What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Endometrial Cancer

Thursday, April 25, 2024
6:00 AM – 7:30 AM

Faculty

Jennifer Filipi, MSN, NP
Kathryn M Lyle, MSN, WHNP-BC, AGNP-C
David M O'Malley, MD
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Jennifer Filipi, MSN, NP
Department of Gynecologic Oncology
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts

Kathryn M Lyle, MSN, WHNP-BC, AGNP-C
Nurse Practitioner
Division of Gynecologic Oncology
The University of Alabama at Birmingham
Birmingham, Alabama

David M O'Malley, MD
Director and Professor
Division of Gynecologic Oncology in Obstetrics and Gynecology
John G Boutselis Chair in Gynecologic Oncology
The Ohio State University and The James Comprehensive Cancer Center
Columbus, Ohio

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

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH TO PRACTICE

Ms Filipi — Disclosures

No relevant conflicts of interest to disclose

RTP
RESEARCH
TO PRACTICE

Ms Lyle— Disclosures

No relevant conflicts of interest to disclose

Dr O'Malley — Disclosures

Advisory Committees and Consulting Agreements (Personal Fees)	AbbVie Inc, Adaptimmune, Agenus Inc, Arcus Biosciences, Arquer Diagnostics, AstraZeneca Pharmaceuticals LP, Atossa Therapeutics, Cardiff Oncology, Celcuity, Clovis Oncology, Corcept Therapeutics, Duality Biologics, Eisai Inc, Elevar Therapeutics, Exelixis Inc, F Hoffmann-La Roche Ltd, Genelux Corporation, Genentech, a member of the Roche Group, GSK, ImmunoGen Inc, Imvax Inc, InterVenn Biosciences, InxMed, Iovance Biotherapeutics, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Laekna Therapeutics, Leap Therapeutics Inc, Luzsana Biotechnology, Merck, Mersana Therapeutics Inc, MSD, Myriad Genetic Laboratories Inc, Novartis, Novocure Inc, OncoC4, Onconova Therapeutics Inc, Regeneron Pharmaceuticals Inc, Replimune, Roche Diagnostics, R-Pharm US, Seagen Inc, Sorrento Therapeutics, Sumitomo Dainippon Pharma Oncology Inc, Sutro Biopharma, Tarveda Therapeutics, Toray Industries Inc, Trillium Therapeutics Inc, Umoja Biopharma, VBL Therapeutics, Verastem Inc, Vincerx Pharma, Xencor, Zentalis Pharmaceuticals
Contracted Research (Institution Received Funds)	AbbVie Inc, Advaxis Inc, Agenus Inc, Alkermes, Aravive Inc, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol Myers Squibb, Clovis Oncology, Deciphera Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Exelixis Inc, F Hoffmann-La Roche Ltd, Genentech, a member of the Roche Group, Genmab US Inc, GSK, ImmunoGen Inc, Incyte Corporation, Iovance Biotherapeutics, Karyopharm Therapeutics, Leap Therapeutics Inc, Merck, Mersana Therapeutics Inc, MSD, Novartis, Novocure Inc, OncoC4, OncoQuest Inc, Pfizer Inc, Predictive Oncology Inc, Prelude Therapeutics, Regeneron Pharmaceuticals Inc, Rubius Therapeutics, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Sutro Biopharma, Tesaro, A GSK Company, Verastem Inc
Nonrelevant Financial Relationships	GOG Foundation Inc, Ludwig Institute for Cancer Research Ltd, National Cancer Institute, NRG Oncology, RTOG, SWOG

RTP
RESEARCH
TO PRACTICE

Dr Westin — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Caris Life Sciences, Clovis Oncology, Eisai Inc, EQRx, Genentech, a member of the Roche Group, Gilead Sciences Inc, GSK, Immunocore, ImmunoGen Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mereo BioPharma, Mersana Therapeutics Inc, NGM Biopharmaceuticals, Nuvectis Pharma Inc, pharmaand GmbH, Seagen Inc, Verastem Inc, Vincerx Pharma, Zentalis Pharmaceuticals, ZielBio
Contracted Research	AstraZeneca Pharmaceuticals LP, Avenge Bio, Bayer HealthCare Pharmaceuticals, Bio-Path Holdings, Clovis Oncology, Genentech, a member of the Roche Group, GSK, Jazz Pharmaceuticals Inc, Mereo BioPharma, Novartis, Nuvectis Pharma Inc, pharmaand GmbH, Zentalis Pharmaceuticals

RTP
RESEARCH
TO PRACTICE

Commercial Support

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

Research To Practice NCPD Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

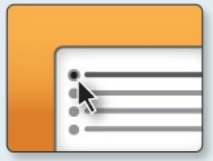
This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

RTP
RESEARCH
TO PRACTICE

Clinicians in the Meeting Room

Networked iPads are available.

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



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

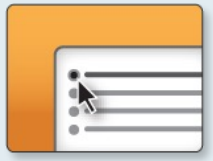
Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

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

RTP RESEARCH TO PRACTICE

Clinicians Attending via Zoom

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



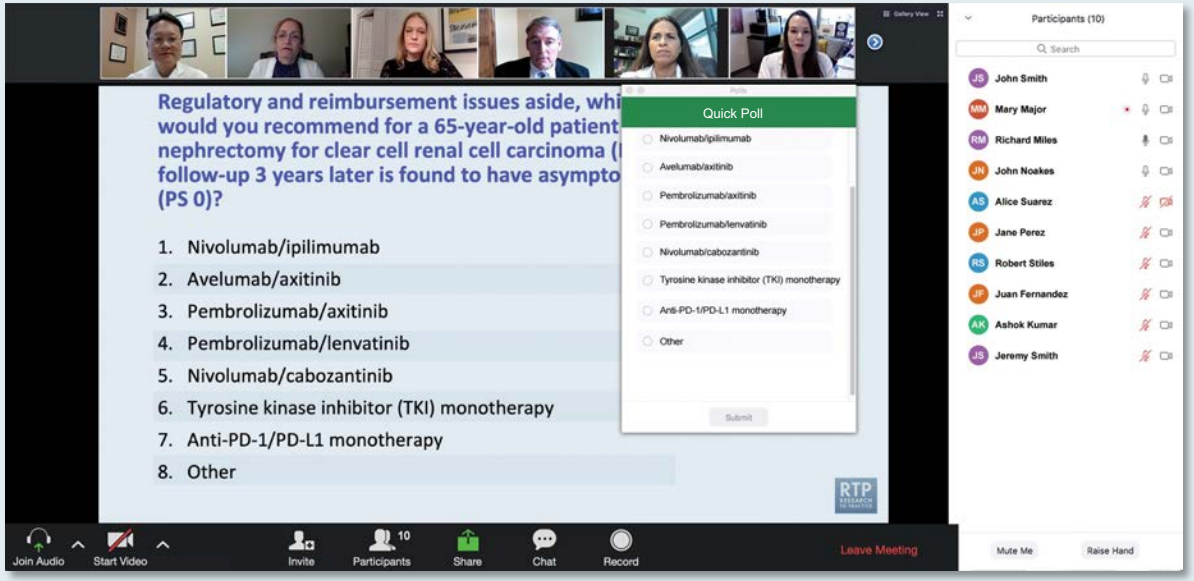
Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

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

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

RTP
RESEARCH
TO PRACTICE

Clinicians, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

About the Enduring Program

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

RTP
RESEARCH
TO PRACTICE

“What I Tell My Patients”
Sixteenth Annual RTP-ONS NCPD Symposium Series

Wednesday April 24	**Hormone Receptor–Positive Breast Cancer** 6:00 PM – 8:00 PM ET
Thursday April 25	**Endometrial Cancer** 6:00 AM – 7:30 AM ET
	Antibody–Drug Conjugates 12:15 PM – 1:45 PM ET
	Chronic Lymphocytic Leukemia and Bispecific Antibodies in Lymphoma 6:00 PM – 8:00 PM ET
Friday April 26	**Head and Neck Cancer** 6:00 AM – 7:30 AM ET
	Non–Small Cell Lung Cancer with an EGFR Mutation 12:15 PM – 1:45 PM ET
	Ovarian Cancer 6:00 PM – 7:30 PM ET
Saturday April 27	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM ET
	Myelofibrosis 12:15 PM – 1:45 PM ET
	Gastroesophageal and Colorectal Cancers 6:00 PM – 8:00 PM ET
Wednesday, May 1	**LIVE WEBINAR — Prostate Cancer** 7:00 PM – 8:00 PM ET

RTP
RESEARCH TO PRACTICE

How was it different to take care of this patient versus another patient in the same oncologic setting?

What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

Consulting Nurse Faculty

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kathleen D Burns, RN, MSN, AGACNP-BC, OCN
City of Hope Comprehensive Cancer Center
Duarte, California

Sonia Glennie, ARNP, MSN, OCN
Swedish Cancer Institute Center for Blood Disorders
Seattle, Washington

Amy Goodrich, CRNP
The Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

Jessica Mitchell, APRN, CNP, MPH
Mayo Clinic College of Medicine and Science
Rochester, Minnesota

Tiffany A Richards, PhD, ANP-BC, AOCNP
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Ronald Stein, JD, MSN, NP-C, AOCNP
USC Norris Comprehensive Cancer Center
Los Angeles, California

https://www.ResearchToPractice.com/ONS2024Clips

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Endometrial Cancer

Thursday, April 25, 2024
6:00 AM – 7:30 AM

Faculty

Jennifer Filipi, MSN, NP
Kathryn M Lyle, MSN, WHNP-BC, AGNP-C
David M O'Malley, MD
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

Consulting Nursing Faculty Comments

People with newly diagnosed cancer

Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC

RTP RESEARCH TO PRACTICE

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

Dr O'Malley
Columbus, Ohio

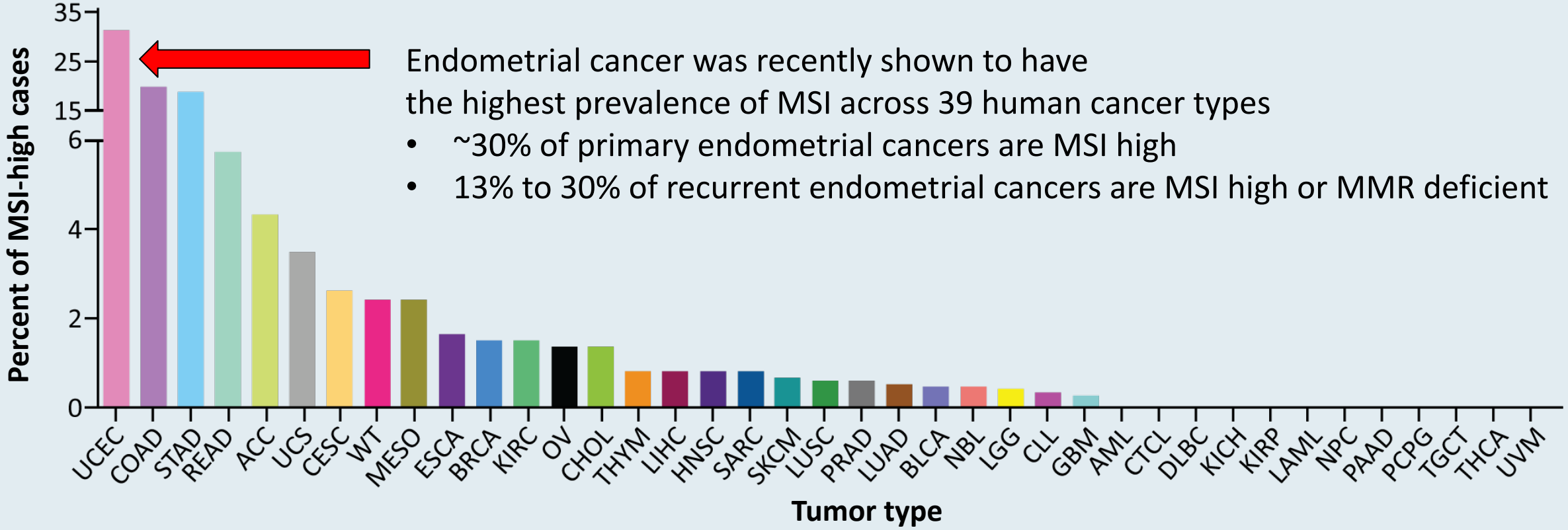
Incidence and Biology of Endometrial Cancer (EC)

Dr Westin
Houston, Texas

- **Incidence and prognosis of EC in the United States and the rest of the world**
- **Appreciation of various molecular subtypes of EC and implications for prognosis and current management**
- **Frequency of microsatellite instability (MSI)/mismatch repair (MMR) deficiency in patients with EC**
- **Optimal timing of and approach to MSI/MMR assessment**

High MSI Across 39 Cancer Types

Whole-exome data from 11,139 tumor-normal pairs from The Cancer Genome Atlas and Therapeutically Applicable Research to Generate Effective Treatments projects



Endometrial cancer was recently shown to have the highest prevalence of MSI across 39 human cancer types

- ~30% of primary endometrial cancers are MSI high
- 13% to 30% of recurrent endometrial cancers are MSI high or MMR deficient

UCEC = uterine corpus endometrial carcinoma

Bonneville R et al. *JCO Precis Oncol* 2017;1:1-15; Green AK et al. *ASCO Educational Book* 2020.

RTP RESEARCH TO PRACTICE

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

Dr O'Malley
Columbus, Ohio

Use of Immune Checkpoint Inhibitors for EC

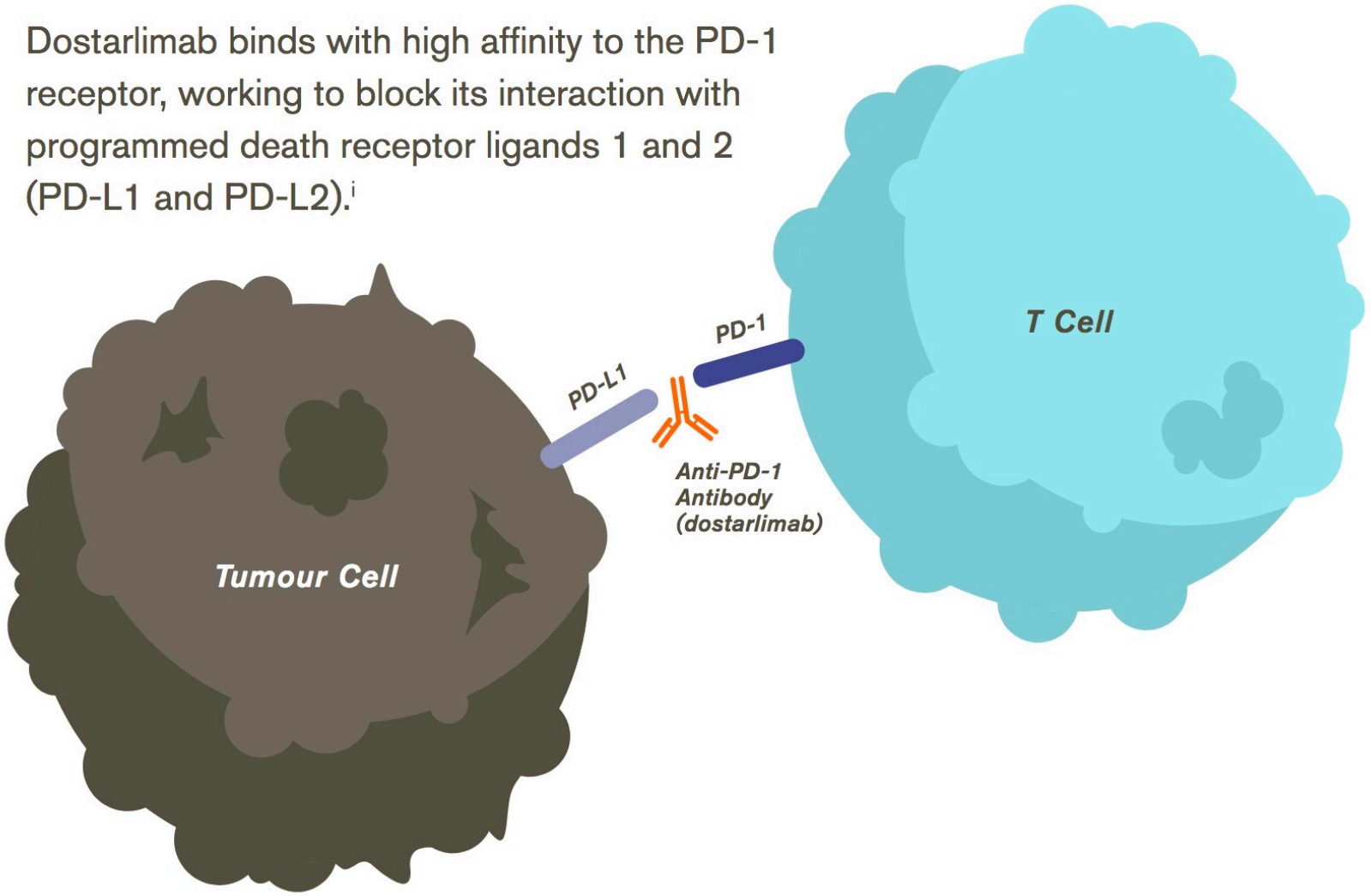
Dr Westin
Houston, Texas

- **Mechanism of action of anti-PD-1/PD-L1 antibodies**
- **Similarities and differences among different currently available anti-PD-1/ PD-L1 antibodies**
- **Published efficacy and safety data with anti-PD-1/PD-L1 antibody monotherapy for MSI-high (MSI-H)/MMR-deficient (dMMR) recurrent EC**
- **Optimal integration of pembrolizumab and dostarlimab into the care of patients with recurrent MSI-H/dMMR EC**

RTP
RESEARCH
TO PRACTICE

Dostarlimab Mechanism of Action

Dostarlimab binds with high affinity to the PD-1 receptor, working to block its interaction with programmed death receptor ligands 1 and 2 (PD-L1 and PD-L2).[i]



https://us.gsk.com/media/5875/dostarlimab-infographic_approved-0422.pdf

RTP RESEARCH TO PRACTICE

Dostarlimab

Mechanism of action

- Anti-PD-1 monoclonal antibody

Indication as single agent

- For patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer that has progressed during or after a prior platinum-containing regimen in any setting who are not candidates for curative surgery or radiation

Recommended dose as single agent

- 500 mg IV q3wk doses 1-4, then 1,000 mg IV q6wk

Dostarlimab package insert, 3/2024.

RTP RESEARCH TO PRACTICE

Pembrolizumab

Mechanism of action

- **Anti-PD-1 monoclonal antibody**

Indication as single agent

- **For patients with advanced MSI-H or dMMR EC who have disease progression after prior systemic therapy in any setting and are not candidates for curative surgery or radiation**

Recommended dose

- **200 mg IV every 3 weeks or 400 mg IV every 6 weeks**

Pembrolizumab package insert, 3/2024.

