Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Ovarian Cancer

Friday, April 11, 2025

12:15 PM – 1:45 PM

Faculty

Courtney Arn, CNP
Jennifer Filipi, MSN, NP
David M O'Malley, MD
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Neil Love, MD

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Faculty

Courtney Arn, CNP
The James Cancer Hospital
and Solove Research Institute
The Ohio State University
Columbus, Ohio

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

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

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

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Ms Arn — Disclosures

Speakers Bureaus	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Eisai Inc, Genmab US Inc, ImmunoGen Inc, Merck, Pfizer Inc

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Ms Filipi — Disclosures

No relevant conflicts of interest to disclose.

Dr O'Malley — Disclosures

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

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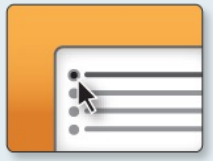
Clinicians in the Meeting Room

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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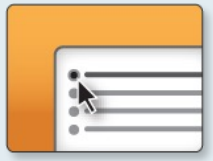
Clinicians Attending via Zoom

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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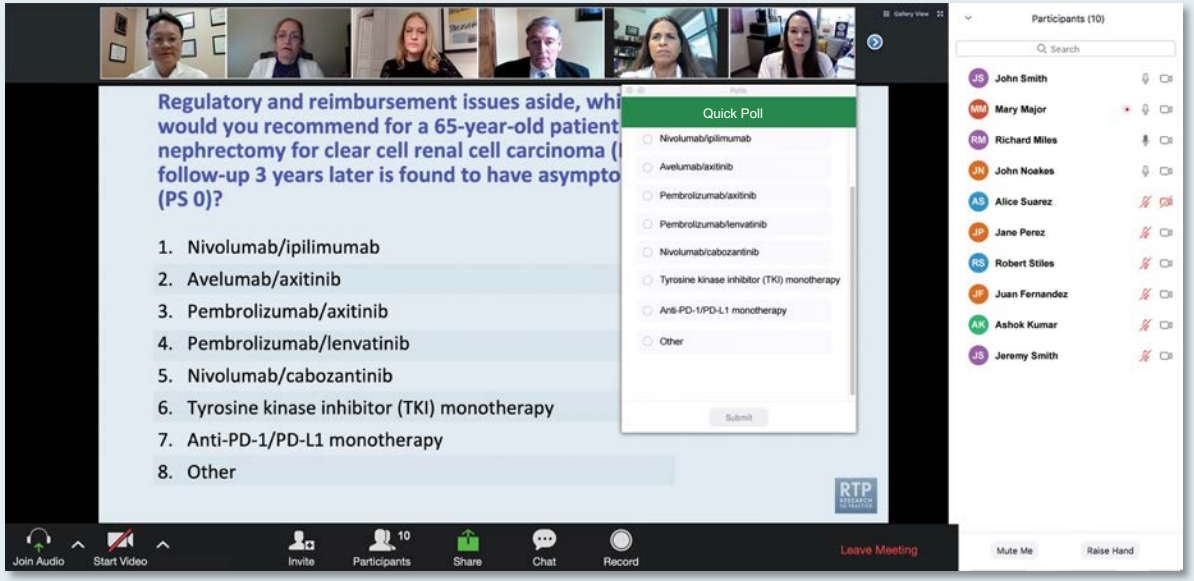
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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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.
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ONCOLOGY NURSING UPDATE WITH DR NEIL LOVE

Bispecific Antibodies in Lymphoma Part 1 — An Interview with Ms Robin Klebig for Oncology Nurses

MS ROBIN KLEBIG
MAYO CLINIC

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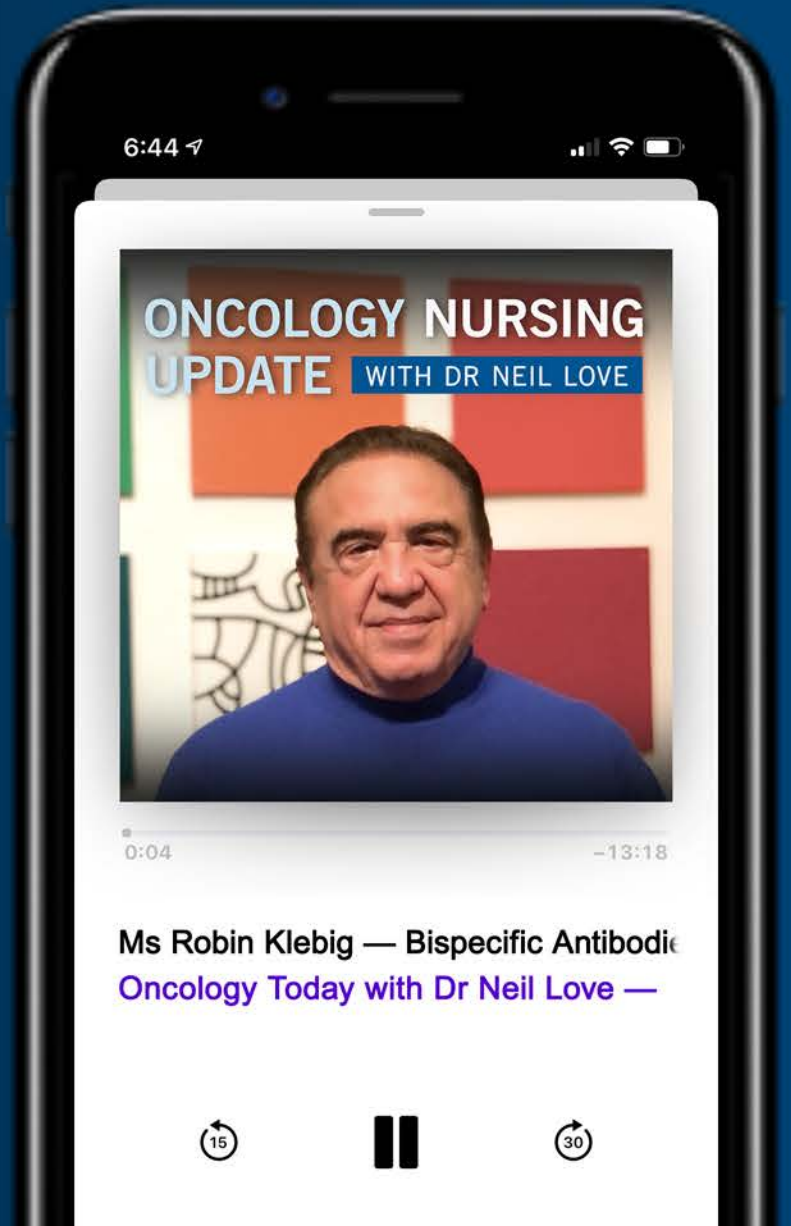
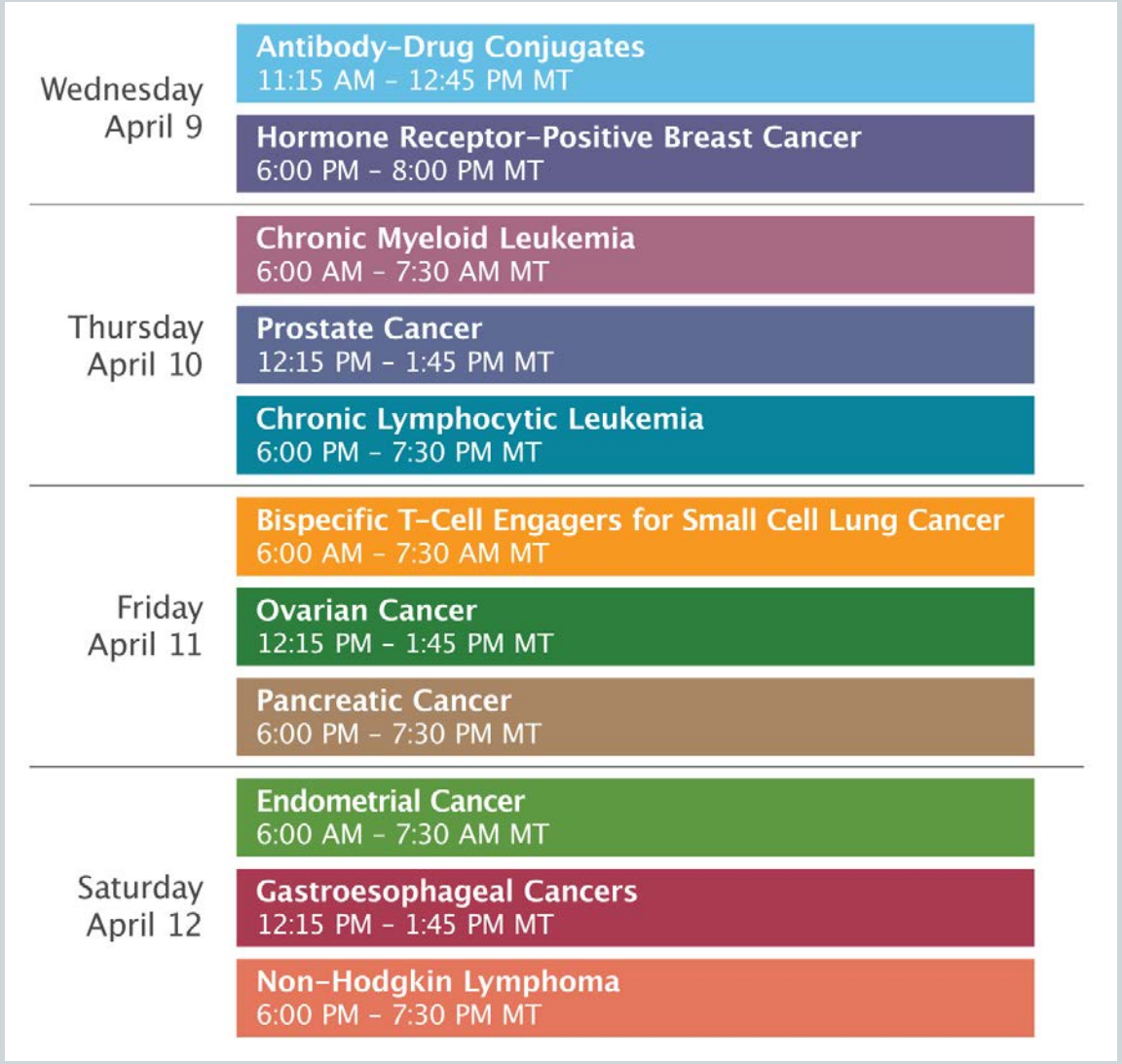


“Understanding the Current Paradigm and New Approaches”
Seventeenth Annual RTP-ONS NCPD Symposium Series



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Understanding the Current Paradigm and New Approaches
RTP Faculty at ONS 2025

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Agenda

Introduction: Overview of Ovarian Cancer (OC) Management

Module 1: Genetic Testing for Newly Diagnosed Advanced OC

Module 2: Role of PARP Inhibitor Maintenance in Newly Diagnosed Advanced OC

Module 3: Other Available and Investigational Novel Strategies for OC

Module 4: Current and Future Role of Mirvetuximab Soravtansine in OC Treatment

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CASE STUDY

- Patient with history of IIIC high grade serous ovarian cancer
- Initially presented with abdominal pain and was found to have bilateral pelvic masses and elevated CA-125
- Underwent debulking surgery and 6 cycles of carboplatin/paclitaxel
- Germline **BRCA2 mutation**
- Counseled on parp inhibitors immediately
- Completed 2 years of maintenance Olaparib 300 mg BID in 2022
- Tolerated treatment well, currently has no evidence of disease
- Biopsychosocial Issues: Adopted, good family support, history of stroke

Courtesy of Courtney Arn, CNP

Agenda

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Overview of Ovarian Cancer Management; Importance of Genetic Testing in Newly Diagnosed Advanced OC

Shannon N. Westin, MD, MPH

Professor

Department of Gynecologic Oncology and Reproductive Medicine

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MD Anderson Cancer Center
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Typical Course of Advanced Ovarian Cancer

Surgery (primary or IDS)
+ primary or adjuvant chemotherapy
carboplatin/paclitaxel
+/- bevacizumab
+/- PARPi

Platinum Sensitive
Progression **>6 months** after completion
of
platinum-based chemotherapy: Good Prognosis

First-Line

GENETIC TESTING!!!!!

Relapse/ Progression (70%-80%)

Second Response/ Disease Stabilization Maintenance?

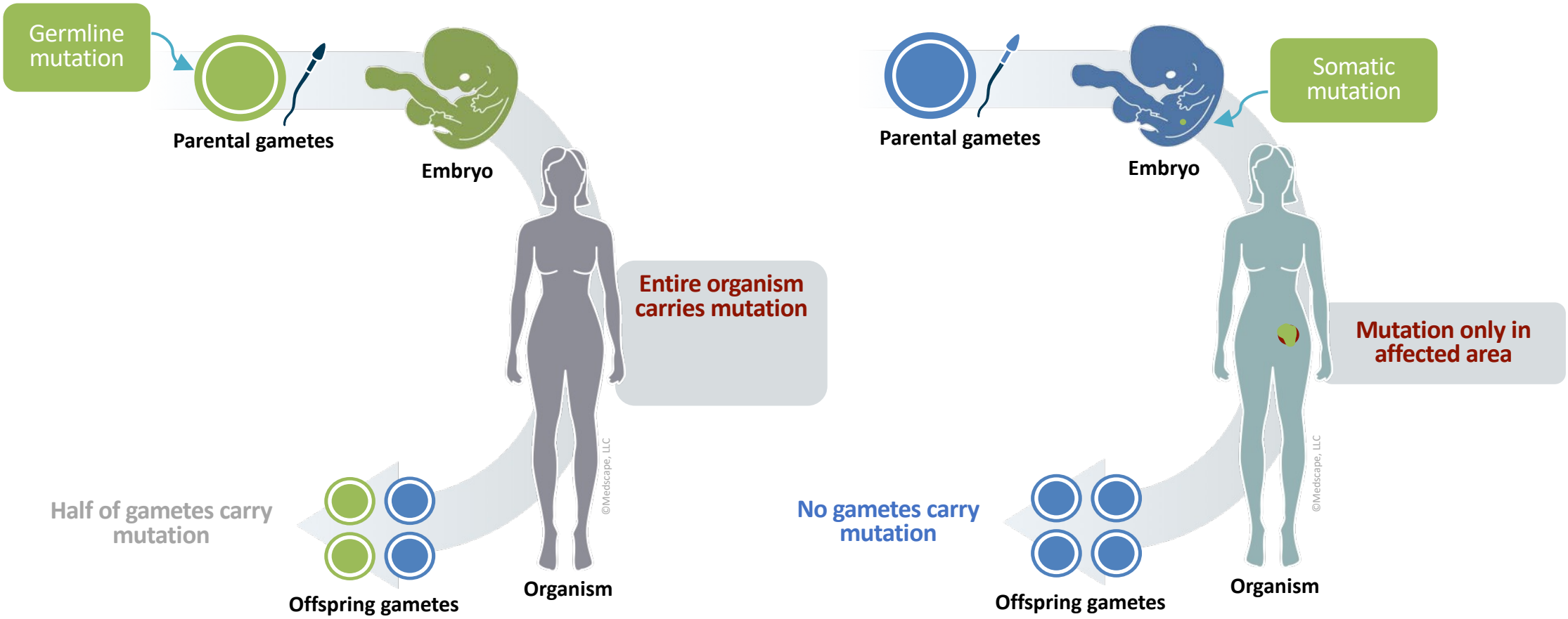
Relapse/ Progression (100%)

Surveillance every 3 months?
Maintenance Therapy?
Which Agent to Consider

Platinum Resistant
Progression **<6 months** after completion of **platinum**-based chemotherapy: Poor Prognosis

Ledermann JA, et al. *Ann Oncol. 2013,* Pignata S, et al. *Ann Oncol.* 2017; du Bois A, et al. *Cancer* 2009, Wilson MK, et al. *Ann Oncol*. 2017

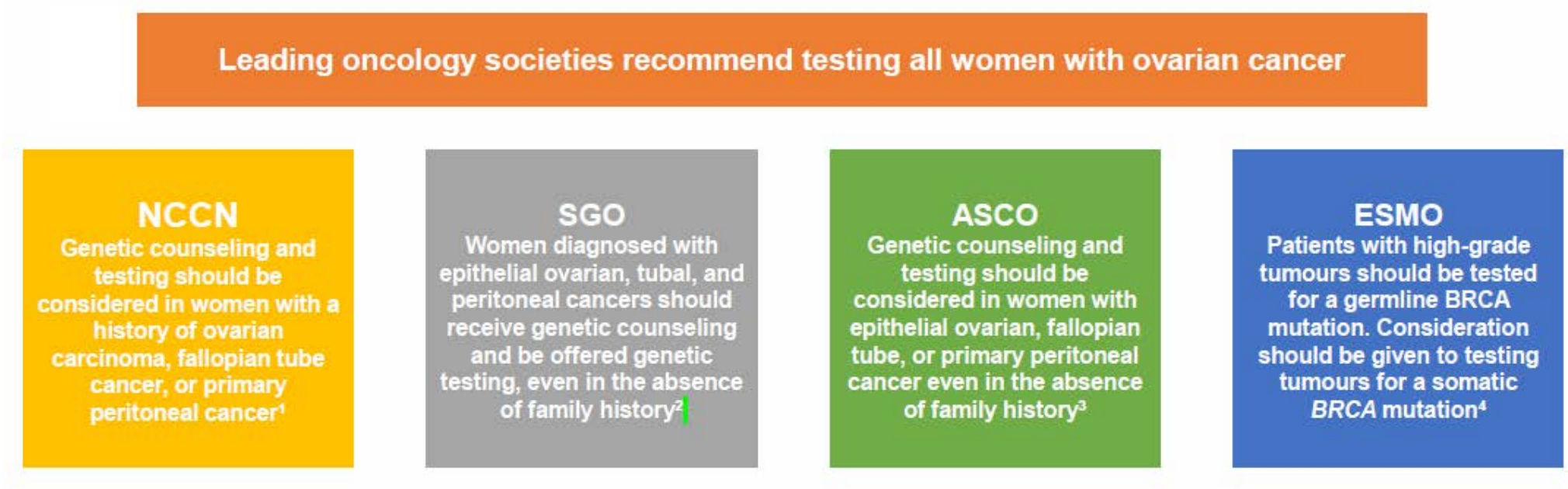
Germline vs Somatic Mutations



Germline mutations are inherited and found in all cells – they are stable and do not change.
Somatic mutations are not inherited and are found within the tumor – they can change over time.
Both can impact cancer risk

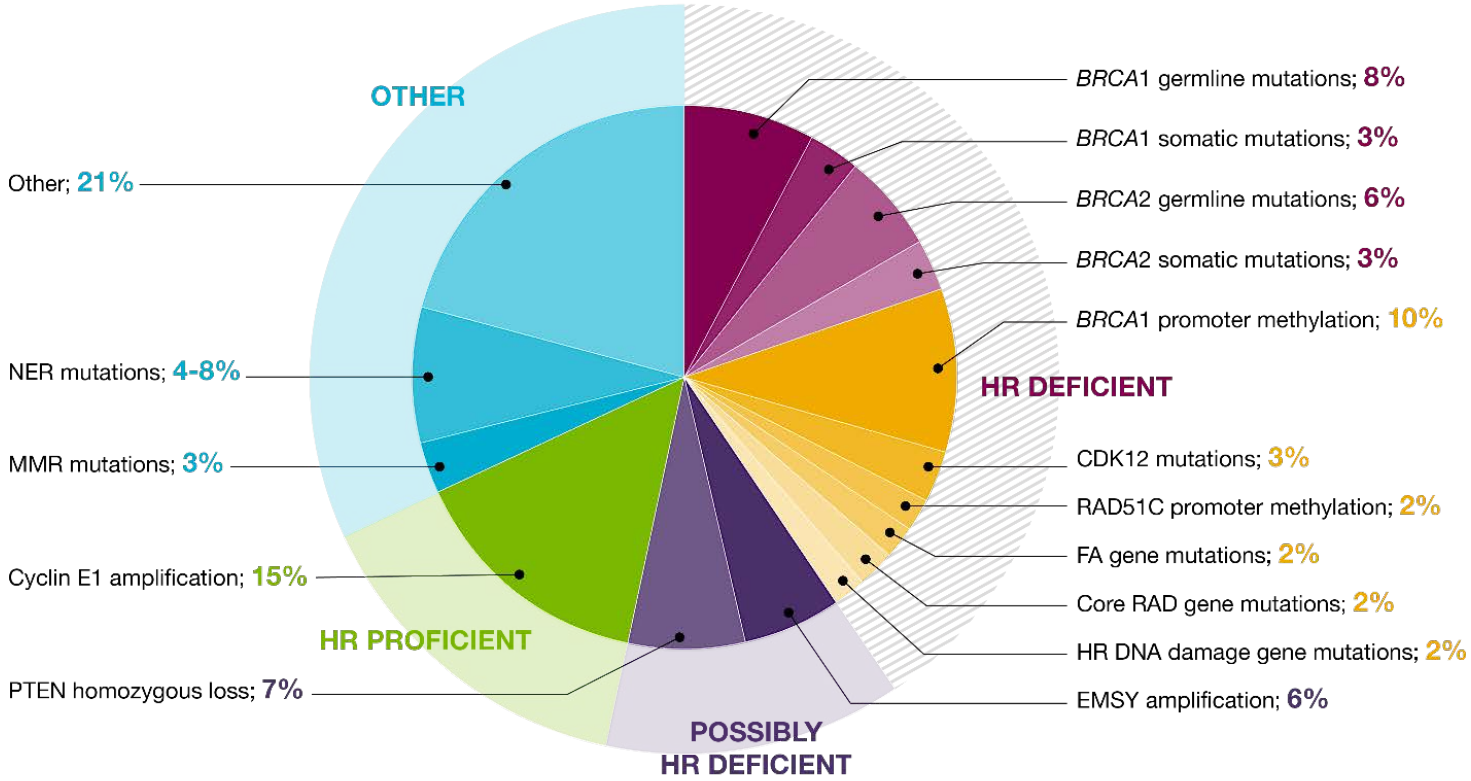
Which genes are associated with ovarian cancer risk and who should we test?

