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

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

Management of Ovarian Cancer

Wednesday, May 13, 2026

6:00 PM – 7:30 PM

Faculty

Bradley J Monk, MD
Kathryn M Schlenker, MSN, WHNP-BC, AGNP-C
Jaclyn Shaver, MS, APRN, CNP, WHNP

Moderator

David M O'Malley, MD

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Faculty

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Professor at the University of Central Florida
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Vice President and Member, Board of Directors
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Dr Monk — Disclosures

Consulting Agreements	AbbVie Inc, Alkermes, AstraZeneca Pharmaceuticals LP, BioNTech SE, Corcept Therapeutics Inc, Daiichi Sankyo Inc, Eisai Inc, Genentech, a member of the Roche Group, Genmab US Inc, GSK, ImmunoGen Inc, Incyte Corporation, Karyopharm Therapeutics, Lilly, Merck, Mersana Therapeutics Inc, Mural Oncology Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Novocure Inc, OncoC4, Panavance Therapeutics, Pfizer Inc, pharmaand GmbH, ProfoundBio, Regeneron Pharmaceuticals Inc, Seagen Inc, Sutro Biopharma, Takeda Pharmaceuticals USA Inc, Tubulis, Verastem Inc, Zai Lab, Zentalis Pharmaceuticals, Zymeworks Inc
Speakers Bureaus	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Eisai Inc, GSK, ImmunoGen Inc, Merck, Takeda Pharmaceuticals USA Inc, Zai Lab

Ms Schlenker — Disclosures

No relevant financial relationships to disclose.

Ms Shaver — Disclosures

No relevant financial relationships to disclose.

Dr O'Malley — Disclosures

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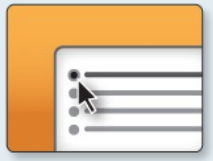
Clinicians in the Meeting Room

Networked iPads are available.

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



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

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

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

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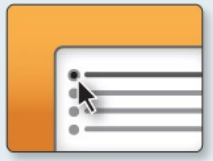
Clinicians Attending via Zoom

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



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

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. 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**

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RTP RESEARCH TO PRACTICE ONCOLOGY NURSING UPDATE WITH NEIL LOVE, MD

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

Overview of nonmelanoma skin cancers (12 min)

Systemic therapy for nonmelanoma skin cancers (8 min)

Immune checkpoint inhibitors for special patient populations (12 min)

Hedgehog inhibitors for basal cell carcinoma (6 min)

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

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

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

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

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Feedback (Please!)

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“Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse”
Eighteenth Annual RTP-ONS NCPD Symposium Series

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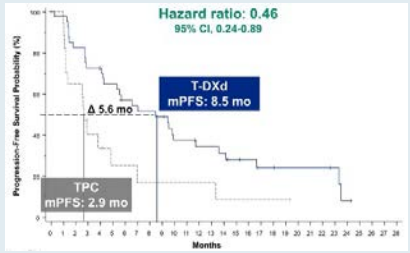
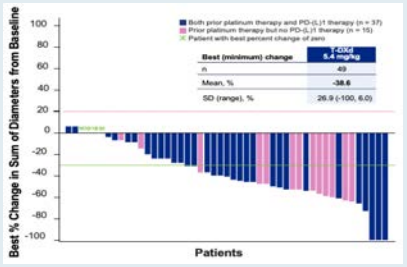
Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

New Agents, Therapies and Regimens

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



  - Waterfall plots



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Agenda

Module 1: Overview of Ovarian Cancer (OC)

Module 2: Role of PARP Inhibitors in Advanced OC

Module 3: Current and Potential Future Role of Mirvetuximab Soravtansine in OC

Module 4: Role of Relacorilant in Advanced OC

Module 5: Utility of Immune Checkpoint Inhibition in Advanced OC

Agenda

Module 1: Overview of Ovarian Cancer (OC)

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Discussion Questions

How do you approach genetic testing for patients with ovarian cancer (OC)? Who should be tested, when and how? What specific alterations (eg, germline and somatic BRCA mutations, other germline or somatic alterations, homologous recombination deficiency [HRD]) are you looking for, and how do you explain these to patients?

How do you counsel patients with germline BRCA and other germline alterations about the potential utility of genetic counseling and genetic testing for children or grandchildren?

How do you decide which patients with advanced OC should receive neoadjuvant versus adjuvant chemotherapy? How do you determine whether bevacizumab should be included?

Agenda

Module 1: Overview of Ovarian Cancer (OC)

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Module 5: Utility of Immune Checkpoint Inhibition in Advanced OC

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ROLE OF PARP INHIBITORS IN ADVANCED OVARIAN CANCER

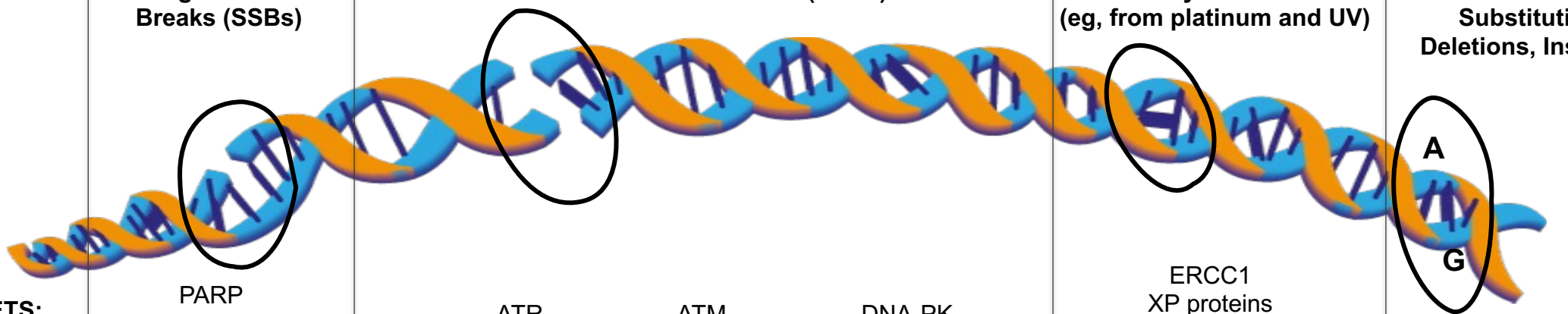
Bradley J. Monk, MD, FACS, FACOG

- Florida Cancer Specialists and Research Institute
  West Palm Beach, FL 33401
- Professor at University of Central Florida College of Medicine
- Vice President and Member Board of Directors GOG-Foundation
- Director GOG-Partners

Any fool can make something complicated. It is hard to keep things simple.

Sir Richard Branson
(Virgin Atlantic/Virgin Galactic Innovator)

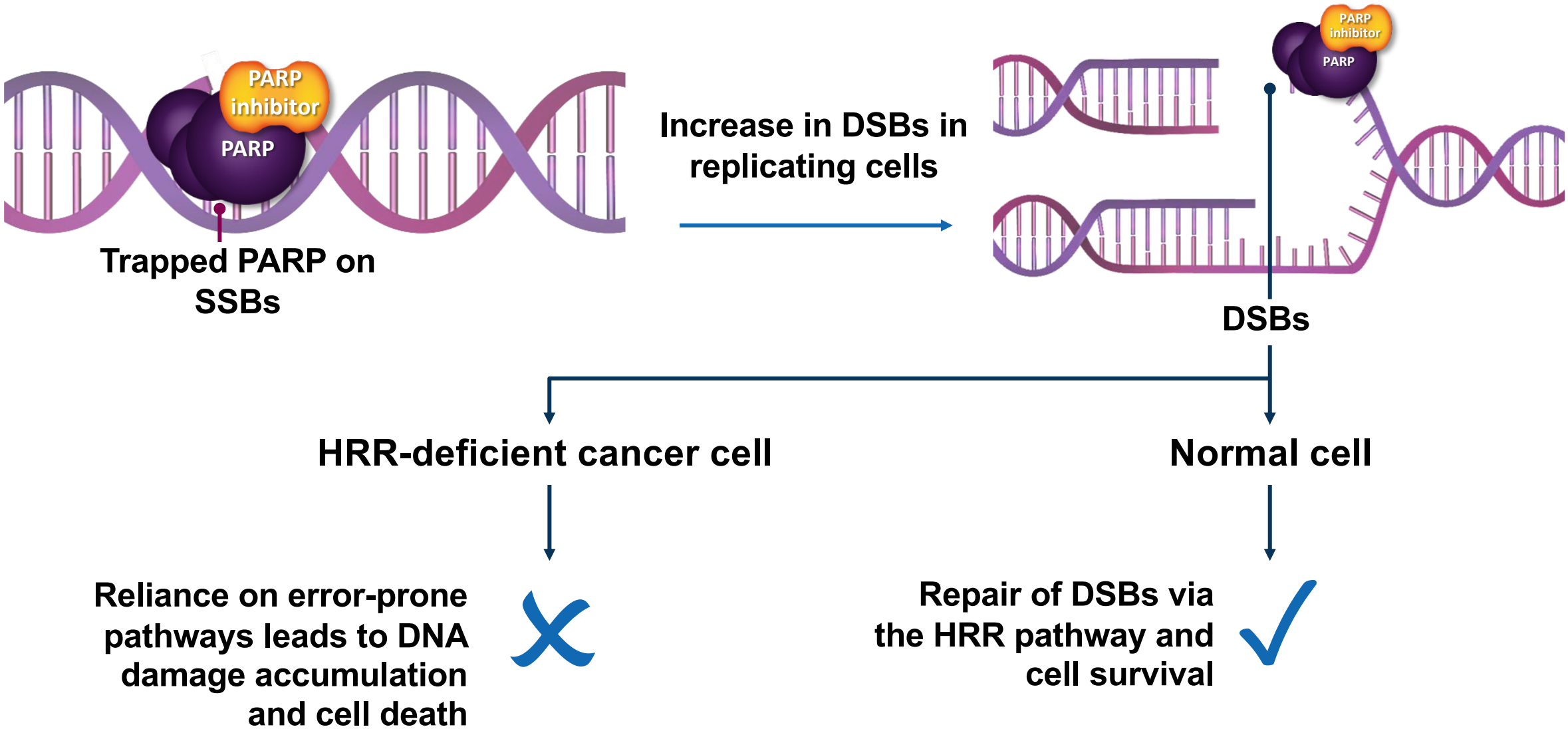
DNA Damage Response Pathway Drug Targets[1]



TYPE OF DAMAGE:	**Single-Strand Breaks (SSBs)**	**Double-Strand Breaks (DSBs)**		**Bulky Adducts (eg, from platinum and UV)**	**Nucleotide Mutations, Substitutions, Deletions, Insertions**
REPAIR TARGETS:	PARP APE1	ATR	ATM DNA-PK	ERCC1 XP proteins Polymerases	MLH, MSH, etc
REPAIR PATHWAY:	**B**ase **E**xcision **R**epair	**H**omologous **R**ecombination **R**epair	**N**on-**H**omologous **E**nd **J**oining	**N**ucleotide **E**xcision **R**epair and **T**ranslesion **S**ynthesis	**M**is**M**atch **R**epair
DAMAGING AGENTS:	Radiotherapy Alkylating agents	Radiotherapy Topo I inhibitors Nucleoside analogue	Radiotherapy Topo II inhibitors	UV light Platinum agents	Replication errors Alkylating agents
RATIONALE FOR TARGETING:	**The most common lesion**	**The most cytotoxic lesion**		**Platinum potentiation but safety concern over UV sensitization**	**Increased mutational load**

1. Adapted from O'Connor MJ. *Mol Cell*. 2015;60:547-560.

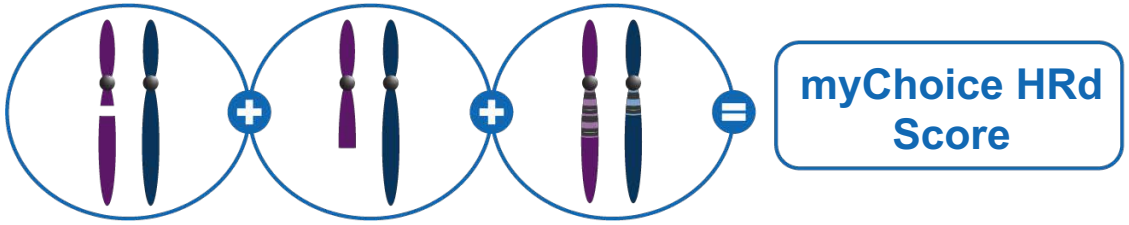
PARP Inhibitor Exploits the Baseline Vulnerability of Cells With Inherent DNA Repair Deficiency[1]



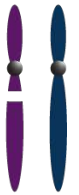
1. O'Connor MJ. *Mol Cell*. 2015;60:547-560.

How to Identify Homologous Recombination Deficiency[1,a]

myChoice
(CDx olaparib, niraparib)



FoundationOne LOH
(CDx rucaparib, olaparib)



HR status is determined by genomic instability score (GIS)

- **HR-deficient tumors:** tissue GIS ≥42 **OR** a *BRCA*m
- **HR-proficient tumors:** tissue GIS <42
- HR not determined

- **HRR pathway–related genes**
  BRCA (germline, somatic)
- **Non-*BRCA* HRR gene mutations**
  (eg, *RAD51C, RAD51D, BRIP1, ATM, CDK12, CHEK1, CHEK2*)

[a] Tests have not been compared head to head. Paired with development of respective drugs.

1. https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm.

Integrated Maintenance Treatment Paradigm for Use in 1-L Ovarian Cancer (2020)

Supporting Phase 3 NEJM Publications

Testing
- Germ line panel testing (all EOC)
- Tumor HRD testing (if germ line BRCAwt)

Decision #1
NACT vs
Primary debulking

IV q 3 week carboplatin + paclitaxel

Decision #2
Bevacizumab Y/N

No bevacizumab

- ***BRCA* mut HRd:** Add PARPi (preferred) — SOLO-1, PRIMA, ATHENA
- **HRd neg:** Add PARPi or Observation — PRIMA, ATHENA

Bevacizumab during chemotherapy and in maintenance

- ***BRCA* mut HRd:** Add PARPi (preferred) — PAOLA-1
- **HRd neg:** Continue bevacizumab — GOG 218, GOG 262

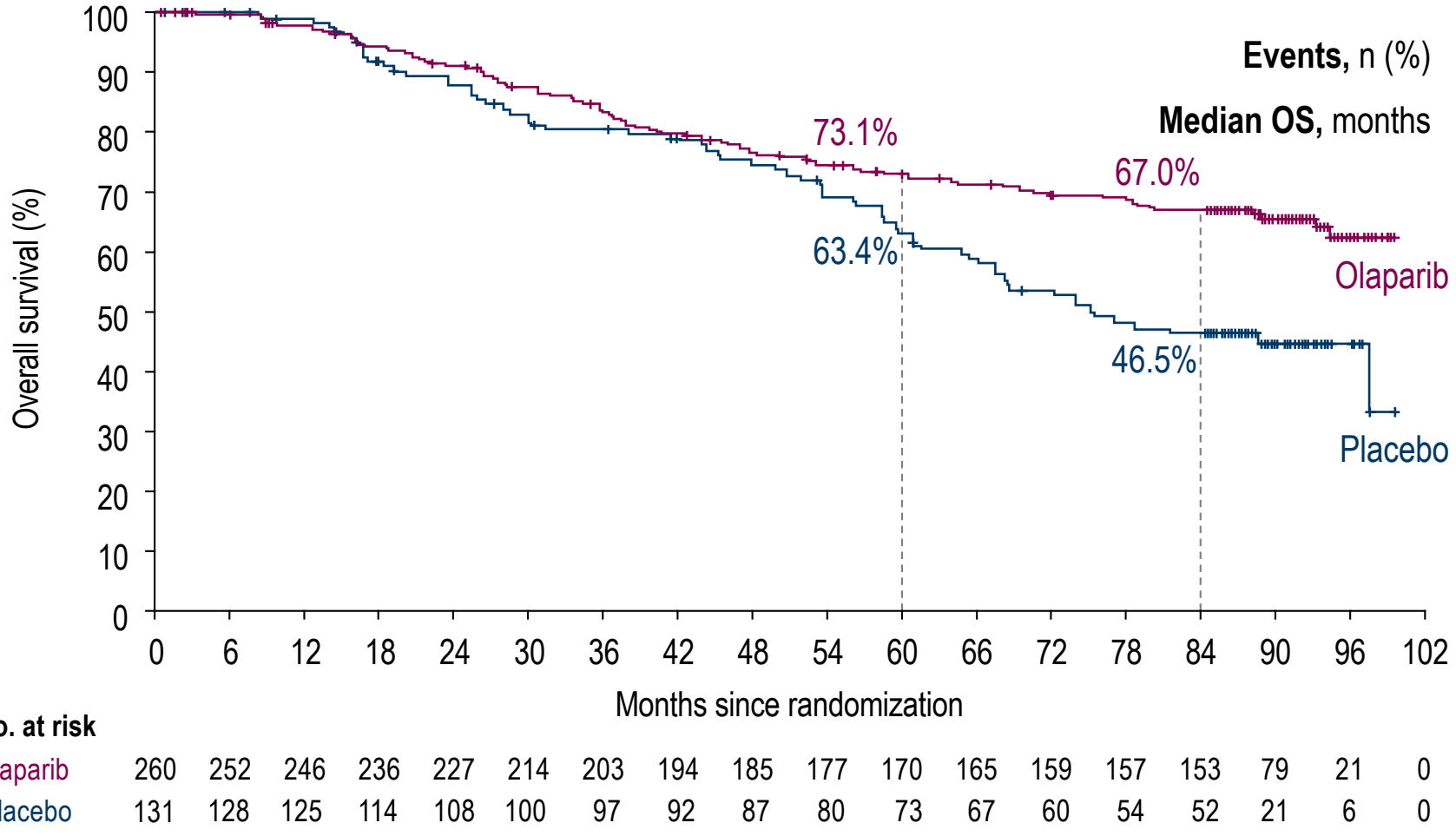
Decision #3
Add PARPi?

1. NACT = Neoadjuvant chemotherapy
2. EOC=Epithelial ovarian cancer
3. HRD = Homologous recombination deficient
4. HRP = Homologous recombination proficient
5. PARPi = Poly ADP Ribose inhibitor
6. NEJM = New England Journal of Medicine

Chan JK, Liang SY, Kapp DS, Chan JE, Herzog TJ, Coleman RL, Monk BJ, Richardson MT. Gynecol Oncol. 2020 Dec;159(3):604-606.

2022 SOLO1 7-year Survival Analysis (BRCA mutation carriers only)

(ESMO 2022, JCO 9/2022)



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	84 (32.3)	65 (49.6)
Median OS, months	**NR**	**75.2**
	HR 0.55 (95% CI 0.40–0.76); *P*=0.0004*	

No. at risk																		
Olaparib	260	252	246	236	227	214	203	194	185	177	170	165	159	157	153	79	21	0
Placebo	131	128	125	114	108	100	97	92	87	80	73	67	60	54	52	21	6	0

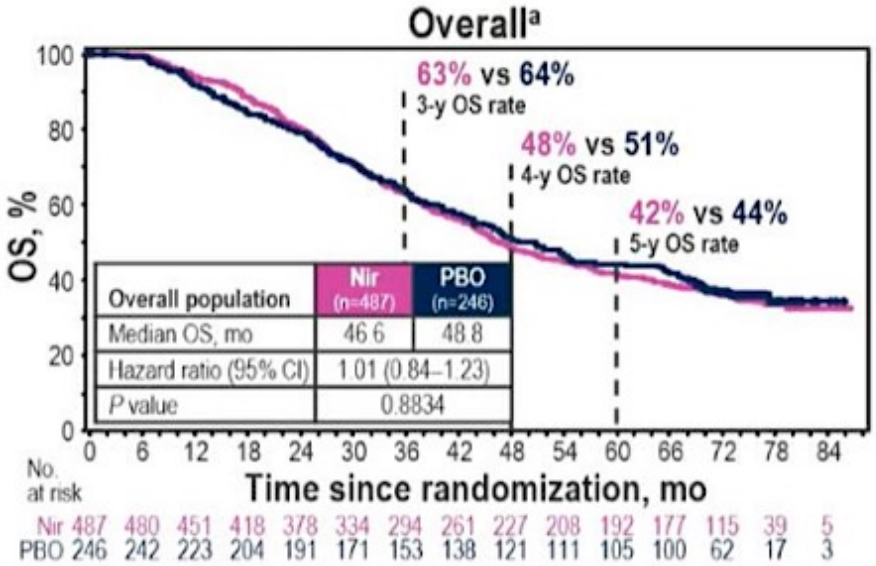
44.3% of patients in the placebo group received subsequent PARP inhibitor therapy, compared with 14.6% of patients in the olaparib group

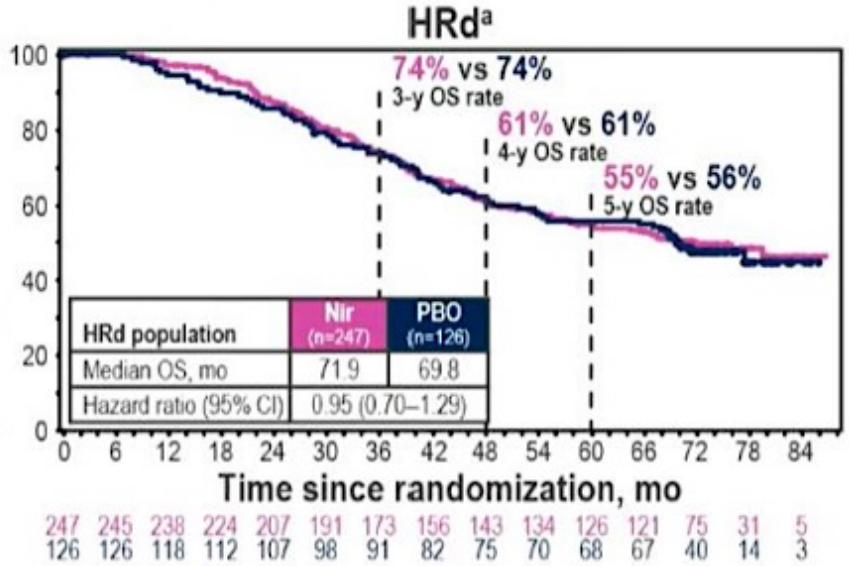
*P<0.0001 required to declare statistical significance

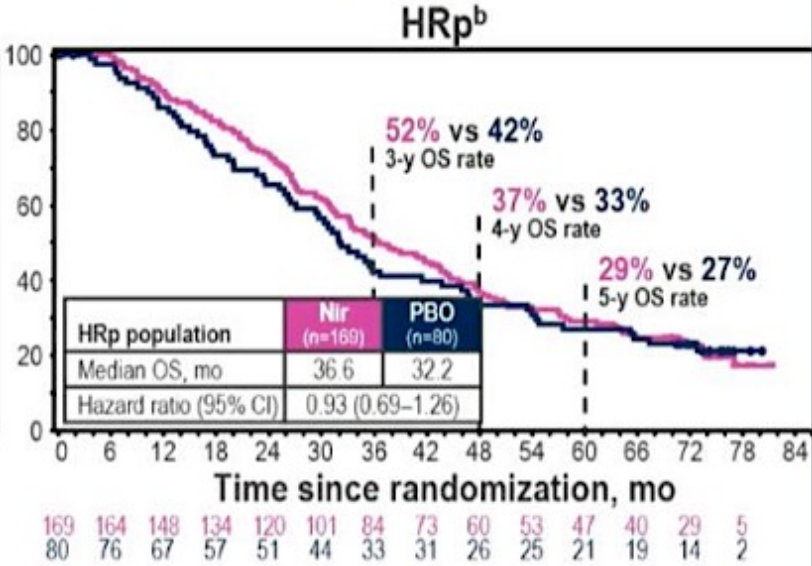
SOLO1 7-year OS: DiSilvestro P. et al. J Clin Oncol. 2022 Sep 9;JCO2201549. Online ahead of print. PMID: 36082969

PRIMA Final OS (62.5% maturity in overall population)

No difference in OS between niraparib and placebo arms in the overall, HRd, and HRp populations







- OS results for all prespecified biomarker-defined subgroups consistent with overall population[c]
- Assessment of long-term efficacy outcomes in high-risk aOC may be complicated by multiple factors[1]
  - Patient population[2–4]
  - Extended postprogression survival[1,5]
  - Subsequent therapy[1,5]

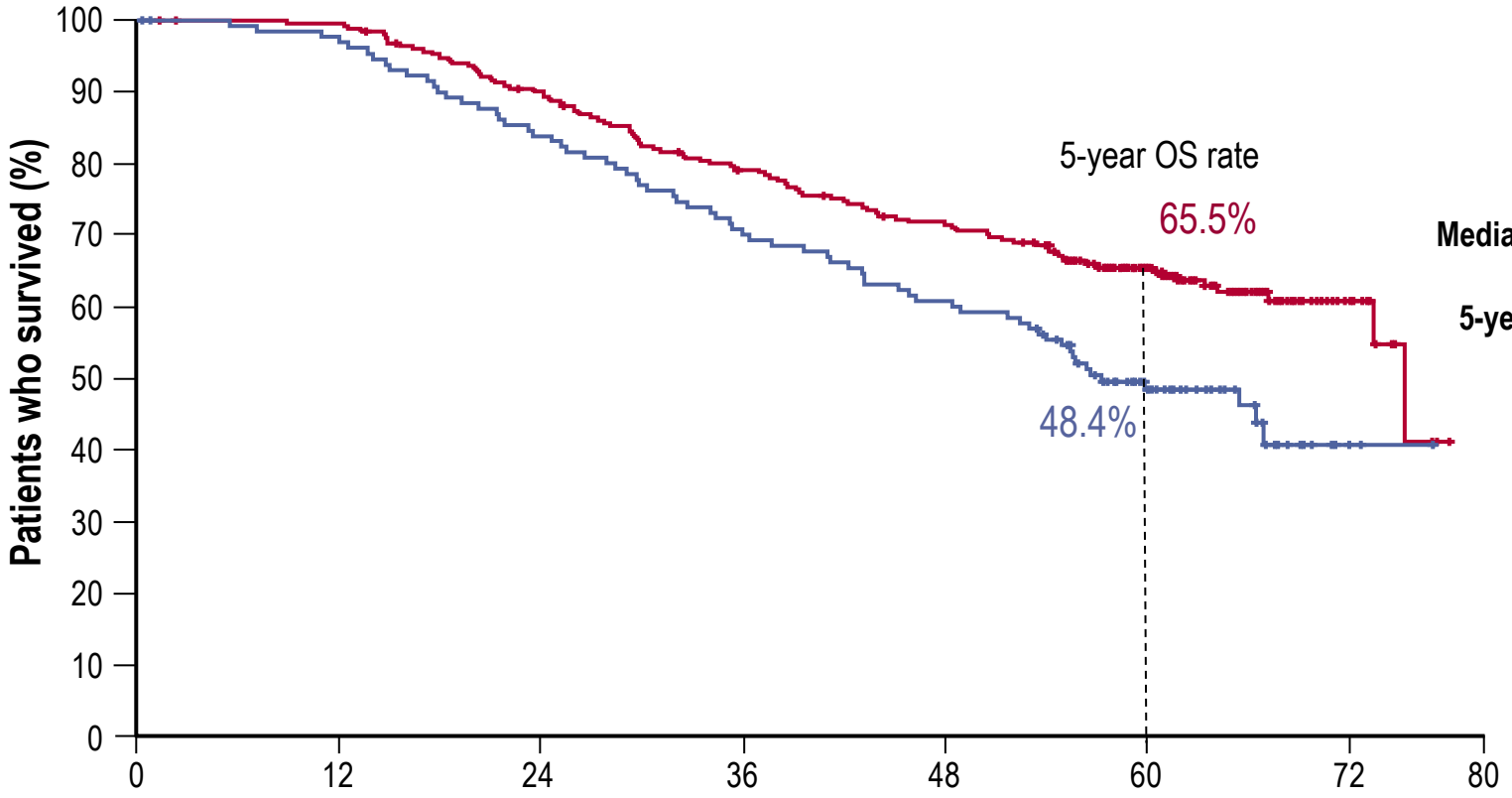
3-fold higher subsequent PARP inhibitor use in placebo than niraparib arms

[a]Hazard ratios and 95% CIs for overall and HRd populations calculated using stratified Cox proportional hazards model with randomization stratification factors. [b]Hazard ratio and 95% CI for HRp population calculated using unstratified Cox proportional hazards model. [c]OS results for the HRnd population (unstratified): hazard ratio (95% CI), 1.39 (0.88–2.19). aOC, advanced ovarian cancer; HRd, homologous recombination deficient; HRnd, homologous recombination status not determined; HRp, homologous recombination proficient; OS, overall survival; Nir, niraparib; PBO, placebo. 1. Matulonis UA, et al. *Cancer*. 2015;121(11):1737–1746. 2. Siegel RL, et al. *CA Cancer J Clin*. 2024;74(1):12–49. 3. Elattar A, et al. *Cochrane Database Syst Rev*. 2011;201(8):CD007565. 4. Sun C, et al. *PLoS One*. 2014;9(5):e95285. 5. Delgado A, et al. *Am J Cancer Res*. 2021;11(4):1121–1131.