Kathryn M Lyle, MSN, WHNP-BC, AGNP-C

What I tell my patients with MSI-H/dMMR EC about to begin treatment with an anti-PD-1/PD-L1 antibody

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

First-Line Therapy for Primary Advanced or Recurrent EC

Dr O'Malley
Columbus, Ohio

Dr Westin
Houston, Texas

- **Historical role of and outcomes achieved with chemotherapy as first-line treatment for primary advanced or recurrent EC**
- **Biological rationale for the evaluation of anti-PD-1/PD-L1 antibodies in combination with chemotherapy for patients with EC**
- **Similarities and differences among the Phase III RUBY, NRG-GY018 and AtTEnd trials evaluating dostarlimab, pembrolizumab and atezolizumab, respectively, in combination with chemotherapy as first-line treatment for primary advanced or recurrent EC**
- **Key efficacy findings from the RUBY, NRG-GY018 and AtTEnd trials; outcomes reported in the MSI-H/dMMR and microsatellite-stable (MSS)/MMR-proficient (pMMR) cohorts**
- **Recent FDA approval of dostarlimab in combination with carboplatin and paclitaxel, followed by single-agent dostarlimab, for primary advanced or recurrent dMMR/MSI-H EC; optimal integration into current management**

Dostarlimab

Mechanism of action

- **Anti-PD-1 monoclonal antibody**

Indication as combination therapy

- **In combination with carboplatin and paclitaxel, followed by single-agent dostarlimab, for patients with primary advanced or recurrent endometrial cancer (EC) whose disease is mismatch repair deficient (dMMR) or microsatellite instability high (MSI-H).**

Recommended dose as combination therapy

- **In combination with carboplatin/paclitaxel: 500 mg IV q3wk doses 1-6, then as monotherapy 1,000 mg IV q6wk**

Dostarlimab package insert, 3/2024.

RTP RESEARCH TO PRACTICE

Symptoms of Immunotherapy Toxicity

Hypophysitis
(fatigue)

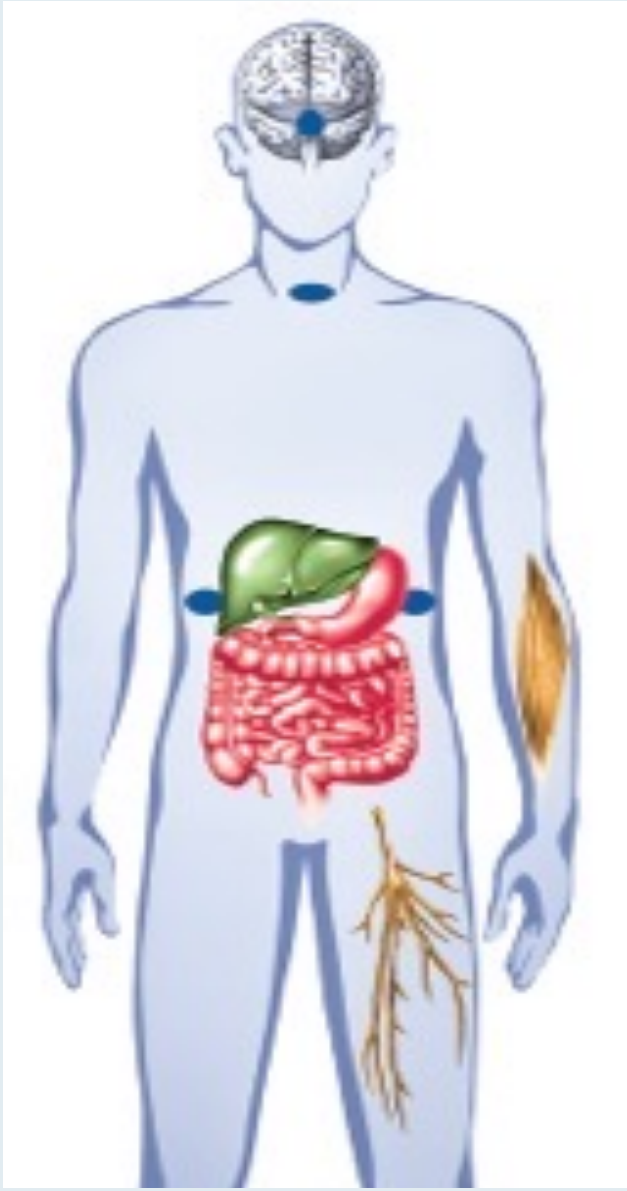
Thyroiditis
(over/underactive thyroid)

Adrenal Insufficiency
(fatigue)

Diabetes Mellitus
(type I, II, fatigue, DKA)

Colitis
(diarrhea, abd pain)

Dermatitis
(rash, itch, blistering)



Pneumonitis
(dyspnea, cough)

Myocarditis
(chest pain, dyspnea)

Hepatitis
(abn LFTs, jaundice)

Pancreatitis
(abd pain)

Neurotoxicities
(MG, encephalitis)

Arthritis
(joint pain)

RTP
RESEARCH
TO PRACTICE

Jennifer Filipi, MSN, NP

What I tell my patients with EC about to begin treatment with an anti-PD-1/PD-L1 antibody in combination with chemotherapy

RTP
RESEARCH
TO PRACTICE

Consulting Nursing Faculty Comments

Patient self-advocacy and shared treatment decision-making

Tiffany A Richards, PhD, ANP-BC, AOCNP

RTP
RESEARCH
TO PRACTICE

PARP Inhibitors Combined with Immunotherapy for Advanced EC

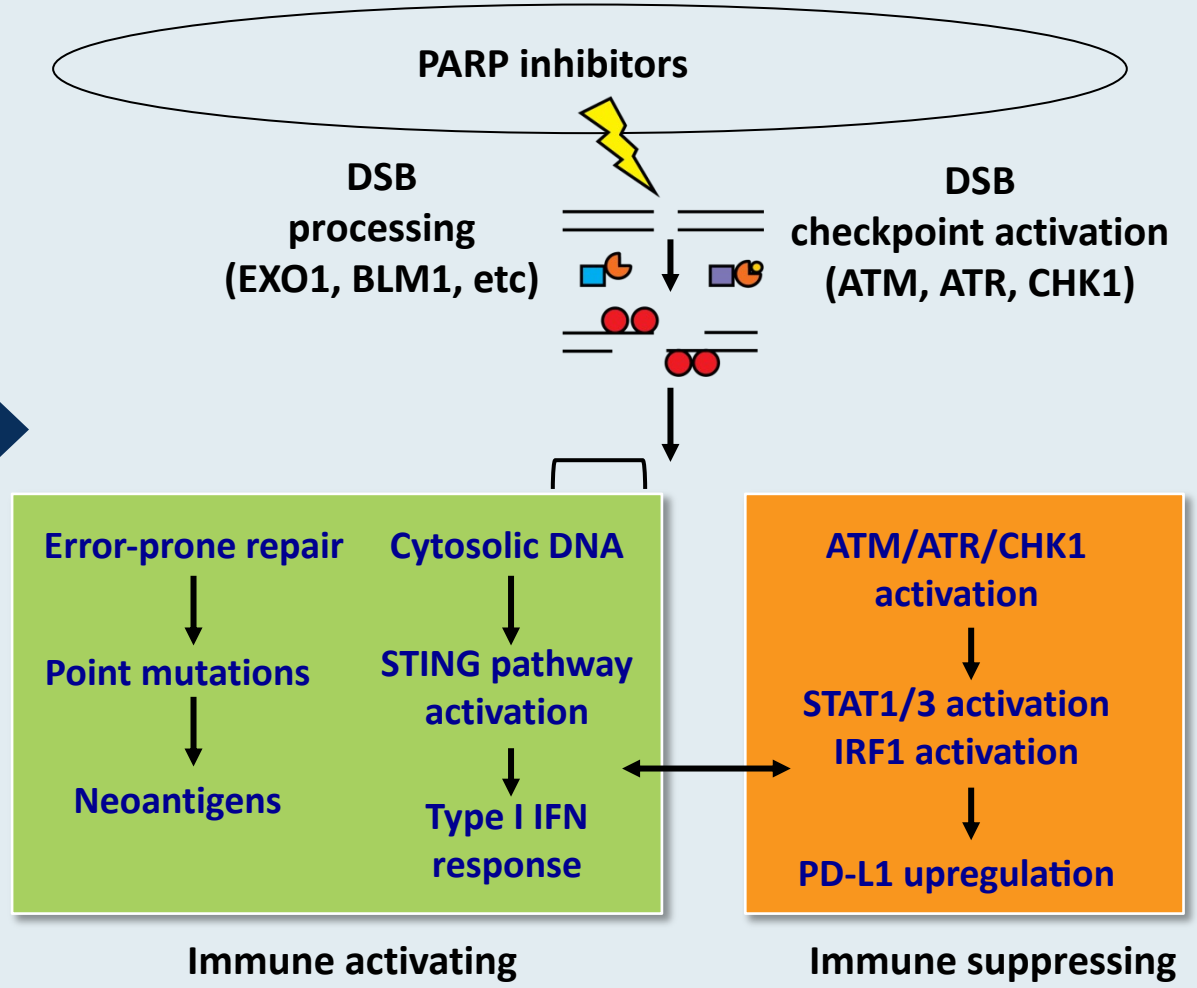
Dr O'Malley
Columbus, Ohio

Dr Westin
Houston, Texas

- **Mechanism of antitumor activity of PARP inhibitors and biological rationale for their investigation for EC; potential therapeutic synergy between PARP inhibitors and immune checkpoint inhibitors (ICIs)**
- **Key efficacy findings from the Phase III DUO-E trial evaluating first-line durvalumab in combination with chemotherapy followed by maintenance durvalumab with or without olaparib for newly diagnosed advanced or recurrent EC**
- **Similarities and differences between the designs of the DUO-E trial and part 2 of the RUBY trial; recently presented data with maintenance dostarlimab/niraparib in RUBY part 2**
- **Potential role of anti-PD-1/PD-L1 antibodies in combination with PARP inhibitors in the future care of patients with EC**

Biological Rationale for Combining a PARP Inhibitor (PARPi) with an Immune Checkpoint Inhibitor

Preclinical models indicate synergy between PARPi and anti-PD-1 agents regardless of BRCA mutation status or PD-L1 status



Preclinical data demonstrate synergy with PARPi and anti-PD-1 combinations.

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

RTP RESEARCH TO PRACTICE

Practical Considerations with Anti-PD-1/ PD-L1 Antibodies Alone or in Combination with Chemotherapy or a PARP Inhibitor

Dr O'Malley
Columbus, Ohio

Dr Westin
Houston, Texas

- **Pathophysiology, incidence and spectrum of immune-mediated and other adverse events (AEs) observed with anti-PD-1/PD-L1 antibodies as monotherapy or in combination with chemotherapy or a PARP inhibitor**
- **Recommended monitoring and management paradigms for immune-related and other AEs with ICIs for gynecologic cancers**
- **Strategies to discern whether toxicities relate to chemotherapy, a PARP inhibitor, immune checkpoint inhibition or combinations of these agents**
- **Role of rechallenge for patients for whom ICI therapy has been held due to immune-mediated toxicity**
- **Relative and absolute contraindications to anti-PD-1/PD-L1 antibody therapy; role, if any, in therapy for patients with preexisting autoimmune conditions or a history of solid organ transplant**

Kathryn M Lyle, MSN, WHNP-BC, AGNP-C

What I tell my patients with EC who are being considered for or are about to enroll on a clinical trial with a PARP inhibitor

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

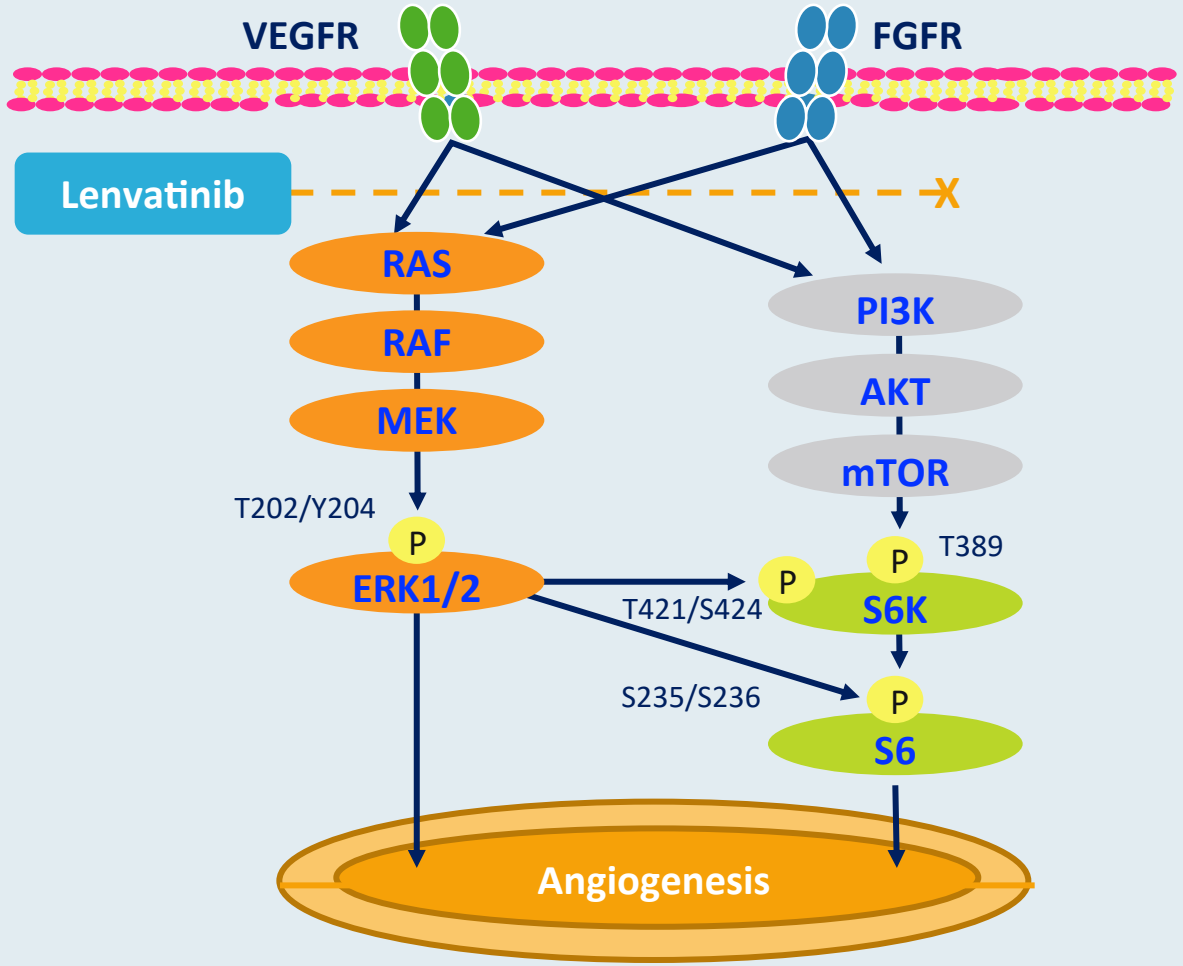
Lenvatinib/Pembrolizumab in the Management of Mismatch Repair Proficient (pMMR) Metastatic EC

Dr O'Malley
Columbus, Ohio

Dr Westin
Houston, Texas

- **Biological rationale for combining ICIs with agents targeting the VEGF pathway for EC**
- **Major findings, including overall survival data, supporting the use of lenvatinib in combination with pembrolizumab for patients with advanced pMMR EC with disease progression after prior systemic therapy**
- **Optimal integration of pembrolizumab/lenvatinib into current EC management algorithms**
- **Recent announcement of failure of the Phase III LEAP-001 trial evaluating lenvatinib/pembrolizumab in the up-front setting; implications for current practice and future research**

Mechanism of Action of Lenvatinib

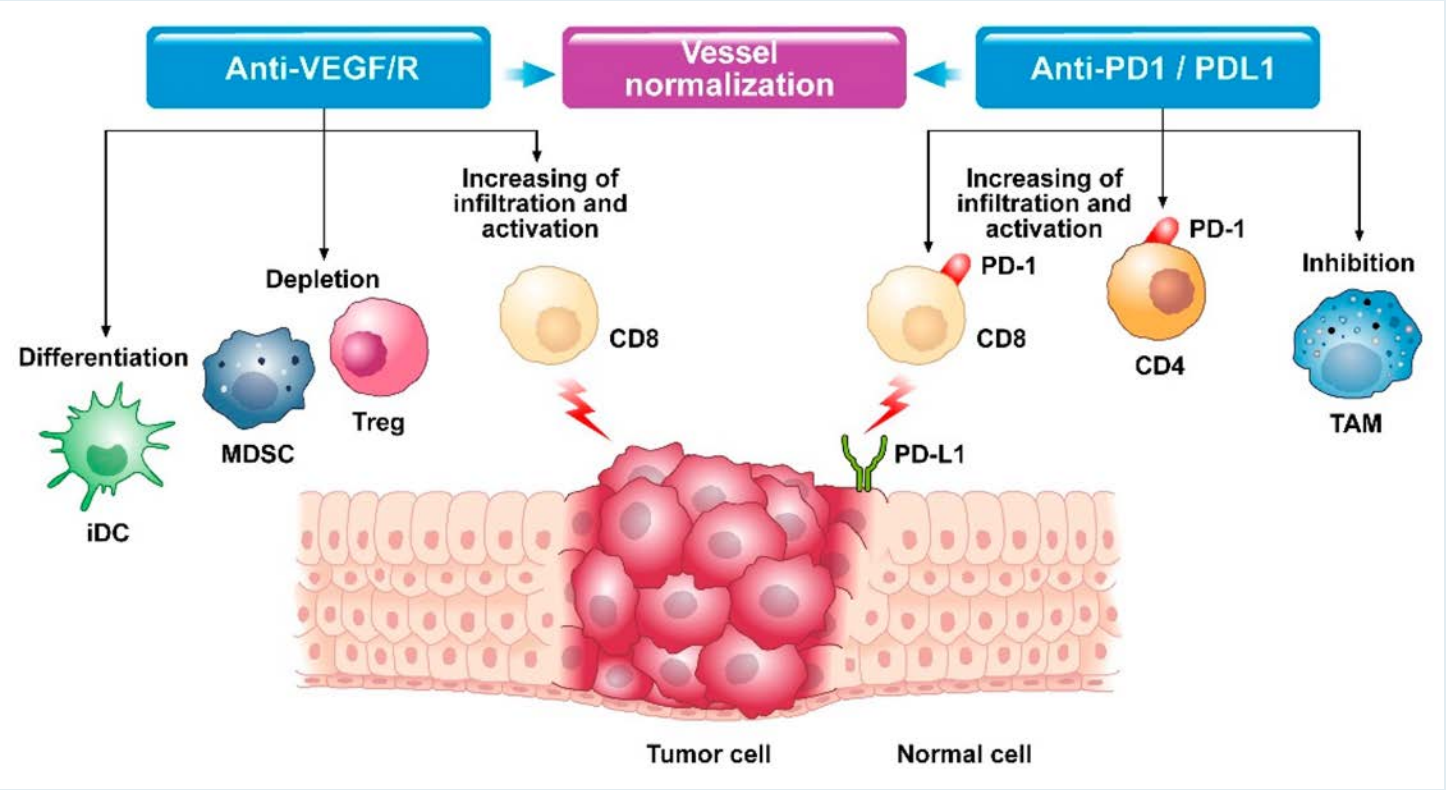


- Orally available inhibitor of multiple tyrosine kinases including VEGF receptors, FGFR, RET, PDGFR and KIT
- Demonstrated promising radiographic response rates and survival results in Phase II and III trials in hepatocellular carcinoma

Finn RS et al. *Proc ASCO* 2014;Abstract TPS4153; Stjepanovic N et al. *Biologics* 2014;8:129-39; Cheng AL et al. *Proc ASCO* 2017;Abstract 4001; Ikeda K et al. *J Gastroenterol* 2017;52(4):512-9.

