Sussex, United Kingdom; [12]Epworth Healthcare and Peter MacCallum Cancer Centre, Melbourne, Australia; [13]Leiden University Medical Center on behalf of the Dutch Gynecology Oncology Group (DGOG), Leiden, Netherlands; [14]Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil; [15]Kortrijk Cancer Centre, AZ Groeninge, Kortrijk, and Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Leuven, Belgium; [16]Seoul National University, Seoul, South Korea; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Centre Eugene Marquis, Rennes, France; [19]Fudan University Shanghai Cancer Center, Shanghai, China

18 October 2025

KEYNOTE-B96 Study Design

Key Eligibility Criteria

- Histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal carcinoma
- 1 or 2 prior lines of therapy; at least 1 platinum-based chemotherapy
  - Prior anti-PD-1 or anti-PD-L1, PARPi and bevacizumab permitted
- Radiographic progression within 6 months after the last dose of platinum-based chemotherapy
- ECOG PS 0 or 1



Stratification Factors

- Planned bevacizumab use (yes vs no)
- Region (US vs EU vs ROW)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)[b]

Primary Endpoint: PFS per RECIST v1.1 by investigator

Key Secondary: OS

[a]Docetaxel (75 mg/m² Q3W) may be considered in participants with severe hypersensitivity reaction to paclitaxel or an adverse event requiring discontinuation of paclitaxel after consultation with the Sponsor. [b]The combined positive score (CPS) was assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx and defined as the number of PD-L1 CPS ≥1 cells (tumor cells, lymphocytes, macrophages) divided by the total number of tumor cells × 100.

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Colombo N et al. ESMO 2025;Abstract LBA3.

RTP RESEARCH TO PRACTICE

KEYNOTE-B96: Baseline Characteristics

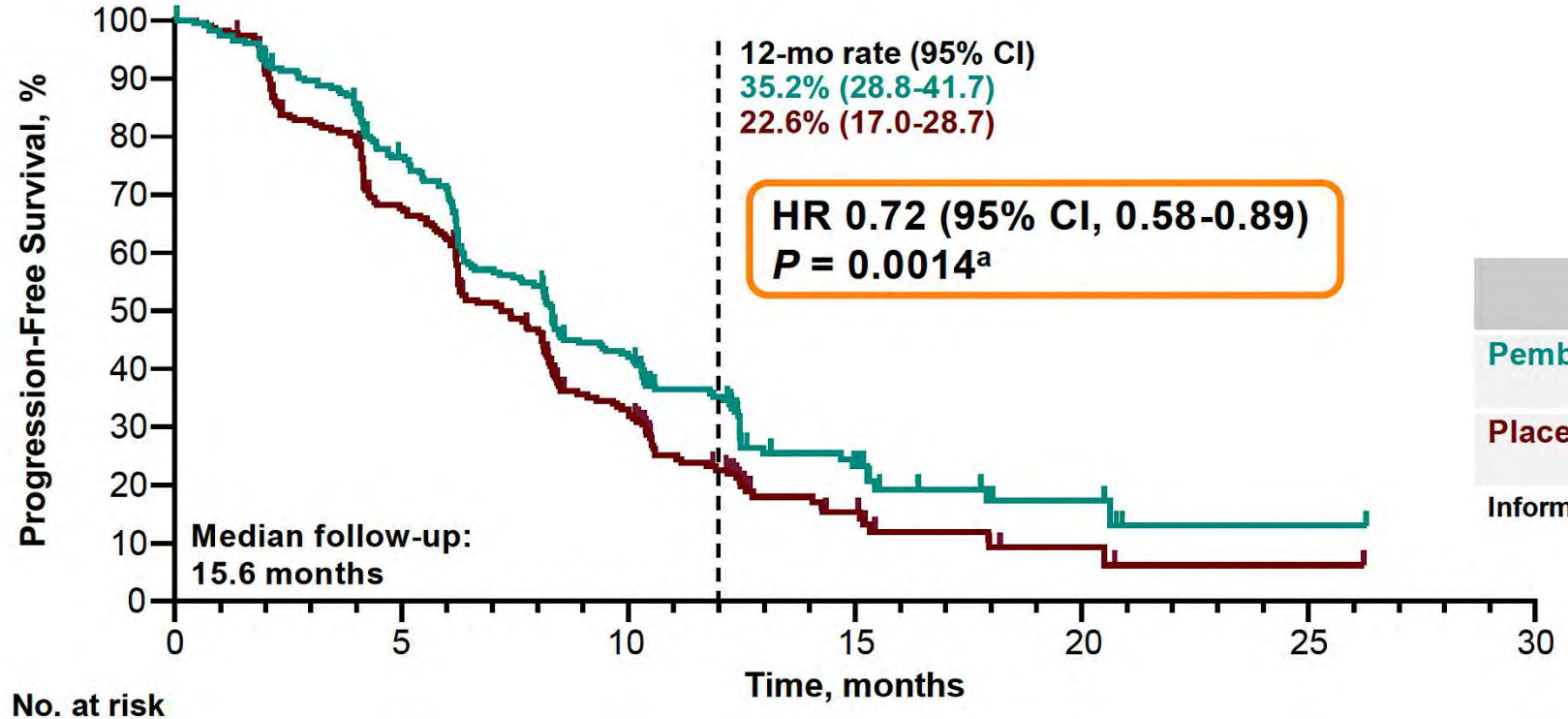
	Pembro Arm (N = 322)	Placebo Arm (N = 321)
Age, median (range)	62 y (37-85)	61 y (37-82)
Race[a]		
White	207 (64.3%)	217 (67.6%)
Asian	72 (22.4%)	58 (18.1%)
Multiple	12 (3.7%)	17 (5.3%)
Black or African American	8 (2.5%)	6 (1.9%)
Hawaiian/Pacific Islander	1 (0.3%)	1 (0.3%)
PD-L1 CPS		
<1	88 (27.3%)	89 (27.7%)
1 to <10	133 (41.3%)	132 (41.1%)
≥10	101 (31.4%)	100 (31.2%)
Stage at diagnosis (FIGO 2014 criteria)		
IA-IIB	25 (7.8%)	26 (8.1%)
III-IIIC	183 (56.8%)	189 (58.9%)
IVA-IVB	114 (35.4%)	106 (33.0%)

	Pembro Arm (N = 322)	Placebo Arm (N = 321)
ECOG PS 1	142 (44.1%)	144 (44.9%)
High-grade serous histology[b]	278 (86.3%)	275 (85.7%)
Bevacizumab use	235 (73.0%)	236 (73.5%)
Prior lines of therapy[c]		
1 line	121 (37.6%)	113 (35.2%)
2 lines	200 (62.1%)	207 (64.5%)
Prior anticancer therapy		
Anti-PD-1 or PD-L1	7 (2.2%)	7 (2.2%)
Bevacizumab	149 (46.3%)	146 (45.5%)
PARP inhibitor	112 (34.8%)	123 (38.3%)
Platinum-free interval[d]		
<3 mo	137 (42.5%)	162 (50.5%)
≥3 to ≤6 mo	183 (56.8%)	154 (48.0%)
>6 mo	2 (0.6%)	4 (1.2%)

[a]44 participants had missing information for race, 22 (6.8%) in the pembro arm and 22 (6.9%) in the placebo arm. [b]Other histology subtypes in the pembro and placebo arms, respectively, were clear cell in 24 (7.5%) and 26 (8.1%), endometrioid in 9 (2.8%) and 4 (1.2%), low-grade serous in 6 (1.9%) and 10 (3.1%), carcinosarcoma in 3 (0.9%) and 5 (1.6%), and other carcinoma in 2 (0.6%) and 1 (0.3%). [c]2 participants had 3 prior lines of therapy, 1 (0.3%) in each treatment arm. [d]1 participant in the placebo arm had missing information for platinum-free interval. Data cutoff date: March 5, 2025.

Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: PFS in the CPS ≥1 Population at Interim Analysis 1 (IA1)



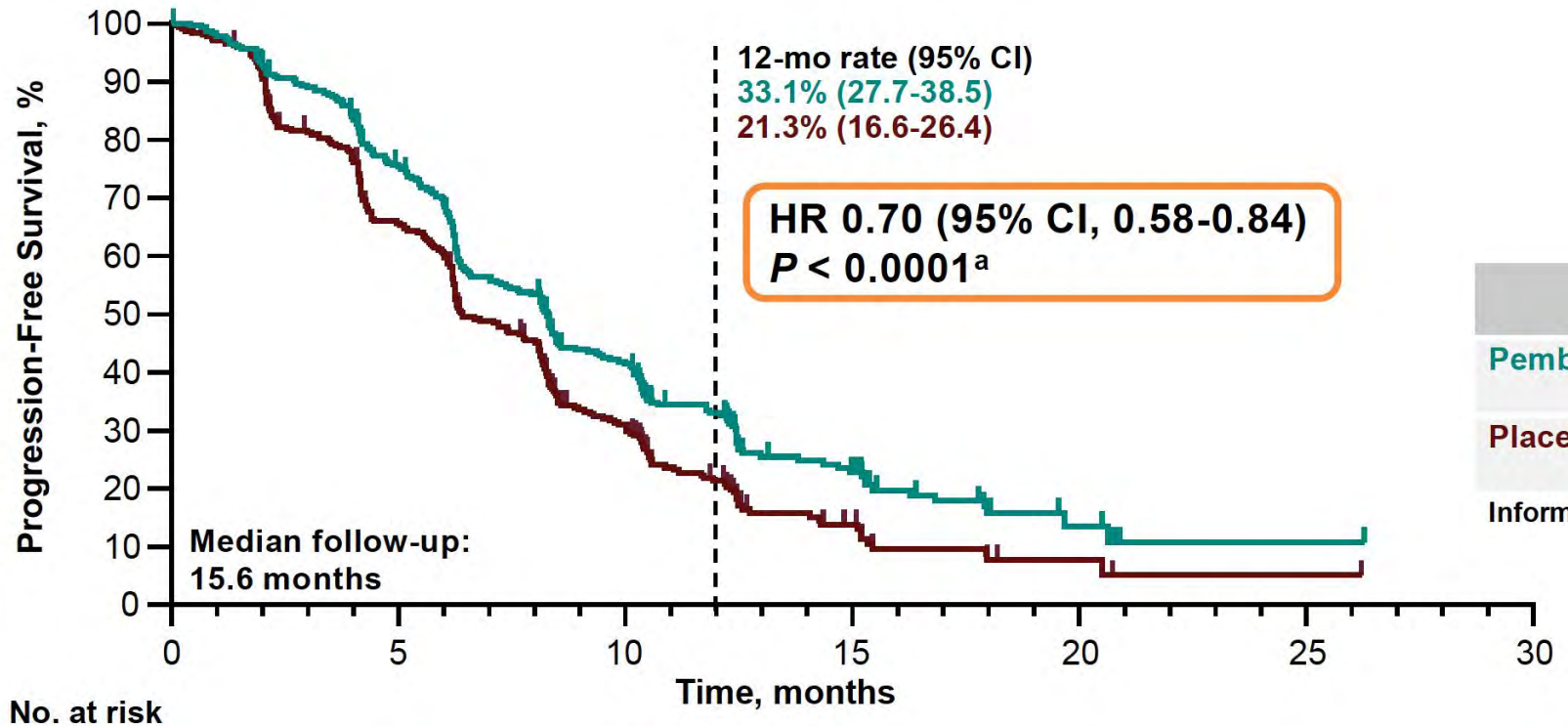
	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	69.2%	8.3 (7.0-9.4)
Placebo Arm	77.6%	7.2 (6.2-8.1)

Information fraction: 87.9%

Response assessed per RECIST v1.1 by investigator review. [a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. The observed p-value crossed the prespecified nominal boundary of 0.0116 at this planned first interim analysis; because the success criterion of the PFS hypothesis was met, no formal testing of PFS will be performed at later analyses. Data cutoff date: April 3, 2024.

Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: PFS in the Intent-to-Treat Population at IA1



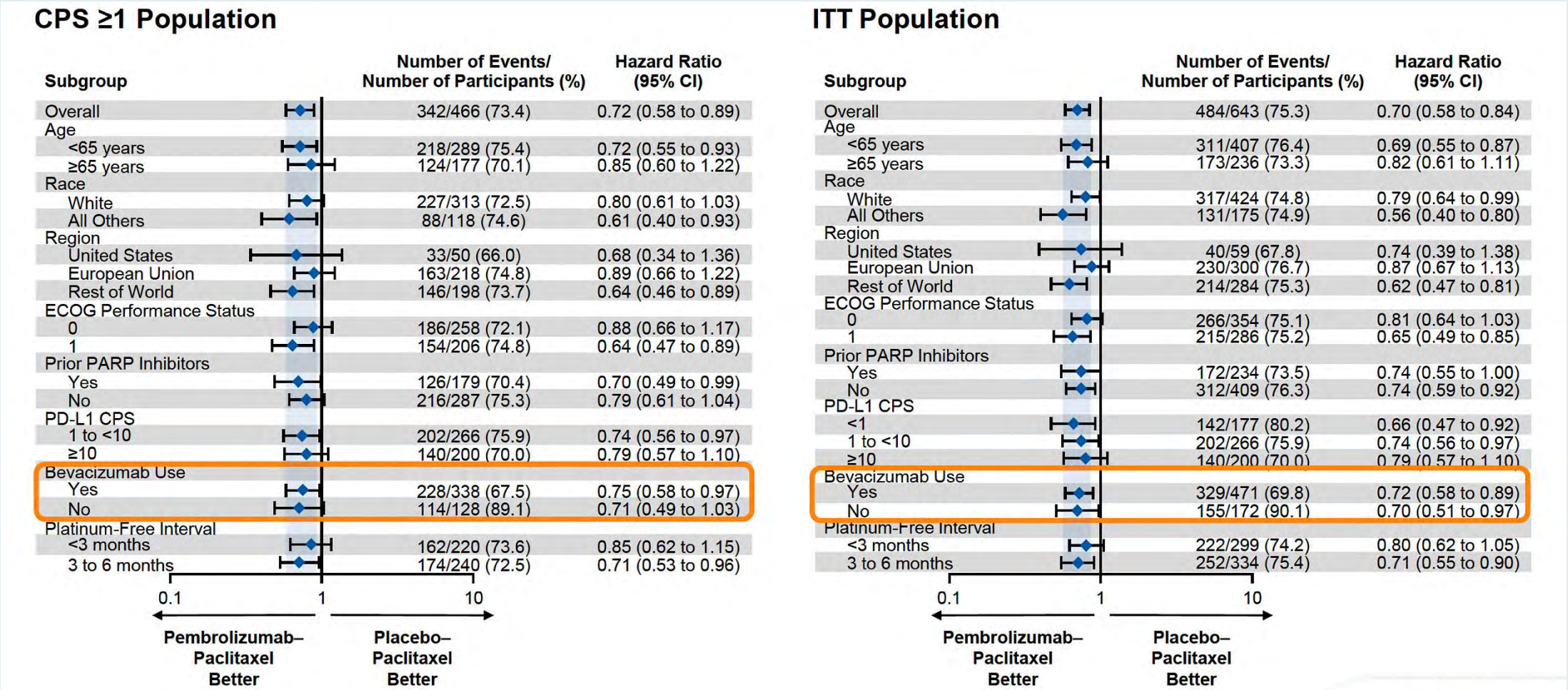
	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	71.7%	8.3 (7.2-8.6)
Placebo Arm	78.8%	6.4 (6.2-8.1)

Information fraction: 89.5%

Response assessed per RECIST v1.1 by investigator review. [a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. The observed p-value crossed the prespecified nominal boundary of 0.0023 at this planned first interim analysis; because the success criterion of the PFS hypothesis was met, no formal testing of PFS will be performed at later analyses. Data cutoff date: April 3, 2024.

Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: PFS in Subgroups in the CPS ≥1 and Intent-to-Treat (ITT) Populations at IA1

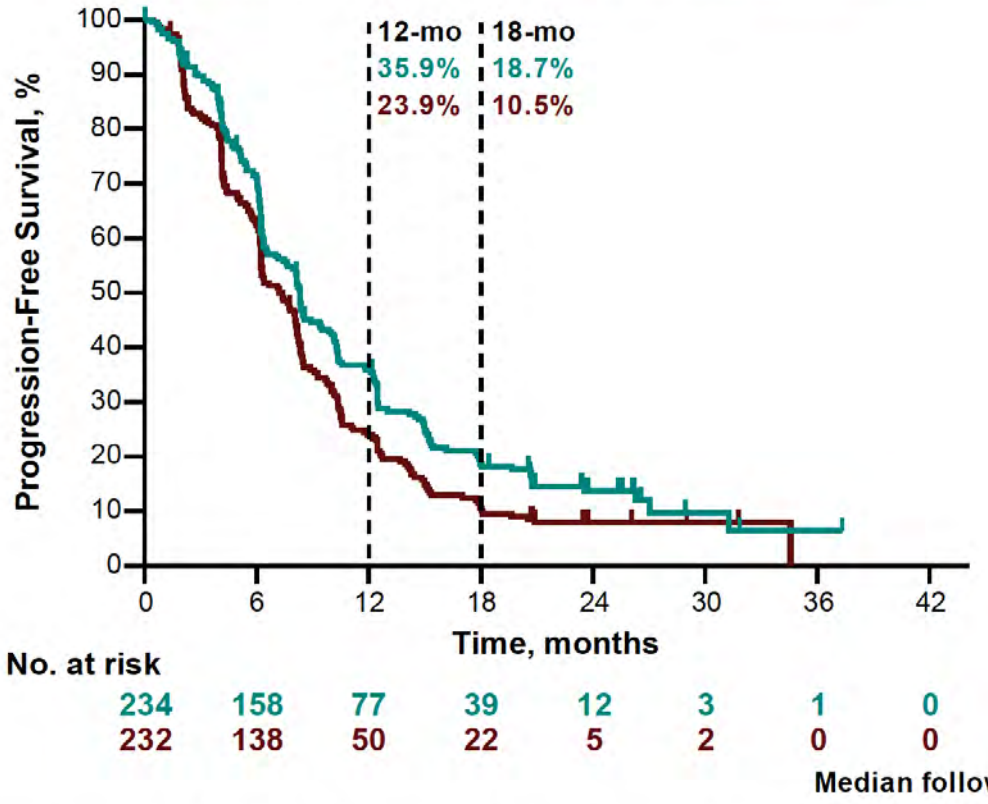


Response assessed per RECIST v1.1 by investigator review. The subgroup results shown in the forest plot were based on an unstratified Cox model, so the results for CPS ≥1 may differ slightly compared with those of the primary analysis, which were based on a stratified Cox model. Data cutoff date: April 3, 2024.

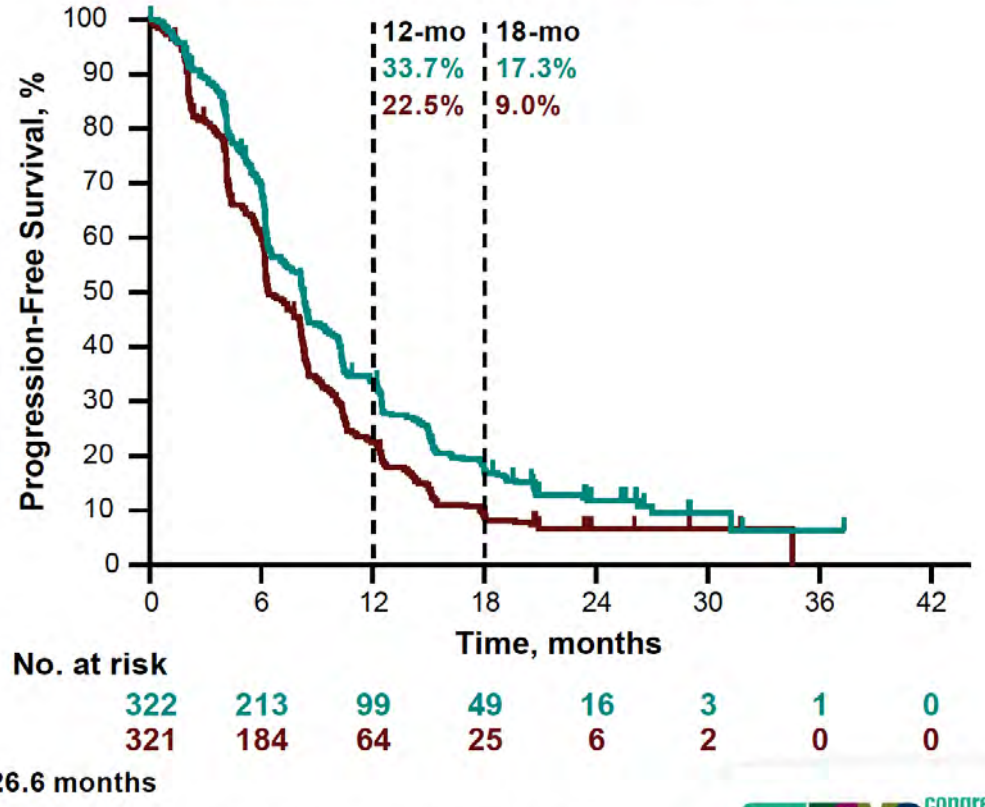
Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: PFS in the CPS ≥1 and ITT Populations at Interim Analysis 2 (IA2)

CPS ≥1 Population	Median, months	Events	HR (95% CI)
Pembro Arm	8.3	81.6%	0.75[a] (0.61-0.91)
Placebo Arm	7.2	86.6%	



ITT Population	Median, months	Events	HR (95% CI)
Pembro Arm	8.3	83.2%	0.73[a] (0.62-0.86)
Placebo Arm	6.4	87.2%	



Median follow-up: 26.6 months

Response assessed per RECIST v1.1 by investigator review. [a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. No statistical testing for PFS was done at this analysis because significance was achieved at IA1. Data cutoff date: March 5, 2025.