- *BRCA1* and *BRCA2*
- *RAD51C*, *RAD51D*, *BRIP1, PALB2*
- Lynch syndrome (*MLH1, MSH2, MSH6, PMS2, EPCAM*)



Common Aberrations in Ovarian Cancer

These defects can be identified using different clinical and molecular biomarkers

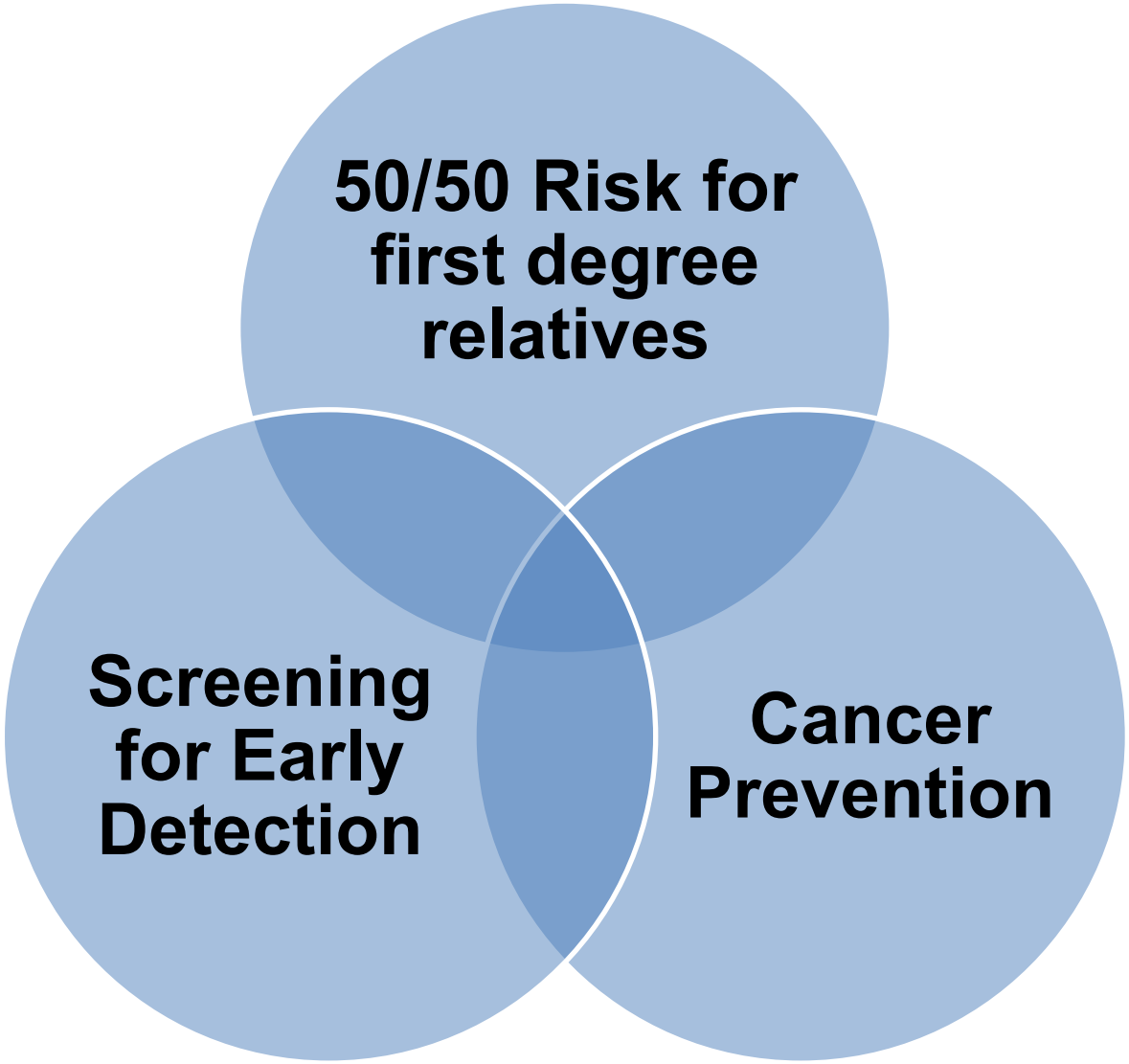


Clinical Implications:

Approximately 50% High Grade Epithelial Ovarian Cancers Characterized by HRD
Is this targetable in recurrent epithelial ovarian cancer?

Konstantinopoulos PA, et al. *Cancer Discov*. 2015

Importance of Cascade Testing



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Universal Genetic Testing: Missed Opportunities

- Meta-analysis (n=35 studies)
- 39% Referral to genetic counseling
- 30% Completion of genetic testing

Table 1
Pooled proportions of referral to genetic counseling and completion of genetic testing by race and insurance status.

	% Referred to counseling (95% CI)	% Completed genetic testing (95% CI)
Race		
White	43% (26–62%)	40% (25–57%)
Black	24% (13–42%)	26% (17–38%
Asian	23% (2–83%)	14% (2–51%)
Insurance status		
Private insurance	39% (26–54%)	47% (30–64%)
Medicare/Medicaid	27% (18–38%)	26% (16–40%)
Uninsured	24% (13–51%)	23% (18–28%)

Lin et al Gyn Onc 2021

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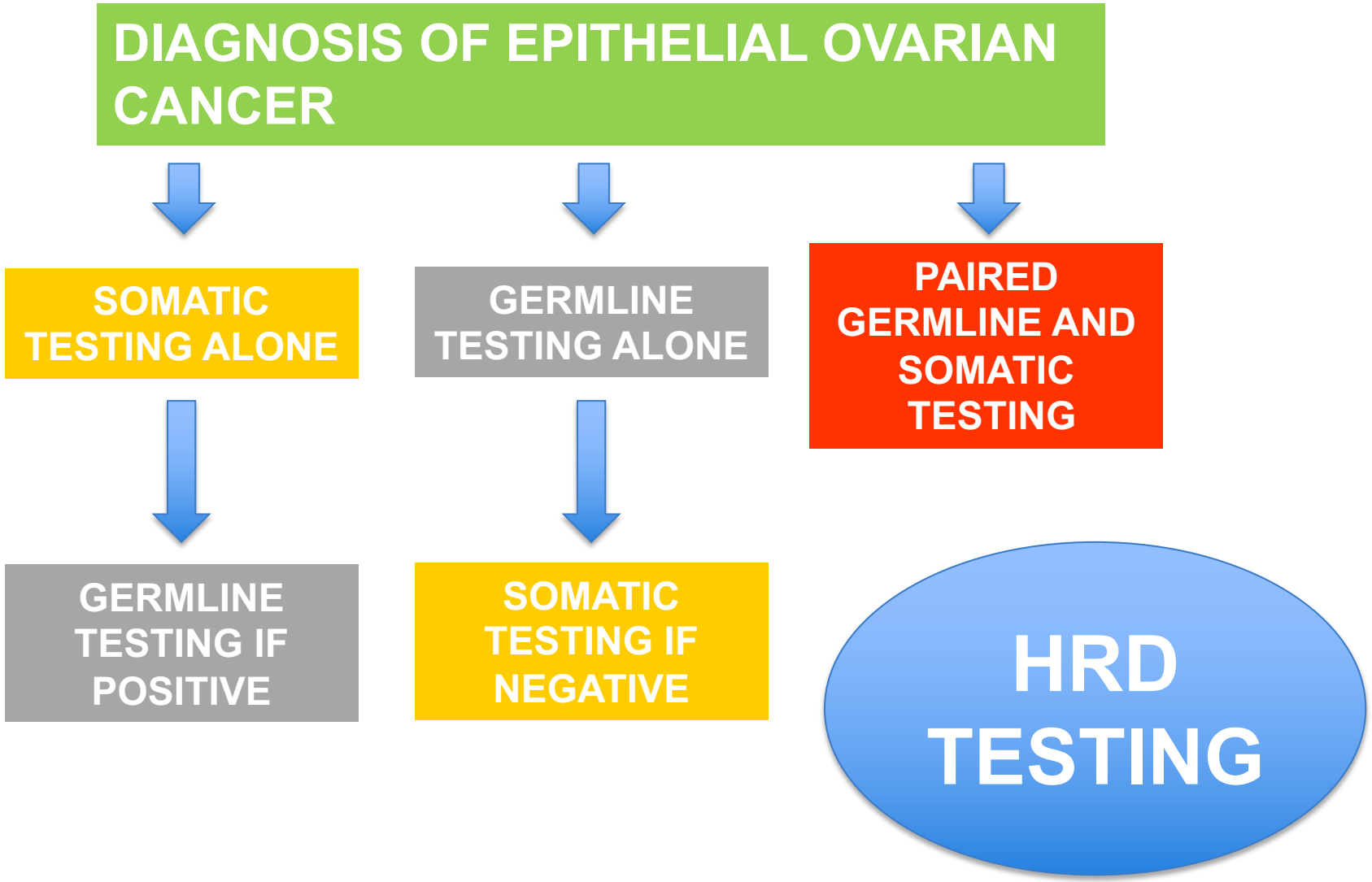
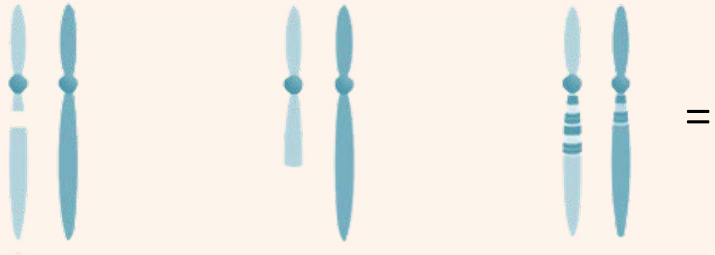
New Testing Paradigm



Molecular Testing in Ovarian Cancer: Which Tests Should Be Used?

MyChoice®

(CDx olaparib, niraparib, veliparib)



Loss of Heterozygosity | Telomeric Allelic Imbalance | Large-Scale State Transitions = MyChoice "GIS" Score

Homologous recombination status is determined by genomic instability score:

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

FoundationOne®

(CDx rucaparib)

Loss of Heterozygosity

HR-deficient tumors: LOH ≥16

Caris®

- Genomic scar score (LOH + LST)
- HRD genes, including *BRCA1* and *BRCA2*

Tempus®

- *BRCA* LOH and somatic genome-wide LOH
- HRD genes, including *BRCA1* and *BRCA2*

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

NCCN Guidelines Version 1.2025
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

NCCN Guidelines Index
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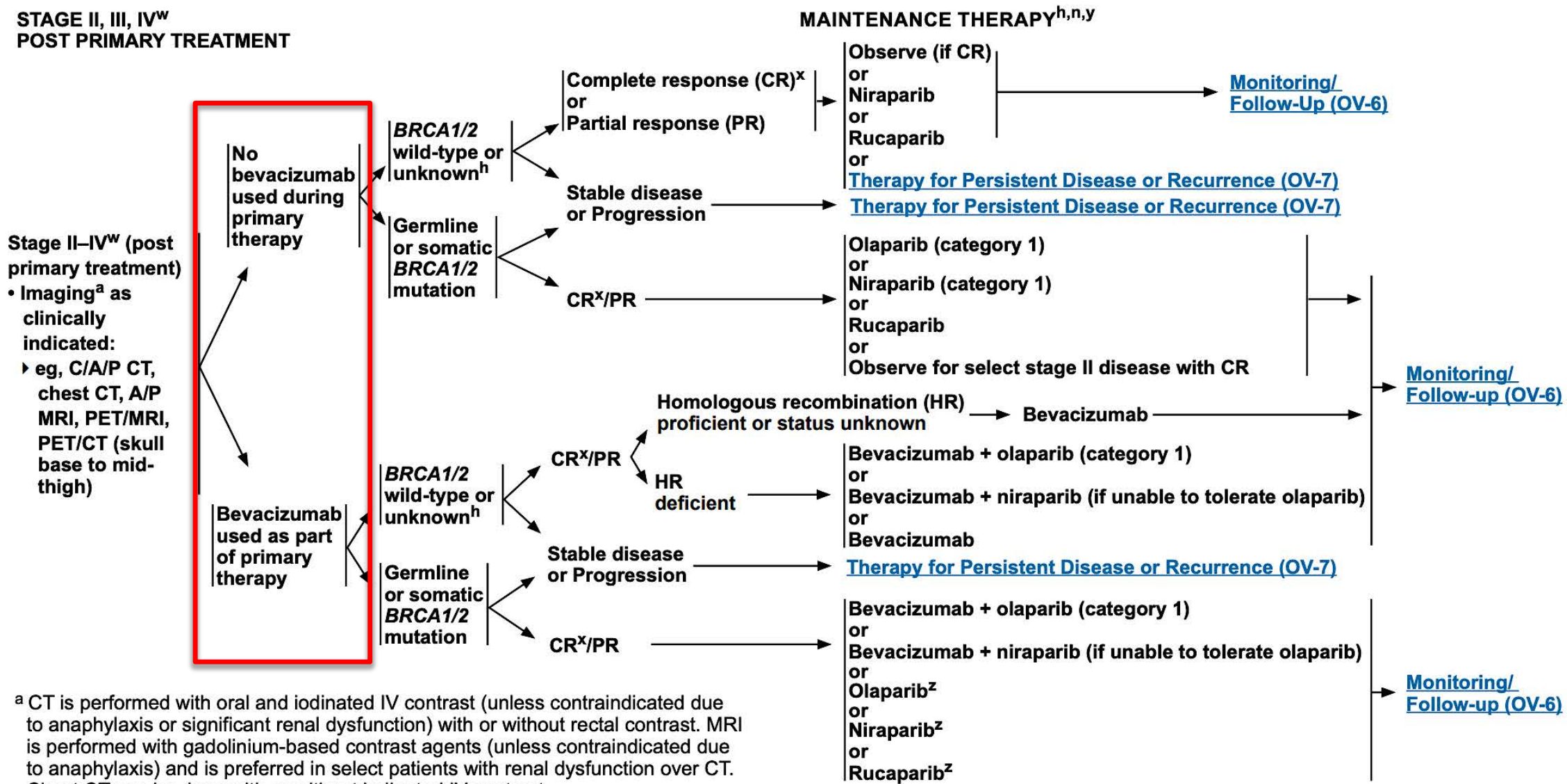
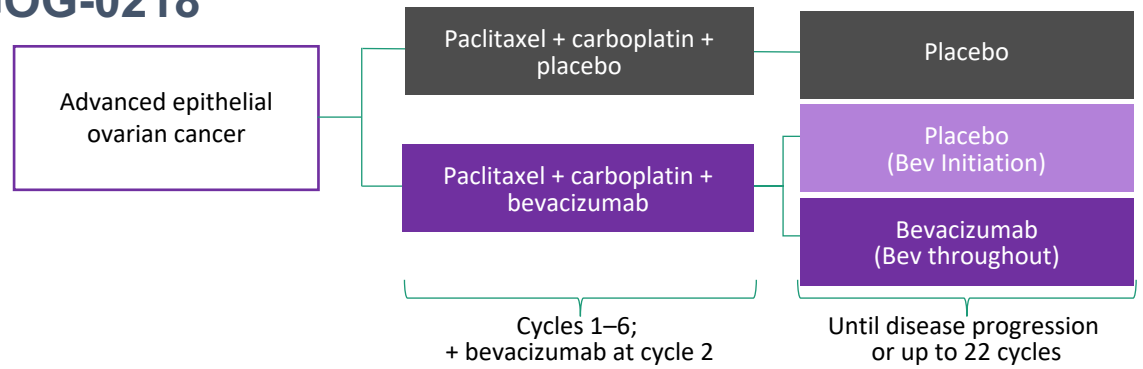
Discussion



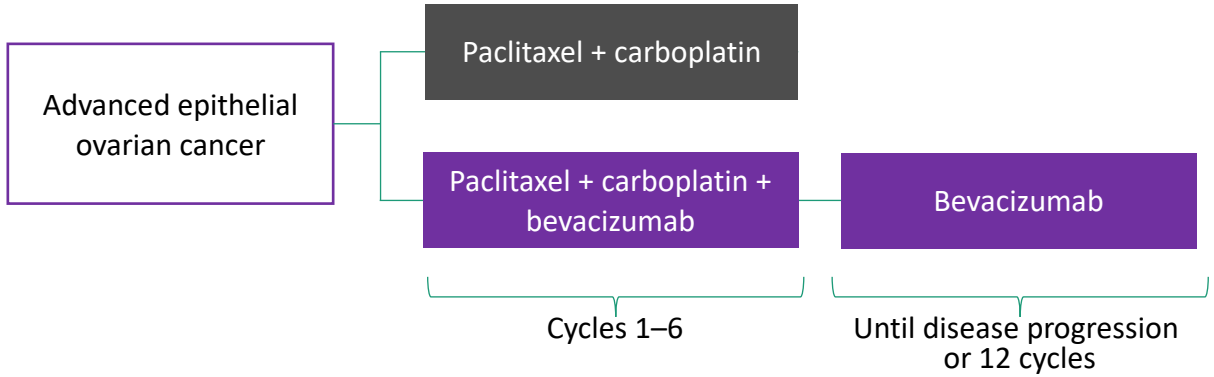
[a] CT is performed with oral and iodinated IV contrast (unless contraindicated due to anaphylaxis or significant renal dysfunction) with or without rectal contrast. MRI is performed with gadolinium-based contrast agents (unless contraindicated due to anaphylaxis) and is preferred in select patients with renal dysfunction over CT. Chest CT can be done with or without iodinated IV contrast.

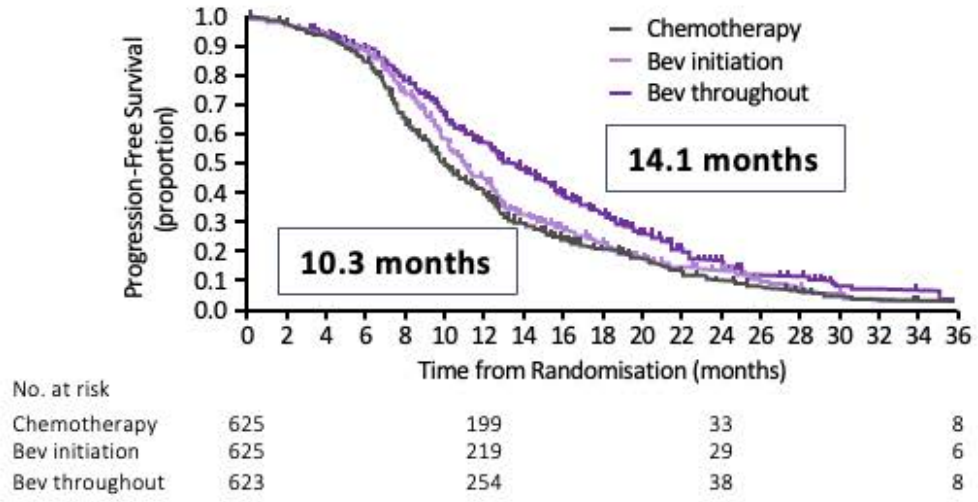
First-Line Chemotherapy Standard of Care: Carboplatin, Paclitaxel & Bevacizumab + Maintenance

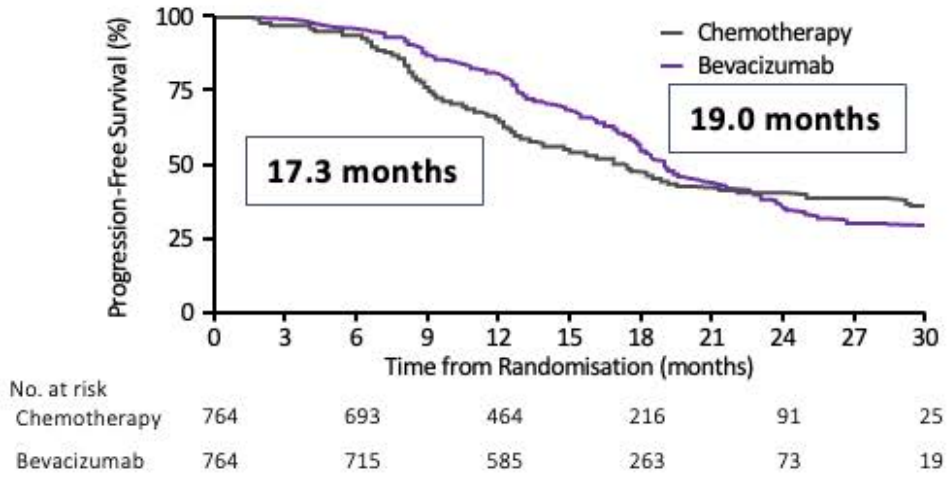
GOG-0218



ICON7







Burger RA et al. *N Engl J Med.* 2011; Perren TJ et al. *N Engl J Med.* 2011

Roundtable Discussion

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Agenda

Introduction: Overview of Ovarian Cancer (OC) Management

Module 1: Genetic Testing for Newly Diagnosed Advanced OC

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Clinical Scenario

A patient with newly diagnosed advanced OC with a germline BRCA2 mutation has undergone debulking surgery and 6 cycles of carboplatin/paclitaxel and is about to start PARP inhibitor maintenance

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ADVANCES IN OVARIAN CANCER

David O'Malley, MD
Professor
Division Director, Gynecologic Oncology
Co-Director, Gyn Oncology Phase I Program

The James

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




PARPi in The First Line

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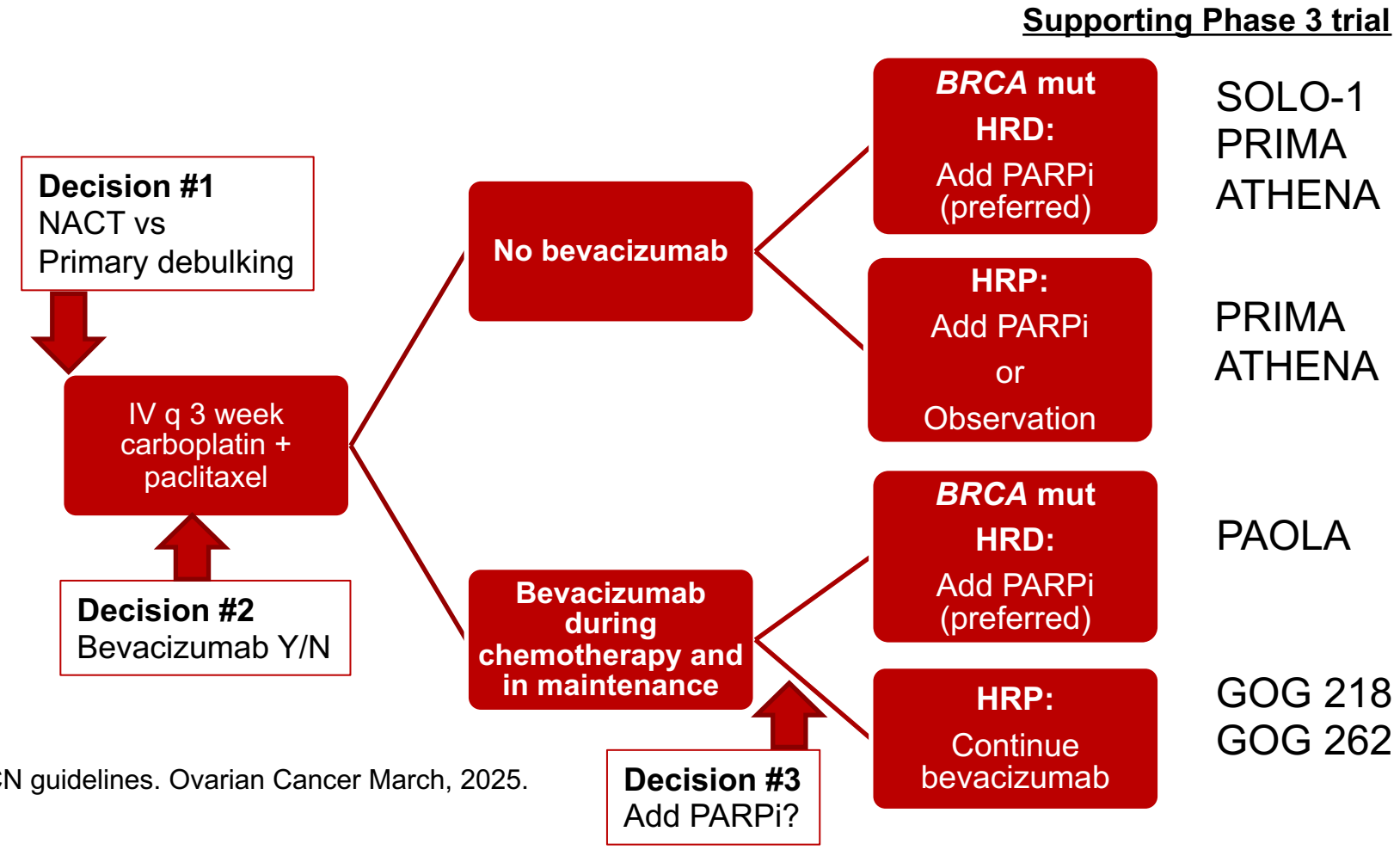
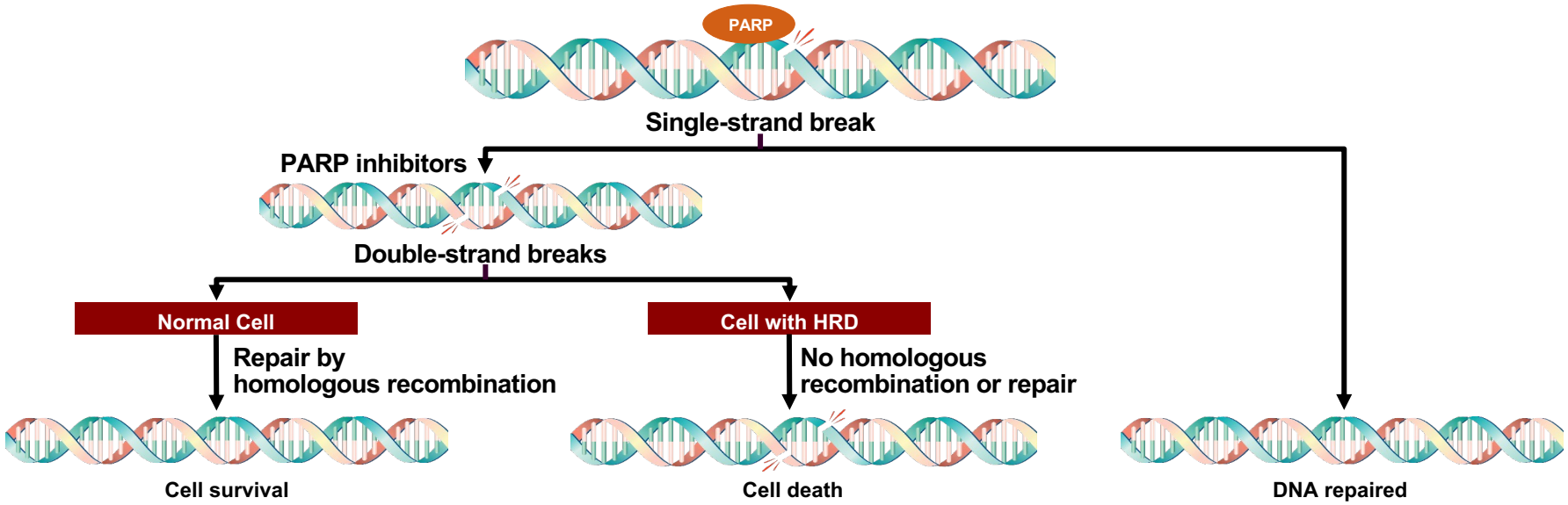
Integrated Maintenance Treatment Paradigm for Use in 1-L Ovarian Cancer (2022)



