An Industry Supported Symposium at the IGCS 2025 Annual Global Meeting

Evidence Based Biomarker-Driven Advances in Ovarian & Endometrial Cancer: Equitable, Individualized and Accessible Care

This session is not included in the main event CME/CPD credit.

Cape Town, South Africa

Friday, November 7, 2025

7:45 am – 8:45 am (GMT+2)

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Welcome & Symposium Objectives

Bradley Monk, MD

Florida Cancer Specialists & Research Institute
West Palm Beach, Florida, USA

MODERATOR

Bradley Monk, MD

Florida Cancer Specialists &
Research Institute
West Palm Beach, Florida, USA

FACULTY

Scott Jordan, MD

Broward Health Medical Center
Fort Lauderdale, FL

Shannon Westin, MD

MD Anderson Cancer Center
Houston, Texas, USA

R. Wendel Naumann, MD

Levine Cancer Institute,
Atrium Health
Charlotte, North Carolina, USA

Faculty Disclosures

Name	Role in Activity	Disclosures
Bradley Monk, MD	Moderator	Honorarium and consulting from: AstraZeneca Pharma& (Clovis), Genentech/Roche, GSK (Tesaro), Merck, Myriad
Scott Jordan, MD	Speaker	Advising: GSK, AstraZeneca, Karyopharm, Caris Speaking: Pfizer/Genmab, GSK, Merck, Natera
Shannon Westin, MD	Speaker	**Research Support:** AstraZeneca, AvengeBio, Bayer, Bio-Path, Clovis Oncology/Pharma&, Daiichi Sankyo, GSK, Jazz Pharmaceuticals, Mereo, Novartis, Nuvectis, Pfizer, Roche/Genentech, Zentalis **Consultant:** AstraZeneca, Bayer, Caris, Clovis Oncology/Pharma&, Corcept, Daiichi Sankyo, Eisai, EQRX, Gilead, GSK, Immunocore, Immunogen, Incyte, Lilly, Loxo, Merck, Mereo, Mersana, NGMBio, Nuvectis, Pfizer, Roche/Genentech, SeaGen, Verastem, Vincerx, Zentalis, ZielBio
R. Wendel Naumann, MD	Speaker	Consulting - AstraZeneca, Eisai, SutroBio, Immunogen, GOG, GSK, Incyclix, Merck, Serno, Genmab, Addi (White Hawk), Ethicon Research – AstraZeneca, SutroBio, Immunogen, Schrödinger, Immunogen DSMB - GOG (Intuitive), Genelux, Virtual Incision (Chair)

Learning Objectives

Upon completion of the activities in this series, learners will demonstrate increased knowledge regarding:

1. **Apply evidence-based treatment strategies for ovarian and endometrial cancers.**
   - Focus on guideline-aligned approaches and biomarker-informed therapies

2. **Integrate biomarker testing into clinical decision-making.**
   - Understand the role of BRCA, HRD, MMR/MSI, Folate Receptor Alpha, HER2, KRAS, and p53 in treatment selection
   - Interpret test results and apply them across disease types and clinical context

3. **Identify practical challenges to biomarker testing and treatment access**
   - Explore disparities in testing availability and therapeutic access
   - Implement strategies to promote equitable care, particularly in resource-limited settings

4. **Recognize emerging therapeutic targets and evolving biomarkers.**
   - Discuss ADCs, including HER2 and Folate Receptor Alpha, and other novel approaches within the context of approved and investigational options
   - Stay informed about evolving biomarker algorithms and their clinical implications

Agenda

07:45 - 08:00: **Welcome & Symposium Objectives**
Bradley Monk, MD, Florida Cancer Specialists & Research Institute, West Palm Beach, Florida, USA

08:00 - 08:15: **Integrating Biomarker Testing in Clinical Practice**
Shannon Westin, MD, MD Anderson Cancer Center, Houston, Texas, USA

08:15 - 08:30: **Applying Evidence-Based Treatments in OC and EC**
Scott Jordan, MD, Broward Health Medical Center, Fort Lauderdale, Florida, USA

08:30 - 08:40: **Barriers to Access and Equitable Care Delivery**
R. Wendel Naumann, MD, Atrium Health Wake Forest Baptist Comprehensive Cancer Center, Charlotte, North Carolina, USA

08:40 - 08:45: **Interactive Panel Discussion: Emerging Targets, Real-World Decision Making, Summary & Closing Remarks**
All Faculty

1. What region of the world are you from?

a. North America,
b. South America,
c. Asia,
d. Europe,
f. Africa,
g. Other

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What is your primary specialty?

a. Gynecologic Oncology (But don't give chemo),
b. Gynecologic Oncology with Chemotherapy,
c. Pharma
d. Radiation Oncology
e. Medical Oncology
f. Other

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3. What biomarkers do you generally have access to? (select all that apply)

a. p53
b. Her-2
c. BRCA
d. HRD
e FOLR1
f. PD-L1
g. POL-E
h. MMR/MSI
i. NGS (Next Generation Sequencing)

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Integrating Biomarker Testing in Clinical Practice

Shannon Westin, MD
MD Anderson Cancer Center
Houston, Texas, USA

Biomarker Testing Primer

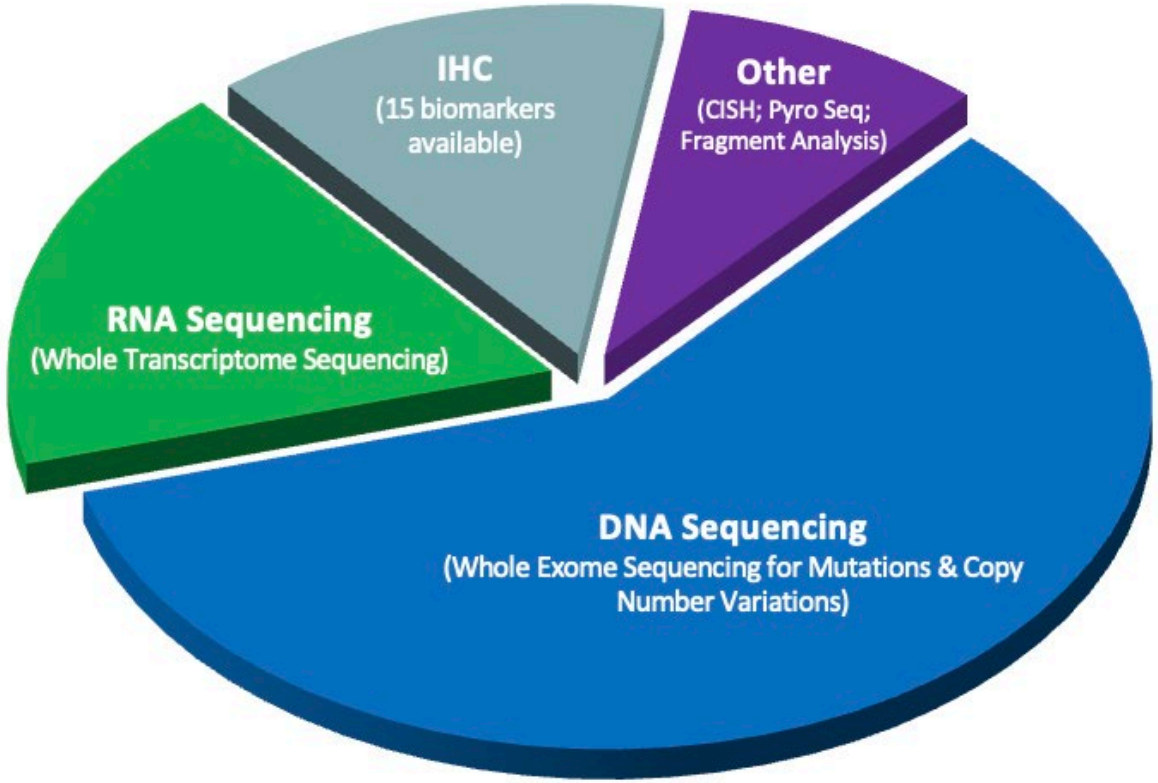
DNA Sequencing:
- Next generation sequencing – NGS – most rapid evaluation of hundreds to thousands of regions
- Focus on hotspots in cancer genomes

Immunohistochemistry (IHC):
- Protein expression

RNA Sequencing (RNASeq):
- Whole transcriptome
- Detection of gene fusions, expression levels and gene expression signatures

Quantitative Polymerase Chain Reaction (qPCR):
- Amplifies and quantifies a targeted DNA molecule

Fragment Analysis (FA/Frag. Analysis):
- Changes in DNA or RNA to indicate the presence or absence of genetic marker



MANY COMMERICIAL AND INSTITUTIONAL OPTIONS

How can biomarkers help us?

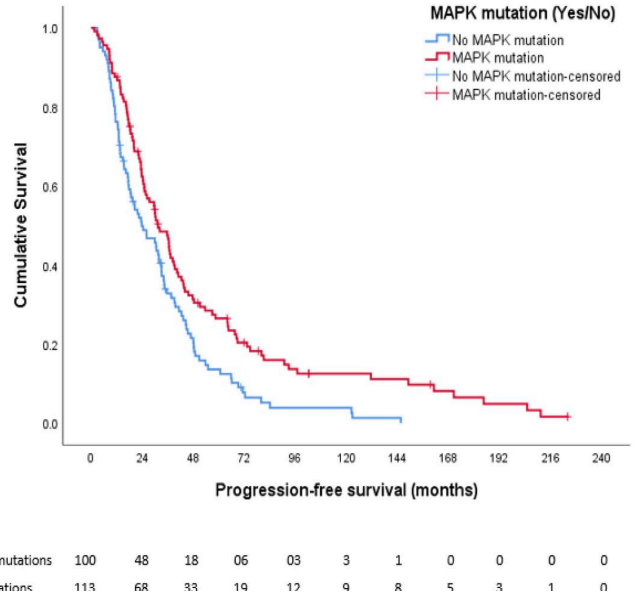
PROGNOSTIC vs. PREDICTIVE BIOMARKER	
PROGNOSTIC BIOMARKER	**PREDICTIVE BIOMARKER**
Definition: Indicates the overall cancer outcome, regardless of therapy	**Definition:** Predicts the response to a specific therapy
Purpose: Provides information about patient's prognosis and risk of recurrence	Identifies patients who are likely to benefit from a certain treatment
Examples: Tumor size Mutation in *TP53*	**Examples:** HER2 amplification BRAF mutation

INFORMATIVE

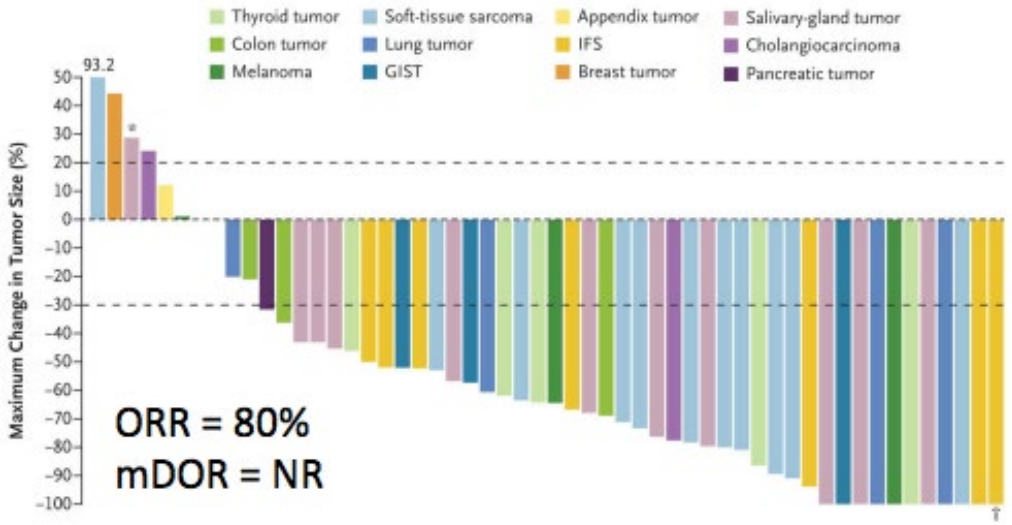
ACTIONABLE

KRASm LGSOC == Improved Survival

A



Larotrectinib in TRK Fusion Positive Cancers



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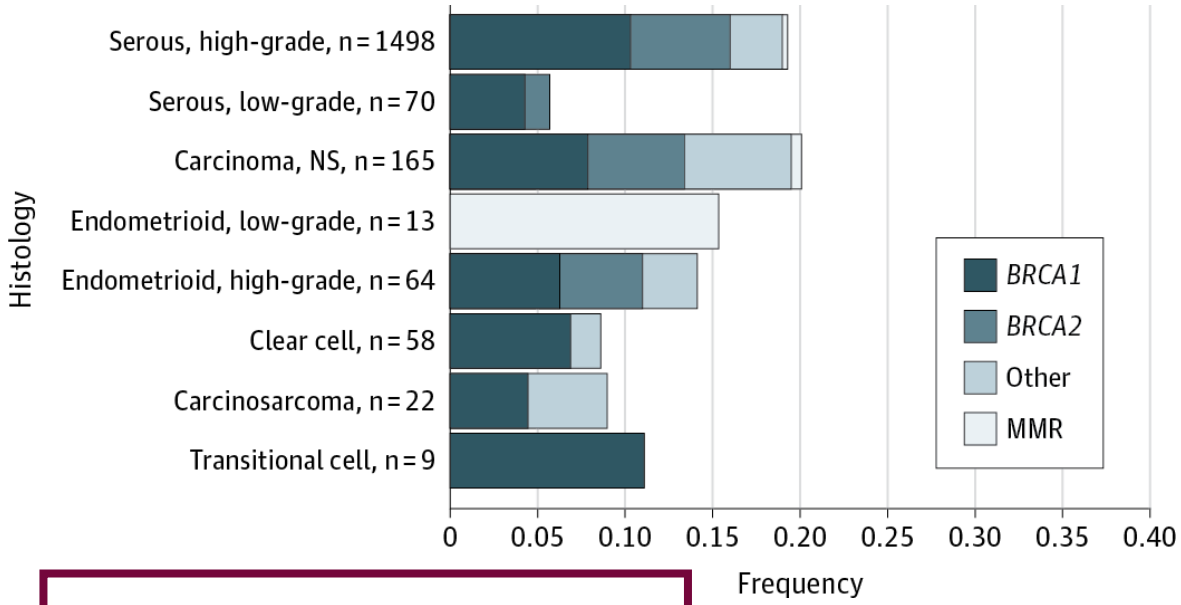
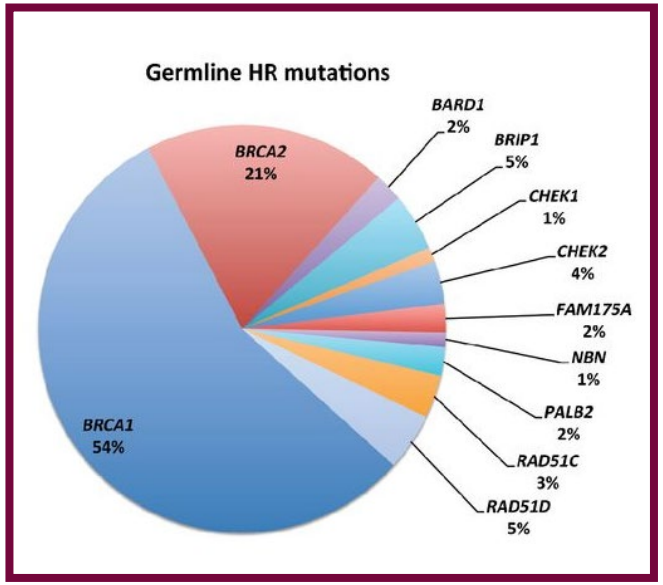
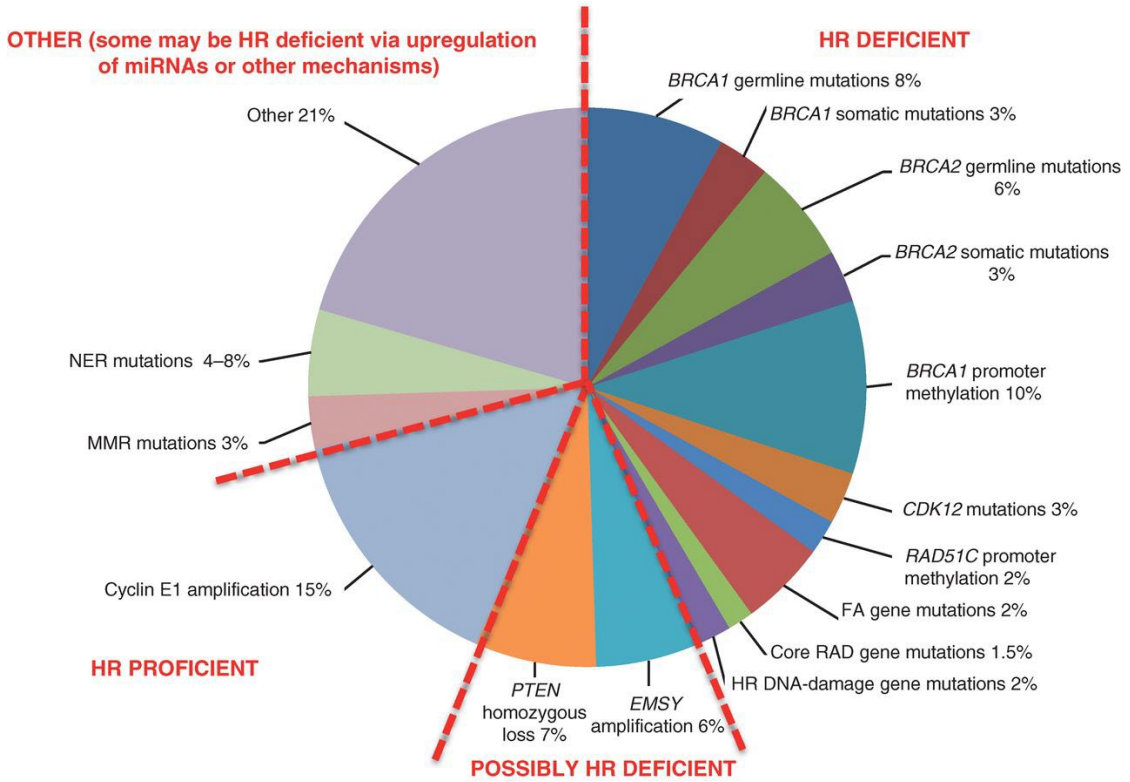
Cobb Gyn Onc 2022, Hyman NEJM 2018

BRCA mutations and HRD are common in epithelial ovarian cancer





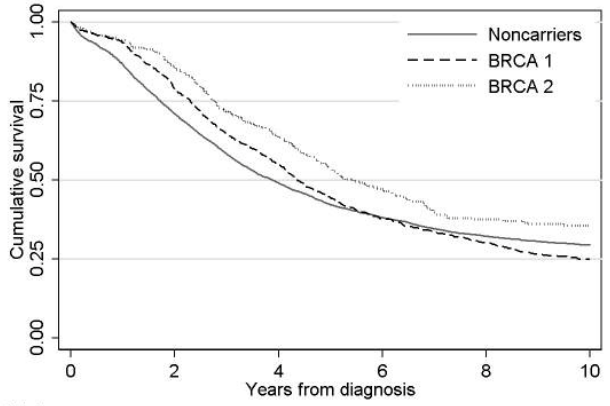


- 24% of patients with ovarian cancer carry a germline mutation in HR genes – majority *BRCA1/2*
- Additional 9% harbor somatic mutations in HR genes
- HRD in ~ 50% of all ovarian cancer

Norquist et al, JAMA Oncol, 2016, Konstantinopoulos et al, Cancer Discov, 2015

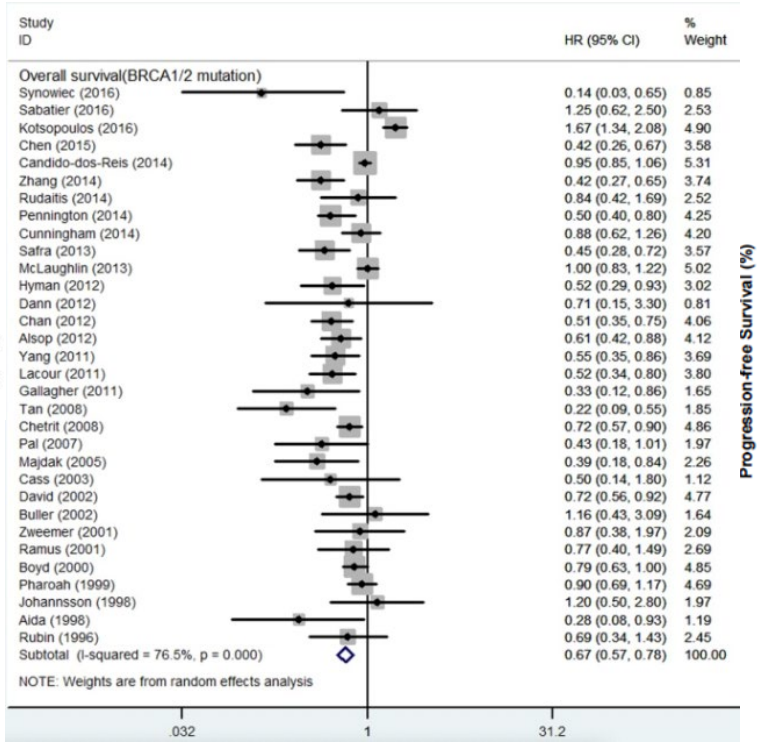
Testing for *BRCA* (and related genes) is critical in ovarian cancer

Prognostic: Improved Survival



Number at risk

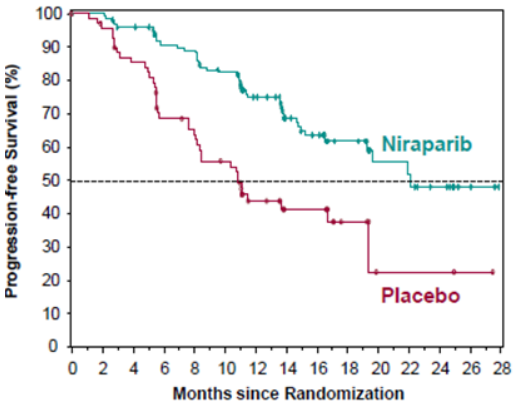
Noncarriers	1924	2914	2295	1657	1120	812
Carriers						
BRCA1	404	676	499	323	198	118
BRCA2	162	278	239	152	86	58



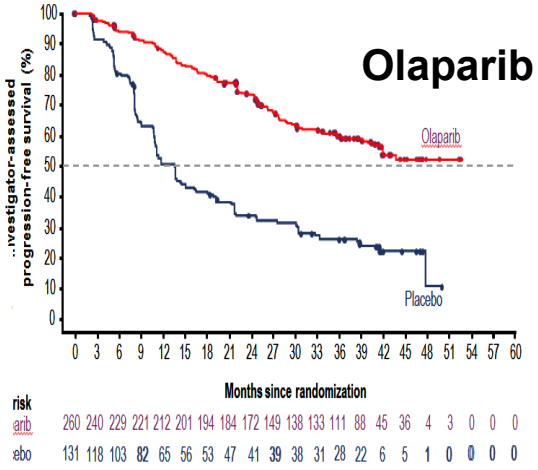
Clearly Predictive (PARPi)

Niraparib

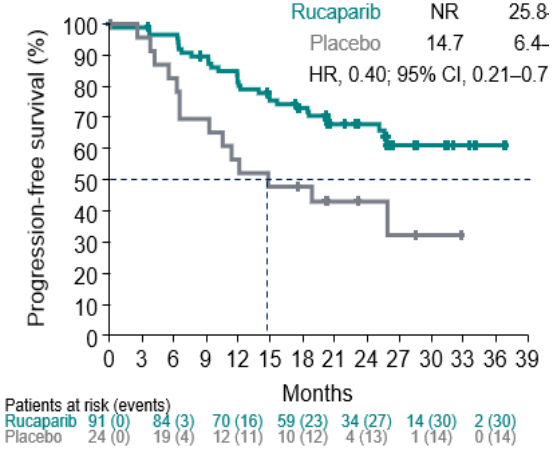
HRd/*BRCA*mut



Olaparib



Rucaparib



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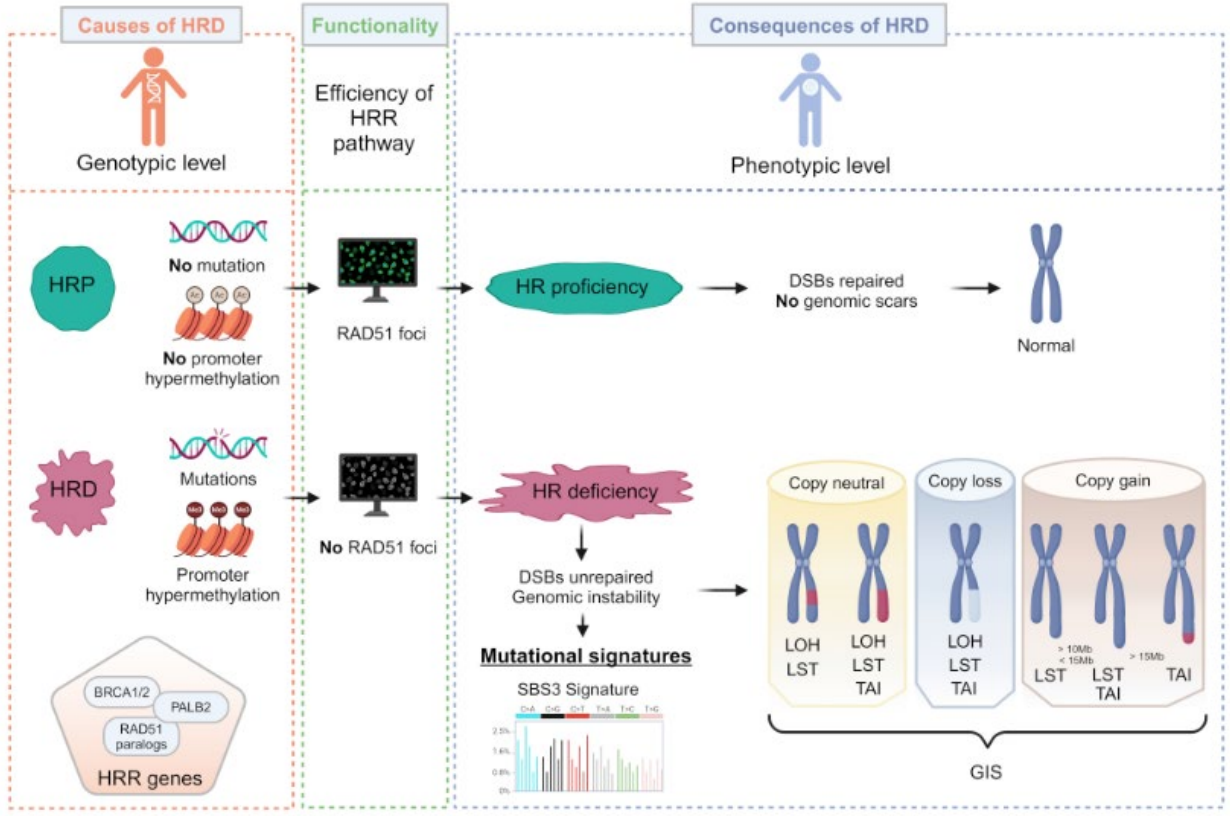
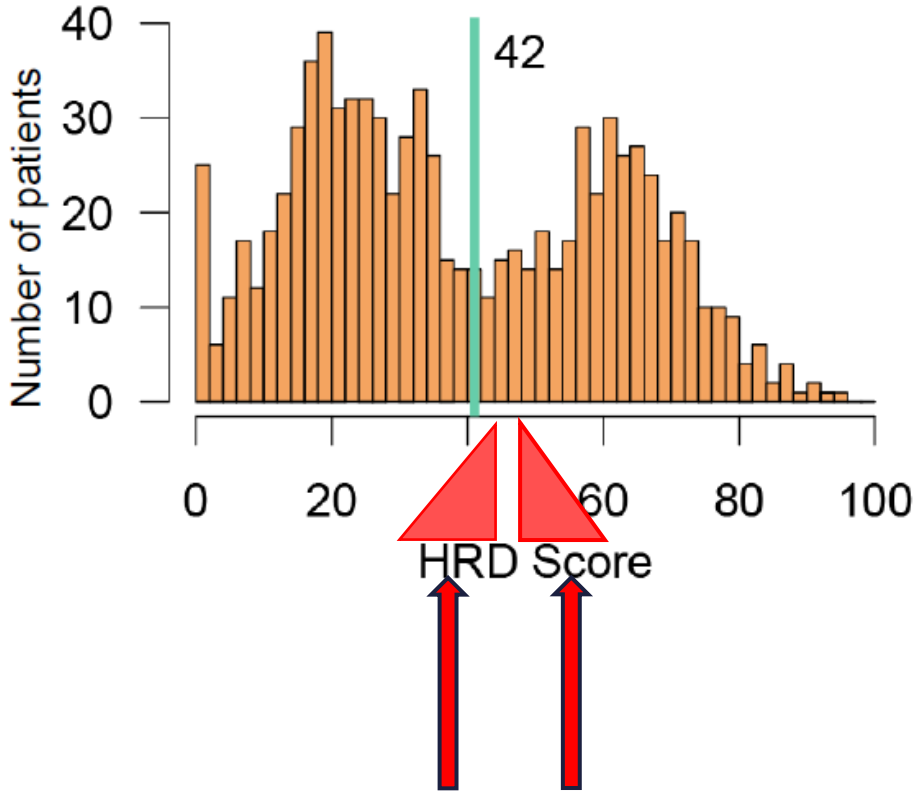
Candido-dos-Reis, et al CCR 2014, Xu et al, Oncotarget 2016; Moore N Engl J Med 2018; Gonzalez-Martin N Engl J Med 2019; Monk J Clin Oncol 2022

Testing for Homologous Recombination Deficiency (HRD)





Possibly misclassified!!!