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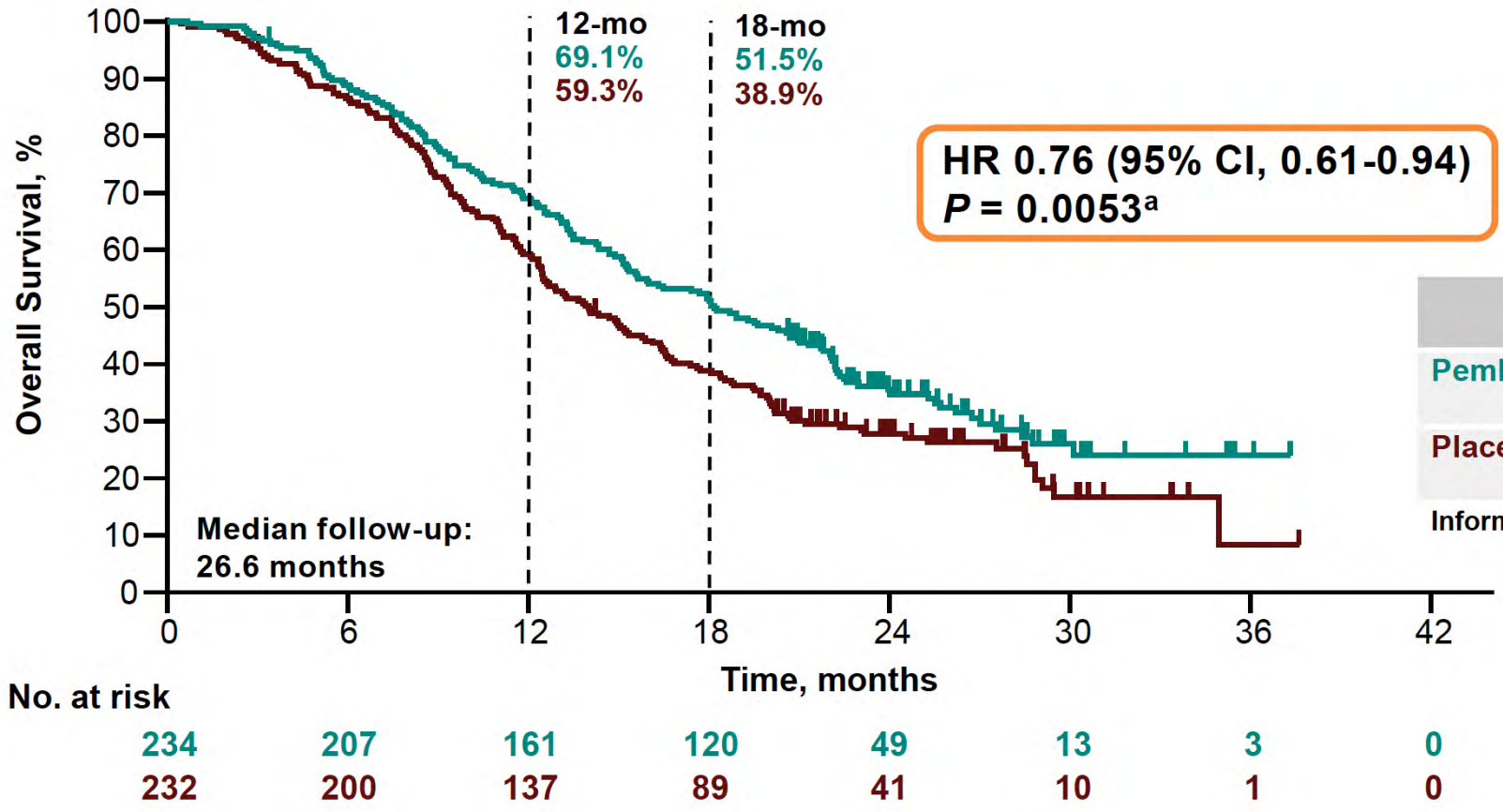
Colombo N et al. ESMO 2025;Abstract LBA3.

RTP RESEARCH TO PRACTICE

KEYNOTE-B96: OS in the PD-L1 CPS ≥1 Population at IA2



HR 0.76 (95% CI, 0.61-0.94)
P = 0.0053[a]

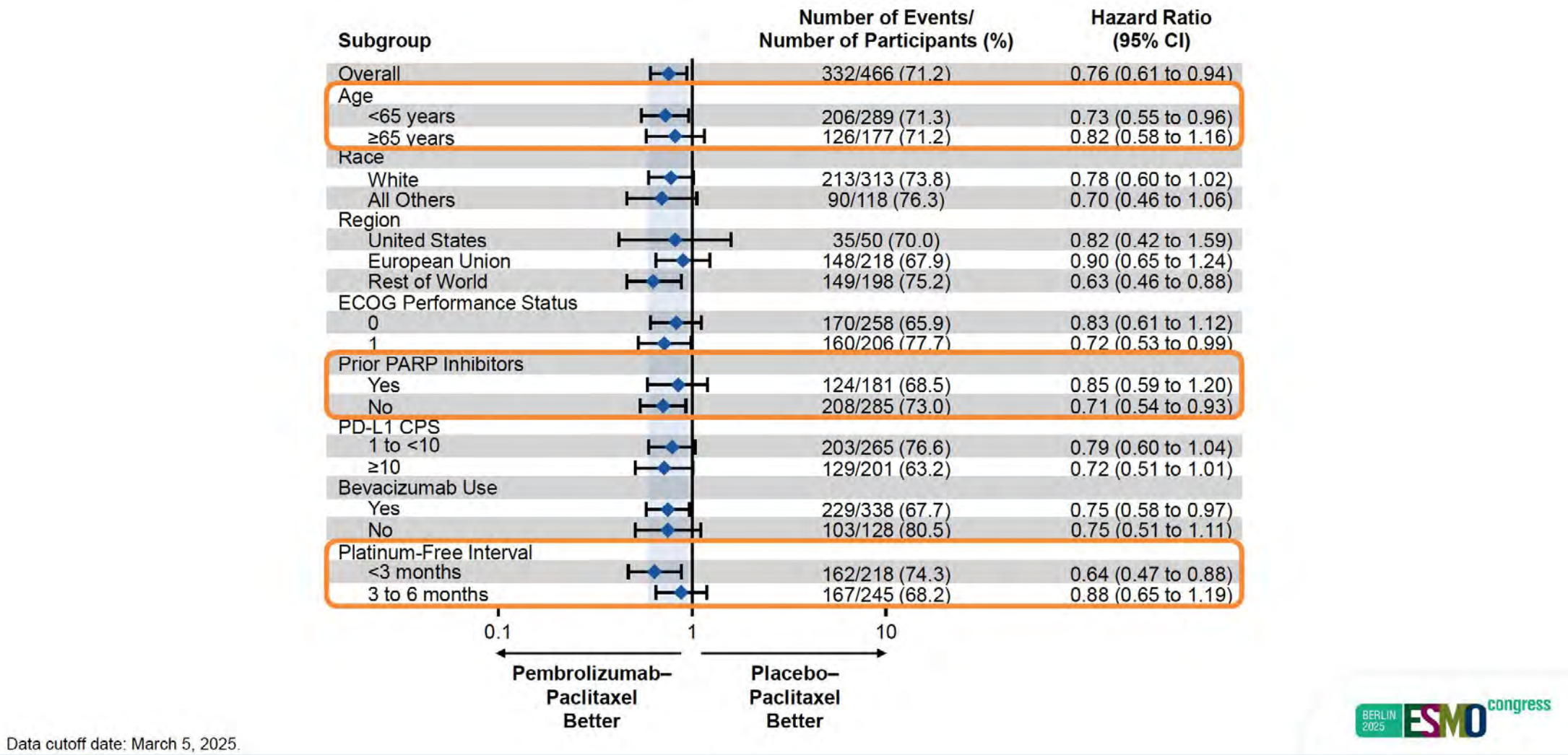
	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	67.1%	18.2 (15.3-21.0)
Placebo Arm	75.4%	14.0 (12.5-16.1)

Information fraction: 90.0%

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. The observed p-value crossed the prespecified nominal boundary of 0.0083 at this planned second interim analysis. Data cutoff date: March 5, 2025.

Colombo N et al. ESMO 2025;Abstract LBA3.

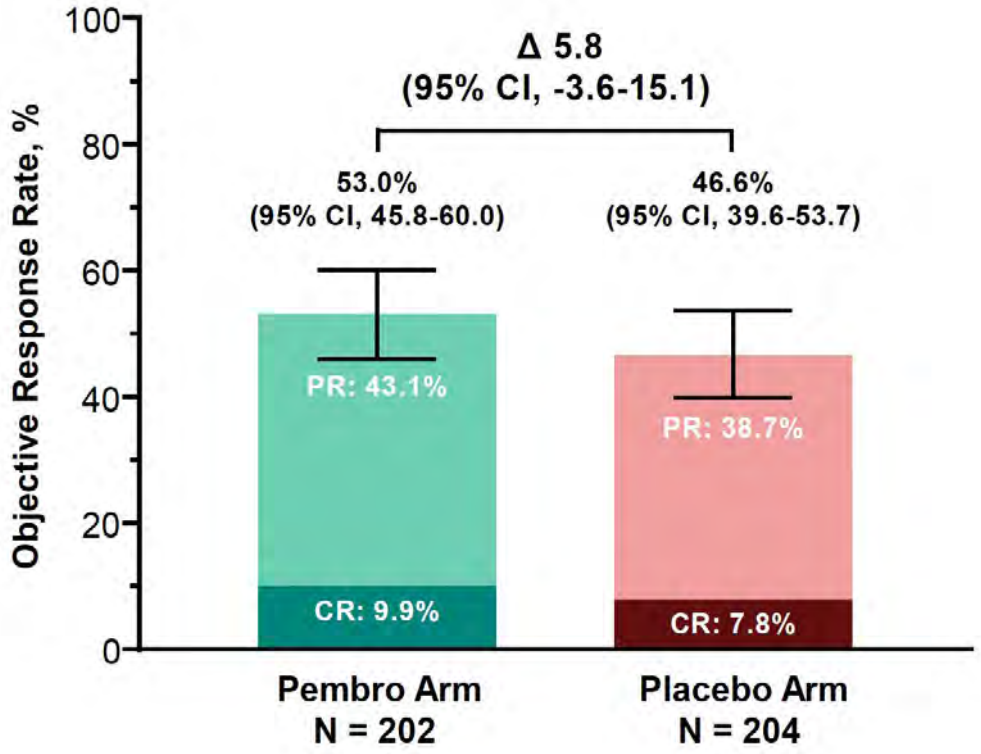
KEYNOTE-B96: OS in Subgroups in the PD-L1 CPS ≥1 Population at IA2

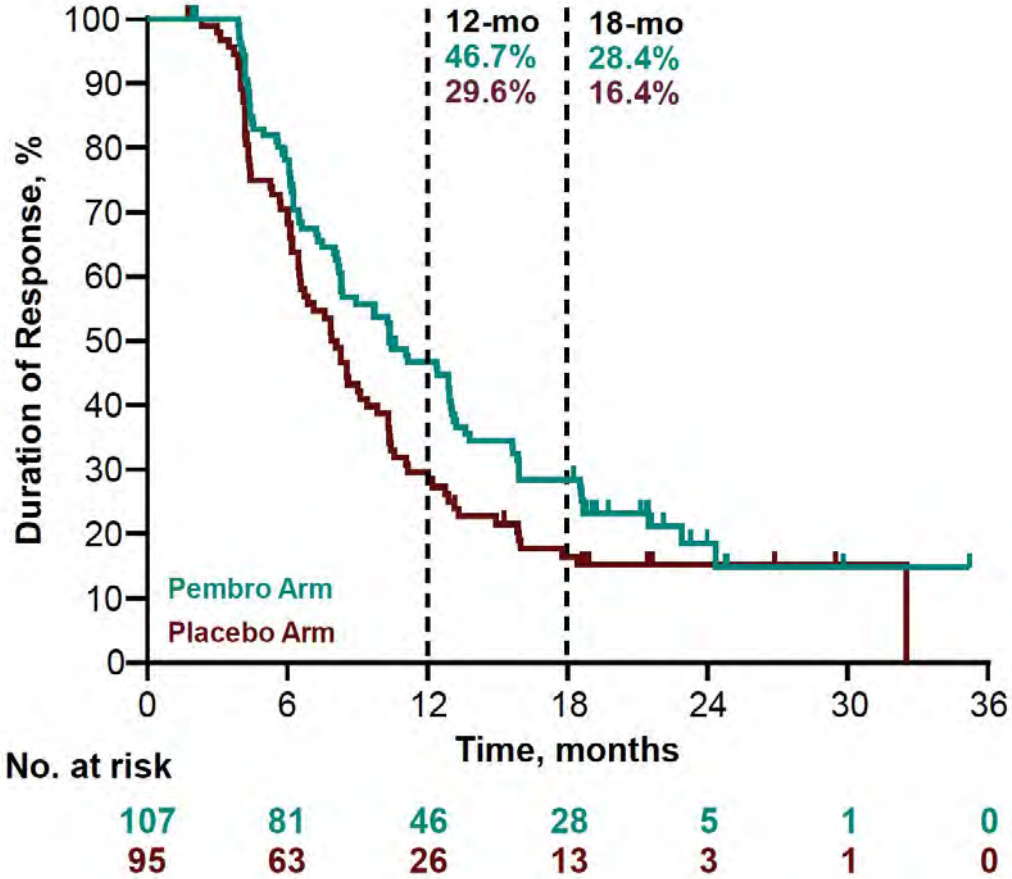


Data cutoff date: March 5, 2025.

Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: Objective Response Rate and Response Duration in the PD-L1 CPS ≥1 Population at IA2

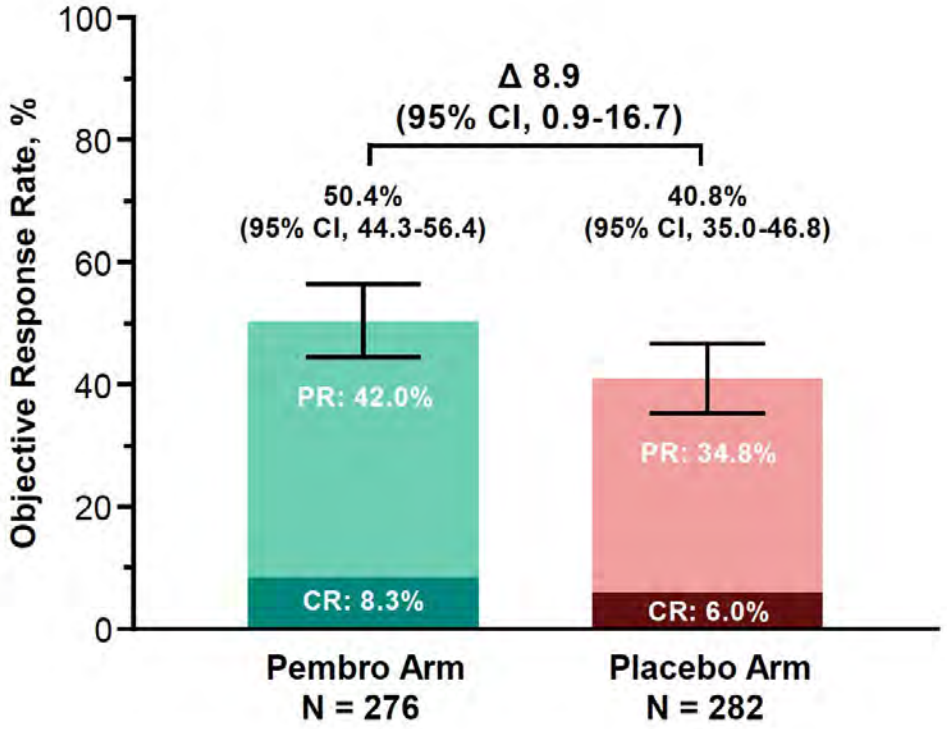


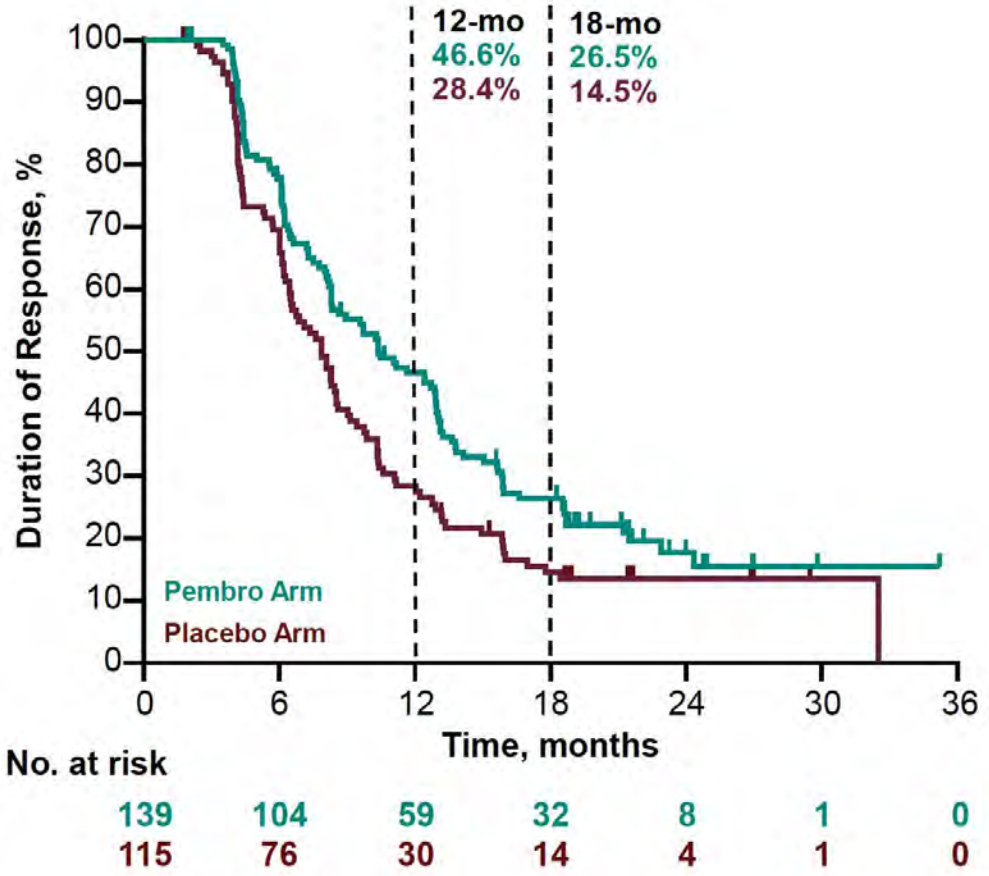


Response assessed per RECIST v1.1 by investigator review. Data cutoff date: March 5, 2025.

Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: Objective Response Rate and Response Duration in the ITT Population at IA2





Response assessed per RECIST v1.1 by investigator review. Data cutoff date: March 5, 2025.

Colombo N et al. ESMO 2025;Abstract LBA3.