1. NCCN guidelines. Ovarian Cancer March, 2025.

PARP Inhibitors Yield Synthetic Lethality in Patients With HRD

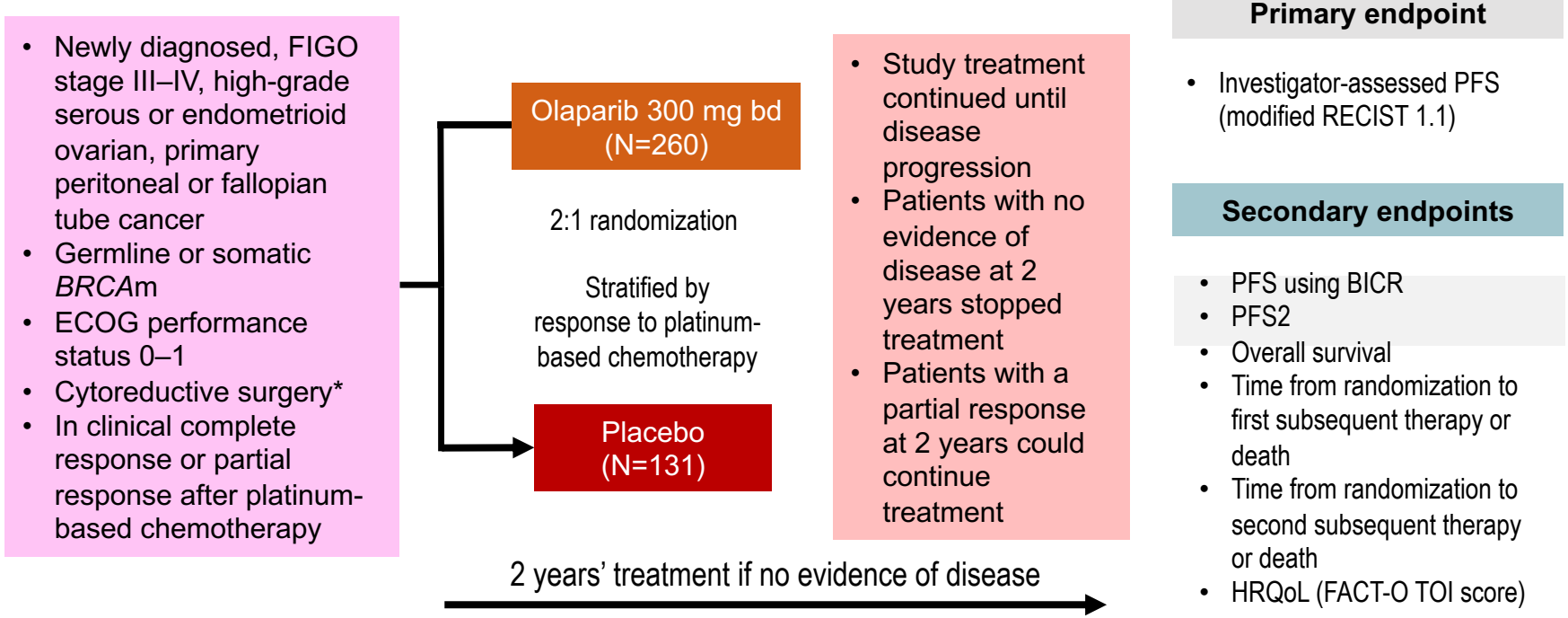
- **PARP inhibitors prevent repair of single-strand breaks, which accumulate and generate double-strand breaks**
- **People with HRD cannot repair double-strand breaks, which triggers cell death**



HRD, homologous recombination deficiency

Sonnenblick A, et al. *Nat Rev Clin Oncol.* 2015;12(1):27-41.

SOLO-1: PHASE III TRIAL INVESTIGATING MAINTENANCE THERAPY WITH A PARP INHIBITOR IN NEWLY DIAGNOSED ADVANCED *BRCA*^{MUT} OVARIAN CANCER



*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease. BICR, blinded independent central review; ECOG, Eastern Cooperative Oncology Group; FACT-O, Functional Assessment of Cancer Therapy – Ovarian Cancer; FIGO, International Federation of Gynecology and Obstetrics; HRQoL, health-related quality of life; PFS, progression-free survival; PFS2, time to second progression or death; RECIST, Response Evaluation Criteria in Solid Tumours; TOI, Trial Outcome Index

Moore et al ESMO 2018; NEJM 2018

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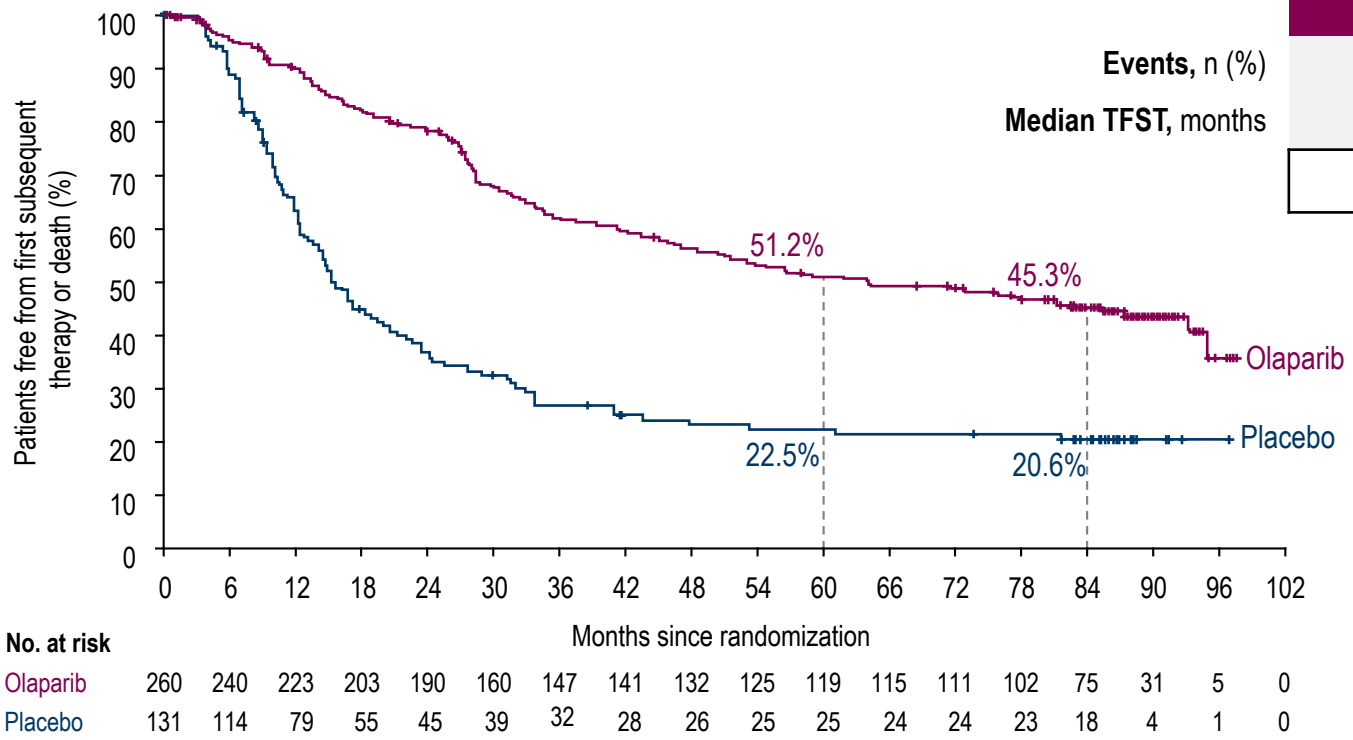
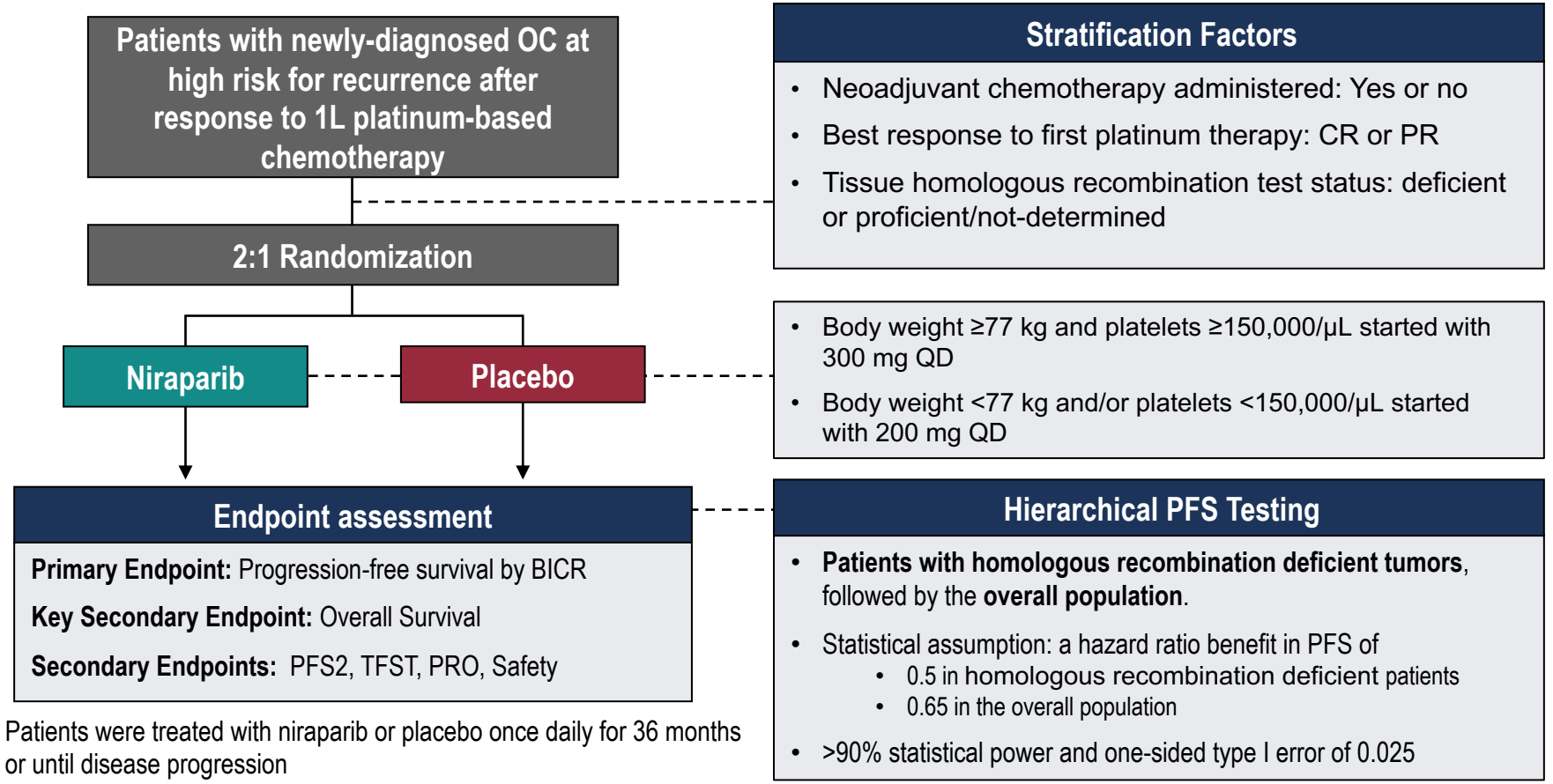
SOLO-1 TFST substantially delayed by maintenance olaparib



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	135 (51.9)	98 (74.8)
Median TFST, months	**64.0**	**15.1**
HR 0.37 (95% CI 0.28–0.48)		

Paul DiSilvestro, et al ESMO 2022

PRIMA Trial Design



1L, first-line; BICR, blinded independent central review; CR, complete response; OC, ovarian cancer; PFS2, progression-free survival 2; PR partial response; PRO, patient-reported outcomes; TFST, time to first subsequent therapy.

Modified from González-Martín A, Presented at ESMO 2019, Barcelona, Spain
González-Martín A, et al. *N Engl J Med*. 2019. doi:10.1056/NEJMoa1910962.

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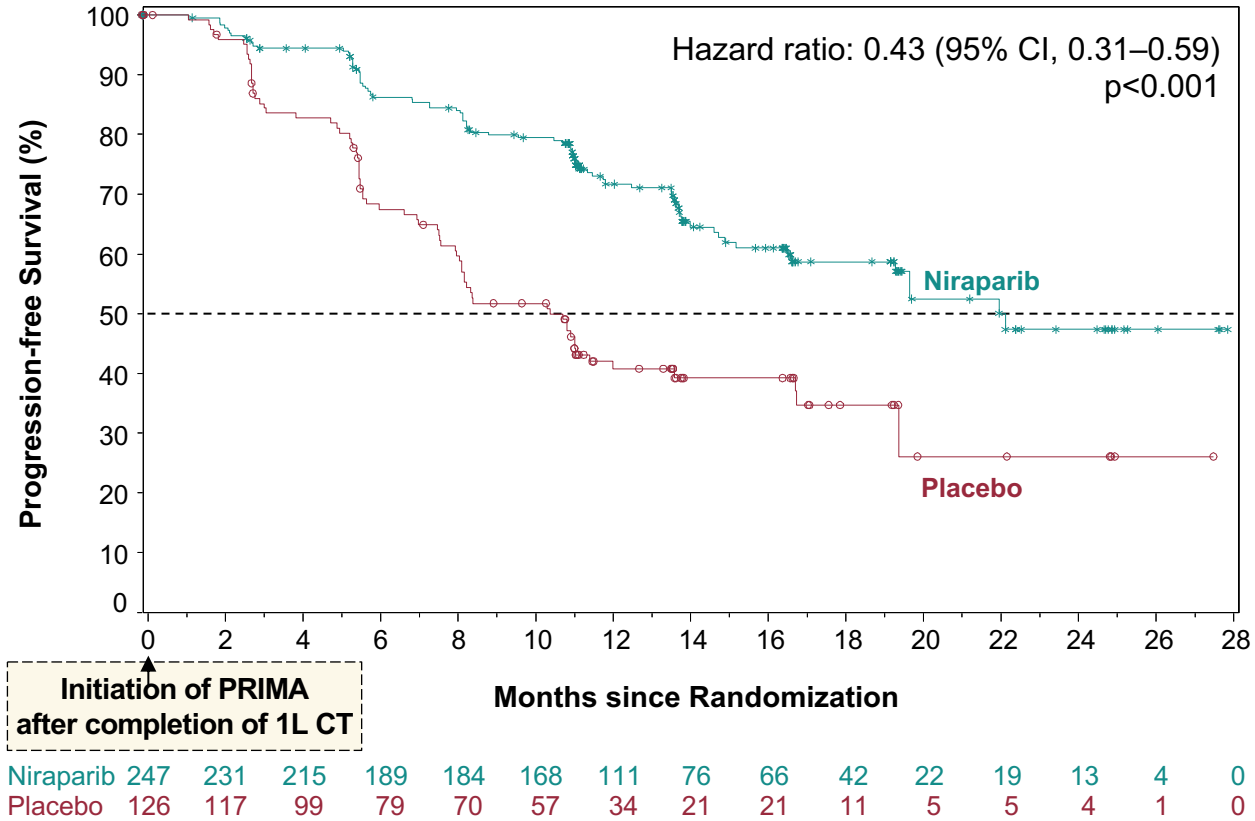
PRIMA Primary Endpoint, PFS Benefit in the HR-deficient Population



57% reduction in hazard of relapse or death with niraparib

	Niraparib (n=247)	Placebo (n=126)
Median PFS		
months (95% CI)	**21.9 (19.3–NE)**	**10.4 (8.1–12.1)**
Patients without PD or death (%)		
6 months	**86%**	**68%**
12 months	**72%**	**42%**
18 months	**59%**	**35%**

1L, first-line; CI, confidence interval; CT, chemotherapy; HR, homologous recombination; NE, not estimable; PD, progressive disease; PFS, progression-free survival.
Sensitivity analysis of PFS by the investigator was similar to and supported the BICR analysis.

Modified from González-Martín A, Presented at ESMO 2019, Barcelona, Spain
González-Martín A, et al. *N Engl J Med*. 2019. doi:10.1056/NEJMoa1910962.

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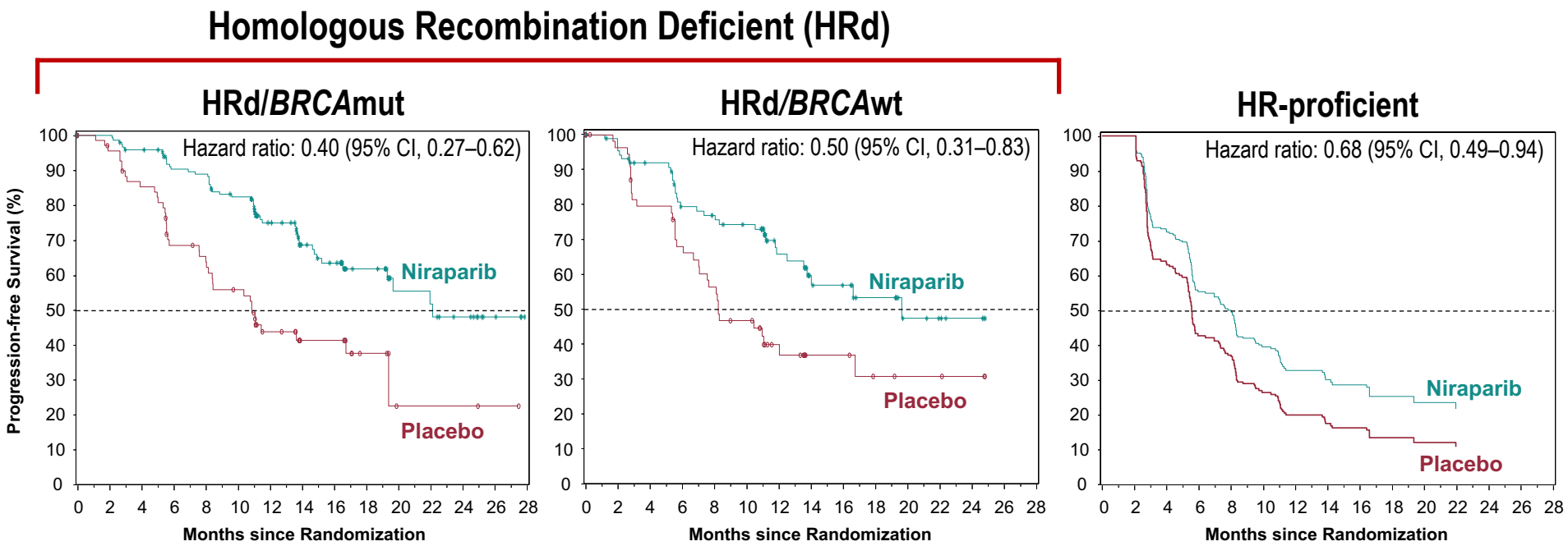
PRIMA PFS Benefit in Biomarker Subgroups



- Niraparib provided similar clinical benefit in the HRd subgroups (*BRCA*mut and *BRCA*wt)
- Niraparib provide clinically significant benefit in the HR-proficient subgroup with a 32% risk reduction in progression or death

CI, confidence interval; HR, homologous recombination; mut, mutation; PFS, progression-free survival wt, wild-type.

Modified from González-Martín A, Presented at ESMO 2019, Barcelona, Spain
González-Martín A, et al. *N Engl J Med*. 2019. doi:10.1056/NEJMoa1910962.

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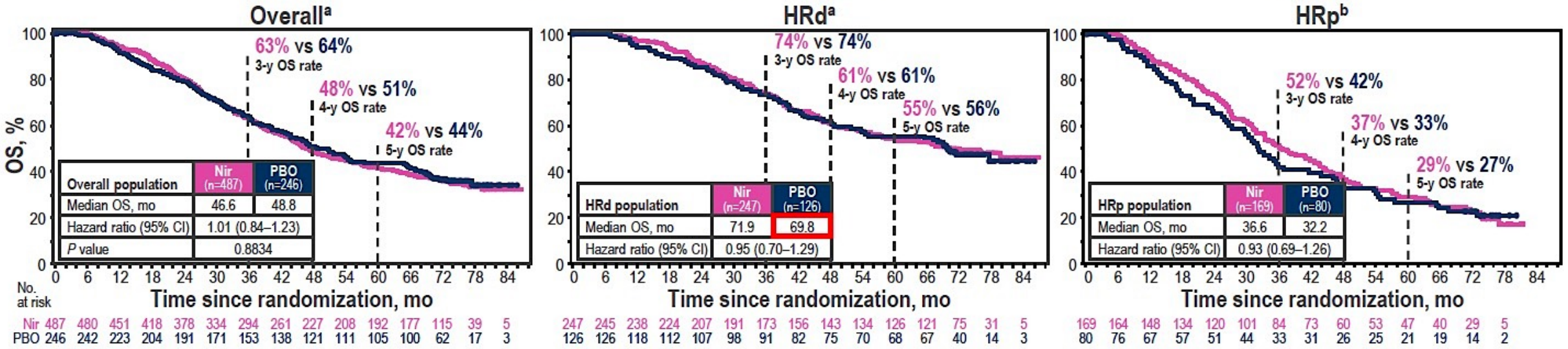
PRIMA/ENGOT-OV26/GOG-3012 Trial of Niraparib 1L Maintenance *cont.*

Final OS (62.5% maturity in overall population)

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



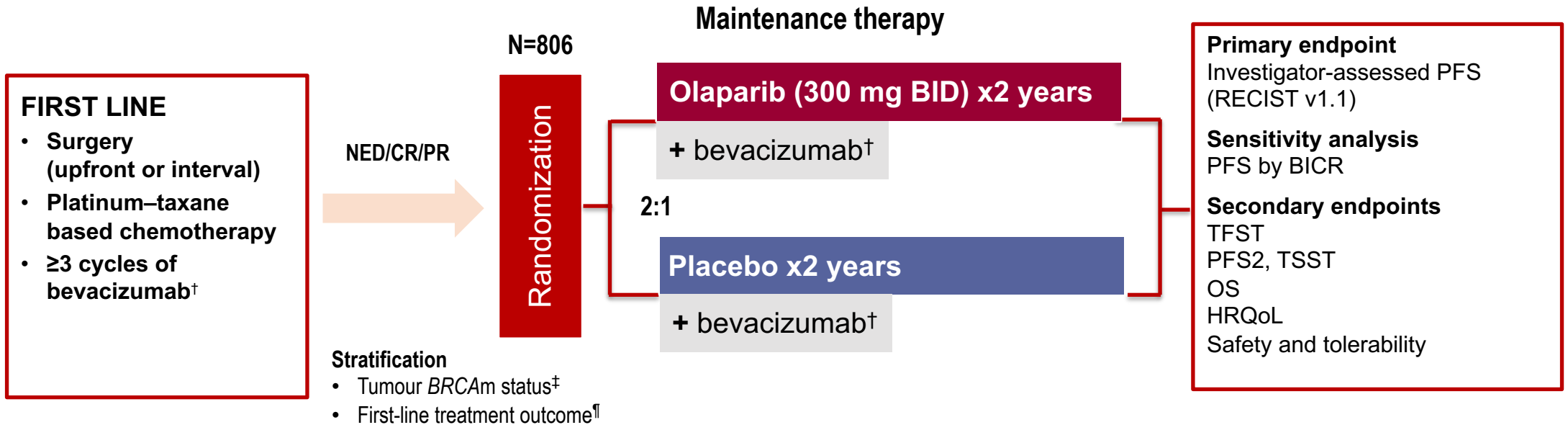
- OS results for all prespecified biomarker-defined subgroups consistent with overall population[c]
- Assessment of long-term efficacy outcomes in high-risk aOC may be complicated by multiple factors[1]
  - Patient population[2–4]
  - Extended postprogression survival[1,5]
  - Subsequent therapy[1,5]

[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.