Biological Rationale for Combining Immune Checkpoint Inhibitors with VEGF Pathway Targeted Agents

- Reduction in Treg activity
- Reversal of immunosuppressive effects of VEGF
- Improved T-cell trafficking and infiltration of CD8+ into the tumor bed



Oaknin A. ASCO 2022; Education Session.

Lenvatinib

Mechanism of action

- **Oral multikinase inhibitor**

Indication in combination with pembrolizumab

- **For patients with advanced endometrial carcinoma that is pMMR or not MSI-H who have disease progression after prior systemic therapy in any setting and are not candidates for curative surgery or radiation**

Recommended dose in combination with pembrolizumab

- **20 mg orally once daily**

Lenvatinib package insert, 4/2024.

Pembrolizumab

Mechanism of action

- **Anti-PD-1 monoclonal antibody**

Indication in combination with lenvatinib

- **For patients with for advanced EC that is pMMR or not MSI-H who have disease progression after prior systemic therapy in any setting and are not candidates for curative surgery or radiation**

Recommended dose in combination with lenvatinib

- **200 mg IV every 3 weeks or 400 mg IV every 6 weeks**

Pembrolizumab package insert, 3/2024.

Update on Phase III LEAP-001 Trial Evaluating Pembrolizumab Plus Lenvatinib as First-Line Treatment for Patients with Advanced or Recurrent Endometrial Carcinoma

Press Release – December 8, 2023

"…the Phase 3 LEAP-001 trial evaluating pembrolizumab plus lenvatinib did not meet its dual primary endpoints of overall survival (OS) and progression-free survival (PFS) for the first-line treatment of patients with advanced or recurrent endometrial carcinoma whose disease is mismatch repair proficient (pMMR)/not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)/MSI-H.

At the final analysis, pembrolizumab plus lenvatinib did not improve OS or PFS sufficiently to meet the study's prespecified statistical criteria in the first-line treatment of certain patients with advanced or recurrent endometrial carcinoma versus a standard of care, platinum-based chemotherapy doublet (carboplatin plus paclitaxel). The safety profile of pembrolizumab plus lenvatinib was consistent with that observed in previously reported studies evaluating the combination. A full evaluation of the data from this study is ongoing."

https://www.merck.com/news/merck-and-eisai-provide-update-on-phase-3-leap-001-trial-evaluating-pembrolizumab-plus-lenvima-lenvatinib-as-first-line-treatment-for-patients-with-advanced-or-recurrent-endometrial-carcinom/

Dr O'Malley
Columbus, Ohio

Toxicities with Lenvatinib/Pembrolizumab

Dr Westin
Houston, Texas

- **Incidence, severity, timing and management of AEs observed in patients with EC receiving lenvatinib/pembrolizumab, such as hypertension, gastrointestinal issues, weight loss and hand-foot syndrome**
- **Approaches to encourage adequate nutrition among patients receiving the combination of lenvatinib and pembrolizumab**
- **Initial dosing and dose-modification strategies for pembrolizumab/lenvatinib for EC; available data exploring the effect of lenvatinib dose reductions on antitumor activity**
- **Strategies to determine the cause of toxicities that could stem from either lenvatinib or pembrolizumab**

RTP
RESEARCH
TO PRACTICE

Jennifer Filipi, MSN, NP

What I tell my patients with EC about to begin treatment with lenvatinib/pembrolizumab

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

Potential Role of Selinexor in the Management of EC

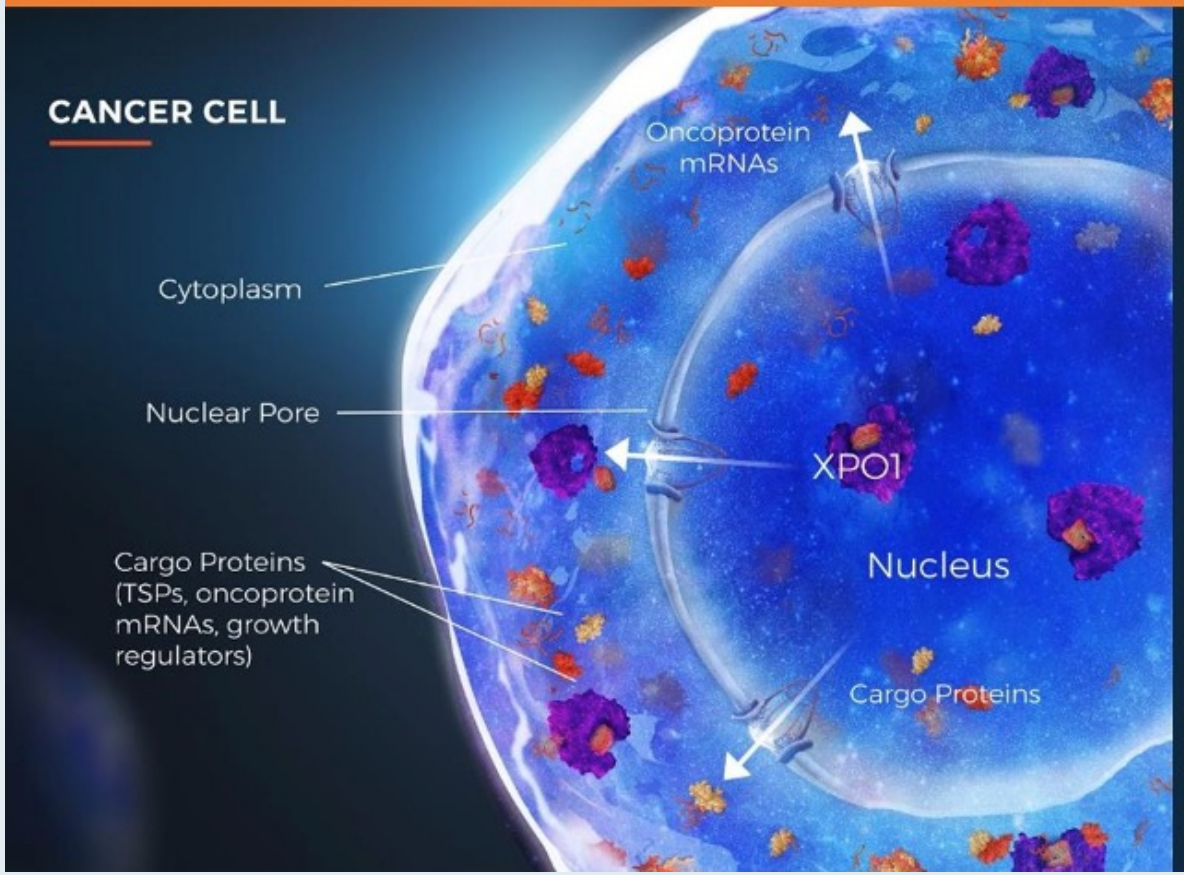
Dr O'Malley
Columbus, Ohio

Dr Westin
Houston, Texas

- **Mechanism of antitumor activity of selinexor and biological rationale for its investigation as maintenance therapy for EC**
- **Progression-free survival advantage documented with selinexor as maintenance therapy after first-line chemotherapy in patients with advanced or recurrent EC in the SIENDO trial; outcomes achieved in the p53 wild-type subgroup**
- **Design, eligibility criteria and key endpoints of the Phase III XPORT-EC-042 trial assessing selinexor maintenance after first-line chemotherapy for p53 wild-type advanced EC**
- **Spectrum, frequency, severity and management of commonly encountered toxicities with selinexor for EC; lessons learned from the multiple myeloma experience**

RTP
RESEARCH
TO PRACTICE

Mechanism of Action of Selinexor



Selinexor is an oral selective inhibitor of XPO1-mediated nuclear export (SINE) compound

- XPO1 exports the major tumor suppressor proteins (TSPs) including p53 away from the nucleus, where TSPs carry out their function
- Tumor cells overexpress XPO1
- Tumor cells inactivate cytoplasmic *p53* through protein degradation
- Selinexor inhibits XPO1 nuclear export, leads to retention / reactivation of TSPs in the nucleus and stabilization of p53
- Retention of wild-type *p53* (p53wt) and other TSPs in the cell nucleus leads to selective killing of cancer cells, while largely sparing normal cells

Makker V et al. ASCO 2022;Abstract 5511.

Selinexor

Mechanism of action

- Inhibitor of the nuclear exporter XPO1

Indication

- Investigational in endometrial cancer

Key clinical trial

- Phase III SIENDO trial evaluating selinexor as front-line maintenance therapy in advanced or recurrent endometrial cancer

Vergote I et al. *J Clin Oncol* 2023;41(35):5400-10.

Kathryn M Lyle, MSN, WHNP-BC, AGNP-C

What I tell my patients with EC who are being considered for or are about to enroll on a clinical trial with selinexor

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

Module 1: Incidence and Biology of Endometrial Cancer (EC)

Module 2: Use of Immune Checkpoint Inhibitors as Monotherapy for EC

Module 3: First-Line Therapy for Primary Advanced or Recurrent EC

Module 4: Lenvatinib/Pembrolizumab in the Management of Metastatic EC

Module 5: Potential Role of Selinexor in the Management of EC

Module 6: Incidence and Management of HER2-Positive EC

Incidence and Management of HER2-Positive EC

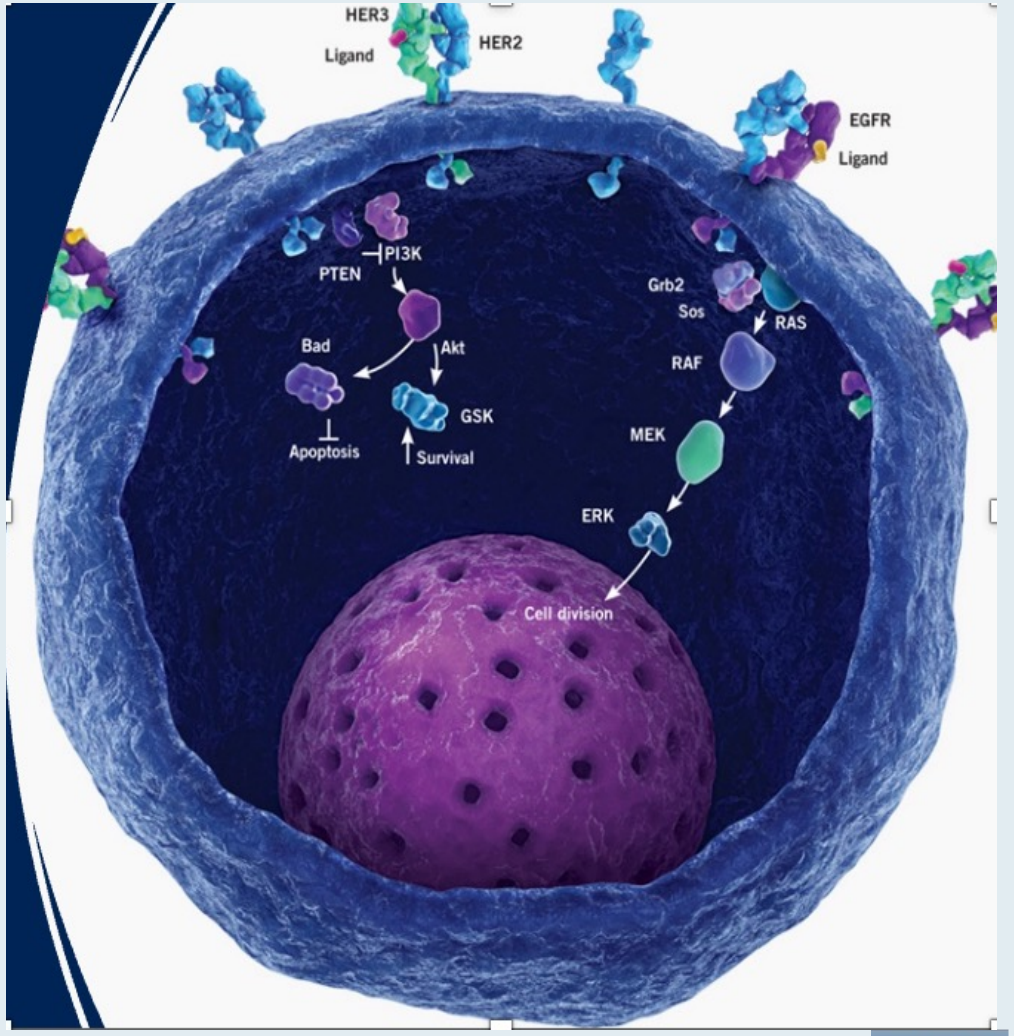
Dr O'Malley
Columbus, Ohio

Dr Westin
Houston, Texas

- **Frequency of HER2 expression in advanced EC; optimal timing of and approach to testing**
- **Published clinical research studies supporting the use of trastuzumab as a component of therapy for HER2-positive uterine serous carcinoma and carcinosarcoma**
- **Efficacy and safety outcomes achieved with T-DXd among patients with advanced EC in the DESTINY-PanTumor02 study**
- **Potential implications of DESTINY-PanTumor02 for biomarker evaluation and clinical management for advanced EC**

HER2/neu in Endometrial Cancer

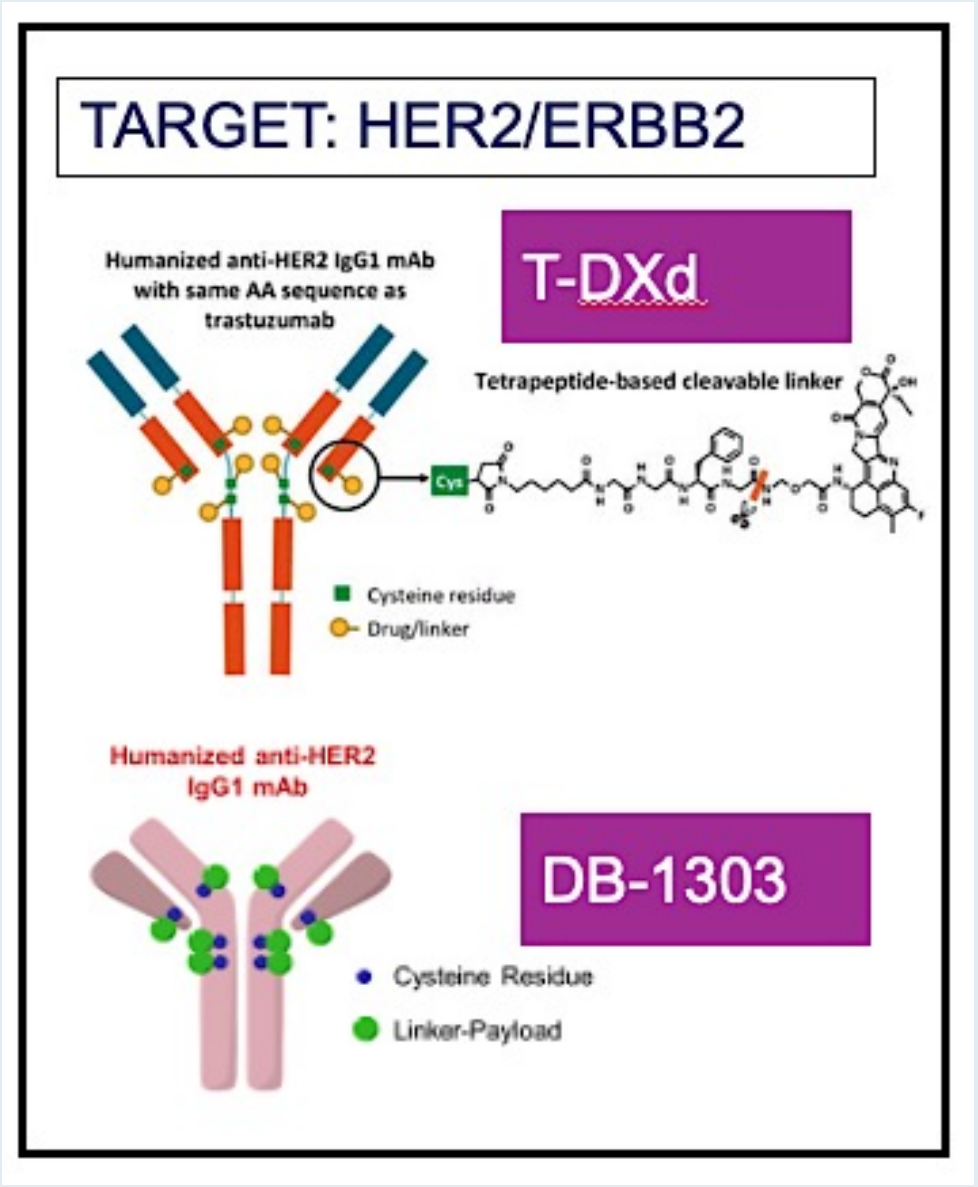
- *Her2/neu* overexpression by IHC demonstrated in 14-60% of USC. Estimates vary widely due to lack of standardized algorithms for interpretation and scoring of Her2 immunostains in endometrial cancer
- Dysregulation of *Her2/neu oncogene* reported in 27% of USC in Whole Exome Sequencing (WES) studies performed by TCGA network (Levine DA , Nature 2013)
- HER2/neu functions as preferred partner for heterodimerisation with any of the other members of the EGF receptor family (HER1, HER3 and HER4) and responsible for regulating cell growth and differentiation



USC = uterine serous carcinoma

Courtesy of Matthew A Powell, MD.

Trastuzumab Deruxtecan



Courtesy of Matthew A Powell, MD.

Trastuzumab Deruxtecan

Mechanism of action

- **Antibody-drug conjugate directed against HER2**

Indication

- **Unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options**

Key clinical trial

- **Phase II DESTINY-PanTumor02 trial evaluating trastuzumab deruxtecan in patients with HER2-expressing solid tumors**

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

Jennifer Filipi, MSN, NP

What I tell my patients with EC about being tested for HER2 and potentially enrolling on a trial of trastuzumab deruxtecan

RTP
RESEARCH
TO PRACTICE

APPENDIX

Use of Immune Checkpoint Inhibitors as Monotherapy for EC

2023;29(22):4564-74

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Safety, Efficacy, and Biomarker Analyses of Dostarlimab in Patients with Endometrial Cancer: Interim Results of the Phase I GARNET Study

Ana Oaknin[1], Bhavana Pothuri[2], Lucy Gilbert[3], Renaud Sabatier[4], Jubilee Brown[5], Sharad Ghamande[6], Cara Mathews[7], David M. O'Malley[8], Rebecca Kristeleit[9], Valentina Boni[10], Adriano Gravina[11], Susana Banerjee[12], Rowan Miller[13], Joanna Pikiel[14], Mansoor R. Mirza[15], Ninad Dewal[16], Grace Antony[17], Yuping Dong[16], Eleftherios Zografos[18], Jennifer Veneris[16], and Anna V. Tinker[19]

GARNET: Phase I Study of Dostarlimab for Advanced EC

dMMR/MSI-H EC	dMMR (*N* = 141)	dMMR/MSI-H (*N* = 143)
Median follow-up, months	27.6	
ORR, *n*, % (95% CI)	64, 45.4% (37.0–54.0)	65, 45.5% (37.1–54.0)
Best confirmed response, *n* (%)		
CR	22 (15.6)	23 (16.1)
PR	42 (29.8)	42 (29.4)
SD	21 (14.9)	21 (14.7)
PD	51 (36.2)	51 (35.7)
NE	5 (3.5)	6 (4.2)
DCR, *n* (%)	85 (60.3)	86 (60.1)
Median DOR (95% CI), months	NR (38.9–NR)	NR (38.9–NR)
Duration ≥12 months, *n* (%)	51 (79.7)	52 (80.0)
Duration ≥24 months, *n* (%)	28 (43.8)	29 (44.6)
Probability of maintaining response (95% CI)		
At 12 months	93.1 (82.7–97.4)	93.3 (83.0–97.4)
At 24 months	83.4 (70.3–91.0)	83.7 (70.8–91.2)

MMRp/MSS EC	MMRp (*N* = 142)	MMRp/MSS (*N* = 156)
Median follow-up, months	33.0	
ORR, *n*, % (95% CI)	21, 14.8% (9.4–21.7)	24, 15.4% (10.1–22.0)
Best confirmed response, *n* (%)		
CR	4 (2.8)	4 (2.6)
PR	17 (12.0)	20 (12.8)
SD	28 (19.7)	29 (18.6)
PD	80 (56.3)	88 (56.4)
NE	13 (9.1)	15 (9.6)
DCR, *n* (%)	49 (34.5)	53 (34.0)
Median DOR (95% CI), months	19.4 (7.3–38.1)	19.4 (8.2–NR)
Duration ≥12 months, *n* (%)	10 (47.6)	12 (50.0)
Duration ≥24 months, *n* (%)	6 (28.6)	8 (33.3)
Probability of maintaining response (95% CI)		
At 12 months	59.2 (34.7–77.2)	60.3 (37.5–77.0)
At 24 months	40.0 (17.7–61.5)	44.2 (22.7–63.8)

Oaknin A et al. *Clin Cancer Res* 2023;29(22):4564-74.