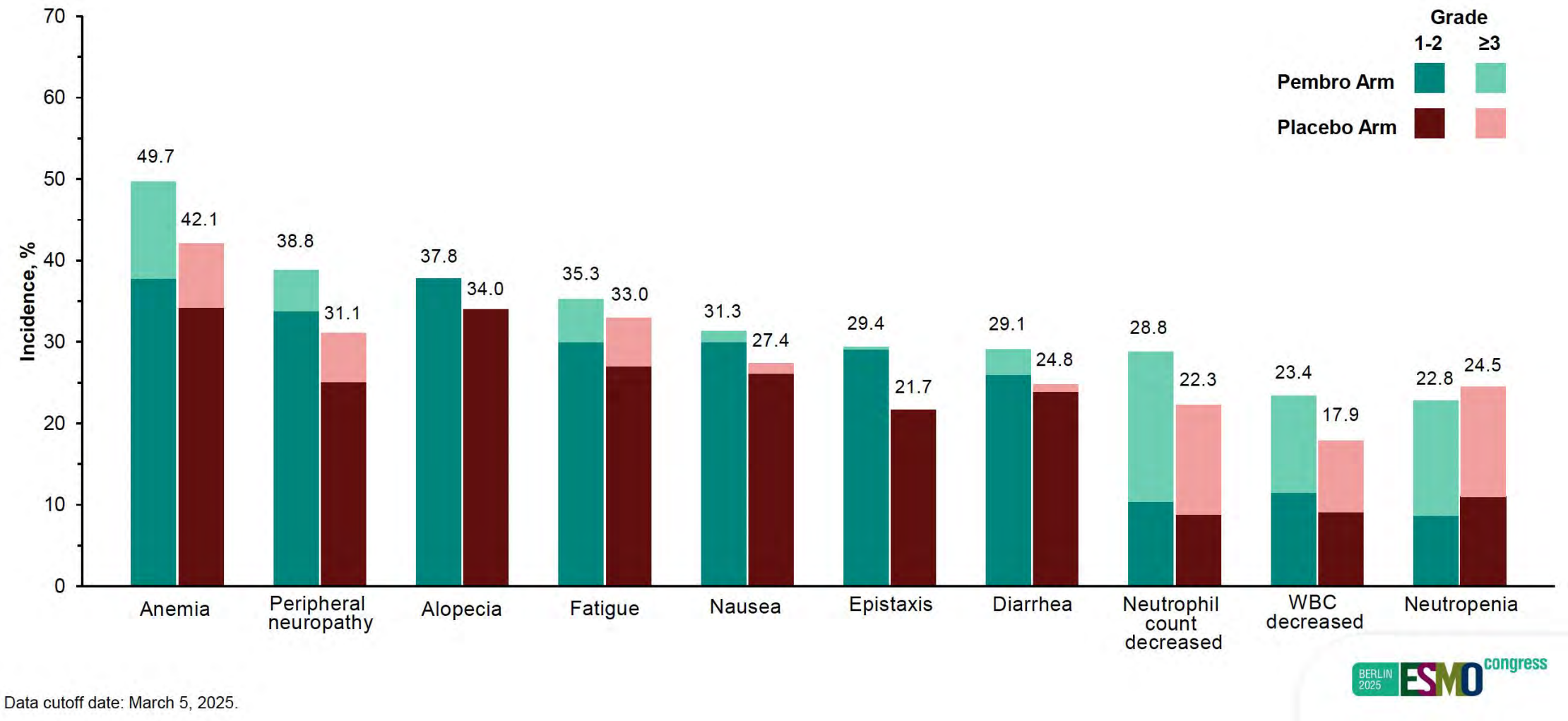
KEYNOTE-B96: Summary of Adverse Events at IA2

	All-Cause AEs		Treatment-Related AEs[a]		Immune-Mediated AEs[b]	
	Pembro Arm (N = 320)	Placebo Arm (N = 318)	Pembro Arm (N = 320)	Placebo Arm (N = 318)	Pembro Arm (N = 320)	Placebo Arm (N = 318)
Any grade	318 (99.7%)	316 (99.4%)	313 (97.8%)	303 (95.3%)	125 (39.1%)	60 (18.9%)
Grade ≥3	264 (82.5%)	225 (70.8%)	216 (67.5%)	176 (55.3%)	37 (11.6%)	11 (3.5%)
Serious	178 (55.6%)	122 (38.4%)	106 (33.1%)	62 (19.5%)	35 (10.9%)	7 (2.2%)
Led to death	15 (4.7%)	14 (4.4%)	3 (0.9%)[c]	5 (1.6%)[d]	2 (0.6%)[e]	0
Led to discontinuation of any treatment	132 (41.3%)	108 (34.0%)	115 (35.9%)	89 (28.0%)	22 (6.9%)	8 (2.5%)

The median duration of therapy was 33 weeks in the pembro arm and 28 weeks in the placebo arm. [a]Per investigator assessment. [b]Events were based on a list of preferred terms intended to capture the known risks of pembrolizumab and considered regardless of attribution to treatment by the investigator. [c]Colitis, interstitial lung disease, and intestinal perforation. [d]Cardiac failure, intestinal perforation (in 2), and large intestine perforation (in 2). [e]Colitis and pneumonitis (reported by the investigator as treatment-related interstitial lung disease). Data cutoff date: March 5, 2025.

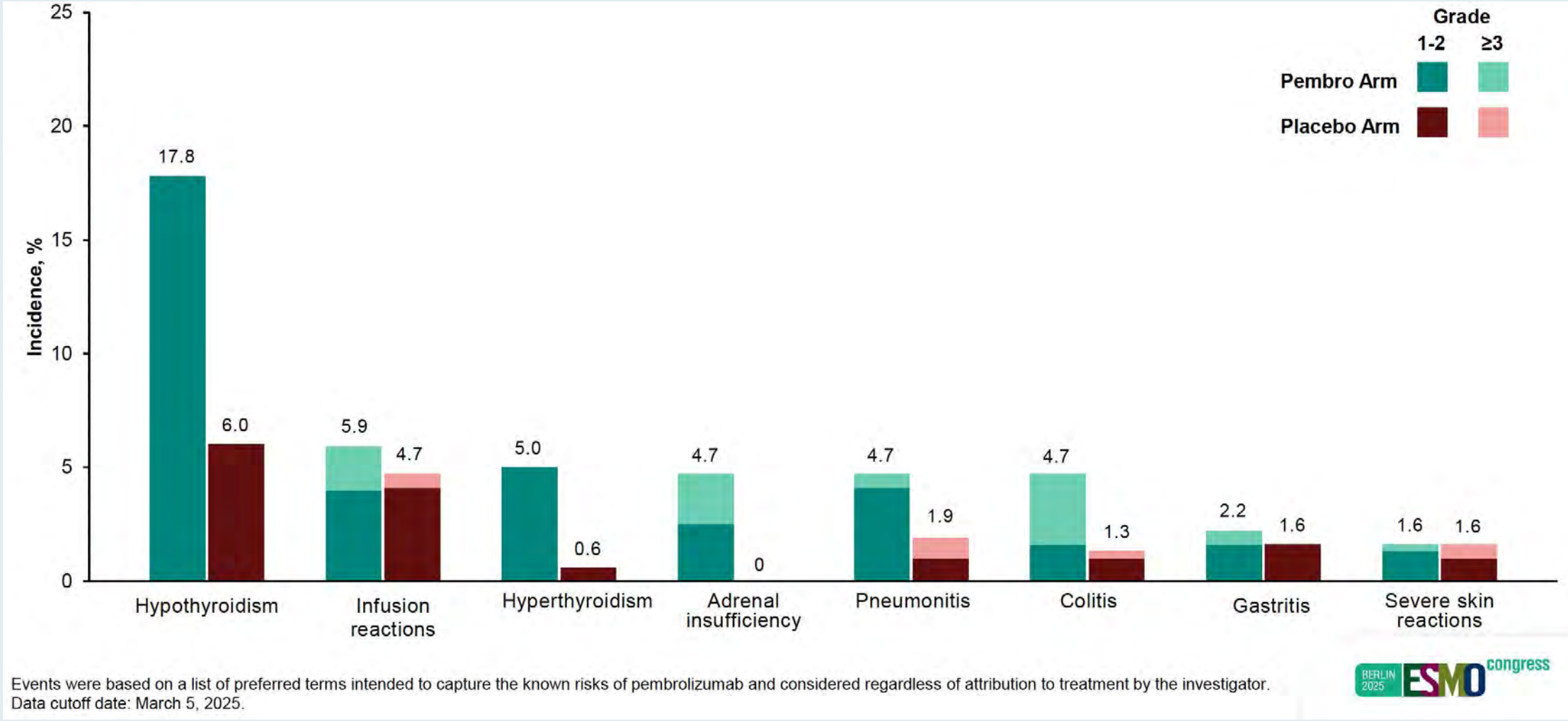
Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: Treatment-Related Adverse Events at IA2



Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96: Immune-Mediated Adverse Events and Infusion Reactions at IA2



Events were based on a list of preferred terms intended to capture the known risks of pembrolizumab and considered regardless of attribution to treatment by the investigator.
Data cutoff date: March 5, 2025.

Colombo N et al. ESMO 2025;Abstract LBA3.

KEYNOTE-B96 Study Conclusions

- Pembrolizumab in combination with weekly paclitaxel, with or without bevacizumab, demonstrated statistically significant and clinically meaningful improvements in PFS regardless of PD-L1 status and in OS in participants with PD-L1-expressing tumors in ENGOT-ov65/KEYNOTE-B96
- This is the first phase 3 study to report a statistically significant improvement in OS with an immune checkpoint inhibitor-based regimen in ovarian cancer
- The observed OS is among the longest reported in any clinical trial for PRROC, showing a clinically meaningful benefit of this regimen relative to the most active standard-of-care control arm, weekly paclitaxel with bevacizumab in bevacizumab-eligible patients
- The safety profile of pembrolizumab plus weekly paclitaxel, with or without bevacizumab, was consistent with the known profiles of the individual therapies, with no new safety signals
- **These data support the use of pembrolizumab plus weekly paclitaxel, with or without bevacizumab, as a new standard-of-care for patients with PRROC**

PRROC = platinum-resistant recurrent ovarian cancer

Colombo N et al. ESMO 2025;Abstract LBA3.

CHAIRS: GIUSEPPE CURIGLIANO, BRIGETTE MA

BERLIN 2025 ESMO congress

Combining Pembrolizumab Plus Weekly Paclitaxel +/- Bevacizumab for Platinum-Resistant Recurrent Ovarian Cancer

Insight from ENGOT-ov65/KEYNOTE-B96 Study

Prof Isabelle Ray-Coquard
Centre Leon Berard
GINECO Group – ENGOT President
France

October 2025

Isabelle Ray-Coquard

Invited Discussant LBA3

RTP RESEARCH TO PRACTICE

Overall Survival Primary Endpoint Met in Phase III ROSELLA Trial of Relacorilant for Patients with Platinum-Resistant Ovarian Cancer

Press Release: January 22, 2026

It was announced today that ROSELLA, a pivotal Phase III trial of relacorilant with *nab*-paclitaxel to treat patients with platinum-resistant ovarian cancer, met its overall survival (OS) primary endpoint.

"In ROSELLA, patients treated with relacorilant in addition to *nab*-paclitaxel chemotherapy experienced a 35 percent reduction in the risk of death compared to patients treated with *nab*-paclitaxel alone (hazard ratio: 0.65; *p*-value: 0.0004). The median OS for patients receiving relacorilant was 16.0 months, compared to 11.9 months for patients receiving *nab*-paclitaxel alone, a difference of 4.1 months. Relacorilant in combination with *nab*-paclitaxel was well-tolerated, consistent with its known safety profile. Importantly, the type, frequency and severity of adverse events in the combination arm were comparable to those in the *nab*-paclitaxel monotherapy arm. Relacorilant conferred its benefit without increasing the safety burden of the patients who received it."

Complete results from ROSELLA will be presented at an upcoming medical conference.

https://ir.corcept.com/news-releases/news-release-details/overall-survival-primary-endpoint-met-corcepts-pivotal-phase-3

RTP RESEARCH TO PRACTICE

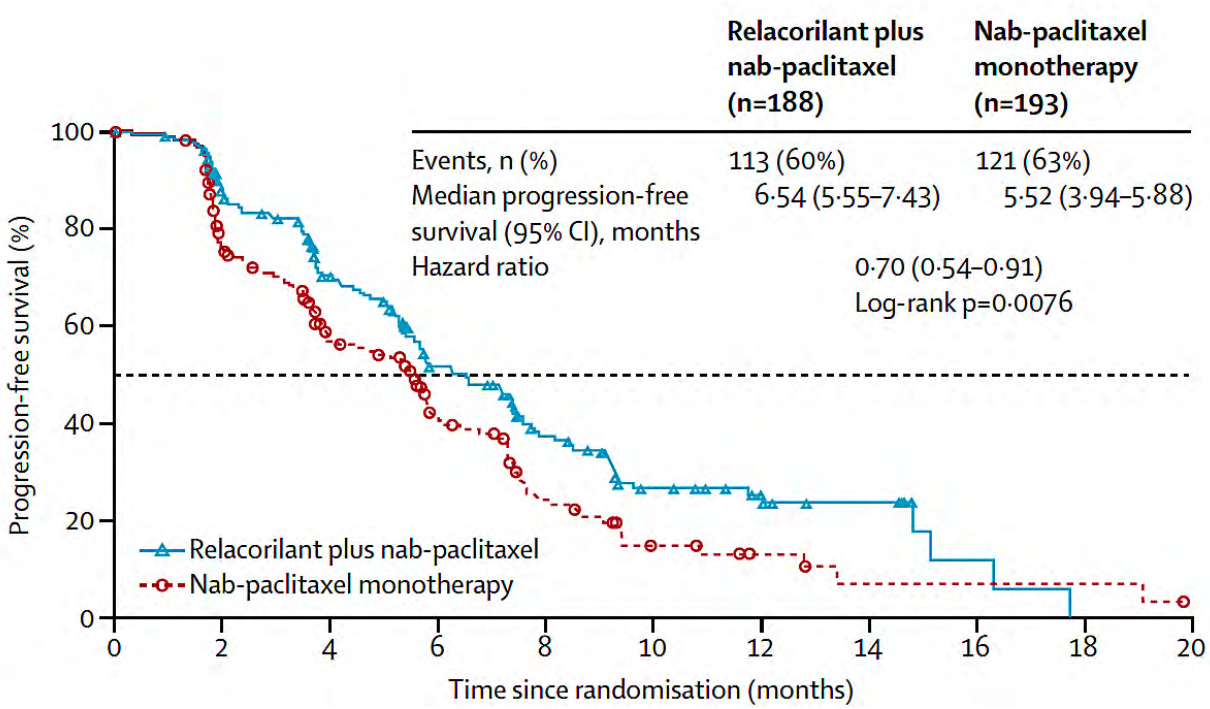
Lancet 2025;405(10496):2205-16.

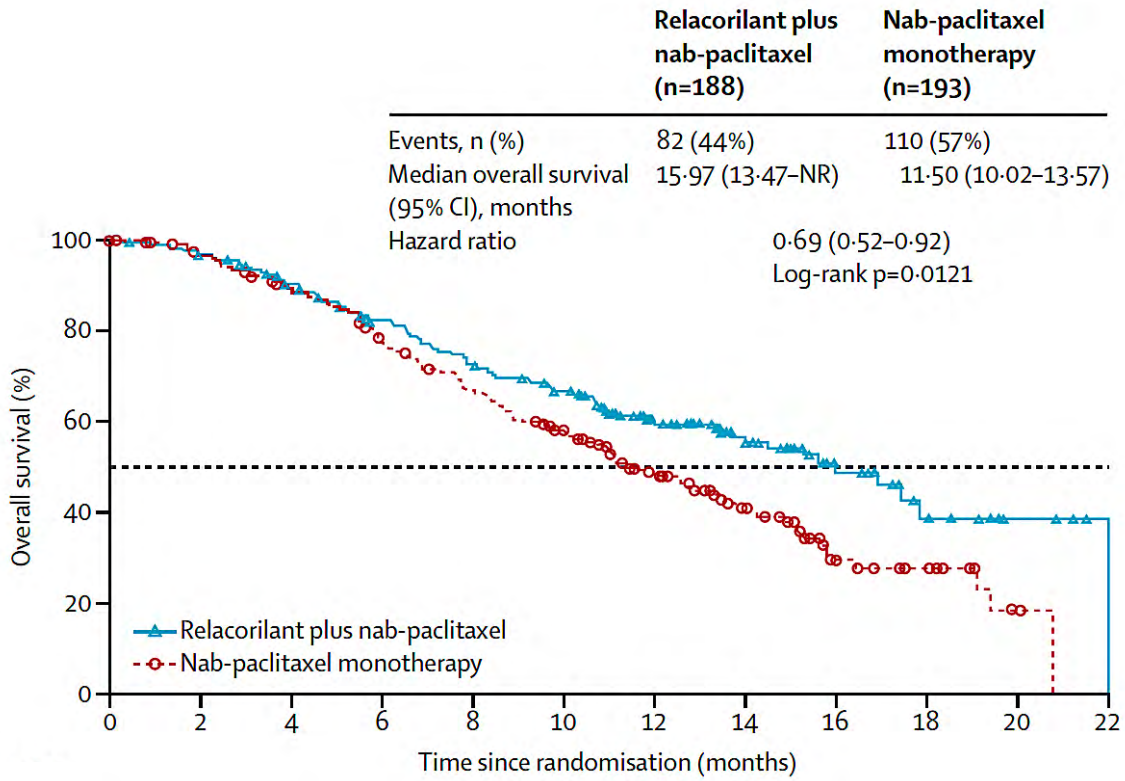
Articles

Relacorilant and nab-paclitaxel in patients with platinum-resistant ovarian cancer (ROSELLA): an open-label, randomised, controlled, phase 3 trial

Alexander B Olawaiye, Laurence Gladieff, David M O'Malley, Jae-Weon Kim, Gabriel Garbaos, Vanda Salutari, Lucy Gilbert, Linda Mileshkin, Alix Devaux, Elizabeth Hopp, Yong Jae Lee, Ana Oaknin, Mariana Scaranti, Byoung-Gie Kim, Nicoletta Colombo, Michael E McCollum, Connie Diakos, Andrew Clamp, Aliza L Leiser, Boglárka Balázs, Bradley J Monk, Giuseppa Scandurra, Emily McClung, Emilie Kaczmarek, Brian Slomovitz, Helena De La Cueva, Aknar Freire de Carvalho Calabrich, Chiara Cassani, Benoit You, Toon Van Gorp, Cristina Churruca, Giuseppe Caruso, Shibani Nicum, Andrea Bagaméri, Grazia Artioli, Lubomir Bodnar, Sokbom Kang, Ignace Vergote, Amanda Kesner-Hays, Hristina I Pashova, Sachin G Pai, Iulia Cristina Tudor, Adrian M Jubb, Domenica Lorusso

ROSELLA: PFS and Interim OS Analysis with Relacorilant and *nab* Paclitaxel





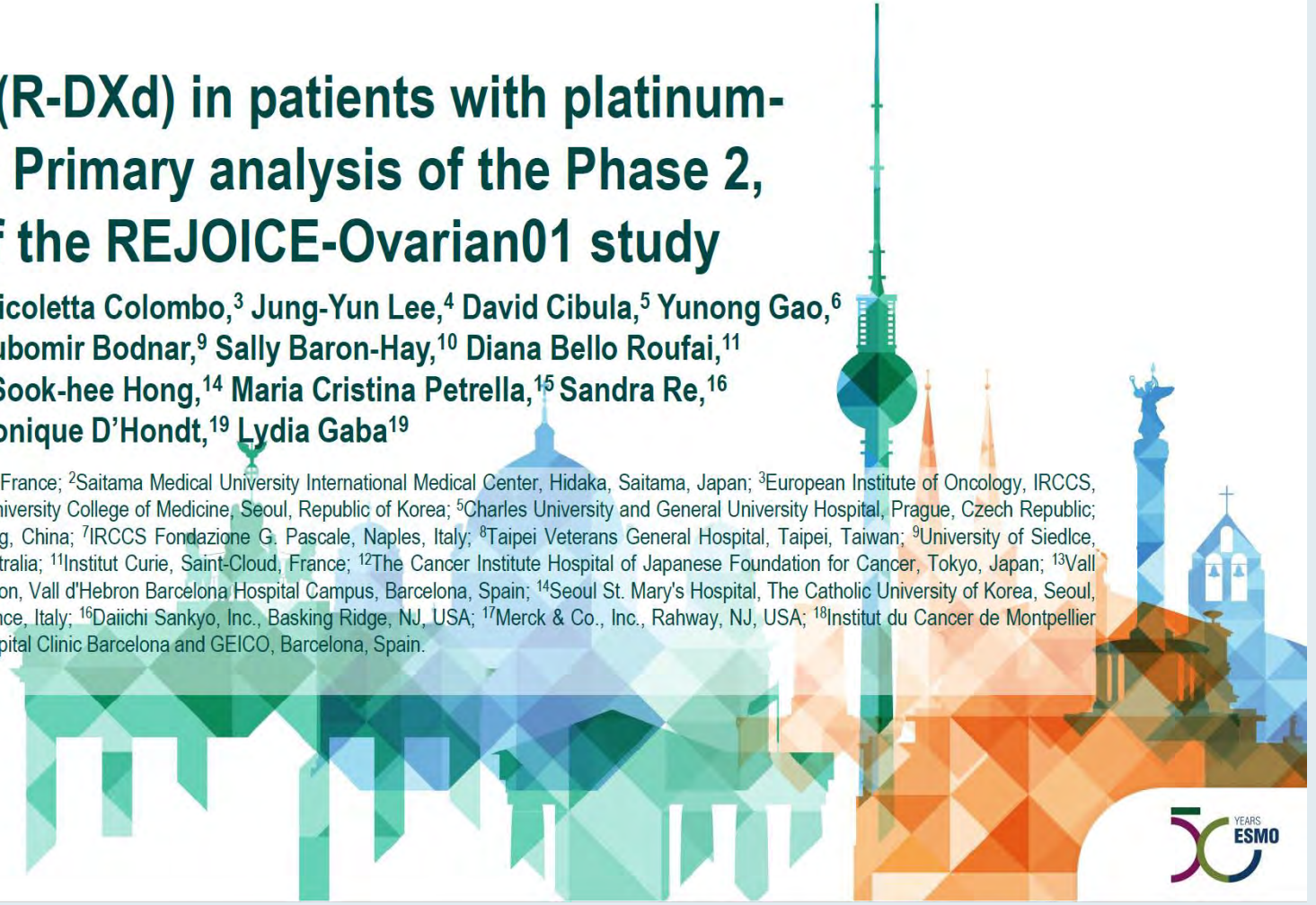
Olawaiye AB et al. *Lancet* 2025;405(10496):2205-16.