NCT02655016

Phase III PAOLA-1/ENGOT-ov25: maintenance olaparib with bevacizumab in patients with newly diagnosed, advanced ovarian cancer treated with platinum-based chemotherapy and bevacizumab as standard of care

Newly diagnosed FIGO stage III–IV high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer*



*Patients with other epithelial non-mucinous ovarian cancer were eligible if they had a germline *BRCA1* and/or *BRCA2* mutation
†Bevacizumab: 15 mg/kg, every 3 weeks for a total of 15 months, including when administered with chemotherapy; ‡By central labs; ¶According to timing of surgery and NED/CR/PR
BICR, blinded independent central review; HRQoL, health-related quality of life; PFS2, time to second progression or death; RECIST, Response Evaluation Criteria in Solid Tumours; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death

Ray-Coquard IL, *et al.* Oral Presentation LBA2_PR at ESMO, September 27–October 1, 2019, Barcelona, Spain

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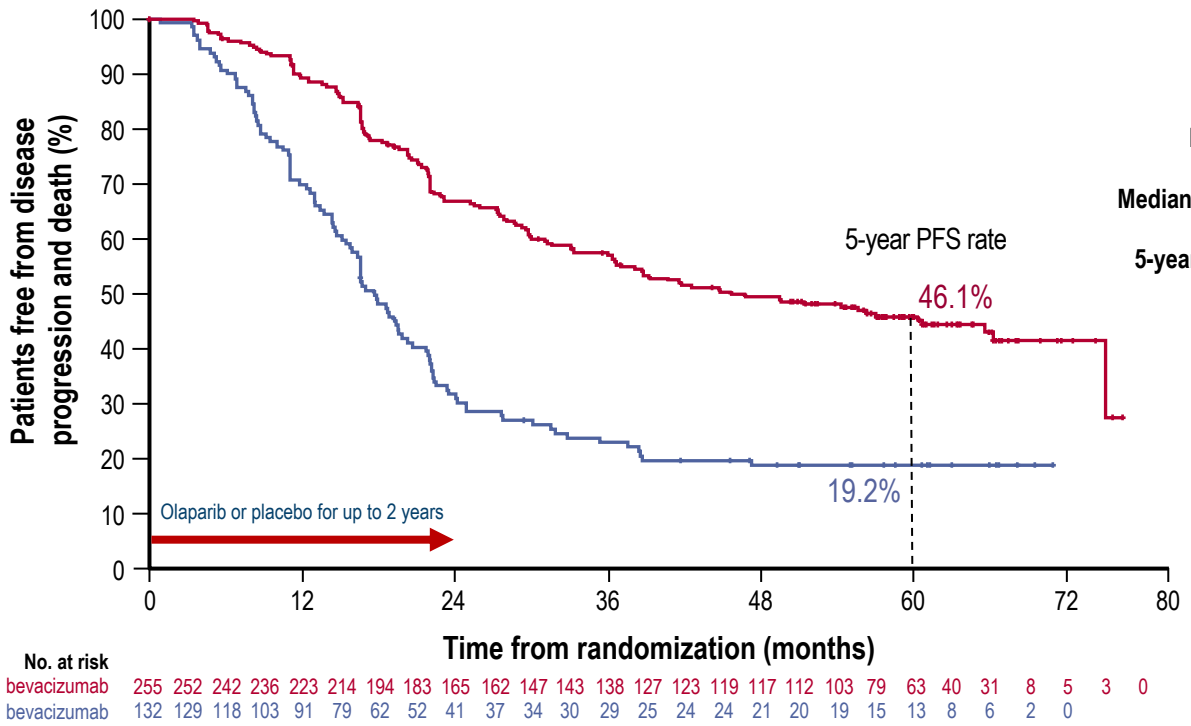
Updated PFS: HRD-positive population*



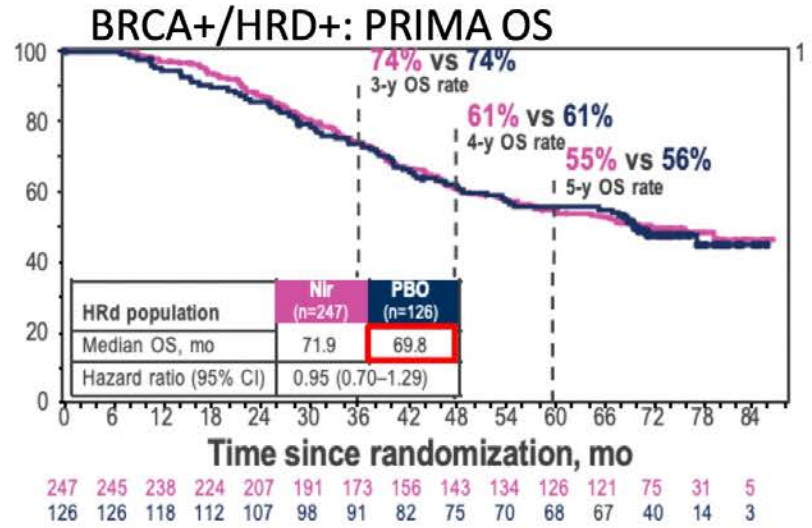
	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	136 (53.3)	104 (78.8)
Median PFS, months	**46.8**	**17.6**
5-year PFS rate, %	**46.1**	**19.2**

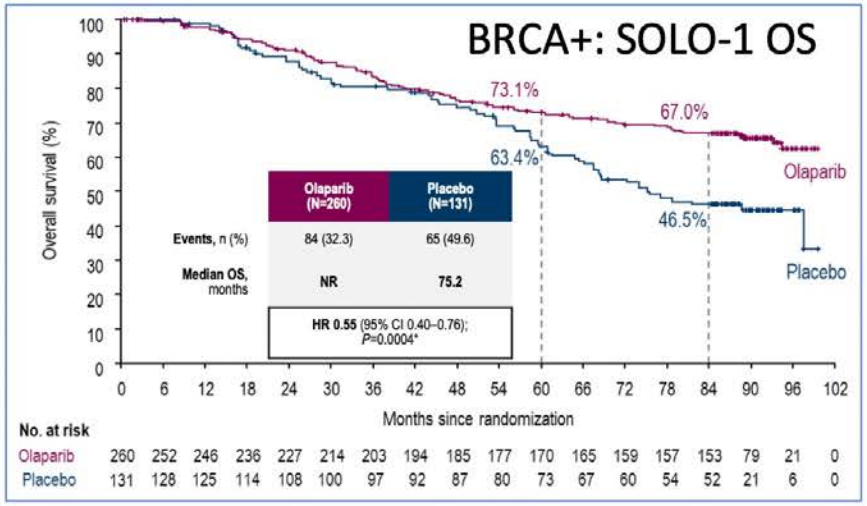
HR 0.41 (95% CI 0.32–0.54)

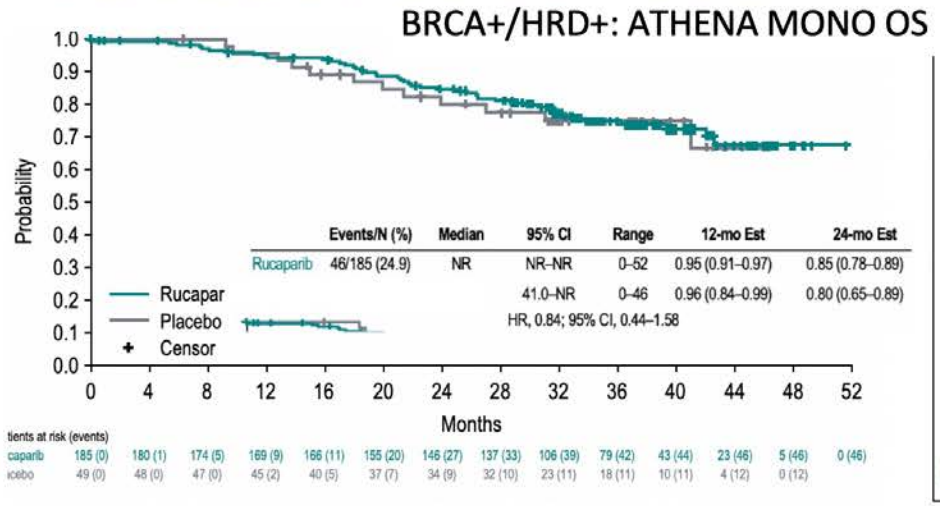
59% reduction in risk of disease progression or death for olaparib + bevacizumab vs bevacizumab alone

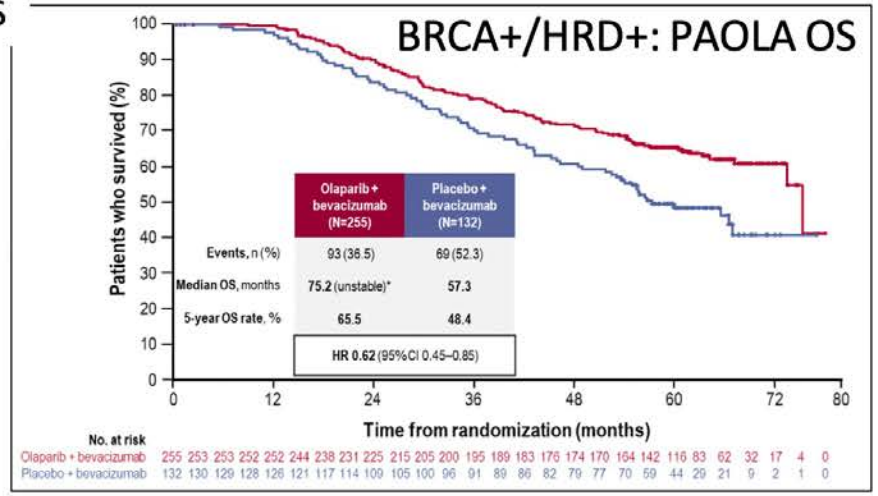
*Descriptive analysis; PFS by investigator-assessment (modified RECIST v1.1).

Updated OS – First Line Ovarian Cancer









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Upfront Ovarian Cancer Maintenance Treatment

- PARPi versus Bev versus Both
- Curative intent is the goal
- Biomarker derived therapy is now the standard.
- Management of Toxicity is essential

PARPi + IO in Ovarian Cancer

Trial	Anti-angiogenic	PARPi	ICI	Median PFS	PFS HR
FIRST ENGOT OV-44	± Bevacizumab	Niraparib	Dostarlimab	Statistically significant improvement (press release)	
DUO-O ENGOT OV-46	Bevacizumab	Olaparib	Durvalumab	25.1 mo (ITT population)	0.61 (0.51-0.73)
ATHENA GOG-3020 ENGOT OV-45	-	Rucaparib	Nivolumab	15.0 mo (ITT population)	1.29 (1.08–1.53)
ENGOT OV-43 KEYLYNK-001	± Bevacizumab	Olaparib	Pembrolizumab	23.9 mo (CPS ≥10 population)	0.66 (0.53-0.83)

Trillsch et al. ESMO GU 2024;Abstract 43O.
Monk et al. ESMO 2024;Abstract LBA30.
Vergote et al. ESGO 2025.
https://www.gsk.com/en-gb/media/press-releases/gsk-announces-first-trial-met-its-primary-endpoint-of-progression-free-survival-in-first-line-advanced-ovarian-cancer/

RTP RESEARCH TO PRACTICE

Recurrent Serous Carcinoma of the Ovary, Stage IIIC
BRCA1+, PD-L1+, FOLR1 negative (0%), Her2 negative (score=0)

Diagnosed in 2006 - TAH/BSO/LND/Omentectomy/Extensive TRS - Stage IIIC Ovarian Cancer

- Followed by Taxol/Carbo x 6 cycles

- Recurred approximately 36 months later with GI symptoms (N/V with GERD), abdominal distention, elevated CA-125 (60)
- Underwent TRS/Omentectomy/Splenectomy - positive for metastatic serous carcinoma
  - Followed by Carbo/Gem/Bev x 6 cycles
- Diagnosed with recurrence 13 years later
  - Followed by Gem/Carboplatin/Bev
  - Started maintenance Bev
  - Started Olaparib, discontinued after 1 dose due to allergic reaction
  - Switched to Niraparib Cycle 2
  - Completed 5 cycles of maintenance Bev, discontinued Cycle 6 due to persistent hypertension.
  - Continued Niraparib

Roundtable Discussion

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CONSIDERATIONS FOR PATIENTS RECEIVING A PARP INHIBITOR

Courtney Arn, CNP

The Ohio State University

James Comprehensive Cancer Center

Columbus, Ohio

INITIATION OF PARP INHIBITORS

- Baseline Labs
- Patient Education:
  - MOA
  - Indication
  - Side effects/expectations
  - Treatment Plan/Schedule
- Supportive Care
- Co-pay Evaluation/Financial Support

MECHANISM OF ACTION

- PARP inhibitors block the activity of PARP enzymes, disrupting the normal DNA repair process and ultimately causing cell death, particularly in cancer cells with impaired DNA repair mechanisms like BRCA mutations.

- Tumor cells carrying a *BRCA* mutation have been shown to be significantly more sensitive to PARP inhibition than tumors that do not carry a *BRCA* mutation

SIDE EFFECTS - NIRAPARIB

- Thrombocytopenia (66%)
- Anemia (64%)
- Nausea (57%)
- Fatigue (51%)
- Neutropenia (42%)
- Constipation (40%)
- Musculoskeletal pain (39%)
- Hypertension (18%)
- Warnings & Precautions: MDS/AML, Hematologic, Hypertension, PRES, Embryo-Fetal Toxicity

Niraparib prescribing information.

SIDE EFFECTS – OLAPARIB

- Nausea (77%)
- Fatigue (67%)
- Abdominal pain (45%)
- Vomiting (40%)
- Anemia (38%)
- Diarrhea (37%)
- Warnings & Precautions: MDS/AML, Pneumonitis, VTE, Embryo-Fetal Toxicity

Olaparib prescribing information.

MONITORING & MANAGING SIDE EFFECTS

- Nausea: Prophylactic anti-emetics 30-60 minutes prior to dosing and PRN
- Constipation: Stool softeners, Laxatives, Diet, Physical Activity
- Diarrhea: Anti-diarrheal, Diet, Fluids, Electrolytes
- Fatigue: Hydration, Exercise, PT, consider stimulants
- Hematologic: Plan for monitoring labs, transfuse as needed

GRADE ≥3 AES OF INTEREST

	PRIMA		PAOLA-1		SOLO-1	
	Niraparib	Placebo	Bevacizumab + Olaparib	Bevacizumab + Placebo	Olaparib	Placebo
n	484	244	535	267	260	130
Anemia	**31%**	2%	17%	<1%	22%	2%
Neutropenia	**13%**	1%	6%	3%	9%	5%
Thrombocytopenia	29%	<1%	2%	<1%	1%	2%
Fatigue	2%	1%	5%	1%	4%	2%
MDS/AML	Not reported	Not reported	1%	<1%	1%	0
Nausea	1%	1%	2%	1%	1%	0%
Vomiting	1%	1%	1%	2%	<1%	1%
Diarrhea	1%	**********	2%	2%	3%	0
Constipation	<1%	0	Not Reported	Not Reported	0	0
Hypertension	6%	1%	**19%**	**30%**	Not Reported	Not Reported

Cross-trial comparisons are not head-to-head studies; varying study designs, methodology, and populations limit ability to draw conclusions of comparative efficacy and safety.
AE, adverse event; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; thrombo, thrombocytopenia; ↓plt, decreased platelets.
1. González-Martín A, et al. *N Engl J Med*. 2019. doi:10.1056/NEJMoa1910962. 2. González-Martín A, et al. Presented at: ESMO Congress; September 27-October 1, 2019; Barcelona, Spain. Abstract LBA1.
3. Ray-Coquard IL, et al. Presented at: ESMO Congress; September 27-October 1, 2019; Barcelona, Spain. Abstract LBA2. 4. Moore K, et al. *N Engl J Med*. 2018;27;379(26):2495-2505.

AML/MDS WITH PARP INHIBITOR TREATMENT

Trial	Placebo	Parp Inhibitor
SOLO-2 Olaparib	4%	8%
NOVA Niraparib	1.7% (3.1% in BRCA)	3.5% (6.6% in BRCA)
ARIEL3 Rucaparib	3.2	3.8

Poveda A, Floquet A, Ledermann JA, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive relapsed ovarian cancer and *BRCA1/2* mutation (SOLO2/ENGOT-Ov21): a final analysis of a double-blind, randomised, placebo-controlled, phase 3 trial. Supplementary appendix [published online March 18, 2021]. *Lancet Oncol.*
Matulonis UA, Herrstedt J, Oza A, et al. Long-term safety and secondary efficacy endpoints in the ENGOT-OV16/NOVA phase 3 trial of niraparib in recurrent ovarian cancer. Presented at: Society of Gynecological Oncology 2021 Virtual Annual Meeting on Women's Cancer; March 19-21, 2021; Virtual. Abstract 37
Coleman et al. Overall Survival Results From ARIEL3: A Phase 3 Randomized, Double-blind Study of Rucaparib vs Placebo Following Response to Platinum-Based Chemotherapy for Recurrent Ovarian Carcinoma. IGCS 2022

AML/MDS WITH PARP INHIBITOR TREATMENT

Trial	Placebo	Parp Inhibitor
SOLO-1 Olaparib	0.8%	1.5%
PRIMA Niraparib	1.6%	2.3%
PAOLA-1 Olaparib + bevacizumab	2.2%	1.7%

DiSilvestro P et al. *J Clin Oncol* 2022;41(3):609-17; Monk BJ et al. *Ann Oncol* 2024;35(11):981-92; Ray-Coquard I et al. *Ann Oncol* 2023;34(8):681-92.

DOSING & ADMINISTRATION

	Olaparib	Niraparib
Dosage Forms	Tablets: 100 mg or 150 mg	Tablets: 100 mg
Dose	300 mg bid	300 mg daily
Starting Dose Modifications	Moderate renal impairment CYP3A inhibitor use	If baseline weight: <77 kg OR platelets: <150,000/uL
Monitor	CBC at baseline and monthly thereafter	• CBC weekly for the first month, then monthly for the next 11 months, and then periodically • BP monthly during the first year and periodically

NIRAPARIB INDIVIDUALIZED STARTING DOSE

Niraparib prescribing information. Accessed 4/2025.

DOSE MODIFICATION

	PRIMA		PAOLA-1		SOLO-1	
	Niraparib	Placebo	Bevaci-zumab + Olaparib	Bevaci-zumab + Placebo	Olaparib	Placebo
n	484	244	535	267	260	130
Dose reduction	71%	8%	41%	7%	28%	3%
Dose interruption	80%	18%	54%	24%	52%	17%
AE leading to discontinuation	12%	3%	20%	6%	12%	2%
Grade >/= 3 AEs	71%	19%	57%	51%	39%	18%

AE, adverse event.

1. González-Martín A, et al. *N Engl J Med*. 2019. doi:10.1056/NEJMoa1910962. 2. González-Martín A, et al. Presented at: ESMO Congress; September 27-October 1, 2019; Barcelona, Spain. Abstract LBA1. 3. Ray-Coquard IL, et al. Presented at: ESMO Congress; September 27-October 1, 2019; Barcelona, Spain. Abstract LBA2. 4. Moore K, et al. *N Engl J Med*. 2018;27;379(26):2495-2505.

Roundtable Discussion

RTP
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TO PRACTICE

Agenda

Introduction: Overview of Ovarian Cancer (OC) Management

Module 1: Genetic Testing for Newly Diagnosed Advanced OC

Module 2: Role of PARP Inhibitor Maintenance in Newly Diagnosed Advanced OC

Module 3: Other Available and Investigational Novel Strategies for OC

Module 4: Current and Future Role of Mirvetuximab Soravtansine in OC Treatment

RTP
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TO PRACTICE

Clinical Scenario

A patient with advanced OC undergoes resection, receives adjuvant carboplatin/paclitaxel and PARP inhibitor maintenance, experiences disease progression and then receives 2 subsequent lines of platinum-based chemotherapy. Her disease is now platinum resistant and is found to be HER2-positive, and she is about to start treatment with trastuzumab deruxtecan (T-DXd).