Monk BJ et al. *Ann Oncol* 2024;35(11):981-92.

2022 PAOLA: OS prolonged in the HRD+ subgroup

HRD positive defined as a tBRCAm and/or genomic instability score of ≥42 on the Myriad myChoice HRD Plus assay



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	93 (36.5)	69 (52.3)
Median OS, months	**75.2** (unstable)*	**57.3**
5-year OS rate, %	**65.5**	**48.4**
HR 0.62 (95% CI 0.45–0.85)		

38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: **17.3%** (44/255)
Placebo + bevacizumab: **50.8%** (67/132)

No. at risk																										
Olaparib + bevacizumab	255	253	253	252	252	244	238	231	225	215	205	200	195	189	183	176	174	170	164	142	116	83	62	32	17	4	0
Placebo + bevacizumab	132	130	129	128	126	121	117	114	109	105	100	96	91	89	86	82	79	77	70	59	44	29	21	9	2	1	0

*Median unstable; <50% data maturity.

HRD positive defined as a tBRCAm and/or genomic instability score of ≥42 on the Myriad myChoice HRD Plus assay.

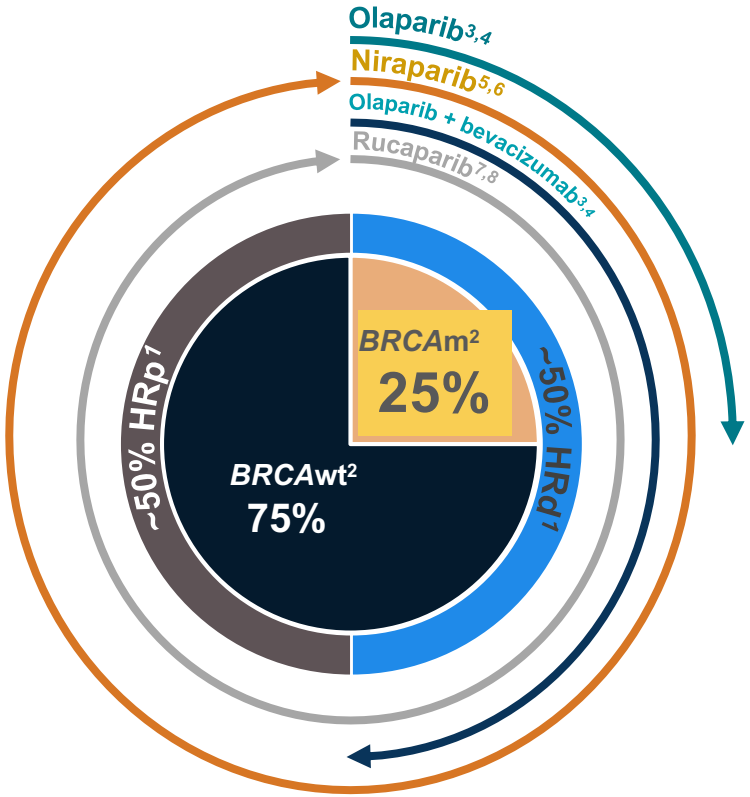
PARIS 2022 ESMO congress

Isabelle Ray-Coquard

Ray-Coquard I et al. *Ann Oncol* 2023;34(8):681-92.

PARPi as 1L Maintenance Therapies were Studied Across Biomarker Subgroups with Different Indications

PARP inhibitor 1L maintenance therapy options



Olaparib[3,4]	Niraparib[5,6]	Olaparib + bevacizumab[3,4]
*BRCA*m	*BRCA*m HRd/*BRCA*m, HRd/*BRCA*wt	*BRCA*m HRd/*BRCA*m, HRd/*BRCA*wt

The data presented are not intended to make comparisons and are used merely for didactic purposes. Direct or indirect comparisons between drugs should be based on head-to-head/comparative trials with level I or II of evidence. In the absence of comparative studies, efficacy and safety cannot be compared and are not intended.

1L, first-line; *BRCA*m, breast cancer gene mutant; *BRCA*wt, breast cancer gene wild type; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PARP, poly(ADP-ribose) polymerase; PARPi, poly(ADP-ribose) polymerase inhibitor.

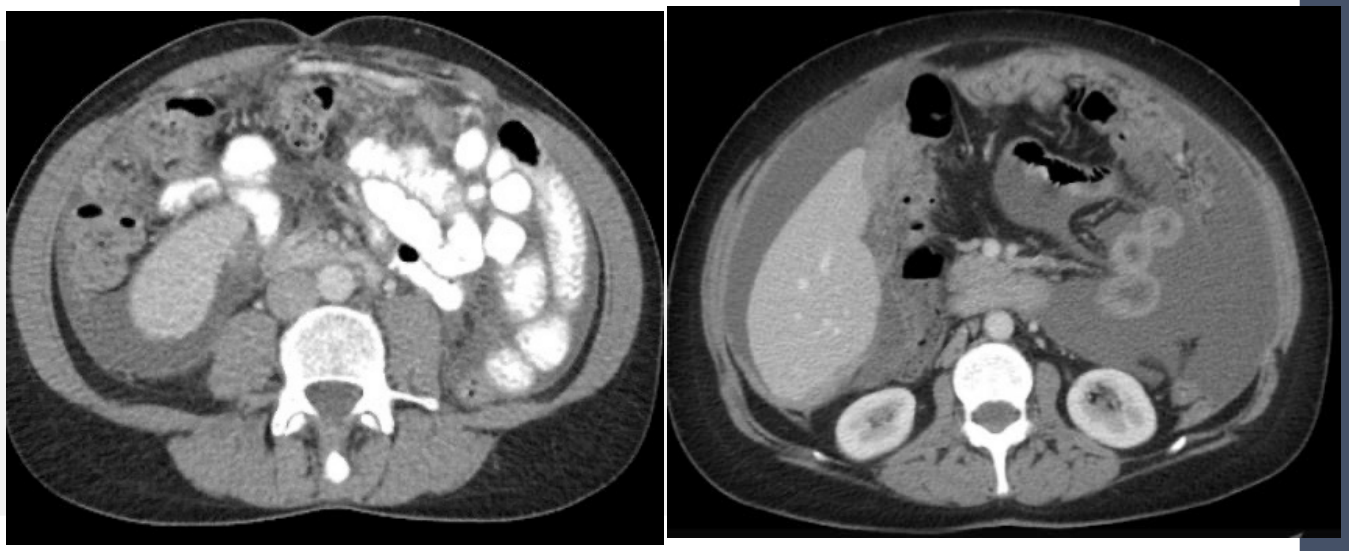
1. Cancer Genome Atlas Research Network. Nature. 2011 Jun 29;474(7353):609-15. 2. Pennington KP, Walsh T, Harrell MI, et al. Clin Cancer Res. 2014 Feb 1;20(3):764-75. 3. Olaparib; 2023 Nov. US prescribing information.
4. Olaparib; 2022. Summary of product characteristics. 5. Niraparib; 2022. Summary of product characteristics. 6. Niraparib; 2024 May. Prescribing information 7. Rucaparib; 2023 Jun. Prescribing information. 8. Rucaparib). Summary of product characteristics. 2022.

Case Study

56-Year-Old Woman With Abdominal Pain

Presentation:

- 65 kg; platelet count 240,000
- CA-125: 2257 IU/mL
- ECOG PS 0
- Hypertension controlled
- Aunt with breast cancer at 39 years of age



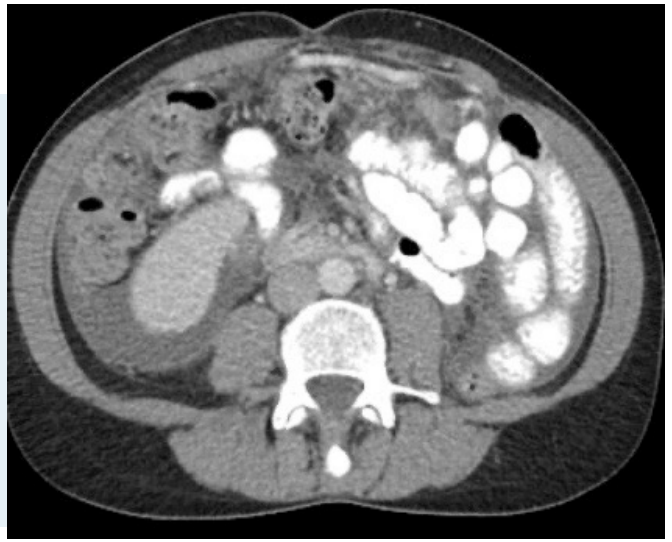
CA-125, cancer antigen 125; ECOG PS, Eastern Cooperative Oncology Group performance status.

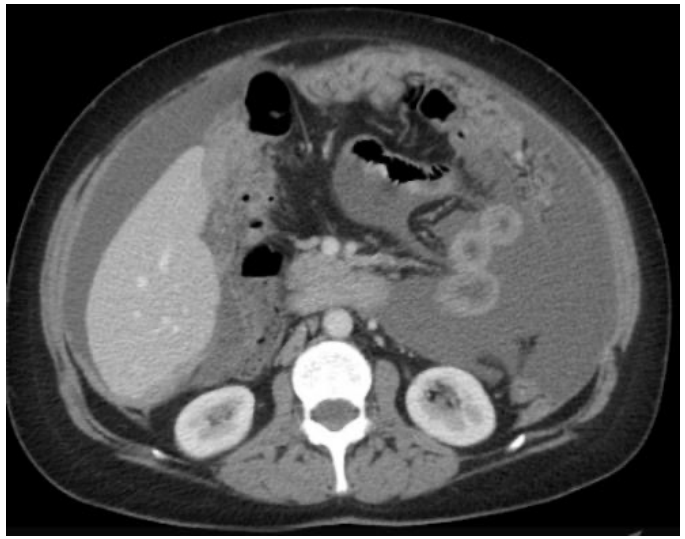
Case Study

56-Year-Old Woman With Abdominal Pain

Key Questions:

1. What type of cancer (GYN vs non-GYN)?
2. Histologic cell type?
3. Grade (low grade vs high grade)?
4. Molecular testing





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Case Study

56-Year-Old Woman With Abdominal Pain

Presentation:

- 65 kg; platelet count 240,000
- CA-125: 2257 IU/mL
- ECOG PS 0
- Hypertension controlled
- Relevant personal history of diverticulitis
- Aunt with breast cancer at 39 years of age

Diagnostic Work-Up

- **High-grade serous OC**
- **FIGO stage IIIC**

Germline Panel Testing

- **Confirmed g*BRCA*wt; HRD score 44, HER2 IHC 1+, FR-alpha 70% 2+, PD-L1 CPS 6**
- **Surgeon recommends neoadjuvant therapy**

FIGO, International Federation of Gynecology and Obstetrics; OC, ovarian cancer.

Case Study

56-Year-Old Woman With Abdominal Pain

Presentation:

- 65 kg; platelet count 240,000
- CA-125: 2257 IU/mL
- ECOG PS 0
- Hypertension controlled
- No relevant personal history
- Aunt with breast cancer at 39 years of age

Diagnostic Work-Up

- High-grade serous OC
- FIGO stage IIIC

Germline Testing (48 genes, normal)

- **Confirmed g*BRCA*wt; HRD score 44, HER2 IHC 1+, FR-alpha 70% 2+, PD-L1 CPS 6**
- Surgeon recommends neoadjuvant therapy

First-Line Treatment

Three cycles of:

- **Paclitaxel (175 mg/m^2 IV over 3h) + carboplatin (AUC6) + bevacizumab (15mg/kg cycles 1,2 5,6 and maintenance)**
- **Interval debulking, R0, three additional cycles**
- **Normal CA-125: 25 IU/mL**

PAOLA-1: Add olaparib in the maintenance phase

Discussion Questions

Should all patients with advanced OC be offered a PARP inhibitor as up-front maintenance therapy? How do you decide which of these to use for individual patients and whether to include bevacizumab or not?

Side Effects and Other Practical Considerations with PARP Inhibitors

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PARP Inhibitors in Ovarian, Fallopian tube, or Primary Peritoneal Cancer

- Olaparib
  - First Line Maintenance with a BRCAm
  - First Line Maintenance HRD + with Bevacizumab
  - Recurrent - Maintenance with BRCAm
- Niraparib
  - First –Line maintenance with a BRCAm or HRD +
  - Recurrent – maintenance with BRCAm
- Rucaparib
  - First line Maintenance with BRCA
  - Recurrent – Maintenance with BRCAm

Dosing of PARP Inhibitors

- Optimal Start Time – 4-6 weeks post last dose of chemo with maximum window of 12 weeks in first line maintenance and no longer than 8 weeks in the recurrent setting
- Key Considerations
  - Resolution of most adverse effect from chemo such as neutropenia and thrombocytopenia to grade 1
- Olaparib
  - 300 mg (2- 150 mg tablets) twice daily with or without food
  - 1st dose reduction to 250 mg twice daily
  - 2nd dose reduction to 200 mg twice daily

Dosing of PARP Inhibitors

- Niraparib
  - With or without food
  - First line maintenance – weight and platelets
  - <77kg(<170lbs) or Plt <150,000= 200 mg once daily
  - 1st dose reduction -> 100 mg/day, 2nd discontinue
  - >77 kg (>170lbs) AND Plt >150,000 = 300 mg once daily
  - 1st dose reduction -> 200 mg/day, 2nd dose reduction-> 100 mg/day
  - Moderate Hepatic Impairment – 200 mg/day regardless of weight or platelets
- Rucaparib
  - 600 mg twice daily with or without food
  - 1st dose reduction 500 mg BID
  - 2nd dose reduction 400 mg BID
  - 3rd dose reduction 300 mg BID

Adverse Reactions

- More common within the first 1-3 months
- Olaparib
  - Nausea, fatigue, vomiting, anemia, neutropenia, thrombocytopenia
- Niraparib
  - Thrombocytopenia, anemia, neutropenia, nausea, vomiting, constipation, fatigue, joint pain, loss of appetite, HTN, headaches, insomnia, dizziness, cough
- Rucaparib
  - Nausea, vomiting, constipation, diarrhea, abd pain, fatigue, dysgeusia, rash, increased sensitivity to sunlight, increased ALT/AST, creatinine, anemia, and thrombocytopenia

Safety Information
Warning and Precautions

- Olaparib
  - No contraindications
  - MDS/AML - ~ 1.2%
  - Pneumonitis – 1.0%
  - Embryo- Fetal Toxicity
  - Hepatotoxicity, including Drug – Induced Liver Injury
    - Monitor- Bilirubin and Transaminases
- Niraparib
  - No contraindications
  - MDS/AML ~ 2.4-3.3%
  - Bone marrow suppression –increased risk for G3/4 toxicity
  - HTN
  - PRES – Posterior Reversible Encephalopathy Syndrome – 0.1%
    - Seizure, headache, altered mental status, visible disturbance, cortical blindness
  - Embry-Fetal Toxicity

Safety Information
Warning and Precautions

- Rucaparib
  - No contraindications
  - MDS/AML – 1.6%
  - Pneumonitis -rare
  - Embryo- Fetal toxicity
  - Photosensitivity – use SPF 30+ sunscreen, protective clothing, hats when outdoors

Key Monitoring

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

Patient Education

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

Case Study

- 53 y/o AAF G1P1
- Comorbidites: HTN, obesity, hypercholesterolemia. Family history – mother and maternal aunt (breast cancer in their 60's)
- Lives with her husband in Oklahoma City
- She presented to her PCP with complaints of abd bloating and constipation for several months. CT scan was ordered and was found to have a large 10.5 cm pelvic mass. She had not seen her gynecologic provider in several years
- CA 125 - 765
- She was referred to gyn/onc at SCC for further evaluation

Case Study

- She was scheduled for tumor debulking surgery and was resected to no gross residual
- Diagnosed with IIIC HGSOC. Germline and tumor testing was completed and was found to be BRCA 1+
- She was counseled and started on carboplatin and paclitaxel for 6 cycles. Overall tolerated treatment well, but did need to undergo blood transfusion for anemia prior to cycle #6
- CT scan after cycle #6 was NED and CA 125 was now wnl – 10. Her hemoglobin after cycle # 6 was 8.3 with some G1-2 fatigue. She was then counseled on starting olaparib maintenance 300 mg BID for 2 years
- Her hemoglobin 5 weeks after her last chemo infusion was 10.3 and she felt ready to start olaparib, but with some grade 1 fatigue

Case Study

- Weekly labs were drawn to include CBC and CMP. **Week 2 of olaparib her hemoglobin did drop to 7.8. She was given 2 units of blood and olaparib was held until grade 1.**
- **Her dose was reduced 1 level to 250 mg BID.**
- She continued weekly labs for the next month and did not need any further interruptions or dose reductions.
- **At her 1-month f/u she also complained of fatigue grade 1-2 and some grade 1-2 nausea. She was sometimes forgetting to take her anti-emetics prior to each olaparib dose.**
- **At her 2-month f/u her fatigue was still grade 1-2, but tolerable and nausea controlled with her anti-emetics.**

Case Study

- At her 3-month f/u she was feeling better with occasional nausea and fatigue. Her labs were grade 1 and we were able to able to extend her office visits out to 3M. CT scan was NED and CA 125 -6.
- At her 6M follow up she was feeling well with no side effects. CA 125 remained normal at 5.
- She completed 2 years of olaparib maintenance and was NED.
- She is currently in surveillance – 1 year from last olaparib and NED – Ca 125 normal at 7.
- Her daughter did get tested for BRCA 1 and is negative.

Discussion Questions

How, if at all, do the tolerability profile and other practical considerations with individual PARP inhibitors affect your selection among them?

Agenda

Module 1: Overview of Ovarian Cancer (OC)

Module 2: Role of PARP Inhibitors in Advanced OC

Module 3: Current and Potential Future Role of Mirvetuximab Soravtansine in OC

Module 4: Role of Relacorilant in Advanced OC

Module 5: Utility of Immune Checkpoint Inhibition in Advanced OC

Current and Potential Future Role of Mirvetuximab Soravtansine in OC Treatment

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The James

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Creating a cancer-free world. One person, one discovery at a time.




Agenda

- Frequency of and rationale for targeting folate receptor alpha (FRα) in OC
- Mechanism of action and structural components of mirvetuximab soravtansine
- Mirvetuximab soravtansine in patients with FRα-high, platinum-resistant OC
- Mirvetuximab soravtansine in FRα-high, platinum-sensitive advanced OC

Rationale for targeting FRα in ovarian cancer

"**FRα has emerged as one of the most attractive candidates** for molecularly targeted approaches for OC due to its **almost ubiquitous expression on the surface of HGSOC** and its **ability to internalize large molecules containing a cytotoxic payload**"[1]

FRα in ovarian tumours

- Expression **varies by sub-type**, e.g., a consortium-based analysis of data from 12 studies showed FRα expression in:[2]
  - **76%** of high-grade serous
  - **50%** of low-grade serous
  - **32%** of clear cell carcinomas
- Expression is **retained in recurrent and metastatic** tumours and is **not significantly altered in response to chemotherapy**[3-5]

FRα in non-malignant ovarian tissues

- FRα is **scarcely expressed** in non-malignant ovarian tissues[6]
- Limited to polarized epithelia, such as in the choroid plexus, kidney, lung, and placenta[3,7]
- FRα has a **minimal physiological role in non-malignant tissues** after embryogenesis[6]

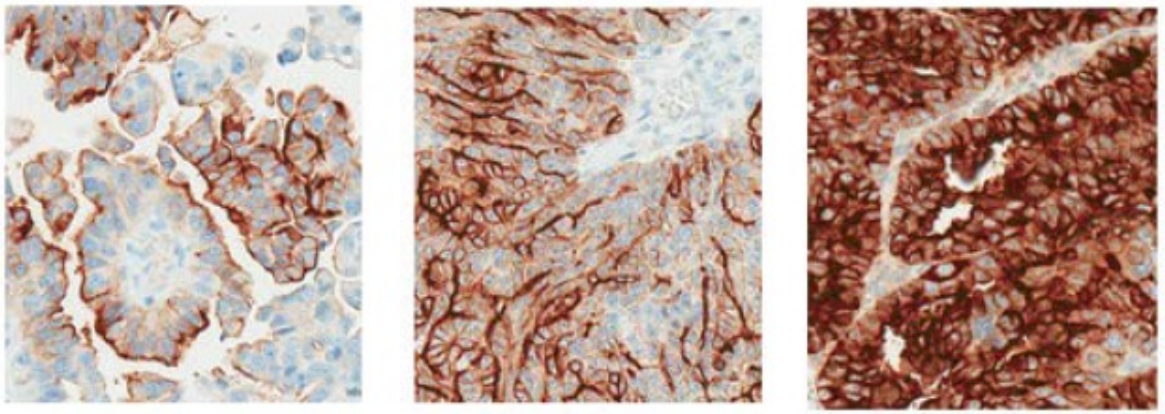
Following the disappointing activity of FRα-targeted antibodies and early folate–drug conjugates, reproducible single-agent activity has been seen with FRα-targeted antibody–drug conjugates and small molecules[6]

FR, folate receptor; HGSOC, high-grade serous ovarian cancer; OC, ovarian cancer.