RTP RESEARCH TO PRACTICE

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study

M. Maio[1*], P. A. Ascierto[2], L. Manzyuk[3], D. Motola-Kuba[4], N. Penel[5], P. A. Cassier[6], G. M. Bariani[7], A. De Jesus Acosta[8], T. Doi[9], F. Longo[10], W. H. Miller, Jr[11,12], D.-Y. Oh[13,14,15], M. Gottfried[16], L. Xu[17], F. Jin[17], K. Norwood[17] & A. Marabelle[18]

Ann Oncol 2022;33(9):929-38

KEYNOTE-158 Cohort K: Objective Responses with Pembrolizumab in the Efficacy Analysis Population

Response	*N* = 321
ORR, % (95% CI)	30.8 (25.8-36.2)
Best objective response, *n* (%)	
CR	27 (8.4)
PR	72 (22.4)
SD	61 (19.0)
PD	131 (40.8)
Not evaluable	3 (0.9)
No assessment[b]	27 (8.4)
Time to response, median (range), months	2.1 (1.3-12.9)
DOR, median (range), months	47.5 (2.1+ to 51.1+)
Kaplan–Meier estimate of patients with extended response duration, %	
≥1 year	88.0
≥2 years	74.1
≥3 years	70.1

Maio M et al. *Ann Oncol* 2022;33(9):929-38.

First-Line Therapy for Primary Advanced or Recurrent EC

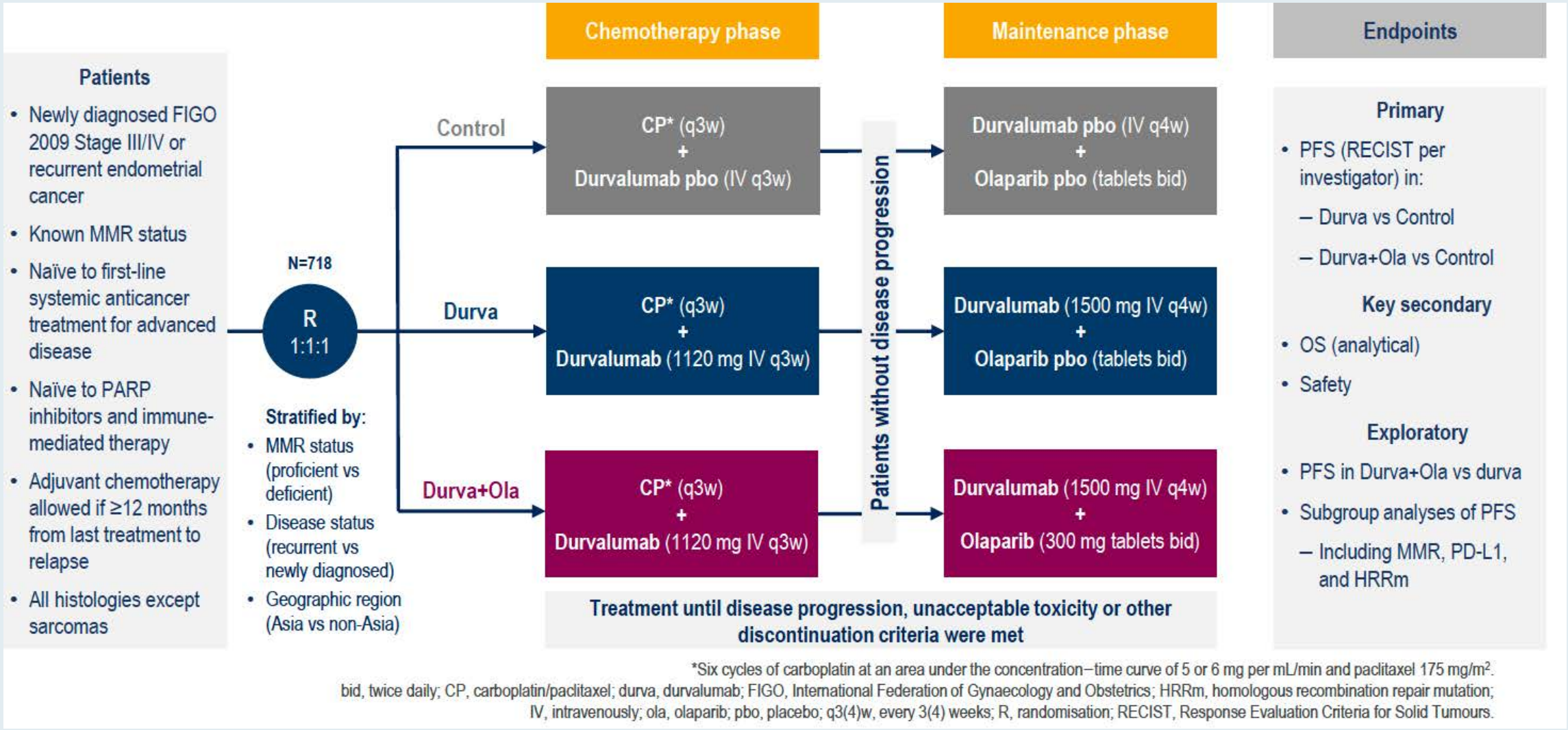
Original Reports | Gynecologic Cancer

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

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

J Clin Oncol 2024;42(3):283-99

DUO-E Study Design

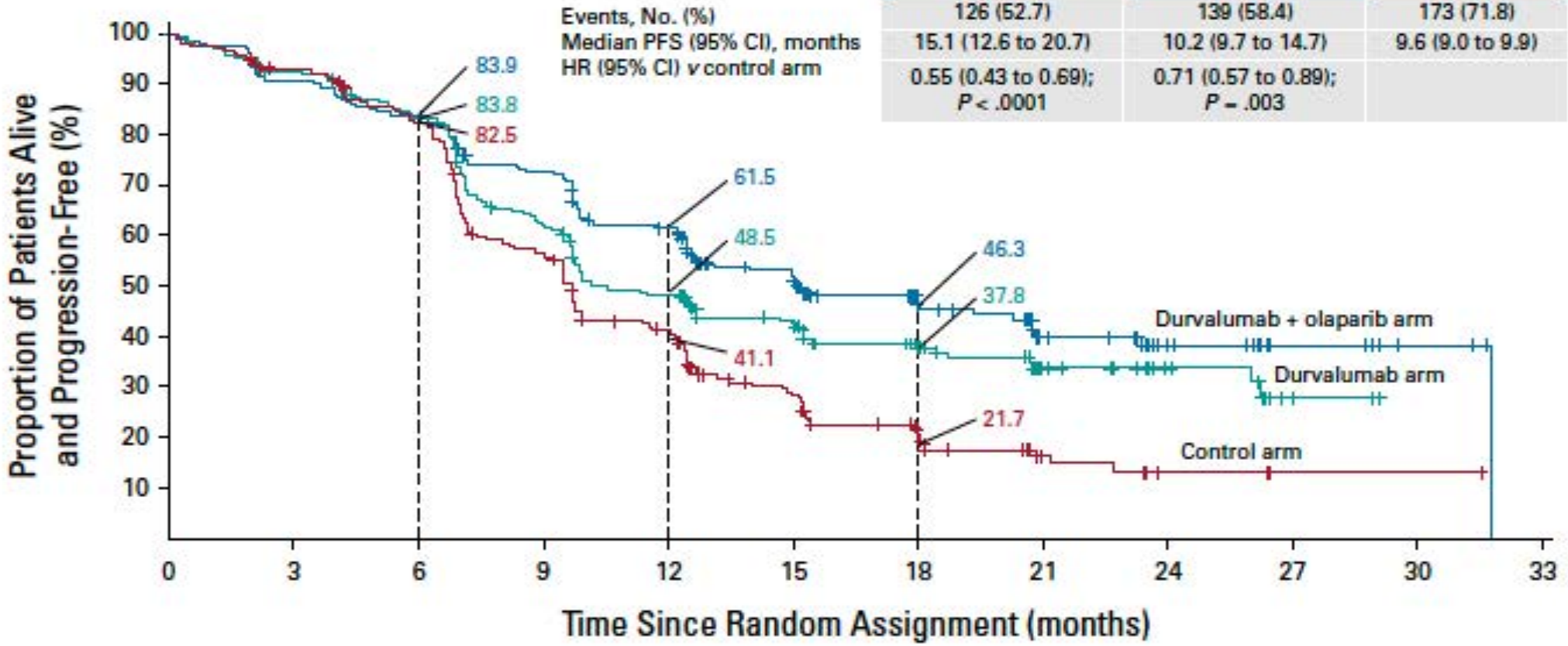


*Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg per mL/min and paclitaxel 175 mg/m².
bid, twice daily; CP, carboplatin/paclitaxel; durva, durvalumab; FIGO, International Federation of Gynaecology and Obstetrics; HRRm, homologous recombination repair mutation; IV, intravenously; ola, olaparib; pbo, placebo; q3(4)w, every 3(4) weeks; R, randomisation; RECIST, Response Evaluation Criteria for Solid Tumours.

Westin SN et al. ESMO 2023;Abstract LBA41.

DUO-E: Progression-Free Survival (PFS) in the Intent-to-Treat Population

	Durvalumab + Olaparib Arm (n = 239)	Durvalumab Arm (n = 238)	Control Arm (n = 241)
Events, No. (%)	126 (52.7)	139 (58.4)	173 (71.8)
Median PFS (95% CI), months	15.1 (12.6 to 20.7)	10.2 (9.7 to 14.7)	9.6 (9.0 to 9.9)
HR (95% CI) *v* control arm	0.55 (0.43 to 0.69); *P* < .0001	0.71 (0.57 to 0.89); *P* = .003	

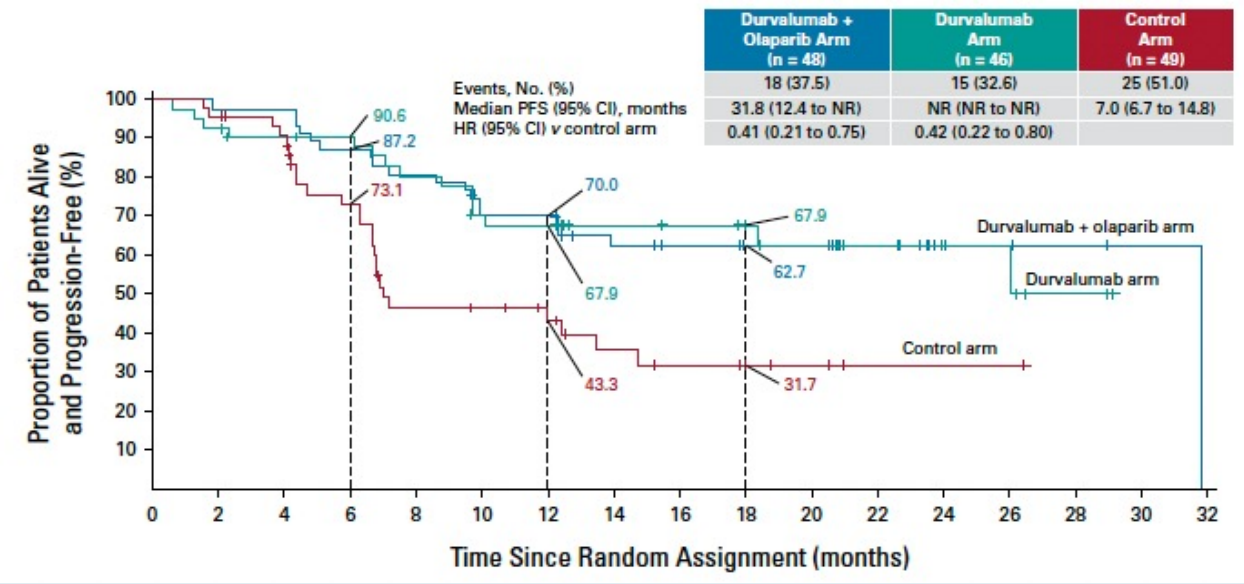


Westin SN et al. *J Clin Oncol* 2024;42(3):283-99.

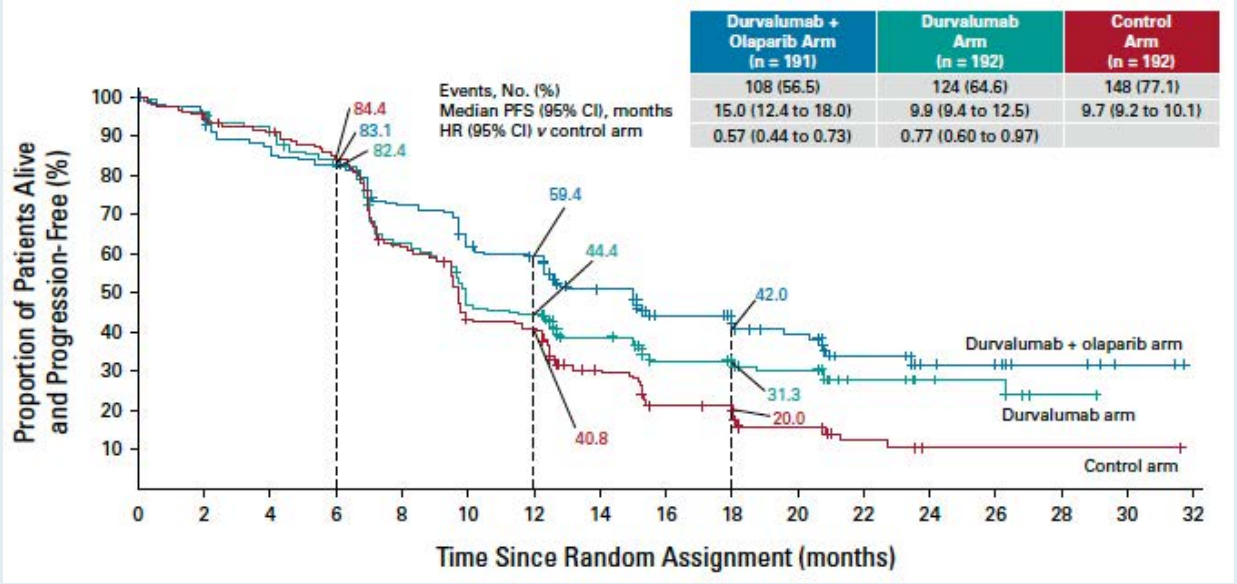
RTP RESEARCH TO PRACTICE

DUO-E: PFS in dMMR and pMMR Populations

dMMR



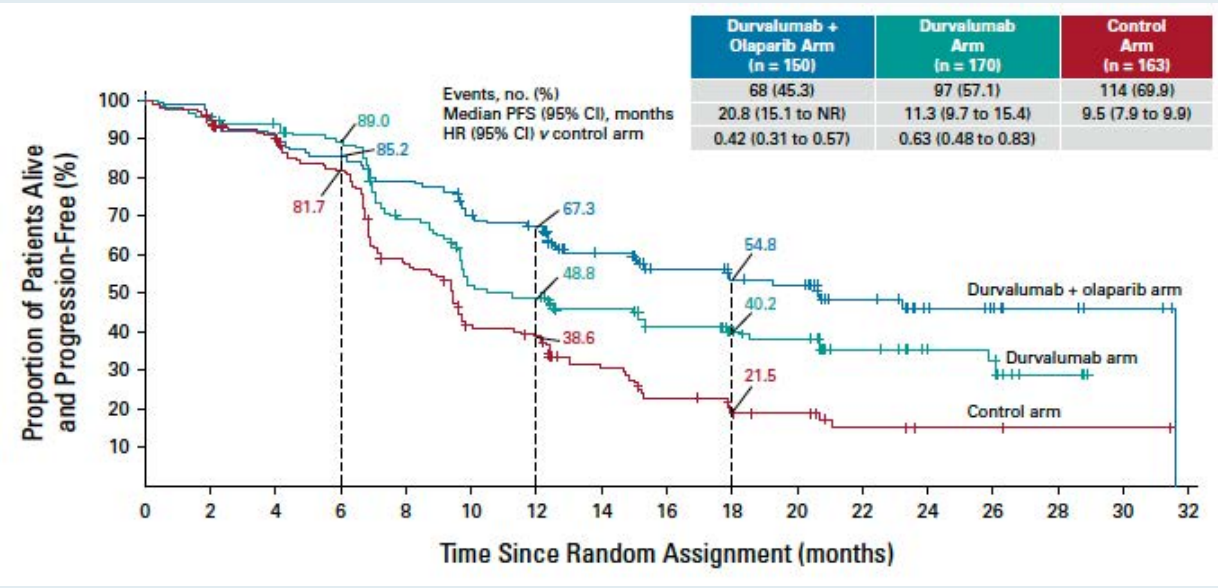
pMMR



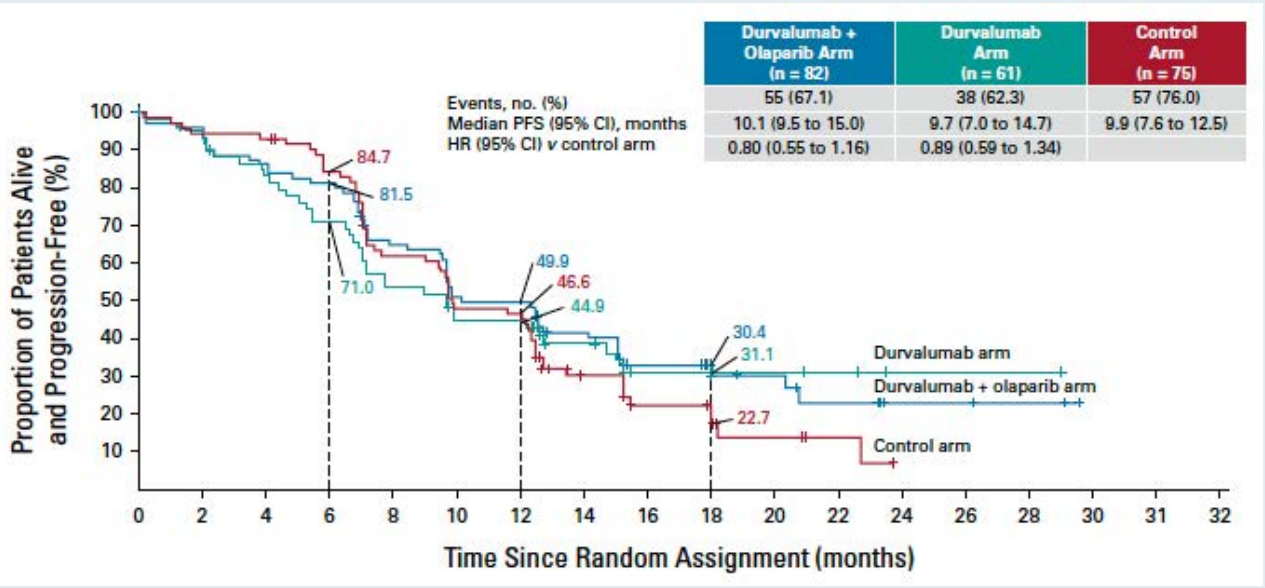
Westin SN et al. *J Clin Oncol* 2024;42(3):283-99.