RTP
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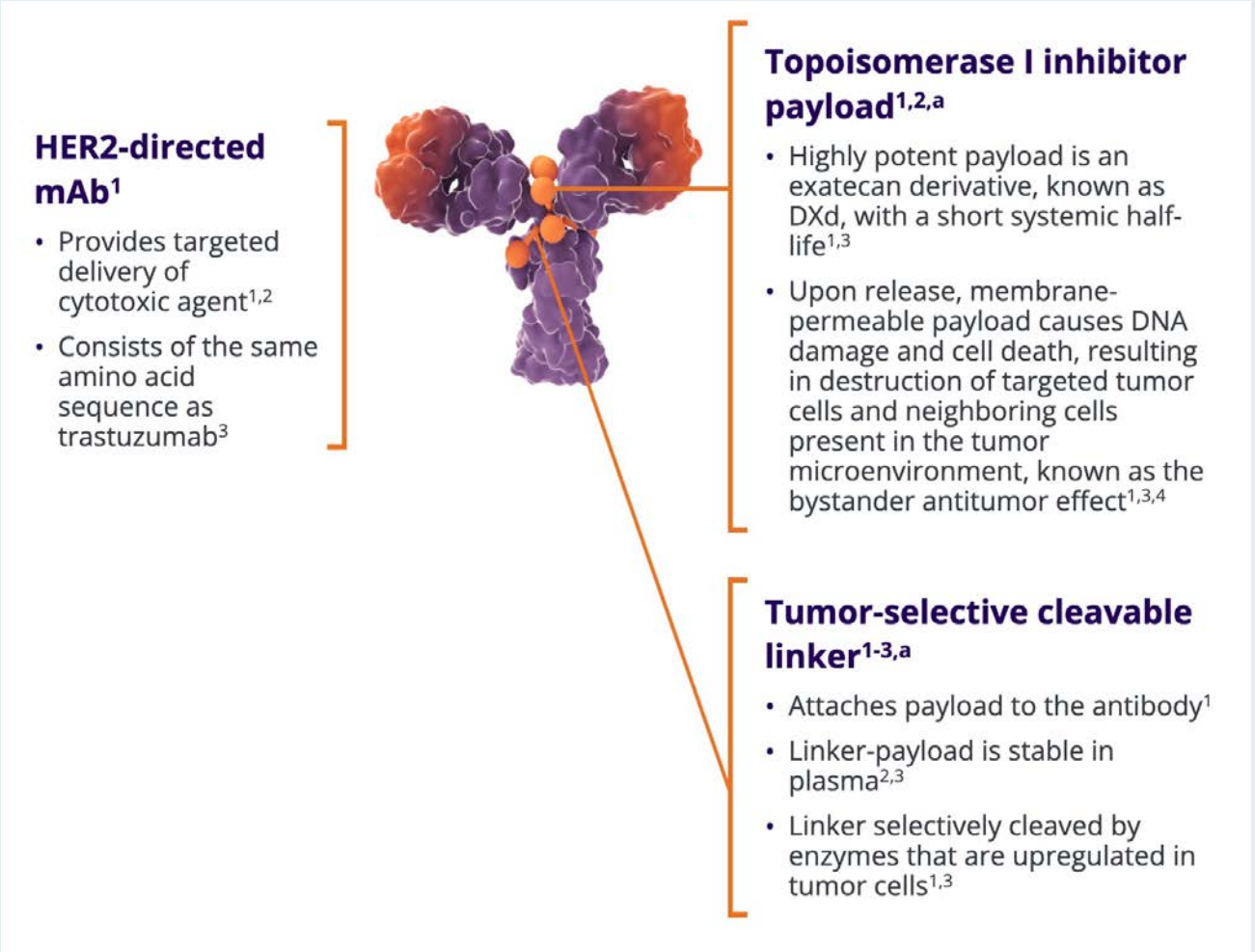
TO PRACTICE

Targeted (ADCs) Therapy - Ovarian Cancer

David M O'Malley, MD
The Ohio State University and
The James Comprehensive Cancer Center
Columbus, Ohio

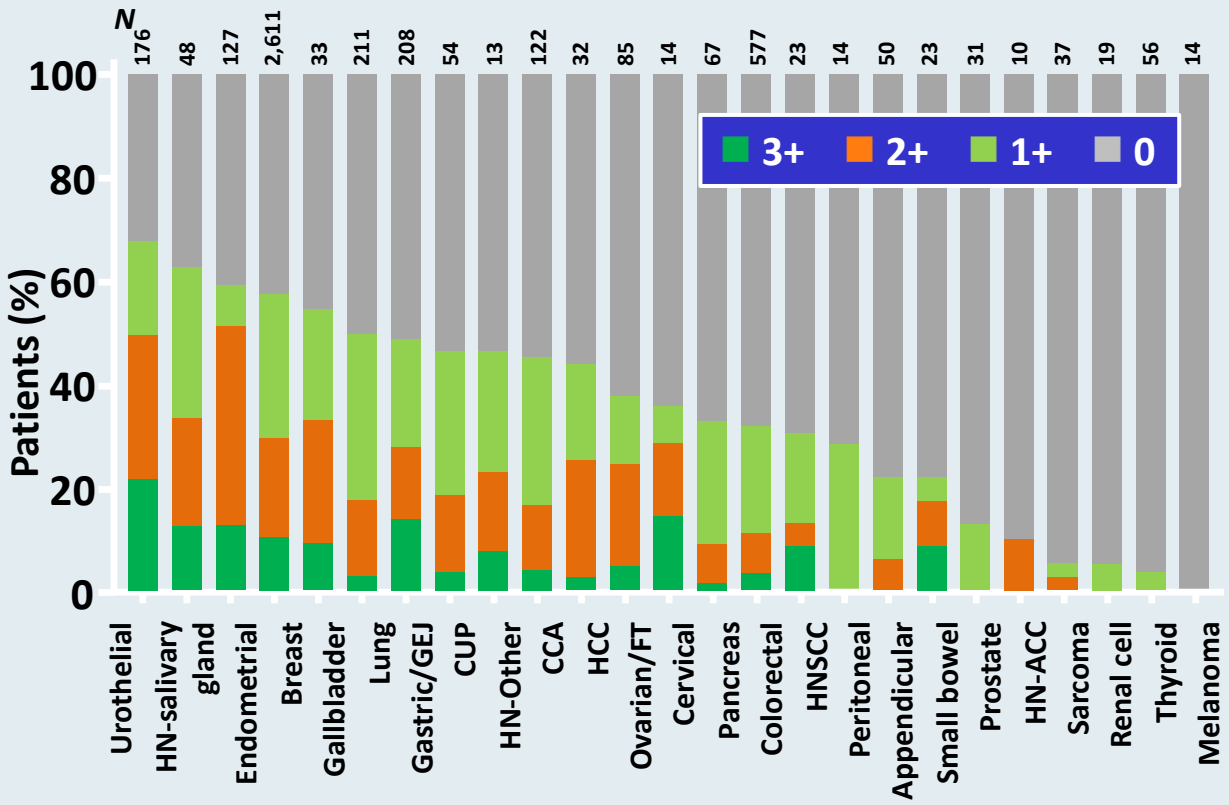
Trastuzumab Deruxtecan



1. Prescribing information. 2025.
2. Ogitani Y, Aida T, Hagihara K, et al. DS-8201a, a novel HER2-targeting ADC with a novel DNA topoisomerase I inhibitor, demonstrates a promising antitumor efficacy with differentiation from T-DM1. *Clin Cancer Res.* 2016;22(20):5097-5108.
3. Nakada T, Sugihara K, Jikoh T, Abe Y, Agatsuma T. The latest research and development into the antibody–drug conjugate, [fam-] trastuzumab deruxtecan (DS-8201a), for HER2 cancer therapy. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185.
[a]Based on in vitro and in vivo non-clinical studies. The clinical relevance of these features is under investigation.
https://www.enhertuhcp.com/en/mechanism-of-action. accessed on 4/6/25

What Is the Incidence of HER2 Expression Across Solid Tumors?

Distribution of HER2 IHC expression levels across cancers



CCA = cholangiocarcinoma; CNS, central nervous system; CUP = cancer of unknown primary; FT = fallopian tube cancer; GEJ = gastroesophageal; GI = gastrointestinal; HCC = hepatocellular carcinoma; HER2 = human epidermal growth factor receptor 2; HN = head and neck; HN-ACC = head and neck-adenoid cystic carcinoma; HNSCC = head and neck squamous cell carcinoma; IHC = immunohistochemistry. *Row percentages were used in the construction of this table.

HER2 expression across solid tumors

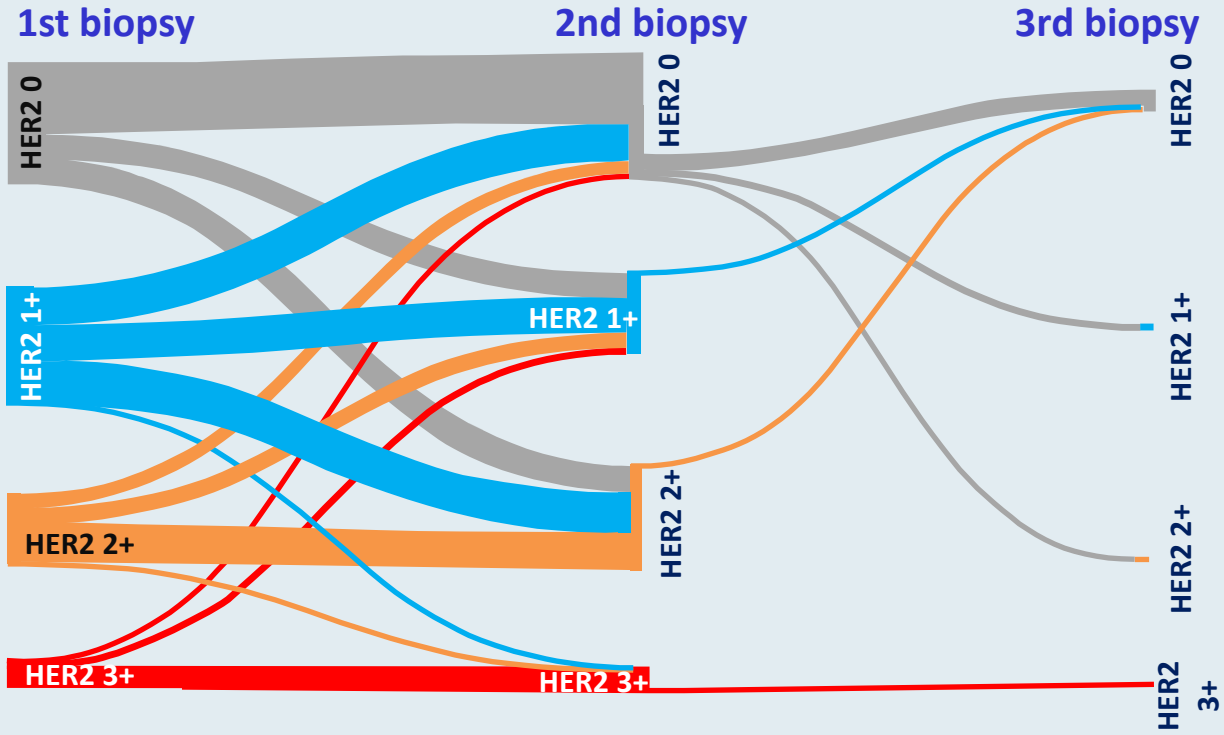
Cancer types		Distribution of HER2 IHC scores across cancers				
		HER2 IHC expression levels, %				
		0	1+	2+	3+	Total, n
Breast		43	28	19	10	2611
Gastric/GEJ		51	21	14	14	208
Biliary tract	CCA	55	29	12	4	122
	Gallbladder	46	21	24	9	33
	Ampullary	50	33	17	0	6
GI—lower	Colorectal	68	21	8	3	577
	Appendiceal	78	16	6	0	50
	Small bowel	78	4	9	9	23
	Anal	100	0	0	0	5
GI—other	Pancreas	67	24	8	2	67
	HCC	56	19	25	0	32
	Mixed CCA and HCC	67	33	0	0	6
Gynecological	Endometrial	41	8	39	13	127
	Ovarian/FT	62	13	20	5	85
	Peritoneal	71	29	0	0	14
	Cervical	64	7	14	14	14
	Vaginal	100	0	0	0	2
	Vulvar	29	14	43	14	7
Head and neck	HN-ACC	90	0	10	0	10
	HN-Other	54	23	15	8	13
	HN-salivary gland	38	30	21	13	48
	HNSCC	70	17	4	9	23
Genitourinary	Urothelial	32	18	28	21	176
	Prostate	87	13	0	0	31
	Renal cell	95	5	0	0	19
	Germ cell/testicular	100	0	0	0	3
	Penile	100	0	0	0	1
Thoracic	Lung	50	32	15	3	211
	Thymic	100	0	0	0	4
Skin	Melanoma	100	0	0	0	14
	Non-melanoma skin	71	14	14	0	7
Other	Adrenal	67	0	33	0	3
	CUP	54	28	15	4	54
	CNS	50	50	0	0	2
	Sarcoma	95	3	3	0	37
	Thyroid	96	4	0	0	56
Total		2361 (50)	1137 (24)	796 (17)	407 (9)	4701

Uzunparmak B et al. *Ann Oncol* 2023;34:1035-46.

Does It Change With the Tissue Tested (primary vs metastatic breast cancer)?

		HER2 metastasis *n*, %			Total
		HER2–	HER2-low	HER2+	
HER2 primary *n*, %	HER2–	157 (65.4)	78 (32.5)	5 (2.1)	240
	HER2-low	96 (34.8)	171 (62.0)	9 (3.3)	276
	HER2+	4 (3.5)	14 (12.4)	95 (84.1)	113
Total		257 (40.9)	263 (41.8)	109 (17.3)	629

Across Time?



		HER2 secondary biopsy *n*, %				Total
		HER2 0	HER2 1+	HER2 2+	HER2 3+	
HER2 first biopsy *n*, %	HER2 0	26 (57.8)	9 (20.0)	10 (22.2)	0 (0)	45
	HER2 1+	14 (32.6)	13 (30.2)	15 (34.9)	1 (2.3)	43
	HER2 2+	5 (19.2)	6 (23.1)	14 (53.8)	1 (3.8)	26
	HER2 3+	1 (10.0)	2 (20.0)	0 (0)	7 (70.0)	10
Total		46 (37.1)	30 (24.2)	39 (31.5)	9 (7.3)	124

Uzunparmak B et al. *Ann Oncol* 2023;34:1035-46.

Original Reports | Gynecologic Cancer

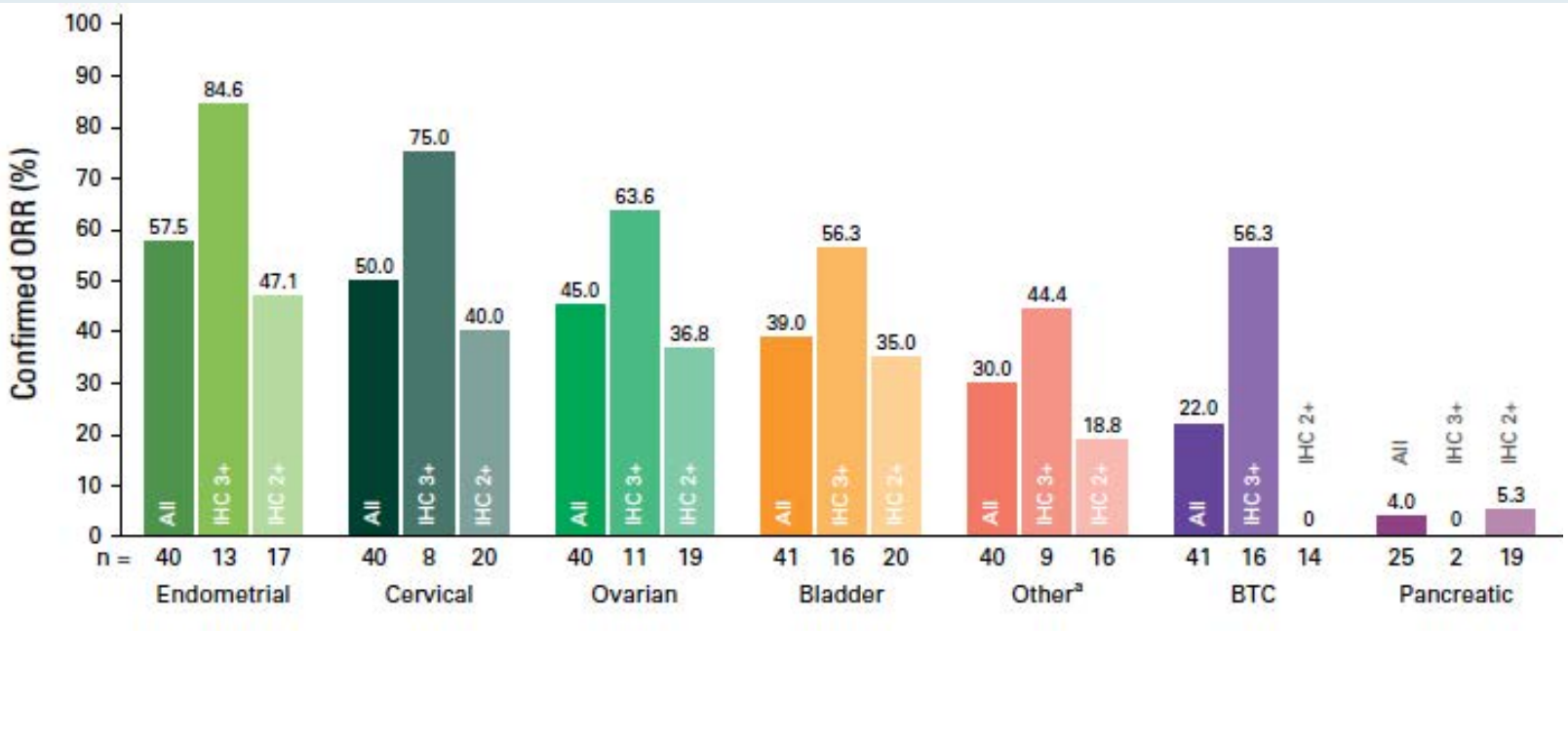
Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

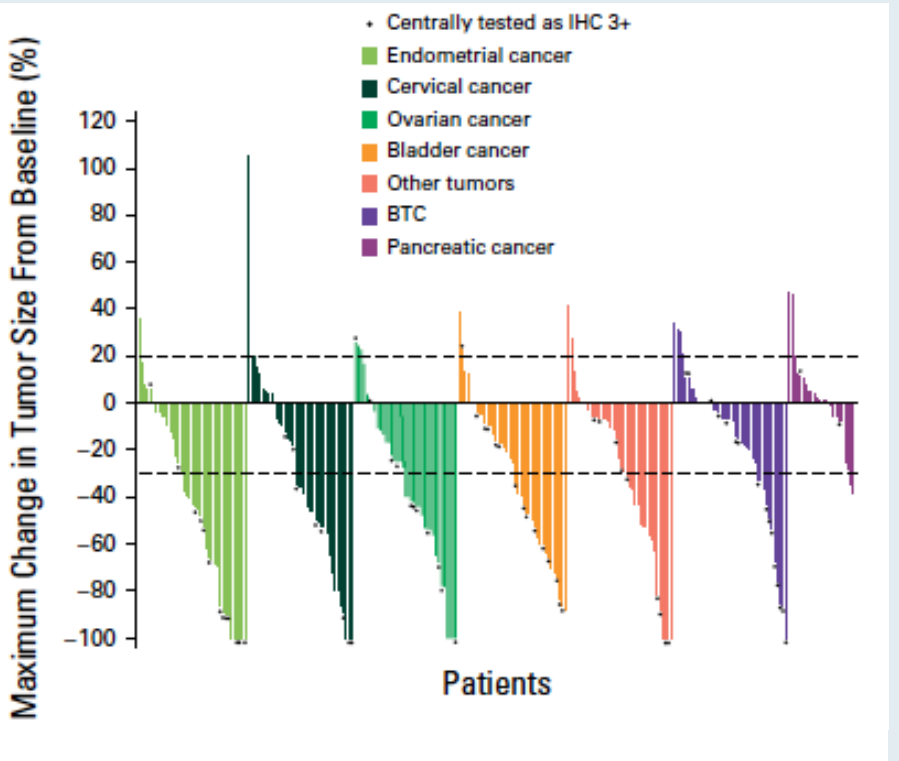
Funda Meric-Bernstam, MD[1]; Vicky Makker, MD[2,3]; Ana Oaknin, MD[4]; Do-Youn Oh, MD[5]; Susana Banerjee, PhD[6]; Antonio González-Martín, MD[7]; Kyung Hae Jung, MD[8]; Iwona Ługowska, MD[9]; Luis Manso, MD[10]; Aránzazu Manzano, MD[11]; Bohuslav Melichar, MD[12]; Salvatore Siena, MD[13]; Daniil Stroyakovskiy,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

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

RTP RESEARCH TO PRACTICE

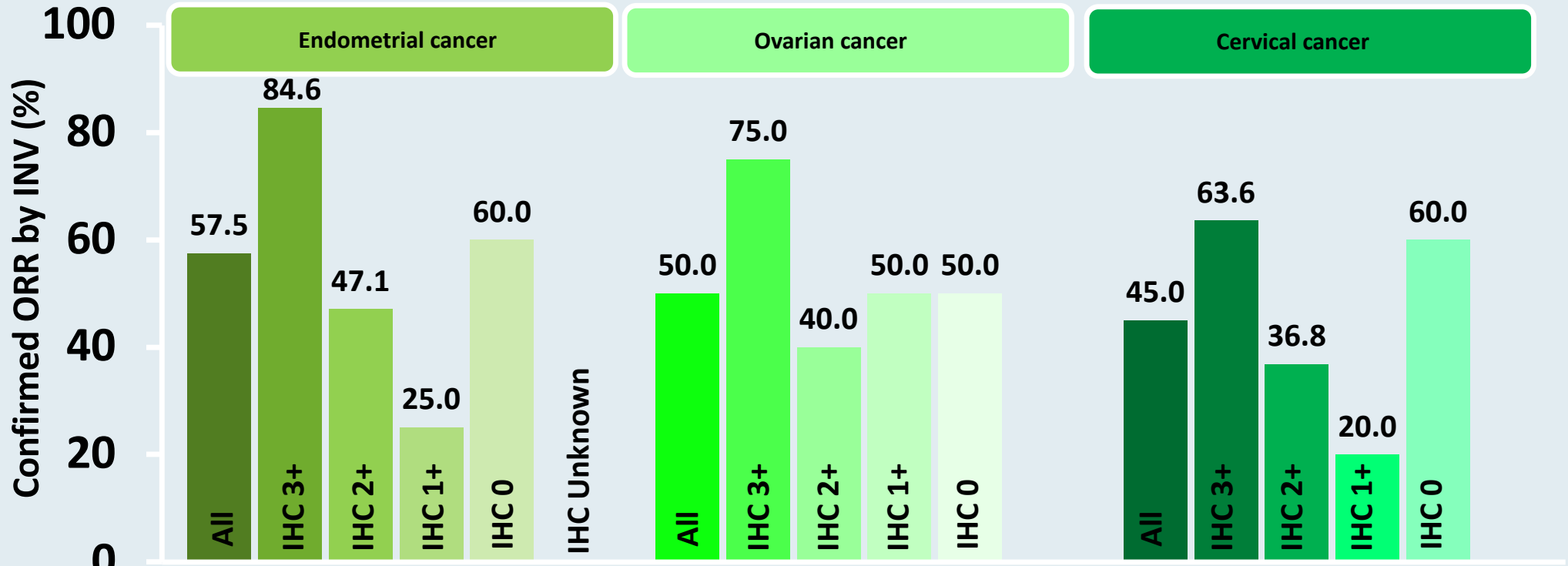
DESTINY-PanTumor02: Phase II Trial of Trastuzumab Deruxtecan in Patients with HER2-Expressing Solid Tumors





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

DESTINY-PanTumor02
Response by HER2 Expression Level (central)



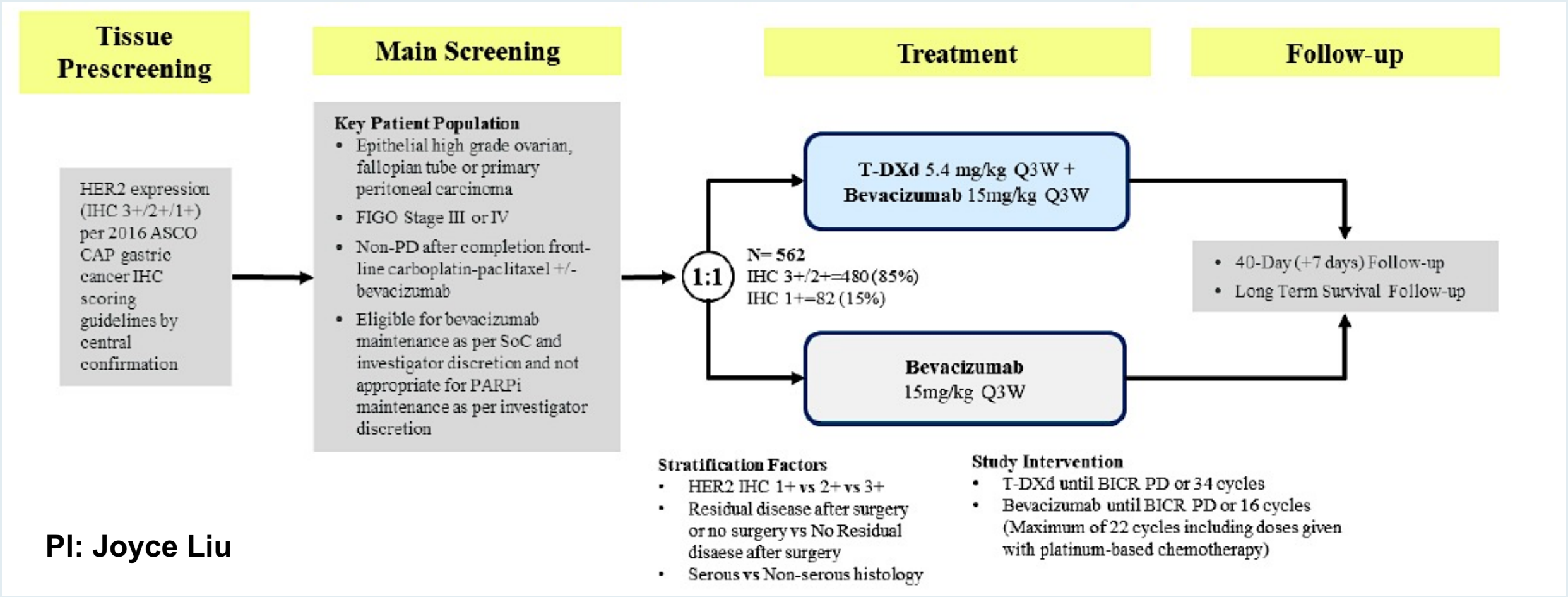
	Endometrial cancer						Ovarian cancer					Cervical cancer				
	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	IHC Unknown	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	All	IHC 3+	IHC 2+	IHC 1+	IHC 0
Total n in subgroup	40	13	7	4	5	1	40	8	20	8	4	40	11	19	5	5
n of responders	23	11	8	1	3	0	20	6	8	4	2	18	7	7	1	3
Median DOR, months	NR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

GYN = gynecological; NE = not estimable; NR = not reached.