1. Chelariu-Raicu A, et al. Int J Gynecol Cancer. 2023;33(3):420-429. 2. Köbel M, et al. Br J Cancer. 2014;111(12):2297-307. 3. Birrer MJ, et al. Oncologist. 2019;24(4):425-429. 4. Despierre E, et al. Gynecol Oncol. 2013;130(1):192-9. 5. Rubinsak LA, et al. Appl Immunohistochem Mol Morphol. 2018;26(8):567-572. 6. Scaranti M, et al. Nat Rev Clin Oncol. 2020;17(6):349-359. 7. Elnakat H, et al. Adv Drug Deliv Rev. 2004;56(8):1067-84. Elnakat

Characterization of folate receptor alpha (FRα) expression

Representative low, medium, and high staining patterns for FRα from archival tumour specimens[1]



Low
25–49% of cells with ≥2+ intensity

Medium
50–74% of cells with ≥2+ intensity

High
≥75% of cells with ≥2+ intensity

Figure adapted from Martin LP, et al.[1]

Prevalence of PS2+ FRα expression in 2,869 pooled samples from patients with HGSOC[2]

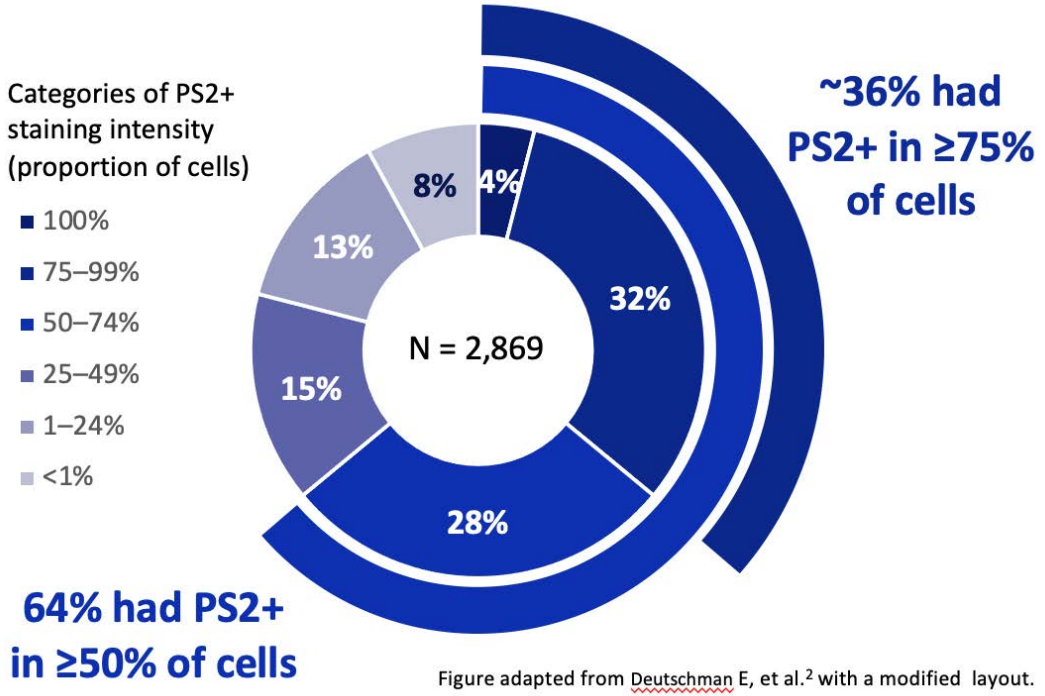
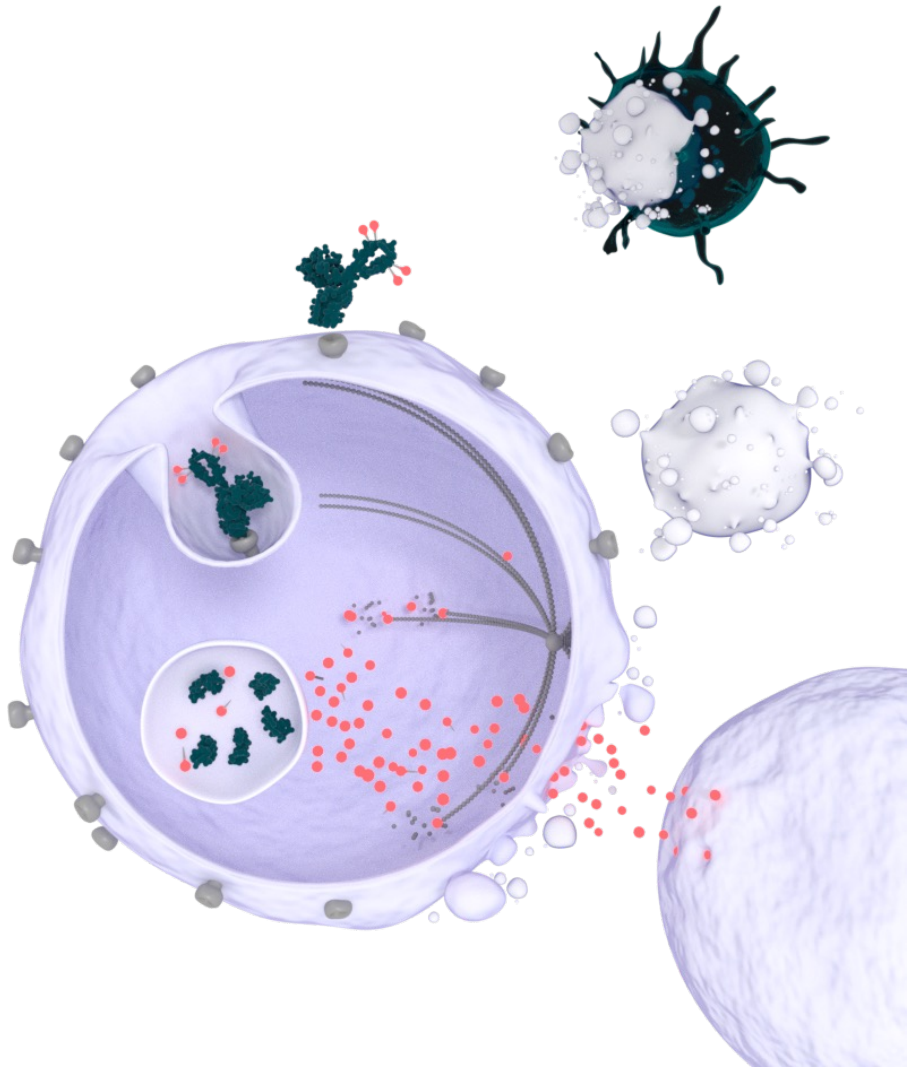


Figure adapted from Deutschman E, et al.[2] with a modified layout.

Background

- No randomized phase 3 trial has shown an overall survival (OS) benefit of a novel therapy in platinum-resistant ovarian cancer (PROC)[1, 2]
- **Mirvetuximab soravtansine (MIRV) is an ADC comprising a FRα-binding antibody, cleavable linker, and maytansinoid DM4, a potent tubulin-targeting agent[3,4]**
- FRα is expressed in ~90% of ovarian carcinomas,[5, 6] with 35-40%[7] of PROC tumors exhibiting high FRα expression (≥75% of tumor cells positive with ≥2+ intensity)[8]
- MIRV demonstrated an ORR of 32% and mDOR 6.9 months in the single-arm study SORAYA[8] of BEV pre-treated PROC to support accelerated approval by the FDA[9]
- MIRASOL was the confirmatory, randomized, global phase 3 trial designed to support approval worldwide



1. Pujade-Lauraine et al. *J Clin Oncol*. 2014;32(13):1302-1308. **2.** Richardson et al. *JAMA Oncol.* 2023;10.1001/jamaoncol.2023.0197. **3.** Moore et al. *Cancer*. 2017;123(16):3080-3087. **4.** Ab et al. *Mol Cancer Ther*. 2015;14(7):1605-1613. **5.** Markert et al. *Anticancer Res.* 2008;28(6A):3567-3572. **6.** Martin et al. *Gynecol Oncol.* 2017;147(2):402-407. 7. Data on file. **8.** Matulonis et al. *J Clin Oncol*. 2023:41(13):2436-2445. **9.** U.S. FOOD & DRUG ADMINISTRATION. BLA ACCELERATED APPROVAL. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/761310Orig1s000ltr.pdf. Accessed May 23, 2023.

MIRASOL: Phase 3 Trial of Mirv in FRα-High PROC

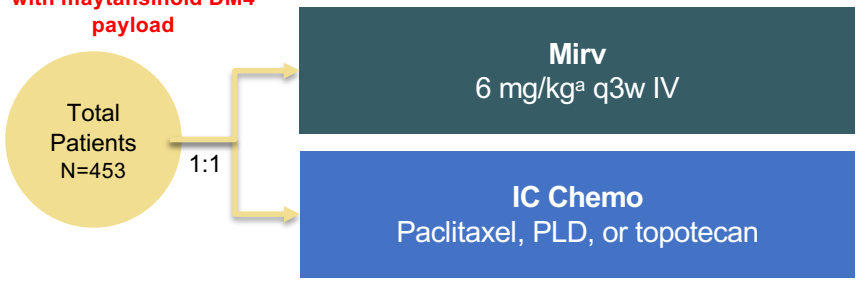
Study Design and Patients

Phase 3 Trial

Key Eligibility Criteria

- Platinum-resistant disease (PFI ≤6 months) with 1-3 prior lines of therapy
- FRα high (≥75% of cells staining positive with ≥2+ staining intensity by IHC)
- Prior bevacizumab and PARPi allowed
- Excludes primary platinum-refractory disease (primary PFI <3 months)

Mirv: FRα-directed ADC with maytansinoid DM4 payload



Primary endpoint: PFS (INV assessed)
Key secondary endpoints: ORR (INV assessed), OS, PROs

[a] Adjusted to ideal body weight.

1. Moore K, et al. *N Engl J Med.* 2023;389(23):2162-2174.

Patient Characteristics		Mirv n=227	IC Chemo n=226
Median age (range), years		63 (32-88)	62 (29-87)
Stage at diagnosis, n (%)	I-II	9 (4)	9 (4)
	III	137 (60)	147 (65)
	IV	76 (33)	65 (29)
*BRCA*mut, n (%)		29 (13)	36 (16)
Prior exposure, n (%)	Bev	138 (61)	143 (63)
	PARPi	124 (55)	127 (56)
	Taxanes	227 (100)	224 (99)
Prior IC Chemo type, n (%)	Paclitaxel	93 (41)	92 (41)
	PLD	82 (36)	81 (36)
	Topotecan	52 (23)	53 (23)
Prior systemic therapies, n (%)	1	31 (14)	32 (14)
	2	91 (40)	91 (40)
	3	105 (46)	103 (46)
PFI, n (%)	≤3 months	88 (39)	99 (44)
	>3 to ≤6 months	138 (61)	124 (55)
Primary PFI, n (%)	≤12 months	146 (64)	142 (63)
	>12 months	80 (35)	84 (37)

MIRASOL: Phase 3 Trial of Mirv in FRα-High PROC

Key Efficacy and Safety[1-4]

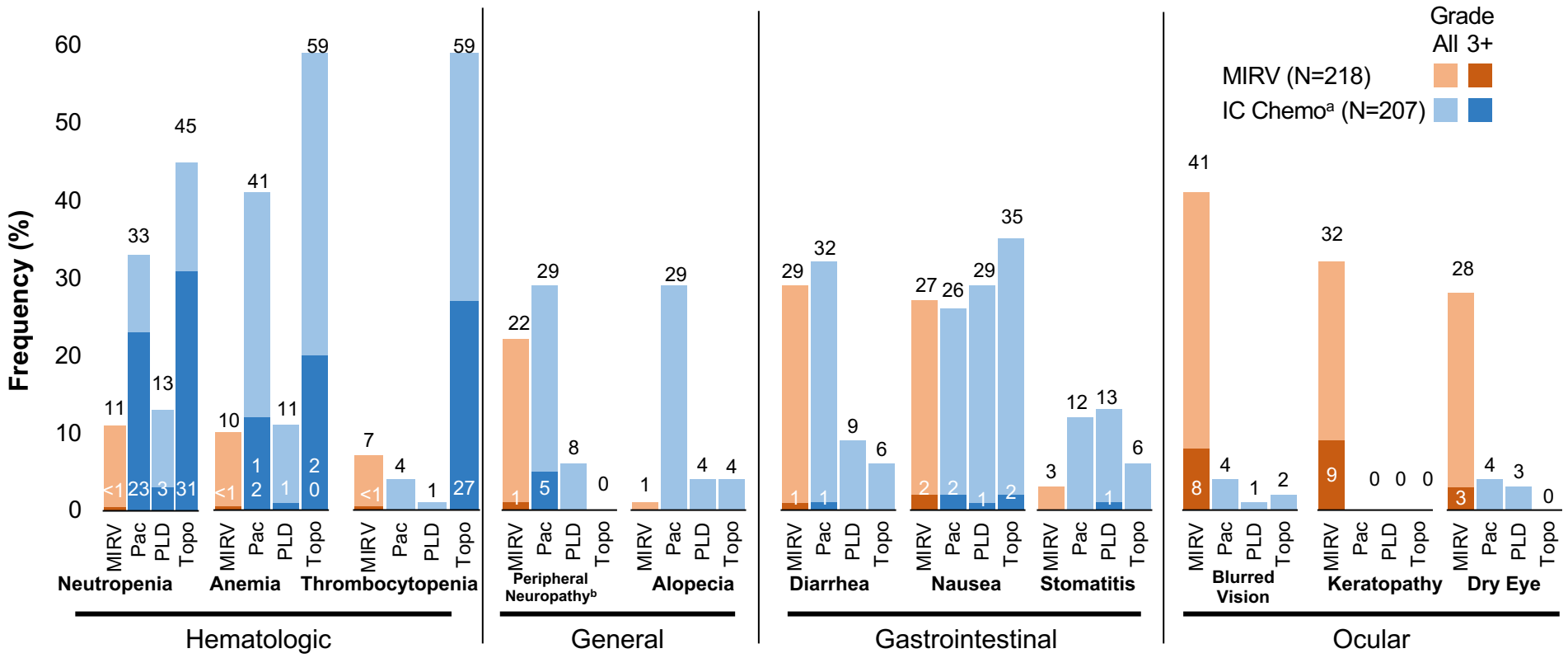
Overall Survival

Key Efficacy	Mirv (n=227)	IC Chemo (n=226)
mOS, mo (95% CI)	**16.85** (14.36-19.78)	**13.34** (11.37-15.15)
mPFS, mo (95% CI)	**5.59** (4.34-5.88)	**3.98** (2.86-4.47)
ORR, % (95% CI)	**41.9** (35.4-48.6)	**15.9** (11.4-21.4)
mPFS2, mo (95% CI)	**11.0** (9.3-12.0)	**7.6** (6.6-8.8)
Any TEAE, n (%)	211 (97)	194 (94)
Grade 3+ TEAE	97 (44)	113 (55)
Any SAE	55 (25)	69 (33)
Death	9 (4)	11 (5)
TEAEs leading to death	4 (2)	5 (2)
TRAEs leading to death	0	1 (<1)

1. Moore K, et al. *N Engl J Med.* 2023;389(23):2162-2174. **2.** Van Gorp T, et al. SGO 2025. Abstract 939696. **3.** Moore KN, et al. ESMO 2025. Abstract 1068P. 4. Mirvetuximab soravtansine-gynx. Prescribing Information. ImmunoGen; 2024.

- **Mirvetuximab soravtansine-gynx can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis.**
- **Conduct an ophthalmic exam including visual acuity and slit lamp exam prior to initiation of mirvetuximab soravtansine-gynx, every other cycle for the first 8 cycles, and as clinically indicated.**
- **Administer prophylactic artificial tears and ophthalmic topical steroids.**
- **Withhold mirvetuximab soravtansine-gynx for ocular toxicities until improvement and resume at the same or reduced dose.**
- **Discontinue mirvetuximab soravtansine-gynx for Grade 4 ocular toxicities.**

Differentiated Safety Profile: Treatment-Emergent Adverse Events



Data cutoff: March 6, 2023

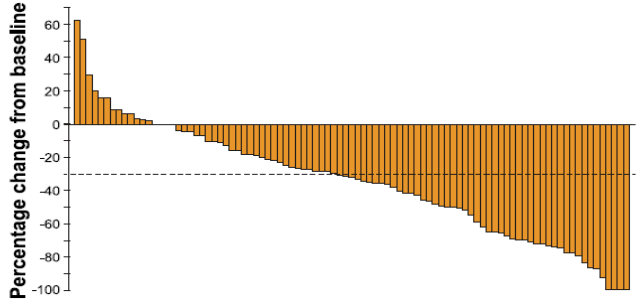
MIRV, mirvetuximab soravtansine; IC Chemo: investigator's choice chemotherapy; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; Topo, topotecan.

[a]Pac n=82 (39%), PLD n=76 (37%), Topo n=49 (24%). [b]Grade 2+ peripheral neuropathy events were observed in 12% and 16% of patients that received MIRV or paclitaxel, respectively.

FORWARD II dose escalation efficacy: Subgroup analysis of MIRV + BEV in FRα-expressing PROC

Efficacy summary		ITT (N = 94)
ORR, n (%) [95% CI]		41 (44) [33-54]
Best overall response, n (%)	CR	5 (5)
	PR	36 (38)
	SD	44 (47)
	PD	8 (9)
Median DOR, mo (95% CI)		9.7 (6.9-14.1)
Median PFS, mo (95% CI)		8.2 (6.8-10.0)

Maximum percentage change in tumour lesion size from baseline for individual patients in the ITT population

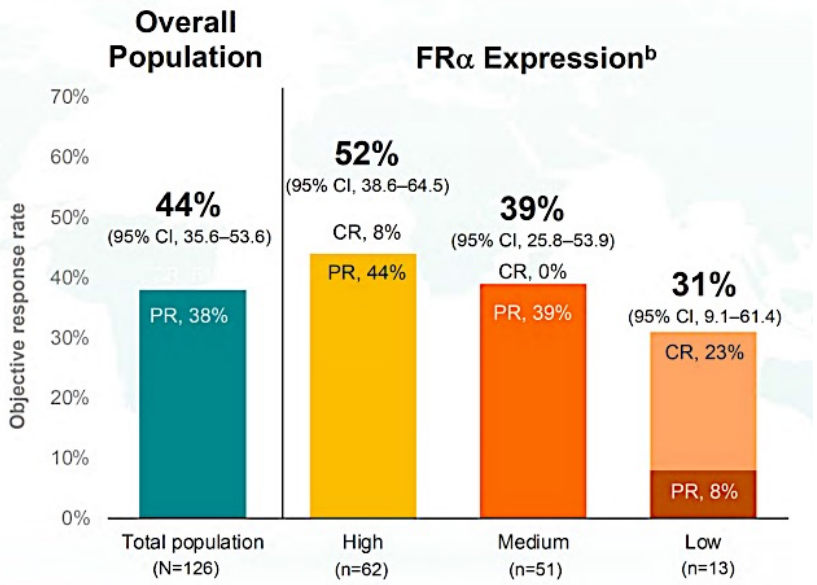


Efficacy summary by subgroup	FRα ≥75% (n = 44)	FRα 50-74% (n = 39)	FRα 25-49% (n = 11)	BEV-naive (n = 39)	BEV-pretreated (n = 55)
ORR, n (%) [95% CI]	21 (48) [33-63]	16 (41) [26-58]	4 (36) [11-69]	22 (56) [40-72]	19 (35) [22-49]
Median DOR, mo (95% CI)	9.7 (6.0-12.0)	9.7 (3.0-NR)	18.5 (NE)	10.4 (6.9-14.5)	9.7 (4.2-NR)
Median PFS, mo (95% CI)	9.7 (6.8-11.0)	6.9 (5.1-9.9)	8.6 (1.3-NR)	10.6 (8.2-14.5)	6.8 (5.3-8.2)

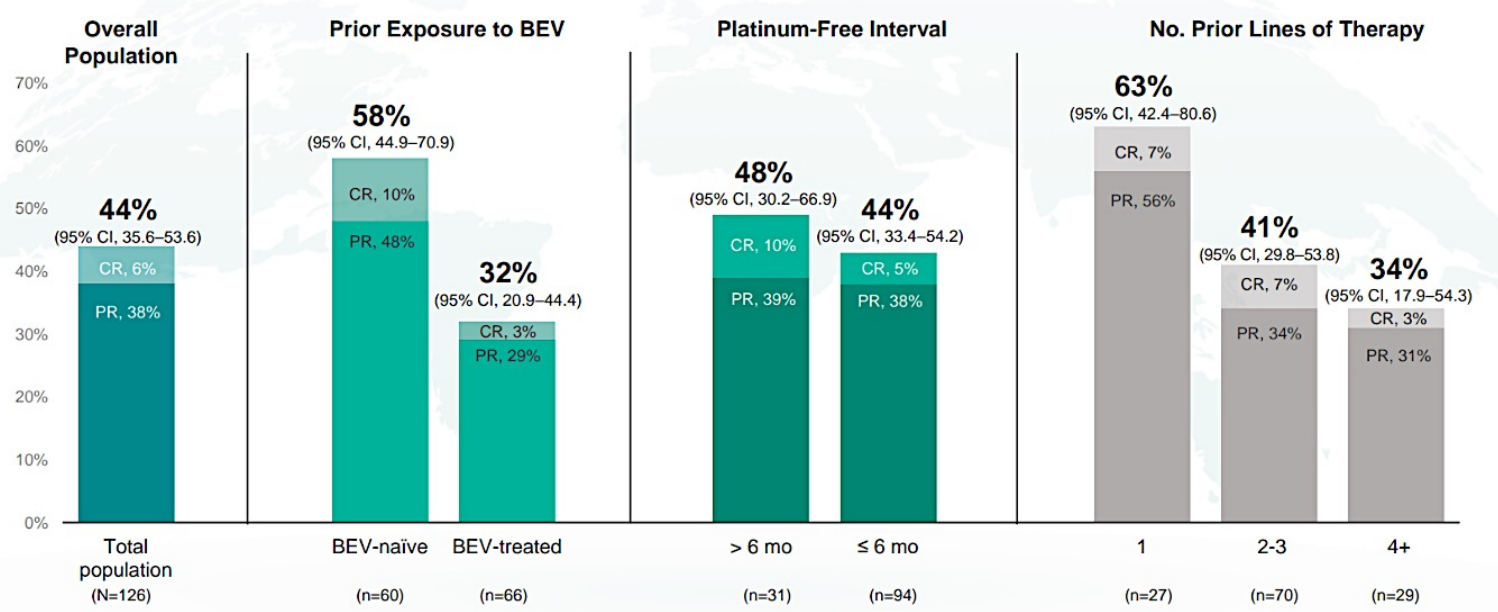
Gilbert L et al…O'Malley DM. Gynecol Oncol. 2023;170:241–247.

Phase 1b/2 FORWARD II: Overall Response Rate Entire Population PROC & PSOC

ORR[a] in the overall population and by FRα expression level subgroups



ORR[a] in subgroups by bev treatment status, platinum-free interval, and prior lines of therapy



[a] DOR (a secondary end point) was defined as the time from the date of first response (complete or partial response) to the date of PD or death from any cause, whichever occurred first.

[b] Low, 25% to 49%; medium, 50% to 74%; high ≥75% of tumor cells with ≥2+ staining intensity.

Bev, bevacizumab; CI, confidence interval; CR, complete response; DOR, duration of response; FRα, folate receptor alpha; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response.

O'Malley DM et al. IGCS 2022. Abstract 496 2. Gilbert L et al…O'Malley DM. Gynecol Oncol. 2023;170:241–247.

Phase 1b/2 FORWARD II: safety summary

Treatment-Related Adverse Events ≥20%

TRAE, n (%)[a]	MIRV 6 mg/kg + BEV 15 mg/kg (N=126)		
	All grades	Grade 3	Grade 4
Diarrhea	74 (59)	2 (2)	0 (0)
Blurred vision	71 (56)	1 (1)	0 (0)
Fatigue	64 (51)	5 (4)	0 (0)
Nausea	64 (51)	1 (1)	0 (0)
Peripheral neuropathy[b]	50 (40)	1 (1)	0 (0)
Keratopathy[c]	43 (34)	0 (0)	0 (0)
Decreased appetite	38 (30)	0 (0)	0 (0)
Dry eye	38 (30)	3 (2)	0 (0)
Hypertension	38 (30)	20 (16)	0 (0)
Thrombocytopenia	35 (28)	4 (3)	1 (1)
AST increased	33 (26)	6 (5)	0 (0)
Headache	33 (26)	0 (0)	0 (0)
Vomiting	33 (26)	1 (1)	0 (0)
ALT increased	29 (23)	6 (5)	0 (0)

- Most TRAEs were low grade; GI, ocular, and fatigue were the most common
- 48% of patients experienced grade ≥3 events; the most common was hypertension (16%)
- Due to treatment-emergent AEs, 30% discontinued MIRV and 37% discontinued BEV
  - 4 patients (3%) discontinued MIRV due to blurred vision
- Patients received a median of 8 cycles of MIRV+ BEV (range 1–35 cycles)
- One patient had a death that was deemed related to a study treatment (intestinal perforation possibly related to BEV)

O'Malley et al. IGCS 2022. Abstract 496.
L Gilbert …..DM OMalley, et al, Gyn Onc 2023

PICCOLO (NCT05041257) – Study Design[1-3]

A single-arm, open-label, phase 2 trial of MIRV in patients with ≥3L platinum-sensitive ovarian cancer with FRα-high expression

PICCOLO Patient Population (N=79)

Enrollment and Key Eligibility

- Platinum-sensitive disease (defined as radiographic progression >6 months from last dose of most recent platinum therapy)
- FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells[a]
- At least 2 prior platinum-containing regimens[b]
- Prior PARPi required if *BRCA*+
- Prior BEV not required
- Appropriate for single-agent therapy

Treatment Regimen

MIRV
(6 mg/kg AIBW Q3W)

Primary Endpoint

ORR by INV

Key Secondary Endpoint

DOR by INV

Other Secondary Endpoints

- Safety and tolerability
- CA-125 response (GCIG criteria)
- PFS
- OS
- Sensitivity analyses[c]

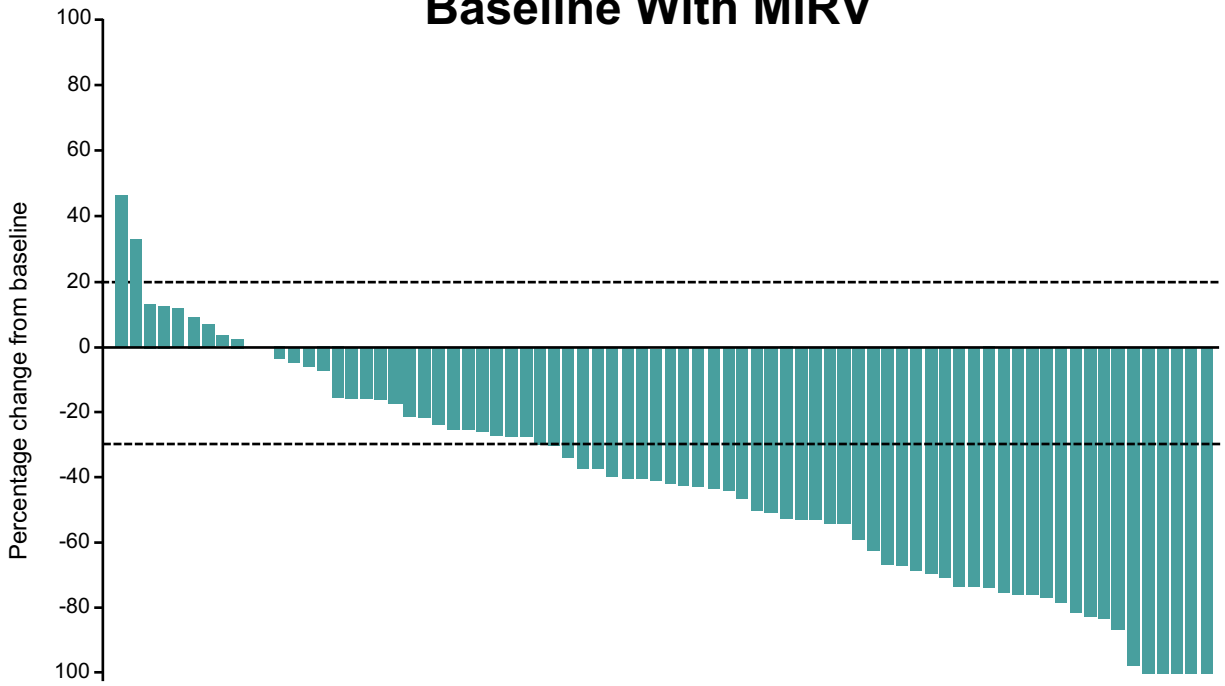
[a]FRα expression measured by the VENTANA FOLR1 (FOLR1-2.1 RxDx) Assay. [b]1 prior line if documented platinum allergy. [c]ORR, DOR, and PFS by BICR will be summarized as sensitivity analyses.