Current Commercial Options:

LOH: Loss of Heterozygosity +/-

LST: Large-Scale State Transitions

TAI: Telomeric Allelic Imbalance

Witz et al, Biomarker Research, 2025, Mills et al., SGO 2016

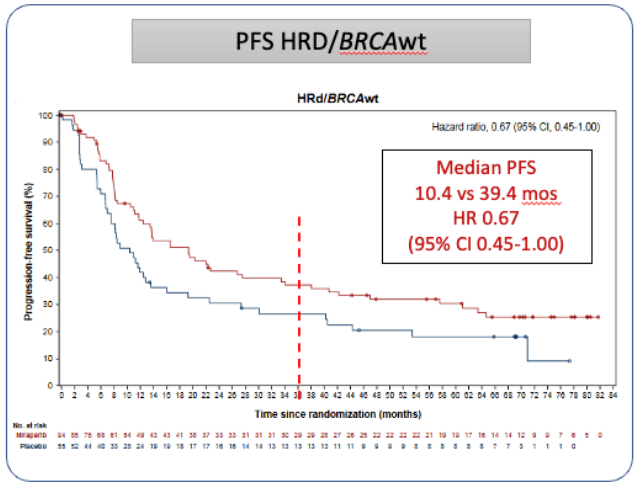
HRD is Prognostic and Predictive in Ovarian Cancer

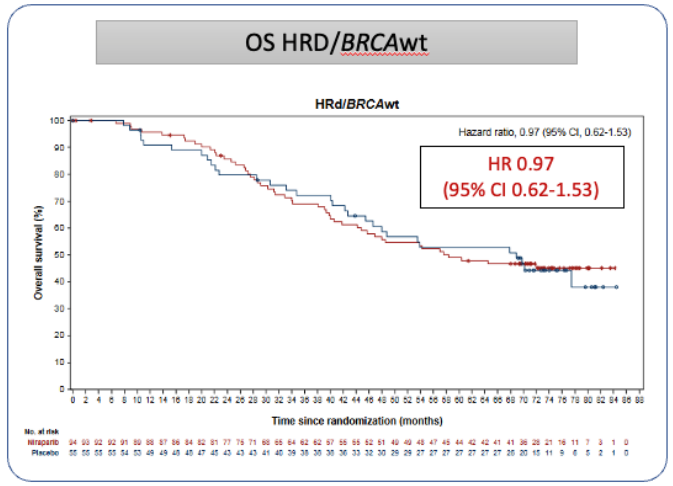
Survival After Chemotherapy

	PFS		OS	
High/Low	P Value	HR	P Value	HR
HRD	**$2x10^{-6}$**	**0.66**	**$1x10^{-8}$**	**0.55**
LOH	$5x10^{-5}$	0.70	$8x10^{-6}$	0.64
TAI	$9x10^{-5}$	0.71	$6x10^{-7}$	0.61
LST	$1x10^{-5}$	0.68	$3x10^{-7}$	0.60

- All of the individual component scores reached significance for both PFS and OS.
- The HRD score was more significant than any of the component scores.

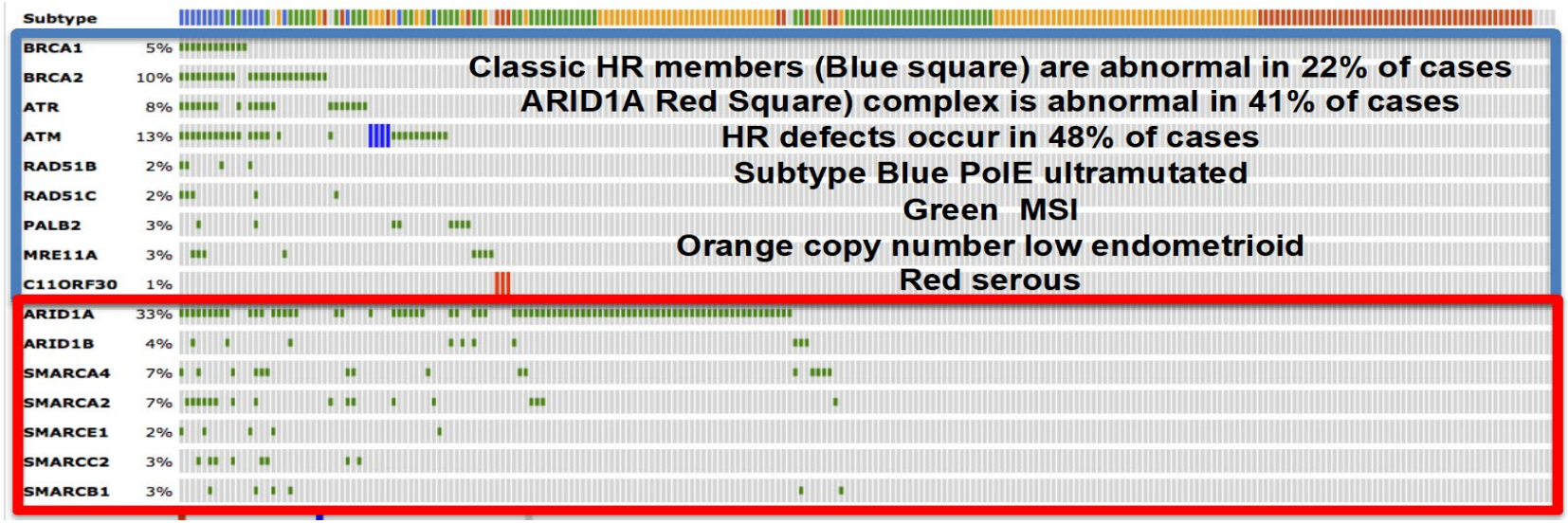
Benefit from PARPi

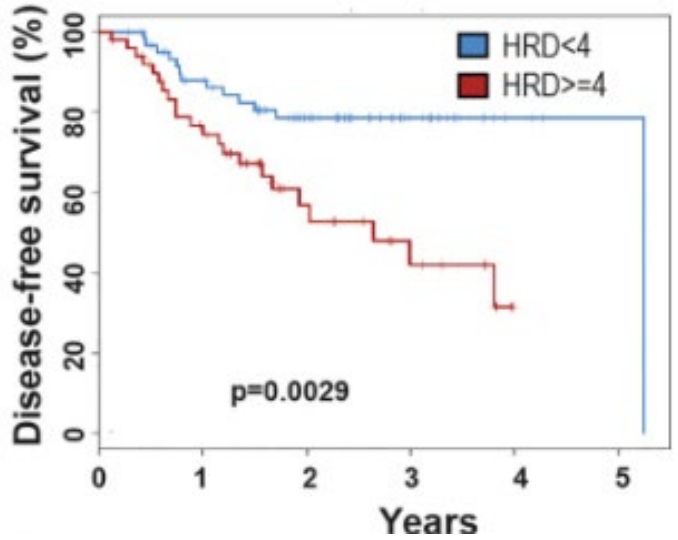


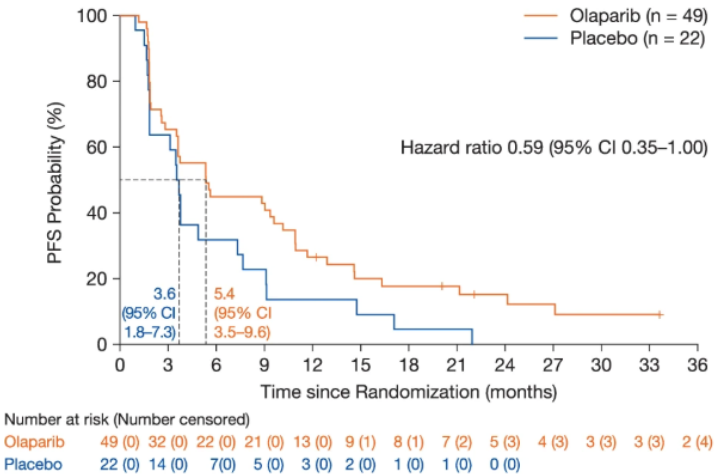


Mills SGO 2016, Gonzalez-Martin, 2024 ESMO Congress; Monk et al., Ann Oncol 2024

BRCA mutations and HRD are less common but still prevalent in endometrial cancer







- Possible up to 50% with aberrations predictive of benefit from PARPi
- Unclear definition of HRD in EC

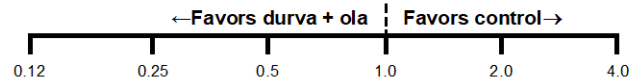
Liang H, et al. *Genome Res*. 2012, Seidel Gyn Onc 2021, Joly et al Nature Communications 2025

Preliminary data regarding HRR mutations and PARPi in EC

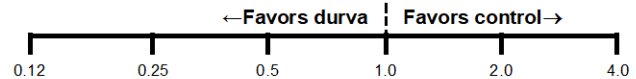
DUO-E exploratory PFS subgroup analysis[1,2]

Overall Population

	HR (95% CI)	Durva + Ola + CP n/N (%)	Control n/N (%)
All patients	0.53 (0.42-0.67)	126/239 (52.7)	173/241 (71.8)
HRRm status			
HRRm	0.30 (0.15-0.58)	16/39 (41.0)	23/32 (71.9)
Non-HRRm	0.59 (0.44-0.80)	81/141 (57.4)	96/132 (72.7)
Unknown	0.57 (0.36-0.89)	29/59 (49.2)	54/77 (70.1)



	HR (95% CI)	Durva + CP n/N (%)	Control n/N (%)
All patients	0.68 (0.55-0.86)	139/238 (58.4)	173/241 (71.8)
HRRm status			
HRRm	0.57 (0.27-1.13)	12/26 (46.2)	23/32 (71.9)
Non-HRRm	0.72 (0.54-0.97)	85/138 (61.6)	96/132 (72.7)
Unknown	0.65 (0.43-0.97)	42/74 (56.8)	54/77 (70.1)

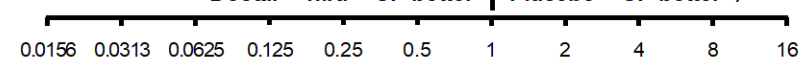


- Enhanced benefit in the pMMR population with Durva + Ola + CP was observed irrespective of *BRCA*m status[4]
- PFS outcomes with Durva + Ola + CP in non-*BRCA*m patients were consistent with the ITT population and pMMR subpopulation[4]

RUBY part 2 exploratory PFS analysis by mutation status[3]

Overall Population

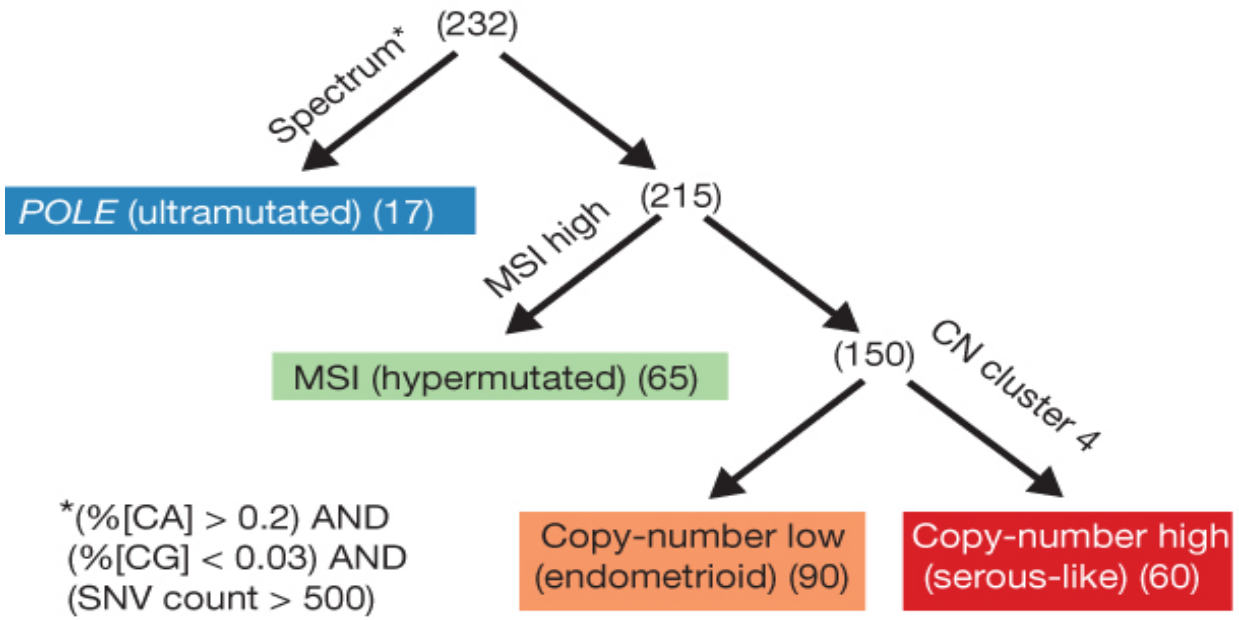
	Dostarlimab + Niraparib + CP (N = 192)	Placebo IV + Placebo PO + CP (N = 99)	HR (95% CI)	HR (95% CI)
All patients	95/192	69/99		0.59 (0.43-0.81)
BRCA mutation status				
Positive	1/6	3/4		NA
Negative	75/148	49/71		0.61 (0.43-0.88)
NE	19/38	17/24		0.71 (0.37-1.37)
HRR mutation status				
Positive	3/20	10/14		NA
Negative	73/134	42/62		0.69 (0.47-1.01)
NE	19/38	17/24		0.71 (0.37-1.37)

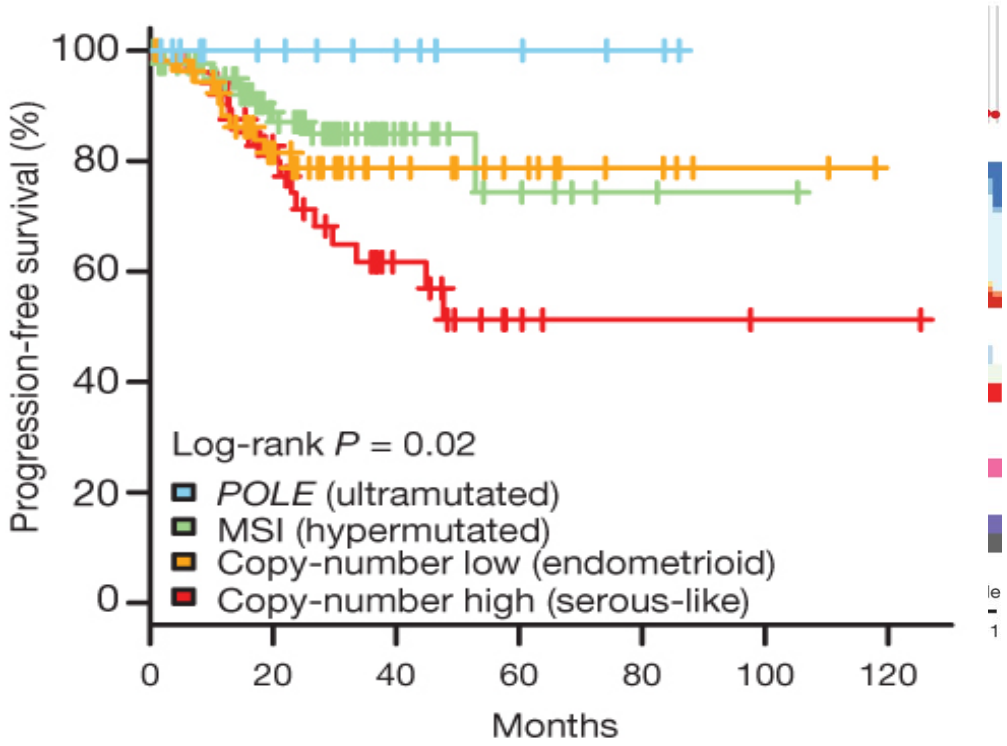


Westin SN et al. JCO 2024. Mirza MR et al. SGO 2024. Abstract LBA2. Van Nieuwenhuysen E et al. ASCO 2024 Abstract 5595.

Shifting the Paradigm in Endometrial Cancer with The Cancer Genome Atlas: Lumping to Splitting

Immunologically Responsive | Immunologically Non-Responsive





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G Getz et al. Nature **497**, 67-73 (2013) doi:10.1038/nature12113

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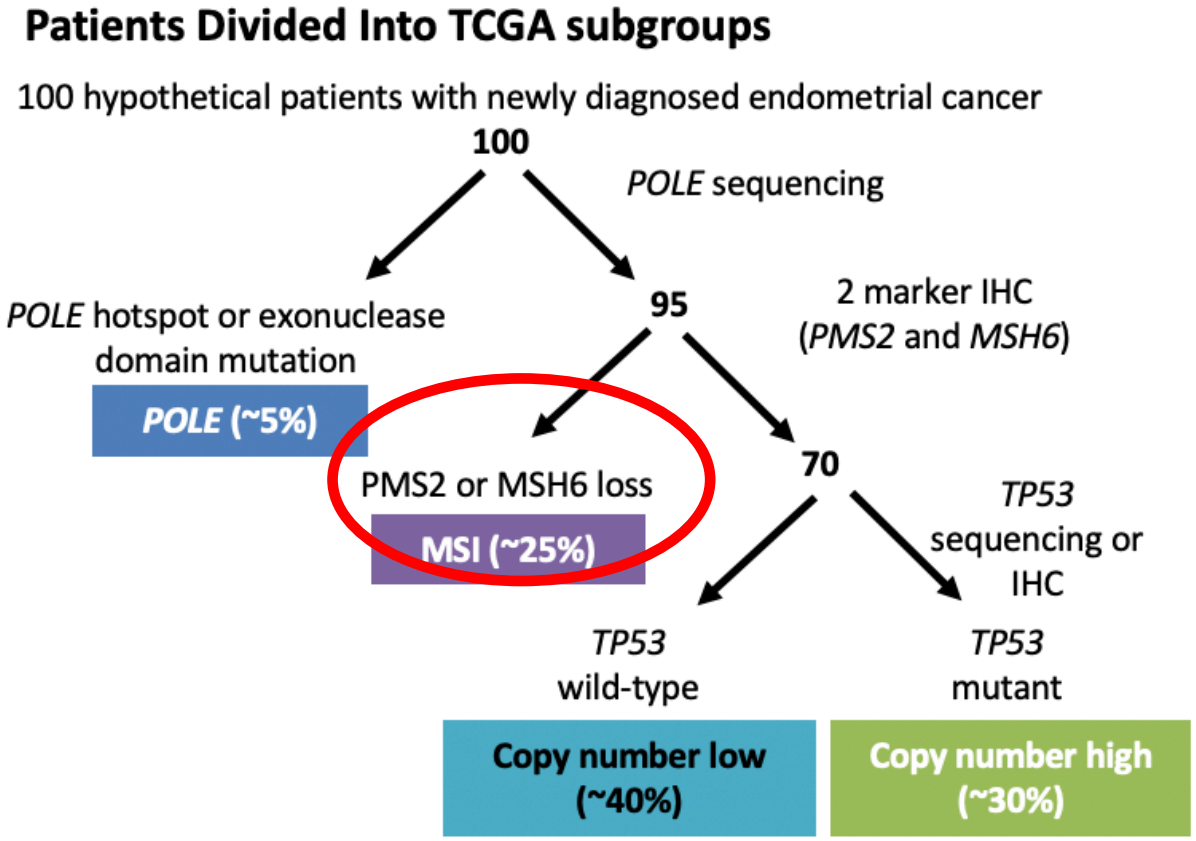
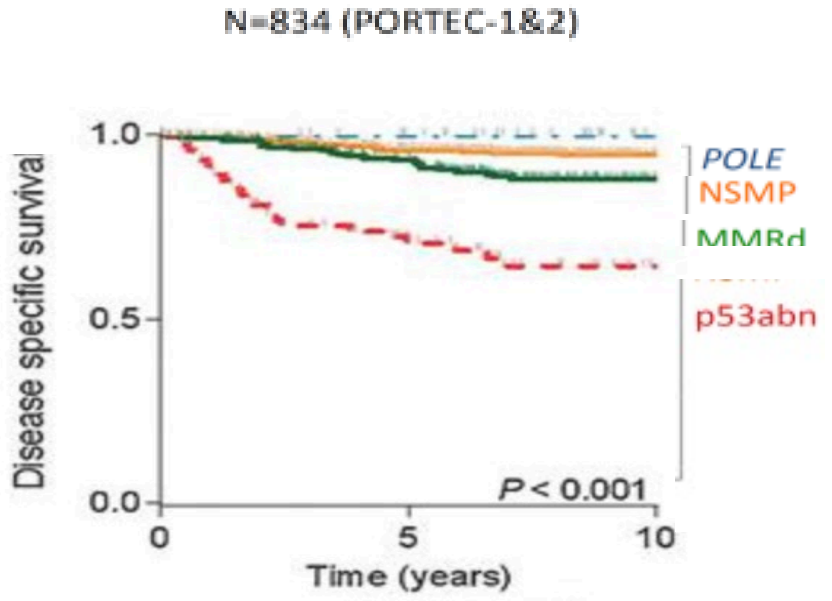
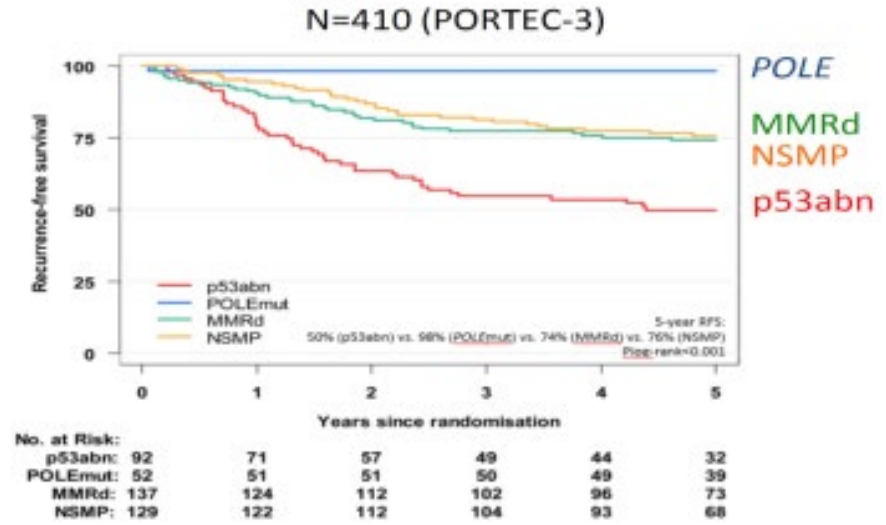
Pragmatic Assessment of Endometrial Cancer – What Matters?