BERLIN 2025 ESMO congress

Raludotatug deruxtecan (R-DXd) in patients with platinum-resistant ovarian cancer: Primary analysis of the Phase 2, dose-optimization part of the REJOICE-Ovarian01 study

Isabelle Ray-Coquard,[1] Kosei Hasegawa,[2] Nicoletta Colombo,[3] Jung-Yun Lee,[4] David Cibula,[5] Yunong Gao,[6] Sabrina Chiara Cecere,[7] Peng-Hui Wang,[8] Lubomir Bodnar,[9] Sally Baron-Hay,[10] Diana Bello Roufai,[11] Mayu Yunokawa,[12] David Garcia-Illescas,[13] Sook-hee Hong,[14] Maria Cristina Petrella,[15] Sandra Re,[16] Madan Gopal Kundu,[16] Karin Yamada,[17] Veronique D'Hondt,[19] Lydia Gaba[19]

[1]Centre Léon Bérard, University Claude Bernard, and GINECO, Lyon, France; [2]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [3]European Institute of Oncology, IRCCS, Milan, Italy; [4]Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [5]Charles University and General University Hospital, Prague, Czech Republic; [6]Beijing Cancer Hospital, Beijing Institute for Cancer Research, Beijing, China; [7]IRCCS Fondazione G. Pascale, Naples, Italy; [8]Taipei Veterans General Hospital, Taipei, Taiwan; [9]University of Siedlce, Siedlce, Poland; [10]GenesisCare North Shore, St Leonards, NSW, Australia; [11]Institut Curie, Saint-Cloud, France; [12]The Cancer Institute Hospital of Japanese Foundation for Cancer, Tokyo, Japan; [13]Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [14]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea; [15]Azienda Ospedaliera Universitaria Careggi, Florence, Italy; [16]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Institut du Cancer de Montpellier Val d'Aurelle, Parc Euromedecine, GINECO, Montpellier, France; [19]Hospital Clinic Barcelona and GEICO, Barcelona, Spain.

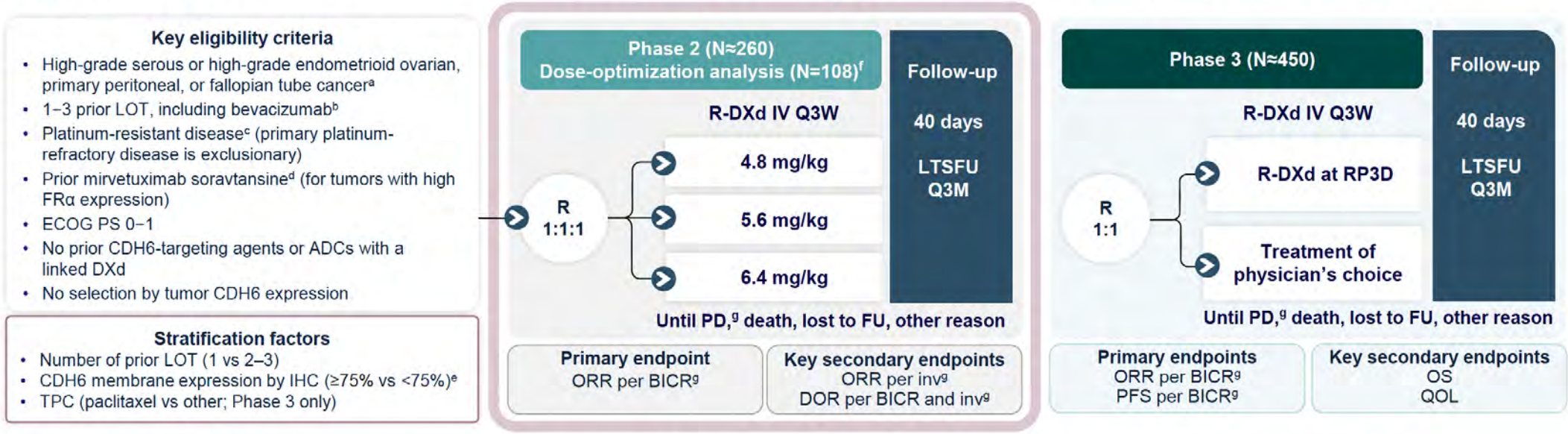


19 October 2025

Presentation number: LBA42

REJOICE-Ovarian01 Phase II/III Study Design

A Phase 2/3 multicenter, randomized study of R-DXd in patients with platinum-resistant, high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer[1,2]



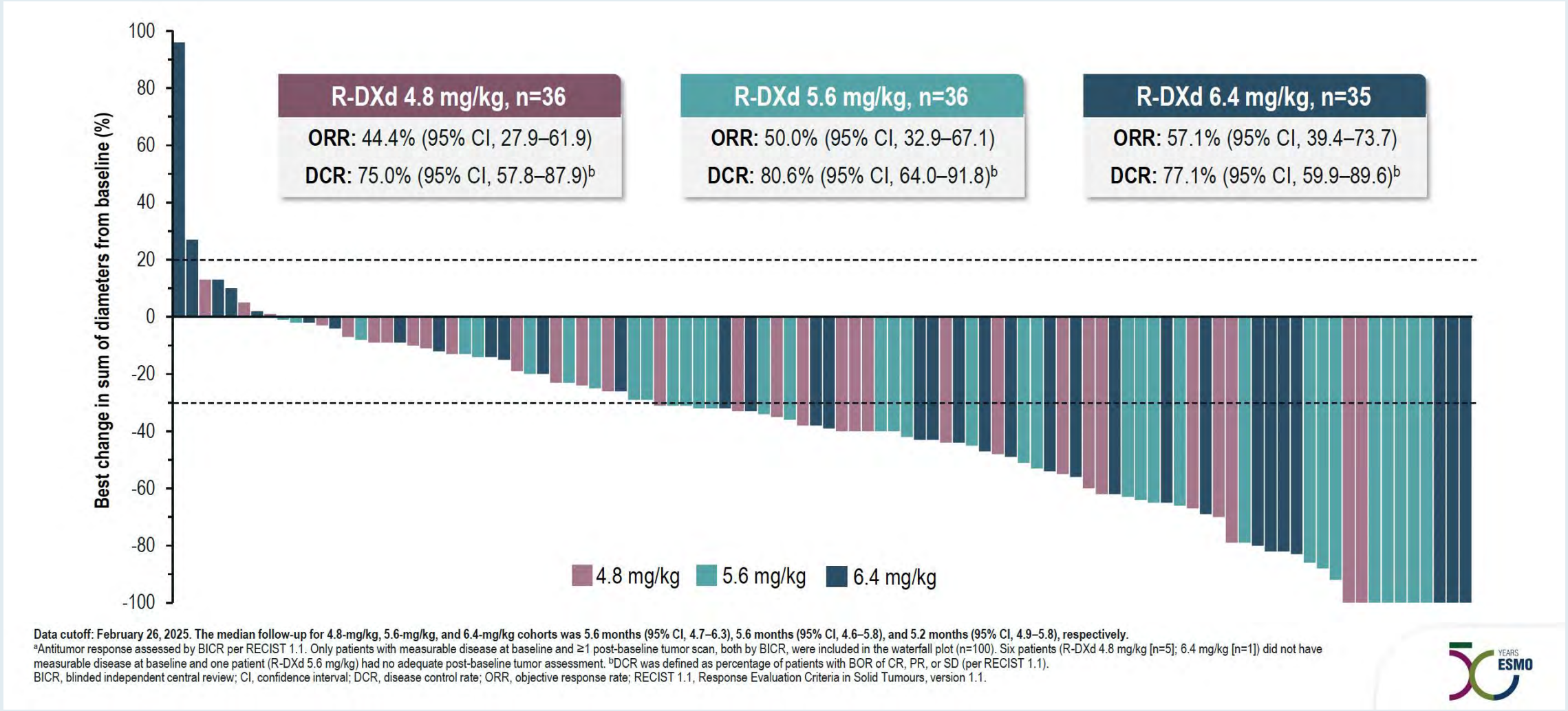
We present the primary analysis from the dose-optimization part of the Phase 2/3 REJOICE-Ovarian01 study, in 107 patients with platinum-resistant OC who had a follow-up of ≥18 weeks or discontinued treatment

[a]Patients must have ≥1 lesion not previously irradiated and amenable to biopsy; must consent to provide a pretreatment biopsy and, in Phase 2 only, an on-treatment biopsy tissue sample and have ≥1 measurable lesion per RECIST 1.1. [b]Unless ineligible. [c]Defined as 1 line of prior platinum therapy (≥4 cycles with best response of not PD) with radiologically documented progression >90 and ≤180 days following last dose of platinum therapy, or 2–3 lines of prior platinum therapy (≥2 cycles) with radiologically documented progression ≤180 days following the last dose of platinum. [d]Unless ineligible, not approved, or not available locally. [e]A stratification cutoff of 75% tumor cell membrane staining at any intensity was selected based on the median observed percentage tumor cell membrane staining (at any intensity) in the Phase 1 study population.[3] [f]Overall, 108 patients were randomized to receive R-DXd. One patient did not receive treatment, so 107 patients were treated and were included in the safety analysis set. [g]Per RECIST 1.1.
ADC, antibody–drug conjugate; BICR, blinded independent central review; CDH6, cadherin 6; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FRα, folate receptor alpha; FU, follow-up; IHC, immunohistochemistry; IV, intravenous; inv, investigator; LOT, lines of therapy; LTSFU, long-term survival follow up; ORR, objective response rate; OS, overall survival; RP3D, recommended phase 3 dose; PD, progressive disease; Q3M, every 3 months; Q3W, every 3 weeks; QOL, quality of life; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; TPC, treatment of physician's choice.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06161025. Accessed October 7, 2025. 2. Ray-Coquard I, et al. Poster presentation at American Society of Clinical Oncology 2024; May 31–June 4; Chicago, IL, USA. Poster TPS5625. 3. Moore KN, et al. Oral presentation at the Society of Gynecologic Oncology 2024 Annual Meeting on Women's Cancer. March 16–18, 2024; San Diego, CA, USA.

Ray-Coquard IL et al. ESMO 2025;Abstract LBA42.

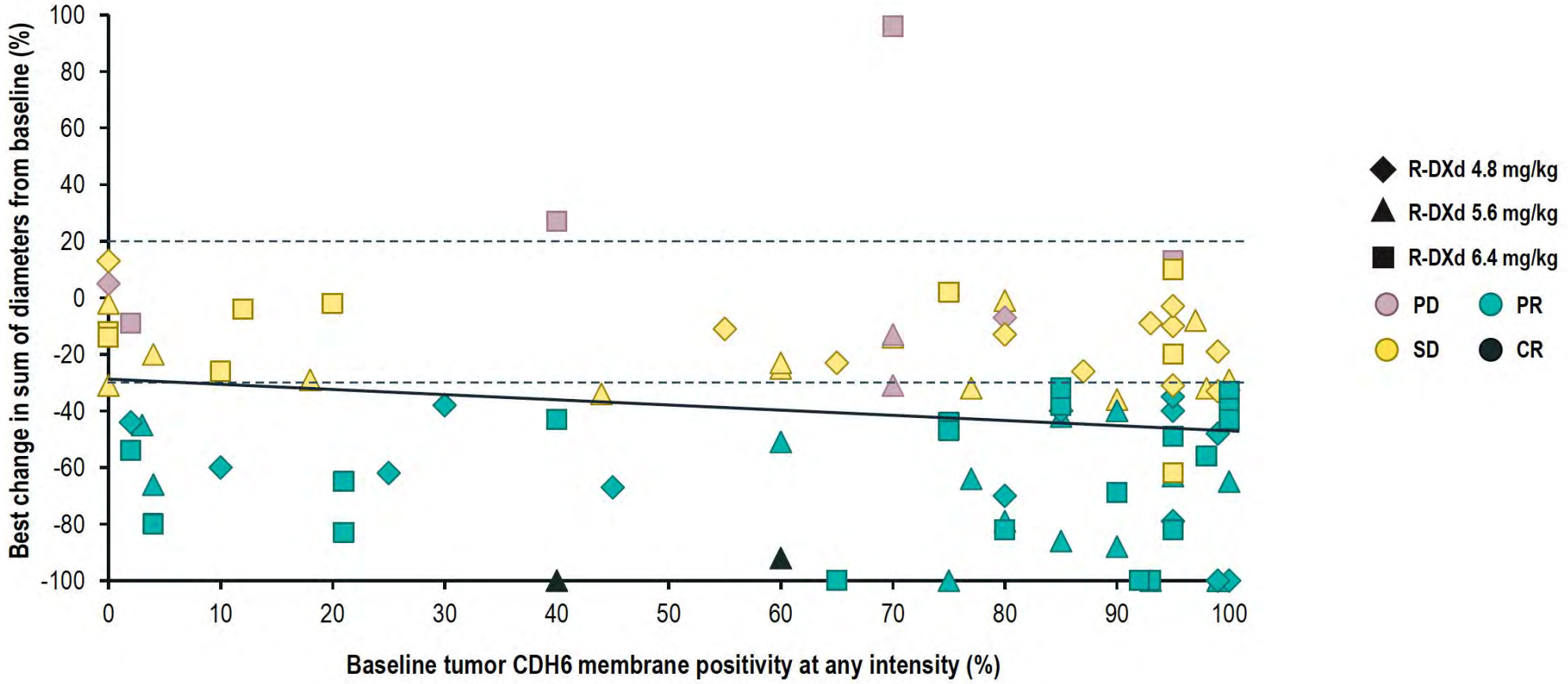
REJOICE-Ovarian01: Antitumor Activity Across Doses



Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 5.6 months (95% CI, 4.7–6.3), 5.6 months (95% CI, 4.6–5.8), and 5.2 months (95% CI, 4.9–5.8), respectively.
[a]Antitumor response assessed by BICR per RECIST 1.1. Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan, both by BICR, were included in the waterfall plot (n=100). Six patients (R-DXd 4.8 mg/kg [n=5]; 6.4 mg/kg [n=1]) did not have measurable disease at baseline and one patient (R-DXd 5.6 mg/kg) had no adequate post-baseline tumor assessment. [b]DCR was defined as percentage of patients with BOR of CR, PR, or SD (per RECIST 1.1).
BICR, blinded independent central review; CI, confidence interval; DCR, disease control rate; ORR, objective response rate; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1.

Ray-Coquard IL et al. ESMO 2025;Abstract LBA42.

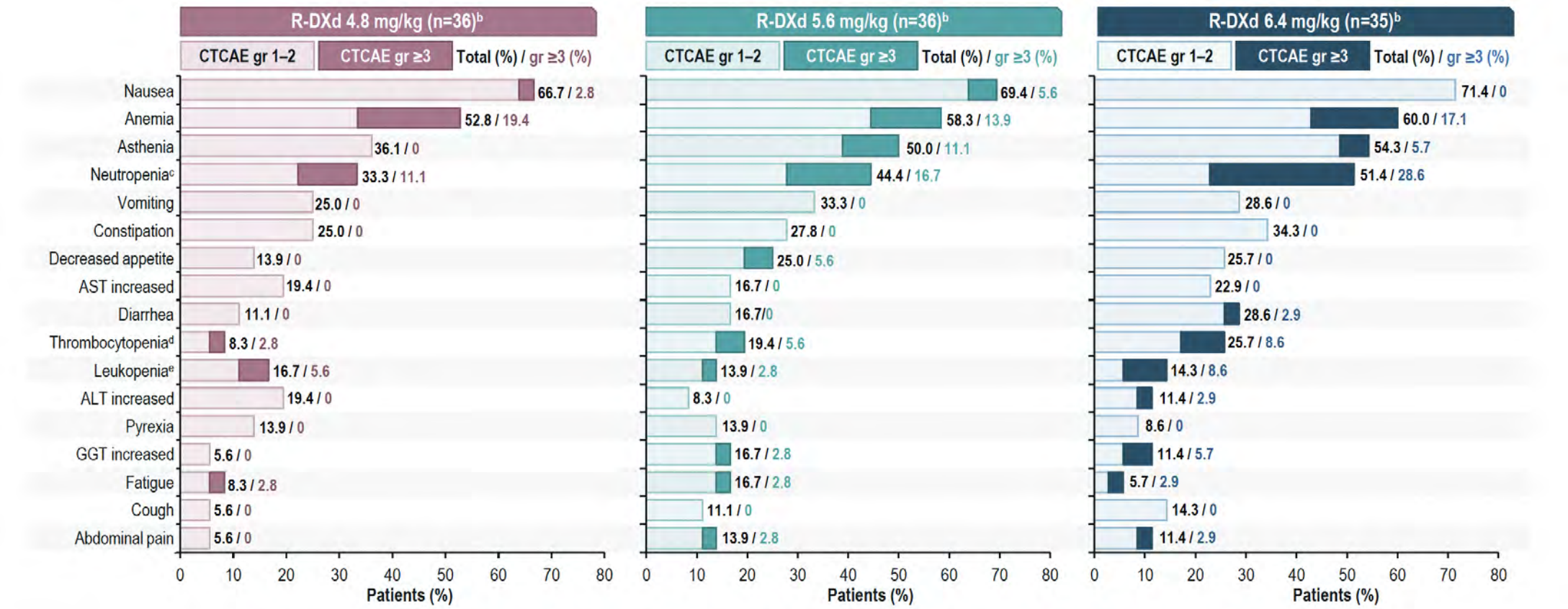
REJOICE-Ovarian01: Antitumor Responses Across CDH6 Expression Levels



Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 5.6 months (95% CI, 4.7–6.3), 5.6 months (95% CI, 4.6–5.8), and 5.2 months (95% CI, 4.9–5.8), respectively.
Patients with available baseline tumor CDH6 expression data, who had measurable disease at baseline and ≥1 post-baseline tumor scan (assessed by BICR), were included in the scatter plot (n=94). Tumor CDH6 positivity was defined as the percentage of viable tumor cells positive for CDH6 membrane staining at any intensity (1+/2+/3+) determined by CDH6 clinical trial assay (SP450; Roche Diagnostics).
BICR, blinded independent central review; CDH6, cadherin 6; CI, confidence interval; CR, complete response; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SD, stable disease.

Ray-Coquard IL et al. ESMO 2025;Abstract LBA42.

REJOICE-Ovarian01: Most Common Treatment-Emergent Adverse Events



Nausea, anemia, asthenia and neutropenia were the most common TEAEs across all doses

Data cutoff: February 26, 2025.

[a]TEAEs reported in ≥10% of all patients who received R-DXd 4.8–6.4 mg/kg. Reported safety events are defined by MedDRA preferred terminology. [b]Grade 4 hematologic TEAEs reported at 4.8 mg/kg: neutropenia[c] (n=2), thrombocytopenia[d] (n=1); at 5.6 mg/kg: neutropenia[c] (n=2), thrombocytopenia[d] (n=1), leukopenia[e] (n=1); at 6.4 mg/kg: neutropenia[c] (n=3), thrombocytopenia[d] (n=1), lymphopenia (n=1). No grade 5 hematologic TEAEs were reported at any dose. Grade 3 febrile neutropenia was reported in 2 patients, one each in the R-DXd 5.6 and 6.4 mg/kg cohorts. [c]Neutropenia was defined as the grouped incidence of events reported under the preferred terms '*neutropenia*' and '*neutrophil count decreased*', with a maximum of one event per patient per grouped preferred term. [d]Thrombocytopenia was defined as the grouped incidence of events reported under the preferred terms '*thrombocytopenia*' and '*platelet count decreased*', with a maximum of one event per patient per grouped preferred term. [e]Leukopenia was defined as the preferred term '*white blood cell count decreased.*'

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; GGT, gamma-glutamyltransferase; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Ray-Coquard IL et al. ESMO 2025;Abstract LBA42.

REJOICE-Ovarian01 Study Conclusions

- In this dose-optimization analysis, 107 patients with platinum-resistant OC received R-DXd at doses of 4.8–6.4 mg/kg
  - In total, 94.1% of tumors demonstrated positive CDH6 membrane expression by IHC
- After a minimum of 18 weeks of follow-up, R-DXd demonstrated promising efficacy across all evaluated doses:
  - The confirmed ORR was 50.5%, including three CRs (2.8%)
  - Clinically meaningful tumor responses were observed across a range of CDH6 expression levels
  - Further follow-up is required to obtain mature data on DOR and PFS
- The safety profile of R-DXd appears manageable and is consistent with the safety findings reported in the Phase 1 study[1,2]
  - One adjudicated treatment-related Grade ≥3 ILD event (Grade 3) was reported in this analysis
- Based on these efficacy and safety results, as well as PK and ER data,[3] R-DXd 5.6 mg/kg provided a positive benefit–risk profile and was considered the optimal dose
- The Phase 3 part of the REJOICE-Ovarian01 study will evaluate R-DXd 5.6 mg/kg versus treatment of physician's choice in patients with platinum-resistant OC

Data cutoff: February 26, 2025.
CR, complete response; DOR, duration of response; ER, exposure–response; IHC. immunohistochemistry; ORR, objective response rate; OC, ovarian cancer; PFS, progression-free survival; PK, pharmacokinetic; PR, partial response.
1. Moore KN, et al. Oral presentation at the European Society for Medical Oncology congress. October 20–24, 2023; Madrid, Spain. Presentation 745MO. 2. Moore KN, et al. Oral presentation at the Society of Gynecologic Oncology 2024 Annual Meeting on Women's Cancer. March 16–18, 2024; San Diego, CA, USA. 3. Daiichi Sankyo, Inc. Data on file.

50 YEARS ESMO

RTP RESEARCH TO PRACTICE

Ray-Coquard IL et al. ESMO 2025;Abstract LBA42.