3L, third-line; AIBW, adjusted ideal body weight; BEV, bevacizumab; BICR, blinded independent central review; *BRCA*, BReast CAncer gene; CA-125, cancer antigen 125; DOR, duration of response; FRα, folate receptor alpha; GCIG, Gynecological Cancer InterGroup; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine-gynx; ORR, objective response rate; OS, overall survival; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; PFS, progression-free survival; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.

1. ClinicalTrials.gov identifier: NCT05041257. Updated April 22, 2024. Accessed July 29, 2024.; 2. Alvarez Secord A, et al. Poster presented at: International Gynecologic Cancer Society (IGCS) Annual Global Meeting; 29 September-1 October 2022; New York City, NY USA [Abstract 1556]. 3. Alvarez Secord A, et al. Poster presented at: Society of Gynecologic Oncology's (SGO) Annual Meeting on Women's Cancer; 18-21 March,2022; Phoenix, AZ USA. [Abstract 300].

Investigator Assessed Efficacy Measures

Maximum Tumor Percentage Change From Baseline With MIRV



Median time to response was 1.58 months
Median number of treatment cycles was 9 (range, 1 to 27)

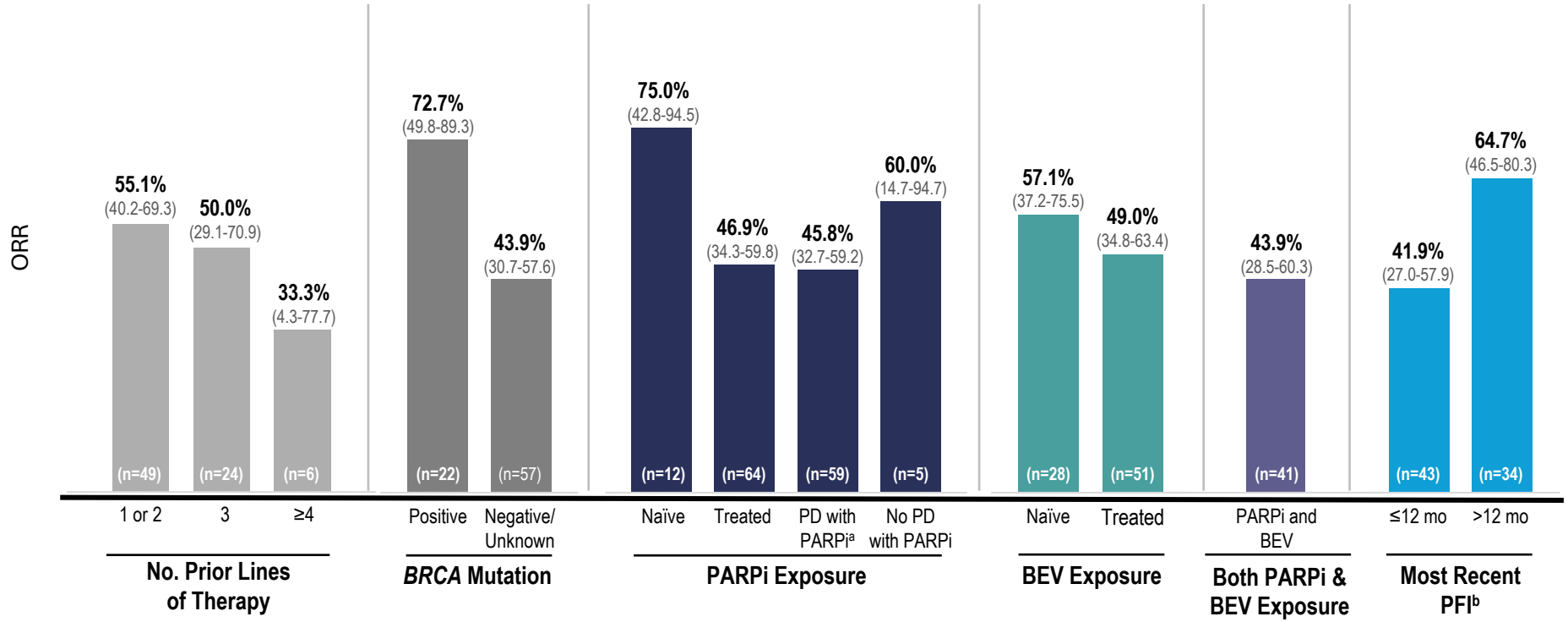
NCT05041257

Primary Endpoint	N=79
ORR, n (%) 95% CI	41 (51.9) 40.4-63.3
Best overall response, n (%)	
CR	6 (7.6)
PR	35 (44.3)
SD	29 (36.7)
PD	7 (8.9)
Secondary Endpoints	
Median DOR[a]	n=41
Months (95% CI)	8.25 (5.55-10.78)
Median PFS	N=79
Months (95% CI)	6.93 (5.85-9.59)
CA-125 response[b]	n=47
n (%)	35 (74.5)
95% CI	59.7-86.1

Data cutoff: January 17, 2024.
aCalculated among participants who had a complete or partial response. bAnalysis performed on the CA-125–evaluable population.
CA-125, cancer antigen 125; CI, confidence interval; CR, complete response; DOR, duration of response; MIRV, mirvetuximab soravtansine-gynx; ORR, objective response rate; PFS, progression-free survival; PD, progressive disease; PR, partial response; SD, stable disease.
1. ClinicalTrials.gov identifier: NCT05041257. Updated April 22, 2024. Accessed July 29, 2024.; 2. Alvarez Secord A, et al. Ann Oncol. 2025 Mar;36(3):321-330.

ORR by Subgroups

Total Population ORR: 51.9% (95% CI, 40.4-63.3)



NCT05041257

Data cutoff: January 17, 2024. ORR presented with 95% CI.

aIf the participant had progression of disease within 30 days after the last dosing of a PARPi or progression was listed as the reason for treatment discontinuation of a PARPi, the participant was defined as having progressive disease on prior PARPi and was included in this category. bPlatinum-free interval is defined as time from last dose of the latest line platinum therapy to the date of disease progression and/or relapse following that line of therapy (time rounded to whole number).

BEV, bevacizumab; BRCA, Breast Cancer gene; CI, confidence interval; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; PD, progressive disease; PFI, platinum-free interval; ORR, objective response rate.

Alvarez Secord A, et al. Ann Oncol. 2025 Mar;36(3):321-330.

Case

Recurrent high grade serous ovarian cancer

- 09/2013: TAH, BSO, pelvic and paraaortic lymphadenectomy, omentectomy and resection of abdominal wall nodule High grade serous carcinoma of the ovary - stage IIIB
- Completed 6 cycles of Carbo/Paclitaxel (dose dense)
- 10/2017 CT C/A/P with significant increase in size of right paracolic gutter soft tissue mass, mild free fluid, thickening of the urinary bladder wall, enlarged lymph node within the upper abdomen
- 12/2017: CT biopsy of right paracolic gutter mass- High grade serous carcinoma
- 2018: Completed 7 cycles of Carbo/Gem
- Progressed within 3 months of completing therapy

Tissue Testing

- NGS testing of Recurrence 12/2017: EGFR D314N, NF1 exon 1 loss, MYC amplification, TP53 D281E, MLH1 R325Q.
- Microsatellite Stable. TMB-intermediate.

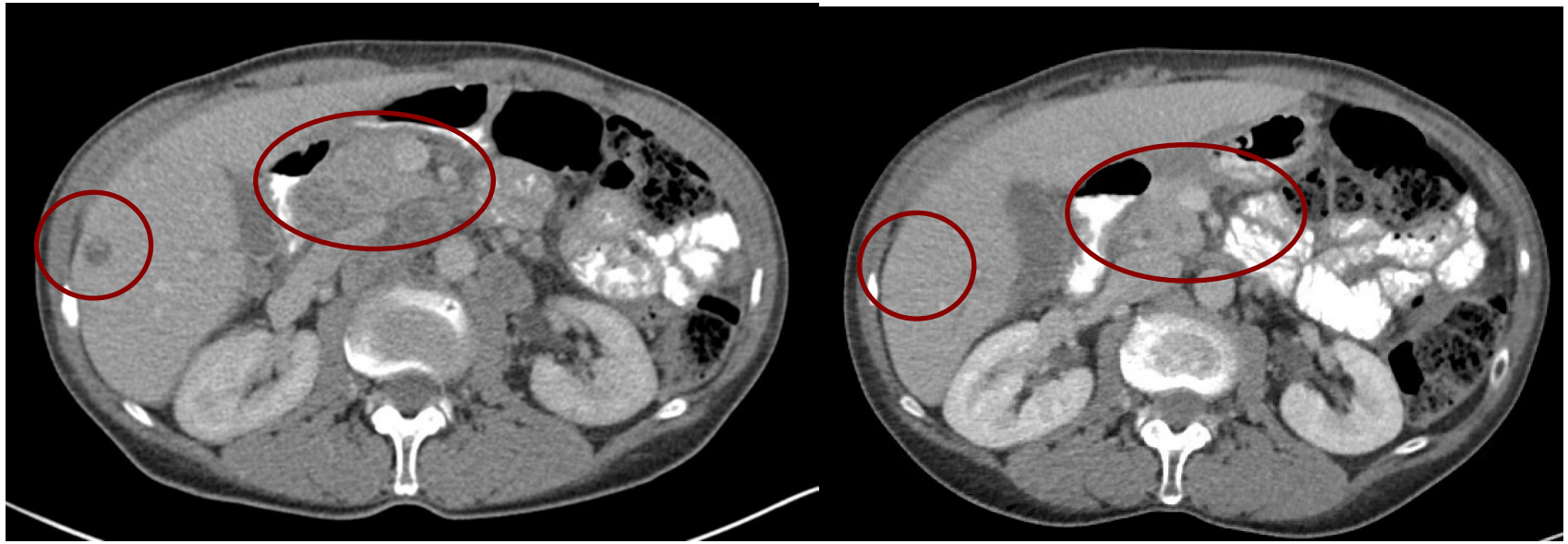
Clinical Trial

- 2018: Clinical trial Olaparib and AZD6738 (WEE1i) x 3 cycles - progressed
- Transfer of Care to The James/OSU
- **1/2019: On clinical trial: C1D1 mirvetuximab 6 mg/kg & Bevacizumab 15 mg/kg**
- **8/2020: C27 delayed 2 weeks due to Grade 2 neuropathy, Mirv reduced to 5 mg/kg**
- 2/2021: Received 35 cycles of mirvetuximab + Bev; clinical trial closed
- 3/2021: Started treatment on Compassionate Use mirvetuximab and Bev (commercial supply) on single patient compassionate use trial.
- Continued on therapy until Oct, 2022 when she elected to take a holiday
- 5/2023: Presented with Brain Mets.

Response

Pre Cycle 1 – multi-focal disease

Cycle 33 – near CR



CA 125 Results	Notes
272	C1 Imgn/Bev
170	C2
96	C3
34	C4
12	C5
7	C6
5	C7

Clinical Trial Participation

November 23, 1958 — July 16, 2025

“Patricia and her husband can still enjoy their lives — taking their three dogs for long walks, tending to the forest they manage on their property and riding a 12-mile bike trail almost every day. The 300-mile round trip to Columbus for treatment is worth that increase in quality of life.”

2/2021

https://cancer.osu.edu/for-patients-and-caregivers/learn-about-cancers-and-treatments/innovation-at-the-james/clinical-trials/clinical-trial-patient-stories/patricia-smith

Discussion Questions

Who should be tested for FRα expression, when and how?

When and for whom do you use mirvetuximab soravtansine in your own practice? What is your FRα expression cutoff? Do you always use mirvetuximab soravtansine as monotherapy, or do you ever combine it with other agents (eg, bevacizumab)?

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Ovarian Cancer Symposium

Research To Practice | ONS 2026

Kathryn Schlenker, MSN, WHNP-BC, AGNP-C

Division of Gynecologic Oncology

University of Alabama at Birmingham

Nursing Considerations for Toxicities Associated with Mirvetuximab Soravtansine

Mirvetuximab Soravtansine

- Antibody drug conjugate (ADC) that targets FOLR1
  - Approximately 40% ovarian cancers have high FOLR1 expression (≥ 75%)
    - Strong correlation with high grade serous histology
  - Currently FDA approved for use in platinum resistant (PR) ovarian cancer
    - Monotherapy (in tumors with ≥ 75% FOLR1 expression)
  - NCCN Guidelines category 2B recommendation
    - In combination with Bevacizumab (in tumors with ≥ 25% FOLR1 expression) in PR setting
    - In combination with Bevacizumab (in tumors with ≥ 50% FOLR1 expression) in PS setting
  - Ongoing clinical trials in the neoadjuvant/platinum sensitive (PS) settings (no current FDA approvals)

- Dosing/route/frequency: 6 mg/kg given IV q21 days
- Premedications (day of treatment):
  - Dexamethasone
  - Diphenhydramine
  - Acetaminophen
  - Palonosetron

Incidence of Ocular Toxicities

- Most common ocular AEs from Mirvetuximab:
  - Blurred vision (48%)
  - Keratopathy (36%)
  - Dry eyes (27%)
  - Photophobia (14%)
  - Eye pain (10%)
- Majority are grade 1-2 and the median time to development is ~5 weeks (after cycle 2)
- Most are managed with dose delay or dose reduction; discontinuation in ~1% patients

Monitoring and Management Ocular Events

- Ocular exams (visual acuity and slit lamp examination)
  - Baseline prior to initiation of Mirvetuximab
  - Every other cycle for the first 8 cycles, then as clinically indicated
  - Ocular assessment form (visual acuity, keratitis/keratopathy/uveitis)
- Prophylactic Eye Drops:
  - Steroid drops (Prednisolone acetate 1%)
    - 6x/day starting the day before infusion through day 4
    - 4x/day days 5-8
  - Artificial tears 4x daily *preservative free* or more if needed
- Helpful measures: avoid contact lenses, use UVA/UVB sunglasses when exposed to sunlight, warm compresses over eyelids in the evening

Other Common Toxicities and Management

- Pneumonitis (10%) – 1% were grade 3 and 1 patient with grade 4
  - Symptoms: Cough, dyspnea, hypoxia, fever
  - High resolution chest CT
  - Rule out infectious etiology
  - Hold until grade 1 or better; permanently discontinue in grade 3 or 4
  - Steroids, PFTs
- Peripheral Neuropathy (36%)
- Lab abnormalities: Anemia, thrombocytopenia, neutropenia, incr AST/ALT/Alk Phos
- GI: Nausea, vomiting, constipation, diarrhea, abdominal pain
- General: Fatigue, decreased appetite

Case Presentation

77yo patient with stage IV high grade serous ovarian cancer initially presented with an abdominal mass in 2023. CT revealed omental nodularity, peritoneal carcinomatosis, ascites, hepatic lesions, and lung nodules. She underwent a Dx LSC with peritoneal and omental biopsies and evacuation of ascites. Path c/w HGSOC. Germline negative. NGS: FOLR1+ (75%), HR proficient, sBRCA1/2 neg, PD-L1 positive CPS:1, ERBB2 neg, P53 mut. Enrolled in UAB2031 (Mirvetuximab + Carboplatin in neoadjuvant setting) and received lead in Carbo dose followed by 3 cycles Mirv/Carbo. She then underwent an Xlap/BSO/OMX/pelvic peritoneal stripping. She resumed NA Mirv/Carbo x3 cycles. **Mirv delayed with cycle 6 for grade 2 keratopathy with reported blurred vision.** CT scan done after 6 cycles – showed a complete response. OV125 normalized. She was put on q3 month surveillance with imaging. In August 2024, she reports some weight gain but was otherwise asymptomatic. CT scan revealed new peritoneal and mesenteric implants and new lung noduled bilaterally. We restarted her on Mirv/Carbo + Bevacizumab. **Reported new blurred vision with cycle 3. Eye exams revealed non-confluent superficial keratitis. We continued treatment but dose reduced to 5mg/kg.** She completed 6 cycles and had a near complete resolution of disease. She continued on Mirv/Bev maintenance for 10 cycles. CT and PET scan negative at that time and she elected to stop treatment and go back on surveillance. She remains NED to date and is actively involved in our local ovarian cancer awareness organization.

Other Approved and Investigational Antibody-Drug Conjugates in OC

Phase II DESTINY-PanTumor02 Study of T-DXd for HER2-Expressing Solid Tumors

A two-part, Phase 2, open-label, multicenter study (NCT04482309)

- **Part 1 (complete)**

Key eligibility criteria

- Locally advanced, metastatic, or unresectable solid tumors
- HER2 expression (IHC 3+ or 2+)* scored using current ASCO/CAP guidelines for scoring HER2 in gastric cancer[1]
- Disease progression following ≥1 prior systemic treatment or without alternative treatment options
  - Prior HER2-directed therapy allowed

Treatment

T-DXd 5.4 mg/kg IV Q3W

Primary endpoint

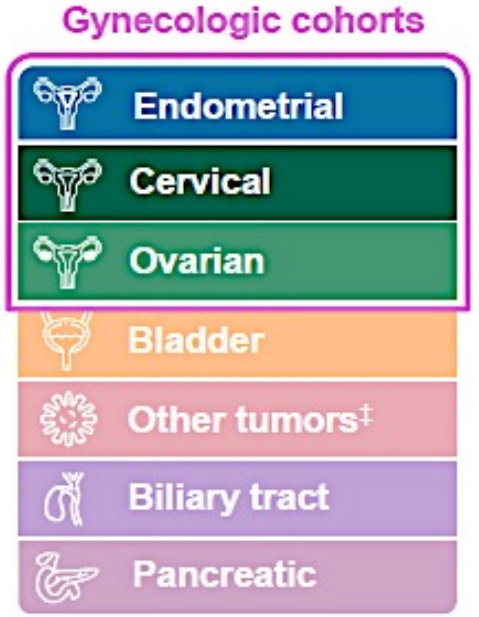
- Confirmed ORR†

Secondary endpoints

- DOR,† DCR,† PFS,† OS
- Safety and tolerability

Final analysis data cutoff

- October 10, 2024



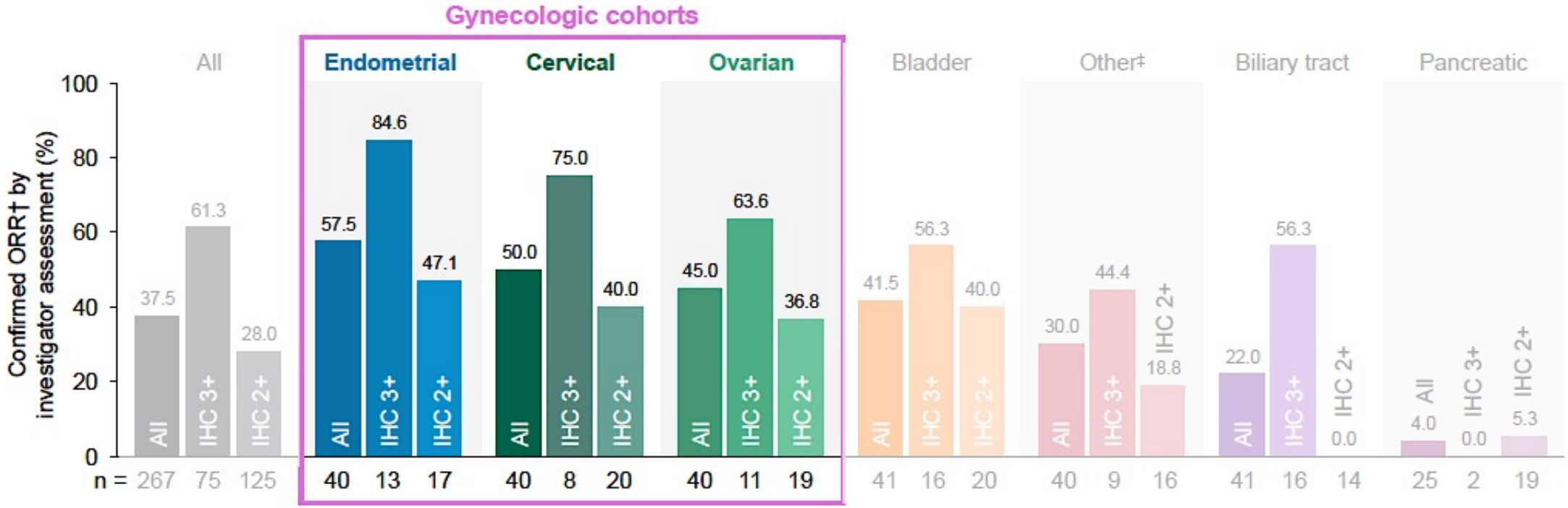
- **Part 2 (recruitment ongoing)**
  T-DXd in any HER2 IHC 3+ and IHC 2+/ISH+ solid tumors, and **HER2 IHC 2+/1+ gynecologic solid tumors**

*HER2 testing at enrollment was based on local testing; however, if local testing was not available, enrollment was determined by central HER2 testing (HercepTest [DAKO]); retrospective central HER2 testing was performed for patients enrolled based on a local HER2 test result; †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). ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan. 1. Bartley AN, et al. *Arch Pathol Lab Med*. 2016;140:1345–1363

Makker V et al. SGO 2026.

RTP RESEARCH TO PRACTICE

DESTINY-PanTumor02 Part 1 Final Analysis: Investigator-Assessed Confirmed ORRs with T-DXd by Tumor Cohort and Central HER2 IHC Status



- Compared with the primary analysis,[1] one additional patient with bladder cancer (HER2 IHC 2+ by central testing) achieved a confirmed objective response by investigator assessment
- Results by investigator assessment were consistent with those by independent central review

Investigator-assessed ORR analyses were performed for patients who received ≥1 dose of T-DXd (n=267). Investigator-assessed confirmed ORR in all patients: 37.5% (95% CI 31.6, 43.6). *Similar to ORRs by central HER2 IHC status, investigator-assessed confirmed ORR was greatest for patients with HER2 IHC 3+ tumors (52.3% [95% CI 42.6, 61.8]; n=111) versus those with IHC 2+ tumors (26.5% [95% CI 19.6, 34.3]; n=151) by the local or central HER2 test result used for enrollment; †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). CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan. 1. Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42:47–58

Makker V et al. SGO 2026.

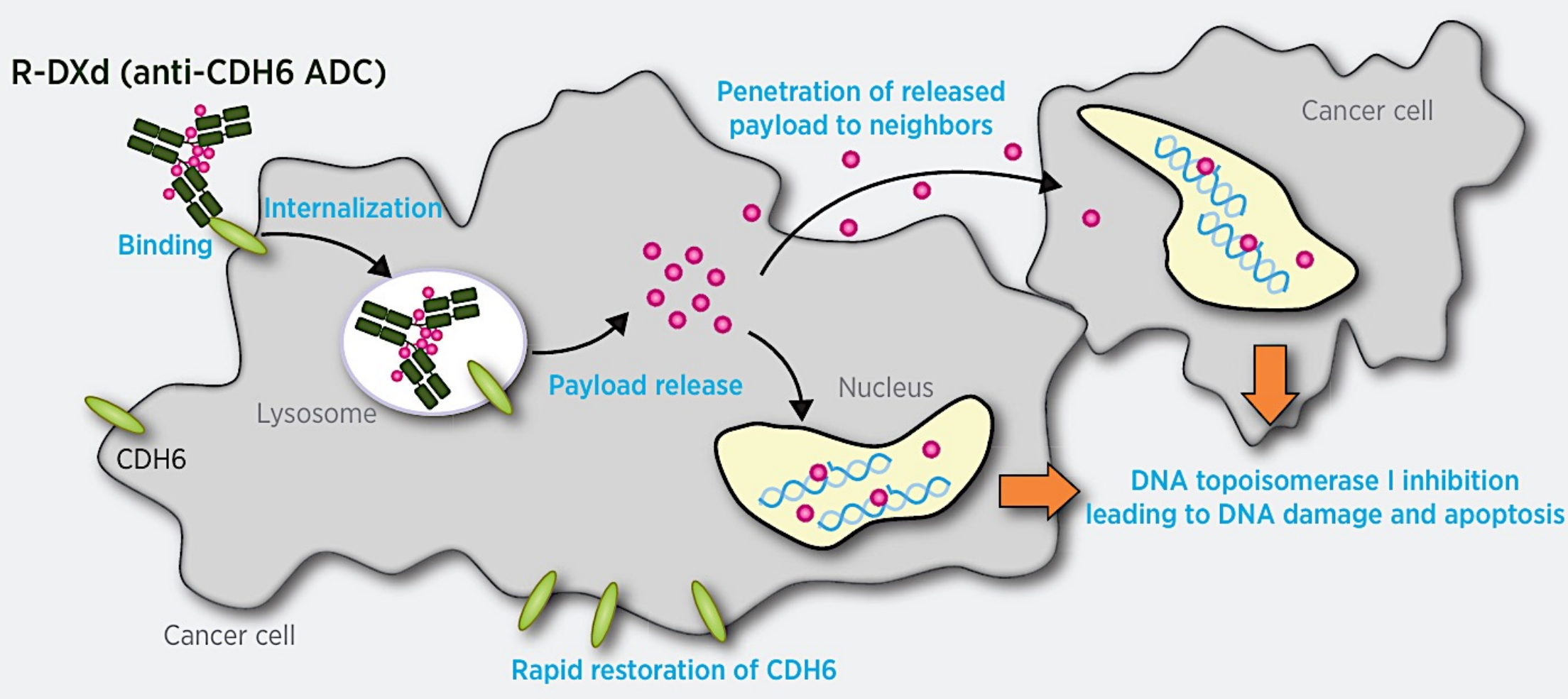
Discussion Questions

Who should be tested for HER2 overexpression, when and how?

When and for whom do you use trastuzumab deruxtecan in your own practice? How do you decide between it and other available strategies for patients who are eligible?

What do you tell your patients about to start T-DXd about potential toxicities? What signs and symptoms should prompt them to contact you?