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

RTP RESEARCH TO PRACTICE

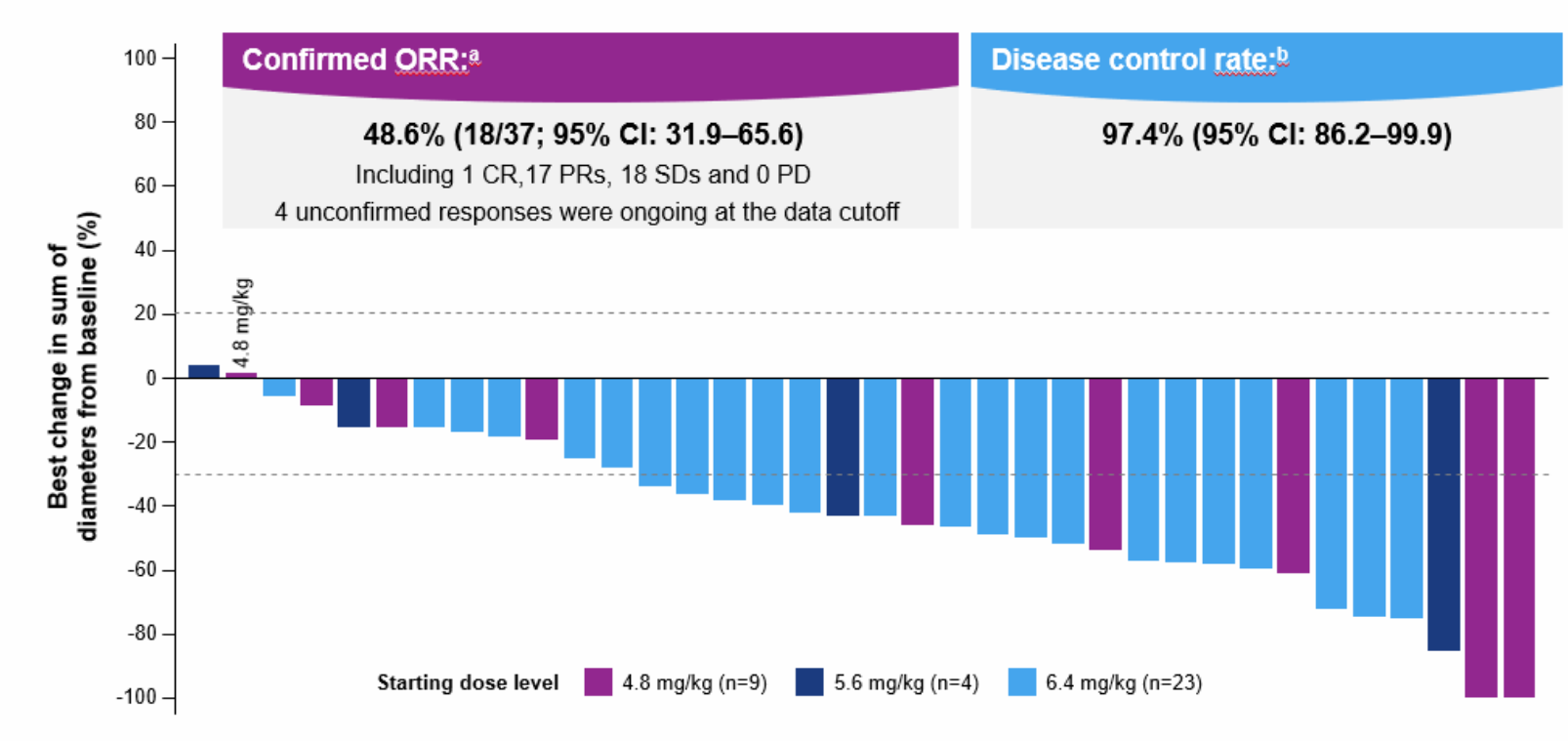
GOG 3112/ENGOT-ov89
Phase 3 DESTINY-Ovarian01: T-DXd + Bevacizumab as 1L Maintenance Therapy in HER2-Expressing Ovarian Cancer



PI: Joyce Liu

NCT06819007

Targeting CDH6



	Raludotatug deruxtecan (DS-6000)[1,2]
Payload	Topoisomerase 1 inhibitor (DXd)
DAR	8
Linker	Cleavable tetrapeptide based linker
Trial	**NCT04707248**

Median DOR:a

11.2 months (95% CI: 3.1–NE)
Median (range) FU: 6.7 months (1.4–16.8)

Median TTR:a

5.7 weeks (95% CI: 5.3–11.4)

Median PFS:b

8.1 months (95% CI: 5.3–NE)
Median (range) FU: 4.0 months (0–25.1)

1. Moore K, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 20-24 October 2023; Madrid, Spain.;
2. NCT04707248. Accessed from: https://clinicaltrials.gov/study/NCT04707248?cond=NCT04707248&rank=1.

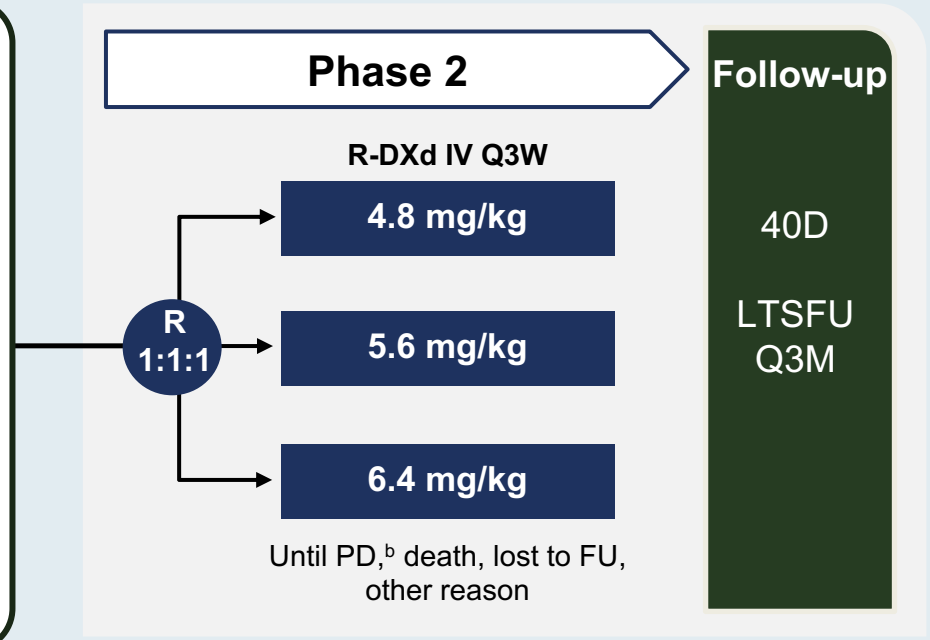
REJOICE-Ovarian01/GOG-3096: Phase 2/3 Randomized Study of R-DXd in Platinum-Resistant EOC

Key eligibility criteria:

- High-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer
- 1−3 prior LOT (inc. bevacizumab)
- Platinum-resistant disease
- Prior MIRV if high FRα[a]
- ECOG PS 0−1
- No prior CDH6-targeting agents or ADCs with linked TOPO I inhibitor
- Patients with primary platinum-refractory disease are not eligible

Stratification:

- Number of prior LOT (1 vs 2/3)
- CDH6 expression (high vs low)
- TPC (paclitaxel vs others; *Ph 3 only*)

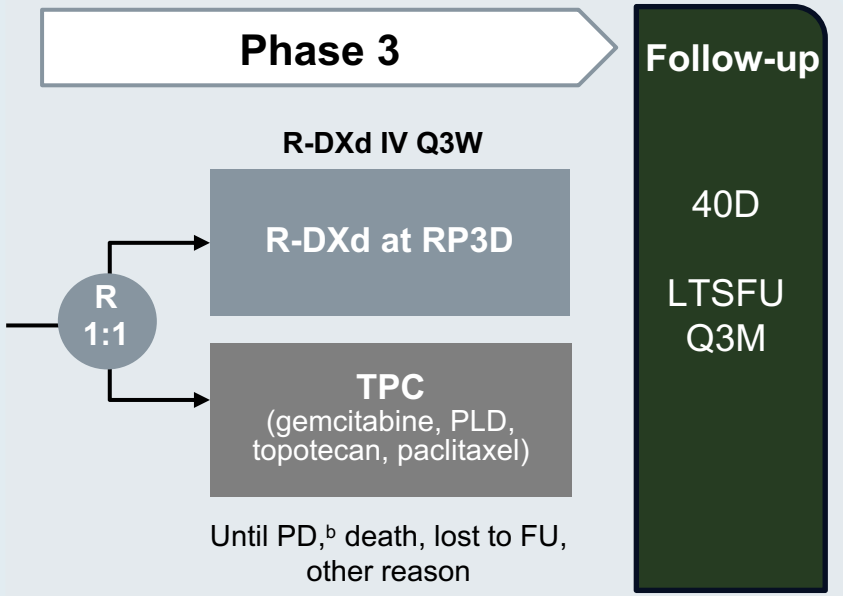


Primary endpoints:

- ORR per BICR[b]

Key secondary endpoints:

- ORR per inv[b]
- DOR



Primary endpoints:

- ORR per BICR[b]
- PFS per BICR[b]

Key secondary endpoints:

- OS
- QOL

NCT06161025

NCT06161025. Accessed from: https://clinicaltrials.gov/study/NCT06161025?term=NCT06161025&rank=1.

Key Takeaways

- Phase 2 DESTINY-PanTumor02, led to tumor-agnostic indication
  - April 5, 2024: FDA granted accelerated approval to T-DXd for unresectable/HER2+ (IHC3+) solid tumors after prior systemic treatment and no satisfactory alternative treatment options
  - Greatest benefit in IHC 3+ population
- Further exploration of T-DXd in HER2 IHC 1+/HER2-low is warranted
- Multiple Trials are being initiated for HER2 expressing gyn cancer
- Next Generation of ADCs is here

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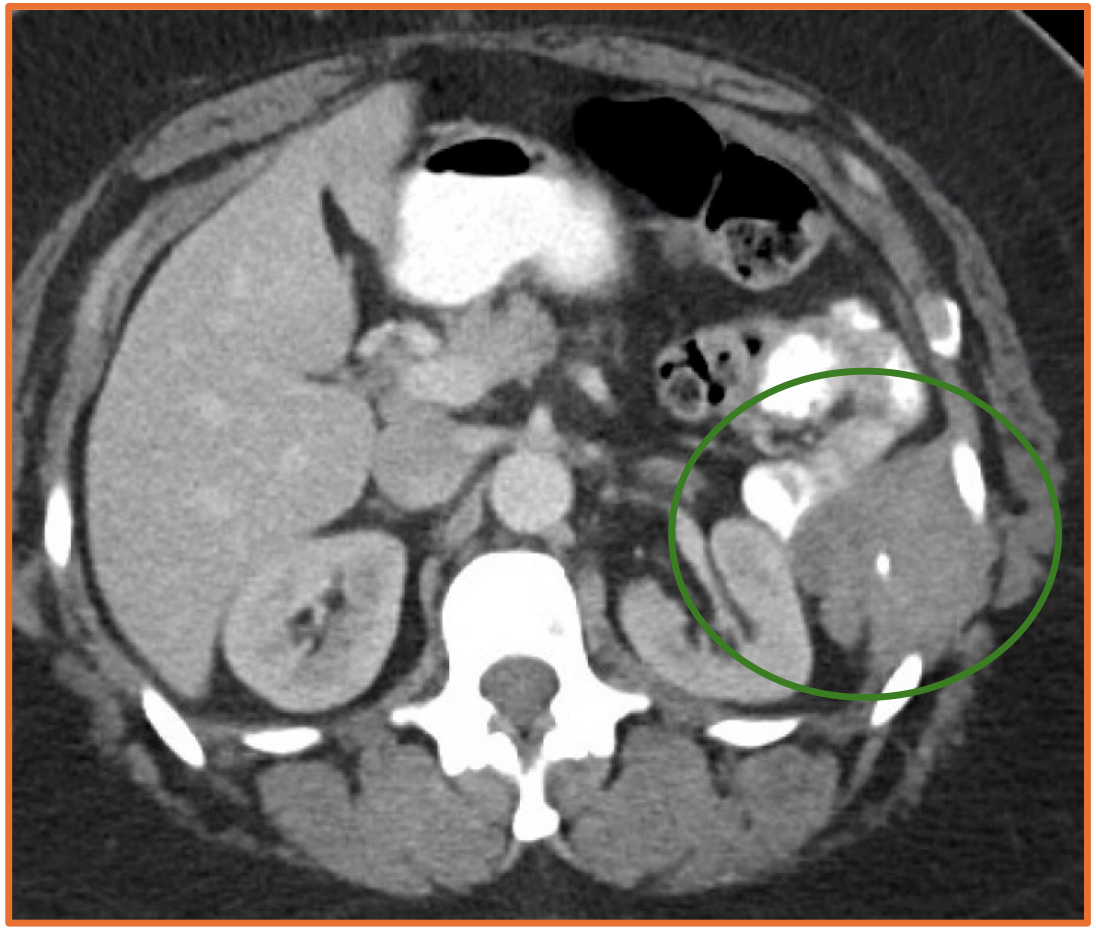
Recurrent Endometrioid Ovarian Cancer

Line of therapy	Therapy
1	Tumor Reductive Surgery + Carboplatin/paclitaxel x 6
2	Carboplatin/paclitaxel x 6
3	PD1i x 5 years
4	Megestrol
5	Letrozole + ribociclib

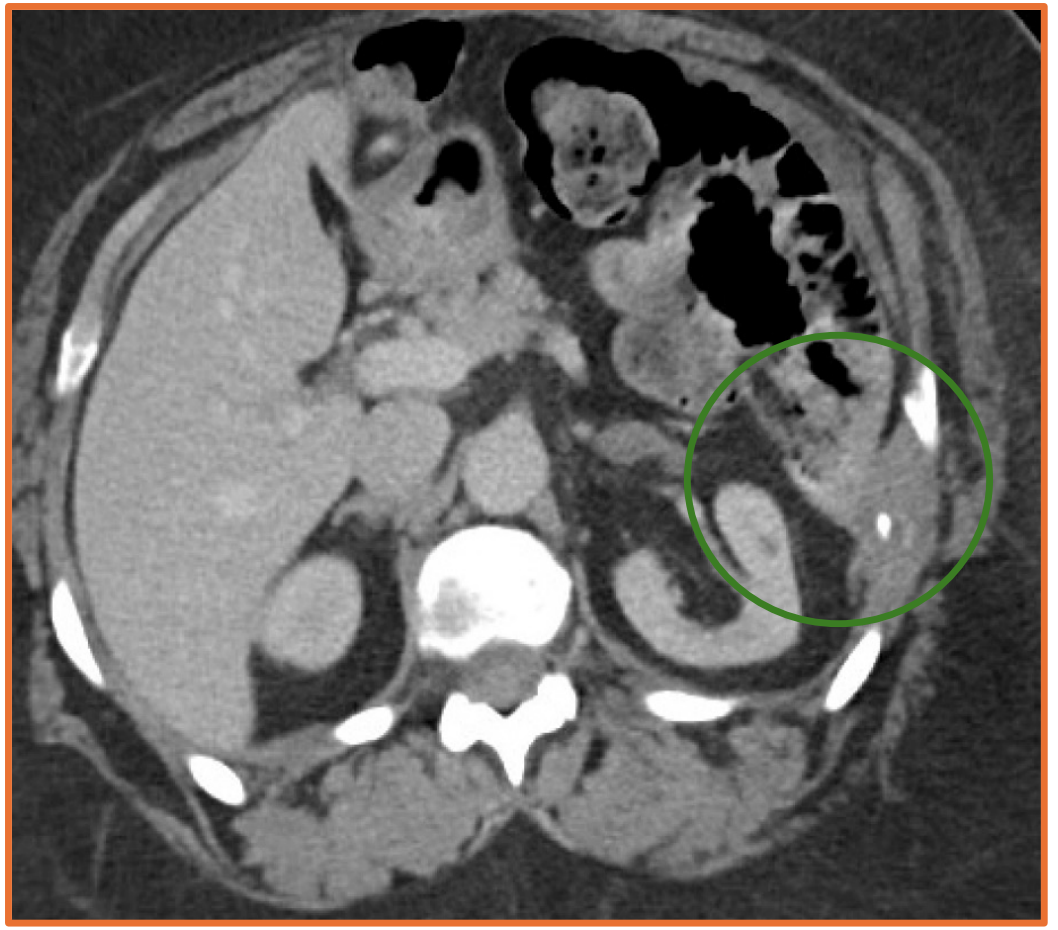
- NGS Testing
  - PTEN Mutation
- HER2 IHC: 3+
- Folate Receptor alpha: 0%

- **Started T-DXd**
- **Reduced dose to 4.4 mg/kg Cycle 3 due to significant fatigue and diarrhea**
- **Reduced dose to 3.2 mg/kg Cycle 9 due to persistent fatigue despite supportive care.**
- **Has Received >20 cycles**

Baseline



After 20 cycles — ongoing PR



Roundtable Discussion

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Nursing Considerations for Patients Receiving T-DXd

Courtney Arn, CNP

The Ohio State University

James Comprehensive Cancer Center

Columbus, Ohio

Patient Education

- MOA/Indication
- Potential Side Effects
- Symptom Management
- Treatment Plan/Schedule
- Pre and post medications
- Baseline labs and procedures (echo)

How does T-DXd work?

HER2-directed mAb

- Provides targeted delivery of cytotoxic agent
- Consists of the same amino acid sequence as trastuzumab

Topoisomerase I inhibitor payload

- Highly potent payload is an exatecan derivative, known as DXd
- Upon release, payload causes DNA damage and cell death, resulting in destruction of targeted tumor cells and neighboring cells present in the tumor microenvironment, known as the bystander antitumor effect

Tumor-selective cleavable linker

- Attaches payload to the antibody

Trastuzumab deruxtecan prescribing information, accessed 4/2025.

Side Effects

- Nausea (72%)
- Fatigue (55%)
- Vomiting (38%)
- Alopecia (37%)
- Constipation (32%)
- Decreased appetite (31%)
- Diarrhea (30%)
- Musculoskeletal pain (24%).
- Hematologic: Leukopenia (73%), Anemia (67%), Neutropenia (65%), decreased lymphocyte count (60%), Thrombocytopenia (48%), increased AST (46%), increased ALT (44%), increased alkaline phosphatase (39%), Hypokalemia (32%)

Trastuzumab deruxtecan prescribing information; accessed 4/2025

ILD/Pneumonitis Associated With T-DXd

- 15% of patients receiving T-DXd
- 87.0% had their first event within 12 months
  - Median: 5.4 months
  - Range: <0.1–46.8 months
- Median time to onset: 5-6 months
- Most patients with ILD/pneumonitis experienced low-grade events (grade 1 or 2, 77.4%)
- Overall rate of fatal events: 2.2%

Powell CA, et al. *ESMO Open*. 2022;7:100554.

Five "S" strategies to help detect and manage ILD/pneumonitis

Screen	Scan	Synergy	Suspend treatment	Steroids
• Careful patient selection • Optimize the monitoring strategies based on the baseline risk; • Screening continues during treatment • Regular clinical assessments to exclude signs/symptoms of ILD • Increased knowledge on the impact of prior ILD with other treatments on future risk of ILD	• The fundamental diagnostic tools for ILD remain CT scans (high-resolution) • Baseline scan is recommended • Repeat scans to be performed every 6 to 12 weeks	• Involves a teamwork • Educating patients • Educate the entire the care team • Multidisciplinary management once ILD is suspected – Pulmonologists – Additional Testing	• T-DXd should always be interrupted if ILD is suspected • Should only be restarted in the case of asymptomatic ILD that fully resolves	• Mainstay for treating are corticosteroids • Dose to be adapted to the toxicity grade

Tarantino P, Tolaney SM. *J Oncol Practice.* Trastuzumab deruxtecan prescribing information. Accessed 4/2025.

Interstitial Lung Disease: Recognition and Management

- **Advise** patients of risks of ILD prior to start of treatment, as well as signs/symptoms of ILD
- **Monitor** for new or worsening cough, dyspnea, or fever

- **Incidental findings on routine scan**
- **Symptomatic findings**

If ILD is suspected…

- Exclude other etiologies, including infectious etiologies
- Initiate evaluation without delay, which may include
  - CT (High-resolution)
  - Consultation with pulmonologist
  - Infectious Workup
  - Additional tests, as clinically indicated

Grade 1 (asymptomatic)

- Hold T-DXd until resolved
- May resume treatment once fully resolved by imaging
- Consider starting systemic steroids (eg, 0.5 mg/kg/day of prednisone or equivalent) until improvement, followed by gradual taper over 4 weeks
- If >28 days to resolve, reduce dose by 1 dose level

Grade 2+ (symptomatic)

- Discontinue T-DXd permanently
- Begin steroid treatment (eg, prednisone ≥1 mg/kg daily) with gradual taper

Trastuzumab deruxtecan prescribing information, Accessed 11/8/2024. Swain SM, et al. *Cancer Treat Rev*. 2022;106:102378.

Anemia/Neutropenia/Thrombocytopenia

- Dose reductions or delays
- Transfusion
- G-CSF for prevention and/or management of neutropenia

Nausea/Vomiting

- Moderate-High emetogenic risk
- Initiate tailored prophylactic antiemetic regimens (2–3 agents) before T-DXd infusion + home regimen for 3-4 days

Fatigue

- Assess/counsel
- Consider holding/dose reductions
- Rule out other causes
- Encourage exercise/physical activity/PT

Left ventricular dysfunction

- Baseline LVEF and regular monitoring (every 3–4 months)
- Dose delay/discontinuations

Diarrhea

- Infectious workup
- Anti-diarrheal (Loperamide, Diphenoxylate / Atropine)
- Fluids/electrolytes

Alopecia

- Patient counseling/education
- Wig prescription
- Scalp cooling

Trastuzumab deruxtecan official website. Accessed 4/2025.

Recommended Dose Reductions

Dose Reduction Schedule	5.4 mg/kg starting dose
First Dose Reduction	4.4 mg/kg
Second Dose Reduction	3.2 mg/kg
Requirement for further dose reduction	Discontinue Treatment

Trastuzumab deruxtecan prescribing information. Accessed 4/2025.

T-DXd: Infusion-Related Reactions

- Prompt recognition and treatment are important for reducing the risk of severe symptoms
  - Signs of T-DXd-related IRRs include fever and chills, N/V, pain, headache, dizziness, dyspnea, and/or hypotension
- Infusion 1 over *90 minutes → if well tolerated → subsequent infusions 30 minutes*
  - **1% to 3% of patients receiving T-DXd experience an IRR with T-DXd 5.4 mg/kg.**

- Grade 1: Reduce infusion rate to 50%
- Grade 2: Temporarily stop infusion
- Grade 3 or 4: Permanently stop

- Keep resources to treat IRR readily on hand
- Suspected anaphylaxis:
  - Follow local management guidelines
  - epinephrine (1 mg/mL IM every 5–15 minutes);
  - normal saline (1–2 L at 5–10 ml/kg for first 5 minutes IV);
  - H1/H2 antagonists

IRR = infusion-related reaction; N/V = nausea and/or vomiting.