BERLIN 2025 ESMO congress

Abstract 1065MO

First-in-human study of AZD5335, a folate receptor α (FRα)-targeted antibody-drug conjugate, in patients with platinum-resistant-ovarian cancer

Ana Oaknin,[1] Ruth Perets,[2] Ronnie Shapira-Frommer,[3] Amit Oza,[4] Joo Ern Ang,[5] Kazuki Sudo,[6] Kate Wilkinson,[7] Rutie Yin,[8] Luis Manso Sanchez,[9] Javier Garcia-Corbacho,[10] Stephen Welch,[11] Qi Zhou,[12] Mihae Song,[13] Linda Mileshkin,[14] Edwin Chow,[15] Claire Myers,[16] Patrick Mitchell,[17] Shreyas Upadhyay,[18] Tim Brier,[19] Funda Meric-Bernstam[20]

[1]Medical Oncology Service, Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [2]Division of Oncology, Rambam Health Care Center, Haifa, Israel; [3]Oncology Department, The Ella Institute for Treatment and Research of Melanoma and Skin Cancer - Sheba Medical Center, Ramat Gan, Israel; [4]Surgical Oncology – Division of Urology GU Clinic, Princess Margaret Cancer Center, Toronto, Ontario, Canada; [5]Department of Oncology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [6]Department of Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; [7]Liverpool Cancer Therapy Centre, Liverpool Hospital, Liverpool, NSW, Australia; [8]Department of Gynecology and Obstetrics, West China Second University Hospital, Chengdu, China; [9]Medical Oncology Service, Hospital Universitario 12 de Octubre, Madrid, Spain; [10]Medical Oncology / Phase 1 Clinical Trials Unit, Hospital Universitario Virgen de la Victoria, Málaga, Spain; [11]Oncology, London Health Sciences Centre London Regional Cancer Program, London, ON, Canada; [12]Department of Gynecologic Oncology, Chongqing Cancer Hospital, Chongqing, China; [13]Department of Surgery, Orange County Lennar Foundation Cancer Center, Irvine, CA, United States; [14]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [15]Clinical Pharmacology, AstraZeneca, Gaithersburg, MD, United States; [16]Translational Medicine, AstraZeneca, Gaithersburg, MD, United States; [17]Early Oncology Statistics, AstraZeneca, Waltham, MA, United States; [18]Global Medicines, AstraZeneca, Cambridge, United Kingdom; [19]Early Global Development, AstraZeneca, Cambridge, United Kingdom; [20]Department of Investigational Cancer Therapeutics, M.D. Anderson Cancer Center, Houston, TX, United States

RTP RESEARCH TO PRACTICE

AZD5335 Background

- FRα is a cell surface protein that binds and internalises folate, a cofactor required for DNA synthesis, cell growth, and proliferation.[1–3]
- FRα is highly expressed in multiple epithelial tumours and a clinically validated ADC target in HGSOC.[2–4]
- AZD5335 is a specific, targeted ADC with a potent TOP1i payload (AZ14170132) that binds to FRα with high affinity.[5]
  - The cleavable peptide linker (mp-PEG8-Val-Ala) is bystander-capable and serum-stable.
  - AZD5335 has an average DAR of 8.

Schematic of AZD5335

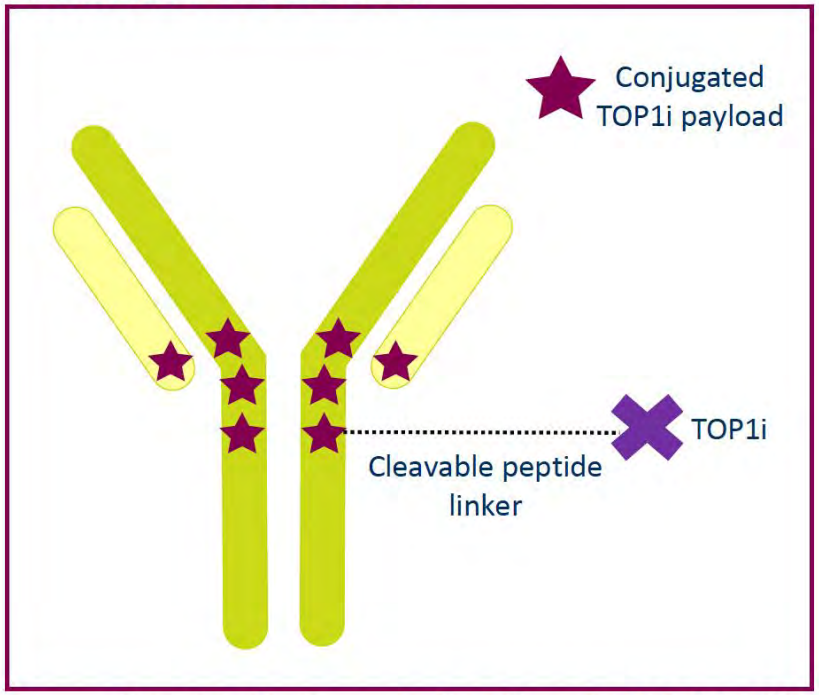


Figure adapted from Gymnopoulos M, et al. Presented at AACR 2023 (LB025).

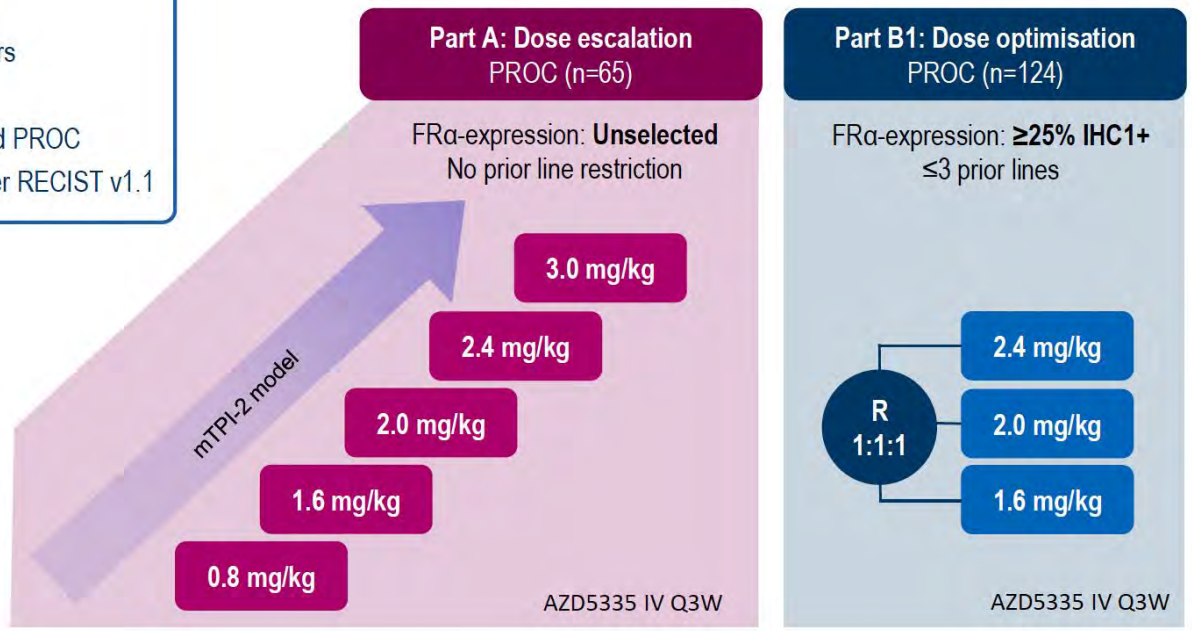
ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; FRα, folate receptor α; OC, ovarian cancer; TOP1i, topoisomerase 1 inhibitor

1. Kelemen LE. *Int J Cancer* 2006;119:243–50;
2. Ledermann JA, et al. *Ann Oncol* 2015;26:2034–43;
3. Scaranti M, et al. *Nat Rev Clin Oncol* 2020;17:349–59;
4. Moore KN, et al. *N Engl J Med* 2023;389:2162–74;
5. Gymnopoulos M, et al. Poster presented at AACR 2023 (Abstract LB025).

FONTANA Module 1: Phase I/IIa Study Design

Key inclusion criteria:

- Patients aged ≥18 years
- ECOG PS 0 or 1
- Histologically confirmed PROC
- Measurable disease per RECIST v1.1



Baseline characteristic	Parts A + B1 N=189
Age, median (range) years	63.0 (40–82)
ECOG PS, n (%)	
0	87 (46.0)
1	102 (54.0)
Median number of prior lines of therapy (range)	3.0 (1–9)
Prior therapy received, n (%)	
PARP inhibitor	119 (63.0)
Bevacizumab	130 (68.8)
FRα-targeted therapy	8 (4.2)
TOP1 inhibitor	8 (4.2)

Primary endpoints: Safety and tolerability including AEs, SAEs, and DLTs

Secondary endpoints: ORR, DoR, PFS

Full analysis set, defined as all patients who received study intervention in Part A and Part B1. Data cutoff: 11 July 2025.
AE, adverse event; DLT, dose-limiting toxicity; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FRα, folate receptor α; IHC1+, immunohistochemistry 1+ intensity; IV, intravenous; mTPI-2, modified toxicity probability interval-2; ORR, objective response rate; PARP, poly(ADP-ribose) polymerase; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; Q3W, every 3 weeks; R, randomisation; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SAE, serious adverse event; TOP1, topoisomerase 1

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Oaknin A et al. ESMO 2025;Abstract 1065MO.

RTP RESEARCH TO PRACTICE

FONTANA: AZD5335 Safety Summary Across Dosing Range

- A dose-safety relationship was observed across the 1.6–2.4 mg/kg dose range.
- The maximum tolerated dose has not been defined.
- One DLT was reported in Part A in the 2.4 mg/kg cohort (Grade 3 decreased appetite).

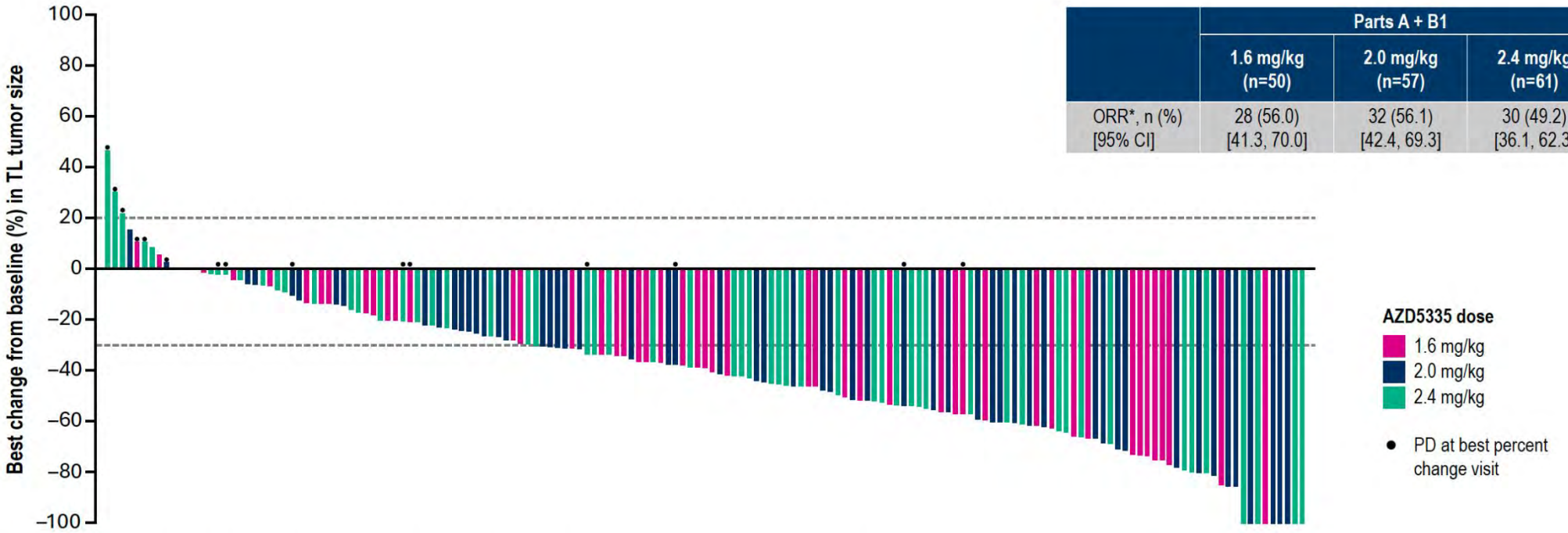
	Parts A + B1		
TEAE, n (%)	1.6 mg/kg (n=50)	2.0 mg/kg (n=58)	2.4 mg/kg (n=61)
Any grade	50 (100)	58 (100)	61 (100)
Grade ≥3	19 (38.0)	35 (55.2)	49 (80.3)
Any serious TEAE	14 (28.0)	17 (29.3)	27 (44.3)
TEAE leading to			
Discontinuation	3 (6.0)	2 (3.4)	6 (9.8)
Dose reduction	6 (12.0)	12 (20.7)	27 (44.3)
Death	0	0	0
DLTs	0	0	1 (1.6)

Safety analysis set, defined as all patients who received study intervention. Data cutoff 11 July 2025.
DLT, dose-limiting toxicity; TEAE, treatment-emergent adverse event

Oaknin A et al. ESMO 2025;Abstract 1065MO.

FONTANA: AZD5335 Tumor Responses Across Dosing Range

	Parts A + B1		
	1.6 mg/kg (n=50)	2.0 mg/kg (n=57)	2.4 mg/kg (n=61)
ORR*, n (%) [95% CI]	28 (56.0) [41.3, 70.0]	32 (56.1) [42.4, 69.3]	30 (49.2) [36.1, 62.3]



Among patients who received 1.6, 2.0, or 2.4 mg/kg AZD5335 in Parts A + B1, the overall ORR* was 53.6% (95% CI: 45.7, 61.3).

Interim response evaluable set, defined as all dosed patients with measurable disease at baseline who have ≥15 weeks follow-up or 2 post-baseline scans ≥4 weeks apart, according to RECIST v1.1 criteria.
Data cutoff: 11 July 2025. *Confirmed ORR.
CI, confidence interval; ORR, objective response rate; PD, progressive disease; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; TL, target lesion

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Oaknin A et al. ESMO 2025;Abstract 1065MO.

FONTANA Study Conclusions

- AZD5335 has a manageable safety profile across the 1.6, 2.0, and 2.4 mg/kg dose levels, consistent with a TOP1i-ADC.
- AZD5335 was associated with a robust ORR, with deep and durable responses in patients with FRα-expressing ovarian cancer across the 1.6, 2.0, and 2.4 mg/kg dose levels.
- The clinical data presented warrant further investigation of AZD5335 monotherapy in PROC.
- Future development will also explore combination approaches and other indications.

Oaknin A et al. ESMO 2025;Abstract 1065MO.

Agenda

Module 1: Up-Front Treatment of Ovarian Cancer (OC)

Module 2: Management of Platinum-Resistant OC

Module 3: Up-Front Management of Metastatic Endometrial Cancer

Module 4: Management of HER2-Positive Gynecologic Cancers

Module 5: Management of Cervical Cancer

Case Presentation: Dr Salani

- 68-year-old (diagnosed at age 64).
- 3/2/21: Endometrial biopsy: Grade 1 endometrial cancer; Pelvic ultrasound: Uterus measures 7.5 x 3.6 x 4.7 cm with a 15 mm stripe.
- 3/18/21: Robotic hysterectomy, bilateral salpingo-oophorectomy, sentinel lymph node dissection: Stage IB (75% myometrial invasion, lymphovascular space invasion), grade 2 endometrial cancer (loss of PMS2 and MLH1-methylated).
- 4/29/21 – 5/11/21: Vaginal brachytherapy (30 Gy) enrolled on GY020 (VB +/- pembrolizumab) to control arm.
- 10/27/21: CT chest/abdomen/pelvis: Subtle liver hypodensity; no evidence of disease.
- 4/22/22: CT chest/abdomen/pelvis: Borderline enlarged left para-aortic lymph node; no other findings.
- 10/22/24: CT abdomen/pelvis: Stable left para-aortic node (9 x 9 mm); interval enlargement of other para-aortic lymph nodes, largest measuring 16 x 21 mm.

Case Presentation: Dr Salani (Continued)

- 11/6/24: Lymph node biopsy: Carcinoma, consistent with history.
- 12/5/24 – 3/13/25: Carboplatin, paclitaxel and dostarlimab x 5 cycles (last cycle held due to side effects).
- 4/3/25: Dostarlimab maintenance started.
- 5/22/25: PET CT: Decrease in left para-aortic lymph node without FDG uptake; no evidence of recurrent or metastatic disease.
- 12/16/25: CT chest/abdomen/pelvis: Interval decreased size of left para-aortic lymph node measuring 6 x 9 mm; no new enlarged lymph nodes. No definite evidence for local recurrence or new distant metastatic disease.
- Current status: Clinically doing well. Traveling the world and plans to continue dostarlimab maintenance.

Key Datasets

- Garcia LG et al. Neoadjuvant dostarlimab in mismatch repair deficient (MMRd) stage II-III endometrioid endometrial cancer (EC): The GEICO137-E/NADIA study. ESMO 2025;Abstract 1224TiP.
- Powell MA et al. Post-hoc survival outcomes based on initial and subsequent treatment in patients with mismatch repair proficient/microsatellite stable (MMRp/MSS) primary advanced or recurrent endometrial cancer (pA/R EC) in the ENGOT-EN6-NSGO/GOG-3031/RUBY trial. ESMO 2025;Abstract 1113P.
- Ginesta MPB et al. Final overall survival (OS) results from the randomized double-blind phase III AtTEND/ENGOT-EN7 trial evaluating atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer. ESMO 2025;Abstract LBA39.
- Westin S et al. Durvalumab plus carboplatin/paclitaxel followed by durvalumab for endometrial cancer: Tumour mutational burden-high subpopulation efficacy analyses from the DUO-E trial. ESMO 2025;Abstract 1117P.

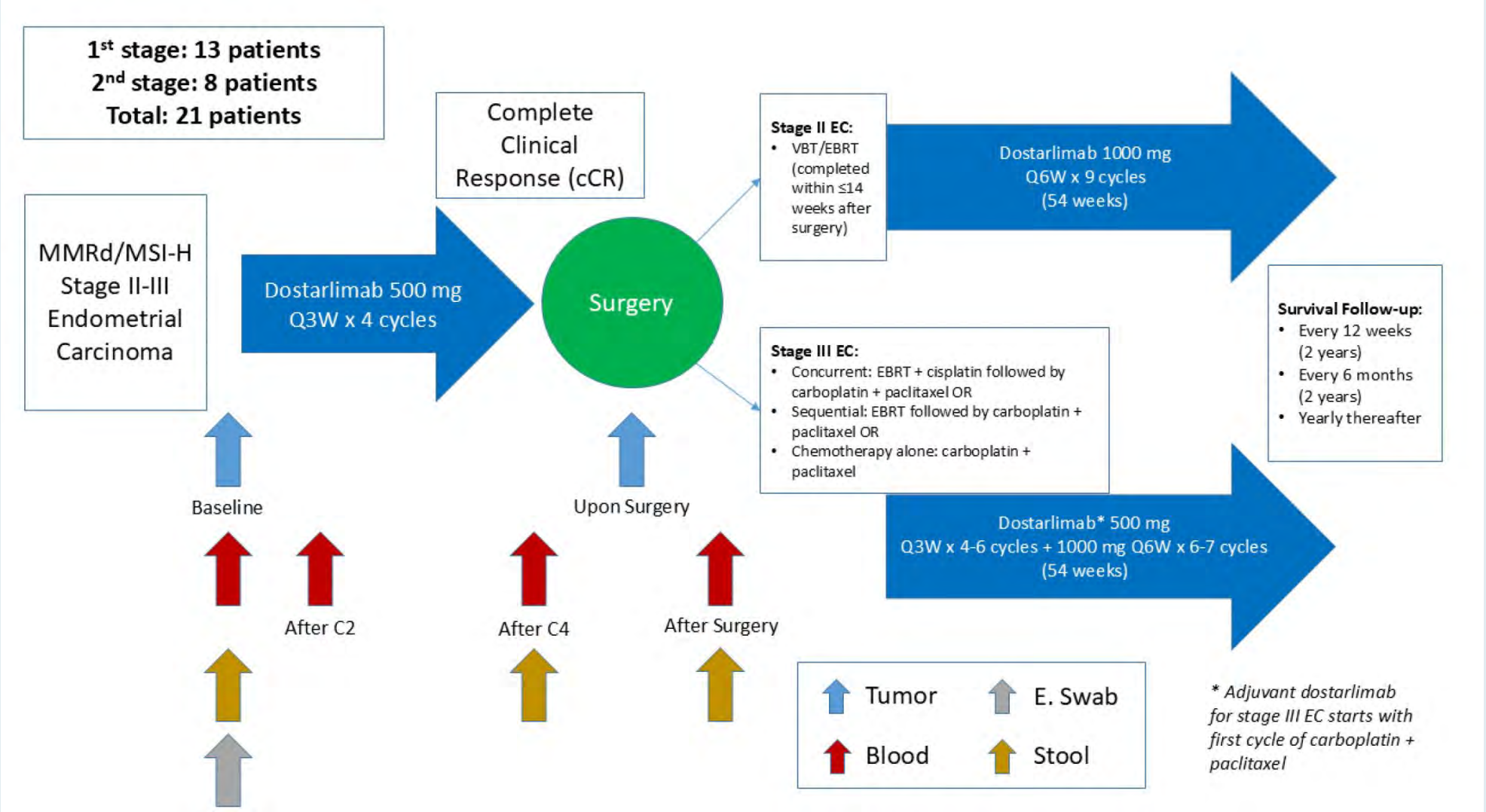
Key Datasets

- Makker V et al. Lenvatinib plus pembrolizumab (L + P) vs treatment of physician's choice (TPC) for advanced endometrial cancer (EC): 5-year outcomes from study 309/KEYNOTE-775. ESMO 2025;Abstract 1119P.
- Akilli H et al. First-line lenvatinib + pembrolizumab (L + P) vs chemotherapy (CT) for advanced or recurrent endometrial cancer (EC): Additional 1-year follow-up results from ENGOT-en9/LEAP-001. ESMO 2025;Abstract 1114P.
- Eminowicz G et al. GOG-3119/ENGOT-en29/TroFuse-033: A phase III, randomized study of sacituzumab tirumotecan (sac-TMT) + pembrolizumab (pembro) vs pembro alone as first-line (1L) maintenance therapy for mismatch repair-proficient (pMMR) endometrial cancer (EC). ESMO 2025;Abstract 1221TiP.