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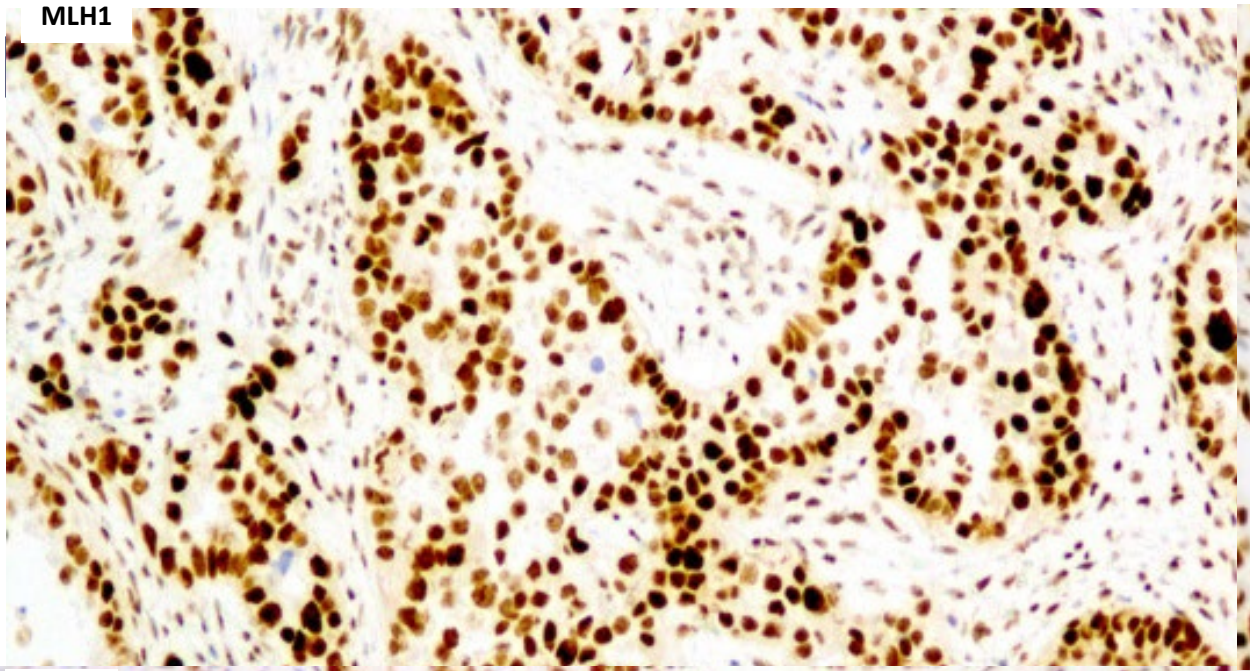
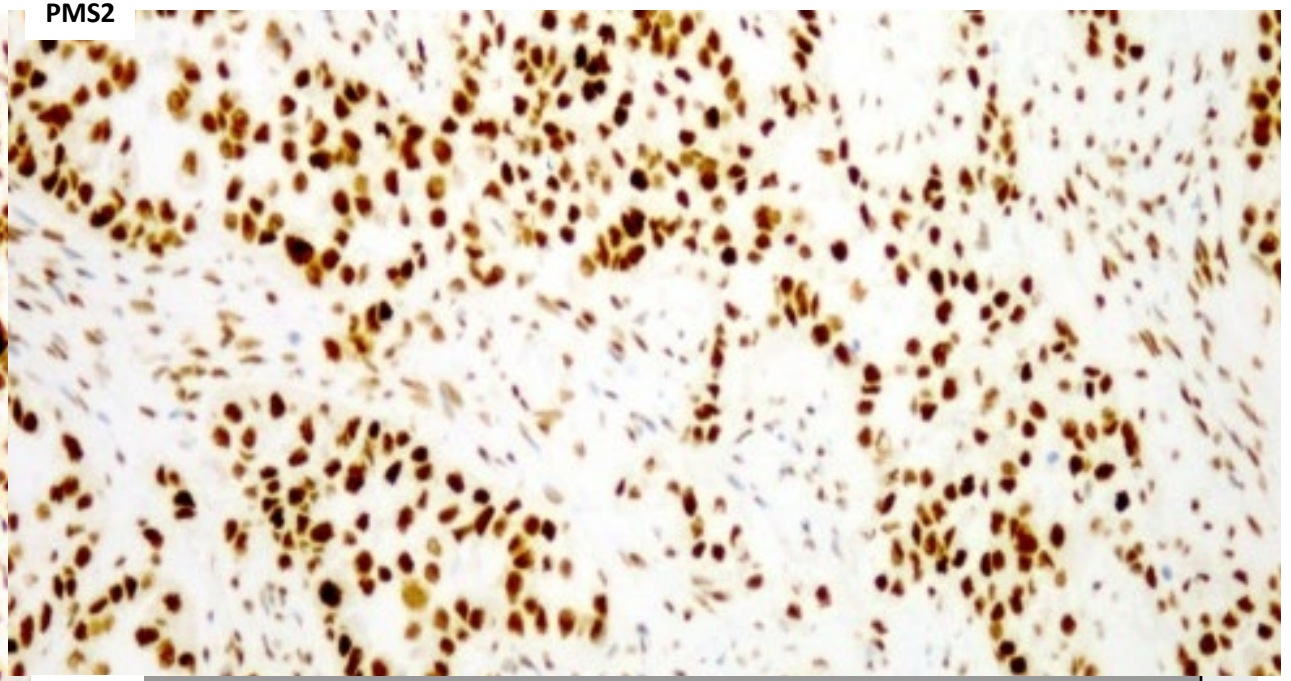
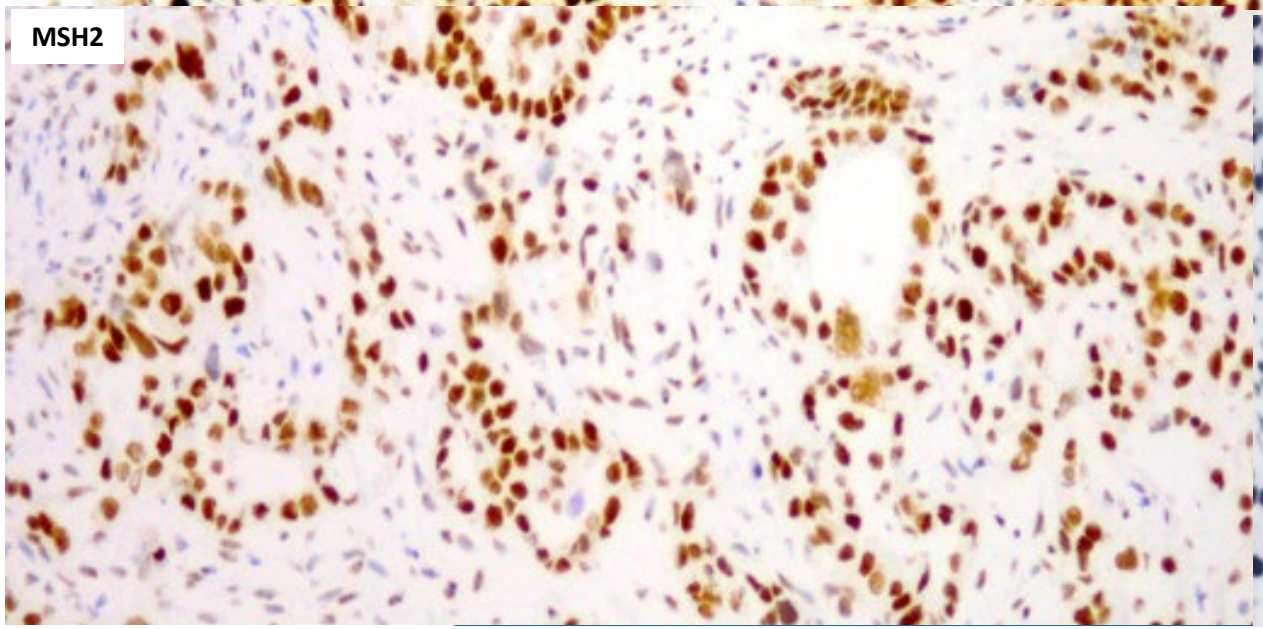
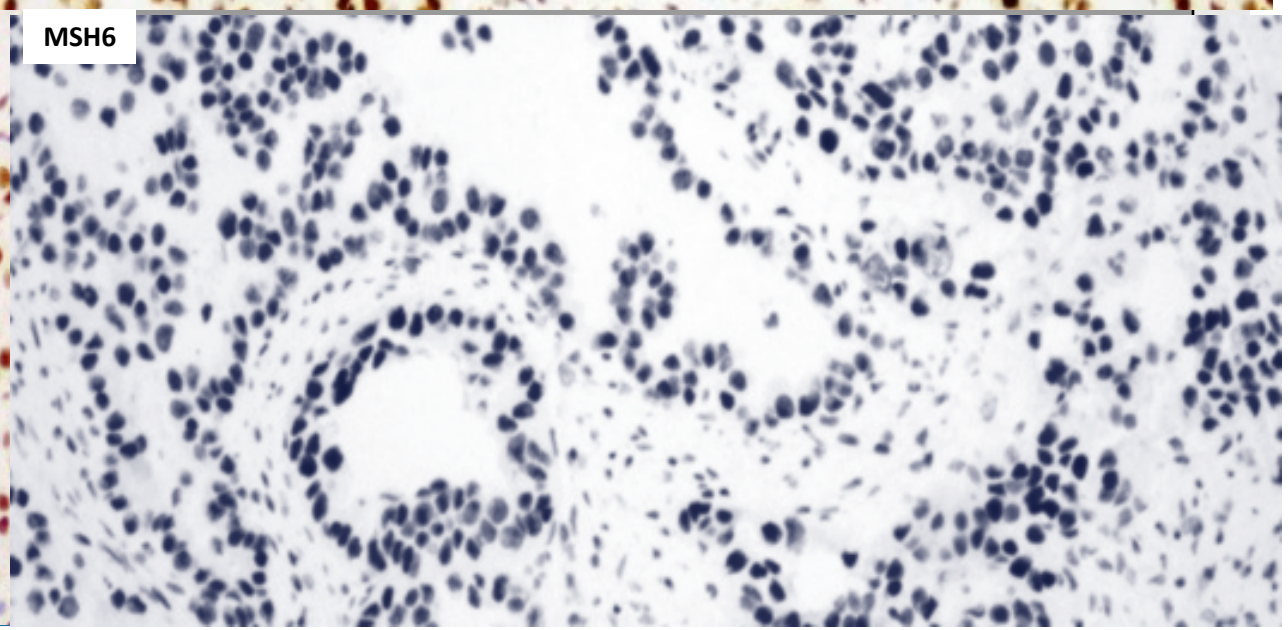
MacKay HJ, et al. Oncotarget. 2017; Leon-Castillo JCO 2020 Stelloo CCR 2016







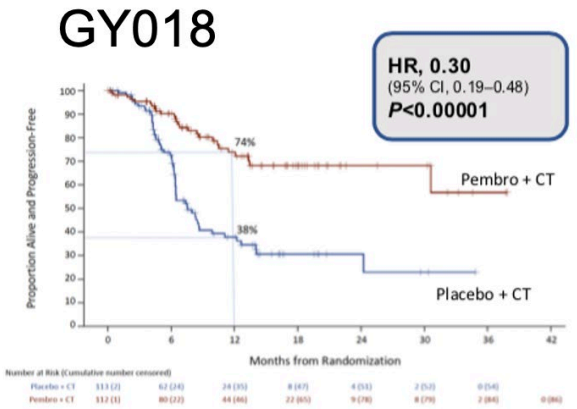


Kloor M et al. Trends Cancer. 2016:121-133. Luchini C et al. Ann Oncol. 2019;30:1232-1243;
Path slides courtesy of Anais Malpica, MD.

Clear Benefit of IO + Chemo in dMMR/MSI-H EC

dMMR population

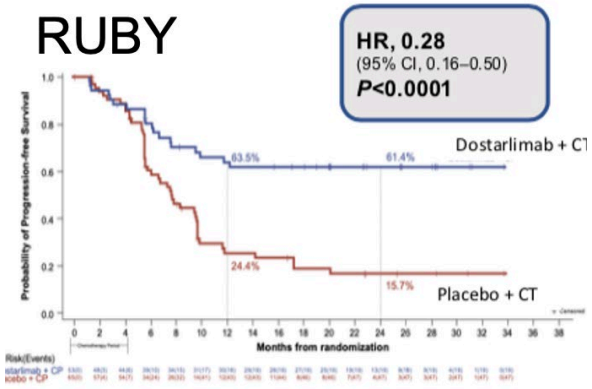
GY018



	No with events%	Median
Pembro + CT	23.2	NR (30.6-NR)
Placebo + CT	52.2	7.6 (6.4-9.9)

dMMR/MSI-H population

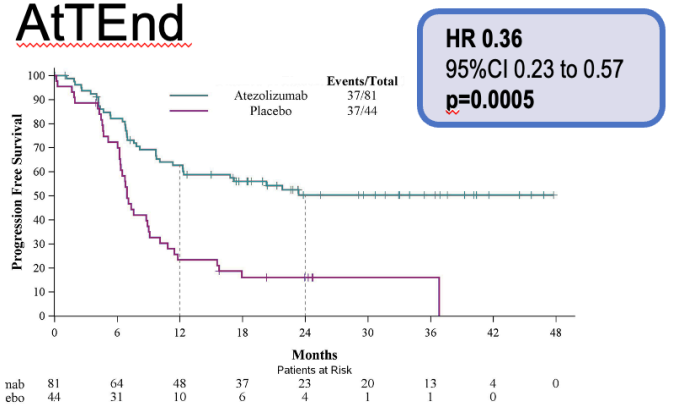
RUBY



	No with events%	Median
Dorsta + CT	35.8	NR (11.8-NR)
Placebo + CT	72.3	7.7 (5.6-9.7)

dMMR population

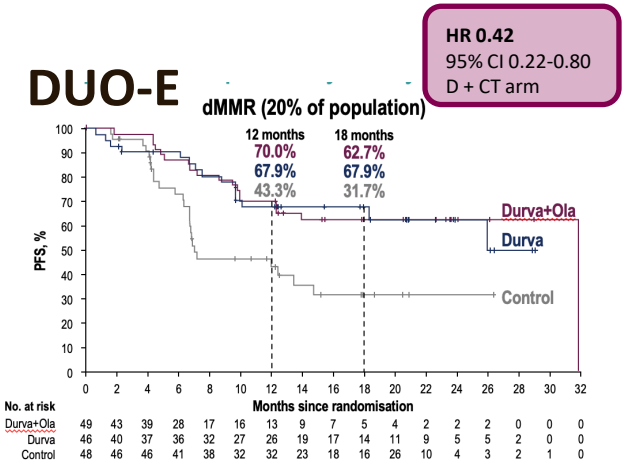
AtTEnd



	No with events%	Median
Atezo + CT	45.7	NR (12.3-NR)
Placebo + CT	84.1	6.9 (6.2-9.0)

dMMR population

DUO-E



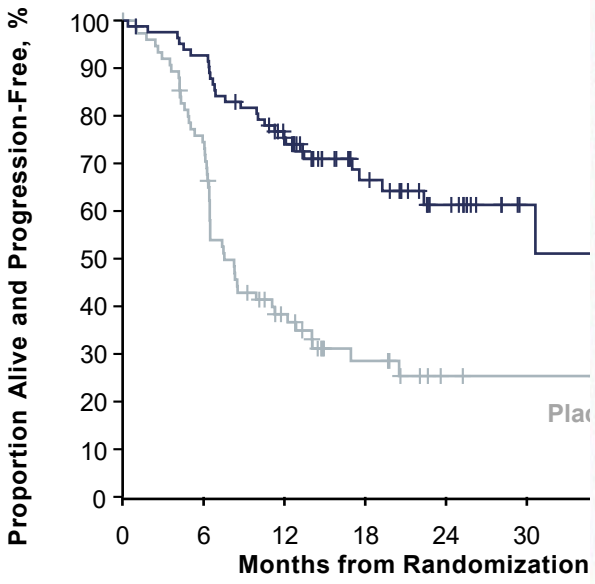
	No with events %	Median
Durva + CT	32.6	NR (NR-NR)
Durva + O + CT	37.5	31.8 (12.4-NR)
Placebo + CT	51	7.0 (6.7-14.8)

Mirza NEJM 2023, Eskander NEJM 2023, Westin JCO 2024, Colombo Lancet Oncology 2024

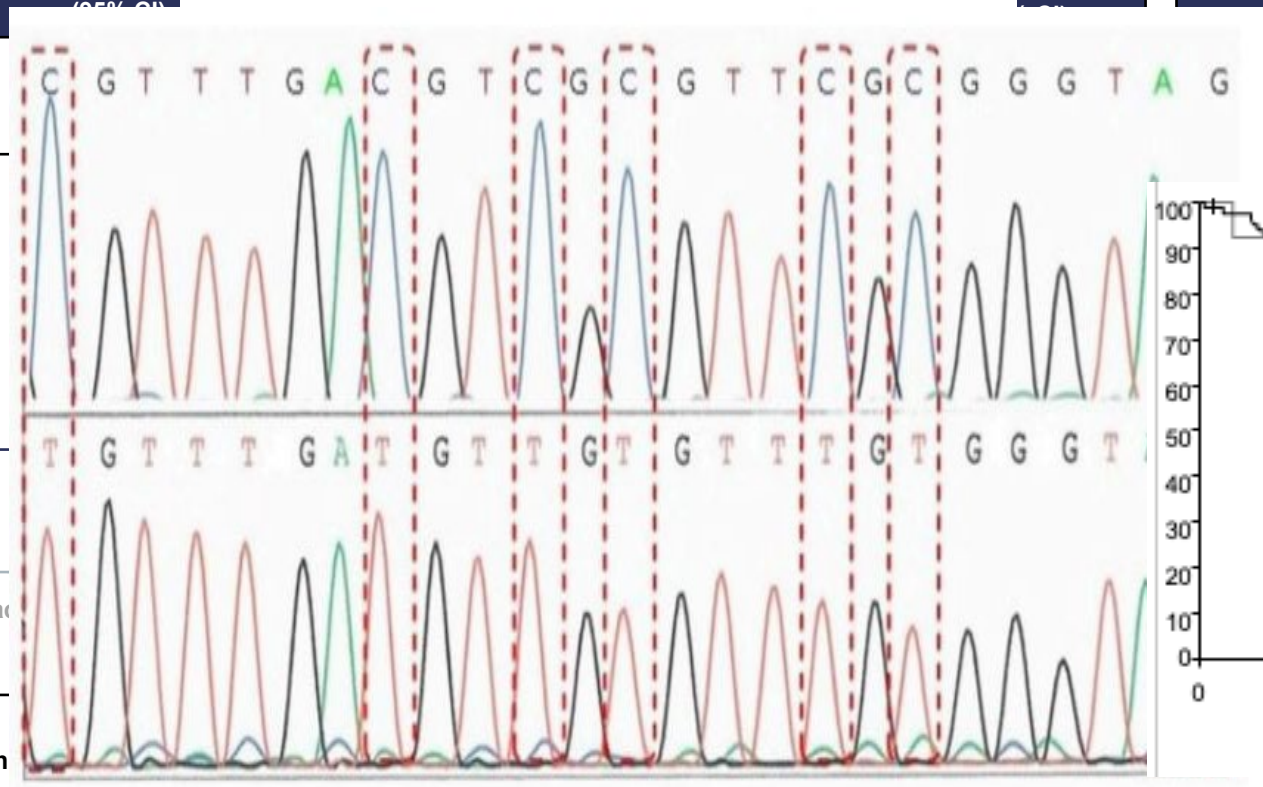
Does mechanism of MSI matter?

Methylation

	Events n/N	Median (95% CI), mo	HR
Placebo + CP	51/77	7.5 (6.4-11.3)	
Pembro + CP	28/83	NR (22.3-NR)	

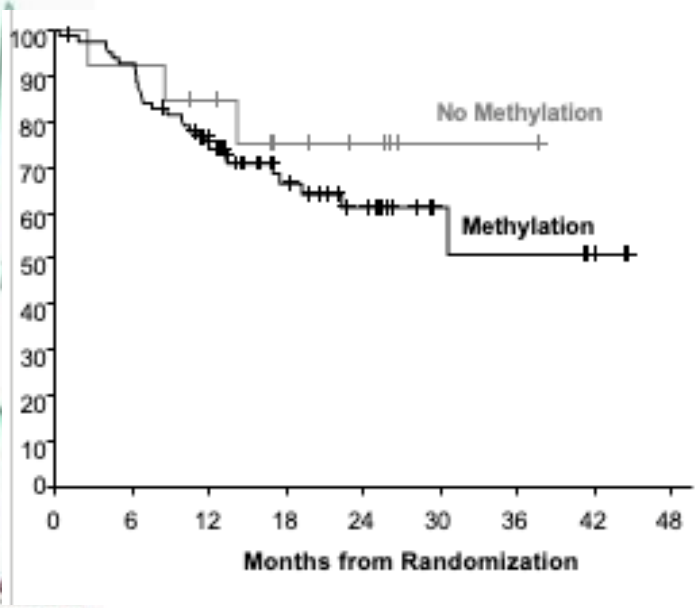


Reflex testing for MLH1 promoter methylation status is recommended if MLH1 protein loss



Methylation Status
Pembro + CP Arm

	Events n/N	Median (95% CI), mo
hylation	3/13	NR (14.2-NR)
ation	28/83	NR (22.3-NR)



The mechanism of MMR loss (mutation vs epigenetic alteration) did not appear to be prognostic of response to chemotherapy or pembrolizumab

Eskander RN et al. ESMO 2023. Abstract 6564.

What do we know about TMB-High in EC?

High degree of overlap between dMMR & TMB-H

Figure 3. Overlap between the dMMR and TMB-H subpopulations (combined dMMR/TMB-H analysis set; N=138)

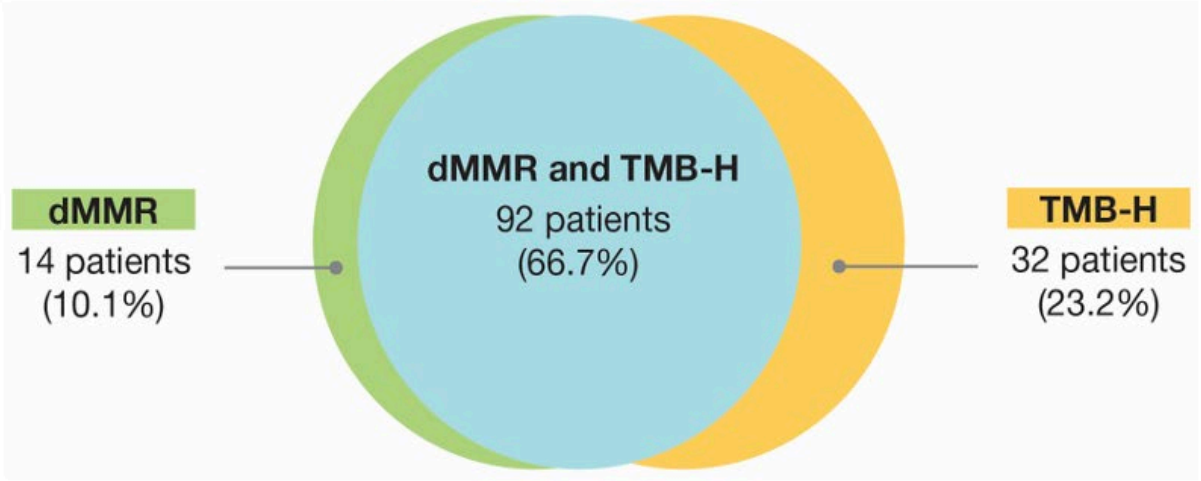


Figure 2. Concordance between MMR and TMB status (concordance analysis set; N=479)

TMB-H
dMMR
TMB and MMR concordance

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

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

Westin et al, 1117P, ESMO 2025; Westin JCO 2024

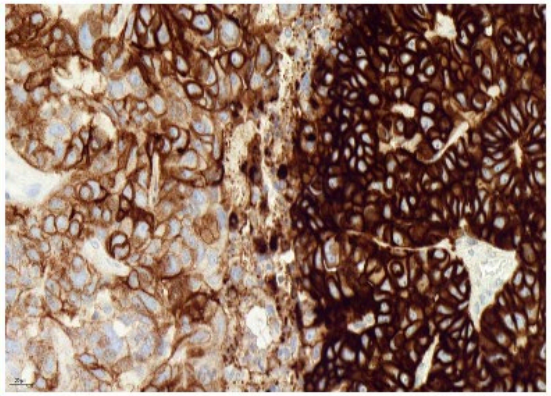
FOLR1 Testing – Assessment of FRα Expression

PS2+ Scoring

Determined by staining intensity and percentage of tumor cells

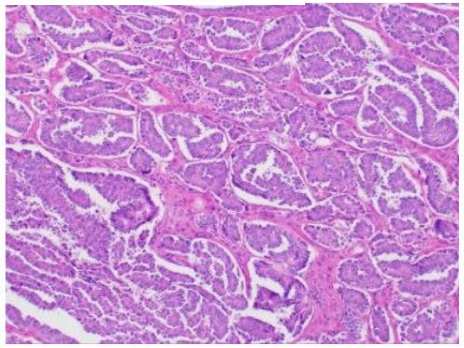
1+ 2+ 3+ intensity

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

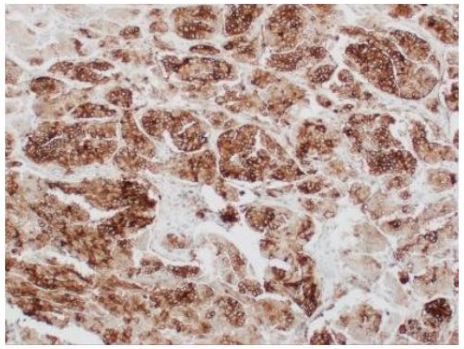


Commercial and institutional options available

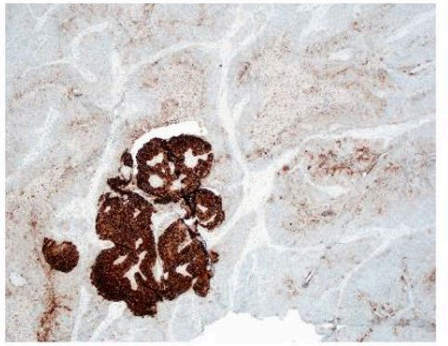
CDx – mirvetuximab sorvtansine at >/= 75%
NCCN – mirvetuximab + bevacizumab at >/= 25%
Future indications for next generation antibody-drug conjugates – potentially at lower expression levels