DUO-E: PFS in PD-L1-Positive and PD-L1-Negative Populations

PD-L1-Positive



PD-L1-Negative



Westin SN et al. *J Clin Oncol* 2024;42(3):283-99.

RTP RESEARCH TO PRACTICE

DUO-E: Safety Summary

AEs, n (%)	Overall (chemotherapy + maintenance phase)			Maintenance phase only		
	Control (N=236)	Durva (N=235)	Durva+Ola (N=238)	Control (N=169)	Durva (N=183)	Durva+Ola (N=192)
Any AEs	236 (100.0)	232 (98.7)	237 (99.6)	143 (84.6)	158 (86.3)	184 (95.8)
Grade ≥3 AEs	133 (56.4)	129 (54.9)	160 (67.2)	28 (16.6)	30 (16.4)	79 (41.1)
Serious AEs	73 (30.9)	73 (31.1)	85 (35.7)	19 (11.2)	22 (12.0)	42 (21.9)
AEs with outcome of death	8 (3.4)	4 (1.7)	5 (2.1)	2 (1.2)	0	3 (1.6)
AEs of special interest to olaparib						
MDS/AML*	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New primary malignancies*	3 (1.3)	1 (0.4)§	2 (0.8)	2 (1.2)	1 (0.5)§	1 (0.5)
Pneumonitis†	1 (0.4)	4 (1.7)	12 (5.0)	0	3 (1.6)	8 (4.2)
Any immune-mediated AEs‡	16 (6.8)	66 (28.1)	56 (23.5)	6 (3.6)	27 (14.8)	27 (14.1)
AEs leading to discontinuation of study treatment	44 (18.6)	49 (20.9)	58 (24.4)	7 (4.1)	11 (6.0)	27 (14.1)
AEs leading to discontinuation of carboplatin/paclitaxel	32 (13.6)	31 (13.2)	31 (13.0)	–	–	–
AEs leading to discontinuation of durvalumab/placebo	19 (8.1)	26 (11.1)	22 (9.2)	4 (2.4)	9 (4.9)	16 (8.3)
AEs leading to discontinuation of olaparib/placebo	5 (2.1)	11 (4.7)	21 (8.8)	5 (3.0)	10 (5.5)	21 (10.9)
AEs leading to dose interruption/delay of study treatment‖	118 (50.0)	128 (54.5)	164 (68.9)	37 (21.9)	52 (28.4)	113 (58.9)
AEs leading to dose reduction of olaparib/placebo	5 (2.1)	14 (6.0)	65 (27.3)	4 (2.4)	13 (7.1)	63 (32.8)

Includes AEs with onset or worsening on or after the date of first dose of durvalumab/placebo or olaparib/placebo (overall) or first dose of olaparib/placebo (maintenance phase) until initiation of the first subsequent anticancer therapy following last dose of study treatment or until the end of the safety follow-up period, whichever occurs first. AEs were graded using National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.0).

*MDS/AML and new primary malignancies include AEs from first dose of investigational product (durvalumab/olaparib/placebo) until the end of the study (includes cases reported beyond the safety follow-up period); †Grouped term: includes pneumonitis, bronchiolitis, and interstitial lung disease; ‡As assessed by the investigator, and programmatically derived from individual causality assessments for combination studies. Missing responses are counted as related; § Excludes one event of basal cell carcinoma; ‖For durvalumab/placebo, this includes dose interruption during infusion as well as doses that were skipped or delayed. AE, adverse event; AML, acute myeloid leukaemia; MDS, myelodysplastic syndrome.

MADRID 2023 ESMO congress

Courtesy of Shannon Westin, MD, MPH.

Westin SN et al. ESMO 2023;Abstract LBA41.

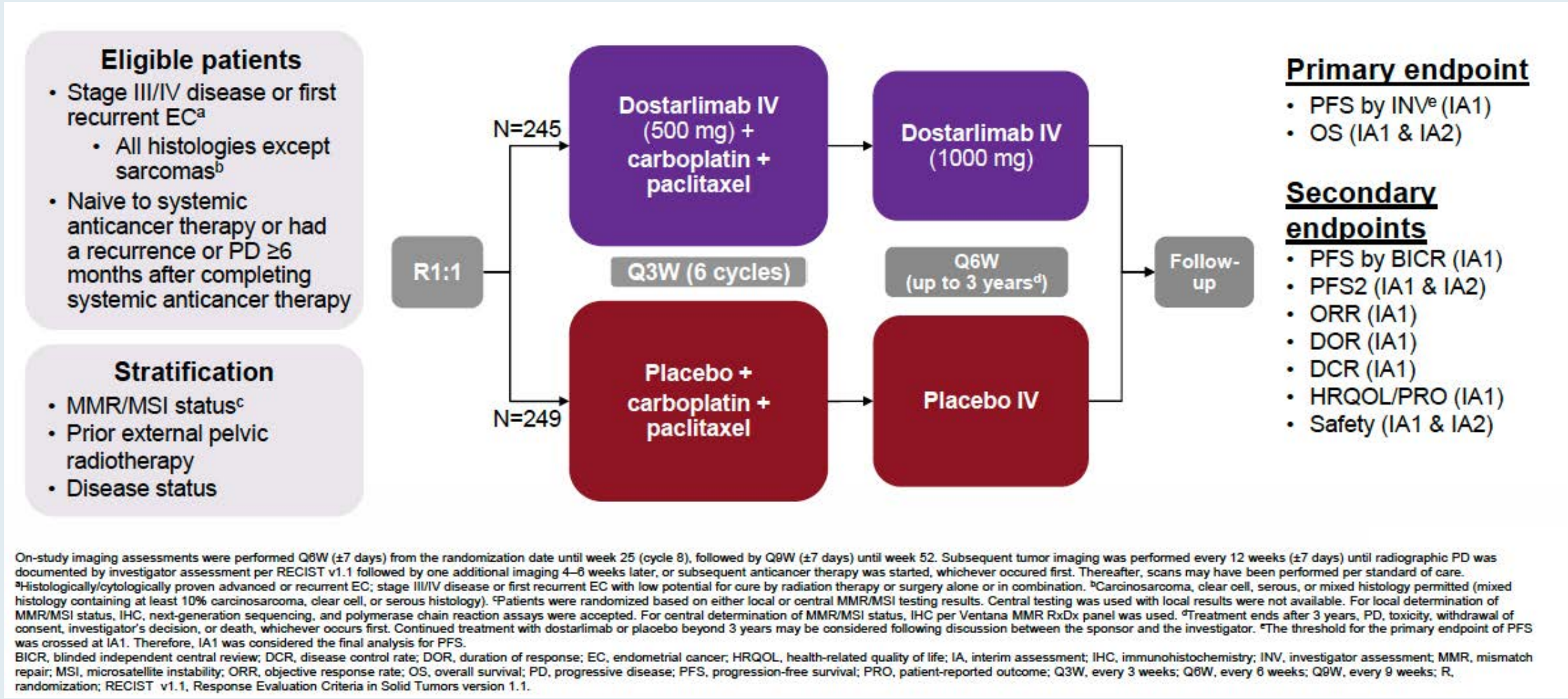
RTP RESEARCH TO PRACTICE

Overall survival in patients with primary advanced or recurrent endometrial cancer treated with dostarlimab plus chemotherapy in Part 1 of the ENGOT-EN6-NSGO/GOG-3031/RUBY trial

Matthew A. Powell,[1] Annika Auranen,[2] Lyndsay Willmott,[3] Lucy Gilbert,[4] Destin Black,[5] David Cibula,[6] Sudarshan Sharma,[7] Giorgio Valabrega,[8] Lisa M. Landrum,[9] Lars C. Hanker,[10] Ashley Stuckey,[11] Ingrid Boere,[12] Michael A. Gold,[13] Mark S. Shahin,[14] Bhavana Pothuri,[15] Brian Slomovitz,[16] Matt Grimshaw,[17] Shadi Stevens,[17] Robert L. Coleman,[18] Mansoor Raza Mirza[19]

SGO 2024 Late-Breaking Abstract

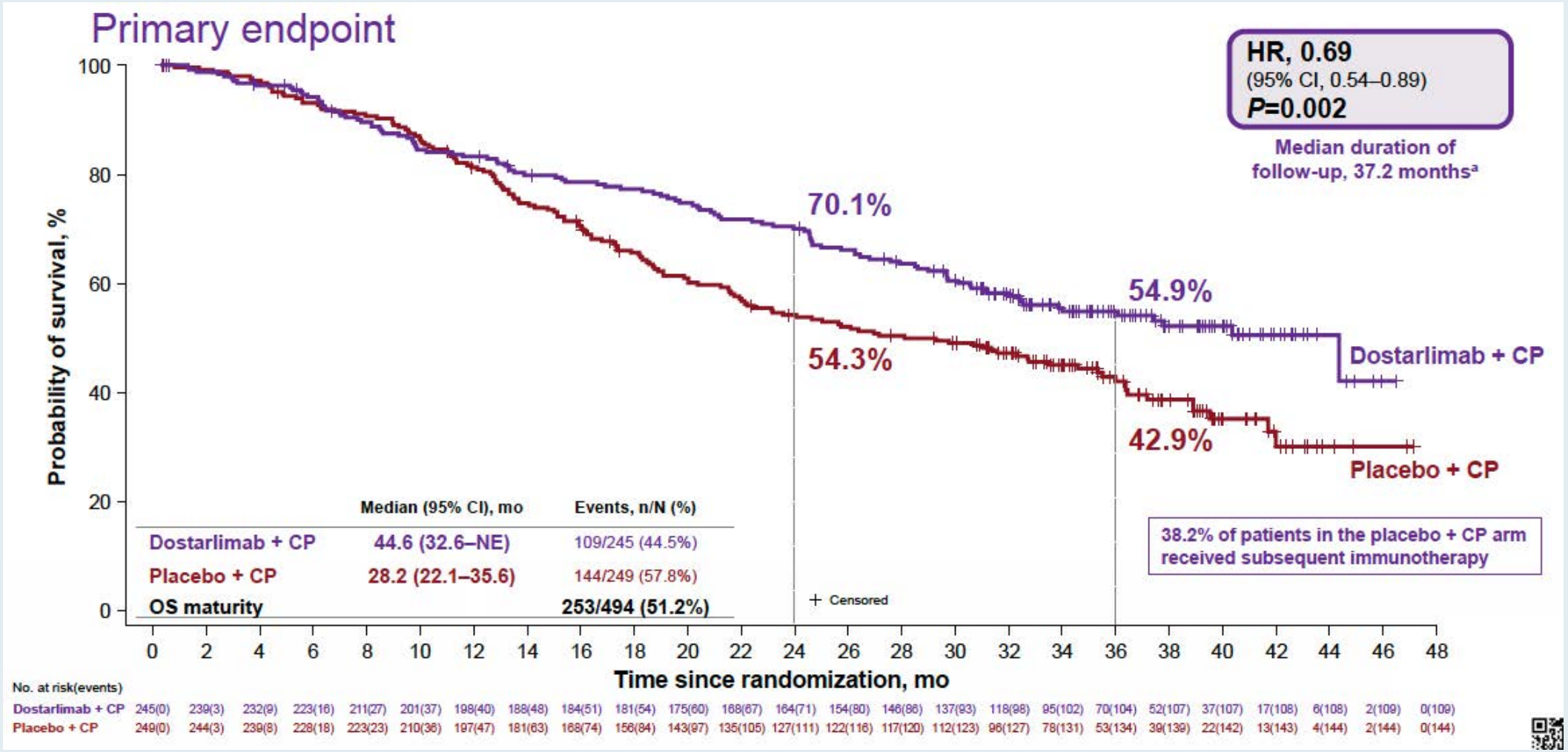
RUBY Part 1: Trial Schema



On-study imaging assessments were performed Q6W (±7 days) from the randomization date until week 25 (cycle 8), followed by Q9W (±7 days) until week 52. Subsequent tumor imaging was performed every 12 weeks (±7 days) until radiographic PD was documented by investigator assessment per RECIST v1.1 followed by one additional imaging 4–6 weeks later, or subsequent anticancer therapy was started, whichever occured first. Thereafter, scans may have been performed per standard of care.
[a]Histologically/cytologically proven advanced or recurrent EC; stage III/IV disease or first recurrent EC with low potential for cure by radiation therapy or surgery alone or in combination. [b]Carcinosarcoma, clear cell, serous, or mixed histology permitted (mixed histology containing at least 10% carcinosarcoma, clear cell, or serous histology). [c]Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used with local results were not available. For local determination of MMR/MSI status, IHC, next-generation sequencing, and polymerase chain reaction assays were accepted. For central determination of MMR/MSI status, IHC per Ventana MMR RxDx panel was used. [d]Treatment ends after 3 years, PD, toxicity, withdrawal of consent, investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered following discussion between the sponsor and the investigator. [e]The threshold for the primary endpoint of PFS was crossed at IA1. Therefore, IA1 was considered the final analysis for PFS.
BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response; EC, endometrial cancer; HRQOL, health-related quality of life; IA, interim assessment; IHC, immunohistochemistry; INV, investigator assessment; MMR, mismatch repair; MSI, microsatellite instability; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; Q6W, every 6 weeks; Q9W, every 9 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Powell MA et al. SGO 2024.

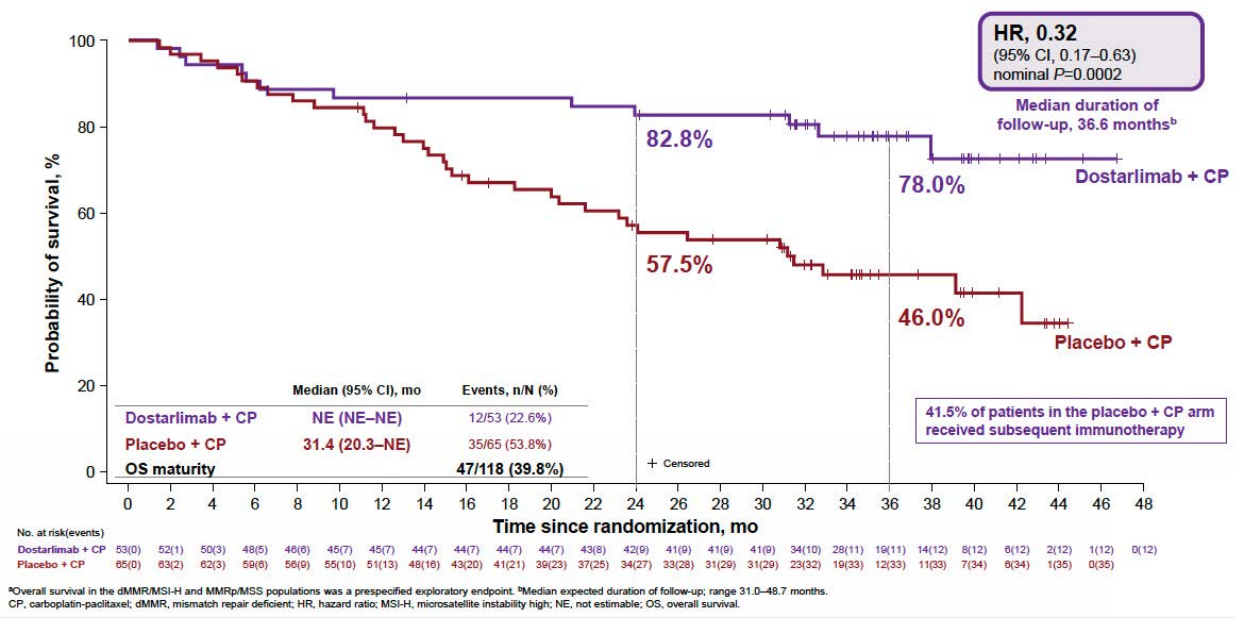
RUBY Part 1: Overall Survival in Intent-to-Treat Population



Powell MA et al. SGO 2024.

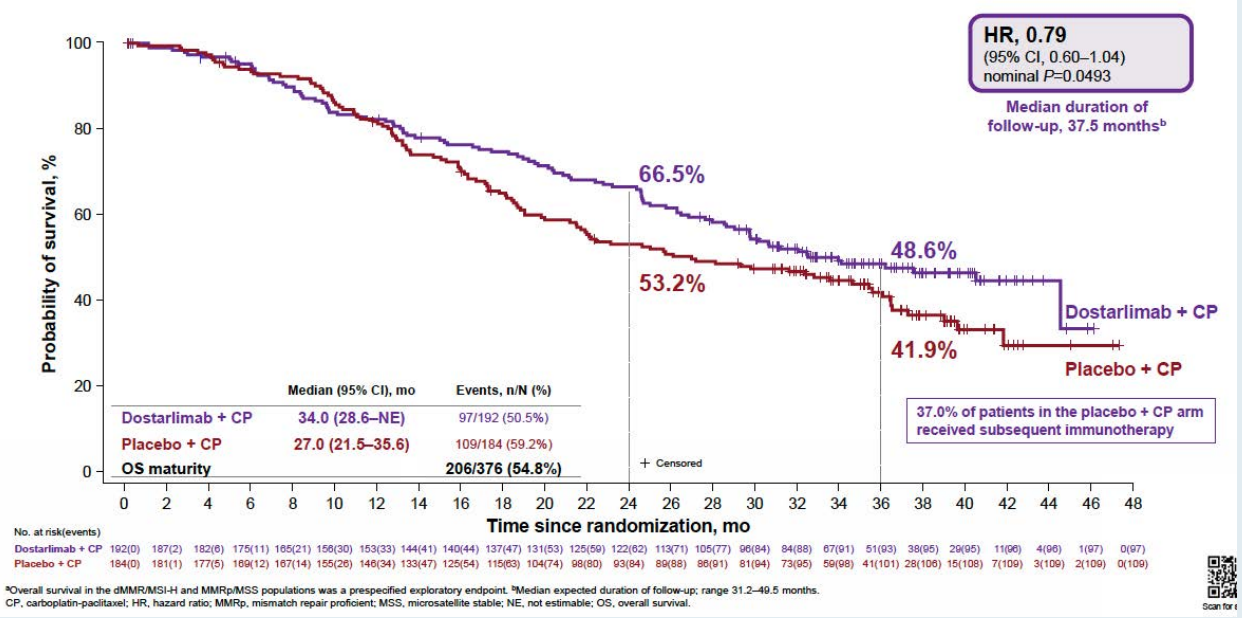
RUBY Part 1: Overall Survival in dMMR/MSI-H and pMMR/MSS Populations

dMMR/MSI-H



[a]Overall survival in the dMMR/MSI-H and MMRp/MSS populations was a prespecified exploratory endpoint. [b]Median expected duration of follow-up; range 31.0–48.7 months.
CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability high; NE, not estimable; OS, overall survival.

pMMR/MSS



[a]Overall survival in the dMMR/MSI-H and MMRp/MSS populations was a prespecified exploratory endpoint. [b]Median expected duration of follow-up; range 31.2–49.5 months.
CP, carboplatin-paclitaxel; HR, hazard ratio; MMRp, mismatch repair proficient; MSS, microsatellite stable; NE, not estimable; OS, overall survival.