Neoadjuvant Dostarlimab in Mismatch Repair Deficient (MMRd) Stage II-III Endometrioid Endometrial Cancer (EC): The GEICO137-E/NADIA Study

Garcia LG et al.
ESMO 2025;Abstract 1224TiP.

GEICO137-E/NADIA Study Design



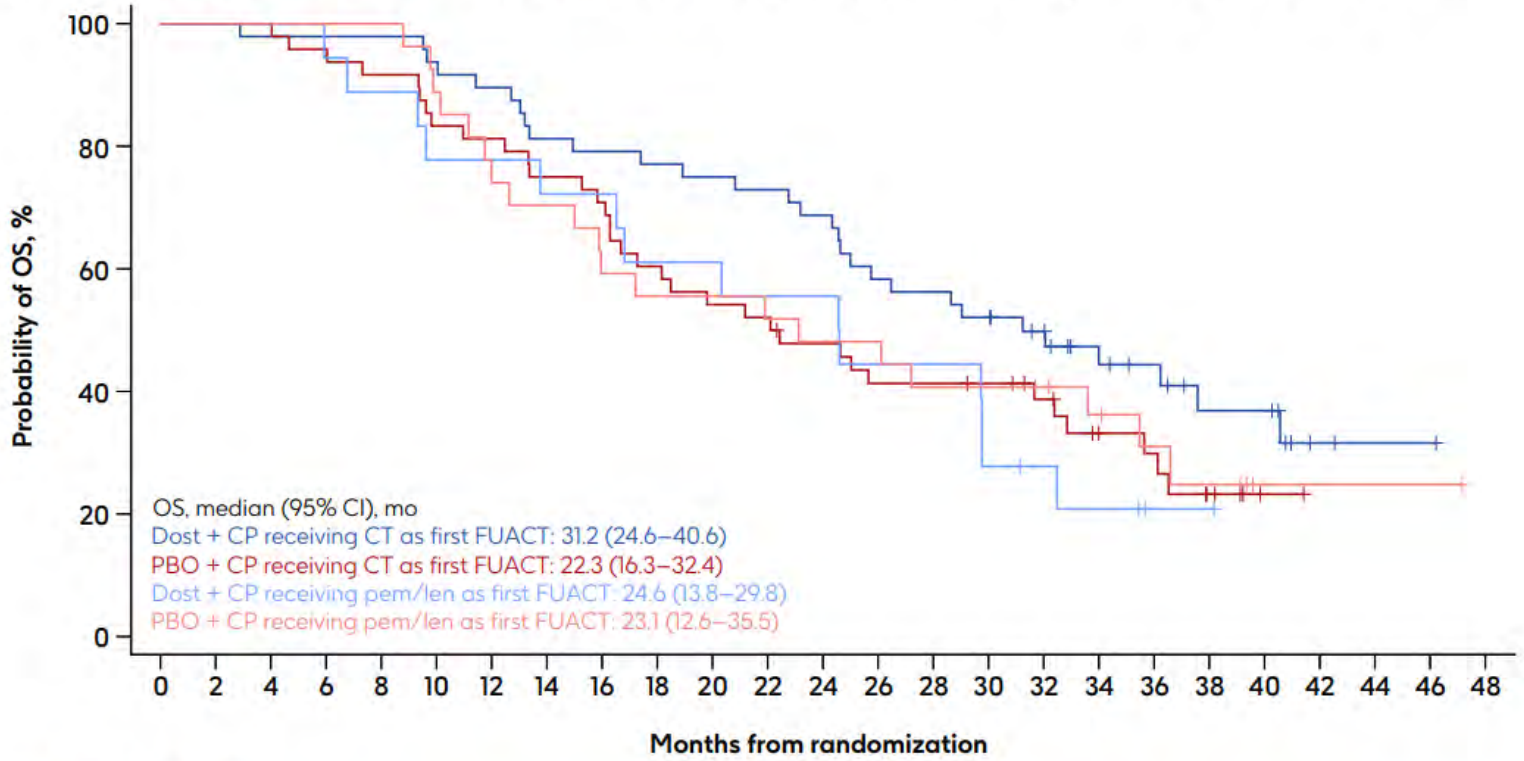
Garcia LG et al. ESMO 2025;Abstract 1224TiP.

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

Powell MA et al.
ESMO 2025;Abstract 1113P.

ENGOT-EN6-GOG-3031/RUBY: OS for Patients with MMRp/MSS Primary Advanced or Recurrent Endometrial Cancer

Figure 3: OS for patients in the MMRp/MSS population who received CT or pem/len as first FUACT



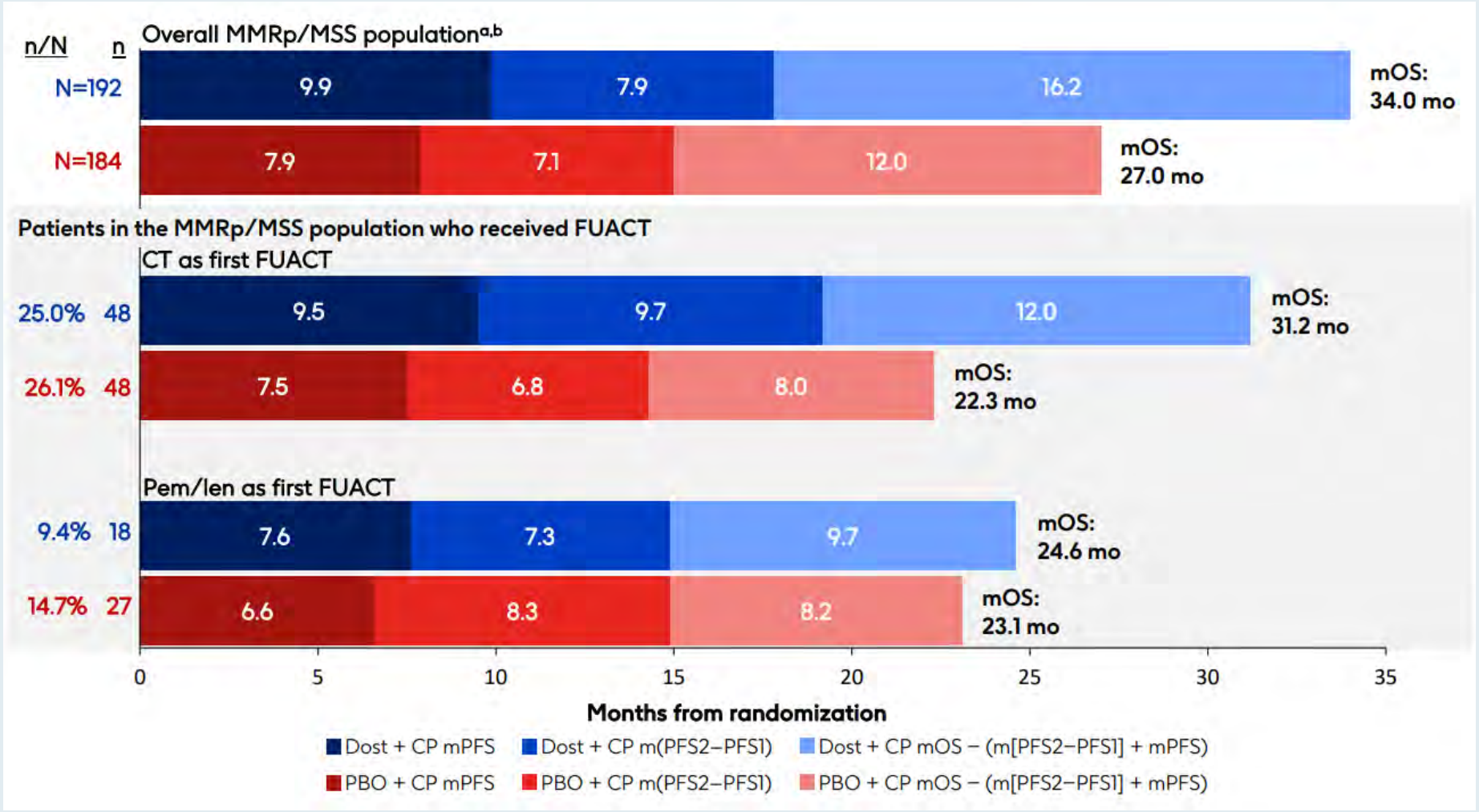
No. at risk (no. of events)

Dost + CP	48 (0)	48 (0)	47 (1)	47 (1)	47 (1)	45 (3)	43 (5)	39 (9)	38 (10)	37 (11)	36 (12)	35 (13)	33 (15)	28 (20)	27 (21)	25 (23)	21 (24)	16 (25)	13 (26)	9 (28)	9 (28)	2 (29)	1 (29)	1 (29)	0 (29)
PBO + CP	48 (0)	48 (0)	48 (0)	46 (2)	44 (4)	40 (8)	39 (9)	36 (12)	34 (14)	29 (19)	26 (22)	25 (23)	22 (25)	19 (28)	19 (28)	18 (28)	15 (29)	11 (31)	9 (32)	5 (34)	1 (34)	0 (34)			
Dost + CP	18 (0)	18 (0)	18 (0)	17 (1)	16 (2)	14 (4)	14 (4)	13 (5)	13 (5)	11 (7)	11 (7)	10 (8)	10 (8)	8 (10)	8 (10)	5 (13)	4 (13)	3 (14)	1 (14)	1 (14)	0 (14)				
PBO + CP	27 (0)	27 (0)	27 (0)	27 (0)	27 (0)	24 (3)	20 (7)	19 (8)	16 (11)	15 (12)	15 (12)	14 (13)	13 (14)	13 (14)	11 (16)	11 (16)	10 (16)	8 (17)	5 (18)	4 (19)	1 (19)	1 (19)	1 (19)	1 (19)	0 (19)

CP, carboplatin-paclitaxel; CT, chemotherapy; dost, dostarlimab; FUACT, follow-up anticancer therapy; HR, hazard ratio; MMRp, mismatch repair-proficient; MSS, microsatellite stable; OS, overall survival; PBO, placebo; pem/len, pembrolizumab/lenvatinib; pts, patients.

Powell MA et al. ESMO 2025;Abstract 1113P.

ENGOT-EN6-GOG-3031/RUBY: Long-Term Outcomes



Powell MA et al. ESMO 2025;Abstract 1113P.

ENGOT-EN6-GOG-3031/RUBY Study Conclusions

- In RUBY Part 1, there were clinically meaningful and consistent benefits across survival endpoints in the difficult-to-treat MMRp/MSS population, including a 7-month improvement in OS and a 24% reduction in the risk of progression[1,4]
- In patients who received FUACT, OS outcomes favored dostarlimab + CP vs placebo + CP for all first FUACTs evaluated, supporting the importance of utilizing effective therapies early in the treatment paradigm
  - Notably, this exploratory (treatment sequencing) analysis further suggests that numerically longer survival outcomes were observed in patients receiving upfront dostarlimab + CP, followed by any FUACT, compared with patients receiving placebo + CP first, followed by any FUACT, including pem/len
- Overall, these data support that frontline use of dostarlimab + CP in MMRp/MSS primary advanced or recurrent EC provides optimal survival outcomes regardless of subsequent treatment, and further reinforce dostarlimab + CP as a standard of care for patients with MMRp/MSS primary advanced or recurrent EC to maximize survival outcomes

Powell MA et al. ESMO 2025;Abstract 1113P.

Abstract LBA39

BERLIN 2025 ESMO congress

Final overall survival results from the randomized double-blind phase III AtTEnd/ENGOT-EN7 trial evaluating atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer

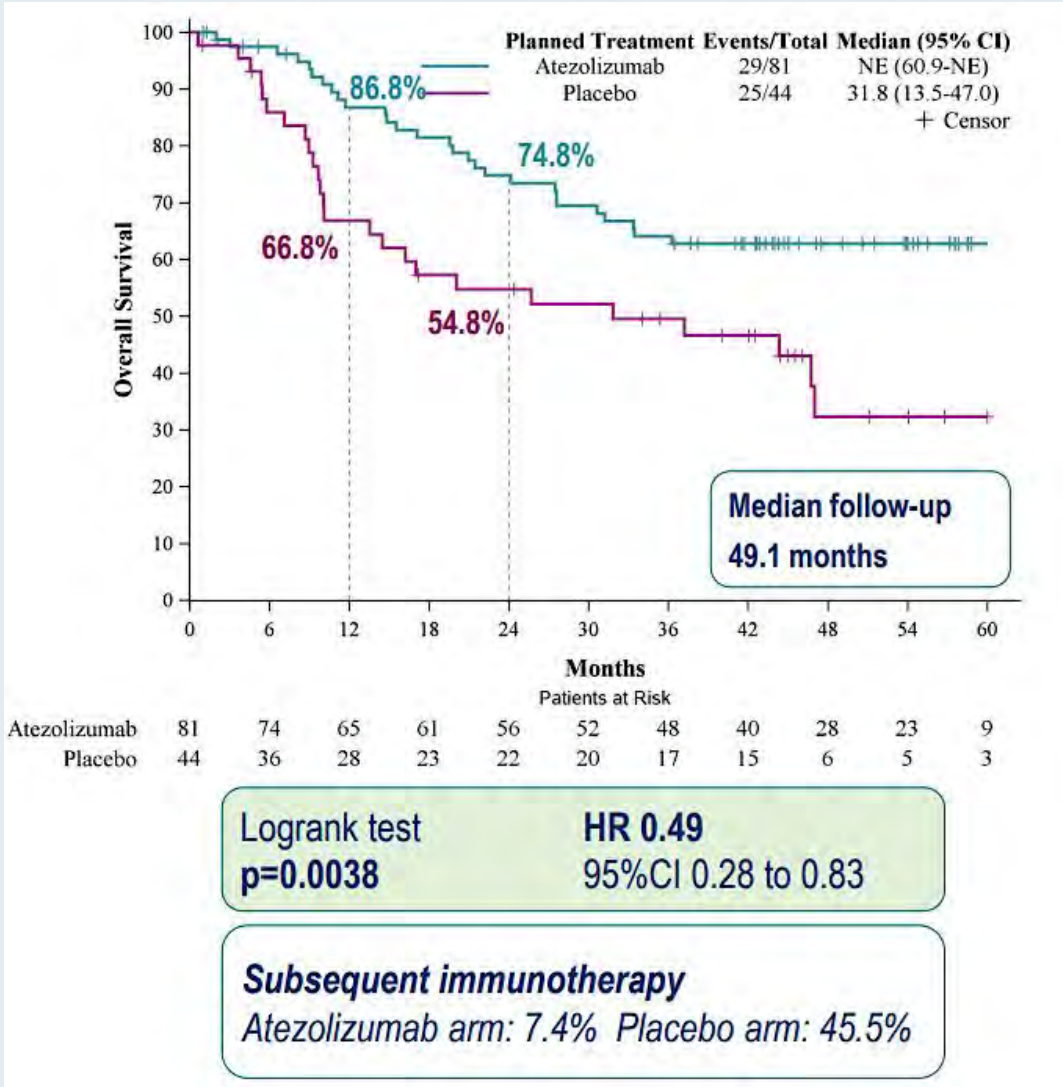
Maria Pilar Barretina Ginesta, Institut Català d'Oncologia, IDIBGI-CERCA, Girona (GEICO, Spain)

On behalf of E. Biagioli (MaNGO, Italy), K. Harano (JGOG, Japan), F. Galli (MaNGO, Italy), E. Hudson (NCRI, United Kingdom), Y. Antill (ANZGOG, Australia-New Zealand), J.-W. Roh (KGOG, Korea), M. Rabaglio (SAKK, Switzerland), F. Marmé (AGO, Germany), E. Piovano (MaNGO, Italy), K. Leitner (AGO-A, Austria), L. Fariñas Madrid (GEICO, Spain), K. Takehara (JGOG, Japan), K. Allan (NCRI, United Kingdom), Y.C. Lee (ANZGOG, Australia-New Zealand), C. Zamagni (MaNGO, Italy), B. Pardo Búrdalo (GEICO, Spain), G. Tasca (MaNGO, Italy), A. Ferrero (MaNGO, Italy), N. Colombo (MaNGO, Italy)

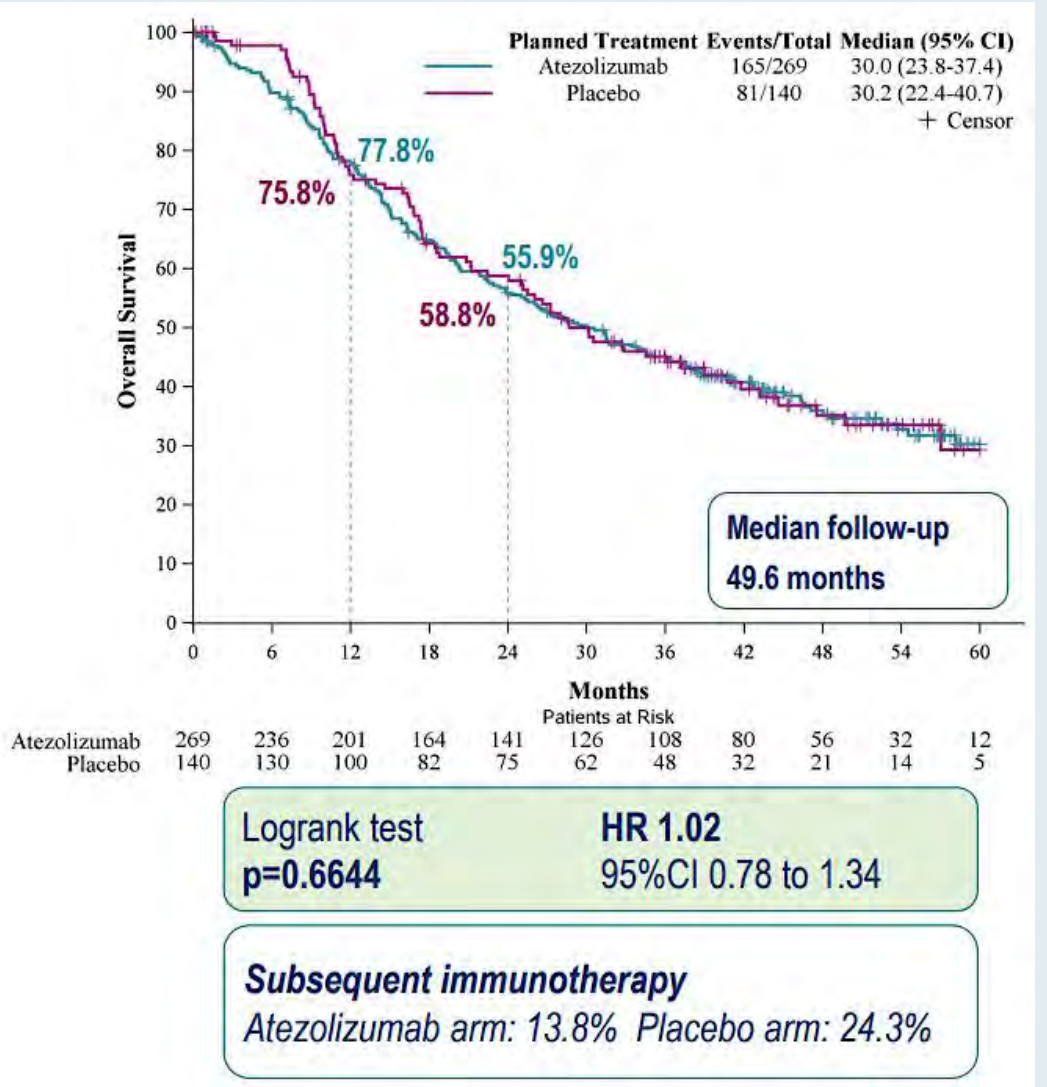
19 October 2025

AtTEnd/ENGOT-EN7: Analysis of OS in the Mismatch Repair-Deficient (MMRd) and Non-MMRd Subgroups