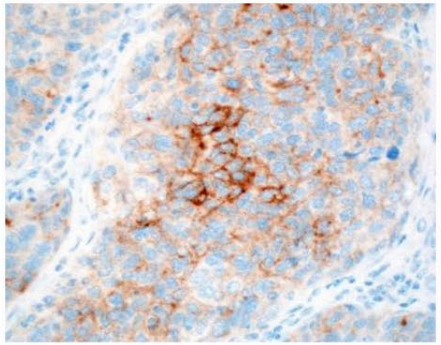
Low Grade Serous



Mod/Strong Membranous Staining



Variable Staining - <75% of cells



Cytoplasmic Staining

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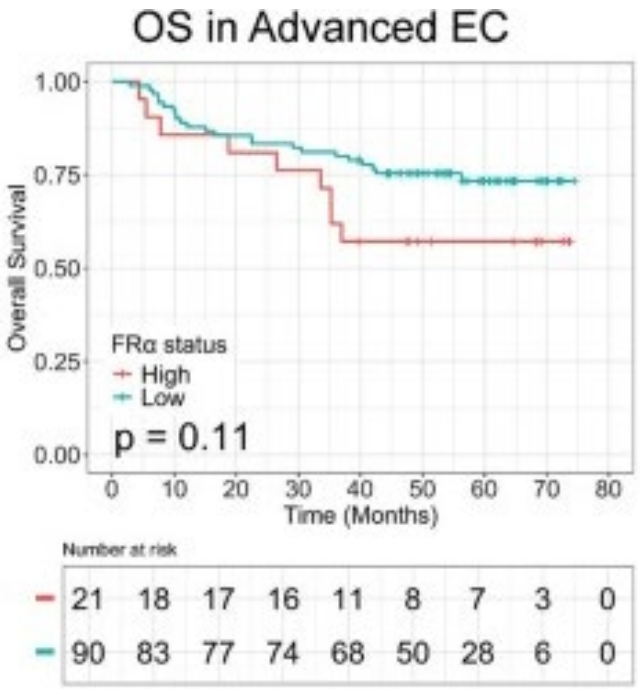
Moore KN et al. ESMO. 2019; Oaknin A et al. ASCO 2023; Chen YL, et al. Mol Oncol 2012, Path slides courtesy of Anais Malpica, MD

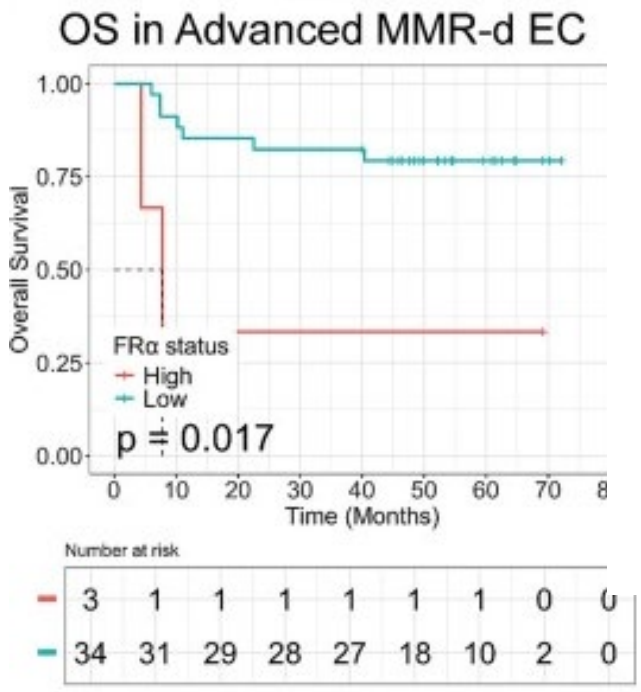
Irrelevant Findings

Relevance of FR α Expression in OC and EC

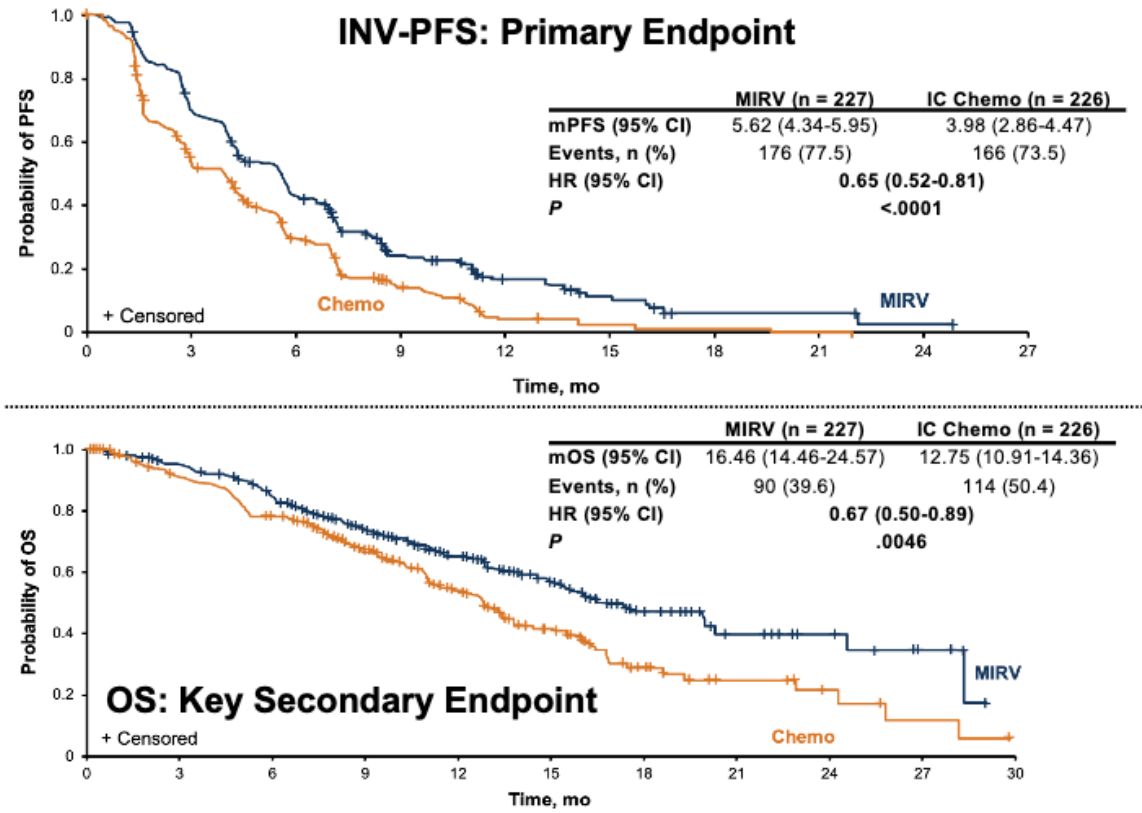
FRα protein over-expression

- Total expression - 80-90% of ovarian carcinomas
  - ~ 35-40% with high expression
- Total expression - 60% of endometrial cancers
  - ~20% with high expression
- FRα expression associated with worse outcomes





MIRASOL – Mirv vs ICC in FOLR1 high

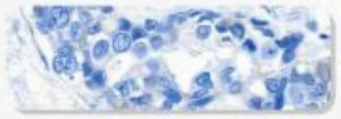
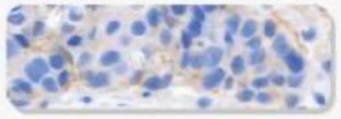


Moore, KN et al. N Eng J Med 2023; Konecny GE et al. Presented at SGO, Xiao Gyn Onc 2025;

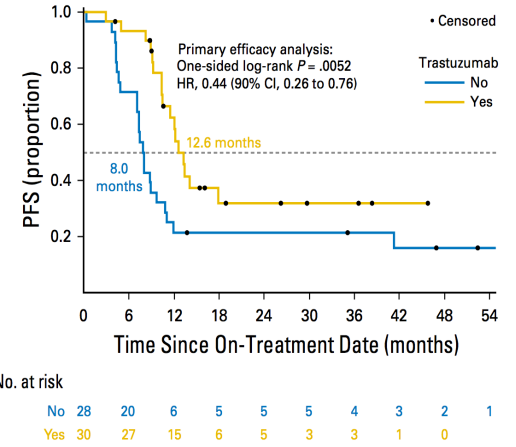
HER2 Testing in Ovarian and Endometrial Cancer

HER2 Gastric Scoring

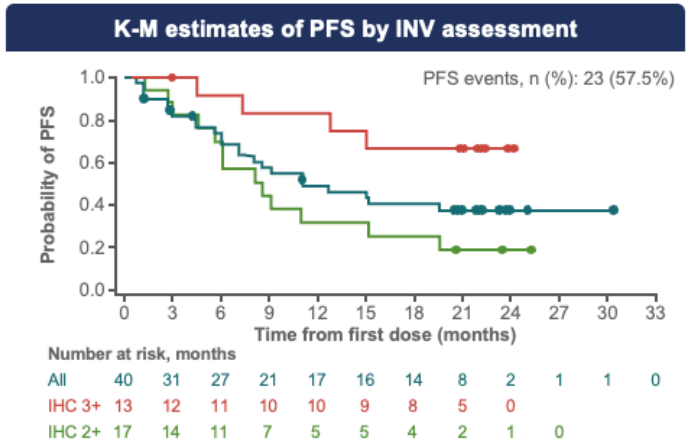
Spectrum of HER2 positivity according to ASCO/CAP guidelines

	IHC score	HER2 test intepretation	HER2 status
	0	No staining or incomplete and faint/barely perceptible membrane staning n ≤10% of tumor cells	Negative
	1+	Incomplete and faint/barely perceptible membrane staining in >10% of tumor cells	Low NO
	2+	Weak-moderate complete membrane staining in >10% of tumor cells OR intense membrane stainingi n ≤10% of tumor cells	ISH amplification? YES
	3+	Complete and intense membrane staining in >10% of tumor cells	Positive

Ivanova M et al. Virchows Arch. 2023, Nickles-Fader J Clin Oncol 2018, Lee et al IGCS 2023



HER2 3+ OR HER 2+/ISH+
Eligible for trastuzumab



HER2 3+ OR HER 2+
Eligible for trastuzumab deruxtecan

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HER2 Impact on Prognosis

High-Grade Serous and High-Grade Endometrioid

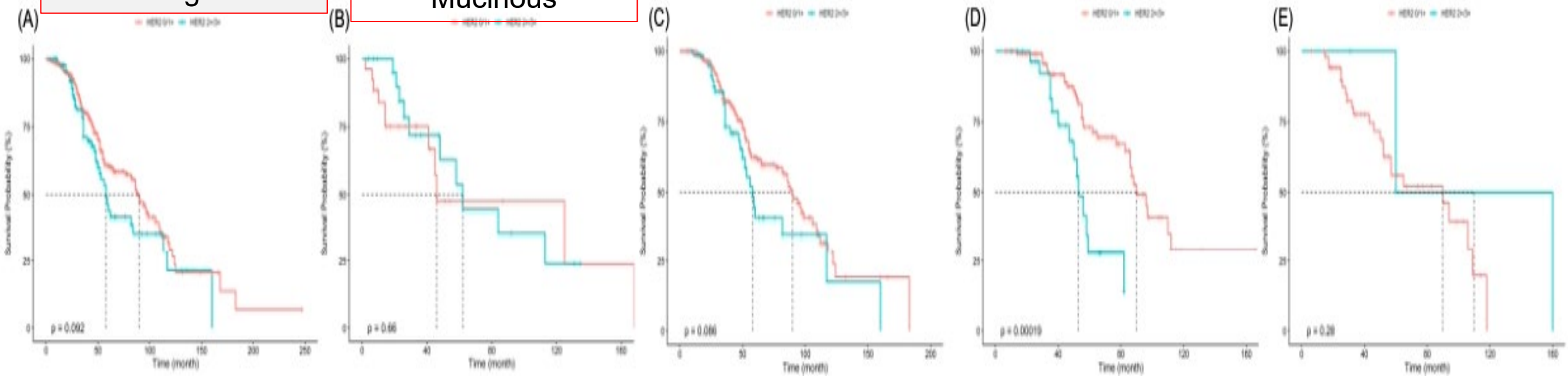
All Histologies

Clear Cell & Mucinous

All Patients

*BRCA*m/HRD status

HRP status



- High HER2 (2-3+) is associated with worse overall survival outcomes in patients with HGSOC and HGEOC characterized by *BRCA*m/HRD status
- Data supports targeting HER2 in patients with clear cell/mucinous, and *BRCA*m/HRD+ HGSOC/HGEOC

HER2 *2-3+*

HER2 *0-1+*

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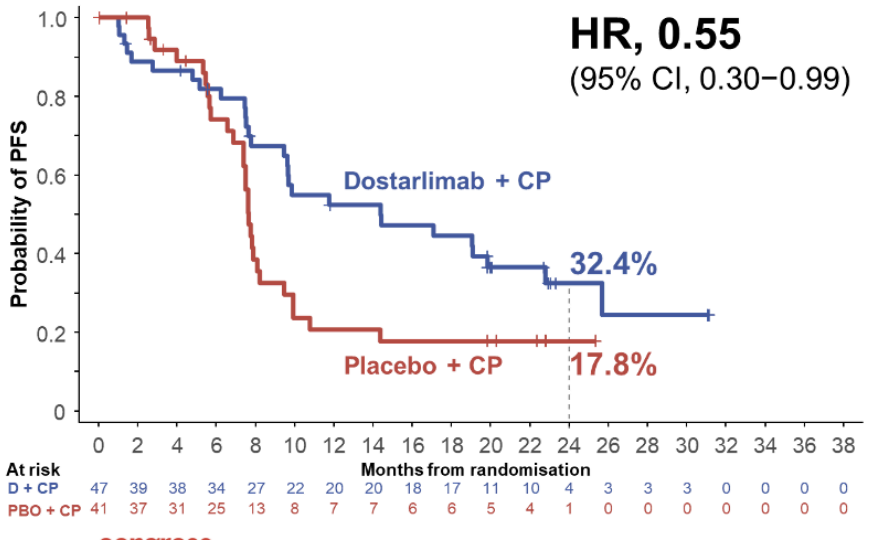
Lee D, ESMO Poster Presentation 2024

GOG PARTNERS

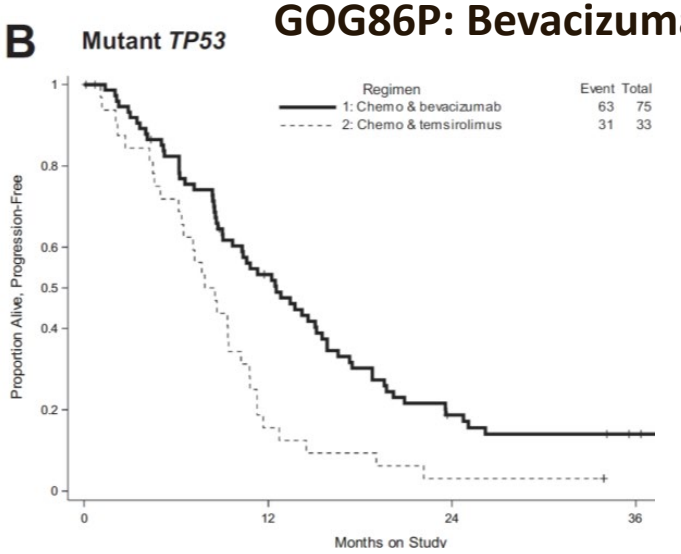
Painting a Picture Based on p53 Status: p53 mutant

TP53 mut

RUBY: Dostarlimab

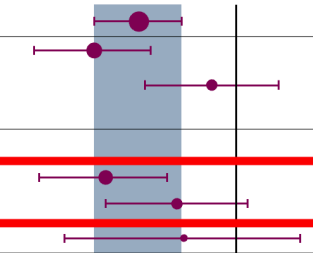


GOG86P: Bevacizumab



pMMR Subpopulation: PFS by Biomarker Subgroup
CP + Durvalumab + Olaparib vs CP

		HR (95% CI)	CP+D+O n/N	CP n/N
All pMMR patients		**0.57 (0.44–0.73)**	108/191	148/192
PD-L1 expression*	Positive (TAP score ≥1%)	**0.44 (0.31–0.61)**	54/112	94/124
	Negative (TAP score <1%)	**0.87 (0.59–1.28)**	52/73	53/67
	Unknown	**NC (NC–NC)**‖	2/6	1/1
***POLE*m and *TP53*m status**†,‡	*POLE*m	**NC (NC–NC)**‖	1/5	0/1
	*TP53*m	**0.47 (0.32–0.67)**	52/89	73/90
	TP53 wild-type	**0.71 (0.47–1.07)**	41/72	54/71
	Unknown	**0.74 (0.37–1.45)**	14/25	21/30



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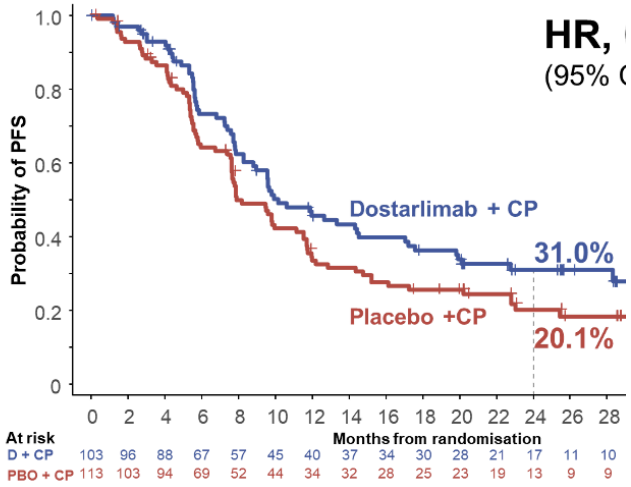
Mirza NEJM 2023, Mirza ESMO 2023
Westin IGCS 2024, Moore SGO 2025

Aghajanian Gynecol Oncol 2018

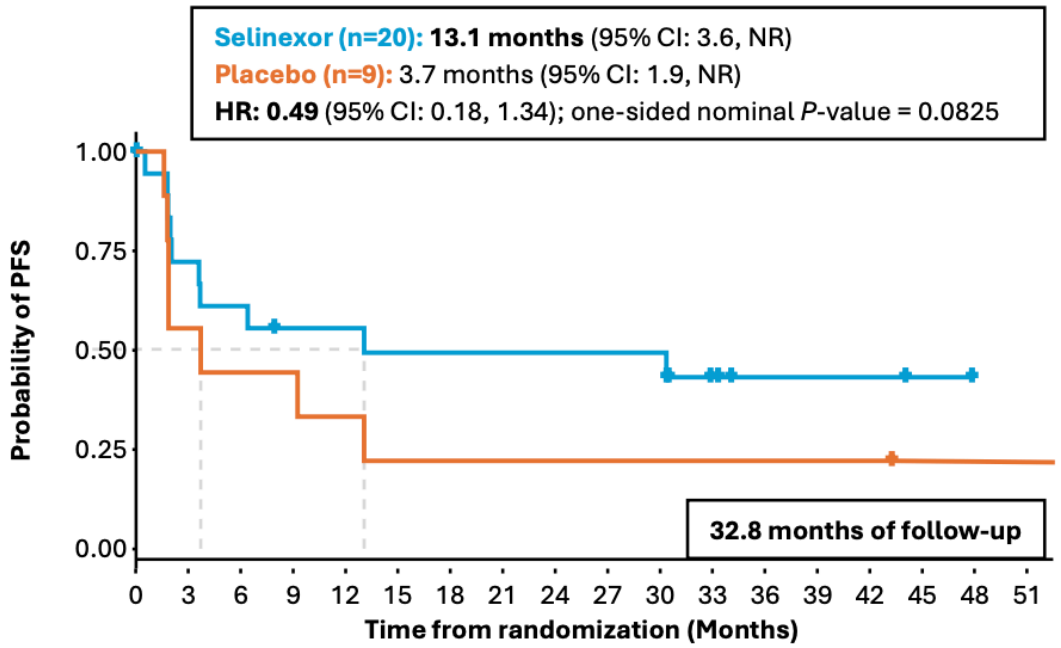
GOG PARTNERS

Painting a Picture Based on p53 Status: p53 wildtype

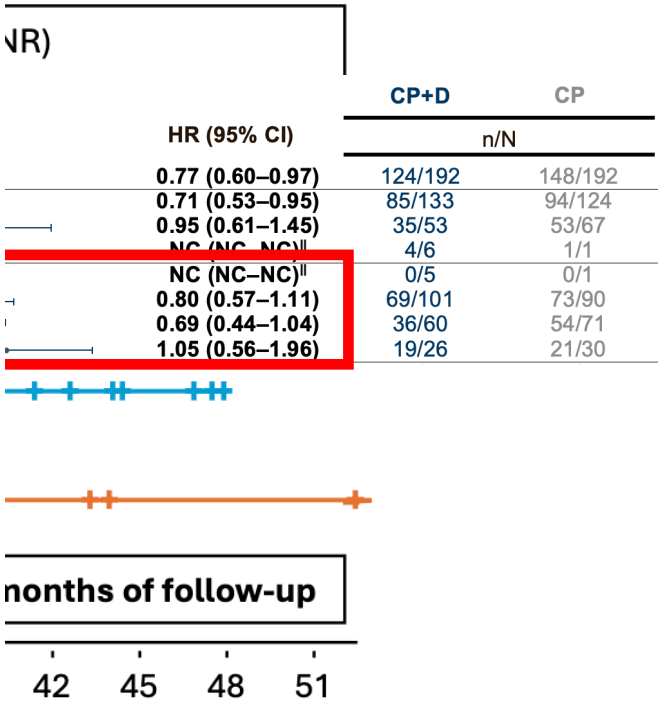
RUBY: Dostarlimab



*TP53*wt/dMMR



rker Subgroup

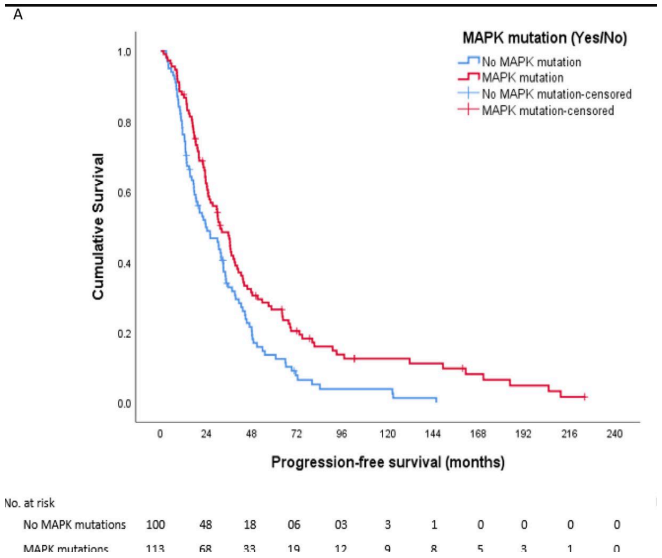


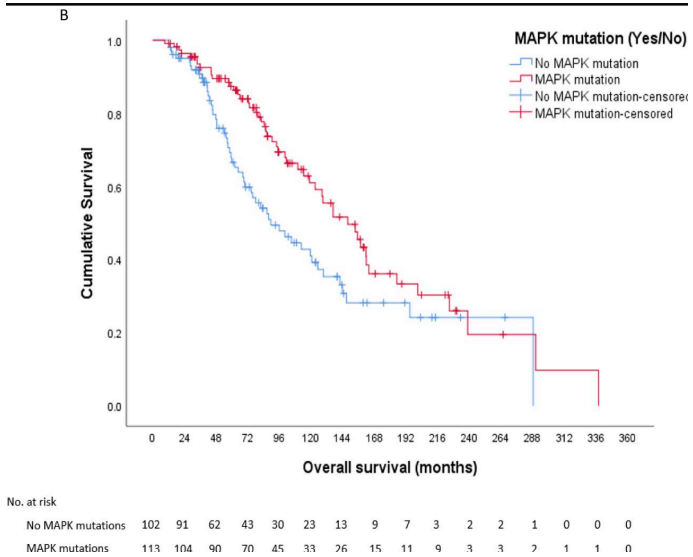
Mirza NEJM 2023, Mirza ESMO 2023
Westin IGCS 2024, Moore SGO 2025

Vergote ESMO 2022, Richardson SGO 2025

KRAS mutation in LGSOC

PROGNOSTIC

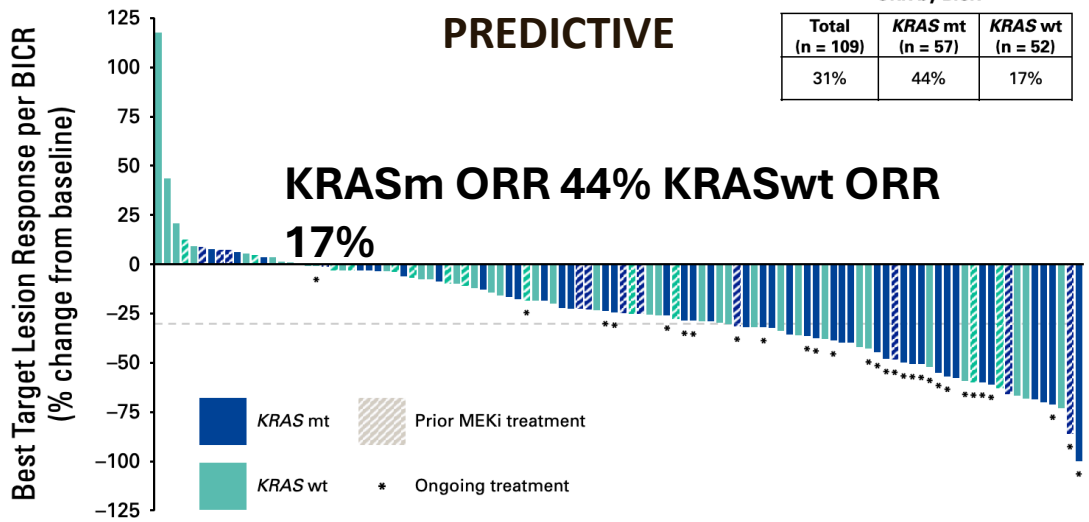


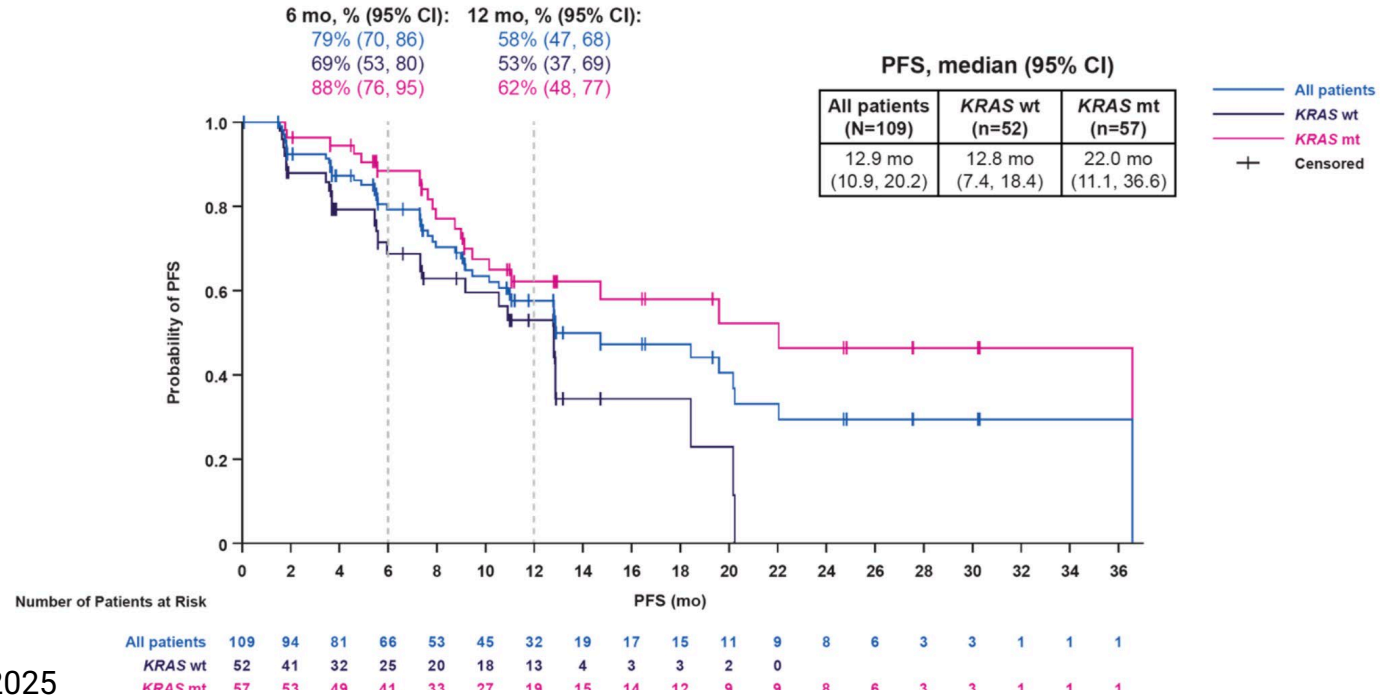


PREDICTIVE

ORR by BICR

Total (n = 109)	*KRAS* mt (n = 57)	*KRAS* wt (n = 52)
31%	44%	17%





Cobb Gyn Onc 2022, Banerjee JCO 2025, Banerjee SGO 2025

Practical Advice – What Do I Do in Clinic Tomorrow?