Rugo HS, et al. *ESMO Open.* 2022;7:100553. Trastuzumab deruxtecan prescribing information.

CASE STUDY

- Patient with recurrent high grade serous ovarian cancer (germline BRCA2+, HER2 IHC 3+, FOLR 0%)
- 2020: Diagnosed
- 2022: Completed adjuvant carboplatin and paclitaxel, followed by PARP maintenance
- 2023: Disease recurrence; Gem/Cis/Bev followed by maintenance Bev x 9 months
- 2024: Disease progression; Gem/Cis/Bev, progressed after 3 cycles of maintenance Bev
- 2025: Started treatment on **trastuzumab deruxtecan (T-DXd).**
- Near CR after 3 cycles, side effects are well controlled with supportive care
- Social History: 2 children in high school, enjoys traveling

Roundtable Discussion

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Other Nursing Considerations Related to OC Management

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

Case Presentation

- 39 year old therapist, artist, and traveler with platinum resistant ovarian cancer, negative genetics, FOLR1 negative, HER2 negative.
- Diagnosed in 2020, Stage III
  - Complete cytoreductive surgery→ Carbo/paclitaxel
  - 2022: Carbo/PLD
  - 2023: platinum resistant→ bev/paclitaxel
  - 2023: clinical trial (ID + immunotherapy)

Stacey's Adventure List, 2nd Ed. 01-2025

Place	Location Activity
The Huntington	CA, San Marino Library, Art Museum, Botanical Gardens, Angeles Nat.Forest
Parc Omega	Canada, Montebello Safari Wildlife Park; Sleep Among Wolves
Biodome de Montreal	Canada, Montreal Indoor Ecosystem Zoo
Montreal Botanical Garden	Canada, Montreal Huge Botanical Gardens & Arboretum; Insectarium
Holmberg Orchards	CT, Gales Ferry Wine Maze!; Lavender; PickUROwn seasonal fruits
Buttonwood Farm	CT, Griswold Ice Cream & Sunflowers
Hartford Flavor Company	CT, Hartford Woman owned distillery; botanically infused
Mystic Aquarium	CT, Mystic Aquarium with animal encounter experiences
Mystic Village	CT, Mystic Restaurants and speciality shoppes
Deviant Donuts	CT, Mystic Gourmet Donuts; Vegan
Mew Cat Cafe	CT, New Haven Cafe with Cat visitation & adoption center
Dinosaur State Park	CT, Rocky Hill dino museum, arboretum, walking trails
Acton Arboretum	MA, Acton Arboretum, gardens, walking trails
Animal Adventures & Rescue Center	MA, Bolton animal rescue shelter; exotic animal encounters
Arnold Arboretum	MA, Boston Arboretum, gardens, walking trails
Franklin Park Zoo	MA, Boston Zoo
Museum of Illusions	MA, Boston Interactive illusion exhibits
Far Out Ice Cream	MA, Boston New Zealand style ice cream
Boston Duck Tours	MA, Boston Tour Boston by land & sea!
Tower Hill Botanical Gardens	MA, Boylston Gardens; Seasonal Light Events at Night
Trillium Brewery	MA, Canton Brewery & Restaurant; Outdoor Patio; Events & Music
Thunderbolt Mountain Coaster	MA, Charlemont Mountain Coaster; Zip lines
Lizzie Borden Ghost Hunt	MA, Fall River ghost HUNT w/equipment; 2 hours
Highfield Hall & Gardens	MA, Falmouth Victorian Mansion & Gardens, Art Exhibits & Music Events
Garden in the Woods	MA, Framingham Beautiful gardens in the woods, as name implies
Jiminy Peak Mountain Resort	MA, Hancock Mountain Coaster, Alpine Slide, Giant Swing, Soaring Eagle, Trampoline
Harvard Alpaca Ranch	MA, Harvard Alpacas & Store
The Farm at Summitwynds	MA, Holden lavender farm; sunflowers; lavender ice cream; events
Castle Hill on the Crane Estate	MA, Ipswich Mansion & Gardens; Hiking to Oceanfront; Festival of Trees
The Mount - Ghost Tours	MA, Lenox ghost tour not for kids!
Tanglewood	MA, Lenox BSO Rehearsals on Sat. mornings
Ventfort Hall	MA, Lenox Gilded Age Mansion, gift shop & events; tarot, ghost tours, tea time
Apex Entertainment	MA, Marlborough Go Karts, Ropes Course, Laser Tag, Bowling, Mini Golf
Southwick Zoo	MA, Mendon Zoo; Seasonal Events
Eustis Estate	MA, Milton Mansion
Mary M.B. Wakefield Arboretum	MA, Milton Dogwood Trees in Spring; Gardens
Nantucket Daffodil Festival	MA, Nantucket Daffodils
Stevens Coolidge House	MA, North Andover Tulip Event
The Tunnel Bar	MA, North Hampton Speakeasy
Tranquil Lake Nursery	MA, Rehoboth Daylilies & Iris
Brilliant Dahlia Flower Farm	MA, Rehoboth Dahlias & Yoga on Saturdays at 10am
Butterflies of Cape Cod	MA, Sandwich Butterfly Gard[illegible]
Heritage Museums & Gardens	MA, Sandwich Carousel, [illegible]
Ward's Berry Farm	MA, Sharon Pick UR [illegible]
Race Brook Falls Trail	MA, Sheffield Hiking, [illegible]
Magic Wings	MA, South Deerfield Huge Indo[illegible]
Dr. Suess Museum	MA, Springfield One of a [illegible]

Clinical Trial Participation

- Advantages: good potential for an active drug (several FDA approvals in last 5-10 years), clinical trial team, opportunity to contribute to the fight
- Barriers: frequency of visits, live far from hospital (not available at satellite sites), eligibility requirements often strict
- Communication: detailed explanations (don’t just assume), “I don’t want to be a guinea pig”- no placebos, will not affect overall care, clinical trial support from pharma company

Optimizing Oncology Nursing Care

- Patient education and support
  - Discuss goals of care with patient, what is important now, may change over time
    - Introduce palliative care early
  - Educate patients on disease and its management
    - Including potential treatment-related adverse events
  - Provide access to support and resources: support groups, social work, lifestyle medicine, nutrition
  - Encourage ALL patients to participate in clinical trials, if available at your work site
  - Be mindful of social and financial burdens, including oral adherence
  - Helpful tips: bring a support person, give handouts for reference back, “never worry alone” motto
- Multidisciplinary approach

Back to our case...

Patient in a PR (over a year on trial)

Roundtable Discussion

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Agenda

Introduction: Overview of Ovarian Cancer (OC) Management

Module 1: Genetic Testing for Newly Diagnosed Advanced OC

Module 2: Role of PARP Inhibitor Maintenance in Newly Diagnosed Advanced OC

Module 3: Other Available and Investigational Novel Strategies for OC

Module 4: Current and Future Role of Mirvetuximab Soravtansine in OC Treatment

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Clinical Scenario

A patient with advanced OC undergoes resection, receives adjuvant carboplatin/paclitaxel and PARP inhibitor maintenance, experiences disease progression and then receives 2 subsequent lines of platinum-based chemotherapy. Her disease is now platinum resistant and has high FRα expression, and she is about to start treatment with mirvetuximab soravtansine.

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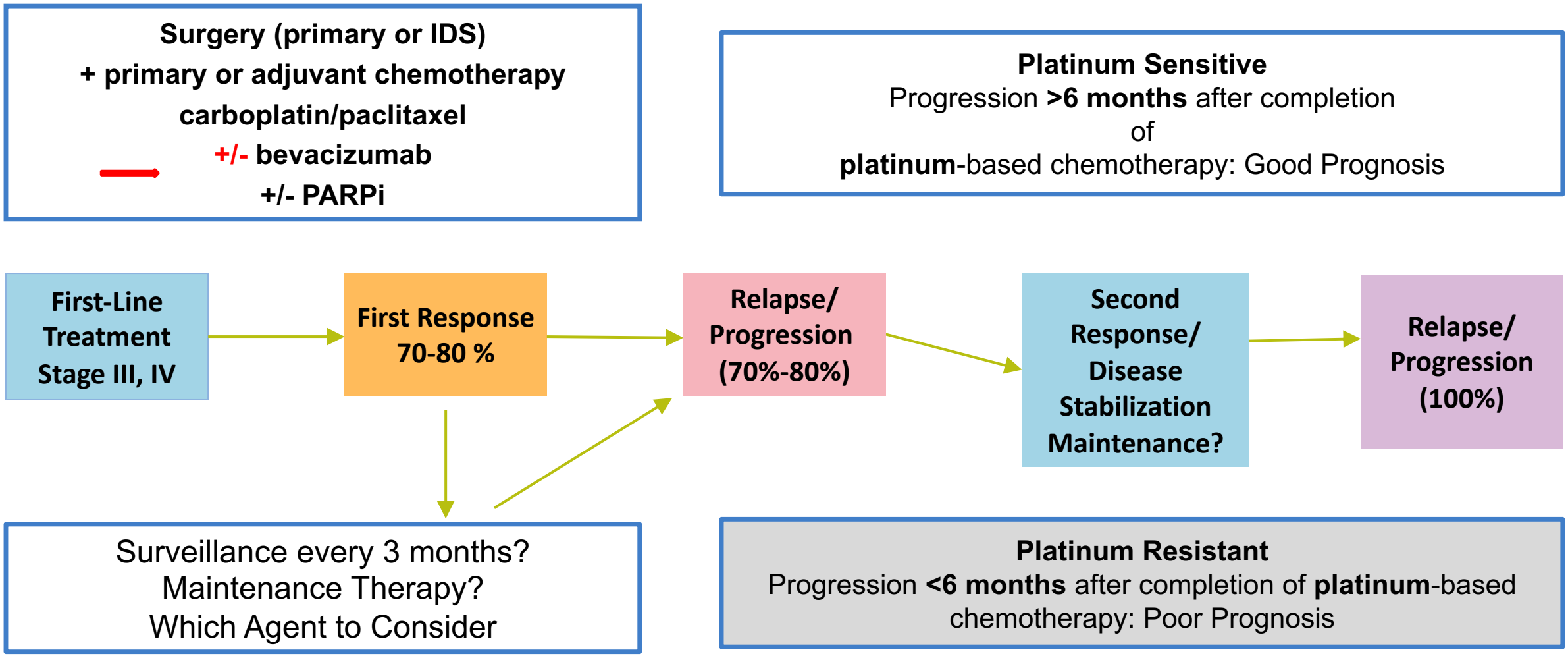
Current and Potential Future Role of Mirvetuximab Soravtansine in Ovarian Cancer Treatment

Shannon N. Westin, MD, MPH
Professor
Department of Gynecologic Oncology and Reproductive Medicine

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Typical Course of Advanced Ovarian Cancer



Ledermann JA, et al. *Ann Oncol. 2013,* Pignata S, et al. *Ann Oncol.* 2017; du Bois A, et al. *Cancer* 2009, Wilson MK, et al. *Ann Oncol*. 2017

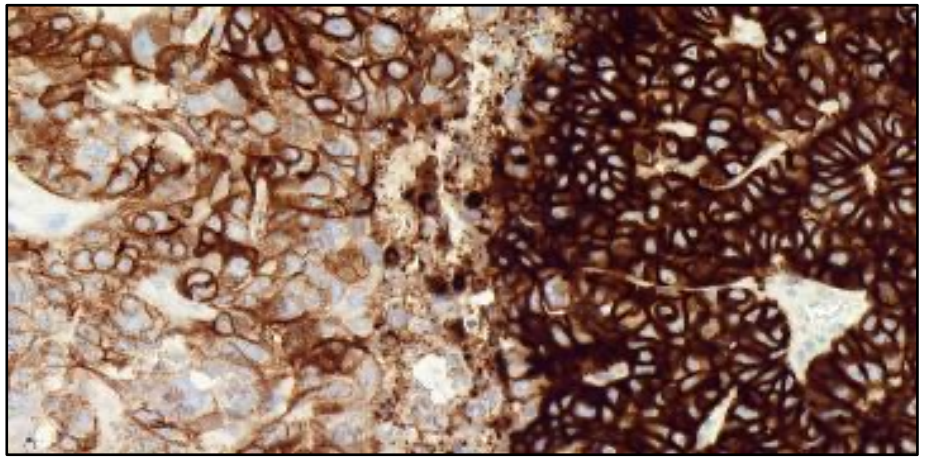
Targeting Folate Receptor Alpha

- FRα is a cell surface folate receptor which mediates folate transport into epithelial cells.
- FRα expression is limited on normal cells, but is upregulated on cancers, primarily ovarian, but also endometrial, and triple negative breast
- FRα may be expressed on the alveoli of the lungs and on renal proximal tubules. However, these receptors are located on the surface of the cell facing the alveolar and tubular lumen, which reduces the exposure of the targets to circulating anti-folate agents
- Expression in ovarian cancer varies by histology (80-90%)
  - 76% HGS
  - 50% LGS
  - 32% clear cell
- Association with prognosis has been mixed

PS2+ Scoring

Determined by staining intensity and percentage of tumor cells staining at 0, 1+, 2+, or 3+

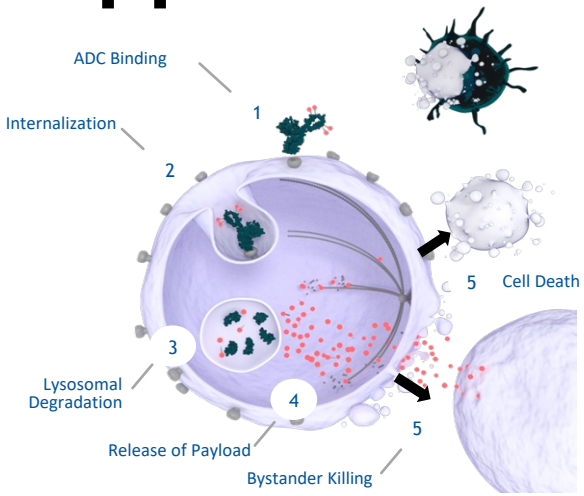
1+ intensity 2+ intensity 3+ intensity



PS2+ Scoring Positive: ≥ 50% tumor cells with ≥ 2+ FRα membrane staining.

Kobel et al. Br. J Cancer (111); 2014; Moore KN et al. ESMO. 2019; Oaknin A et al. ASCO 2023; Chen YL, et al. *Mol Oncol* 2012

Mirvetuximab soravtansine, first FRα-targeted ADC approved for PROC



Antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload

SORAYA (NCT04296890)

Key eligibility criteria

- Platinum-resistant ovarian cancer
- Prior bevacizumab required, prior PARPi allowed
- 1–3 prior lines of therapy
- Patients with *BRCA* mutations allowed
- FRα-positive (≥75% of cells staining positive with ≥2+ staining intensity)

Mirvetuximab soravtansine (N=106)

6.0 mg/kg adjusted ideal body weight (AIBW) q3w

Primary endpoint

- ORR per Investigator

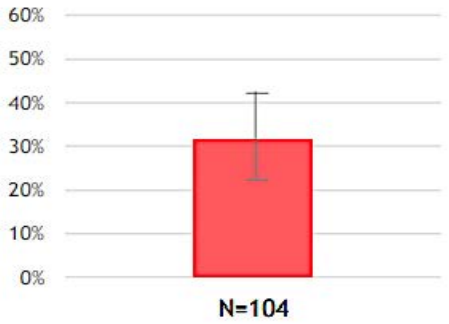
Secondary endpoints

- DOR, PFS, OS, CA-125 response by GCIG criteria, safety

ORR% BY INVESTIGATOR[1]

31.7%

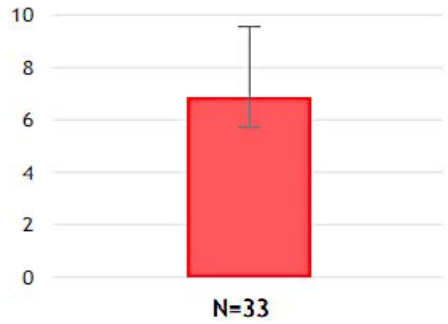
(22.9, 41.6)*



DOR BY INVESTIGATOR[1]

6.9 months

95% CI: (5.6, 9.7)



FDA grants accelerated approval to mirvetuximab soravtansine-gynx for FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or peritoneal cancer

Share Tweet LinkedIn Email Print

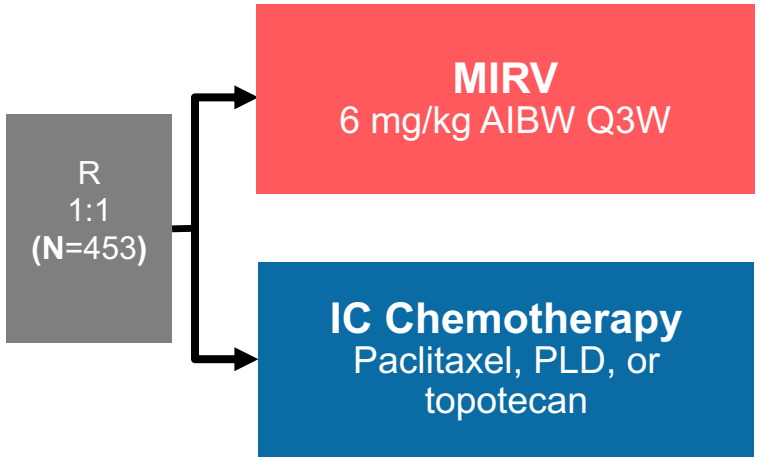
On November 14, 2022, the Food and Drug Administration granted accelerated approval to mirvetuximab soravtansine-gynx (Elahere, ImmunoGen, Inc.) for adult patients with folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Mirvetuximab soravtansine-gynx is a folate receptor alpha directed antibody and microtubule inhibitor conjugate. Patients are selected for therapy based on an FDA-approved test.

Moore KN et al. *Cancer*. 2017; Matulonis UA et al. *J Clin Oncol*. 2023

MIRASOL (NCT04209855): Randomized, phase 3 study of MIRV vs chemotherapy in FRα-high platinum–resistant ovarian cancer

Eligible patients:
- PROC (PFI ≤6 mo)
- FRα detected by IHC with PS2+ among ≥75% of viable tumor cells
- High-grade serous histology
- 1–3 prior lines of therapy
- Prior BEV and PARPi allowed
- Participants with *BRCA* mutations allowed

Excluded patients:
- 1º platinum-refractory disease (primary PFI <3 mo)



Stratification:
- IC chemotherapy: paclitaxel, PLD, or topotecan
- Prior lines of therapy: 1 vs 2 vs 3

Primary endpoint[a]:
- PFS by INV (BICR sensitivity analysis)

Select secondary endpoints:
- ORR by INV (BICR sensitivity analysis)
- OS OV28 abdominal/GI subscale[b]
- Safety and tolerability
- DOR
- CA-125 response[c]
- PFS2

Select exploratory:
- Additional PRO assessments[d]

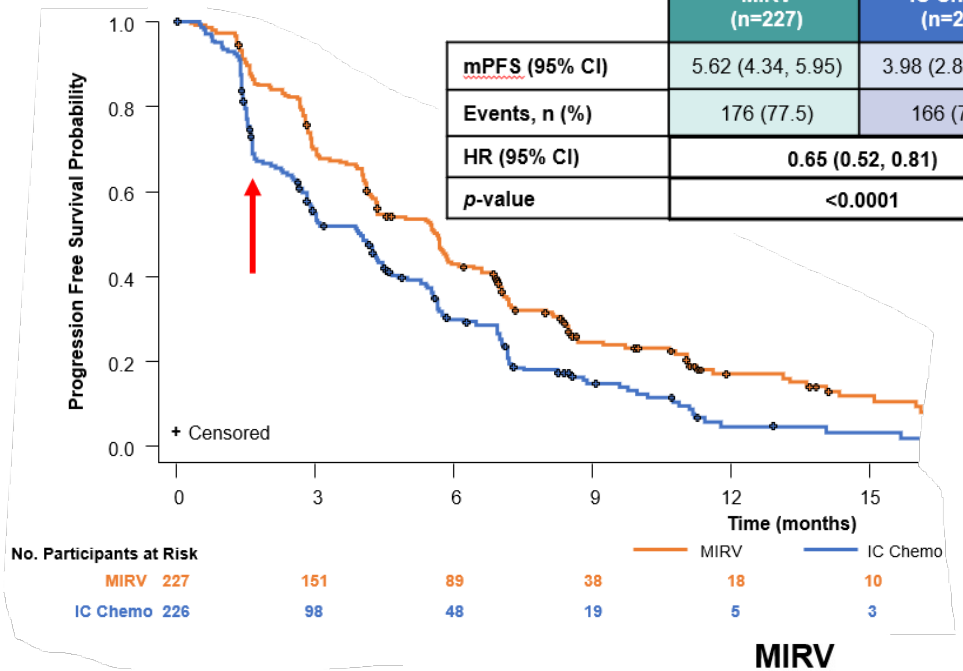
ITT population:
- All randomized patients, regardless of receipt of assigned treatment

Safety population:
- All randomized patients who received ≥1 dose of assigned treatment

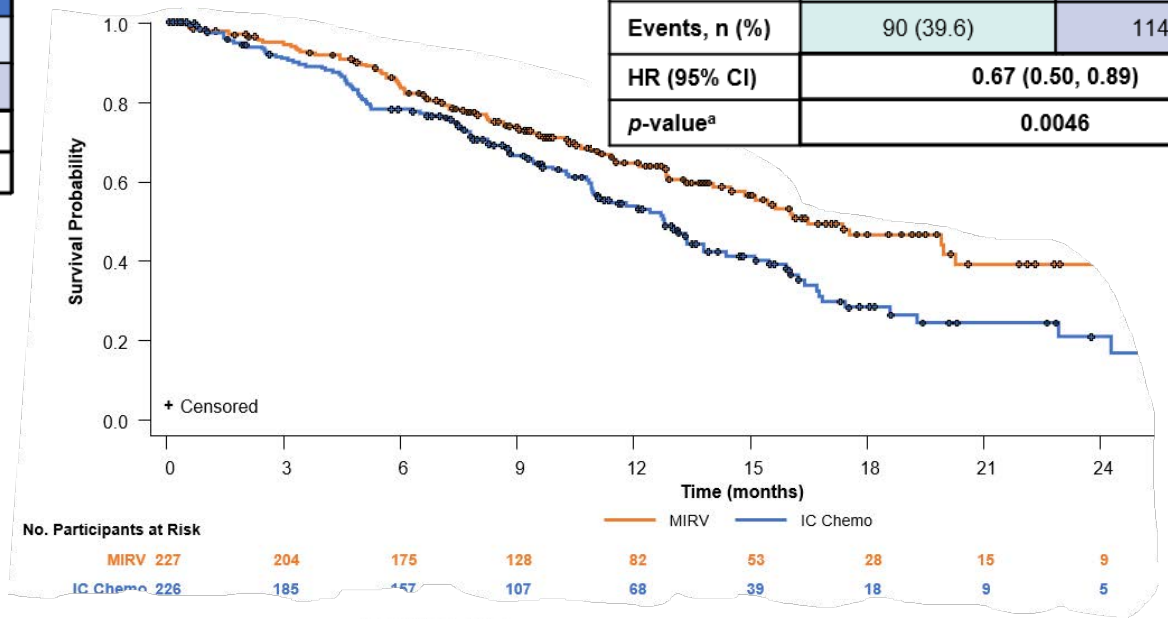
Moore KN, et al. N Engl J Med. 2023;389(23):2162-2174

Confirmation of Superiority – OS Benefit!!!!