MMRd tumors

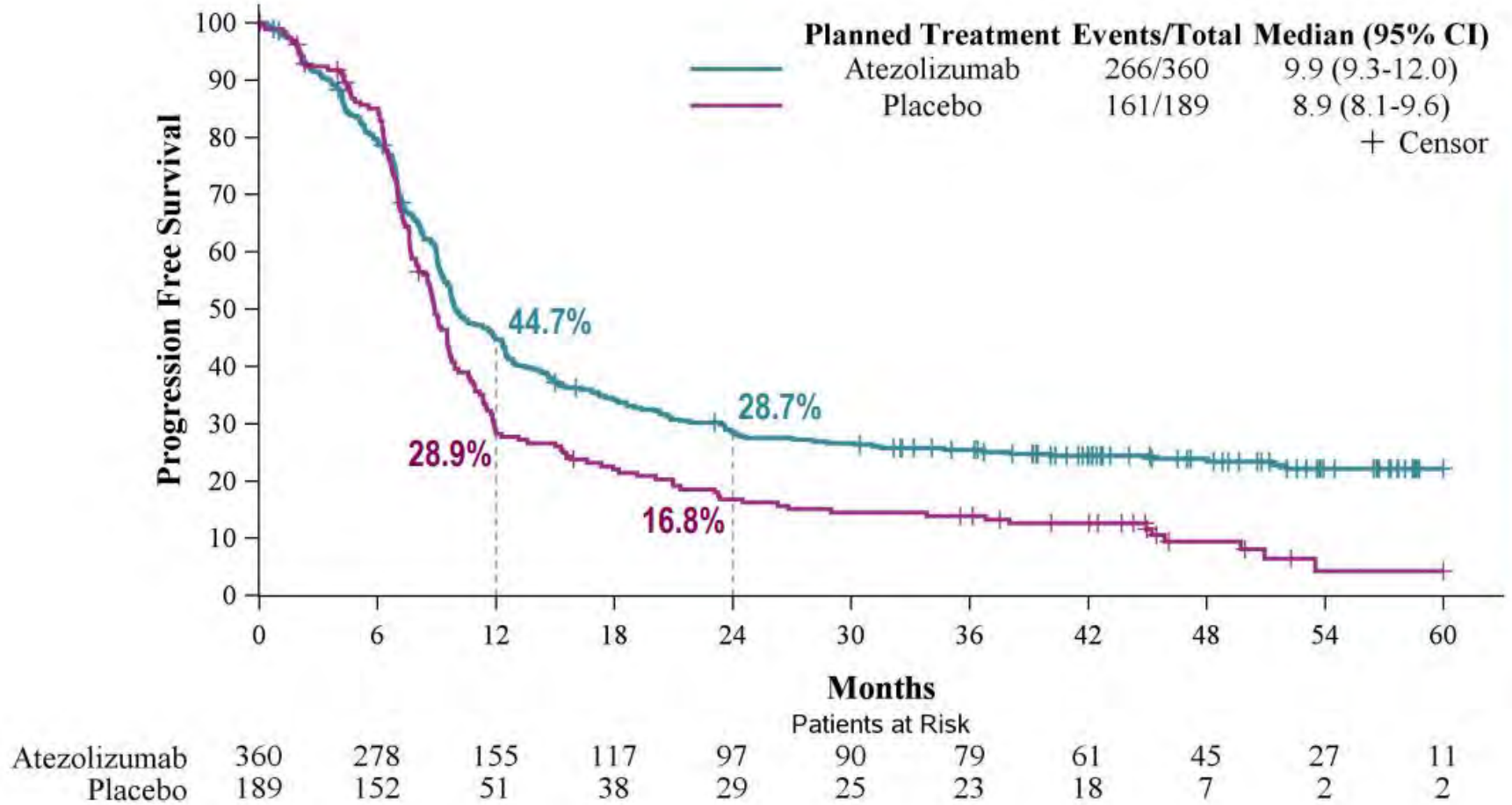


Non-MMRd tumors



Ginesta MPB et al. ESMO 2025;Abstract LBA39.

AtTEnd/ENGOT-EN7: Updated PFS for All Patients



Logrank test
p=0.0055

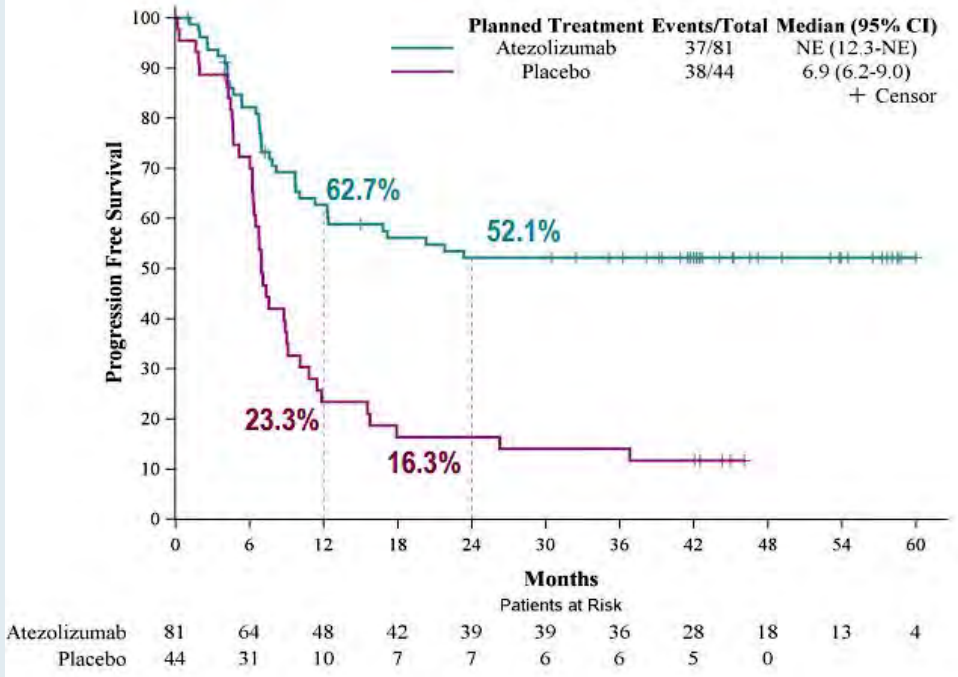
HR 0.70
95%CI 0.58 to 0.86

NON PROPORTIONAL HAZARDS
Restricted Mean Survival Time (RMST) difference at 30 months 2.52 months
95%CI 0.82 to 4.22

Ginesta MPB et al. ESMO 2025;Abstract LBA39.

AtTEnd/ENGOT-EN7: Analysis of PFS in the MMRd and Non-MMRd Subgroups

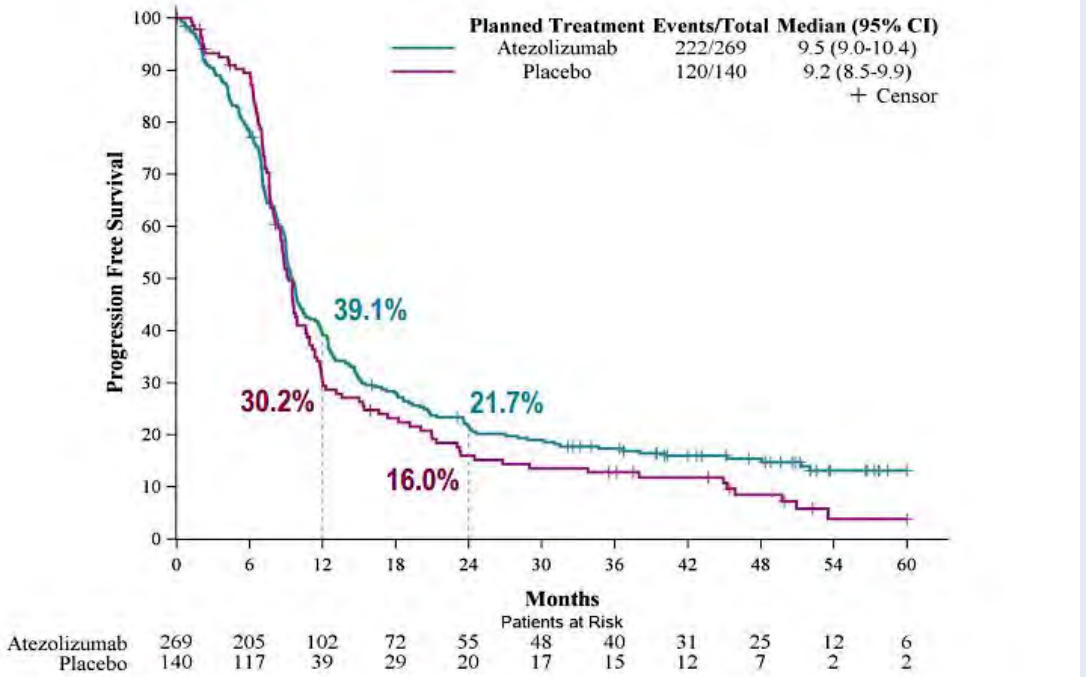
MMRd tumors



Logrank test **p=0.0002**

HR 0.35
95%CI 0.22 to 0.55

Non-MMRd tumors



Logrank test **p=0.1885**

HR 0.86
95%CI 0.69 to 1.08

NON PROPORTIONAL HAZARDS
Restricted Mean Survival Time (RMST) difference at 30 months 0.73 months
95%CI -1.16 to 2.62

Maria Pilar Barretina Ginesta, Girona, Spain

Ginesta MPB et al. ESMO 2025;Abstract LBA39.

AtTEnd/ENGOT-EN7 Study Conclusions

- The addition of atezolizumab to chemotherapy did not demonstrate a statistically significant survival benefit in pts with advanced/recurrent endometrial cancer (HR 0.87; 95%CI 0.69 to 1.10; logrank test p=0.0824)
- In the pre-planned sub-group analysis based on MMR status, a substantial survival improvement was observed in pts with MMRd carcinomas (HR 0.49; 95%CI 0.28 to 0.83; logrank test p=0.0038)
- The previously observed PFS improvement in all comers was confirmed with a longer follow-up (HR 0.70; 95%CI 0.58 to 0.86; p=0.0055). This improvement was particularly notable in MMRd tumors (HR 0.35; 95%CI 0.22 to 0.55; p=0.0002).
- In non-MMRd tumors, an interaction between Asian race and the efficacy of atezolizumab in terms of OS was observed (Non-Asian HR 0.89; 95% CI: 0.67-1.18; p=0.4244; Asian HR 2.22; 95% CI: 1.01-4.87; p=0.0459; interaction test p=0.0336).
- The safety profile of the combination of chemotherapy and atezolizumab was manageable and consistent with expected toxicities
- Overall, these findings confirm that the addition of atezolizumab to chemotherapy offers a significant improvement In PFS in all patients with advanced/recurrent endometrial cancer, while the overall survival benefit is limited to patients with MMRd tumors. Ethnic and genomic factors warrant further investigation to optimize treatment strategies.

Ginesta MPB et al. ESMO 2025;Abstract LBA39.

Final publication number (FPN): 1117P

Durvalumab plus carboplatin/paclitaxel followed by durvalumab for endometrial cancer: tumour mutational burden-high subpopulation efficacy analyses from the DUO-E trial

Shannon N. Westin,[1] Kathleen Moore,[2] Todd Tillmanns,[3] Christen Haygood,[4] Setsuko K. Chambers,[5] Anna Priebe,[6] Young Kim,[7] Brian Slomovitz,[8] Goda Jonuškienė,[9] Maria Pilar Barretina-Ginesta,[10] Tibor Csőszi,[11] Flora Zagouri,[12] Jae-Weon Kim,[13] Qinglei Gao,[14] Fernando Contreras Mejia,[15] Andreia Cristina De Melo,[16] Tadaaki Nishikawa,[17] Matthew Kowgier,[18] Ying Wang,[19] Els Van Nieuwenhuysen[20]

ESMO 2025

Tumor Mutational Burden (TMB) Efficacy Analysis in DUO-E: Concordance Between MMR and TMB Status

TMB-H
dMMR
TMB and MMR concordance

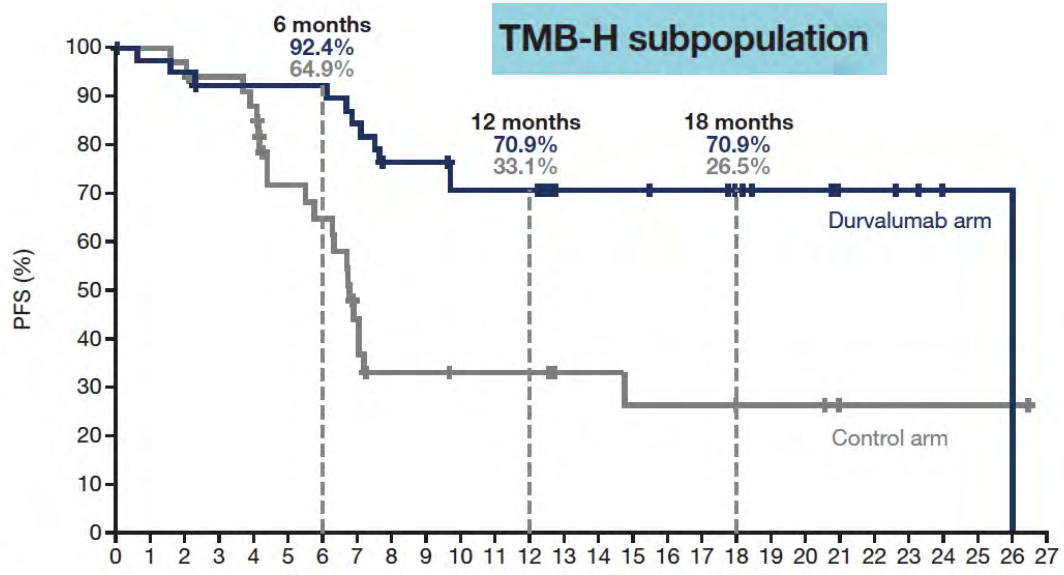
Subpopulation, n (%)	dMMR	pMMR	
TMB-H	92 (19.2%)	32 (6.7%)	124/479 (25.9%)
TMB-L	14 (2.9%)	341 (71.2%)	
	106/479 (22.1%)		433/479 (90.4%)

Concordance between TMB and MMR status: 90.4% (95% CI, 87.4–92.7)
Positive concordance between TMB-H and dMMR status: 86.8% (95% CI, 79.0–92.0)

H = high; L = low

Westin SN et al. ESMO 2025;Abstract 1117P.

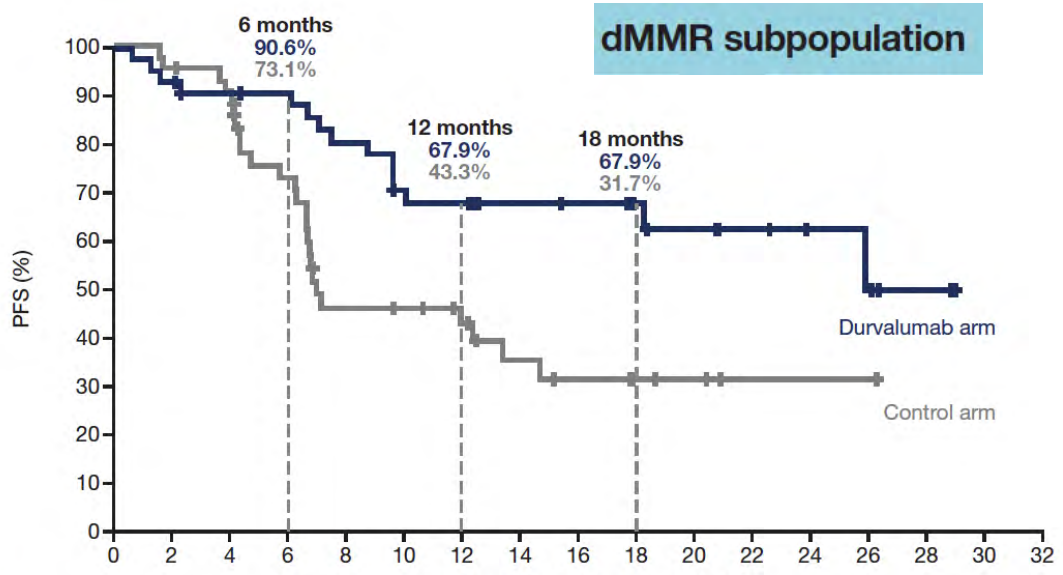
TMB Efficacy Analysis in DUO-E: Post-Hoc PFS Exploratory Analysis



No. at risk

Durvalumab arm	43	39	38	35	35	35	35	32	28	28	25	25	25	16	16	16	14	11	9	9	4	4	3	1	1	1	0
Control arm	36	34	33	31	29	21	19	12	8	8	7	7	7	5	5	4	4	3	3	3	1	1	1	1	1	1	0

	Control arm (N=36)	Durvalumab arm (N=43)
Events, n (%)	21 (58.3)	12 (27.9)
Median PFS (95% CI), months	**6.8** (5.5–14.8)	**26.0** (NR–NR)
HR (95% CI) versus control	**0.30** (0.14–0.60)	



No. at risk

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

	Control arm (N=49)	Durvalumab arm (N=46)
Events, n (%)	25 (51.0)	15 (32.6)
Median PFS (95% CI), months	**7.0** (6.7–14.8)	**NR** (NR–NR)
HR (95% CI) versus control	**0.42** (0.22–0.80)	

Westin SN et al. ESMO 2025;Abstract 1117P.

TMB Efficacy Analysis in DUO-E: Authors' Conclusions

- DUO-E demonstrated statistically significant and clinically meaningful PFS benefit for CP + durvalumab versus CP alone in the ITT population,[1] with the greatest benefit in the dMMR subpopulation.
- In DUO-E, dMMR and TMB-H prevalence was similar, and there was strong concordance between TMB-H and dMMR status.
- Post hoc analyses demonstrated clinically meaningful PFS improvement with the addition of durvalumab to CP in patients with TMB-H EC, consistent with analyses for the dMMR subpopulation.

Westin SN et al. ESMO 2025;Abstract 1117P.

1119P

Lenvatinib Plus Pembrolizumab vs Treatment of Physician's Choice for Advanced Endometrial Cancer: 5-Year Outcomes From Study 309/KEYNOTE-775

V. Makker[1]; N. Colombo[2]; A. Casado Herráez[3]; A.D. Santin[4]; E. Colomba[5]; D.S. Miller[6]; K. Fujiwara[7]; S. Pignata[8]; K. Yonemori[9]; Y.M. Kim[10]; S. Baron-Hay[11]; I. Ray-Coquard[12]; R. Shapira-Frommer[13]; R. Kristeleit[14]; Z. Yu[15]; J. McKenzie[16]; S. Kruger[17]; R. Meng[17]; C.E. Okpara[18]; D. Lorusso[19]

ESMO 2025

KEYNOTE-775 Study Conclusions

- There was continued durable and robust benefit with len + pembro vs TPC in this long-term follow-up of Study 309/ KEYNOTE-775
- Results were consistent with the primary analysis despite increased use of subsequent systemic anticancer therapy and crossover to len + pembro in the TPC group
- The safety profile of len + pembro was manageable, with no new safety signals identified
- Results lend further support for the use of len + pembro as a standard of care therapy in patients with previously treated, advanced or recurrent EC

Makker V et al. ESMO 2025;Abstract 1119P.

1114P

First-Line Lenvatinib + Pembrolizumab vs Chemotherapy for Advanced or Recurrent Endometrial Cancer: Additional 1-Year Follow-Up Results From ENGOT-en9/LEAP-001

H. Akilli[1]; R.G. Moore[2]; C. Marth[3]; T. Díaz-Redondo[4]; J. Korach[5]; A. Stillie[6]; J.-F. Baurain[7]; P. Mach[8]; K. Cadoo[9]; M. Bidziński[10]; K. Ariyoshi[11]; X. Wu[12]; S. Frentzas[13]; A. Mattar[14]; B. Slomovitz[15]; L. Yao[16]; J. McKenzie[17]; R. Meng[18]; L. Gilbert[19]; V. Makker[20]

ESMO 2025

LEAP-001 Study Conclusions

- Efficacy outcomes after an additional year of follow-up in ENGOT-en9/LEAP-001 were consistent with the final analysis
  - In the pMMR and all-comer populations, OS, PFS, and ORR continued to be similar between the len + pembro and chemo groups, with DOR being numerically longer with len + pembro
  - In participants with dMMR EC, OS, PFS, ORR, and DOR continued to favor len + pembro over chemo
- The safety profile of len + pembro was manageable, with no new safety signals identified
- Despite ENGOT-en9/LEAP-001 not meeting its primary endpoints, len + pembro continued to demonstrate antitumor activity with clinical benefit in participants with advanced EC after an additional year of follow-up

Akilli H et al. ESMO 2025;Abstract 1114P.

GOG-3119/ENGOT-en29/TroFuse-033: A Phase 3, Randomized Study of Sacituzumab Tirumotecan (Sac-TMT) + Pembrolizumab (Pembro) vs Pembro Alone as First-Line (1L) Maintenance Therapy for Mismatch Repair-Proficient (pMMR) Endometrial Cancer (EC)

Eminowicz G et al.
ESMO 2025;Abstract 1221TiP.

Agenda

Module 1: Up-Front Treatment of Ovarian Cancer (OC)

Module 2: Management of Platinum-Resistant OC

Module 3: Up-Front Management of Metastatic Endometrial Cancer

Module 4: Management of HER2-Positive Gynecologic Cancers

Module 5: Management of Cervical Cancer

Case Presentation: Dr Salani

- 84 yo (83 at diagnosis) with PMH of hypertension and hypothyroidism.
- 12/2/24: Robotic hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic sentinel lymph node dissection, and omental biopsy: FIGO 2023 Stage IIC high grade serous endometrial cancer; pMMR, HER2 2+, p53m.
- 1/13/25 – 4/8/25: Carboplatin and paclitaxel (1L) x 6 cycles.
- 5/14/25: CT chest/abdomen/pelvis: No evidence of disease; positive for pulmonary embolism.
- 9/9/25: CT abdomen/pelvis: New ascites and omental carcinomatosis.
- 10/7/25: Trastuzumab deruxtecan (2L) started (declined lenvatinib and pembrolizumab due to hypertension).
- 12/4/25: CT chest/abdomen/pelvis: No intrathoracic disease. Improved peritoneal and omental nodularity, resolution of ascites.
- Current status: Tolerating therapy well. Plan to continue current therapy and reassessment after cycle 6 (currently on cycle 4).