- Ovarian Cancer
- Genetic Testing – PANEL
- HRD/GIS Testing
- NGS
- IHC
  - FOLR1
  - HER2

- Endometrial Cancer
- IHC
  - MMR proteins
    - MLH1 hypermethylation if needed
  - HER2
  - ER, PR, p53
- NGS (if able)
  - POLE, p53

Timing: Ideally at diagnosis BUT definitely at recurrence

Final Thoughts

- Biomarker-directed therapy is here to stay in ovarian and endometrial cancer
- Further refinement and continued “splitting” is necessary to improve outcomes
- Unmet needs:
  - Are all molecular aberrations created equal?
  - Understand overlap of biomarkers and determination of sequencing/prioritization of therapies

Applying Evidence-Based Treatments in OC and EC

Scott Jordan, MD
Broward Health Medical Center
Fort Lauderdale, Florida, USA

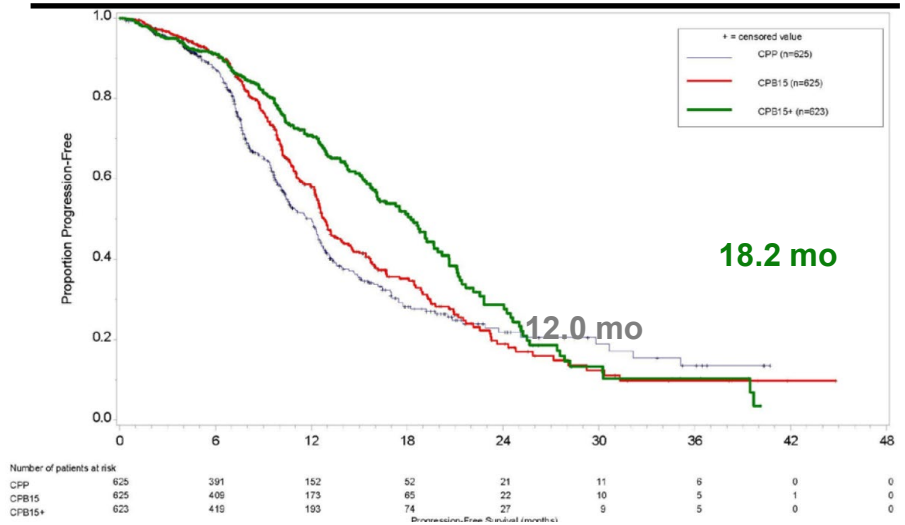
Biomarkers in Ovarian cancer

- BRCA
- HRD
- FOLR alpha
- HER2
- PD-L1
- Other

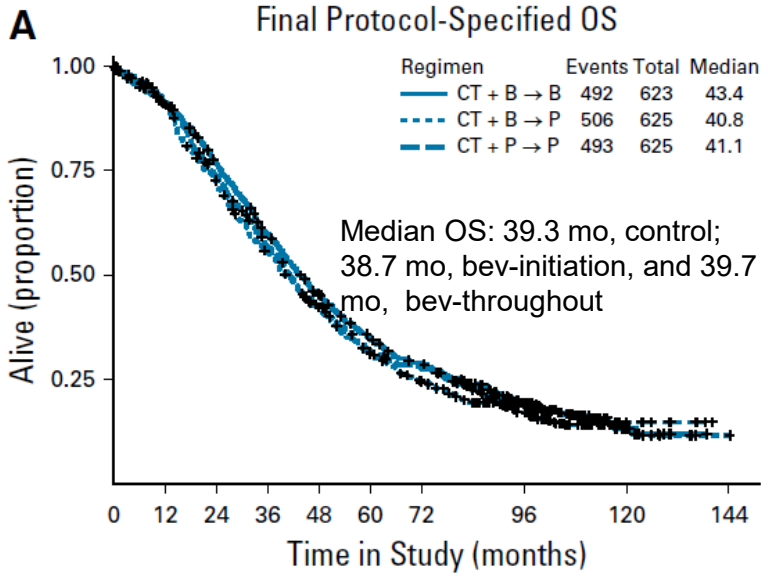
Phase 3 GOG-218 Study of Adjuvant Chemotherapy + Bevacizumab: Efficacy Outcomes

PFS (Primary Endpoint)

	Bev Throughout (CPB15+)	Bev Initiation (CPB15)	Control (CPP)
mPFS (mo)	18.2	12.8	12.0
HR (95% CI) P-value	0.62 (0.52, 0.75) < 0.0001	0.83 (0.70, 0.98) NS	



Final OS (103 month follow up)

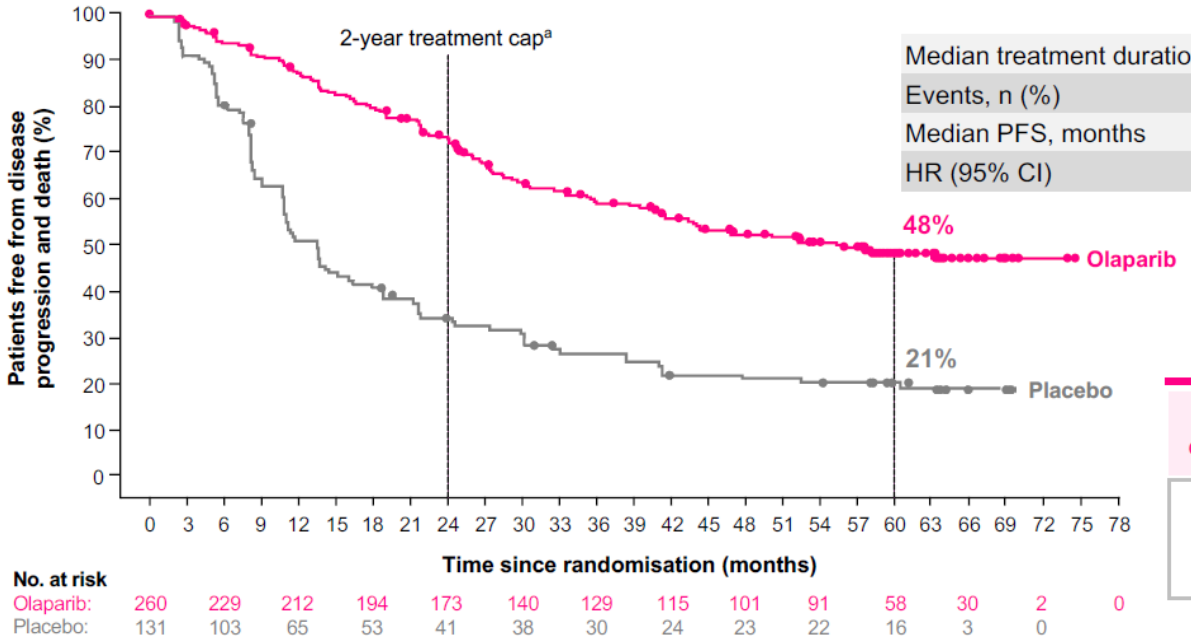


No survival differences observed with addition of bevacizumab compared with CT alone

Burger RA et al N Engl J Med. 2011 Dec 29;365(26):2473-83.
Tewari KS et al J Clin Oncol. 2019 Sep 10;37(26):2317-2328.

SOLO 1

- BRCA mutated advanced high grade serous or endometrioid ovarian ca
- Olaparib vs placebo maintenance



	Olaparib (n=260)	Placebo (n=131)
Median treatment duration, months	24.6	13.9
Events, n (%)	118 (45)	100 (76)
Median PFS, months	56.0	13.8
HR (95% CI)	0.33 (0.25, 0.43)	

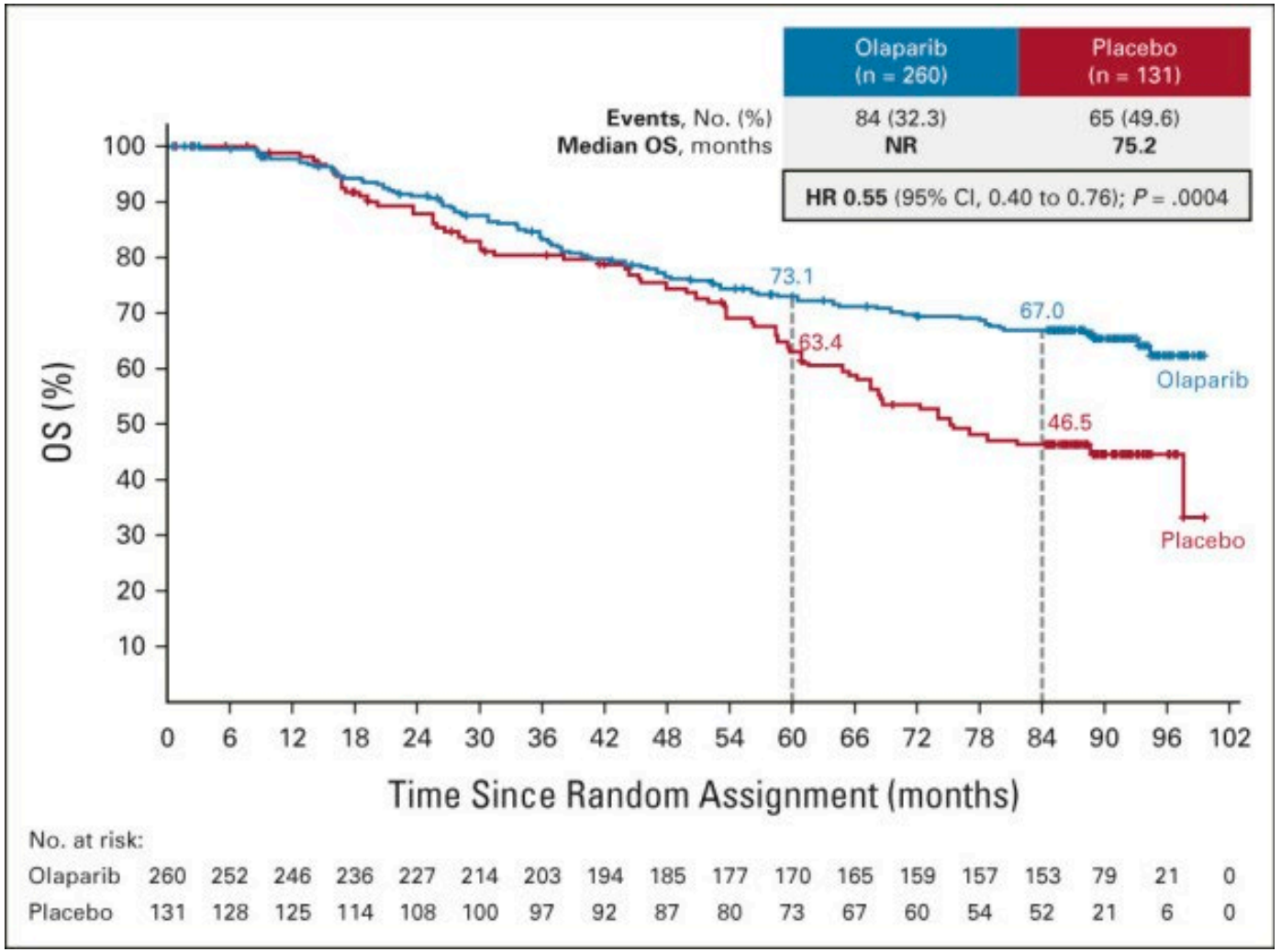
Median PFS difference for olaparib vs placebo: 42.2 months

Median follow-up for PFS:

Olaparib	Placebo
4.8 years	5.0 years

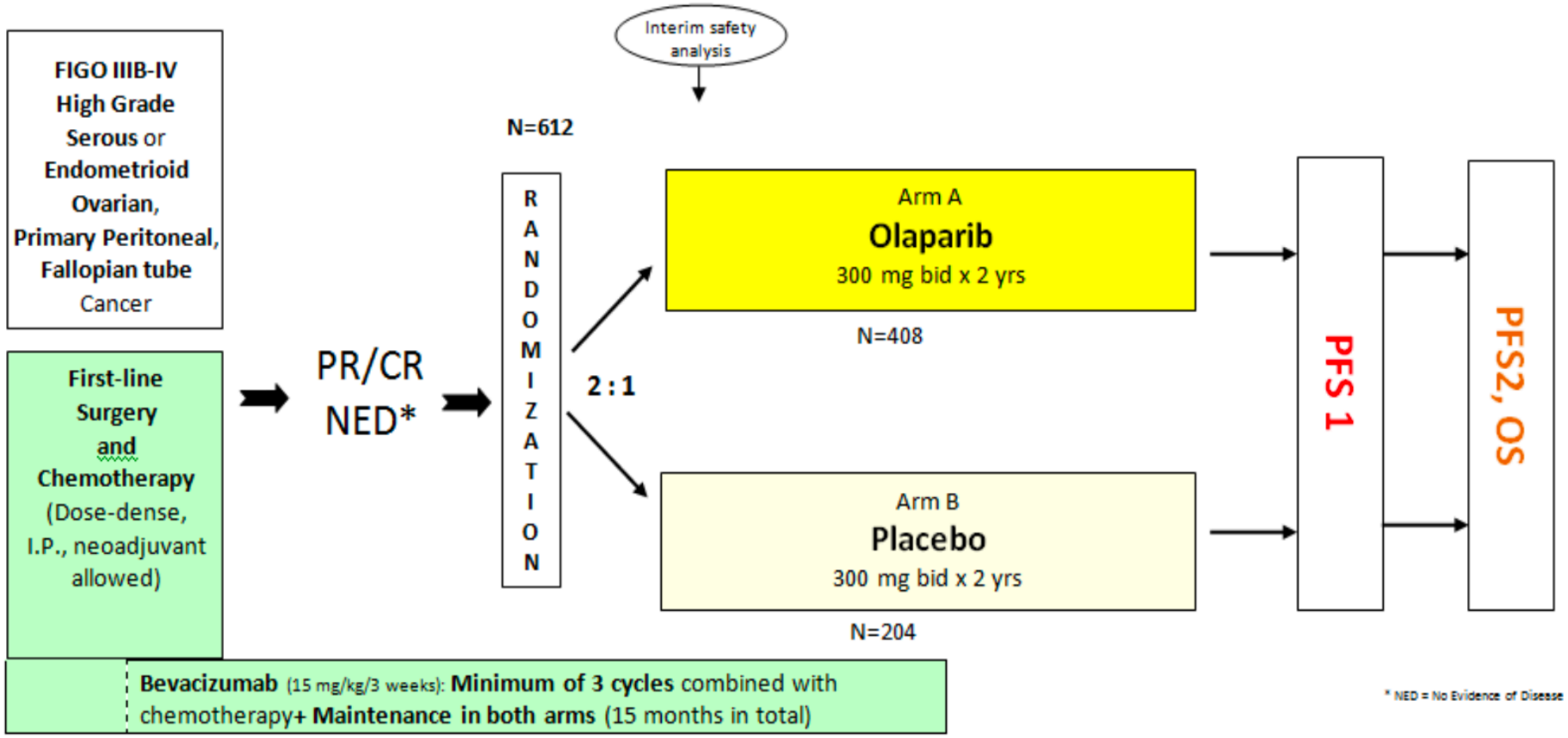
Lancet Oncol. 2021 Dec;22(12):1721-1731

SOLO 1 OS at 7 years



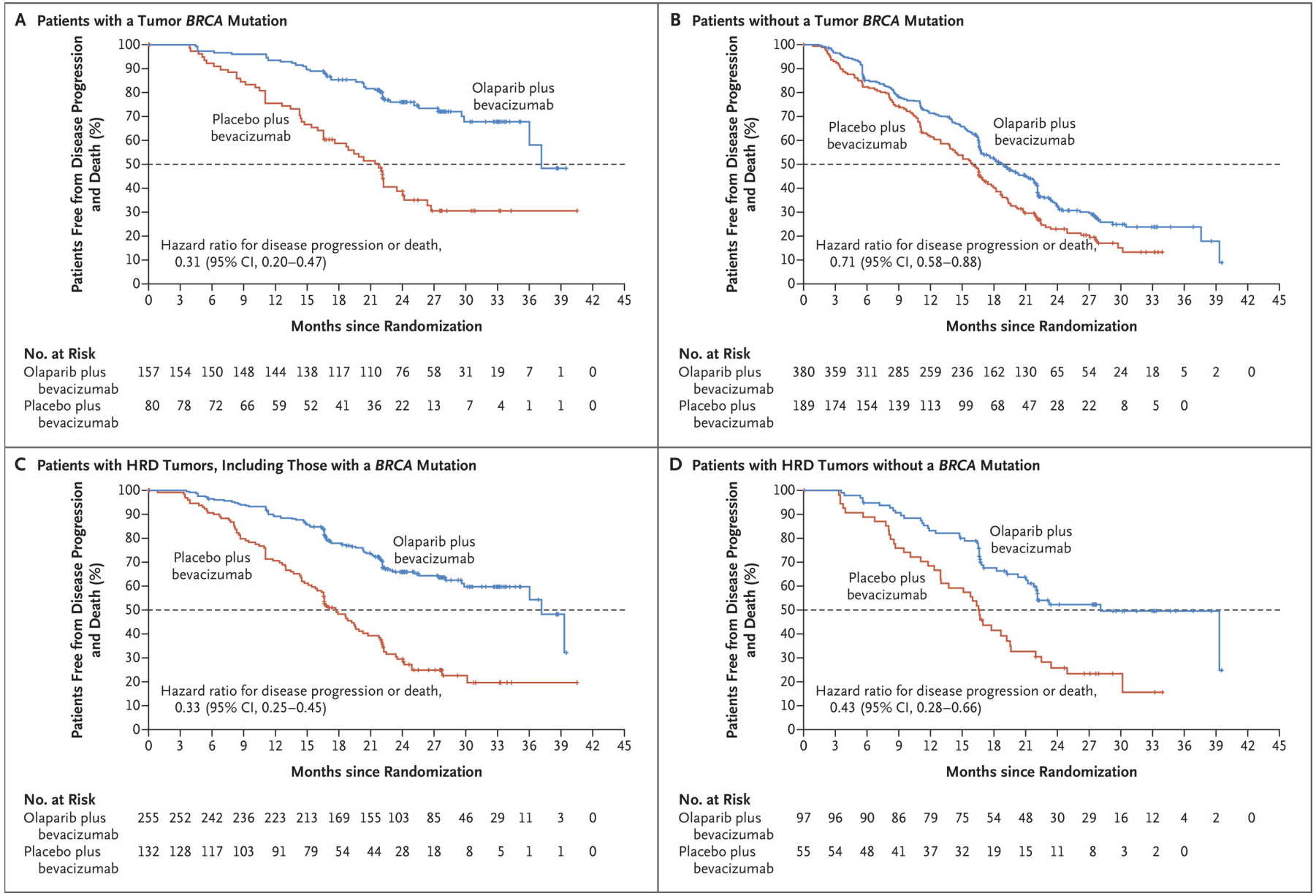
PAOLA 1

- Advanced high grade serous or endometrioid ovarian ca
- Stratified by
- BRCA status and response to 1L