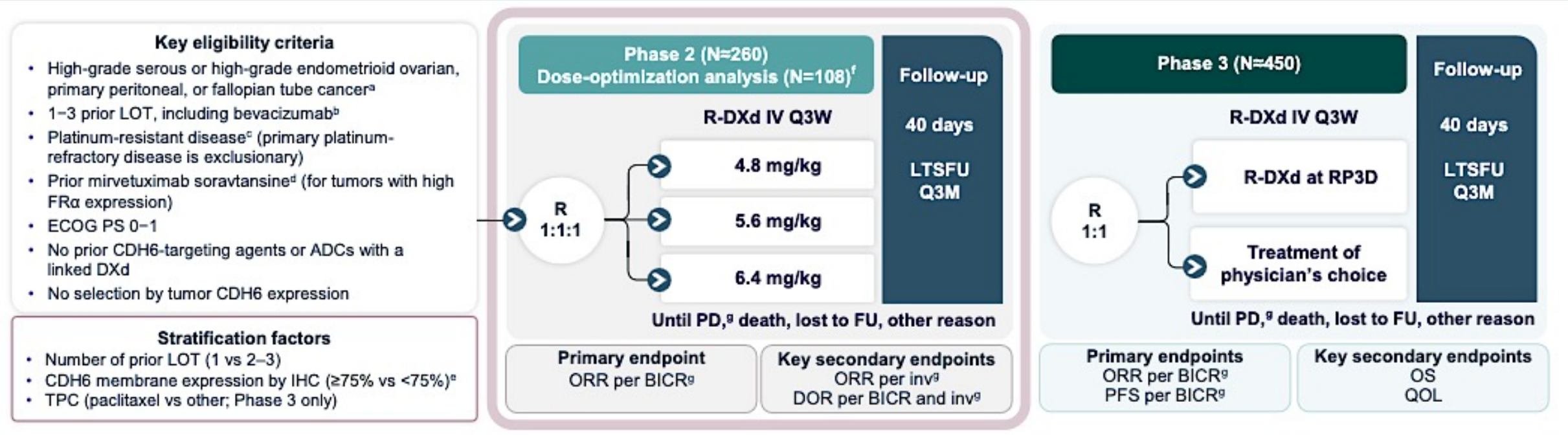
Raludotatug Deruxtecan (R-DXd) Mechanism of Action



ADC = antibody-drug conjugate

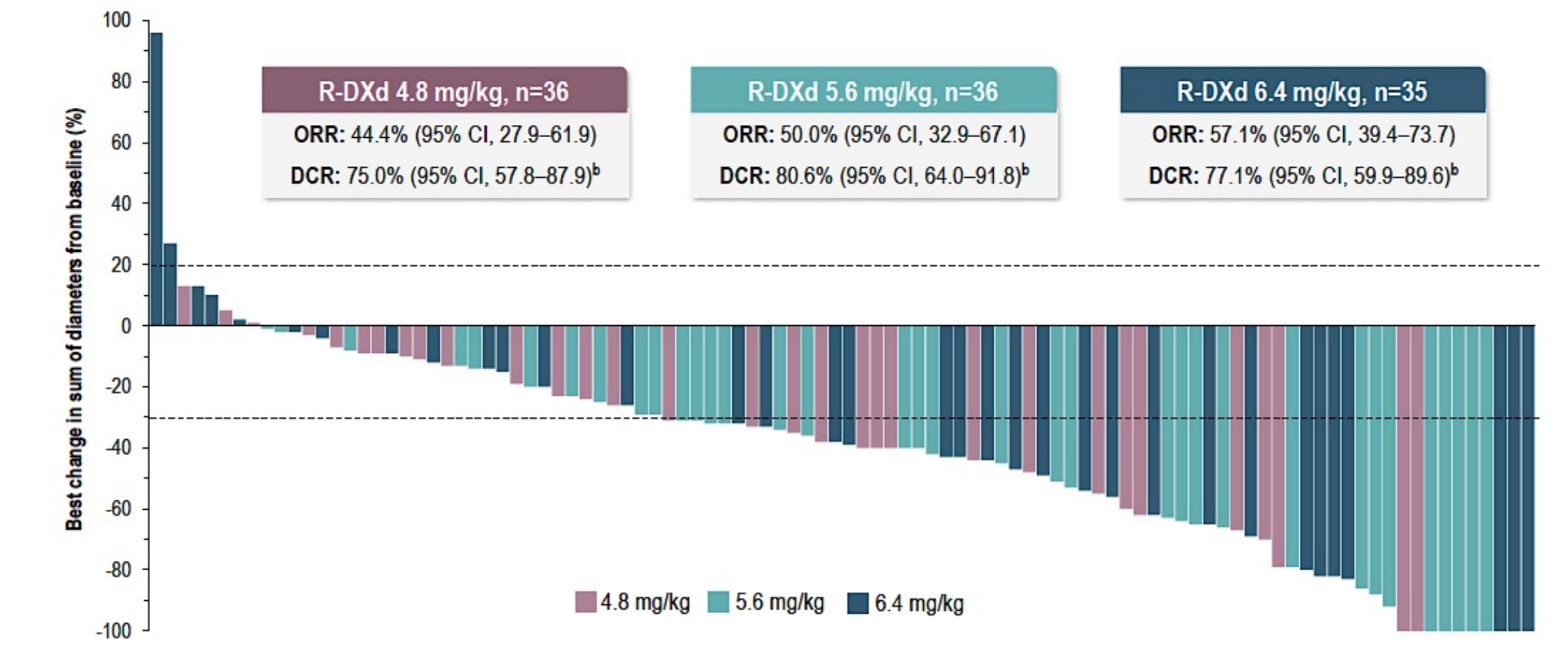
Suzuki H et al. *Mol Cancer Ther* 2024;23(3):257-71.

REJOICE-Ovarian01: A Phase II/III Trial of Raludotatug Deruxtecan (R-DXd) for Platinum-Resistant Ovarian Cancer



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

REJOICE-Ovarian01 Phase II: ORR and Tumor Response with Raludotatug Deruxtecan (R-DXd) for Platinum-Resistant Ovarian Cancer



ORR = objective response rate; DCR = disease control rate

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

RTP RESEARCH TO PRACTICE

Discussion Questions

Based on available data, where do you see R-DXd potentially fitting into the OC treatment paradigm?

What would you tell a patient about to start R-DXd about potential toxicities? How similar and different are they from those with T-DXd?

Schematic Diagram of Torvutatug Samrotecan (AZD5335)

- 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.

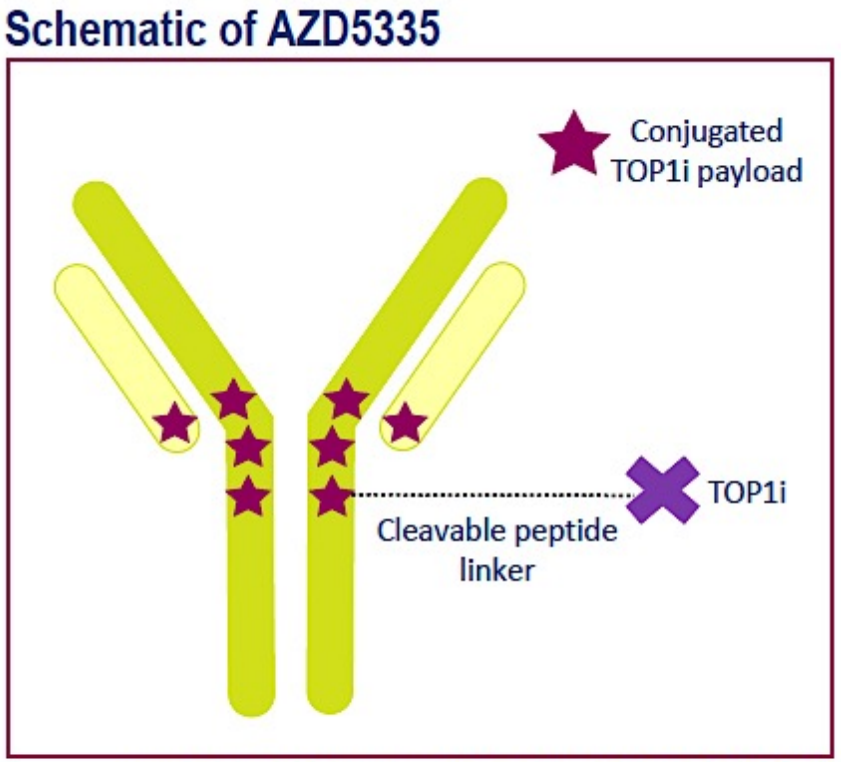


Figure adapted from Gymnopoulos M, et al. Presented at AACR 2023 (LB025).

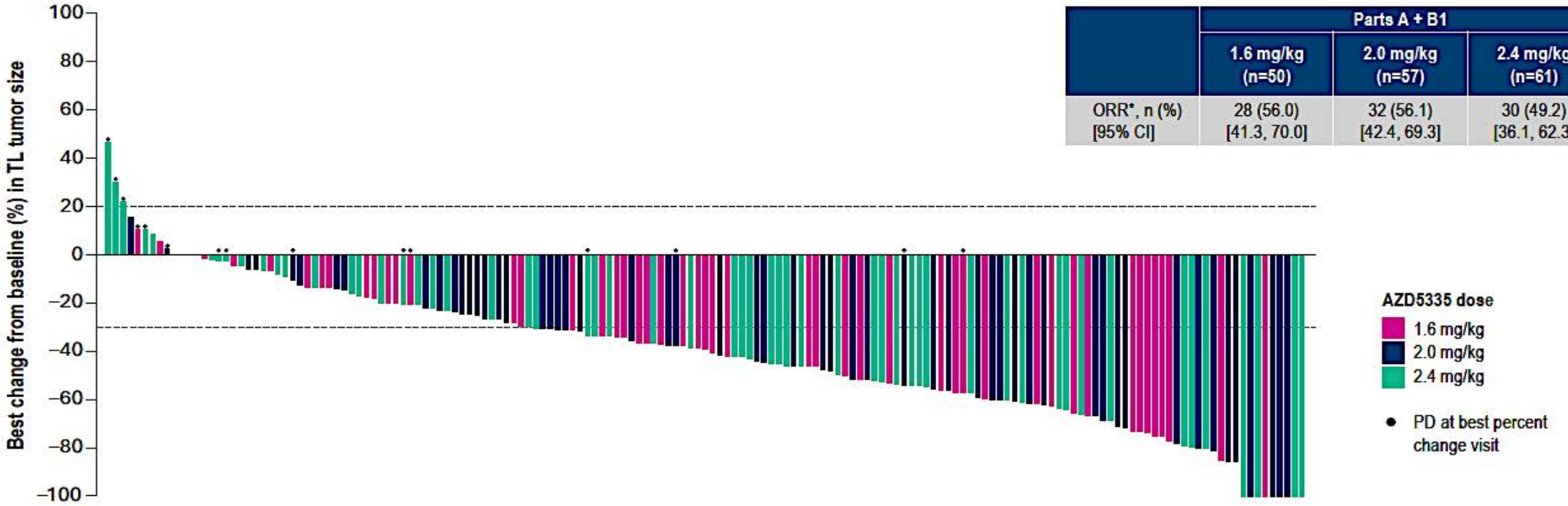
ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; FRα, folate receptor α; OC, ovarian cancer; TOP1i, topoisomerase 1 inhibitor

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).

First-in-Human Study of Torvutatug Samrotecan (AZD5335) for Platinum-Resistant Ovarian Cancer

AZD5335 demonstrates efficacy across 1.6–2.4 mg/kg dose 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).

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

Discussion Questions

Do you believe that any of the FRα-targeted antibody-drug conjugates in development will have significant activity in patients with disease progression on mirvetuximab soravtansine?

Do you believe any of these agents will be more effective or better tolerated than mirvetuximab soravtansine?

Agenda

Module 1: Overview of Ovarian Cancer (OC)

Module 2: Role of PARP Inhibitors in Advanced OC

Module 3: Current and Potential Future Role of Mirvetuximab Soravtansine in OC

Module 4: Role of Relacorilant in Advanced OC

Module 5: Utility of Immune Checkpoint Inhibition in Advanced OC

RTP
RESEARCH
TO PRACTICE

Role of Relacorilant in Advanced OC

David O'Malley, MD
Director for Translational and Clinical Research Partnerships at OSUCCC
Leader of Clinical Trial Innovation in the Center for Cancer Innovation
Professor, Division of Gyn Oncology
John G. Boutselis Chair in Gynecologic Oncology
Co-Director, Gyn Oncology Phase I Program

Ovarian Cancer Portfolio Lead, GOG-P
BOD, GOG Foundation

The James

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Creating a cancer-free world. One person, one discovery at a time.

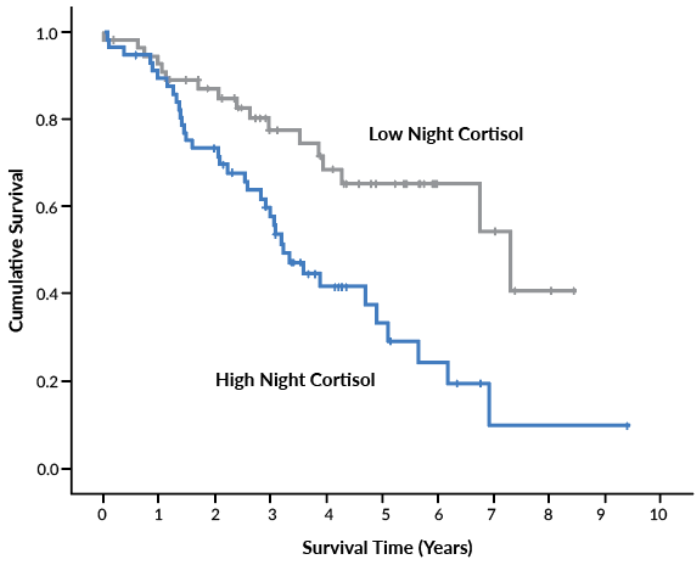



Agenda

- Incidence and clinical relevance of glucocorticoid receptor (GR) overexpression in OC
- Mechanism of action of the selective GR modulator relacorilant; rationale for combining relacorilant with chemotherapy in advanced OC
- Published findings with relacorilant plus nab paclitaxel in patients with platinum-resistant advanced OC

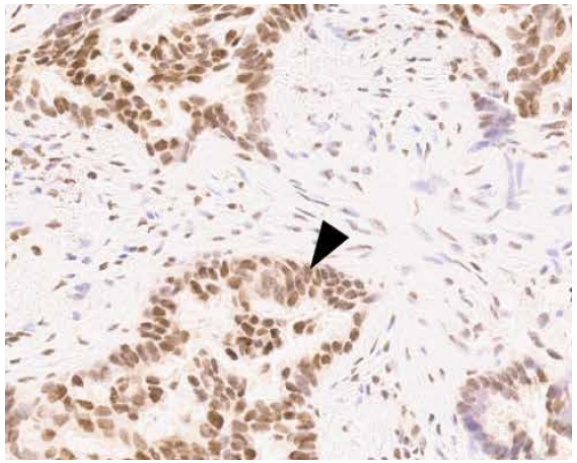
Glucocorticoid Receptor Signaling Is Implicated in the Poor Outcomes of Patients with Ovarian Cancer

Ovarian Cancer Patients With High Nocturnal Cortisol Are Reported to Have Shorter Overall Survival



Psychoneuroendocrinology. 2015;53:256–267.

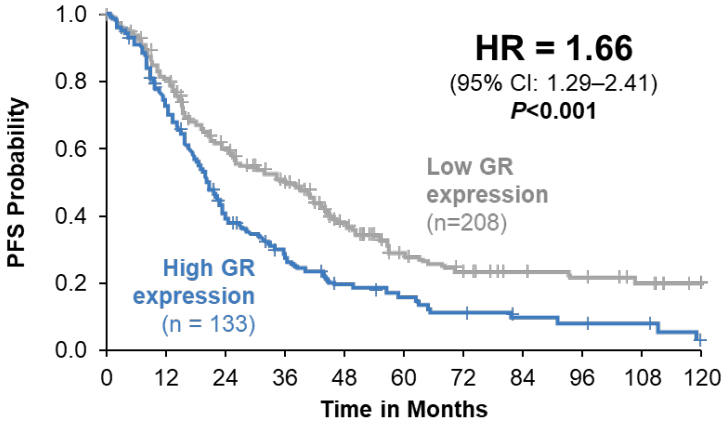
Epithelial Ovarian Tumor Cells Express High Levels of GR



Nuclear expression of the GR in tumor cells (arrowhead) from a high-grade serous carcinoma. Immunoreactivity is shown by brown chromogen against a blue nuclear counterstain.

Lorusso et al. SGO 2026. Poster 247.

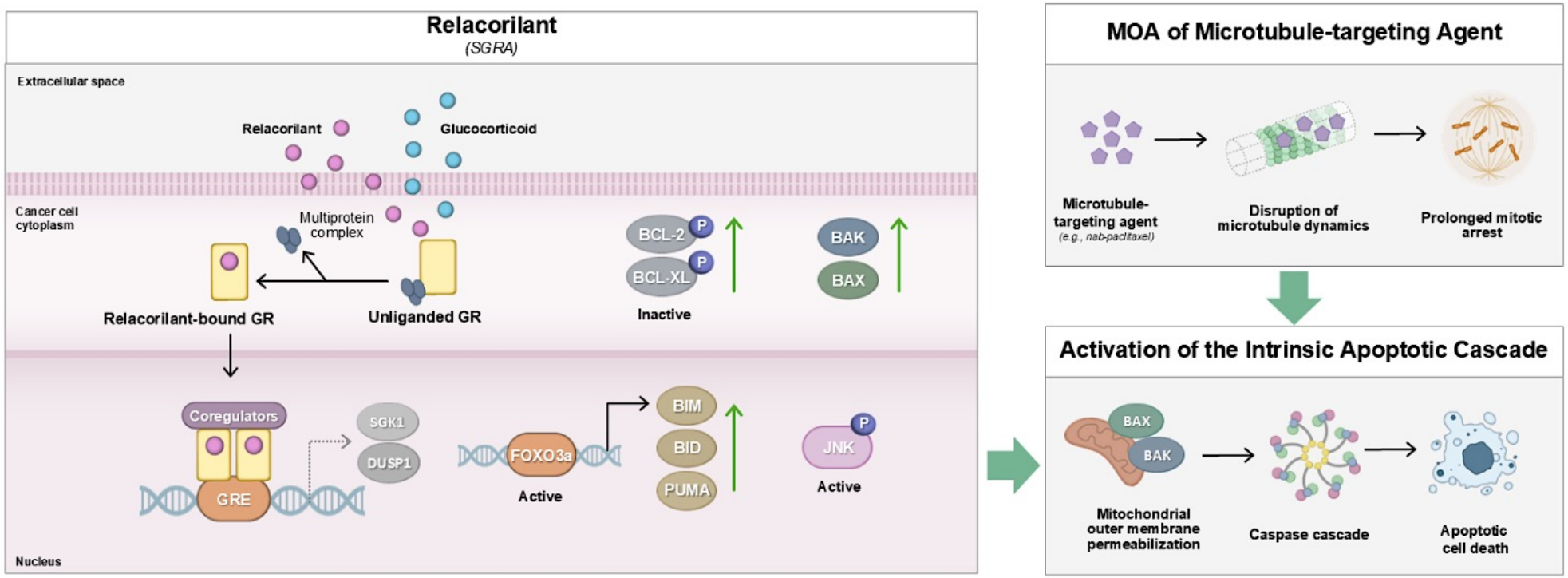
High GR Expression Is Associated With Shorter Progression-Free Survival in Ovarian Cancer



Gynecol Oncol. 2017;146(1):153–160.

CI, confidence interval; GR, glucocorticoid receptor; HR, hazard ratio; PFS, progression-free survival.

Relacorilant Restores Tumor Sensitivity to Chemotherapy

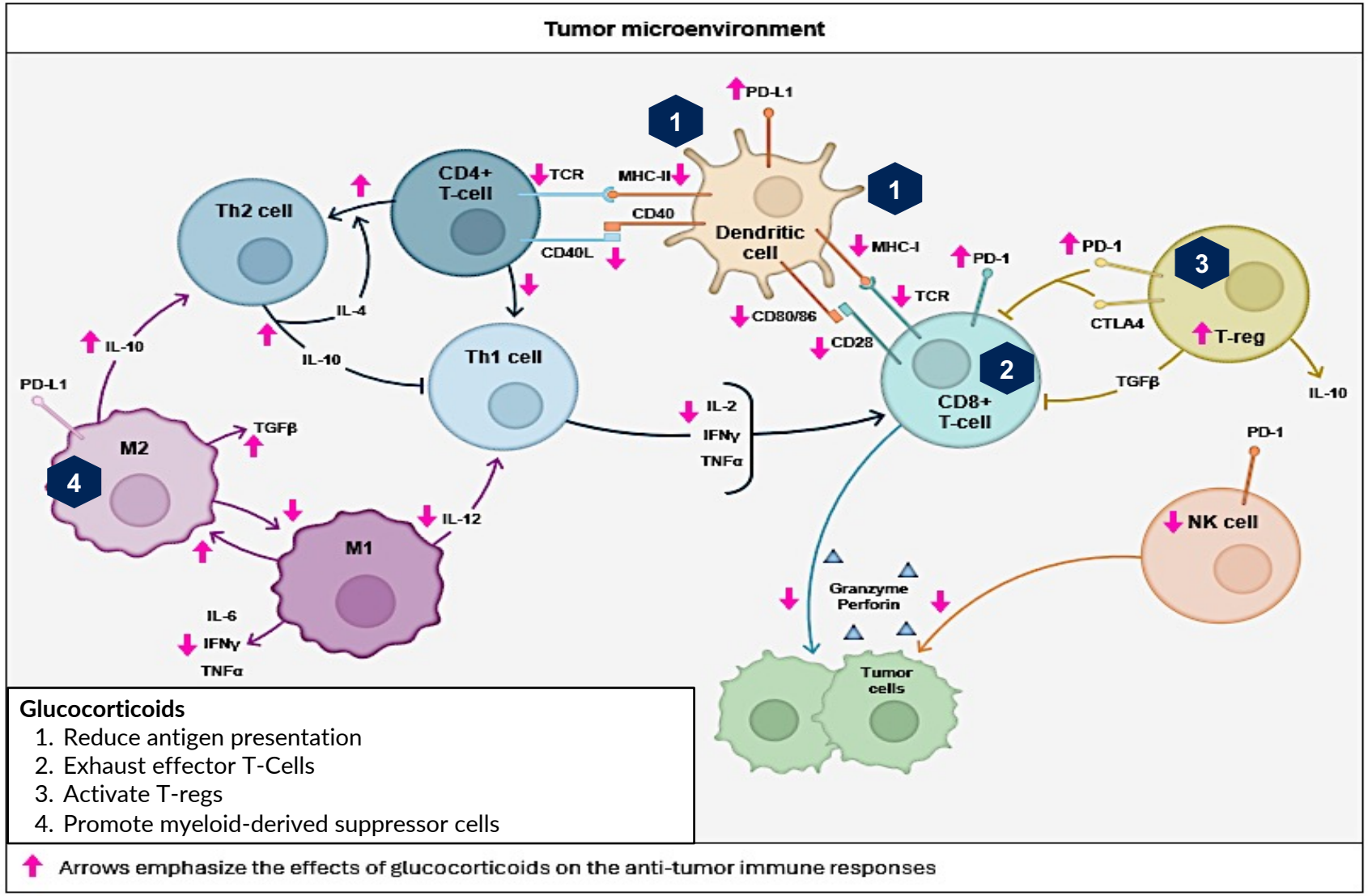


- Relacorilant inhibits the GR, reducing expression of genes that encode for the anti-apoptotic proteins SGK1 and DUSP1
- Reduced SGK1 and DUSP1 increases the activity of pro-apoptotic BCL-2 family members leading to cell death when exposed to chemotherapy

BAK, BCL-2 antagonist/killer; BAX, BCL-2 associated X; BCL-2, apoptosis regulator; BCL-XL, BCL2 like 1; BID, BH3 interacting domain death agonist; BIM, BCL2 like 11; DUSP1, dual-specificity phosphatase 1; FOXO3a, forkhead box O3; GR, glucocorticoid receptor; GRE, glucocorticoid response element; JNK, c-Jun N-terminal kinase; MOA, mechanism of action; MTA, microtubule-targeting agent; P, phosphorylated; PUMA, p53 upregulated modulator of apoptosis; SGK1, serum/glucocorticoid-regulated kinase 1; SGRA, selective GR antagonist.

Int Immunopharmacol. 2023:120:110312, Horm Cancer 2018;9:95-107, Clin Cancer Res 2022;28:3214, Eur J Med Chem. 2014;87:89, Nat Rev Cancer 2004;4:253, Front Pharmacol 2022:13:933112, Biomolecules 2023;13(4):653, Trends Pharmacol Sci 2013;34:518, Mol Cancer 2018;17:104, Oncogene 2008;27:6245

Activation of the GR Suppresses Anti-Cancer Immunity



CTLA-4, cytotoxic T-cell associated protein 4; DC, dendritic cell; IL, interleukin; MHC, major histocompatibility complex; NK, natural killer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand 1; TCR, T-cell receptor; TGFβ, transforming growth factor beta; Th1/2, T helper 1/2; TNFα, tumor necrosis factor alpha; T-reg, T regulatory cell.

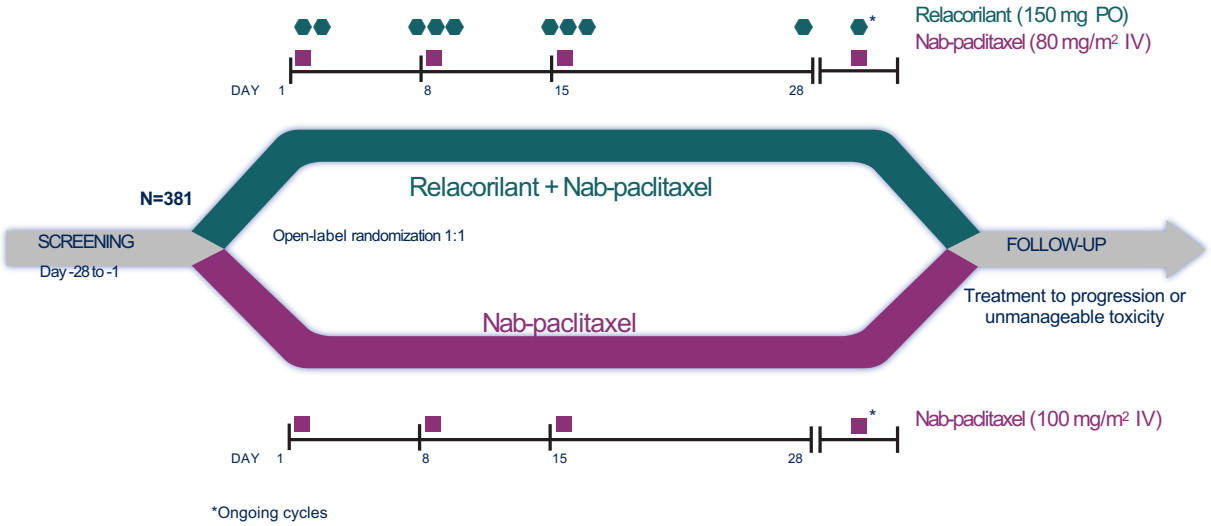
Int Immunopharmacol. 2023:120:110312; *Horm Cancer.* 2018;9(2):95–107; *Clin Cancer Res.* 2022;28(15):3214–3224; *Eur J Med Chem.* 2014;87:89–124; *Nat Rev Cancer.* 2004;4(4):253–265; *Front Pharmacol.* 2022:13:933112; *Biomolecules.* 2023;13(4):653; *Trends Pharmacol Sci.* 2013;34(9):518–530; *Mol Cancer.* 2018;17(1):104; *Oncogene.* 2008;27(48):6245–6251.