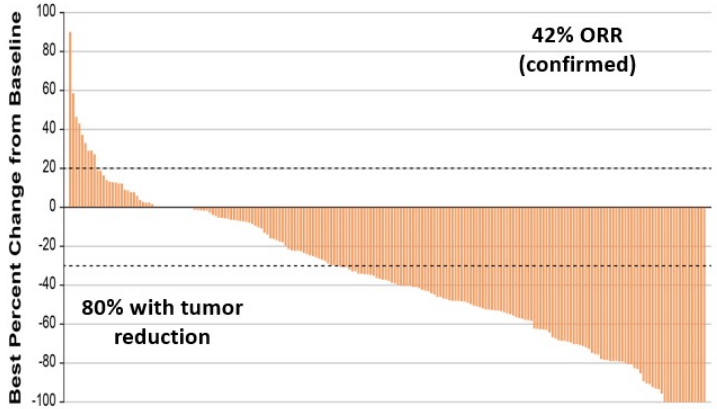
	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
Events, n (%)	176 (77.5)	166 (73.5)
HR (95% CI)	0.65 (0.52, 0.81)	
p-value	<0.0001	



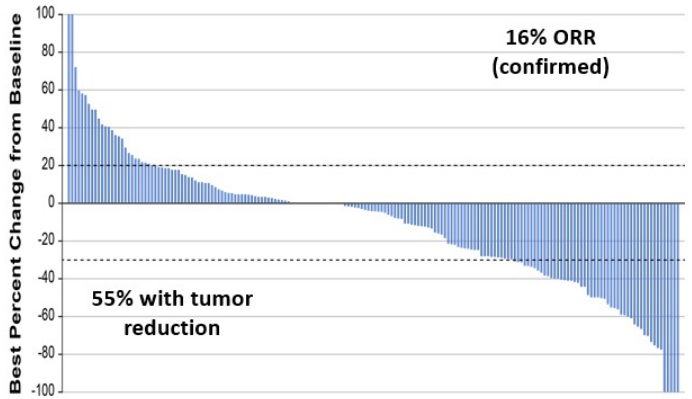
	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value[a]	0.0046	



MIRV



IC Chemo



Moore et al. NEJM 2023

PICCOLO: Mirvetuximab soravtansine in platinum sensitive ovarian cancer

Characteristics	N=79
Age, median (range), years	66 (41-84)
Race, n (%)	
White	65 (82.3)
Black or African American	4 (5.1)
Asian	1 (1.3)
# prior lines of systemic therapy, n (%)	
1-2[a]	49 (62.0)
≥3	30 (37.9)
Prior exposure to taxanes, n (%), Yes	77 (97.5)
Exposed in multiple lines	20 (25.3)
Prior exposure to PARPi[b],n (%), Yes	64 (81.0)
Progression on PARPi[c]	59 (74.7)
Prior exposure to bev, n (%), Yes	51 (64.6)
Most recent PFI (months)[d], n (%)	
≤12	43 (54.4)
>12	34 (43.0)

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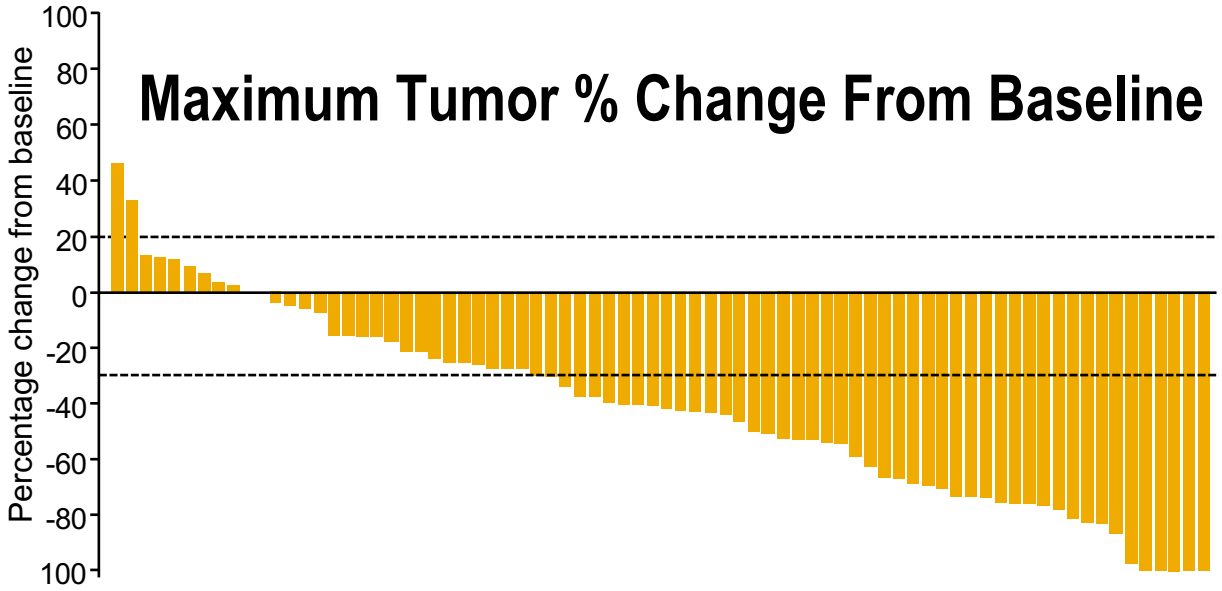
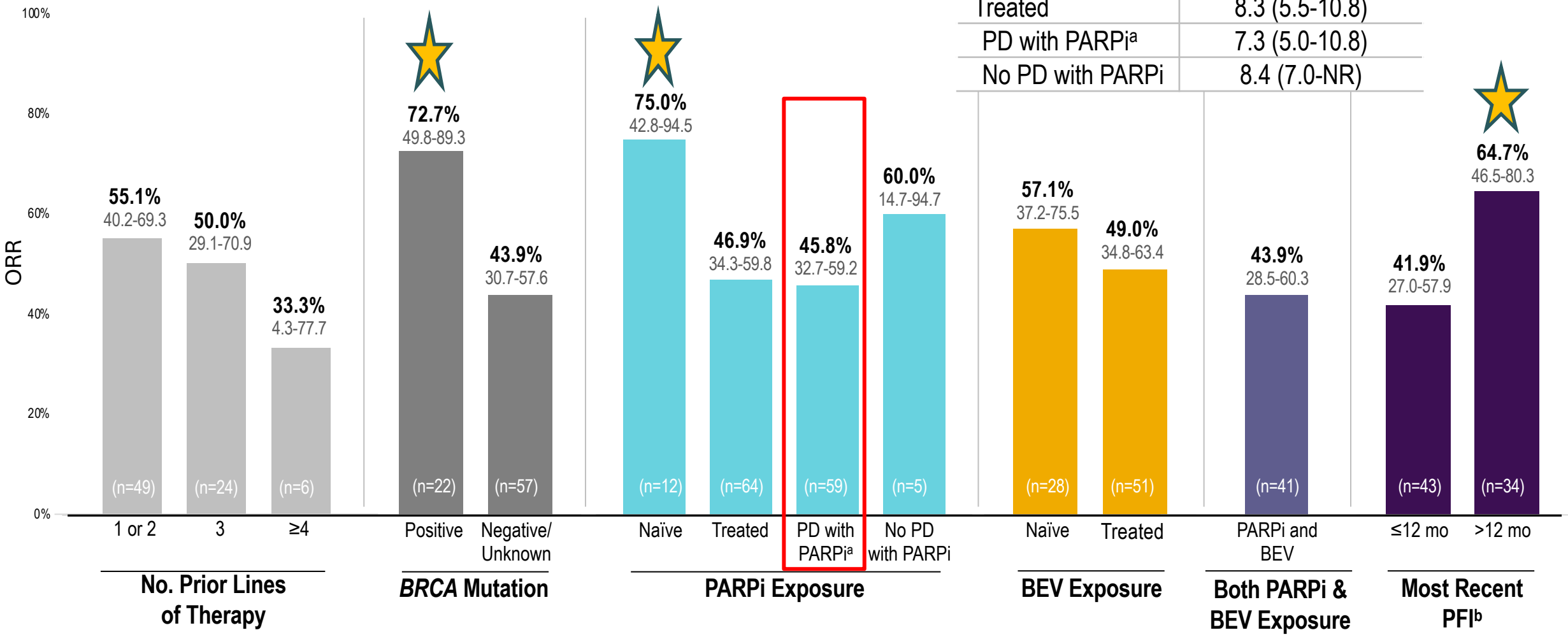


Primary Endpoint	N=79
ORR, n (%)	41 (51.9)
95% CI	40.4-63.3
Best Response, n (%)	
CR	6 (7.6)
PR	35 (44.3)
SD	29 (36.7)
PD	7 (8.9)
Not evaluable	2 (2.5)

Secondary Endpoints	
Median DOR[a]	n=41
Months (95% CI)	8.25 (5.6-10.8)
Median PFS	N=79
Months (95% CI)	6.93 (5.8-9.6)

PICCOLO: Subgroup Analyses

Exposure to PARPis	Median DOR months (95% CI)
Naïve	8.8 (3.5-NR)
Treated	8.3 (5.5-10.8)
PD with PARPi[a]	7.3 (5.0-10.8)
No PD with PARPi	8.4 (7.0-NR)



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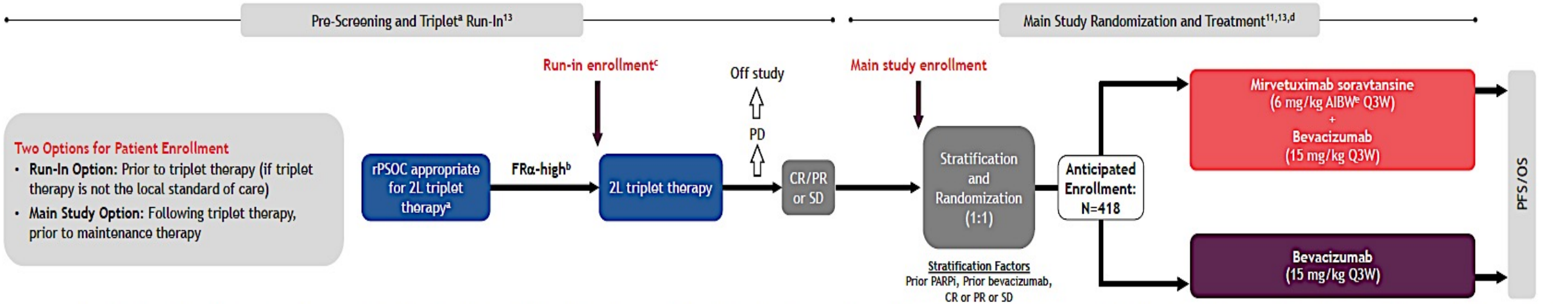
GOG-3078/IMGN853-0421/GLORIOSA

Randomized Phase 3 Trial for Mirvetuximab + Bevacizumab Maintenance in FRα-high Platinum Sensitive Ovarian Cancer



[a]Triplet treatment consists of platinum+chemotherapy+bevacizumab for planned 6 cycles (minimum 4 and maximum 8 cycles), including at least 3 cycles of bevacizumab. [b]Pre-screening consent must be obtained for tissue testing for FRα expression by Ventana FOLR1 Assay. [c]FRα-high patients who desire to be treated and followed while on their run-in triplet therapy must sign a run-in consent as part of the main consent form if they meet eligibility criteria as assessed by the investigator. [d]Maintenance treatment must begin ≤12 weeks from last dose of triplet therapy and within 30 days of randomization. Treatment continues until PD, unacceptable toxicity, withdrawal of consent, death, or sponsor study termination. [e]AIBW, also known as AdjBW, is calculated as IBW (kg) + 0.4 (actual weight − IBW). IBW for females is calculated as 0.9*height (cm) − 92.

Key Eligibility Criteria:

- Platinum-sensitive HGS ovarian cancer
- 1 prior platinum treatment
- Prior PARPi required if BRCA+
- CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

NCT05445778

GOG PARTNERS

Roundtable Discussion

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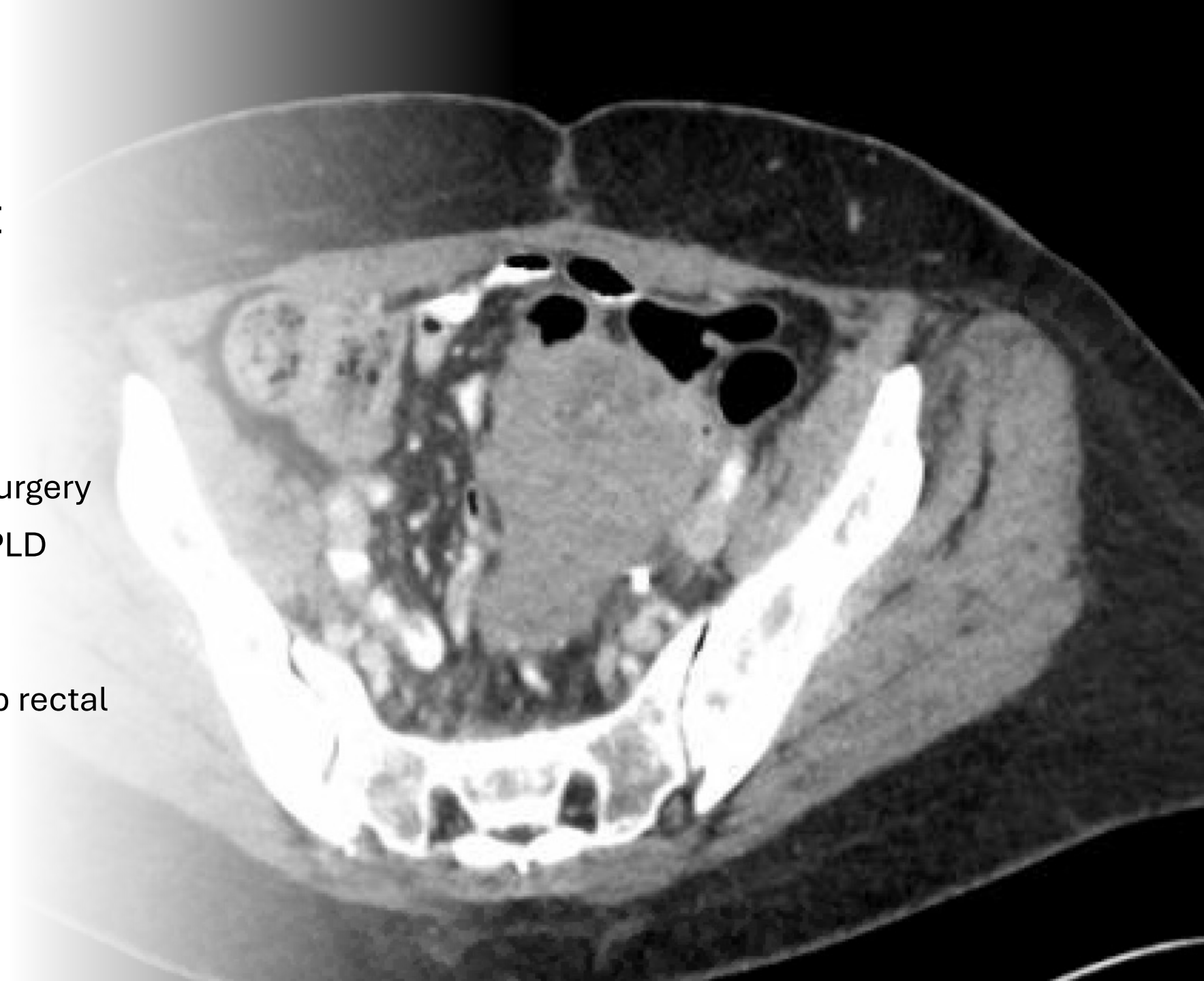
Nursing Considerations for Patients Receiving Mirvetuximab Soravtansine

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

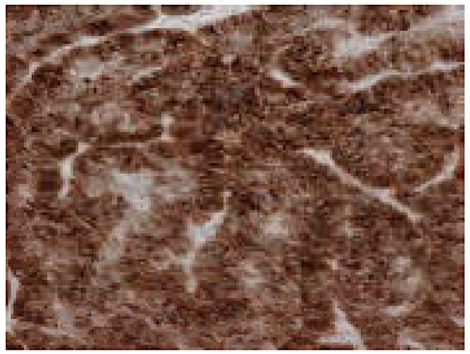
64-year-old new grandmother with platinum resistant ovarian cancer

- Diagnosed in 2019
- Negative genetics
- C/T and cytoreductive surgery
- Recurrence in 2021: C/PLD
- Recurrence in 2023: C/Gem/Bev
- Jan 2025: recurrence c/b rectal bleeding, hydronephrosis, significant pain

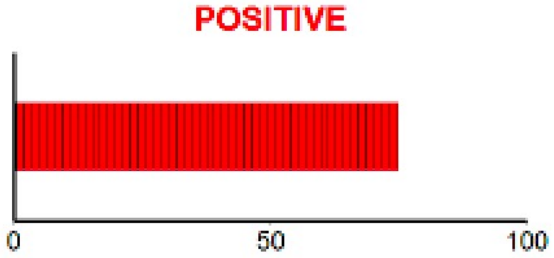


Molecular testing

- Snapshot (in house molecular testing) with no actionable mutations
- HER2 negative (0)
- FOLR1 +



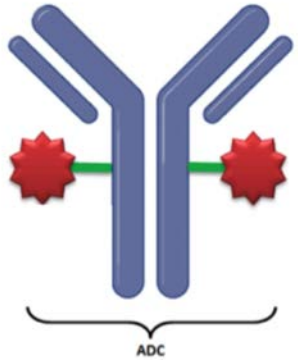
FOLR1 FDA MIRV for Ovarian Carcinoma: POSITIVE
Percentage of Cells with 2+ and/or 3+ Membrane Staining: 75%



Reference Ranges	
Positive	>/=75%
Negative	<75%

Mirvetuximab

- Antibody drug conjugate
  - 3 components
    - Antibody, linker, cytotoxic payload



- Targets folate receptor 1 (FOLR1) on surface of cancer cells
  - Often present in ov ca cells; limited expression in normal cells
- Bystander effect

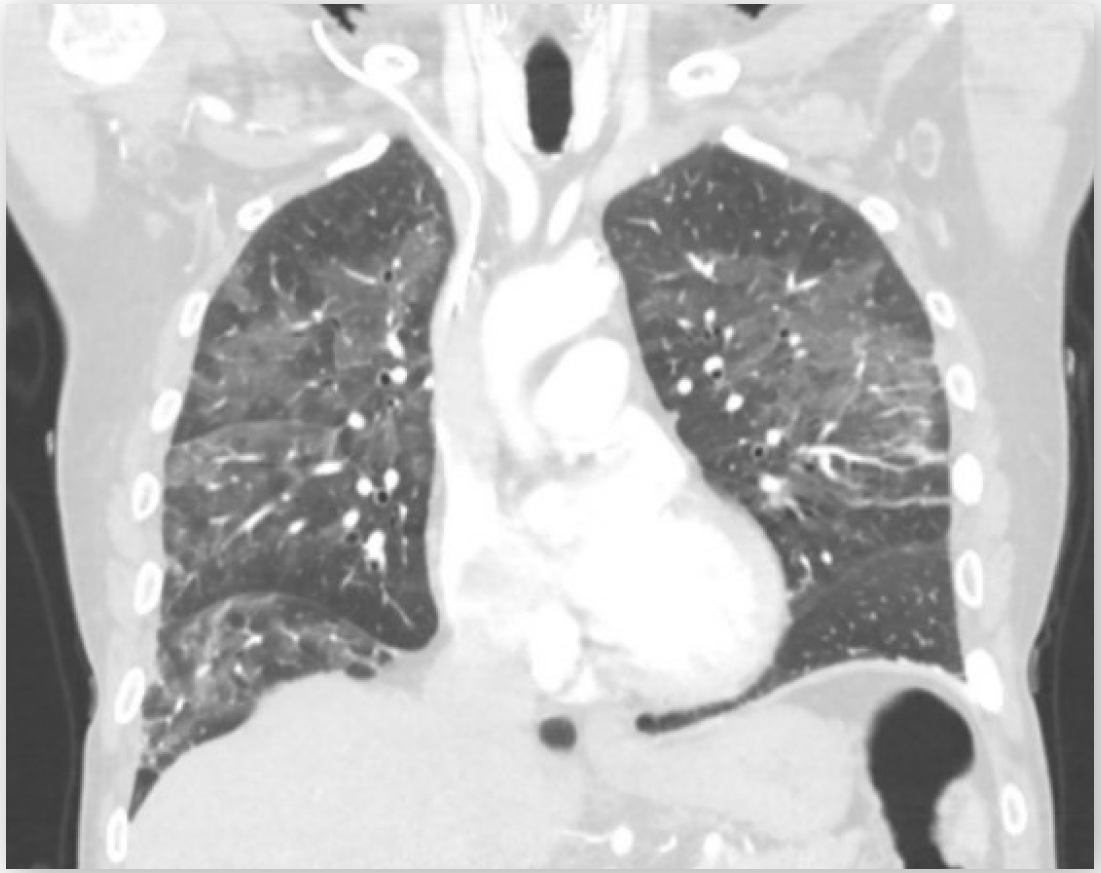
- Approved for platinum resistant ovarian cancer
- + expression = 75% or greater

Mirvetuximab: Common Side Effects

- **Eye disorders:** Blurry vision, dry eyes, eye irritation, eye redness
- **Low blood cell counts**
- **Fatigue**
- **Nausea**, **vomiting**
  - Most common on the day(s) of chemotherapy and for 2-3 days afterwards
- **Diarrhea**, **constipation**
- **Liver enzyme elevations**
- **Peripheral neuropathy**:
  - Numbness, tingling (“pins and needles”), or burning sensations in the hands and/or feet
    - If you already have neuropathy when you start this treatment, it may get worse

Mirvetuximab: Rare but Serious Side Effects

- **Infusion related/hypersensitivity reactions**
  - This reaction is most common with the first infusion and the risk for it after the first infusion significantly declines
- **Inflammation of the lungs**
  - If you experience unexplainable symptoms consisting of but not limited to dry cough, shortness of breath, or difficulty breathing then report it to your oncologist



Eye Care During Treatment

- To decrease risk of visual complications, you will be required to:
  - Have an eye examination (visual acuity and slit lamp) done **prior** to your first infusion
  - Have follow-up eye exams before **every other dose** of mirvetuximab soravtansine during the first 8 treatment cycles, then as directed by your provider
  - Administer **preservative free artificial tears** in each eye at least four times a day, starting with the first treatment and continuing until the end of treatment
  - Administer **corticosteroid eye drops** in each eye starting the day prior to and on days 1 to 8 of each treatment cycle, starting with the first cycle and continuing until the end of treatment
  - Avoid the use of contact lenses
  - Use caution when driving or operating heavy machinery
  - Wear sunglasses when outdoors because your eyes may become more sensitive to sunlight during treatment with mirvetuximab soravtansine
  - If you experience eye toxicity, your oncologist may hold (temporarily stop) this medication until your condition improves

Home medications

- **Corticosteroid eye drops**: Instill the number of drops shown below starting the **day prior** to each treatment cycle and continue use for only the first **eight days** of each treatment cycle

Treatment Day	-1	1	2	3	4	5	6	7	8
Number of eye drops per eye per day	Six					Four			

- **Artificial tears** (preservative free): Instill 1 drop into each eye (waiting at least 10 minutes after administration of dexamethasone eye drops) four times a day **during the treatment period**

Back to our case…

- 3 cycles later, complete resolution of rectal bleeding and pain
- CA125 decreasing
- Mild blurred vision with changes on eye exam.
  - Management: ophthalmologist visit, held x1 week
  - Lower dose by one dose level
- Eye toxicity resolved
- Continues to tolerate well

Roundtable Discussion

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Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Pancreatic Cancer

Friday, April 11, 2025

6:00 PM – 7:30 PM

Faculty

Farshid Dayyani, MD, PhD
Caroline Kuhlman, MSN, APRN-BC
Philip A Philip, MD, PhD
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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

To Claim NCPD Credit

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