Powell MA et al. SGO 2024.

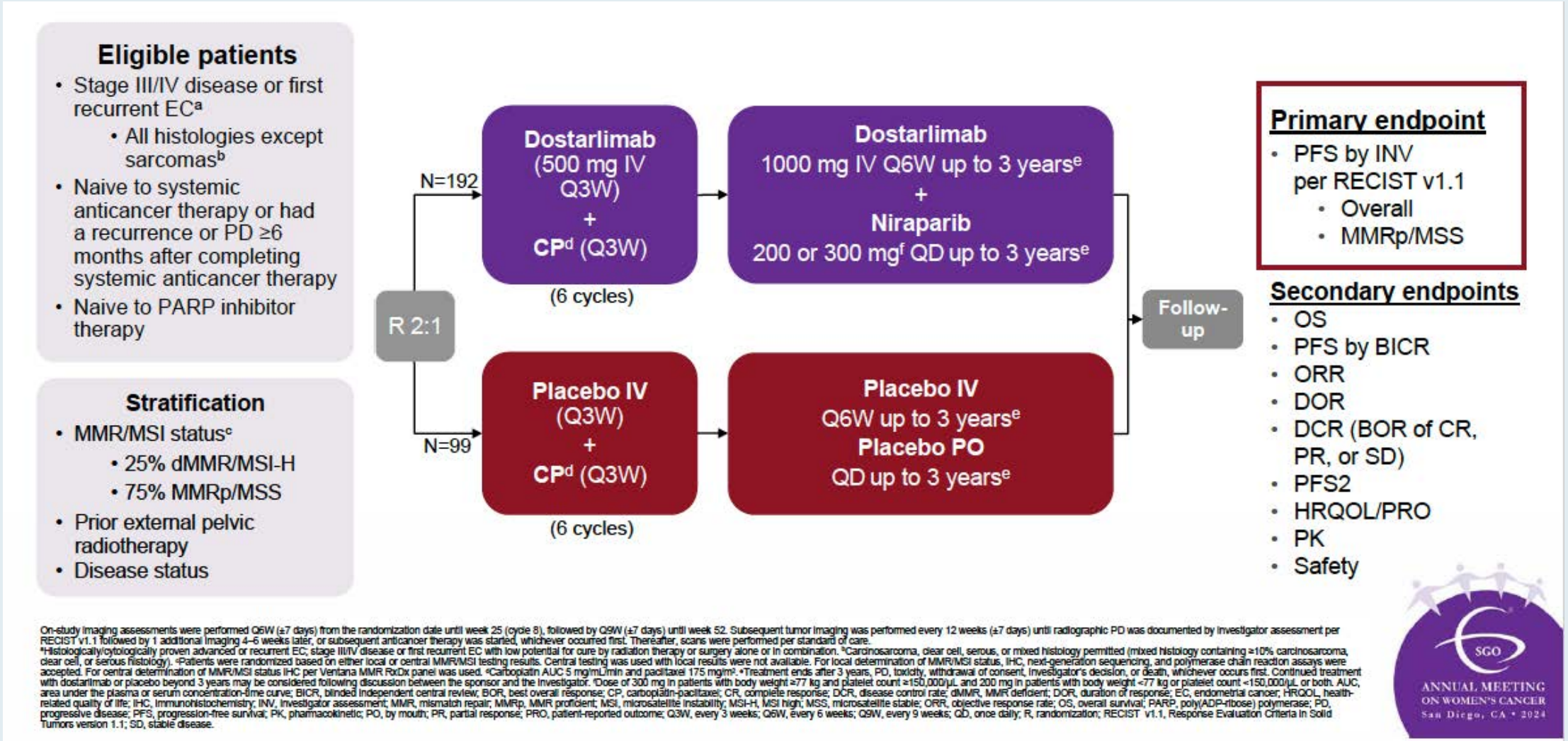
RTP RESEARCH TO PRACTICE

Dostarlimab plus chemotherapy followed by dostarlimab plus niraparib maintenance therapy in patients with primary advanced or recurrent endometrial cancer in Part 2 of the ENGOT-EN6-NSGO/GOG-3031/RUBY trial

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

SGO 2024 Late-Breaking Abstract

RUBY Part 2: Trial Schema



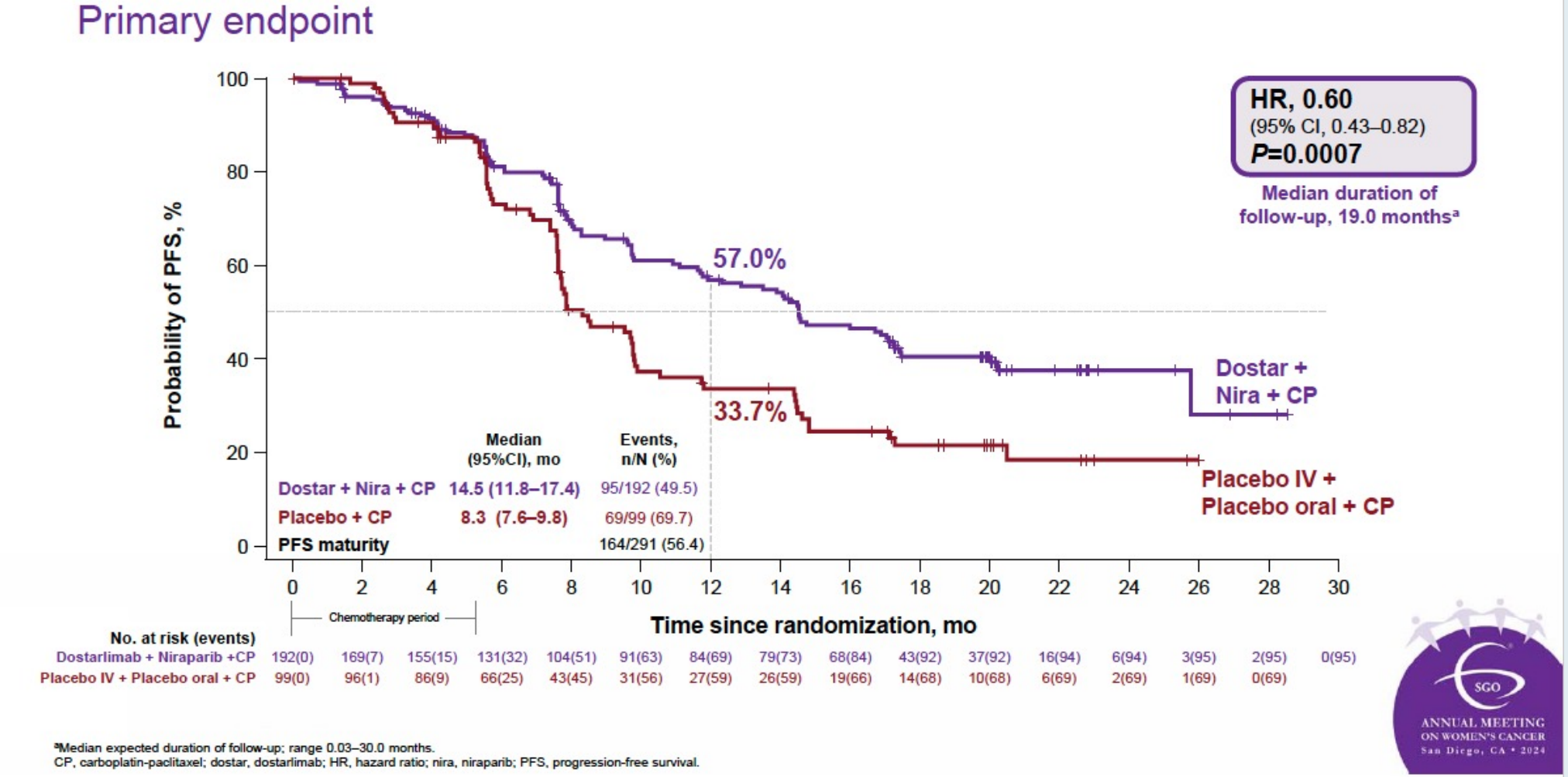
On-study imaging assessments were performed Q6W (±7 days) from the randomization date until week 25 (cycle 8), followed by Q9W (±7 days) until week 52. Subsequent tumor imaging was performed every 12 weeks (±7 days) until radiographic PD was documented by investigator assessment per RECIST v1.1 followed by 1 additional imaging 4–6 weeks later, or subsequent anticancer therapy was started, whichever occurred first. Thereafter, scans were performed per standard of care.
[a]Histologically/cytologically proven advanced or recurrent EC; stage III/IV disease or first recurrent EC with low potential for cure by radiation therapy or surgery alone or in combination. [b]Carcinosarcoma, clear cell, serous, or mixed histology permitted (mixed histology containing ≥10% carcinosarcoma, clear cell, or serous histology). [c]Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used with local results were not available. For local determination of MMR/MSI status, IHC, next-generation sequencing, and polymerase chain reaction assays were accepted. For central determination of MMR/MSI status IHC per Ventana MMR RxDx panel was used. [d]Carboplatin AUC 5 mg/mL/min and paclitaxel 175 mg/m². [e]Treatment ends after 3 years, PD, toxicity, withdrawal of consent, investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered following discussion between the sponsor and the investigator. [f]Dose of 300 mg in patients with body weight ≥77 kg and platelet count ≥150,000/µL and 200 mg in patients with body weight <77 kg or platelet count <150,000/µL or both. AUC, area under the plasma or serum concentration-time curve; BICR, blinded independent central review; BOR, best overall response; CP, carboplatin-paclitaxel; CR, complete response; DCR, disease control rate; dMMR, MMR deficient; DOR, duration of response; EC, endometrial cancer; HRQOL, health-related quality of life; IHC, immunohistochemistry; INV, investigator assessment; MMR, mismatch repair; MMRp, MMR proficient; MSI, microsatellite instability; MSI-H, MSI high; MSS, microsatellite stable; ORR, objective response rate; OS, overall survival; PARP, poly(ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetic; PO, by mouth; PR, partial response; PRO, patient-reported outcome; Q3W, every 3 weeks; Q6W, every 6 weeks; Q9W, every 9 weeks; QD, once daily; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

SGO ANNUAL MEETING ON WOMEN'S CANCER San Diego, CA • 2024

Mirza MA et al. SGO 2024.

RTP RESEARCH TO PRACTICE

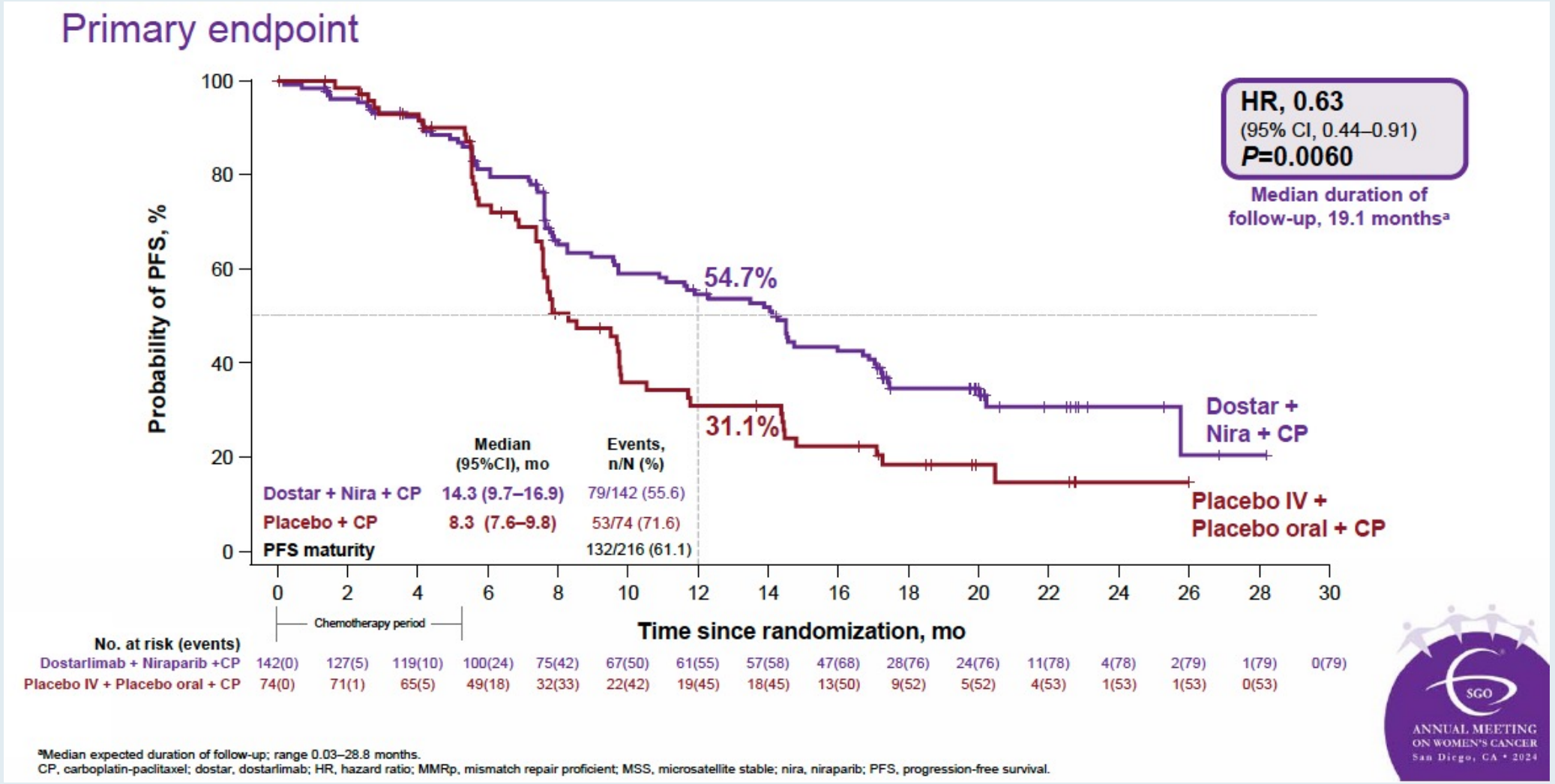
RUBY Part 2: Progression-Free Survival in Overall Population



Mirza MA et al. SGO 2024.

RTP RESEARCH TO PRACTICE

RUBY Part 2: Progression-Free Survival in pMMR/MSS Population



Mirza MA et al. SGO 2024.

RTP RESEARCH TO PRACTICE

Lenvatinib/Pembrolizumab in the Management of Metastatic EC

RTP
RESEARCH
TO PRACTICE

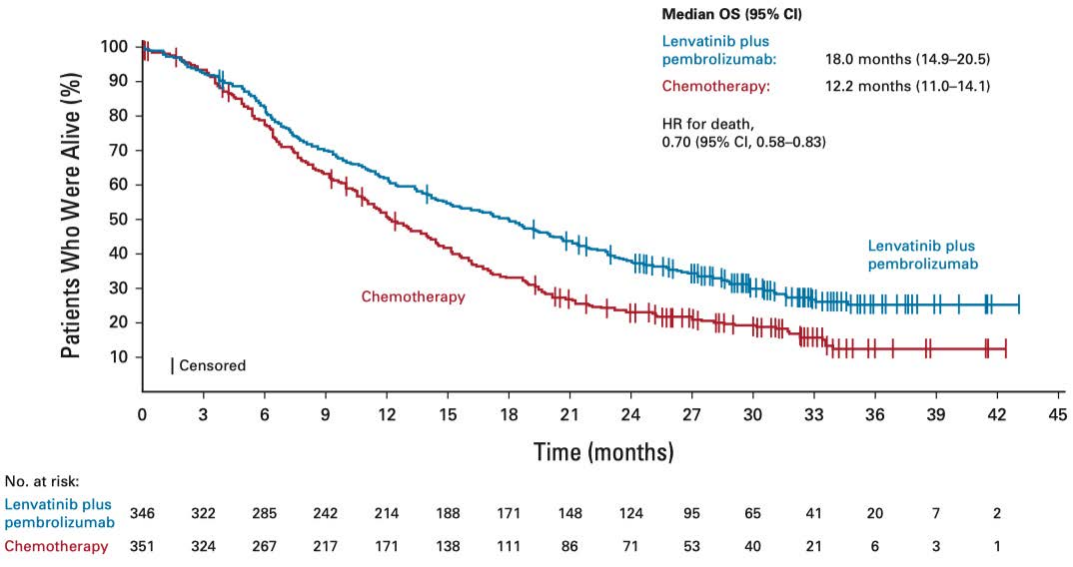
Lenvatinib Plus Pembrolizumab in Previously Treated Advanced Endometrial Cancer: Updated Efficacy and Safety From the Randomized Phase III Study 309/KEYNOTE-775

Vicky Makker, MD[1]; Nicoletta Colombo, MD[2]; Antonio Casado Herráez, MD[3]; Bradley J. Monk, MD[4]; Helen Mackay, MD[5]; Alessandro D. Santin, MD[6]; David S. Miller, MD[7]; Richard G. Moore, MD[8]; Sally Baron-Hay, MBBS[9]; Isabelle Ray-Coquard, MD[10]; Kimio Ushijima, MD[11]; Kan Yonemori, MD[12]; Yong Man Kim, MD[13]; Eva M. Guerra Alia, MD[14]; Ulus A. Sanli, MD[15]; Steven Bird, MS[16]; Robert Orlowski, MD[16]; Jodi McKenzie, PhD[17]; Chinyere Okpara, PhD[18]; Gianmaria Barresi, MD[19]; and Domenica Lorusso, MD[20]