N Engl J Med 2019;381:2416-2428

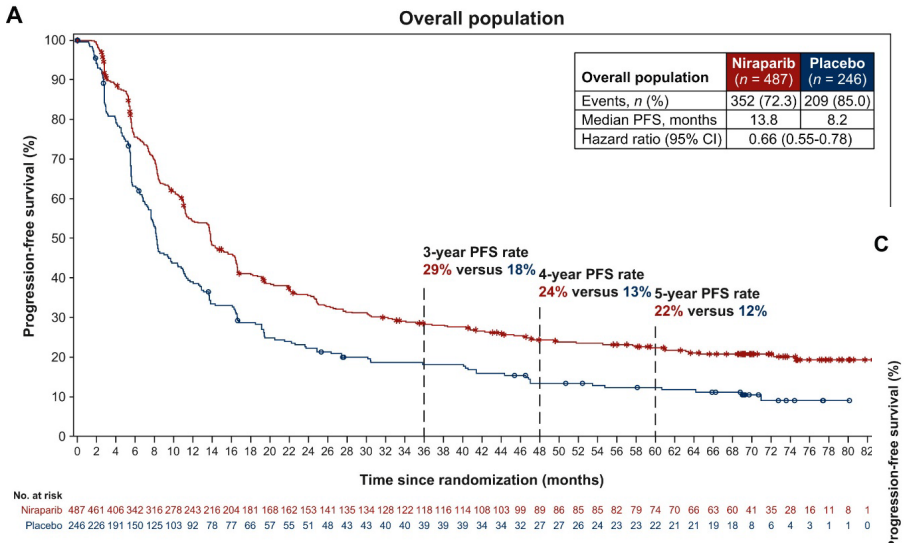
PAOLA 1

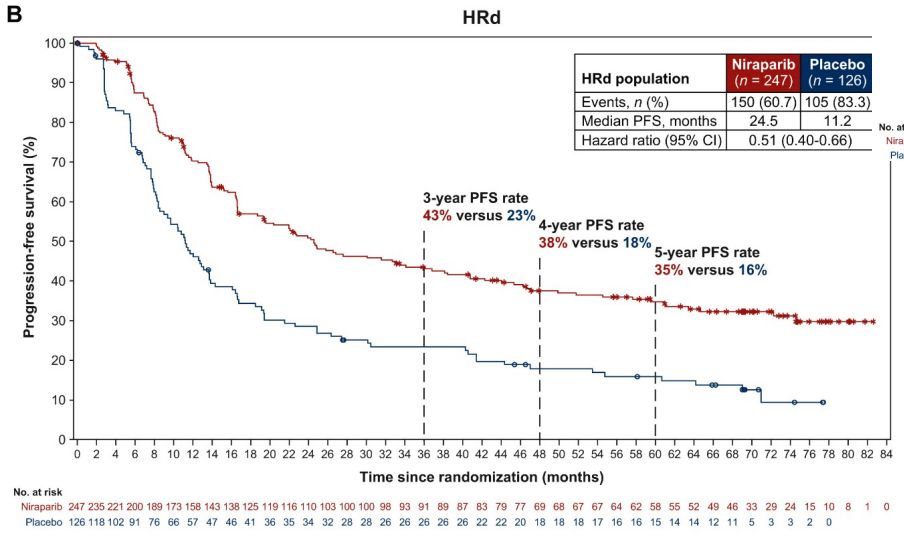


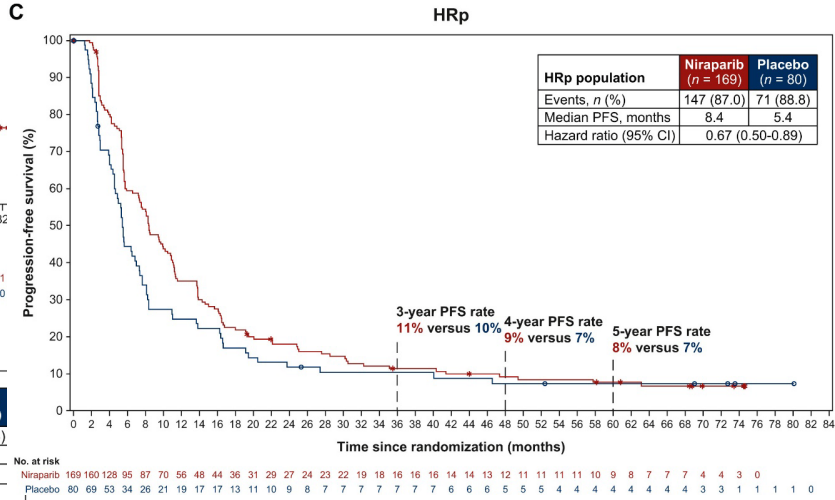
N Engl J Med 2019;381:2416-2428

PRIMA

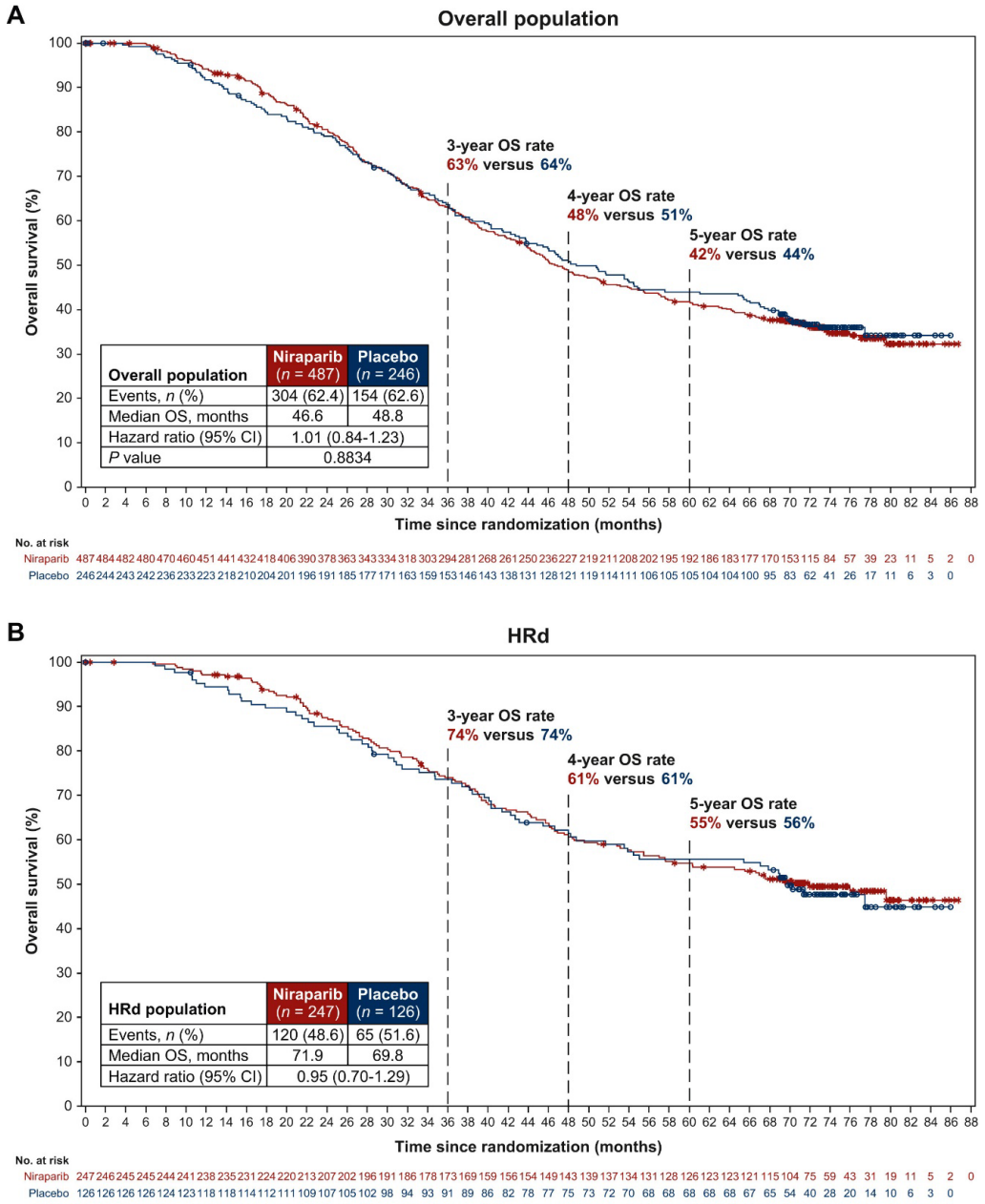
- BRCA mutated advanced high grade serous or endometrioid ovarian ca
- Stratified by response, NACT, and HRD status
- Niraparib vs placebo maintenance







PRIMA OS



Annals of Oncology, Volume 35, Issue 11, 981 - 992

FR alpha- MIRASOL

MIRASOL (NCT04209855) – Study Design[1,2]

An open-label, phase 3 randomized trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high platinum-resistant ovarian cancer

Patient Population
(N=453)

Enrollment and Key Eligibility
Platinum-resistant disease
(PFI ≤6 mo)

FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells

High-grade serous histology

1º platinum-refractory disease excluded (primary PFI <3 mo)

1-3 prior lines of therapy

Prior BEV and PARPi allowed

Patients with BRCA mutations allowed

1:1 Randomization

Treatment Regimen-Experimental

MIRV
(6 mg/kg AIBW Q3W)

Treatment Regimen-Control

Investigator's Choice Chemotherapy
(Paclitaxel, PLD, or Topotecan)

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

Primary Endpoint
PFS by INV
(BICR sensitivity analysis)

Key Secondary Endpoints
1) ORR by INV
2) OS
3) PROs[a]

Secondary Endpoints
Safety and tolerability
DOR
CA-125 response[b]
PFS2

AIBW, adjusted ideal body weight; BEV; bevacizumab; BICR, blinded independent central review; BRCA, BReast CAncer gene; CA-125, cancer antigen 125; chemo, chemotherapy; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PFI, platinum-free interval; PFS, progression-free survival; PFS2, time from randomization until second disease progression; PLD, pegylated liposomal doxorubicin; PROs, patient-reported outcomes; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.

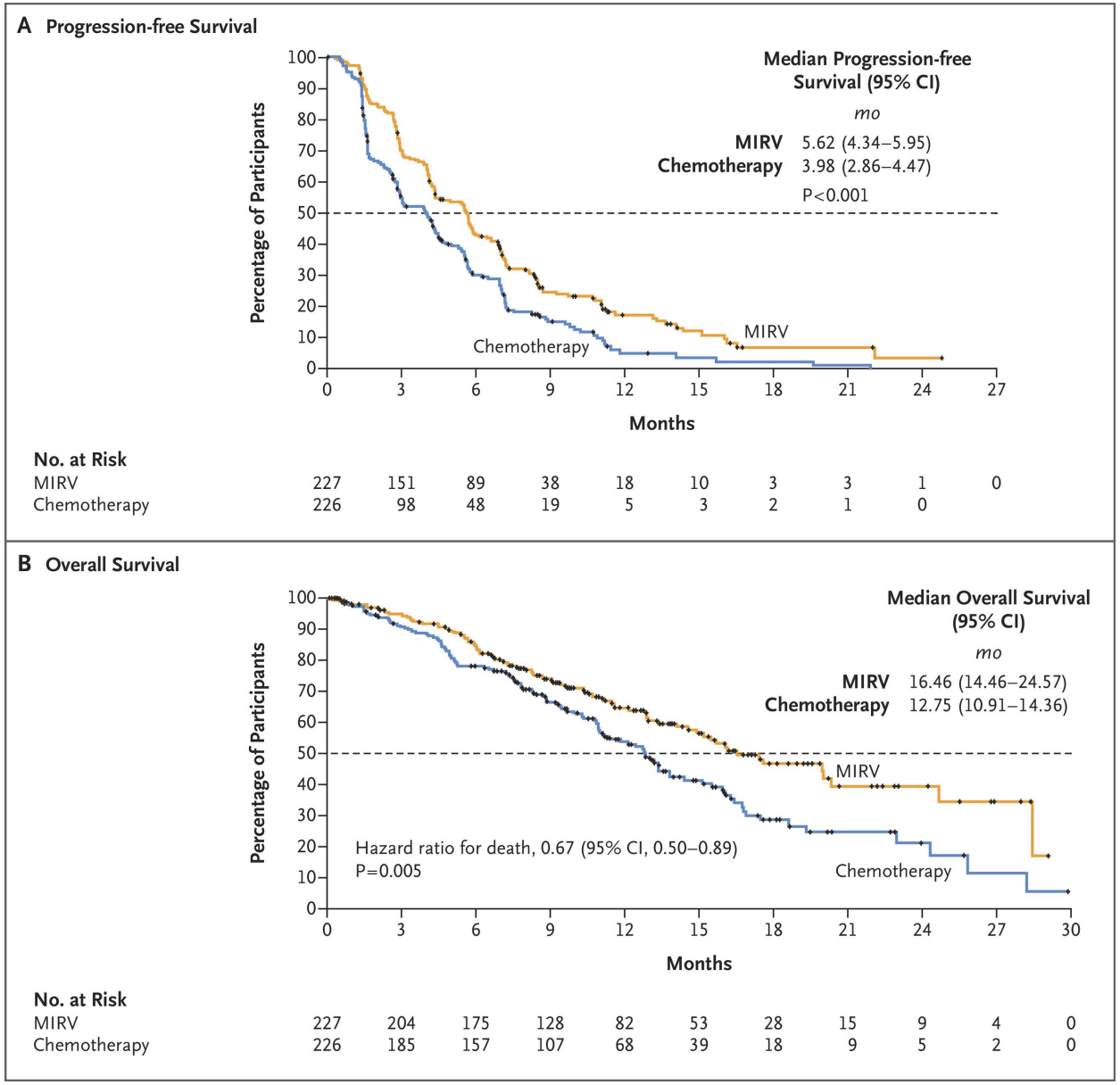
[a]PROs will be measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, 28-item Ovarian Cancer Module (OV28) study instrument.

[b]Gynecological Cancer InterGroup (GCIG) criteria.

1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855

2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting; May 29-31, 2020; Virtual. Abstract TPS6103.

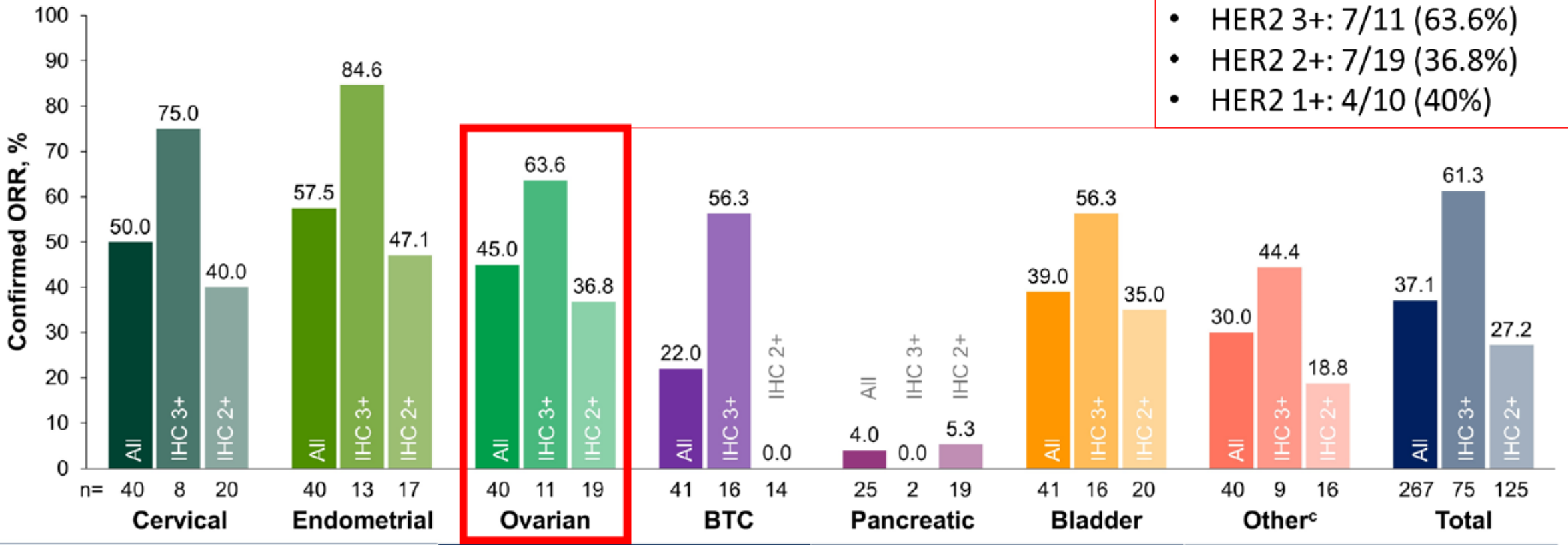
MIRASOL



N Engl J Med 2023;389:2162-2174

Objective Response Rate by HER2 status

Ovarian – 18 responders
- HER2 3+: 7/11 (63.6%)
- HER2 2+: 7/19 (36.8%)
- HER2 1+: 4/10 (40%)



	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

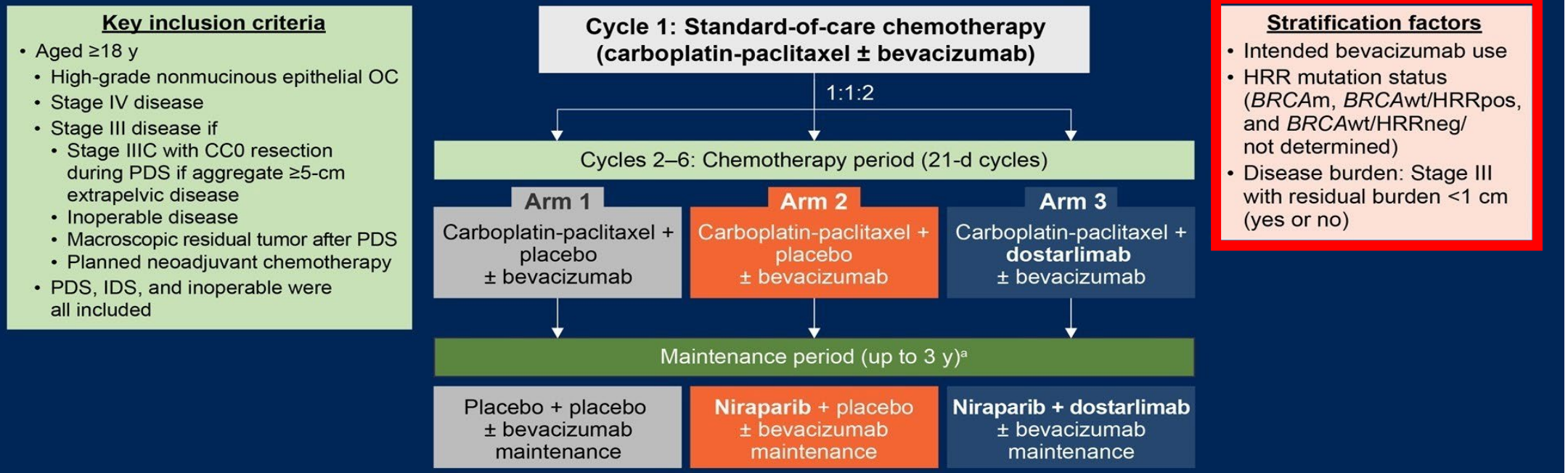
Analysis of ORR was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DOR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. [a]Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.
BTC, biliary tract cancer; CI, confidence interval; DOR, duration of response; IHC, immunohistochemistry; NE, non-estimable; ORR, objective response rate.

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; ERBB2, erb-b2 receptor tyrosine kinase 2; GYN, gynecologic; HER2, human epidermal growth factor receptor 2; OC, ovarian cancer; q3w, every 3 weeks.

1. Meric-Bernstam F et al. ASCO 2022. Abstract TPS623. 2. ClinicalTrials.gov. NCT04482309. Accessed March 1, 2023.

First Trial

FIRST Trial Design



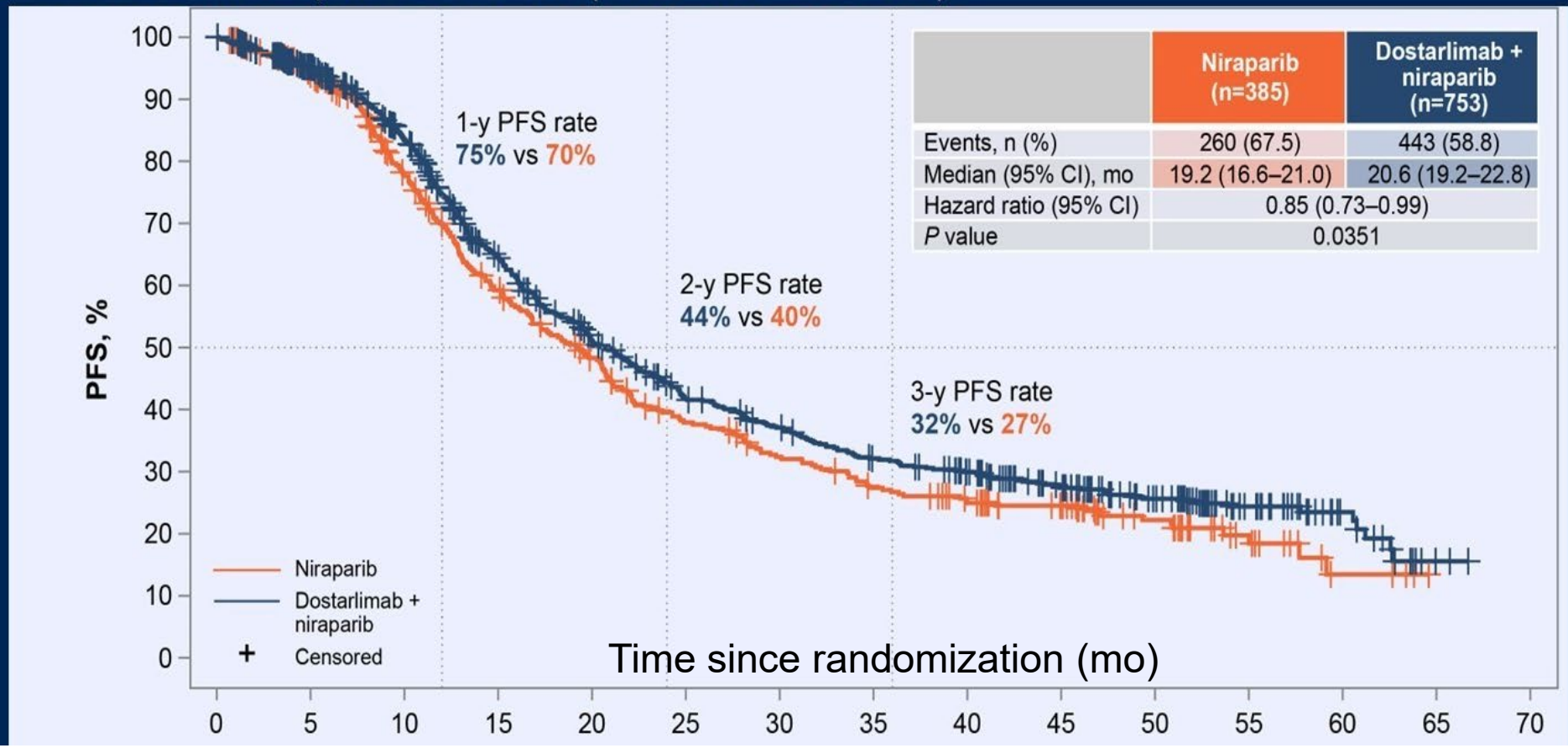
[a]May continue treatment beyond 3 years in consultation with the medical monitor. *BRCA*m, *BRCA*-mutated; *BRCA*wt, *BRCA* wild-type; CC0, complete resection; HRR, homologous recombination repair; IDS, interval debulking surgery; neg, negative; OC, ovarian cancer; PDS, primary debulking surgery; pos, positive.

Hardy-Bessard AC, et al. Ann Oncol. 2025 May 30:S0923-7534(25)00201-7.
https://pubmed.ncbi.nlm.nih.gov/40461381/

First Trial

PFS per RECIST v1.1 in the ITT Population

Median duration of follow-up was 53.1 mo (IQR, 47.5–59.7 mo).



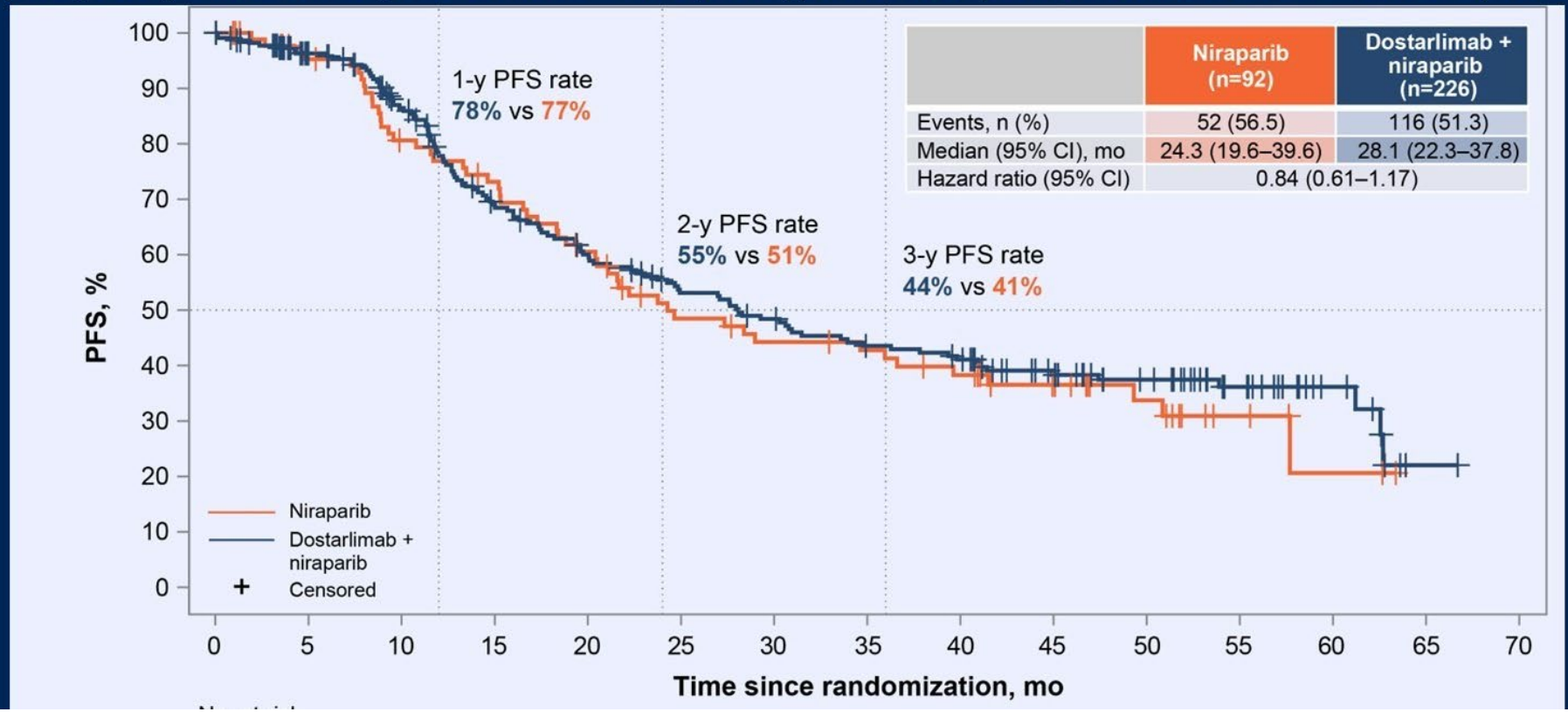
	Niraparib (n=385)	Dostarlimab + niraparib (n=753)
Events, n (%)	260 (67.5)	443 (58.8)
Median (95% CI), mo	19.2 (16.6–21.0)	20.6 (19.2–22.8)
Hazard ratio (95% CI)	0.85 (0.73–0.99)	
P value	0.0351	

Hardy-Bessard AC, et al. Ann Oncol. 2025 May 30:S0923-7534(25)00201-7.
https://pubmed.ncbi.nlm.nih.gov/40461381/

First Trial

PFS per RECIST v1.1 in the PD-L1+ Population

In arm 2 (niraparib) and arm 3 (dostarlimab + niraparib), 27.9% of patients had PD-L1+ tumors (TAP ≥5%).