Key Datasets

- Makker V et al. Trastuzumab deruxtecan (T-DXd) for pretreated patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) part 1 final analysis. ESMO 2025;Abstract 957P.
- Lee J-Y et al. Trastuzumab deruxtecan (T-DXd) in pretreated patients (pts) with HER2-expressing solid tumors: Exploratory biomarker analysis of DESTINY-PanTumor02 (DP-02) Part 1. ESMO 2025;Abstract 145P.
- Slomovitz BM et al. A randomized phase 3 study of first-line (1L) trastuzumab deruxtecan (T-DXd) with rilvegostomig or pembrolizumab in patients with HER2-expressing, mismatch repair proficient (pMMR), primary advanced or recurrent endometrial cancer (EC): DESTINY Endometrial 01/GOG-3098/ENGOT-EN24. ESMO 2025;Abstract 1223TiP.
- González-Martín A et al. An open-label, randomized, multicenter, phase III study of trastuzumab deruxtecan (T-DXd) with bevacizumab (BEV) vs BEV monotherapy as first-line (1L) maintenance therapy in HER2-expressing ovarian cancer: DESTINY-Ovarian01 (DO 01). ESMO 2025;Abstract 127TiP.

Poster 957P

ESMO 2025

Trastuzumab deruxtecan for pretreated patients with HER2-expressing solid tumors: DESTINY-PanTumor02 Part 1 final analysis

Vicky Makker,[1] Funda Meric-Bernstam,[2] Ana Oaknin,[3] Do-Youn Oh,[4] Anastasiya Mochalova,[5] Arunee Dechaphunkul,[6] Igor Kudryavtsev,[7] Chia-Chi Lin,[8] Antonio Gonzalez-Martin,[9] Mairead G McNamara,[10] Iwona Ługowska,[11] Tarek Meniawy,[12] Vanda Salutari,[13] Thatthan Suksombooncharoen,[14] Teerapat Ungtrakul,[15] Chiedozie Anoka,[16] Ann Smith,[17] Soham Puvvada,[18] Jung-Yun Lee[19]

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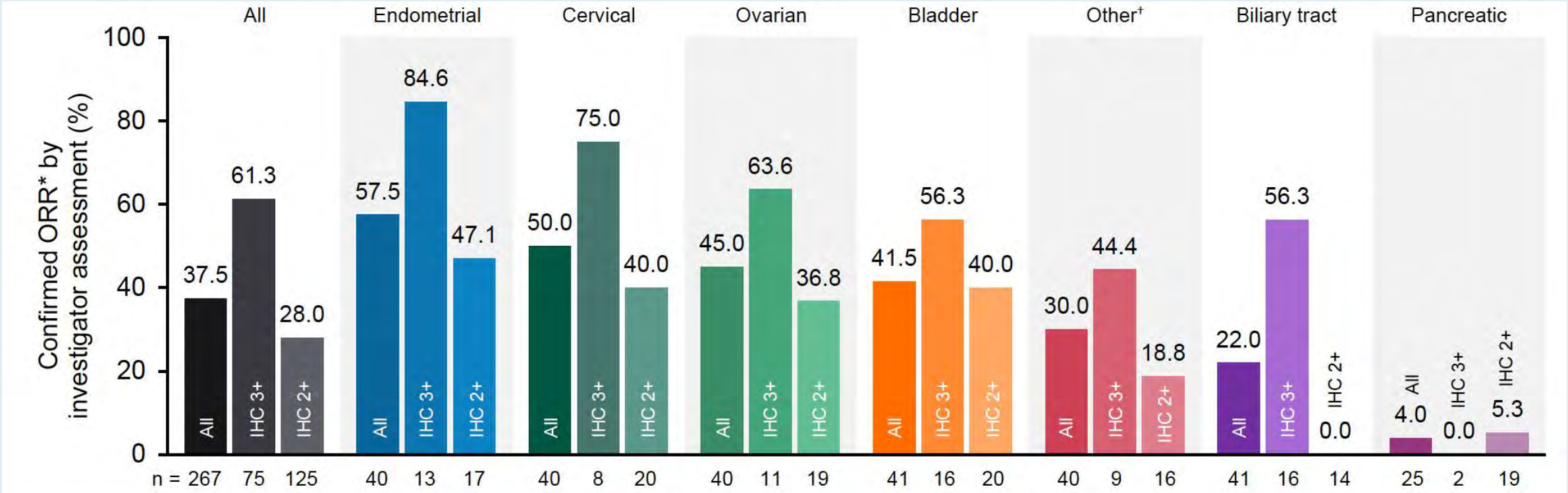
DESTINY-PanTumor02 Part 1 Final Analysis: Investigator-Assessed Confirmed ORR by Tumor Cohort and Central HER2 IHC Status



Investigator-assessed ORR analyses were performed for patients who received ≥1 dose of T-DXd (n=267). *Confirmed ORR per RECIST 1.1; †included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1)
HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan

Makker V et al. ESMO 2025;Abstract 957P.

DESTINY-PanTumor02 Part 1 Final Analysis: Investigator-Assessed Median PFS by Tumor Cohort and HER2 IHC Status

Median PFS, months (95% CI) [n]*	All patients	HER2 IHC status by central testing		HER2 IHC status at enrollment‡	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
All	**6.9** (5.6, 8.0) [267]	**11.9** (8.2, 13.0) [75]	**5.4** (4.2, 6.0) [125]	**9.7** (7.0, 12.5) [111]	**5.1** (4.1, 6.0) [151]
Endometrial	**11.1** (7.1, 25.8) [40]	**28.1** (7.3, NE) [13]	**8.5** (4.6, 15.1) [17]	**24.8** (4.5, 35.7) [16]	**11.0** (6.0, 19.5) [24]
Cervical	**7.0** (4.2, 11.1) [40]	**NE** (3.9, NE) [8]	**4.8** (2.7, 5.7) [20]	**NE** (3.9, NE) [10]	**4.6** (1.4, 8.1) [25]
Ovarian	**5.9** (4.0, 8.3) [40]	**12.5** (3.1, NE) [11]	**4.1** (2.3, 12.6) [19]	**12.6** (4.1, NE) [15]	**4.4** (2.3, 7.1) [25]
Bladder	**7.0** (4.2, 9.7) [41]	**7.4** (3.0, 11.9) [16]	**7.8** (2.6, 11.6) [20]	**7.0** (3.9, 11.5) [27]	**7.0** (2.6, 13.0) [14]
Other†	**8.8** (5.5, 12.5) [40]	**22.3** (5.6, NE) [9]	**5.5** (2.8, 8.7) [16]	**13.0** (6.3, 23.4) [16]	**6.6** (2.9, 8.8) [24]
Biliary tract	**4.6** (3.1, 6.0) [41]	**7.4** (2.8, 12.5) [16]	**4.2** (2.8, 6.0) [14]	**6.9** (3.0, 8.0) [22]	**3.7** (2.8, 5.1) [19]
Pancreatic	**3.2** (1.8, 7.2) [25]	**5.4** (2.8, NE) [2]	**2.8** (1.4, 9.1) [19]	**8.0** (1.2, NE) [5]	**3.2** (1.4, 4.9) [20]

Discrepancies in n numbers are owing to patients with central HER2 IHC status of 1+/0/unknown enrolled as IHC 3+/2+ by local testing

*Investigator assessed per RECIST 1.1; †included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1); ‡HER2 expression for enrollment was based on local assessment, where available, otherwise enrollment was based on central testing

CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NE, not evaluable; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

Makker V et al. ESMO 2025;Abstract 957P.

DESTINY-PanTumor02 Part 1 Final Analysis: Median OS by Tumor Cohort and HER2 IHC Status

Median OS, months (95% CI) [n]	All patients	HER2 IHC status by central testing		HER2 IHC status at enrollment†	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
All	**13.4** (11.9, 15.3) [267]	**21.1** (16.0, 26.0) [75]	**12.2** (10.7, 13.6) [125]	**17.7** (12.8, 23.4) [111]	**12.0** (9.6, 13.5) [151]
Endometrial	**24.2** (12.8, 33.7) [40]	**33.7** (18.9, NE) [13]	**16.4** (8.0, 34.7) [17]	**29.0** (4.5, NE) [16]	**20.3** (8.1, 33.1) [24]
Cervical	**13.6** (11.1, 19.7) [40]	**35.8** (3.9, NE) [8]	**11.6** (5.1, 18.0) [20]	**35.8** (3.9, NE) [10]	**11.7** (8.0, 13.6) [25]
Ovarian	**13.2** (8.0, 17.7) [40]	**20.0** (3.8, NE) [11]	**13.0** (4.7, 21.9) [19]	**20.0** (7.2, NE) [15]	**10.7** (5.9, 14.8) [25]
Bladder	**12.8** (11.2, 15.1) [41]	**13.4** (6.7, 19.8) [16]	**13.1** (11.0, 19.9) [20]	**12.6** (6.7, 17.2) [27]	**13.5** (8.0, 19.9) [14]
Other*	**21.0** (12.9, 25.1) [40]	**25.1** (11.1, NE) [9]	**14.6** (6.8, 22.4) [16]	**25.2** (11.1, 40.0) [16]	**15.5** (9.6, 22.4) [24]
Biliary tract	**7.0** (4.6, 10.2) [41]	**12.4** (2.8, 26.3) [16]	**6.0** (3.7, 11.7) [14]	**7.6** (4.6, 23.7) [22]	**5.3** (3.1, 10.2) [19]
Pancreatic	**5.0** (3.8, 14.2) [25]	**12.4** (8.8, NE) [2]	**4.9** (2.4, 15.7) [19]	**8.8** (2.4, NE) [5]	**4.7** (3.2, 14.2) [20]

Discrepancies in n numbers are owing to patients with central HER2 IHC status of 1+/0/unknown enrolled as IHC 3+/2+ by local testing
*Included patients with salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1); †HER2 expression for enrollment was based on local assessment, where available, otherwise enrollment was based on central testing
CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NE, not evaluable; OS, overall survival

Makker V et al. ESMO 2025;Abstract 957P.

DESTINY-PanTumor02 Part 1 Conclusions

- Consistent with the primary and post-hoc analyses,[1,2] T-DXd continued to show durable and clinically meaningful antitumor activity in patients with HER2-expressing tumors (immunohistochemistry [IHC] 3+/2+), irrespective of whether HER2 IHC status was determined by central or local testing
  - The greatest benefit was observed in patients with HER2 IHC 3+ tumors
  - With extended follow up, safety remained consistent with the known profile of T-DXd, with no new safety signals observed compared with the primary analysis[1]
- These results further reinforce T-DXd as a recommended treatment for pretreated patients with HER2-positive (IHC 3+) tumors[3–5]
  - Part 2 of the study is currently ongoing and is expected to provide further insights into the antitumor activity of T-DXd in pretreated patients with HER2-expressing/amplified solid tumors[6]

Makker V et al. ESMO 2025;Abstract 957P.

ESMO 2025

Poster 145P

Trastuzumab deruxtecan in pretreated patients with HER2-expressing solid tumors: exploratory biomarker analysis of DESTINY-PanTumor02 Part 1

Jung-Yun Lee,[1] Funda Meric-Bernstam,[2] Ana Oaknin,[3] Do-Youn Oh,[4] Soham Puvvada,[5] Robert McEwen,[6] Flavia Michelini,[7] Vicky Makker[8]

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DESTINY-PanTumor02 Part 1 Biomarker Analysis Conclusions

- T-DXd showed clinically meaningful antitumor activity across multiple biomarker subgroups
  - Consistent with the primary analysis,[1] the greatest antitumor activity was observed for patients with human epidermal growth factor receptor 2 (HER2) immunohistochemistry (IHC) 3+ tumors by central testing
  - The lowest confirmed investigator-assessed objective response rate (ORR; 11.6%) was observed for patients with *H/K/NRAS* alterations; however, this subgroup had a limited sample size (n=43) and included only four (9.3%) patients with HER2 IHC 3+ tumors (by central testing)
- Overall, these data further demonstrate clinically meaningful activity for T-DXd in HER2-expressing tumors and HER2 IHC 3+ expression as the greatest predictor of treatment response, consistent with treatment recommendations for T-DXd in pretreated patients with HER2-positive (IHC 3+) tumors[2–4]

Lee J-Y et al. ESMO 2025;Abstract 145P.

A Randomized Phase 3 Study of First-Line (1L) Trastuzumab Deruxtecan (T-DXd) with Rilvegostomig or Pembrolizumab in Patients with HER2-Expressing, Mismatch Repair Proficient (pMMR), Primary Advanced or Recurrent Endometrial Cancer (EC): DESTINY-Endometrial 01/GOG-3-98/ENGOT-EN24

Slomovitz BM et al.
ESMO 2025;Abstract 1223TiP.

An Open-Label, Randomized, Multicenter, Phase III Study of Trastuzumab Deruxtecan (T-DXd) with Bevacizumab (BEV) vs BEV Monotherapy as First-Line (1L) Maintenance Therapy in HER2-Overexpressing Ovarian Cancer: DESTINY-Ovarian01 (DO-01)

González-Martín A et al.

ESMO Gynaecological Cancers Congress 2025;Abstract 127TiP.

Agenda

Module 1: Up-Front Treatment of Ovarian Cancer (OC)

Module 2: Management of Platinum-Resistant OC

Module 3: Up-Front Management of Metastatic Endometrial Cancer

Module 4: Management of HER2-Positive Gynecologic Cancers

Module 5: Management of Cervical Cancer

Case Presentation: Dr Salani

- 75 year old patient, PMH of hypertension and well controlled diabetes.
- 6/13/24: Cervical biopsy: Detached fragments of at least high-grade squamous intraepithelial lesion (HSIL/CIN 3) with papillary features.
- 6/17/24: PET CT: Cervical mass (6.3 x 4.1 x 4.7 cm) with SUV 15.8, intense FDG avid right iliac lymph node and several mild FDG uptake in bilateral pelvic nodes. Concern for pulmonary embolism.
- 6/18/24: Cervical biopsy: Papillary squamous cell carcinoma; CPS>1; consistent with Stage IIIC1r cervical cancer.
- 6/18/24: MRI abdomen/pelvis: Cervical mass measuring 6.5 x 3.5 x 4.7 cm with parametrial extension on the right and uppermost vagina; suspicious pelvic and common iliac lymph nodes.

Case Presentation: Dr Salani (Continued)

- 7/8/24 – 8/9/24: External beam radiation (4500 cGy) with cisplatin and pembrolizumab.
- 8/12/24 – 8/16/24: Cervical brachytherapy (2550 cGy).
- 8/19/24: Pembrolizumab maintenance started.
- 11/1/24: PET CT: Resolution of cervical mass and lymph nodes; stable 4 mm right pulmonary nodules.
- 5/3/25: CT chest/abdomen/pelvis: No evidence of intrathoracic or abdominal disease.
- 10/25/25: CT abdomen/pelvis: No evidence of disease, sustained treatment response.
- Current status: Doing well, plan to receive pembrolizumab maintenance for a total of 15 cycles.

Key Datasets

- Wu X et al. Phase III study of camrelizumab plus famitinib versus platinum-based chemotherapy as first-line therapy for recurrent or metastatic cervical cancer. ESMO 2025;Abstract LBA38.

BERLIN 2025 ESMO congress

Abstract LBA38

Phase 3 study of camrelizumab plus famitinib versus platinum-based chemotherapy as first-line therapy for recurrent or metastatic cervical cancer

Camrelizumab plus famitinib for cervical cancer

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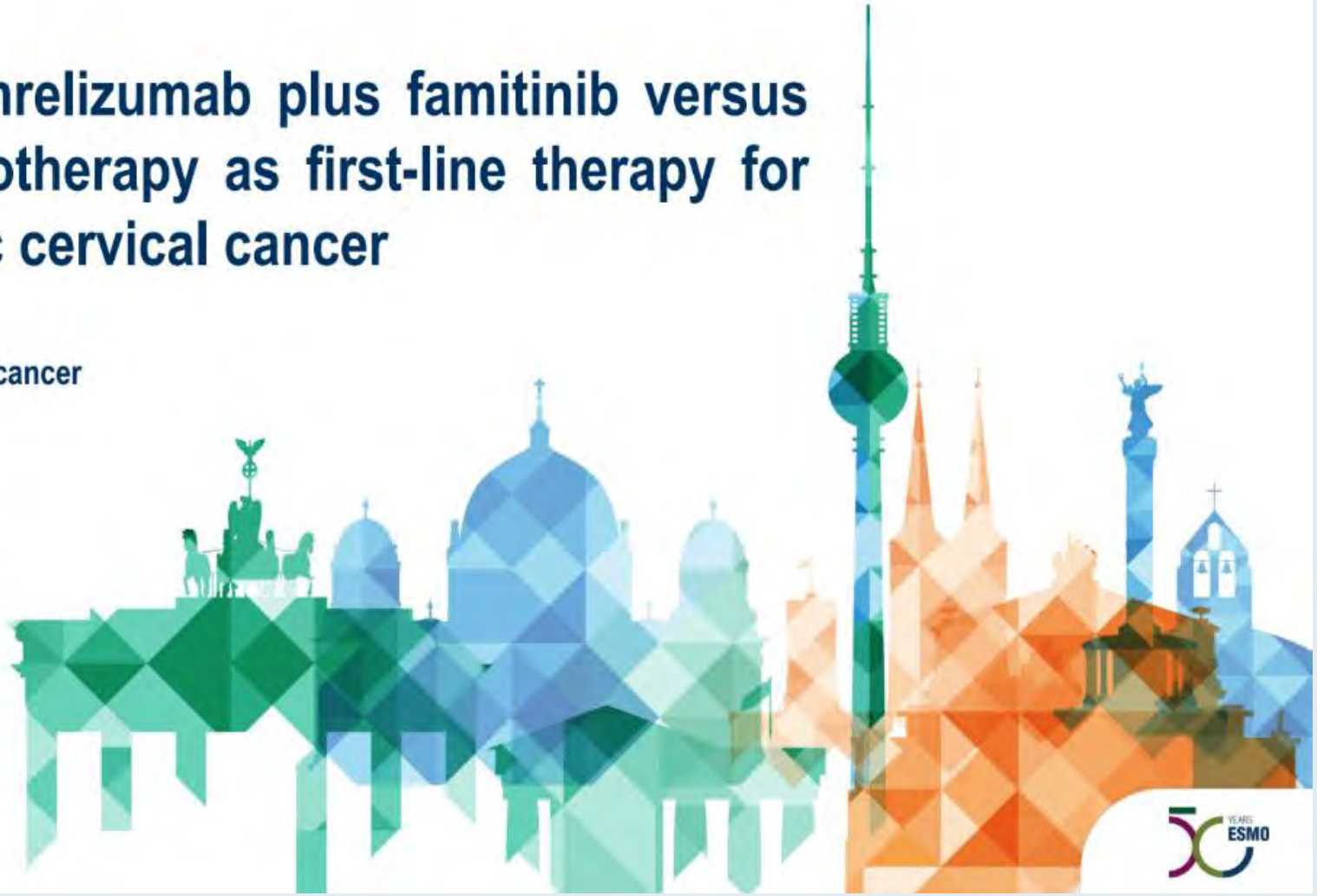
On behalf of Lingfang Xia, Jing Wang, Hanmei Lou, Shanbing Wang, Hui Zhang, Yunyan Zhang, Guonan Zhang, Yin Tang, Shuxia Cheng, Yuhua Gao, Dan Li, Yong Cheng, Guiling Li, Lina Zhao, Hongping Zhang, Guoying Xu, Yuting Wang



Study Conclusions

- **The chemotherapy-free regimen of camrelizumab plus famitinib significantly prolonged PFS and OS compared with platinum-based chemotherapy with or without bevacizumab as first-line treatment in R/M CC, meeting the dual primary endpoints at interim analysis.**
  - Median PFS (per BICR): 11.1 vs 7.5 months; camrelizumab-famitinib vs chemotherapy, HR=0.68 (0.53–0.86), P=0.0007.
  - Median OS: 34.4 vs 23.4 months; camrelizumab-famitinib vs chemotherapy, HR=0.65 (0.49–0.86), P=0.0012.

- **The safety profile was manageable.**
  - Toxicities were consistent with previous reports of camrelizumab and famitinib. No new safety signals were identified.
  - The most common grade ≥3 TRAEs associated with camrelizumab and famitinib were hematological toxicities and hypertension, which were manageable with standard supportive treatment and dose modification.
  - The incidence of grade ≥3 hematological toxicities with camrelizumab and famitinib was lower than that with platinum-based chemotherapy (with or without bevacizumab).

- **Camrelizumab plus famitinib could be a novel first-line treatment option for this patient population.**

Wu X et al. ESMO 2025;Abstract LBA38.

Inside the Issue: The Emerging Role of Cereblon E3 Ligase Modulators in Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Wednesday, January 28, 2026
5:00 PM – 6:00 PM ET

Faculty

Natalie S Callander, MD
Paul G Richardson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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