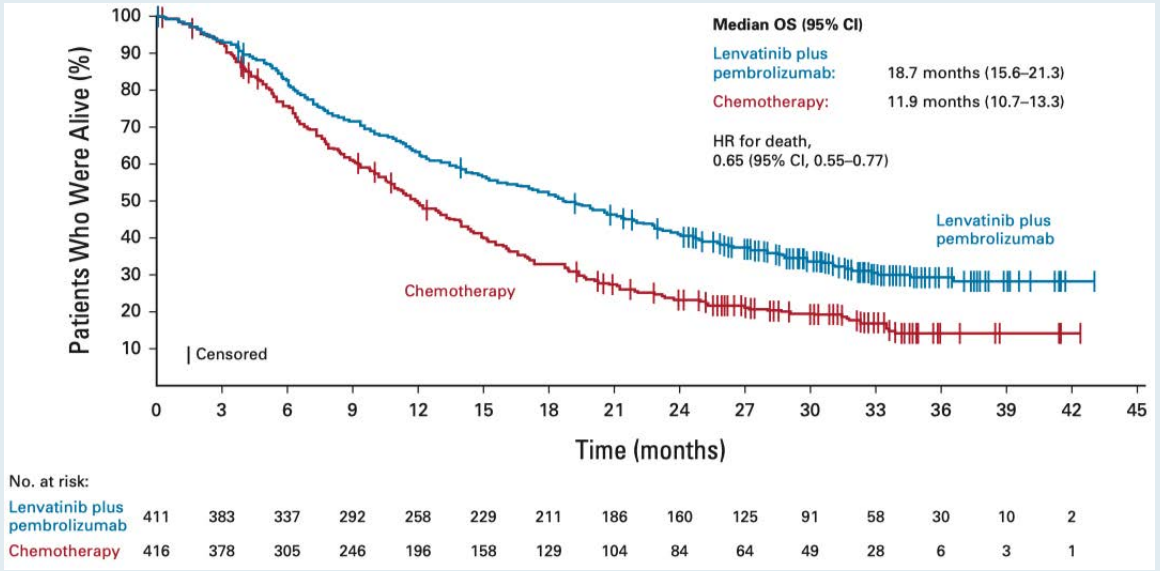
J Clin Oncol 2023;41(16):2904-10

KEYNOTE-775: Overall Survival in pMMR and All-Comer Patient Populations

pMMR population



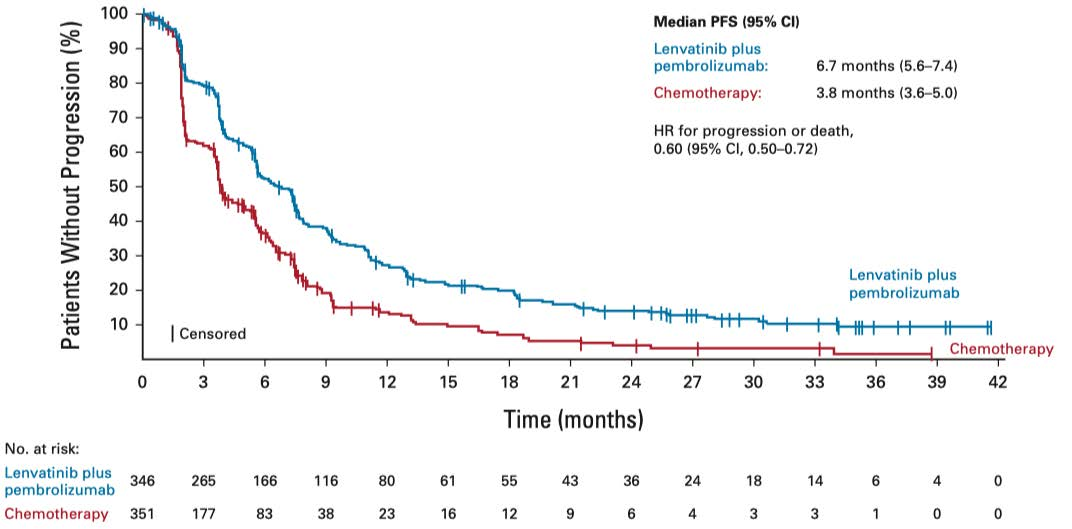
All-Comer population



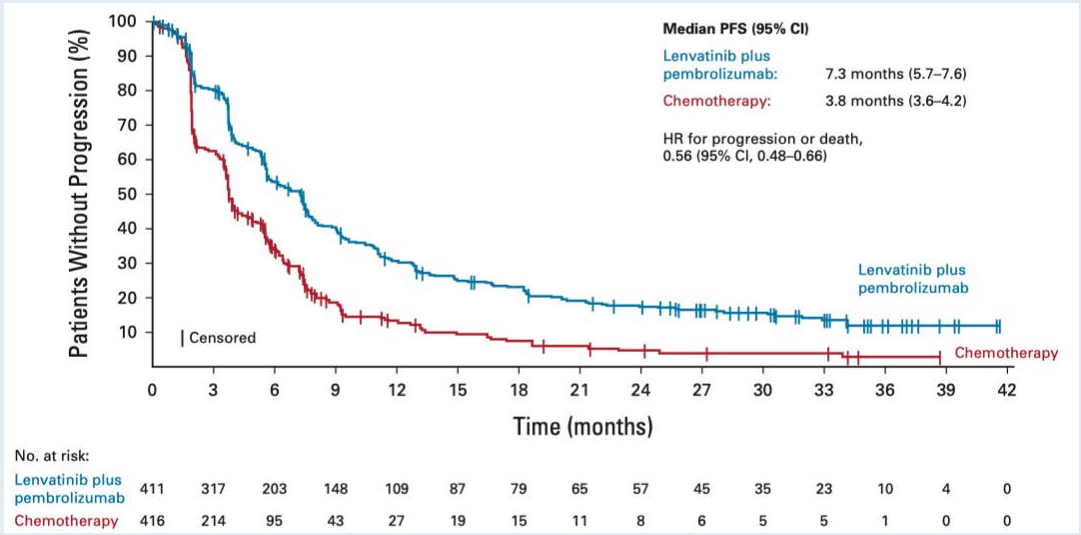
Makker V et al. *J Clin Oncol* 2023;41(16):2904-10.

KEYNOTE-775: Progression-Free Survival in pMMR and All-Comer Patient Populations

pMMR population



All-comer population



Makker V et al. *J Clin Oncol* 2023;41(16):2904-10.

RTP RESEARCH TO PRACTICE

KEYNOTE-775: Treatment-Emergent Adverse Events

	LEN Plus Pembro (n = 406)		Chemotherapy (n = 388)	
Preferred Term[a]	Any Grade	Grade ≥ 3[b]	Any Grade	Grade ≥ 3[b]
TEAEs, No. (%)	405 (99.8)	366 (90.1)	386 (99.5)	286 (73.7)
Hypertension	264 (65.0)	159 (39.2)	20 (5.2)	10 (2.6)
Hypothyroidism	239 (58.9)	6 (1.5)	3 (0.8)	0 (0.0)
Diarrhea	226 (55.7)	33 (8.1)	79 (20.4)	8 (2.1)
Nausea	210 (51.7)	14 (3.4)	180 (46.4)	5 (1.3)
Decreased appetite	189 (46.6)	31 (7.6)	83 (21.4)	2 (0.5)
Vomiting	153 (37.7)	12 (3.0)	82 (21.1)	10 (2.6)
Weight decreased	144 (35.5)	44 (10.8)	23 (5.9)	1 (0.3)
Fatigue	138 (34.0)	22 (5.4)	107 (27.6)	12 (3.1)
Arthralgia	131 (32.3)	7 (1.7)	31 (8.0)	0 (0.0)
Proteinuria	124 (30.5)	21 (5.2)	13 (3.4)	1 (0.3)
Constipation	115 (28.3)	3 (0.7)	95 (24.5)	2 (0.5)
Anemia	114 (28.1)	28 (6.9)	189 (48.7)	60 (15.5)
Urinary tract infection	112 (27.6)	17 (4.2)	40 (10.3)	4 (1.0)
Headache	107 (26.4)	2 (0.5)	35 (9.0)	1 (0.3)
Neutropenia	37 (9.1)	8 (2.0)	132 (34.0)	101 (26.0)
Alopecia	24 (5.9)	0 (0.0)	120 (30.9)	1 (0.3)
Treatment-related TEAEs, No, (%)[c]	395 (97.3)	320 (78.8)	364 (93.8)	233 (60.1)
AEOSIs, No. (%)[d]	279 (68.7)	54 (13.3)	17 (4.4)	1 (0.3)
CSAEs, No. (%)[d]	386 (95.1)	227 (55.9)	149 (38.4)	51 (13.1)

Makker V et al. *J Clin Oncol* 2023;41(16):2904-10.

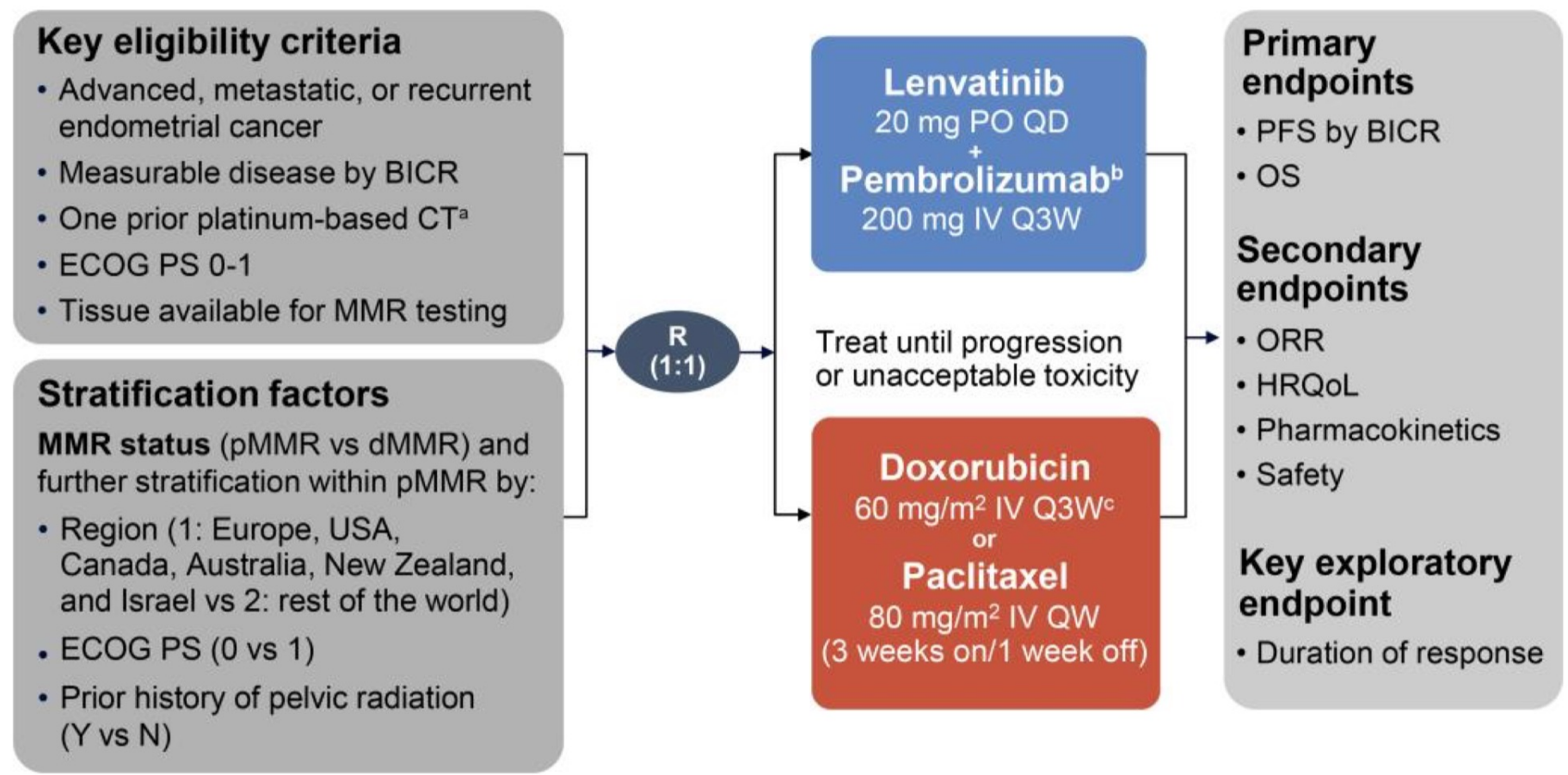
Updated efficacy and safety of lenvatinib plus pembrolizumab versus treatment of physician's choice in patients with advanced endometrial cancer: Study 309/KEYNOTE-775

Vicky Makker[1], Nicoletta Colombo[2], Antonio Casado Herraez[3], Bradley J. Monk[4], Helen Mackay[5], Alessandro D. Santin[6], David S. Miller[7], Richard Moore[8], Sally Baron-Hay[9], Isabelle Ray-Coquard[10], Ronnie Shapira Frommer[11], Kimio Ushijima[12], Kan Yonemori[13], Yong Man Kim[14], Eva M. Guerra Alia[15], Ulus A. Sanli[16], Jie Huang[17], Jodi McKenzie[18], Gianmaria Barresi[19], Domenica Lorusso[20]

PARIS 2022 ESMO congress

Abstract 525MO

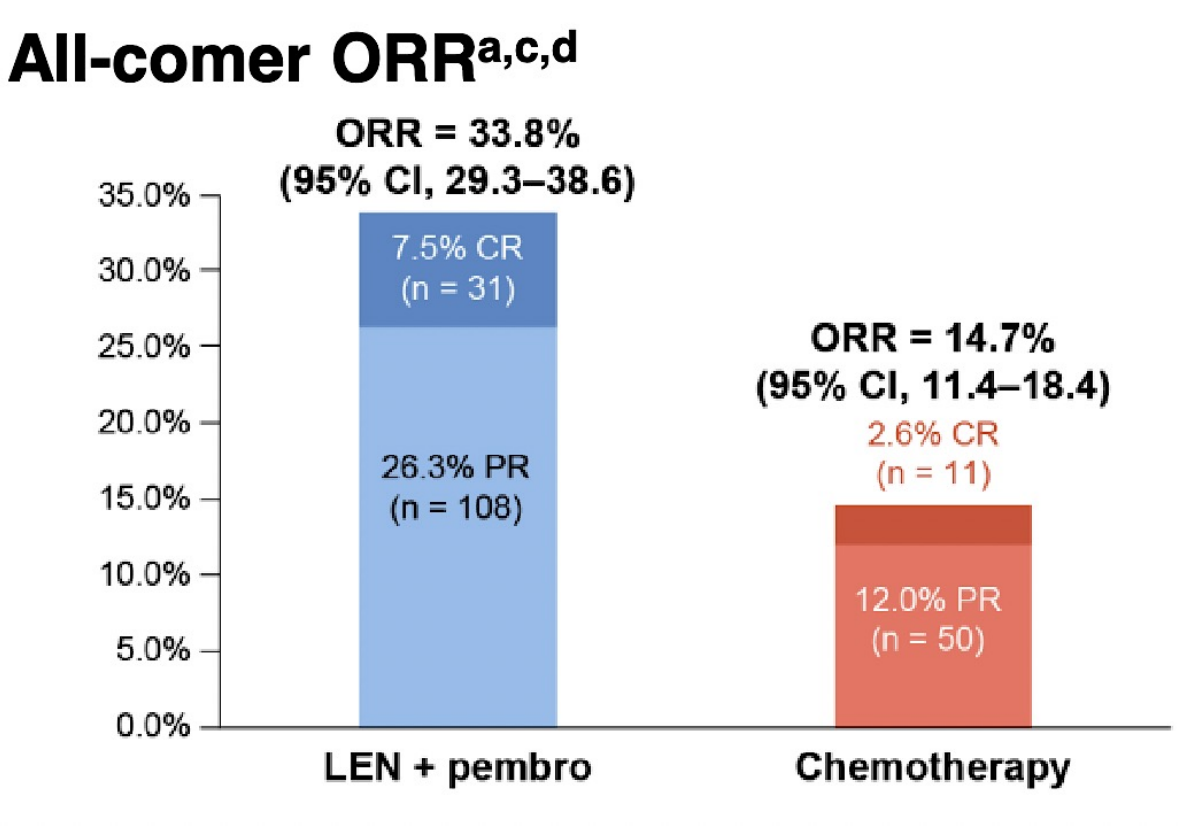
KEYNOTE-775: Lenvatinib and Pembrolizumab for Advanced, Metastatic or Recurrent EC Following Chemotherapy

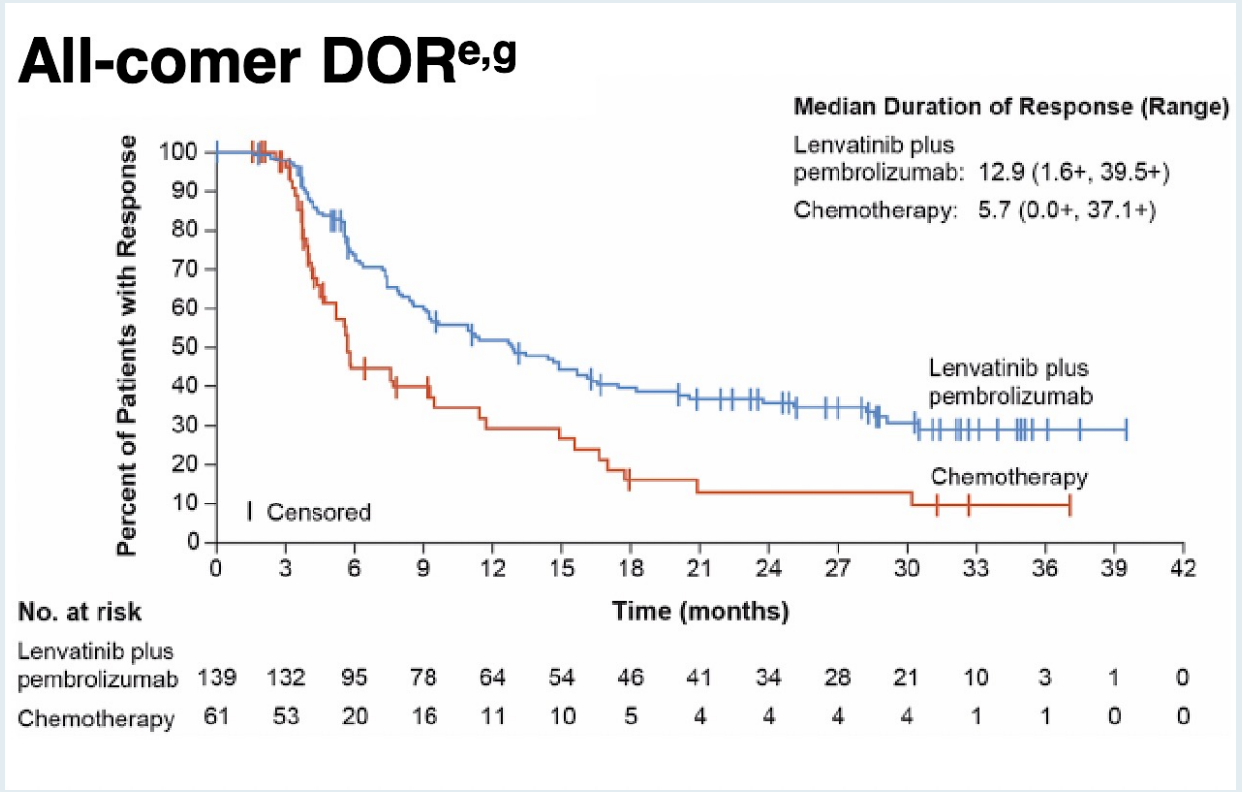


[a]Patients may have received up to 2 prior platinum-based CT regimens if 1 was given in the neoadjuvant or adjuvant treatment setting; [b]maximum of 35 doses; [c]maximum cumulative dose of 500 mg/m².

Makker V et al. ESMO 2022;Abstract 525MO.

KEYNOTE-775: Continued Tumor Responses in pMMR and All-Comer Patients





Makker V et al. ESMO 2022;Abstract 525MO.