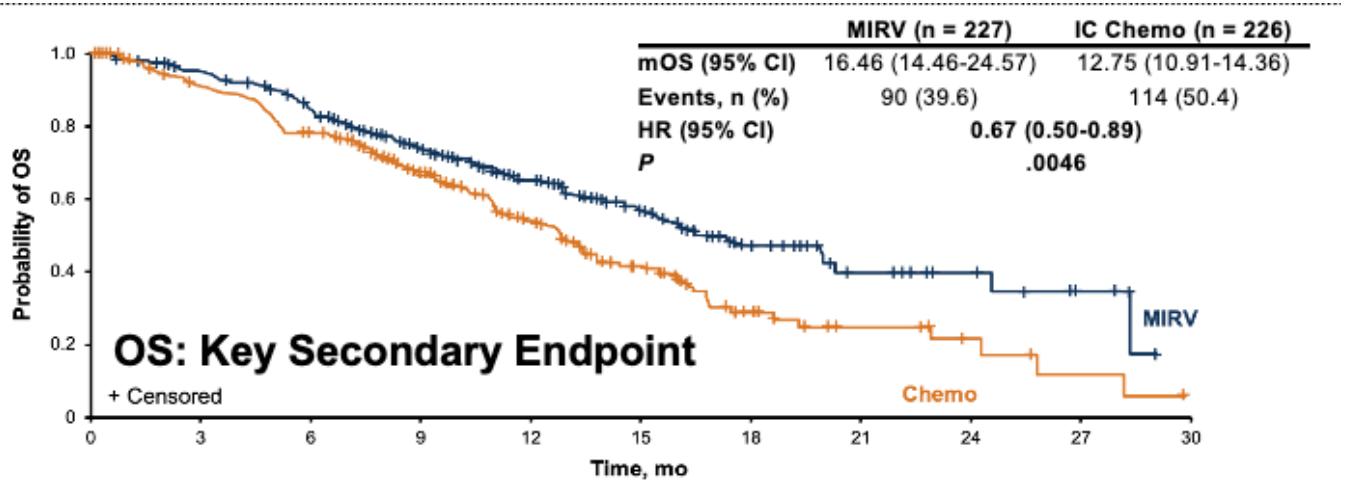


	Niraparib (n=92)	Dostarlimab + niraparib (n=226)
Events, n (%)	52 (56.5)	116 (51.3)
Median (95% CI), mo	24.3 (19.6–39.6)	28.1 (22.3–37.8)
Hazard ratio (95% CI)	0.84 (0.61–1.17)	

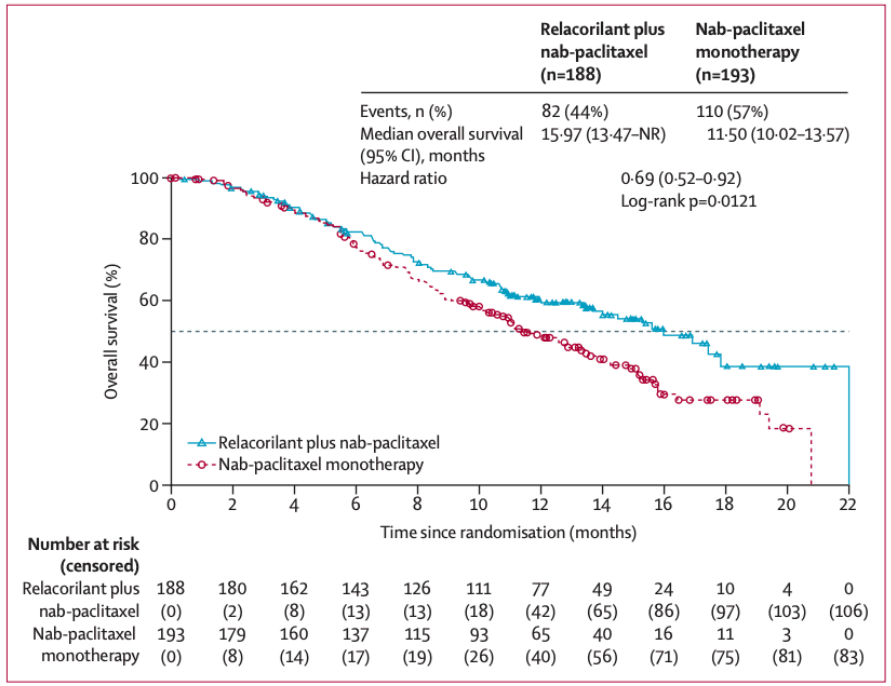
Hardy-Bessard AC, et al. Ann Oncol. 2025 May 30:S0923-7534(25)00201-7.
https://pubmed.ncbi.nlm.nih.gov/40461381/

PROC Current Landscape: Survival is QUEEN!

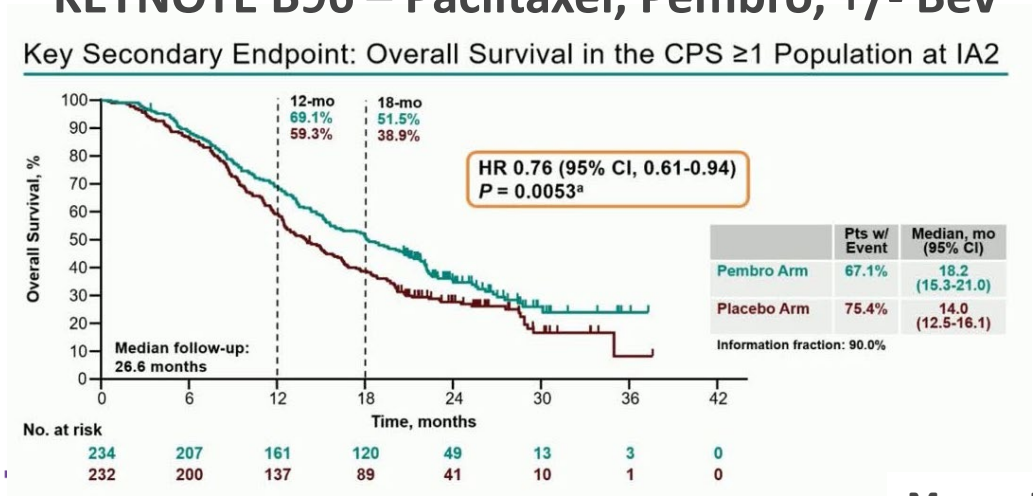
MIRASOL – Mirv vs ICC in FOLR1 high



ROSELLA – relacorilant + nab paclitaxel



KEYNOTE B96 – Paclitaxel, Pembro, +/- Bev



DOR/PFS values mean that we are often looking for new therapies within the year

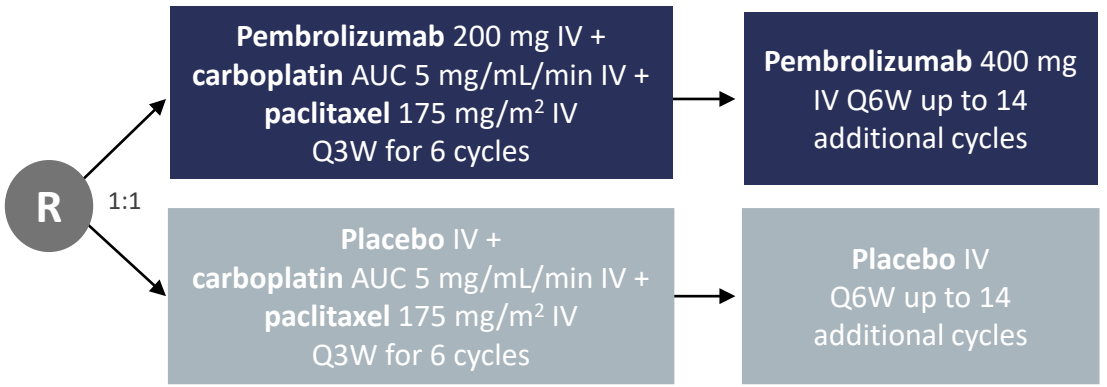
Moore, NEJM 2023; Olawaiye Lancet 2025, Colombo ESMO 2025

Biomarkers in Endometrial Cancer

- MMR/MSI
- HER2
- P53
- ER/PR
- POLE

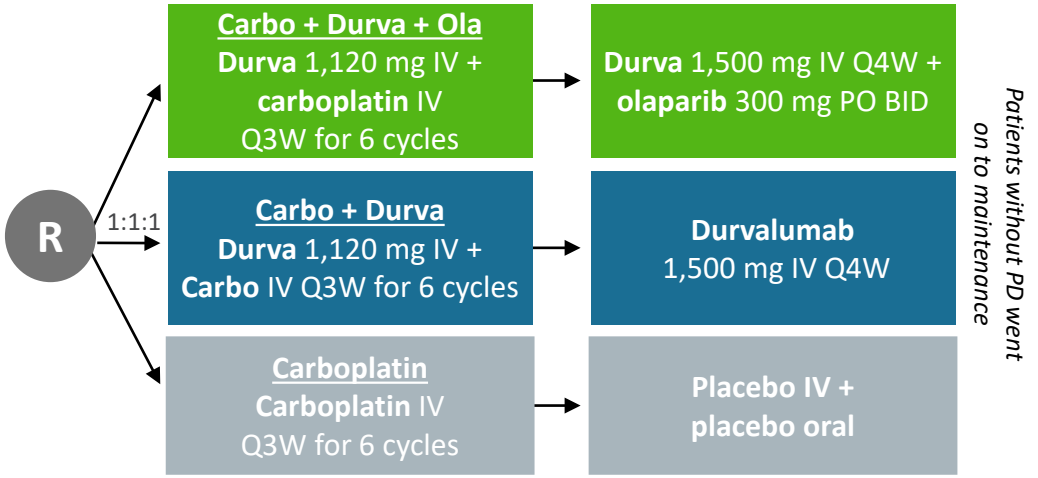
Transformative Clinical Trials in the Advanced Stage and Recurrent Setting

NRG GY018



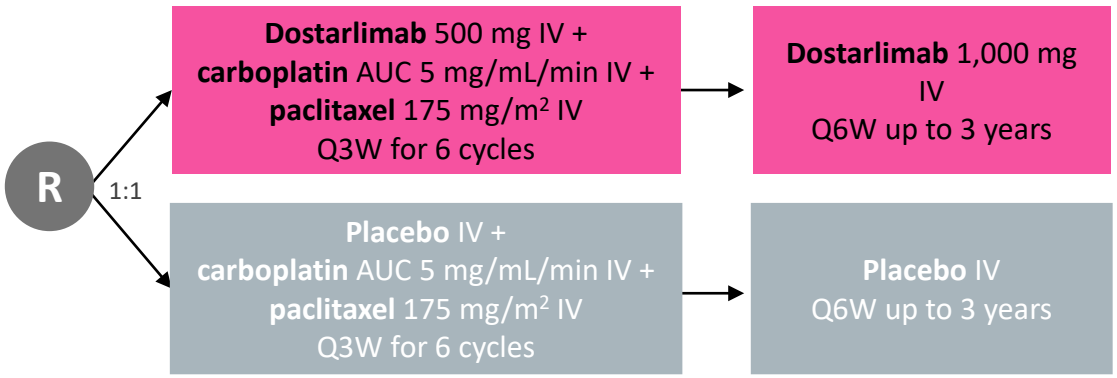
Stratified by MMR status (pMMR vs dMMR), ECOG status, and prior adjuvant chemo

DUO-E/GOG 3041



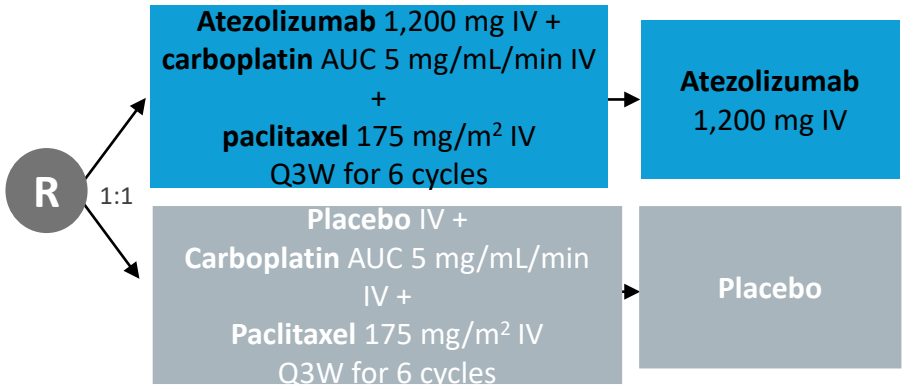
Stratified by MMR status, disease status, region of world

GOG 3031/RUBY



Stratified by MMR/MSI status, prior external pelvic radiotherapy, and disease status

AtTEnd



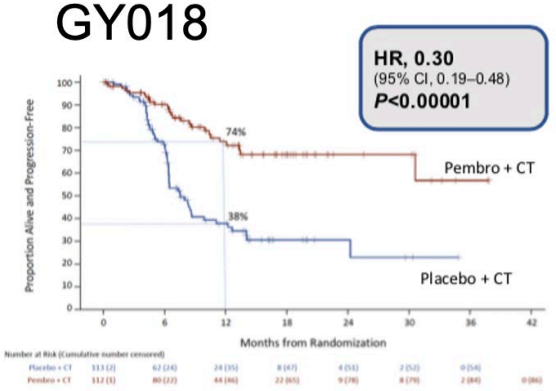
Stratified by MMR status, disease status, region of world, histology

BID, twice a day; Carbo, carboplatin; Durva, durvalumab; Ola, Olaparib; PO, orally.

Eskander RN, et al. N Engl J Med. 2023;388:2159-2170; Mirza MR, et al. N Engl J Med. 2023;388:2145-2158; Westin SN, et al. J Clin Oncol. 2024;42:283-299; Colombo N, et al. Ann Oncol. 2023;34(suppl 2):S1281-S1282.

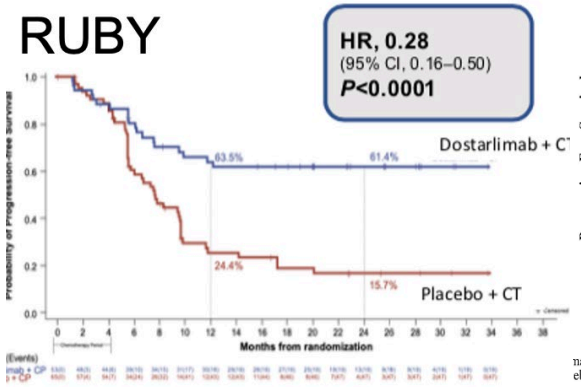
Benefit of IO + Chemo in the dMMR EC population

GY018



	No with events%	Median
Pembro + CT	23.2	NR (30.6-NR)
Placebo + CT	52.2	7.6 (6.4-9.9)

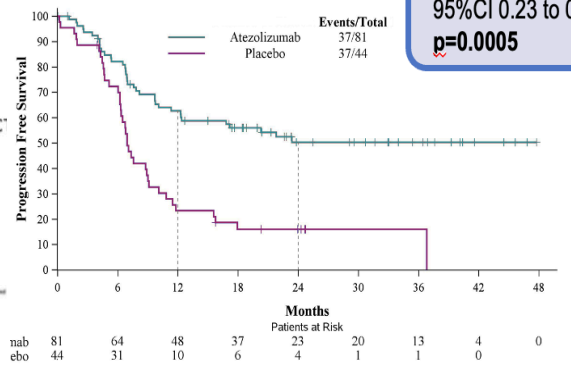
RUBY



	No with events%	Median
Dorsta + CT	35.8	NR (11.8-NR)
Placebo + CT	72.3	7.7 (5.6-9.7)

AtTEnd

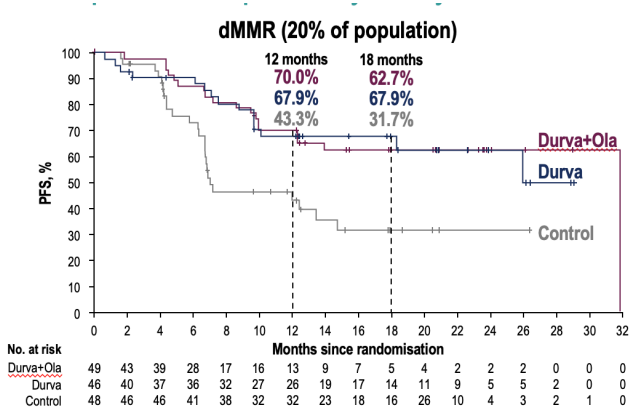
HR 0.36
95%CI 0.23 to 0.57
p=0.0005



	No with events%	Median
Atezo + CT	45.7	NR (12.3-NR)
Placebo + CT	84.1	6.9 (6.2-9.0)

DUO-E

HR 0.42
95% CI 0.22-0.80
D + CT arm

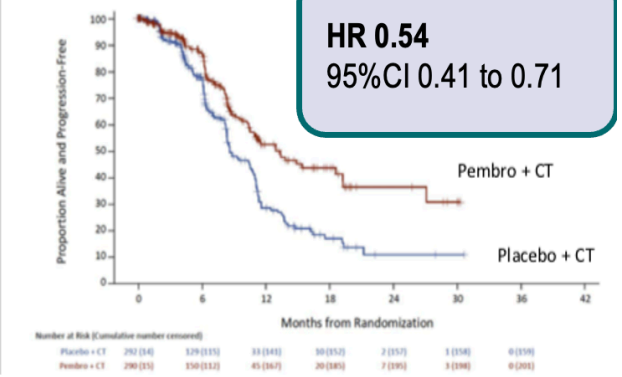


	No with events %	Median
Durva + CT	32.6	NR (NR-NR)
Durva + O + CT	37.5	31.8 (12.4-NR)
Placebo + CT	51	7.0 (6.7-14.8)

Slide courtesy of Dr. David Tan ESMO 2023 - Revised

Benefit of IO + Chemo in the pMMR EC population

GY018

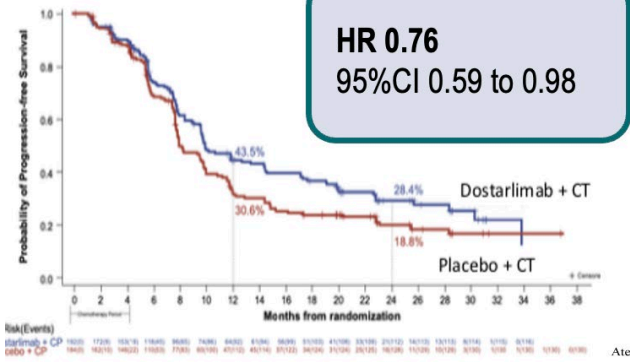


HR 0.54
95%CI 0.41 to 0.71

	No with events%	Median
Pembro + CT	30.6	13.1 (10.5-18.8)
Placebo + CT	45.5	8.7 (8.4-10.7)
Maturity	38.1%	

Only trial with prespecified alpha allocated analysis in pMMR EC cohort as primary endpoint

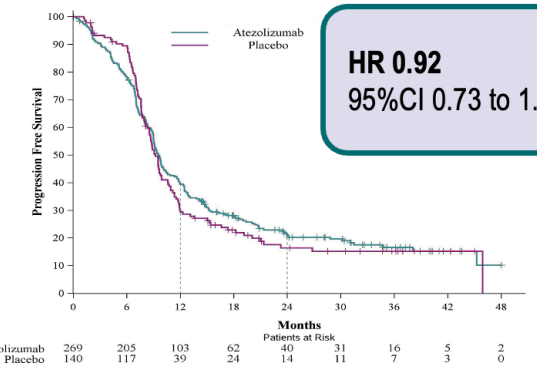
RUBY



HR 0.76
95%CI 0.59 to 0.98

	No with events%	Median
Dorsta + CT	60.4	9.9 (9.0-13.3)
Placebo + CT	70.7	7.9 (7.6-9.8)
Maturity	65.4%	

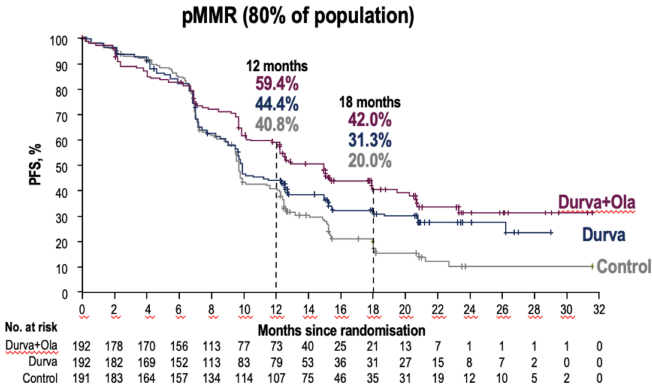
AtTEnd



HR 0.92
95%CI 0.73 to 1.16

	No with events%	Median
Atezo + CT	78	9.5 (9.0-10.4)
Placebo + CT	77	9.2 (8.5-9.9)
Maturity	78%	

DUO-E

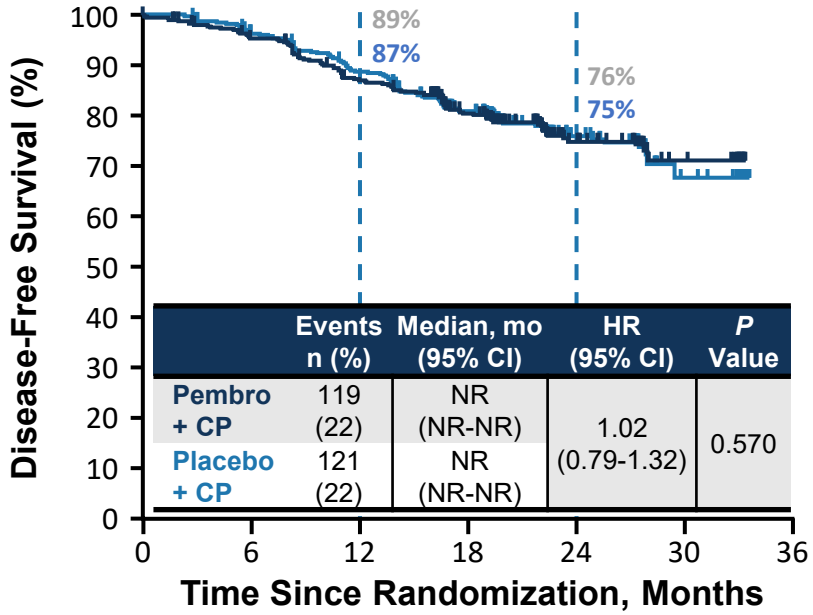


HR 0.57
95% CI 0.44-0.73
D + O + CT arm

	No with events %	Median
Durva + CT	64.6	9.9 (9.4-12.5)
Durva + O + CT	56.5	15 (12.4-18)
Placebo + CT	77.1	9.7 (9.2-10.1)

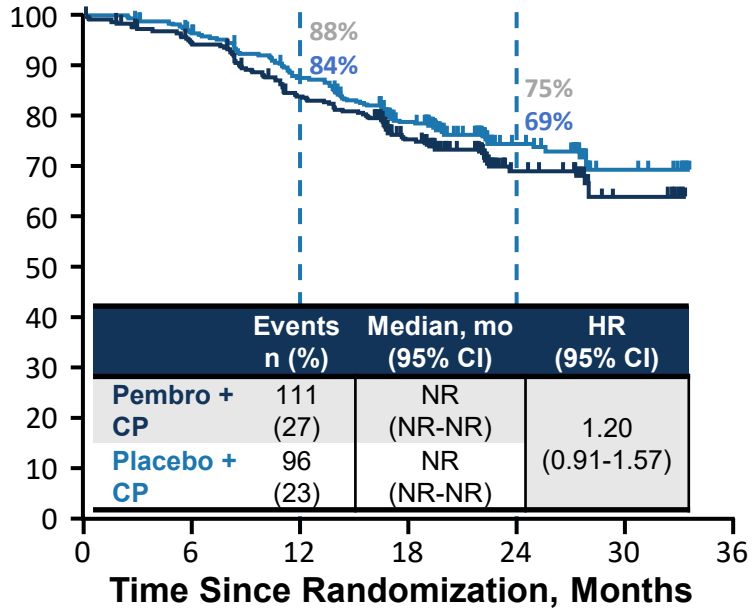
ENGOT-en11/GOG-3053/KEYNOTE-B21: Pembrolizumab in the Adjuvant Setting for Newly Diagnosed, High-Risk EC

DFS in ITT



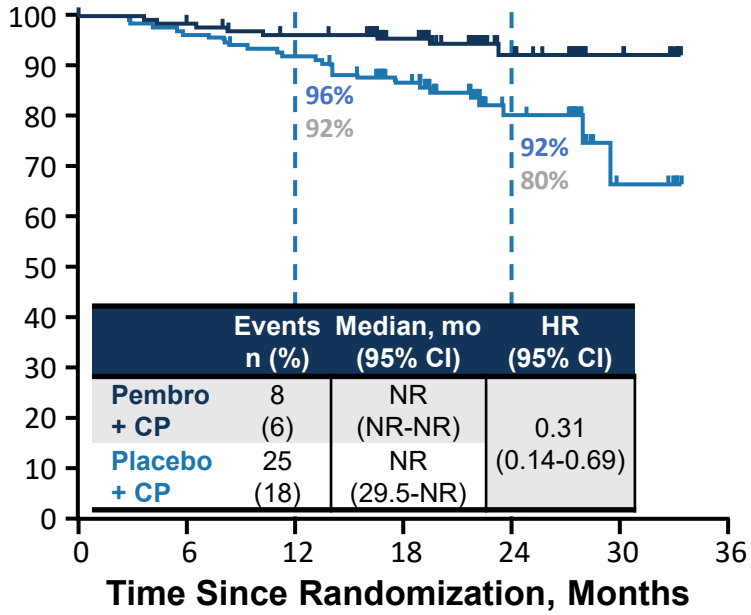
	Events n (%)	Median, mo (95% CI)	HR (95% CI)	*P* Value
Pembro + CP	119 (22)	NR (NR-NR)	1.02 (0.79-1.32)	0.570
Placebo + CP	121 (22)	NR (NR-NR)		

DFS in pMMR



	Events n (%)	Median, mo (95% CI)	HR (95% CI)
Pembro + CP	111 (27)	NR (NR-NR)	1.20 (0.91-1.57)
Placebo + CP	96 (23)	NR (NR-NR)	

DFS in dMMR



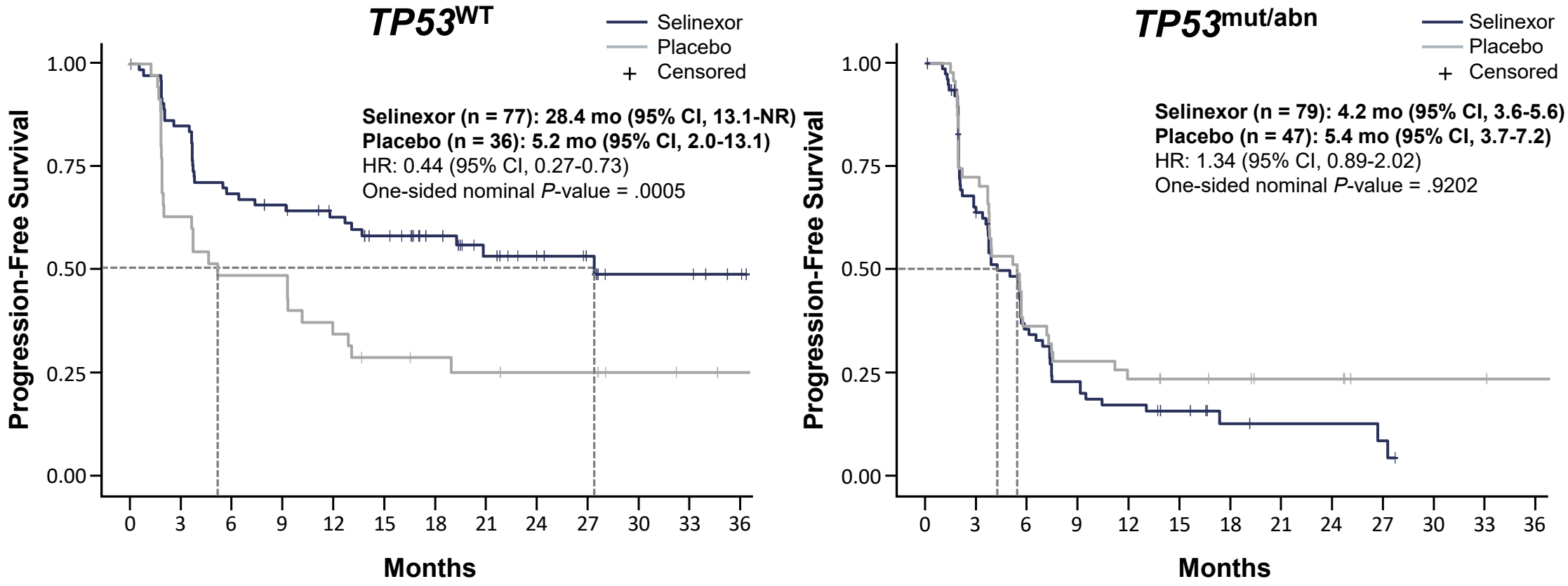
	Events n (%)	Median, mo (95% CI)	HR (95% CI)
Pembro + CP	8 (6)	NR (NR-NR)	0.31 (0.14-0.69)
Placebo + CP	25 (18)	NR (29.5-NR)	

Adjuvant pembrolizumab + chemotherapy did not improve DFS in the newly-diagnosed, high-risk, ITT population but did improve DFS in the dMMR subgroup. Safety profile was as expected and manageable.