ROSELLA | Study Schema

Population

- Epithelial ovarian, primary peritoneal or fallopian tube cancer
- ECOG performance status 0 or 1
- Progression <6 months after the last dose of platinum therapy (excluding no response to, or progression in <1 month of primary platinum)
- 1–3 prior lines of therapy
- Prior bevacizumab required

NCT05257408



Stratification Factors

- Prior lines of therapy (1 vs >1)
- Region (North America vs Europe vs Korea, Australia, & Latin America)

Dual Primary Endpoints

- Progression-free survival (PFS) by RECIST v1.1 per blinded independent central review
- Overall survival

Secondary Endpoints

- PFS by RECIST v1.1 per Investigator
- ORR, DoR, CBR (RECIST v1.1)
- Response by CA-125 GCIG criteria
- Combined response (RECIST v1.1 and CA-125 GCIG criteria)
- Safety

First patient enrolled: 5th January 2023
Last patient enrolled: 8th April 2024
Data cutoff: 24th February 2025
Conducted at 117 sites in 14 countries.

Additional Study Identifiers: APGOT-Ov10, LACOG-0223, and ANZGOG-2221/2023.
CA, cancer antigen; CBR, clinical benefit rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; GCIG, Gynecologic Cancer Intergroup; IV, intravenous; ORR, objective response rate; PFS, progression-free survival; PO, by mouth; RECIST, Response Evaluation Criteria in Solid Tumors.

Relacorilant

Relacorilant is a novel, selective glucocorticoid receptor antagonist that potentially restores the sensitivity of cancers to cytotoxic chemotherapy[3–5]

Ovarian cancers express the glucocorticoid receptor, a marker of poor prognosis[1]

Glucocorticoid receptor signaling reduces sensitivity to chemotherapy[2,3]

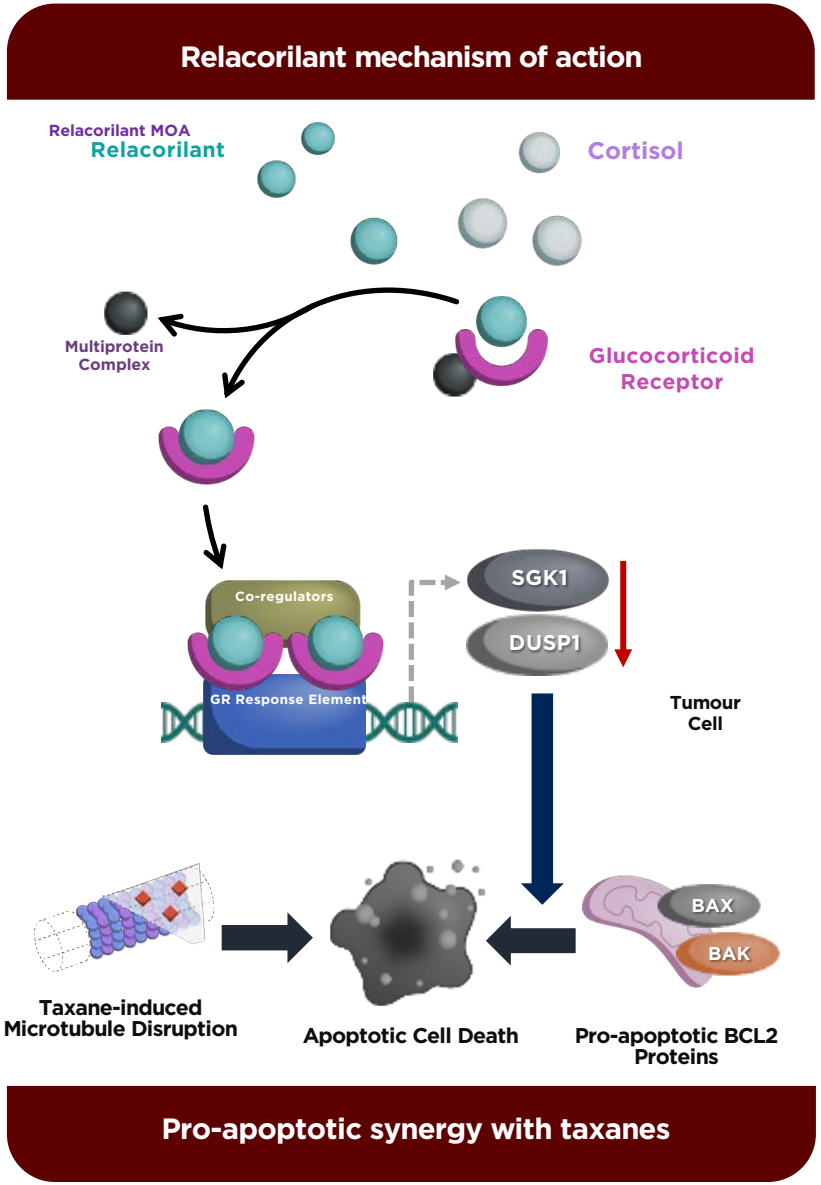


Figure from Olawaiye A, et al. ASCO Annual Meeting. 2025

GR, glucocorticoid receptor; SGRA, selective GR antagonist.

1. Veneris JT, et al. ***Gynecol Oncol***. 2017;146(1):153-60; 2. Greenstein AE, et al. ***Oncotarget.*** 2021;12(13):1243-1255; 3. Melhelm A, et al. ***Clin Cancer Res.*** 2009;15(9):3196-3204; 4. Stringer-Reasor EM, et al. ***Gynecol Oncol.*** 2015;138(3):656-662; 5. Munster PN, et al. ***Clin Cancer Res.*** 2022;28(15):3214-3224.

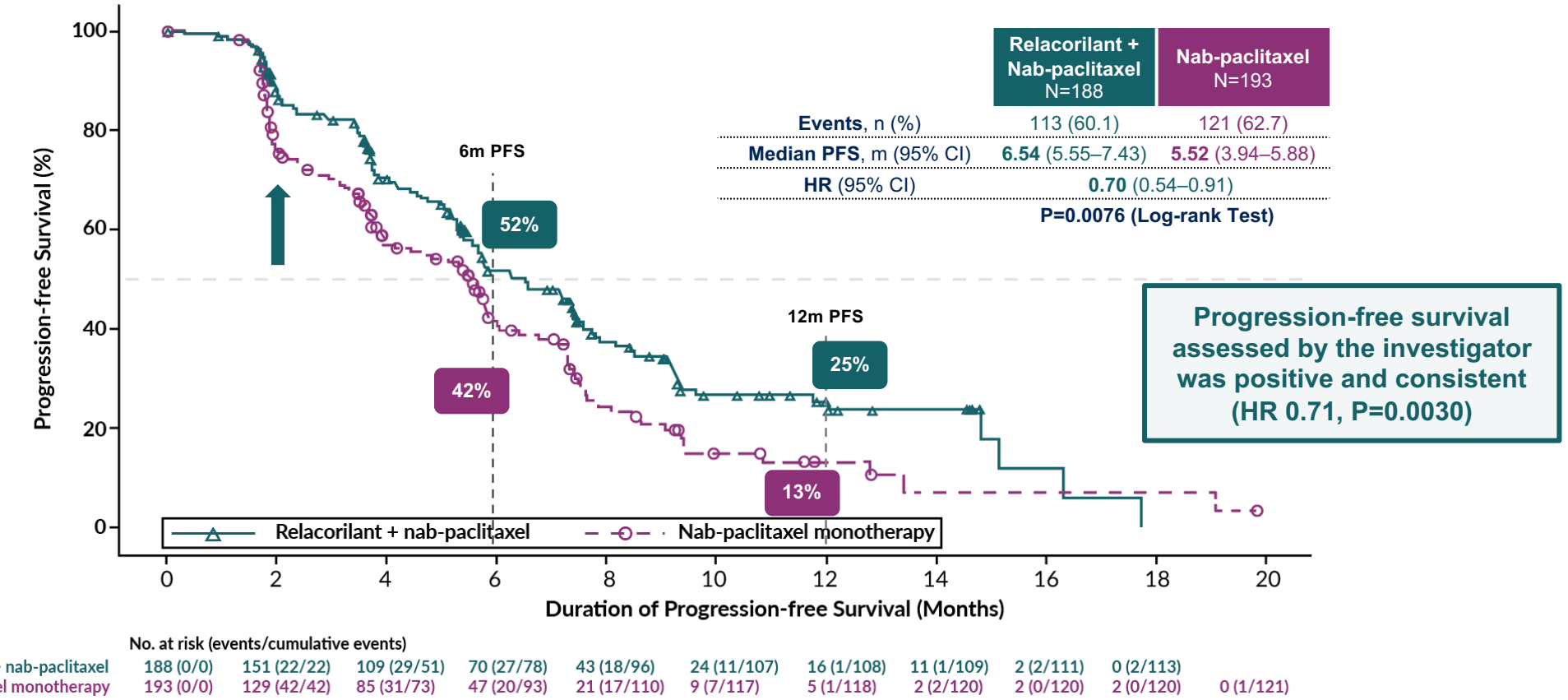
ROSELLA

		Relacorilant + Nab-paclitaxel (N=188)	Nab-paclitaxel (N=193)
Age, median (range), years		**61** (26–85)	**62** (33–86)
Race, n (%)	White Black or African-American Asian (92% Korean) Other / Not Reported	136 **(72.3)** 3 **(1.6)** 22 **(11.7)** 27 **(14.4)**	135 **(69.9)** 2 **(1.0)** 26 **(13.5)** 30 **(15.5)**
Ethnicity, n (%)	Hispanic	16 **(8.5)**	17 **(8.8)**
Region	North America Europe Korea, Australia, and Latin America	45 **(23.9)** 107 **(56.9)** 36 **(19.1)**	45 **(23.3)** 109 **(56.5)** 39 **(20.2)**
ECOG Performance Status, n (%)*	1 or 2	53 **(28.2)**	63 **(32.6)**
BRCA1/2 Mutation, n (%)	Yes	23 **(12.2)**	24 **(12.4)**
Prior Lines of Therapy, n (%)	1 2 3	15 **(8.0)** 92 **(48.9)** 81 **(43.1)**	18 **(9.3)** 89 **(46.1)** 86 **(44.6)**
Primary Platinum Refractory, n (%)†	Yes	13 **(6.9)**	13 **(6.7)**
Prior Lines of Therapy in the Platinum-resistant Setting, n (%)	≥1	67 **(35.6)**	82 **(42.5)**
Prior Taxane in the Platinum-resistant Setting, n (%)	Yes	8 **(4.3)**	7 **(3.6)**
Prior Therapies, n (%)	Bevacizumab Taxanes Pegylated Liposomal Doxorubicin PARP Inhibitor	188 **(100)** 187 **(99.5)** 121 **(64.4)** 114 **(60.6)**	193 **(100)** 192 **(99.5)** 125 **(64.8)** 120 **(62.2)**

*In the nab-paclitaxel monotherapy arm, 1 patient had an ECOG performance status of 2. †Progressed within 3 months of the last dose of platinum from their first line platinum regimen. 97% of patients had high-grade serous carcinoma; 8 patients had high-grade endometrioid carcinoma and 2 patients had carcinosarcoma. BRCA, Breast Cancer Gene; ECOG, Eastern Cooperative Oncology Group.

Data cutoff: Feb 24, 2025

ROSELLA | Progression-Free Survival Assessed by BICR



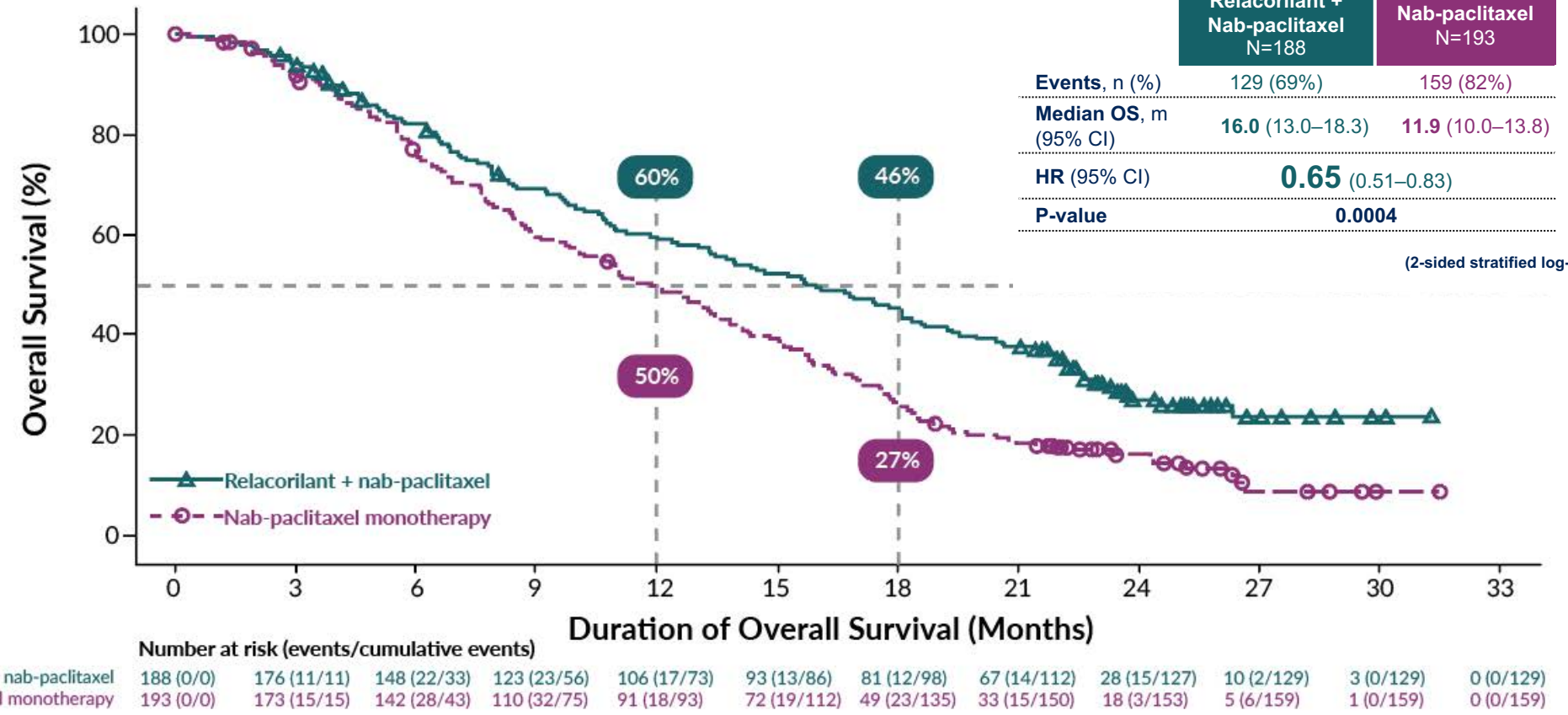
	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	113 (60.1)	121 (62.7)
Median PFS, m (95% CI)	**6.54** (5.55–7.43)	**5.52** (3.94–5.88)
HR (95% CI)	**0.70** (0.54–0.91)	
	P=0.0076 (Log-rank Test)	

Progression-free survival assessed by the investigator was positive and consistent (HR 0.71, P=0.0030)

No. at risk (events/cumulative events)											
Relacorilant + nab-paclitaxel	188 (0/0)	151 (22/22)	109 (29/51)	70 (27/78)	43 (18/96)	24 (11/107)	16 (1/108)	11 (1/109)	2 (2/111)	0 (2/113)	
Nab-paclitaxel monotherapy	193 (0/0)	129 (42/42)	85 (31/73)	47 (20/93)	21 (17/110)	9 (7/117)	5 (1/118)	2 (2/120)	2 (0/120)	2 (0/120)	0 (1/121)

Median follow-up time: 9.0 months; statistical significance threshold: P≤0.04. The Kaplan–Meier method was used to estimate the curves, median estimates and the 95% confidence intervals (CI) for progression-free survival in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates. BICR, blinded-independent central review; CI, confidence interval; HR, hazard ratio; m, months; PFS, progression-free survival.

ROSELLA | Overall Survival at the Final Analysis



	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	129 (69%)	159 (82%)
Median OS, m (95% CI)	**16.0** (13.0–18.3)	**11.9** (10.0–13.8)
HR (95% CI)	**0.65** (0.51–0.83)	
P-value	**0.0004**	

(2-sided stratified log-rank test)

76% maturity

Median follow-up time: 24.9 months; statistical significance threshold at the final analysis: P≤0.0499. The Kaplan–Meier method was used to estimate the curves, median estimates and the 95% CIs for OS in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates.

CI, confidence interval; HR, hazard ratio; m, months; OS, overall survival.

Data cutoff: Jan 8, 2026

ROSELLA | Objective Response and Clinical Benefit Rates (by Investigator)

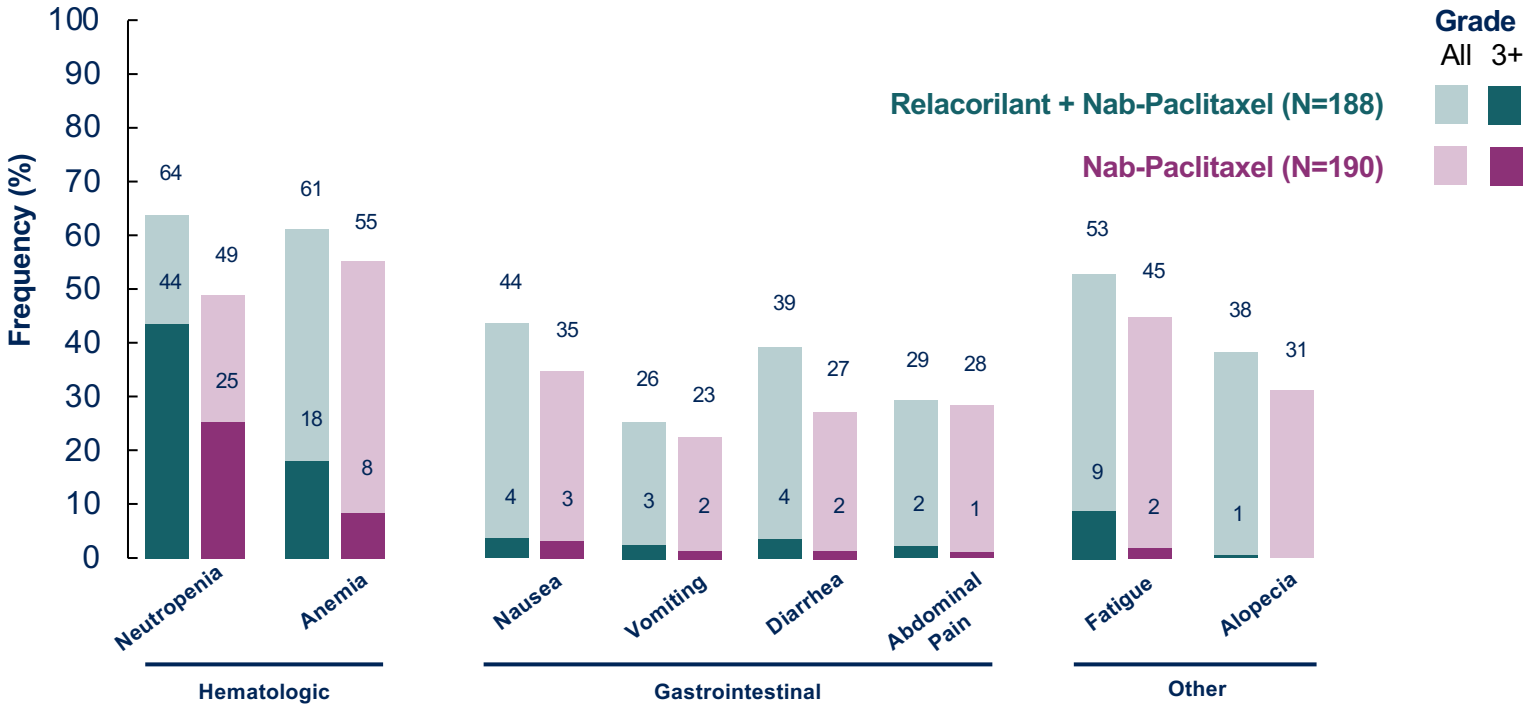
Endpoint	Relacorilant + Nab-paclitaxel	Nab-paclitaxel
Objective Response Rate, n (%)	69 **(36.9)**	58 **(30.1)**
	6.8% improvement P=0.17 (Stratified Cochran-Mantel-Haenszel Test)	
Complete Response, n (%)	6 **(3.2)**	4 **(2.1)**
Partial Response, n (%)	63 **(33.7)**	54 **(28.0)**
Stable Disease, n (%)	77 **(41.2)**	68 **(35.2)**
Progressive Disease, n (%)	32 **(17.1)**	52 **(26.9)**
Not Evaluable, n (%)	9 **(4.8)**	15 **(7.8)**
Clinical Benefit Rate, n (%) (Response or stable disease maintained for 24 weeks)	96 **(51.1)**	75 **(38.9)**
	12.2% improvement P=0.016 (Stratified Cochran-Mantel-Haenszel Test)	

Objective response rate was assessed in the subset of intent-to-treat population with measurable disease at baseline, per investigator assessment (n=380 patients). Clinical Benefit Rate was assessed in the intent-to-treat population (n=381 patients). Per RECIST v1.1 guidelines confirmatory scans were not required for this randomized controlled trial.

RECIST, Response Evaluation Criteria in Solid Tumors.

Data cutoff: Feb 24, 2025

ROSELLA | Common (>20%) Adverse Events



5 SAEs of febrile neutropenia were reported, 4 (2.1%) with relacorilant + nab-paclitaxel and 1 (0.5%) with nab-paclitaxel monotherapy.
5 SAEs of sepsis were reported, 3 (1.6%) with relacorilant + nab-paclitaxel and 2 (1.1%) with nab-paclitaxel monotherapy.

Data cutoff: Feb 24, 2025

TEAEs that occurred in >20% of patients. Assessed in the safety population of patients who received at least one dose of study drug, N=378. Combined terms are presented for neutropenia (neutropenia, reduced neutrophil count, and febrile neutropenia), anemia (anemia, reduced hemoglobin, and reduced red blood cell count) and fatigue (fatigue and asthenia).
SAEs, serious adverse events; TEAEs, treatment-emergent adverse events.

Case Presentation

- A patient in her 70s presented in 2024.
- Found to have stage IVA high grade fallopian tube cancer.
- BRCA/HRD negative
- Received carboplatin/paclitaxel/Bev for a total of 8 cycles (interval tumor reductive surgery after 4)
- Achieved a CR, Received an additional 15 cycles of Bev, where she was found to have progression at 1 year after completing platinum chemotherapy
- PSOC: carboplatin/Gemcitabine/Bev, progressed after 3 cycles with acute worsening of kidney function excluding her from clinical trials and further Bev.
- Her2: 0, Folate Receptor alpha (2+): <25%
- After extensive counseling, patient elected for nab-paclitaxel and Relacorilant

Discussion Questions

How are you sequencing relacorilant/*nab* paclitaxel relative to other available strategies (eg, targeted antibody-drug conjugates, pembrolizumab/chemotherapy) for individual patients?

Do you use glucocorticoid receptor expression levels to inform how you sequence this regimen?

Would you employ relacorilant in combination with any other chemotherapeutic agent beyond *nab* paclitaxel?