RTP RESEARCH TO PRACTICE

Potential Role of Selinexor in the Management of EC

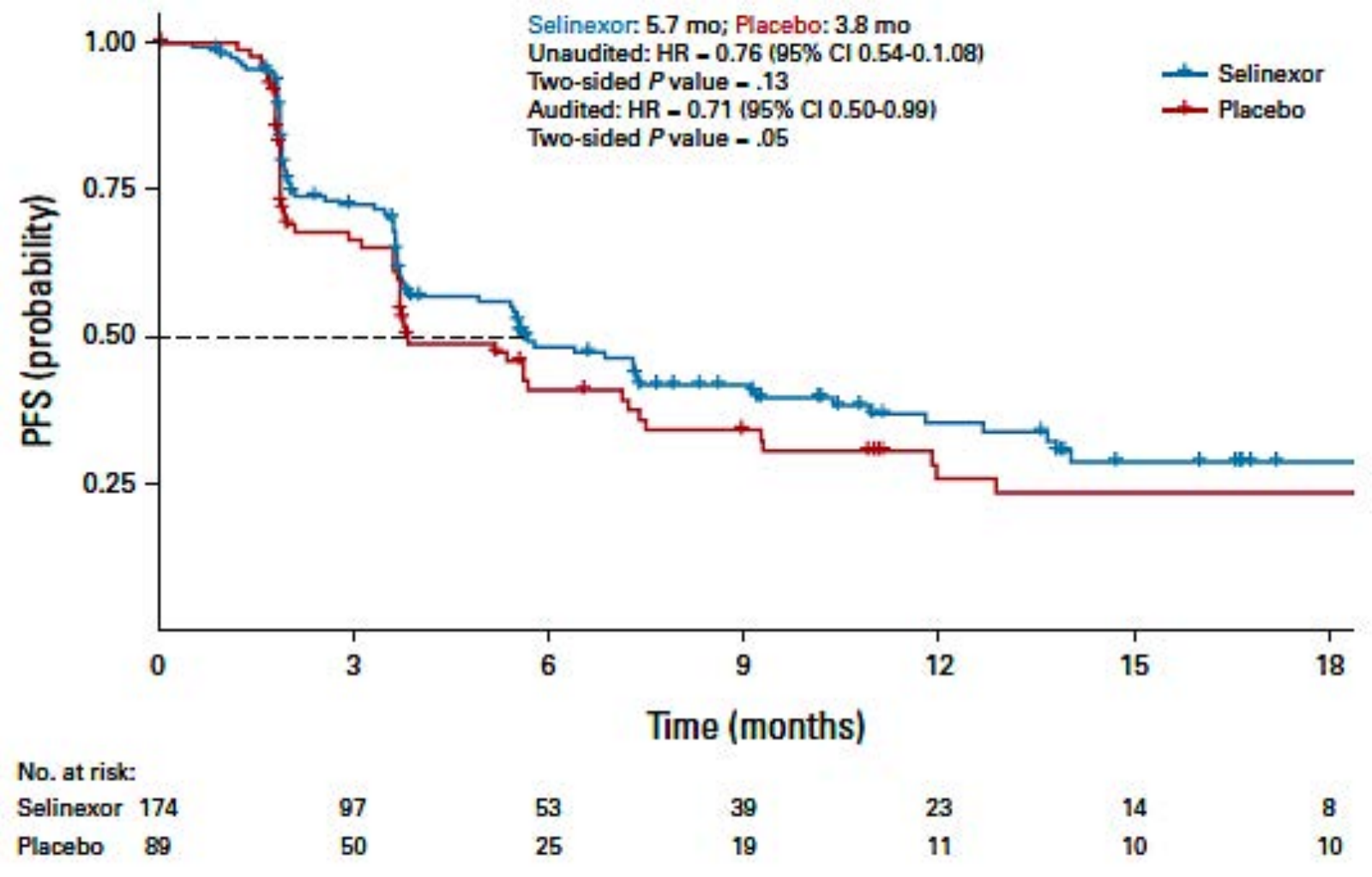
Original Reports | Gynecologic Cancer

Oral Selinexor as Maintenance Therapy After First-Line Chemotherapy for Advanced or Recurrent Endometrial Cancer

Ignace Vergote, MD[1]; Jose Alejandro Pérez-Fidalgo, MD[2]; Erika Paige Hamilton, MD[3]; Giorgio Valabrega, MD[4]; Toon Van Gorp, MD[1]; Jalid Sehouli, MD[5]; David Cibula, MD[6]; Tally Levy, MD[7]; Stephen Welch, MD[8]; Debra L. Richardson, MD[9]; Eva M. Guerra, MD[10]; Giovanni Scambia, MD[11]; Stéphanie Henry, MD[12]; Pauline Wimberger, MD[13]; David S. Miller, MD[14]; Jaroslav Klat, MD[15]; Jerónimo Martínez-Garcia, MD[16]; Francesco Raspagliesi, MD[17]; Bhavana Pothuri, MD[18]; Ignacio Romero, MD[19]; Alice Bergamini, MD[20,21]; Brian Slomovitz, MD[22]; Fabienne Schochter, MD[23]; Estrid Høgdall, MD[24]; Lorena Fariñas-Madrid, MD[25]; Bradley J. Monk, MD[26]; Dayana Michel, MD[27]; Michael G. Kauffman, MD[27]; Sharon Shacham, PhD[27]; Mansoor Raza Mirza, MD[28]; and Vicky Makker, MD[29]; on behalf of the ENGOT-EN5/GOG-3055/SIENDO Investigators

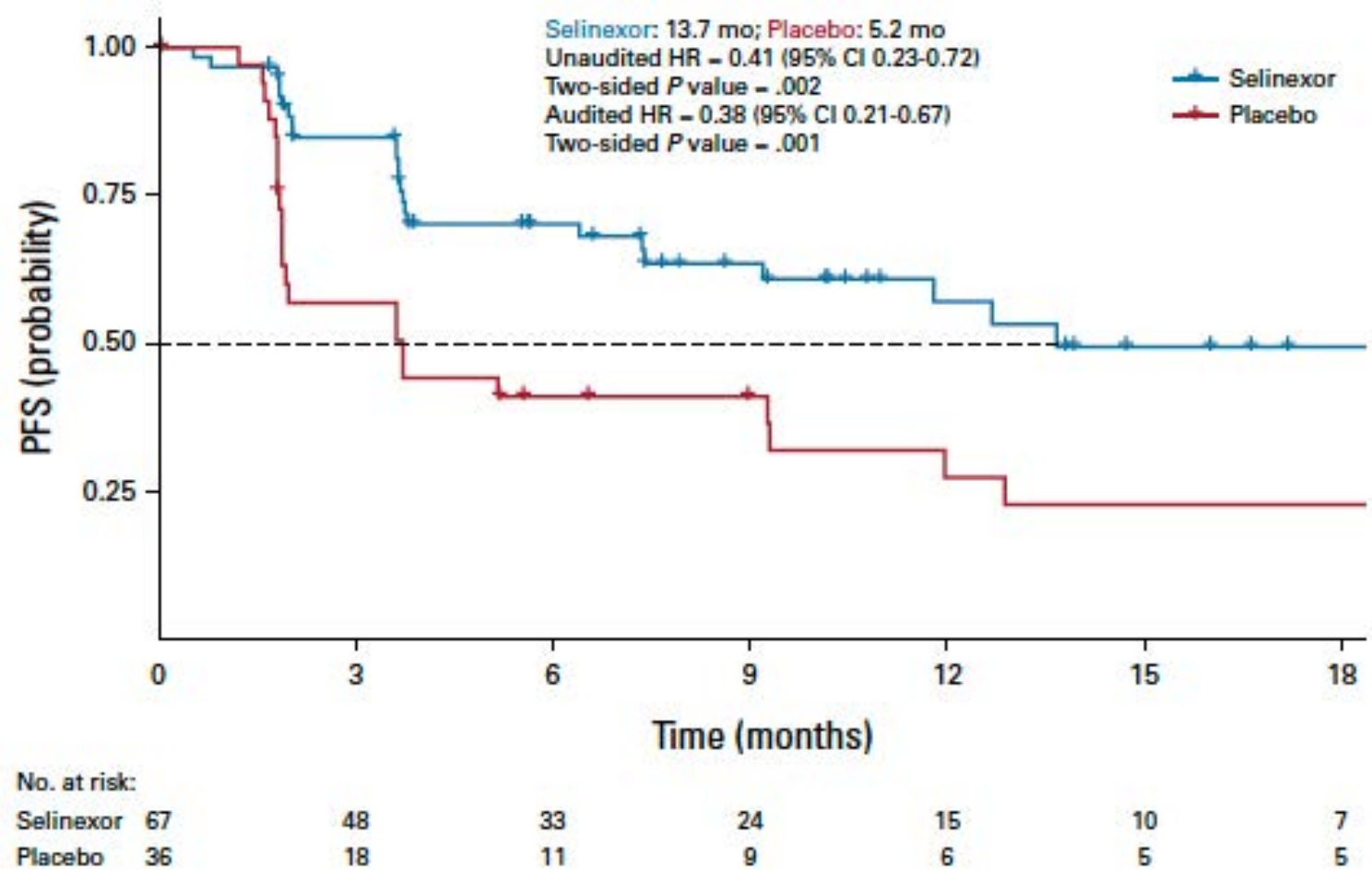
J Clin Oncol 2023;41(35):5400-10

SIENDO: PFS with Selinexor in the Intent-to-Treat Population



Vergote I et al. *J Clin Oncol* 2023;41(35):5400-10.

SIENDO: PFS with Selinexor in the p53 Wild-Type Population



Vergote I et al. *J Clin Oncol* 2023;41(35):5400-10.

Incidence and Management of HER2-Positive EC

2023 ASCO ANNUAL MEETING

Abstract LBA3000

DESTINY-PanTumor02

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

Funda Meric-Bernstam

The University of Texas MD Anderson Cancer Center, Houston, TX, USA

June 5, 2023

Additional authors: Vicky Makker, Ana Oaknin, Do-Yo
Kyung Hae Jung, Iwona Ługowska, Luis Manso, Arán
Daniil Stroyakovskiy, Chiedozie Anoka, Yan Ma, Soha

On behalf of the DESTINY-PanTumor02

2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: Funda Meric-Bernstam, MD

J Clin Oncol 2024;42(1):47-58

Original Reports | Gynecologic Cancer

Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

Funda Meric-Bernstam, MD[1]; Vicky Makker, MD[2,3]; Ana Oaknin, MD[4]; Do-Youn Oh, MD[5]; Susana Banerjee, PhD[6]; Antonio González-Martín, MD[7]; Kyung Hae Jung, MD[8]; Iwona Ługowska, MD[9]; Luis Manso, MD[10]; Aránzazu Manzano, MD[11]; Bohuslav Melichar, MD[12]; Salvatore Siena, MD[13]; Daniil Stroyakovskiy, MD[14]; Anitra Fielding, MBChB[15]; Yan Ma, MSc[16]; Soham Puvvada, MD[15]; Norah Shire, PhD[15]; and Jung-Yun Lee, MD[17]

RTP RESEARCH TO PRACTICE

DESTINY-PanTumor02: Phase II Basket Trial Schema

An open-label, multicenter study (NCT04482309)

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

T-DXd
5.4 mg/kg
q3w

n≈40 per cohort planned

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

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

Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

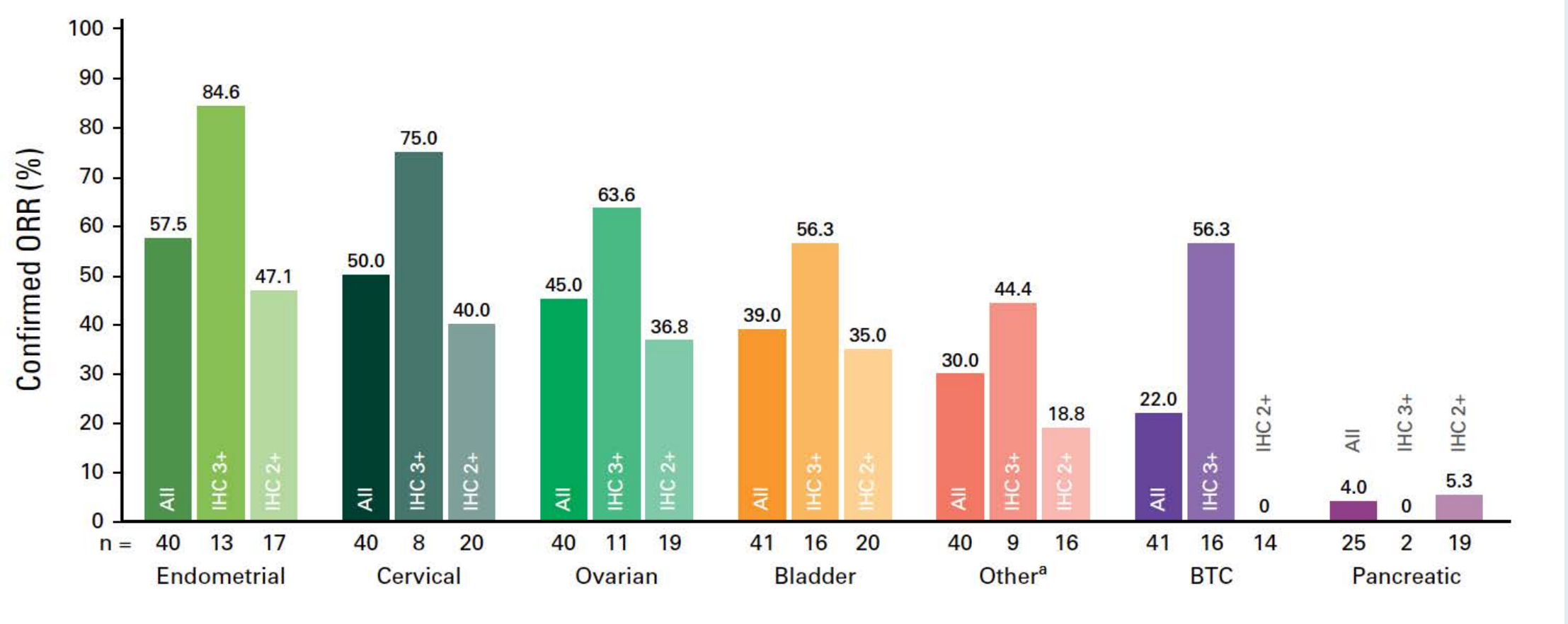
- DOR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

Meric-Bernstam F et al. ASCO 2023;Abstract LBA3000; Meric-Bernstam F et al. *J Clin Oncol* 2024;42(1):47-58.

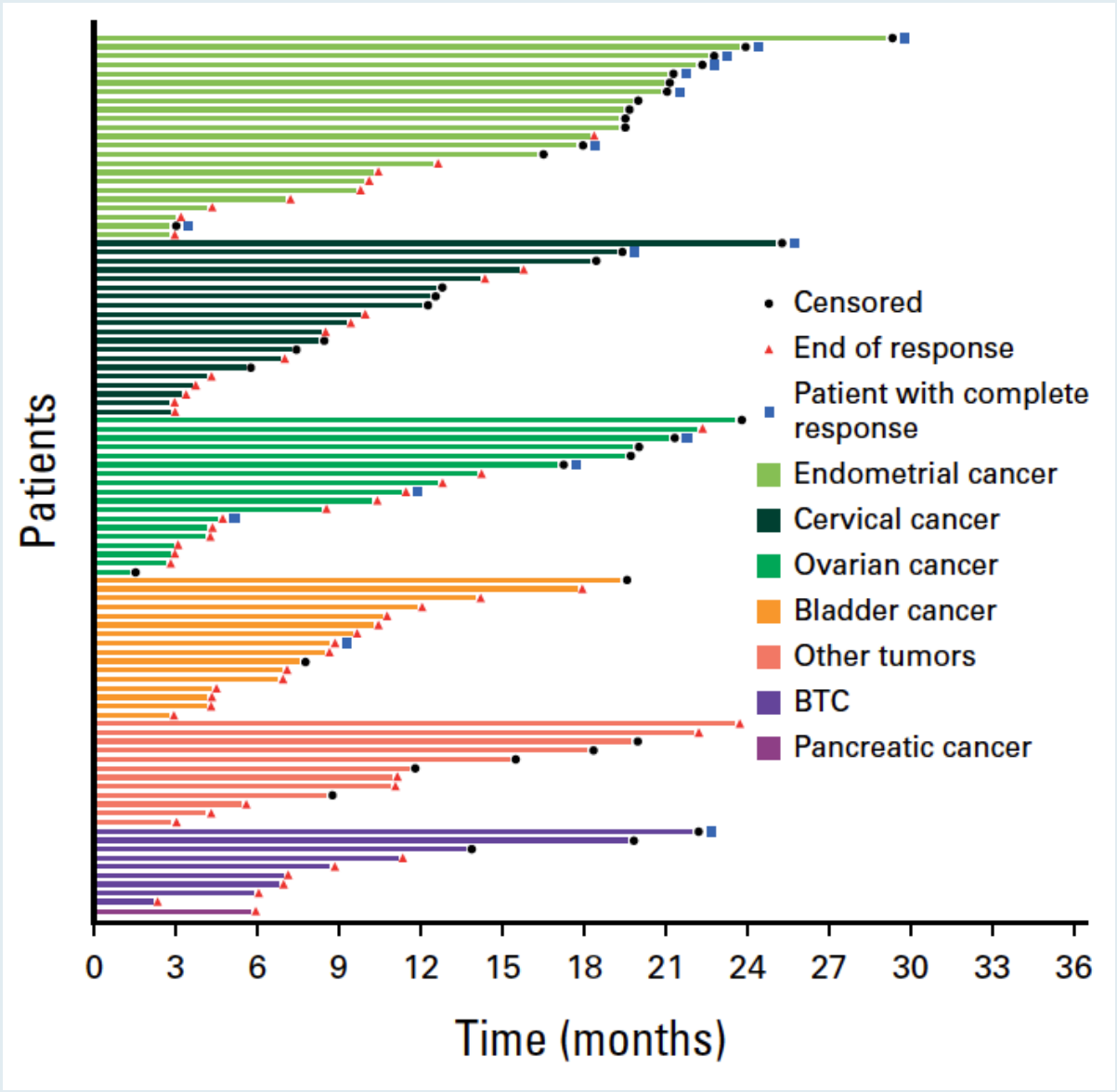
DESTINY-PanTumor02: Objective Response Rate by HER2 Status



Meric-Bernstam F et al. ASCO 2023;Abstract LBA3000; Meric-Bernstam F et al. *J Clin Oncol* 2024;42(1):47-58.

RTP RESEARCH TO PRACTICE

DESTINY-PanTumor02: Duration of Response



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

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Endometrial Cancer

Thursday, April 25, 2024
6:00 AM – 7:30 AM

Faculty

Jennifer Filipi, MSN, NP
Kathryn M Lyle, MSN, WHNP-BC, AGNP-C
David M O'Malley, MD
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Optimal Implementation of Antibody-Drug Conjugates

Thursday, April 25, 2024
12:15 PM – 1:45 PM

Faculty

Jamie Carroll, APRN, MSN, CNP
Kelly EH Goodwin, MSN, RN, ANP-BC
Erika Hamilton, MD
Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

To Claim NCPD Credit

In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.

Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

RTP
RESEARCH
TO PRACTICE