Tolerability Considerations with Relacorilant/Nab Paclitaxel

Jaclyn Shaver, MS, APRN, CNP, WHNP

Section of Gynecologic Oncology

Stephenson Cancer Center

OU Health

Oklahoma City, Oklahoma

Relacorilant/Nab Paclitaxel

- Ideal Combination Partner
- Nab-Paclitaxel is preferred over other taxanes because it does not require corticosteroid premedication
- Relacorilant antagonizes the effect of glucocorticoids
  - May make systemic glucocorticoids less effective
  - Similarly, coadministration may make Relacorilant less effective
    - – Simply they could negate each other and not produce the treatment benefit and cause other conditions such as autoimmune disorders to exacerbate
  - Relacorilant is contraindicated in patients who are receiving systemic glucocorticoids for lifesaving purposes such as immunosuppression after organ transplant

Relacorilant/Nab Paclitaxel

- Dosing
  - Nab Paclitaxel – 80 mg/m^2 IV infusion days 1, 8, and 15 of each 28-day cycle
  - Relacorilant – 150 mg day before, day of, and day after each Nab Paclitaxel
- Oral Administration of Relacorilant
  - Capsules – 100 mg, 25 mg
  - Take with food, swallow capsules whole
- Missed dose
  - <12 hours: take missed dose
  - > 12 hours: Skip missed dose and take next dose at regularly scheduled time
  - Do not take 2 doses at same time to make up for missed dose
  - If vomiting occurs after administration, do not take additional dose

Relacorilant/Nab Paclitaxel

- Well tolerated and manageable – No new safety concerns
- Most common Adverse Reactions
  - Laboratory Abnormalities
    - – Anemia, Neutropenia, Thrombocytopenia
  - Fatigue, Nausea, Rash, Decreases Appetite, Diarrhea

  - May need to hold vs omit based upon grade and day
    - If holding or omitting Nab Paclitaxel you also will hold Relacorilant
    - Continue same dose of Relacorilant when you resume Nab Paclitaxel, unless you have a grade 3 or 4 other hematologic adverse affect

Relacorilant/Nab-paclitaxel

- Dose Adjustment
- Nab-Paclitaxel
  - First Reduction
    - 60 mg/m^2 D1, D8, D15
  - Second Reduction
    - 60 mg/m^2 D1, D15 – so omit D8
  - Third Reduction
    - Permanently Discontinue
- Relacorilant
  - First Reduction (fatigue/loss of appetite)
    - 125 mg on day before, the day of, and day after nab-paclitaxel
  - Second Reduction
    - Permanently discontinue

Relacorilant/Nab Paclitaxel

- Warning and Precautions
  - Neutropenia and Severe Infections
    - Neutropenia and febrile neutropenia reported
    - Monitor CBC before each weekly infusion and as clinically indicated
    - Based on severity may need to delay vs dose reduce or discontinue
    - Consider adding G-CSF – 38% needing growth factor with C1 or C2
    - Consider the possibility of adrenal insufficiency in the setting of serious infection
    - Educate patient to report any episodes of fever

Relacorilant/Nab Paclitaxel

- Warning and Precautions
  - Adrenal Insufficiency- Relacorilant is a reversible glucocorticoid and can cause adrenal insufficiency
    - Can occur at any time during treatment
    - Risk increased in stress – acute illness, infection, surgery
    - Consider supplemental glucocorticoids in perioperative period who have received relacorilant within 30 days of surgery
    - Monitor for signs and symptoms
      - Serum cortisol levels do not provide an accurate assessment in patient receiving relacorilant
    - Educate patients of symptoms of adrenal insufficiency
      - Intense, long-lasting fatigue and muscle weakness, sudden severe pain in the lower back, abd, or legs, severe vomiting, diarrhea, hypotension, dizziness, loss of consciousness, confusion, or delirium
    - **If adrenal insufficiency suspected**
      - Hold Relacorilant and administer glucocorticoid therapy
      - High doses may be required
      - Can resume at previous dose, dose reduce or discontinue based on severity

Relacorilant/Nab Paclitaxel

- Warning and Precautions
  - Exacerbations of conditions treated with glucocorticoids
  - Coadministration of glucocorticoids may make relacorilant less effective
- Embryo-Fetal Toxicity
- Drug interactions
  - Substrate of CYP3A and CY2C8
- Use in Specific Populations
  - Lactation- avoid during treatment and for 1 week after last dose
  - Geriatric Use – Higher incidence of grade 3-4 AE and dose modifications 65y/o and older
  - Hepatic Impairment- Avoid in moderate to severe hepatic impairment (total bilirubin > 1.5 x 10X ULN and any AST)

Case Study

- 67 y/o CF G2P2
- Care giver for her husband who has dementia
- Daughters lives out of state, but has social support with friends at her local church
- Lives in rural Oklahoma – 2 hours outside of OKC where the closest cancer center is
- Comorbidities: HTN, Obesity, Hypothyroidism
- Presented to her local ER with N/V – CT scan revealed 7-cm right pelvic mass with omental caking, and ascites. Was referred to gyn/onc at the SCC for follow-up
- CA 125 was 1463,CEA – 2.0
- Taken to OR for cytoreduction, but had a suboptimal surgery with porta hepatitis disease (Daughters came into town for surgery and helped take care of her husband)
- BRCA negative, + HRD

Case Study

- She was nervous to start treatment – Her daughters had to go back to work and she would have to take care of her husband with dementia
- She was started on Carboplatin and paclitaxel + bevacizumab (C2)
- Friends from church came with her to her infusions and stayed with her husband
- Cycle #3 was delayed for neutropenia – paclitaxel was reduced to 135 mg/m^2 and GCSF was added
- CT scan after cycle #3 showed a decrease in her porta hepatis disease. CA 125 decreasing now to 135. She was able to complete the remainder of her 6 cycles without issues
- CT scan after cycle #6 was NED and Ca 125 was now 43

Case Study

- She was transitioned to Bev and olaparib maintenance. She had no further issues with neutropenia or other hematologic toxicities after starting maintenance that caused dose reduction or delay.
- CT scan after cycle #4 bev/olaparib (12 weeks) showed a recurrence of her HGSOC with a 2.5cm PA node. Now platinum resistant. CA 125 is 112.
- **She was counseled on Relacorilant/nab paclitaxel and reluctant to start this treatment secondary to travel distance, weekly infusions, and care that her husband needed.**

Case Study

- She did start the regimen - her daughter moved back in and they transitioned her husband into a dementia care facility. She was referred to our supportive care team for counseling secondary to depression and placed on an anti-depressant
- She was started on Relacorilant 150 mg day before, day of, and day after her nab paclitaxel IV infusion 80 mg/m^2 D1, D8, D15 until PD or toxicity
- Weekly CBC prior to each Nab paclitaxel infusion
- **Cycle #1D15- ANC = 890. Nab paclitaxel was omitted and short acting GCSF was added to start with cycle #2. Relacorilant was held**
- **Her ANC recovered to 1550 with CBC prior to cycle #2. Nab paclitaxel and Relacorilant was restarted at same dose. Short acting G-CSF was started**
- **She tolerated cycle #2 without further dose adjustment or omittance. She has some grade 1 fatigue and nausea that is controlled with anti-emetics. Her neuropathy has been stable from her previous treatment.** Ca 125 decreasing to 84

Agenda

Module 1: Overview of Ovarian Cancer (OC)

Module 2: Role of PARP Inhibitors in Advanced OC

Module 3: Current and Potential Future Role of Mirvetuximab Soravtansine in OC

Module 4: Role of Relacorilant in Advanced OC

Module 5: Utility of Immune Checkpoint Inhibition in Advanced OC

UTILITY OF IMMUNE CHECKPOINT INHIBITION IN PLATINUM-RESISTANT OVARIAN CANCER

Bradley J. Monk, MD, FACS, FACOG
Florida Cancer Specialists and Research Institute
West Palm Beach, FL 33401

Professor
University of Central Florida College of Medicine

Natural history of ovarian cancer evolution

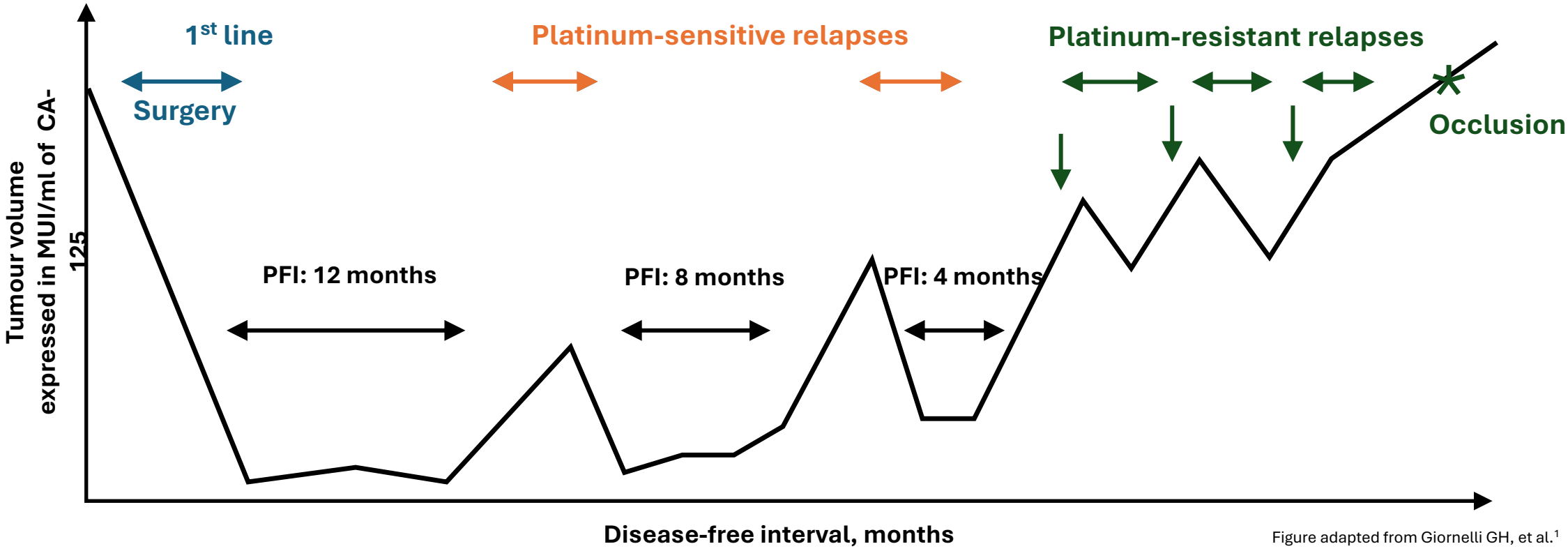
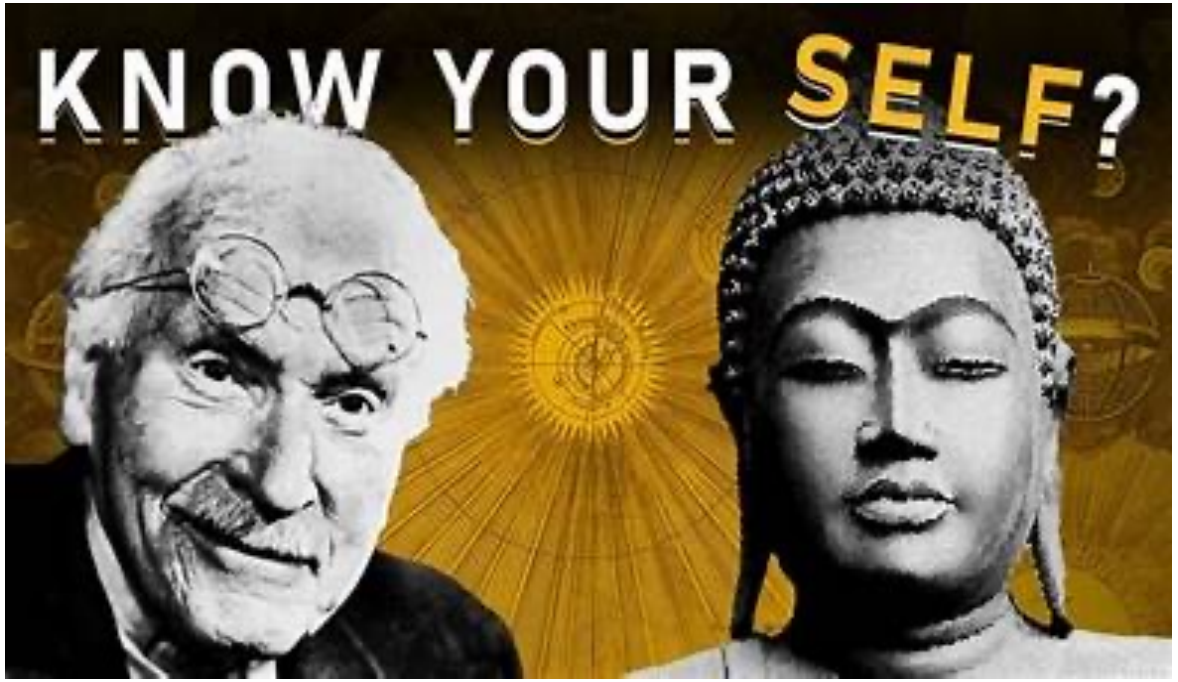


Figure adapted from Giornelli GH, et al.[1]

"Most patients will relapse within the first 2 years after diagnosis, even after an optimal primary cytoreductive surgery and six cycles of the standard adjuvant chemotherapy with carboplatin/paclitaxel"

Giornelli GH. Springerplus. 2016;5(1):1197.



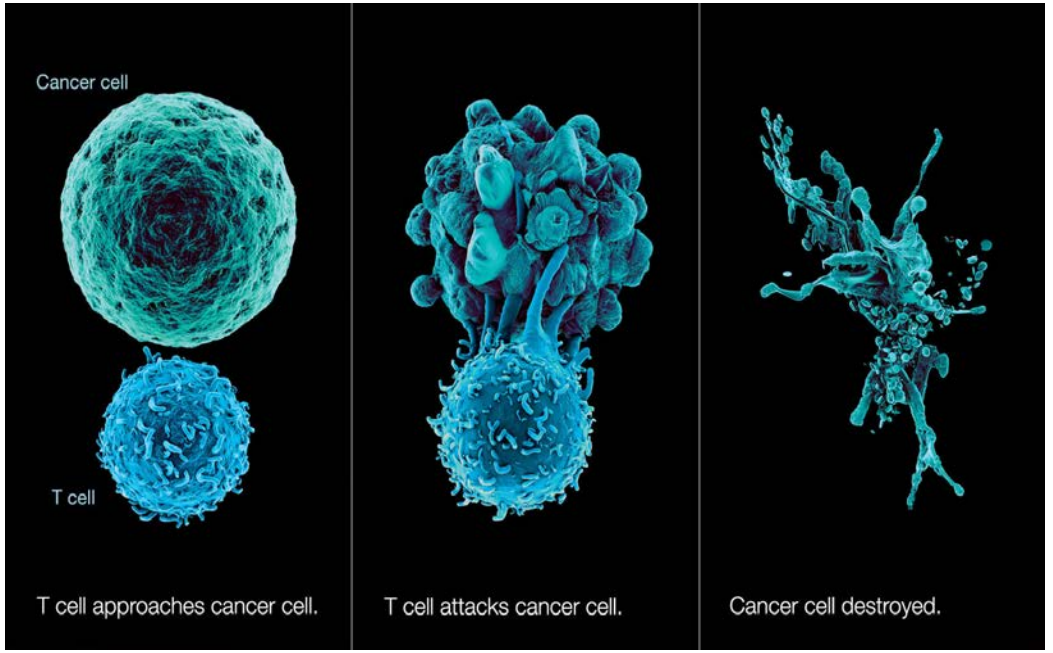
IMMUNOLOGY

The science of

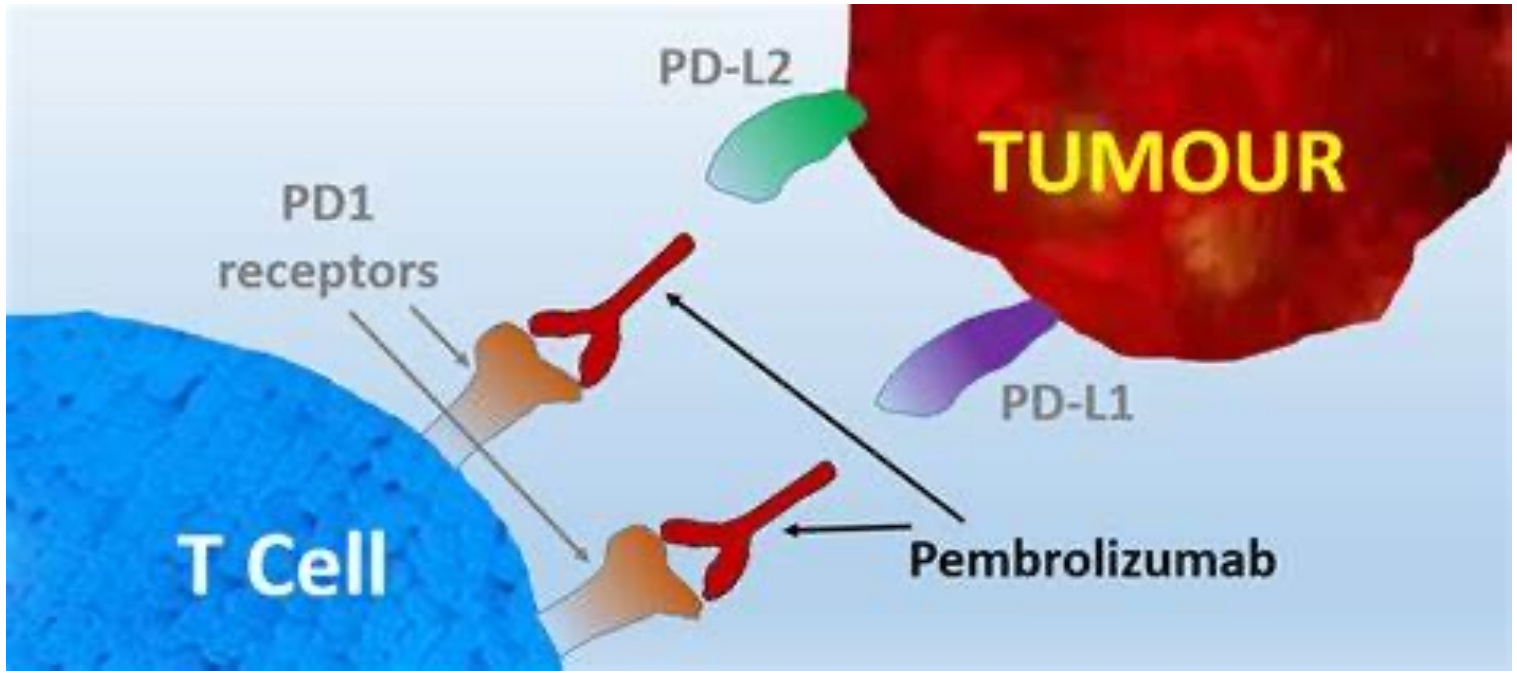
Self / Non-self Discrimination

Self
Well-ordered self

Non-self
(Pathogens)
I. External pathogens
II. Internal pathogens (Disordered Self)



Pembrolizumab



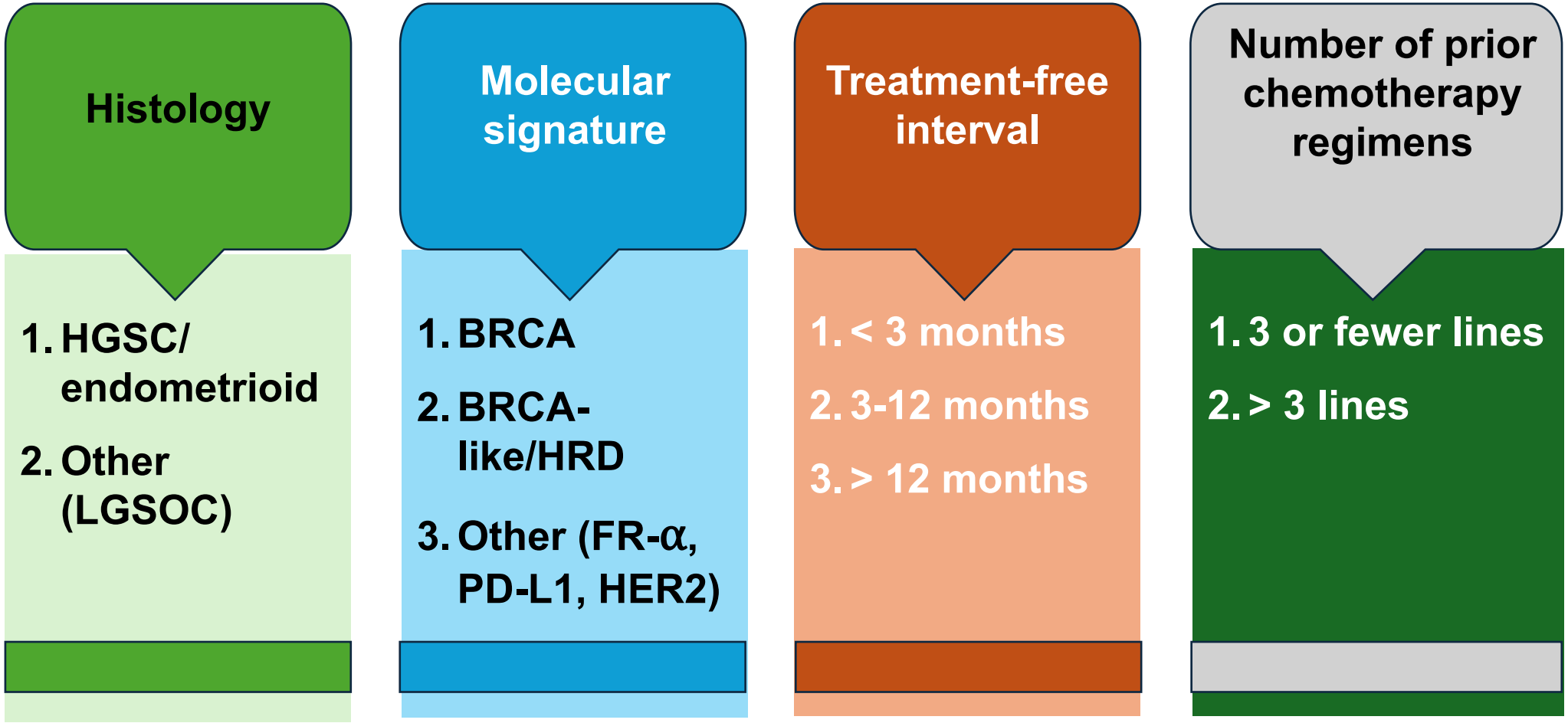
PD-1 ligands (**PD-L1**) bind to the PD-1 receptors and are present on both tumor cells and activated T cells, B cells, and myeloid cells. It plays a major role in immune regulation

Pembrolizumab is a humanized monoclonal antibody binding to the programmed cell death protein 1 (**PD-1**) receptors on lymphocytes.

It is used in cancer immunotherapy to treat many types of cancer and administered by slow intravenous injection.

https://institute-genetics-cancer.ed.ac.uk/news-and-events/news-2022/pembrolizumab

Emerging New Multiplex Classification System



Alvarez RD, Matulonis UA, Herzog TJ, Coleman RL, Monk BJ, **Markman M**. *Gynecol Oncol*. 2016;141(3):405-9.

HGSC = High grade serous cancer
LGSOC = Low grade serous ovarian cancer

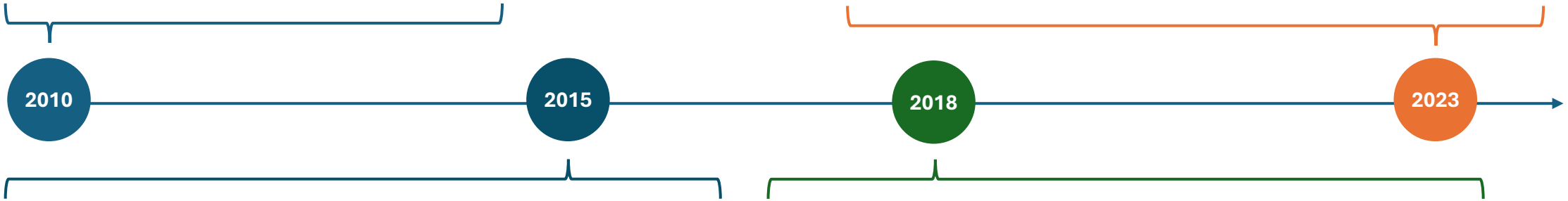
‘Platinum-resistant’ OC redefined as ’not suitable for further platinum therapy ’

Historical definition (regulatory trial standard):
Fourth International Ovarian Cancer Consensus Meeting, Vancouver[1]

- **Platinum-free interval (PFI)**

Contemporary definition (clinical standard): ESMO Guidelines[4]

- **For some patients with recurrent ovarian cancer, platinum rechallenge may not be considered clinically appropriate**



Fifth Gynecological Cancer InterGroup (GCIG) Ovarian Cancer Consensus Conference, Tokyo[2]

- **Treatment-free interval (TFI)**
- **PFI as a continuous variable,** rather than a single fixed time point (6 months)

ESMO-ESGO Consensus Conference on Ovarian Cancer, Milan[3]

- **Patients for whom platinum-based therapy is no longer an option**
  Includes:
  - Symptomatic relapse soon after Pt-based CTx

1. Friedlander M, et al. Int J Gynecol Cancer. 2011;21(4):771-5. 2. Wilson MK, et al. Ann Oncol. 2017;28(4):727-732. 3.. Colombo N et al. Ann Oncol. 2019;30(5):672–705.
4. González-Martín A, et al. Ann Oncol. 2023 Oct;34(10):833-848.

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

ENGOT-ov65/KEYNOTE-B96 Study Design (NCT05116189)

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]

R 1:1
N = 643

Pembrolizumab 400 mg (Q6W, 18 cycles) +
Paclitaxel[a] 80 mg/m² Days 1, 8, 15 of each Q3W cycle
(± bevacizumab 10 mg/kg Q2W)

Placebo (Q6W, 18 cycles) +
Paclitaxel[a] 80 mg/m² Days 1, 8, 15 of each Q3W cycle
(± bevacizumab 10 mg/kg Q2W)

Wkly paclitaxel is most active single agent

Bevacizumab is first target therapy approved in ovarian in 2014

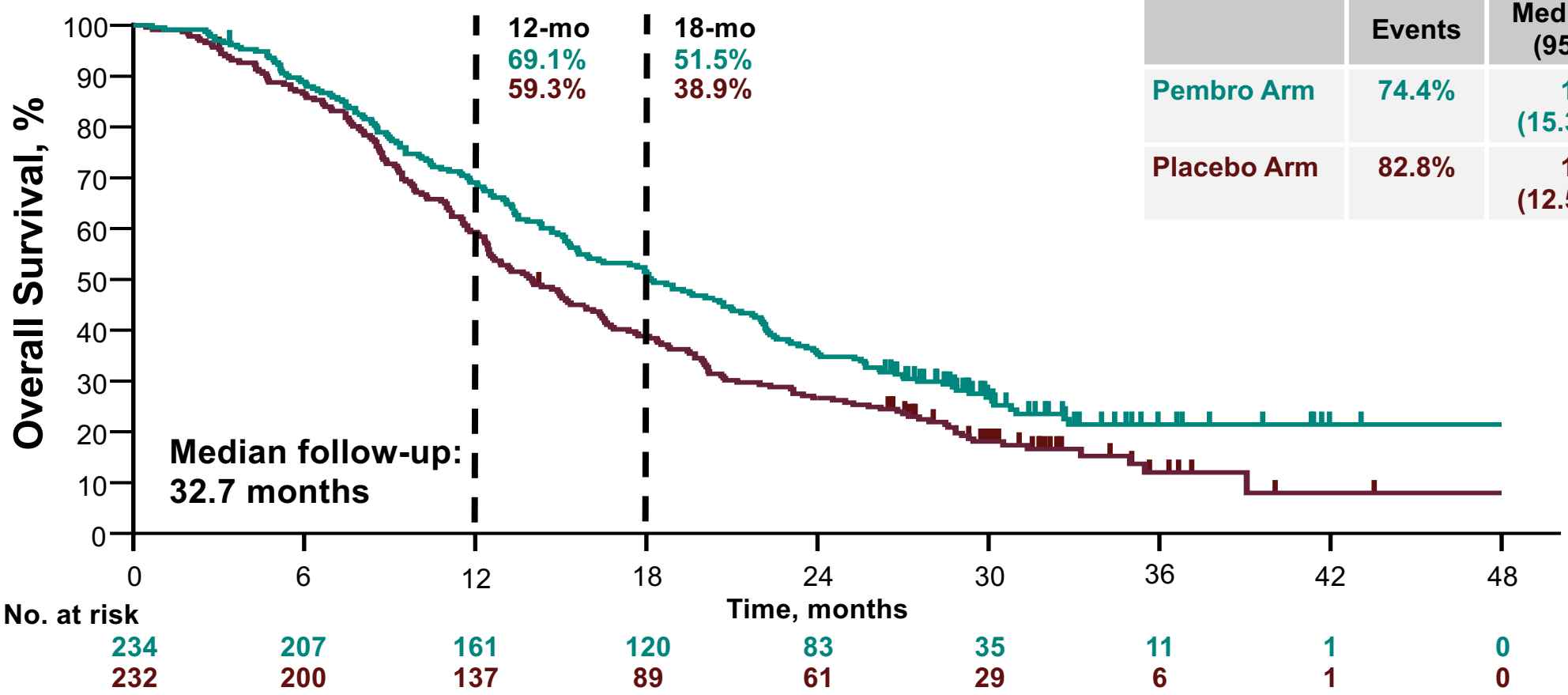
Primary Endpoint: PFS per RECIST v1.1 by investigator

Key Secondary: OS

Monk BJ. et al. Presented at SGO Meeting, April 10, 2026; Colombo N et al. Lancet. 2026 Apr 18;407(10538):1525-1537.

KEYNOTE-B96

OS in CPS ≥1 population at final analysis



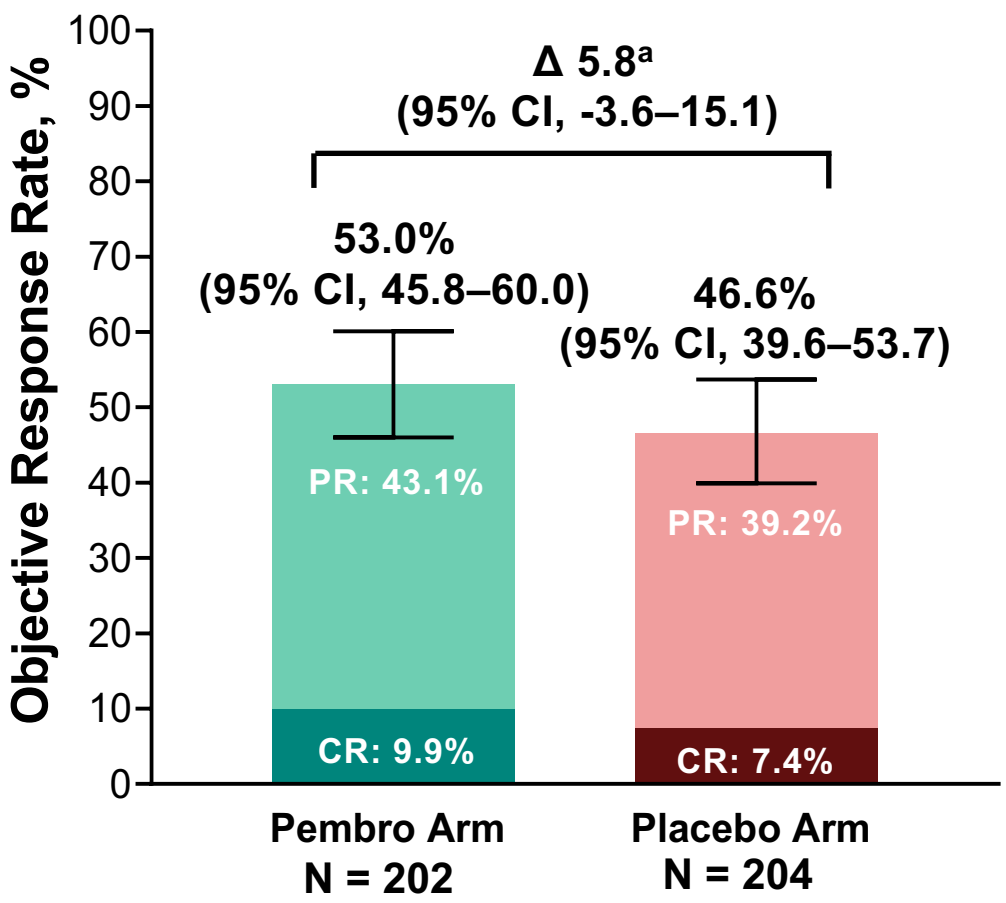
	Events	Median, mo (95% CI)	HR (95% CI)
Pembro Arm	74.4%	18.2 (15.3–21.3)	0.76 (0.62–0.93)
Placebo Arm	82.8%	14.0 (12.5–16.1)	

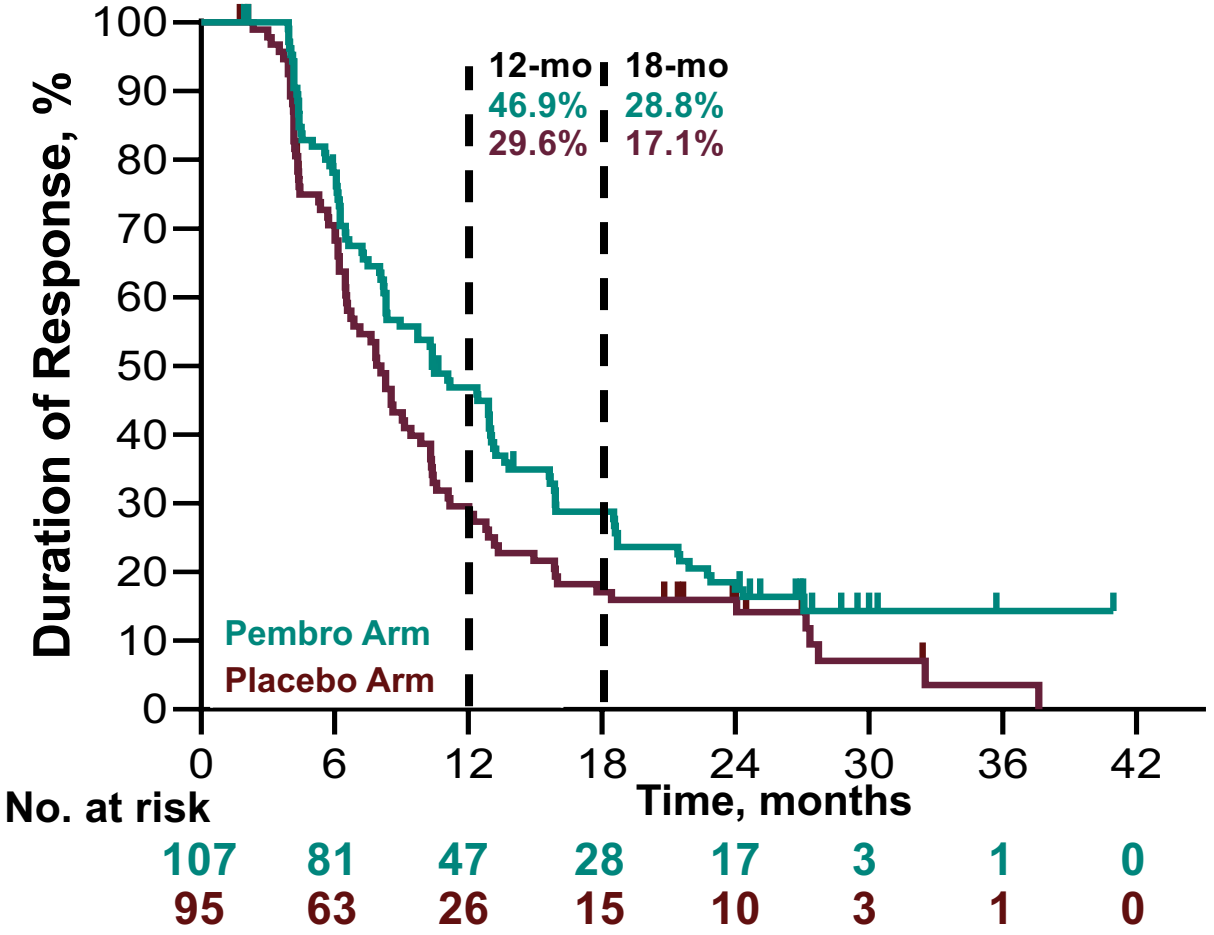
[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff date: September 5, 2025.

Monk BJ. et al. Presented at SGO Meeting, April 10, 2026; Colombo N et al. Lancet. 2026 Apr 18;407(10538):1525-1537.

KEYNOTE-B96

ORR and DOR in CPS ≥1 population*





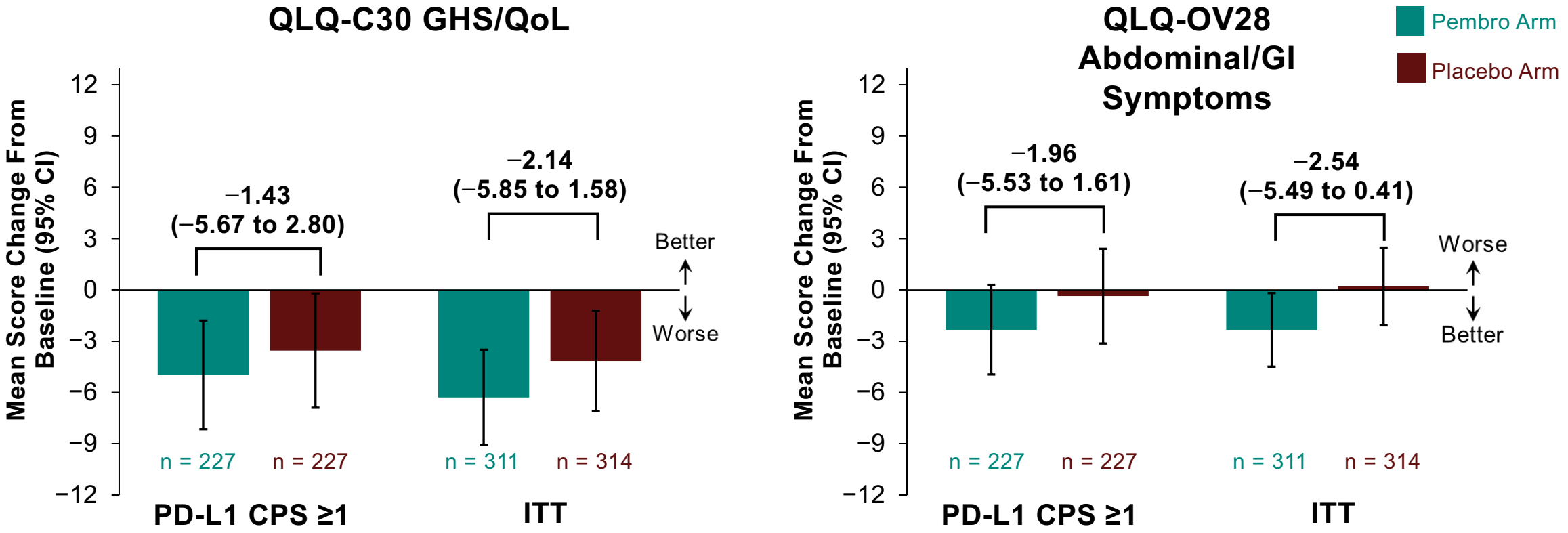
* Final Analysis

Response assessed per RECIST v1.1 by investigator review. [a]Delta estimated using Miettinen & Nurminen method stratified by the randomization stratification factors. Data cutoff date: September 5, 2025.

Monk BJ. et al. Presented at SGO Meeting, April 10, 2026 Lancet. 2026 Apr 18;407(10538):1525-1537.

KEYNOTE-B96

Least-Squares Mean Changes From Baseline to Week 24 for PRO

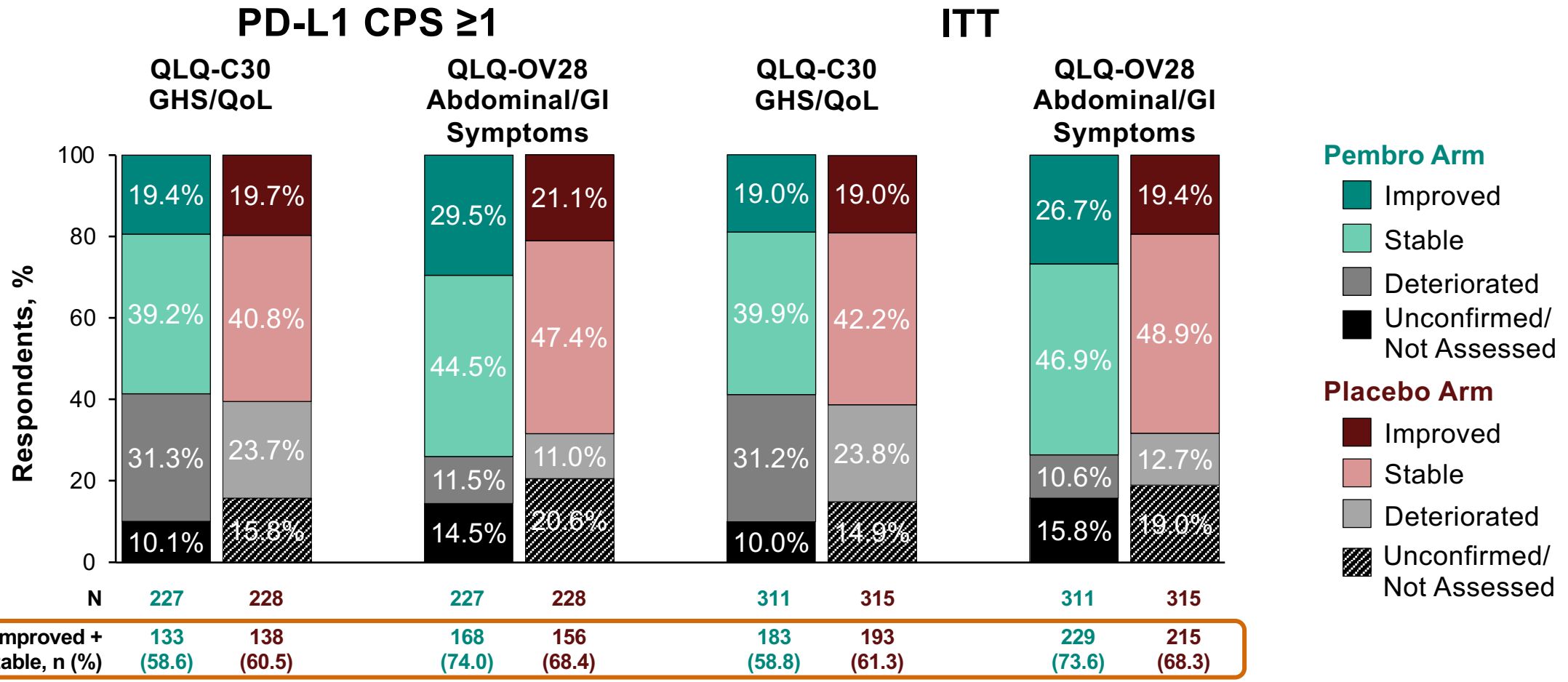


Data cutoff date: 5 September 2025.

Zsiros E et al. Presented at: European Society of Gynaecological Oncology; 26-28 February 2026; Copenhagen, Denmark. Abstract 666.

KEYNOTE-B96

Best Overall Response Score of Improved, Stable, and Deteriorated



Data cutoff date: 5 September 2025.

Zsiros E et al. Presented at: European Society of Gynaecological Oncology; 26-28 February 2026; Copenhagen, Denmark. Abstract 666.

FDA Approves Pembrolizumab with Paclitaxel for Platinum-Resistant Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma

Press Release: February 10, 2026

"The Food and Drug Administration approved pembrolizumab as well as pembrolizumab and berahyaluronidase alfa-pmph in combination with paclitaxel, with or without bevacizumab, for adult patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma whose tumors express PD-L1 (CPS≥1) as determined by an FDA-authorized test, and who have received one or two prior systemic treatment regimens.

FDA also approved the PD-L1 IHC 22C3 pharmDx as a companion diagnostic device to identify patients with epithelial ovarian, fallopian tube, or primary peritoneal carcinoma whose tumors express PD-L1 (CPS≥1) for treatment with pembrolizumab.

Efficacy was evaluated in KEYNOTE-B96 (NCT05116189), a multicenter, randomized, double-blind, placebo-controlled trial that enrolled 643 patients with platinum-resistant, epithelial ovarian, fallopian tube, or primary peritoneal carcinoma who received one or two prior lines of systemic therapy for ovarian carcinoma."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-paclitaxel-platinum-resistant-epithelial-ovarian-fallopian-tube-or

RTP RESEARCH TO PRACTICE

Case Study

59-Year-Old Woman With Abdominal Pain

Diagnostic Work-Up
- High-grade serous OC
- FIGO stage IIIC

Germline Testing (48 genes, normal)
- Confirmed gBRCAwt; HRD score 44, HER2 IHC 1+, FR-alpha 70% 2+, PD-L1 CPS 6
- Surgeon recommends neoadjuvant therapy

First-Line Treatment

Three cycles of:
- **Paclitaxel (175 mg/m^2 IV over 3h) + carboplatin (AUC6) + bevacizumab (15mg/kg cycles 1,2 5,6 and maintenance)**
- **Interval debulking, R0, three additional cycles**
- **Normal CA-125: 25 IU/mL**

Second line:
- Platinum-sensitive recurrence at 2 years treated with carboplatin and liposomal doxorubicin
- Second recurrence 4 months later

A good candidate for bevacizumab retreatment

Recommended wkly paclitaxel - bevacizumab - pembrolizumab

PAOLA-1: Added olaparib in the maintenance phase

Discussion Questions

How are you sequencing pembrolizumab/chemotherapy relative to other available strategies for individual patients? How do you decide whether to include bevacizumab or not?

Would you employ pembrolizumab/chemotherapy with or without bevacizumab for a patient with PD-L1-negative OC under any circumstances?

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Ovarian Cancer Symposium

Research To Practice | ONS 2026

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Nursing Considerations for Patients Receiving an Anti-PD-1/PD-L1 Antibody in Advanced Ovarian Cancer

Incidence of irAEs

KEYNOTE B96 – Phase 3 Trial (Pembrolizumab + Paclitaxel +/- Bevacizumab) in PR ovarian cancer

Pembrolizumab: 400 mg q6 week

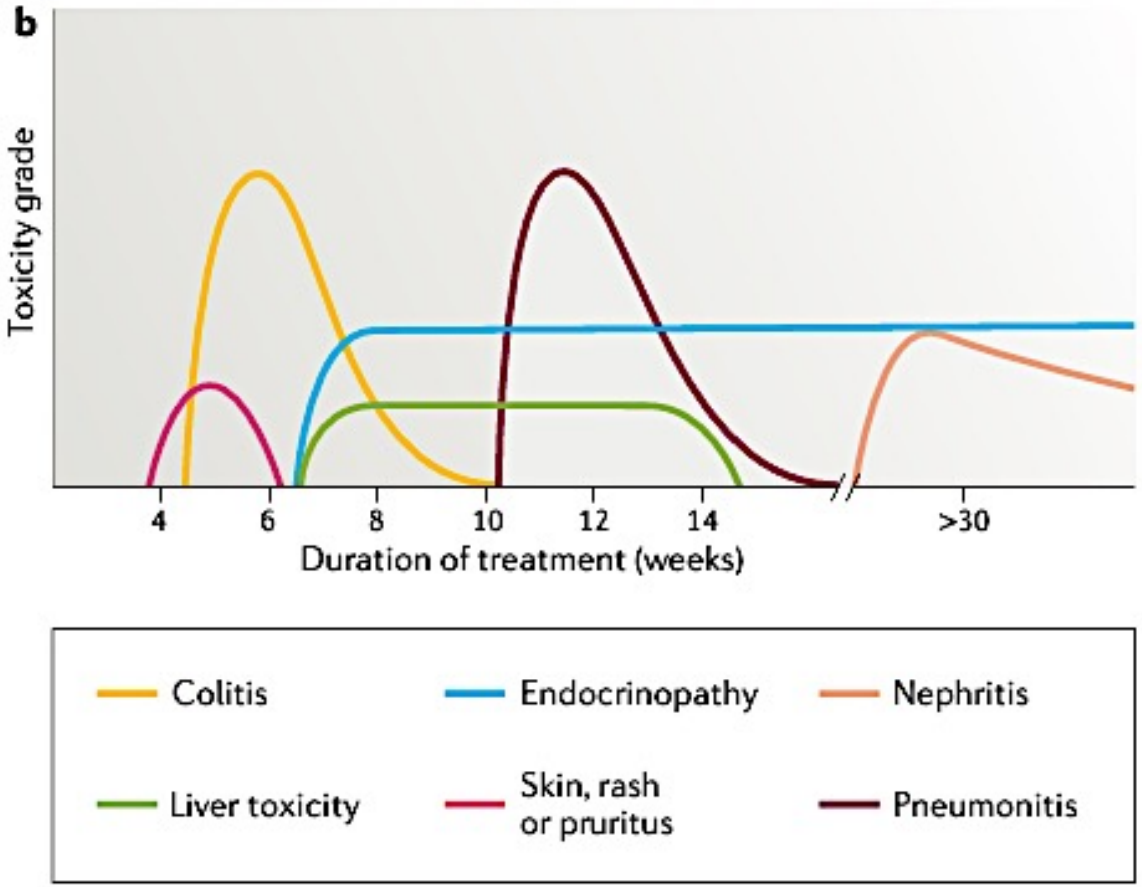
Weekly Paclitaxel (Day 1, 8, 15) q3 week cycle (no off week)

+/- **Bevacizumab** 10 mg/kg q2 weeks

- Most Common AEs in Pembro/Paclitaxel arm:
  - Anemia (50%)
  - Neuropathy (39%)
  - Alopecia (38%)
  - Fatigue (35%)
  - Nausea (31%)
  - Epistaxis (29%)
  - Diarrhea (29%)
  - Neutropenia (23%)
- Immune-mediated AEs in Pembro/Paclitaxel arm:
  - Hypothyroidism (18%)
  - Hyperthyroidism (5%)
  - Adrenal insufficiency (5%)
  - Pneumonitis (5%)

Management of irAEs

- Non-specific activation of the immune system by checkpoint inhibitors causes immune-related adverse events (irAEs)
- The most common irAEs involve the skin, GI tract, endocrine system, and lungs (think *itis*)
- Timing of onset and duration varies
- Some toxicities can be reversible (GI, skin, pulmonary) while others may not be (endocrine)
- Monitoring:
  - Labs: TSH, FT4, LFTs (CBC, CMP, TSH)
  - CXR, CT scans
  - Closely monitor patients with pre-existing autoimmune disorders
- Management: Dose delay +/- steroid taper vs drug discontinuation



Martins, F., Sofiya, L., Sykiotis, G.P. *et al.* Adverse effects of immune-checkpoint inhibitors: epidemiology, management and surveillance. *Nat Rev Clin Oncol* 16, 563–580 (2019).

Management of irAEs

- Patient education is key to early recognition
- Consultation with other specialties may be needed (endocrinology, dermatology, etc)
- Utilize guidelines for patient management (i.e. ASCO Clinical Practice Guidelines, NCCN Guidelines: Management of Immunotherapy-Related Toxicities)
- Toxicity grading can vary some with each organ system, but in general:
  - Grade 1: Continue therapy and closely monitor patient.
  - Grade 2: Hold therapy. May consider steroid taper. Resume therapy once grade 1 or less.
  - Grade 3: Hold therapy and start high-dose corticosteroids with taper.
  - Grade 4: Permanently discontinue therapy.

Special Considerations

- Is there a role for rechallenge after holding immunotherapy for irAE?
  - Depends on the grade and severity of the initial irAE
  - Higher likelihood to experience a subsequent irAE
  - Individualized care and shared decision-making
  - Experience in my clinical practice:
    - 1. Skin rash (generalized): Held therapy, initiated topical and oral steroids, recovered to grade 1. Rechallenged successfully (now 3 months in with no repeat issues and CR on imaging).
    - 2. Increased LFTs: Held therapy, hospitalization (grade 3), steroid taper, unable to rechallenge.
    - 3. Colitis: Held therapy, initiated antidiarrheals, hospitalization (grade 3) steroid taper. Rechallenged 2 months later after resolution of symptoms and completion of steroid taper (limited treatment options remaining) and colitis returned with similar severity. Discontinued immunotherapy.

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

- No absolute label contraindications
- Relative contraindications:
  - Autoimmune disease (IBD/Crohn's/ulcerative colitis, lupus, MS, RA, psoriasis)
  - Solid organ transplant (taking immunosuppressants)
  - Uncontrolled thyroid disorders
  - Severe, uncontrolled asthma
  - Uncontrolled HIV (need to be compliant on ART with well controlled viral load)
- Factors to consider:
  - The degree to which the condition is controlled (well controlled vs poorly controlled)
  - Collaboration with other specialists
  - Increased risk for flares

Case Presentation

61 yo with IIIC ovarian cancer initially presented with abdominal distention and bloating. She underwent diagnostic laparoscopy with biopsy and was found to have ovarian cancer. She received 3 cycles of neoadjuvant Paclitaxel/Carbo followed by IDS (X/BSO/OMX/debulking) – prior Hyst in 2008 for benign indications. She resumed NA chemo and received 3 more cycles Paclitaxel/Carbo followed by Niraparib maintenance, which she took for 3 months before having new disease progression on CT imaging. Of note, she is germline negative. NGS: BRCA1/2 neg, HR proficient, HER2 neg, FOLR1 90%, PD-L1 pos CPS: 1, TP53 mut, MS-stable, TMB low. She was started on Mirvetuximab and received 6 cycles. CT scan showed progression and she enrolled on a clinical trial, which she was on for 2 months before again having disease progression. She then started liposomal doxorubicin/Bev and received 5 cycles. CA-125 was increasing and CT scan ordered, which showed a mixed response. She was eligible for BiTE therapy clinical trial and began treatment. She was subsequently admitted for new pleural effusion and pneumonia. Imaging again showed progression. **She then started weekly Paclitaxel + Pembrolizumab + Bevacizumab. Re-admitted with respiratory symptoms (SOB/hypoxia) and new O2 requirement, which prompted pulmonology consult. Concern for pneumonitis on HR chest CT – initiated steroids. Currently continuing with weekly Paclitaxel and Bev but holding Pembro.** She's feeling much better and her CA-125 is down-trending (354 currently, down from 1,846 in Feb 2026).

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

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

Immunotherapeutic Approaches for Endometrial Cancer

Thursday, May 14, 2026

6:00 AM – 7:30 AM

Faculty

Sarah Karpen, MPAS, PA-C
J Alejandro Rauh-Hain, MD, MPH
Jaclyn Shaver, MS, APRN, CNP, WHNP

Moderator

Dana M Chase, MD

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