DFS, disease-free survival.

Van Gorp T, et al. Presented at: 2024 ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abstract LBA28;
Van Gorp T, et al. Ann Oncol. 2024 Aug 19. [Epub ahead of print].

ENGOT-EN5/GOG-3055/SIENDO: Long-Term Follow-Up of PFS in Prespecified Exploratory *TP53*^{WT} and *TP53*$^{mut/abn}$ Subgroups

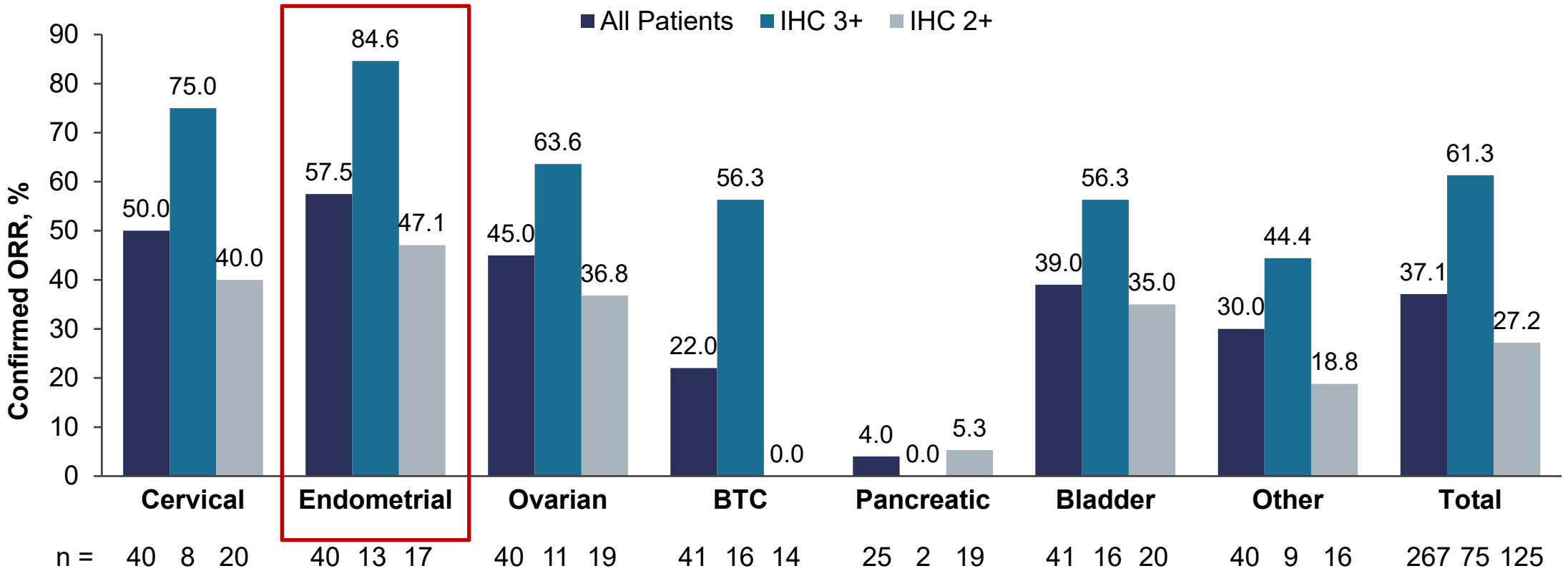


Median follow-up: 36.8 months

Median follow-up: 22.9 months

Makker V, et al. Gynecol Oncol. 2024;185:202-211; Slomovitz BM, et al. J Clin Oncol. 2023;41(suppl 36):427956.

DESTINY-PanTumor02: Response to Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors



	All Patients (N = 99)	IHC 3+ (n = 75)	IHC 2+ (n = 34)
Median DOR, mo (95% CI)	11.3 (9.6-17.8)	22.1 (9.6-NR)	9.8 (4.3-12.6)

BTC, biliary tract cancer.

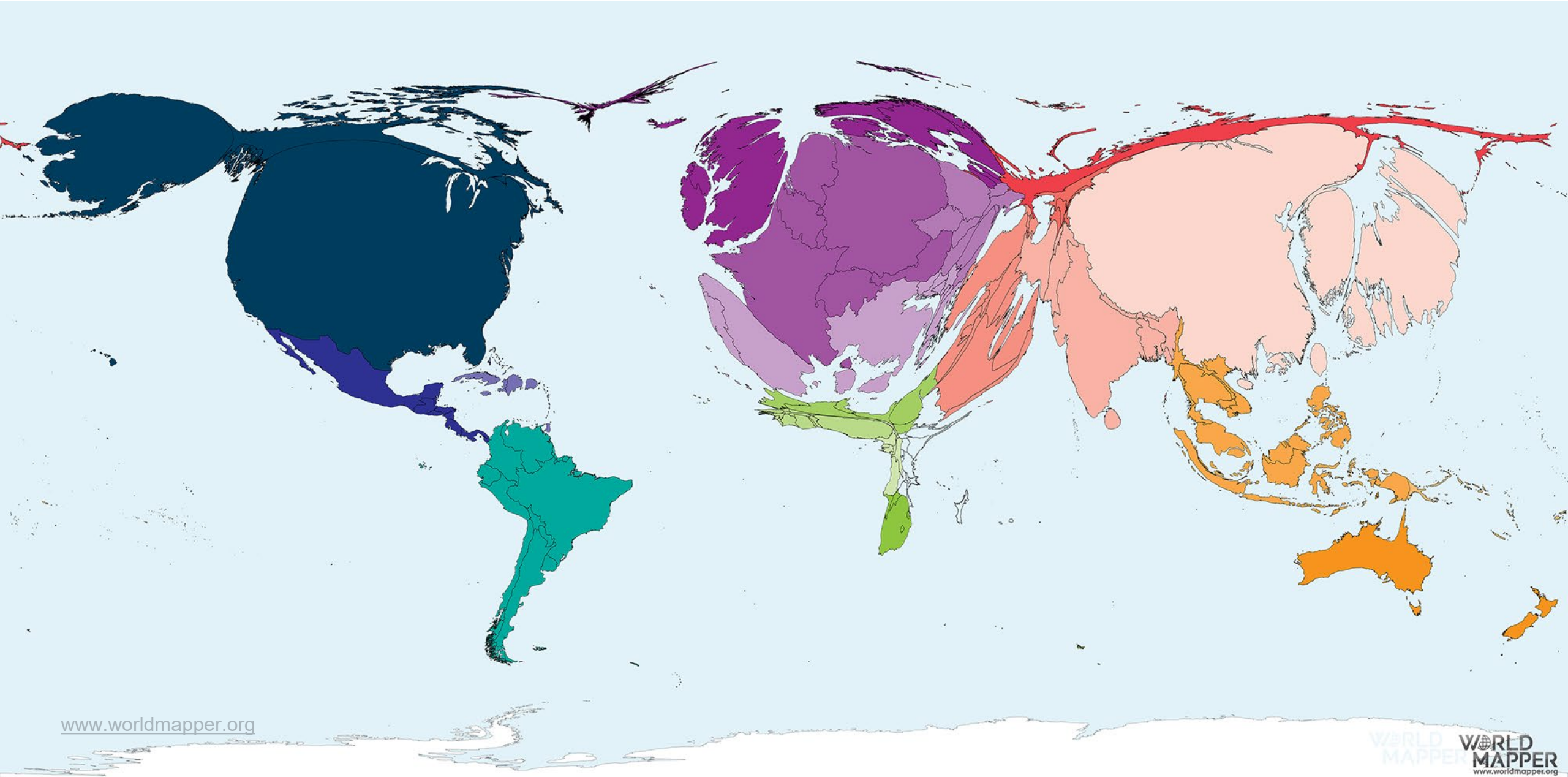
F, et al. J Clin Oncol. 2024;42:47-58.

Barriers to Access and Equitable Care Delivery

R. Wendel Naumann, MD

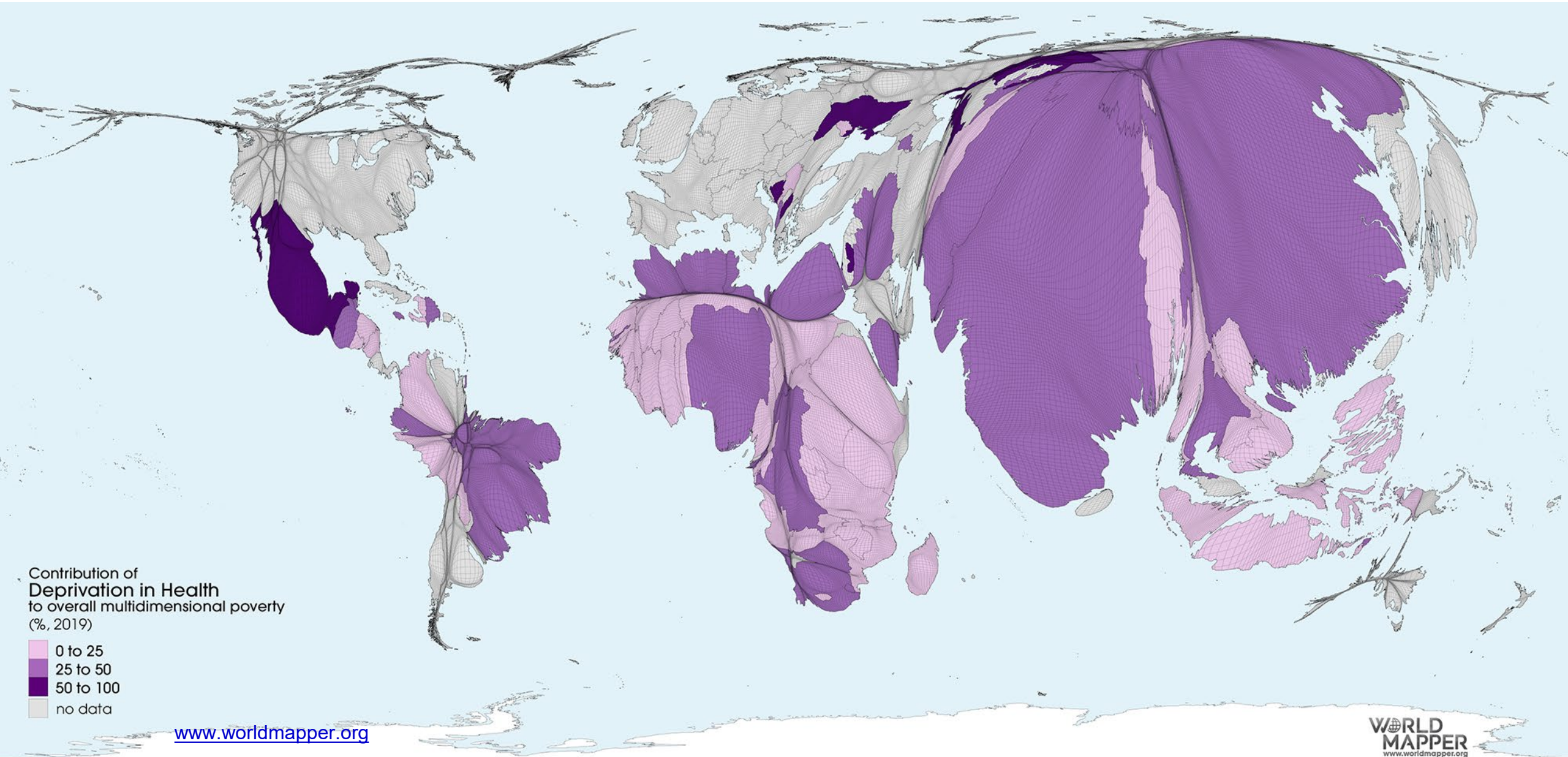
Atrium Health Wake Forest Baptist Comprehensive Cancer Center
Charlotte, North Carolina, USA

Gross National Income

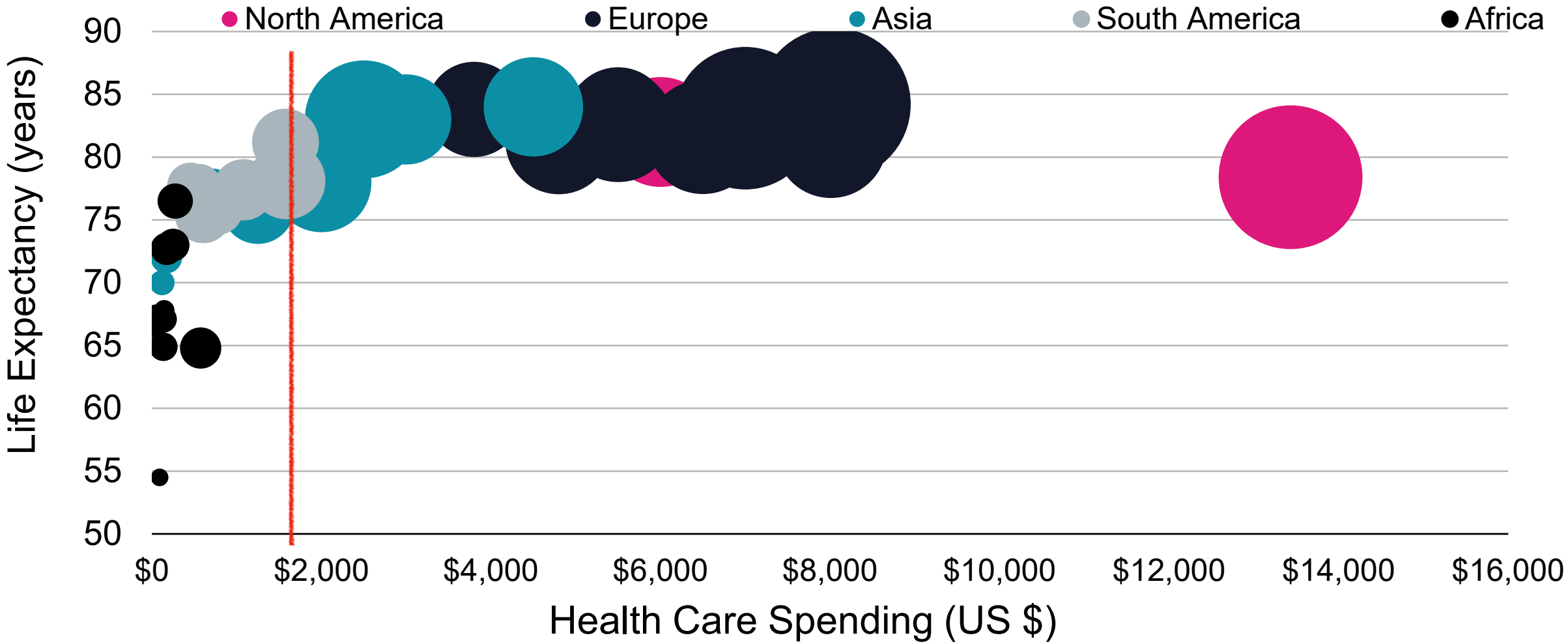


www.worldmapper.org

Deprivation in Health Contributing to Poverty



Health Care Spending and Life Expectancy



Bubble area represents GDP per capita (US$)

GOG FOUNDATION® Transforming the standard of care

GOG PARTNERS

Ovary and Uterine Cancer - 773,000 cases and 304,000 deaths

CANCER SITE	NO. OF NEW CASES (% OF ALL SITES)		NO. OF NEW DEATHS (% OF ALL SITES)	
Female breast	2,261,419	(11.7)	684,996	(6.9)
Lung	2,206,771	(11.4)	1,796,144	(18.0)
Prostate	1,414,259	(7.3)	375,304	(3.8)
Nonmelanoma of skin [a]	1,198,073	(6.2)	63,731	(0.6)
Colon	1,148,515	(6.0)	576,858	(5.8)
Stomach	1,089,103	(5.6)	768,793	(7.7)
Liver	905,677	(4.7)	830,180	(8.3)
Rectum	732,210	(3.8)	339,022	(3.4)
Cervix uteri	604,127	(3.1)	341,831	(3.4)
Esophagus	604,100	(3.1)	544,076	(5.5)
Thyroid	586,202	(3.0)	43,646	(0.4)
Bladder	573,278	(3.0)	212,536	(2.1)
Non-Hodgkin lymphoma	544,352	(2.8)	259,793	(2.6)
Pancreas	495,773	(2.6)	466,003	(4.7)
Leukemia	474,519	(2.5)	311,594	(3.1)

[a] New cases exclude basal cell carcinoma, whereas deaths include all types of nonmelanoma skin cancer.

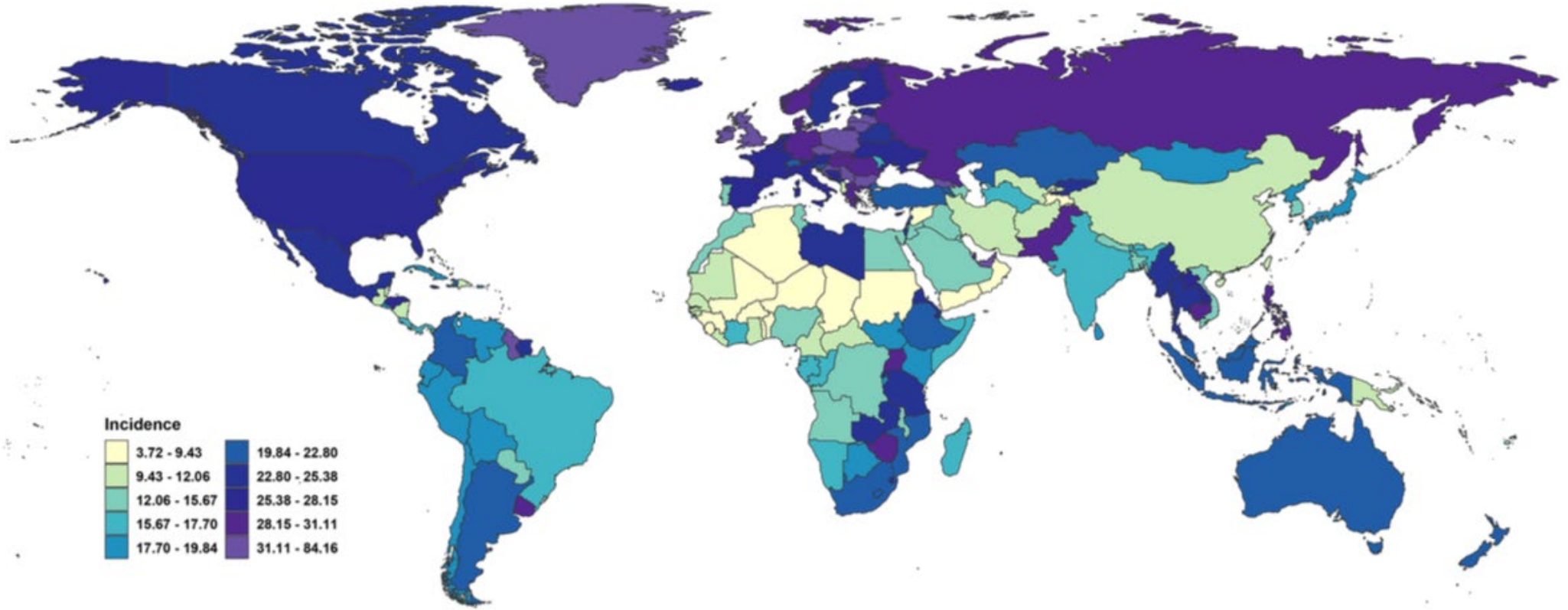
Source: GLOBOCAN 2020.

CANCER SITE	NO. OF NEW CASES (% OF ALL SITES)		NO. OF NEW DEATHS (% OF ALL SITES)	
Non-Hodgkin lymphoma	544,352	(2.8)	259,793	(2.6)
Pancreas	495,773	(2.6)	466,003	(4.7)
Leukemia	474,519	(2.5)	311,594	(3.1)
Kidney	431,288	(2.2)	179,368	(1.8)
Corpus uteri	417,367	(2.2)	97,370	(1.0)
Lip, oral cavity	377,713	(2.0)	177,757	(1.8)
Melanoma of skin	324,635	(1.7)	57,043	(0.6)
Ovary	313,959	(1.6)	207,252	(2.1)
Brain, nervous system	308,102	(1.6)	251,329	(2.5)
Larynx	184,615	(1.0)	99,840	(1.0)
Multiple myeloma	176,404	(0.9)	117,077	(1.2)
Nasopharynx	133,354	(0.7)	80,008	(0.8)
Gallbladder	115,949	(0.6)	84,695	(0.9)
Oropharynx	98,412	(0.5)	48,143	(0.5)
Hypopharynx	84,254	(0.4)	38,599	(0.4)

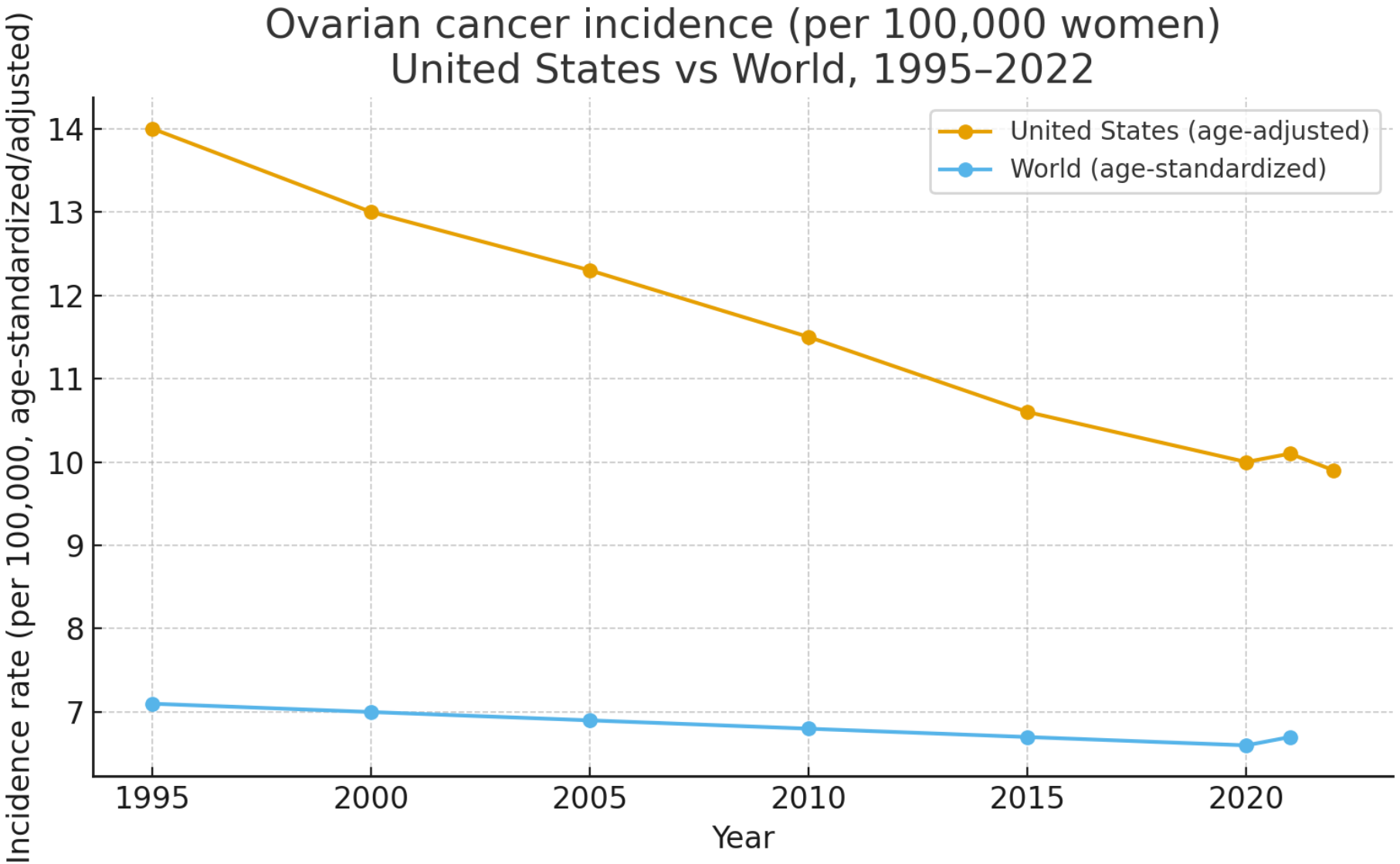
[a] New cases exclude basal cell carcinoma, whereas deaths include all types of nonmelanoma skin cancer.

Sung H, CA CANCER J CLIN 2021;71:209–249

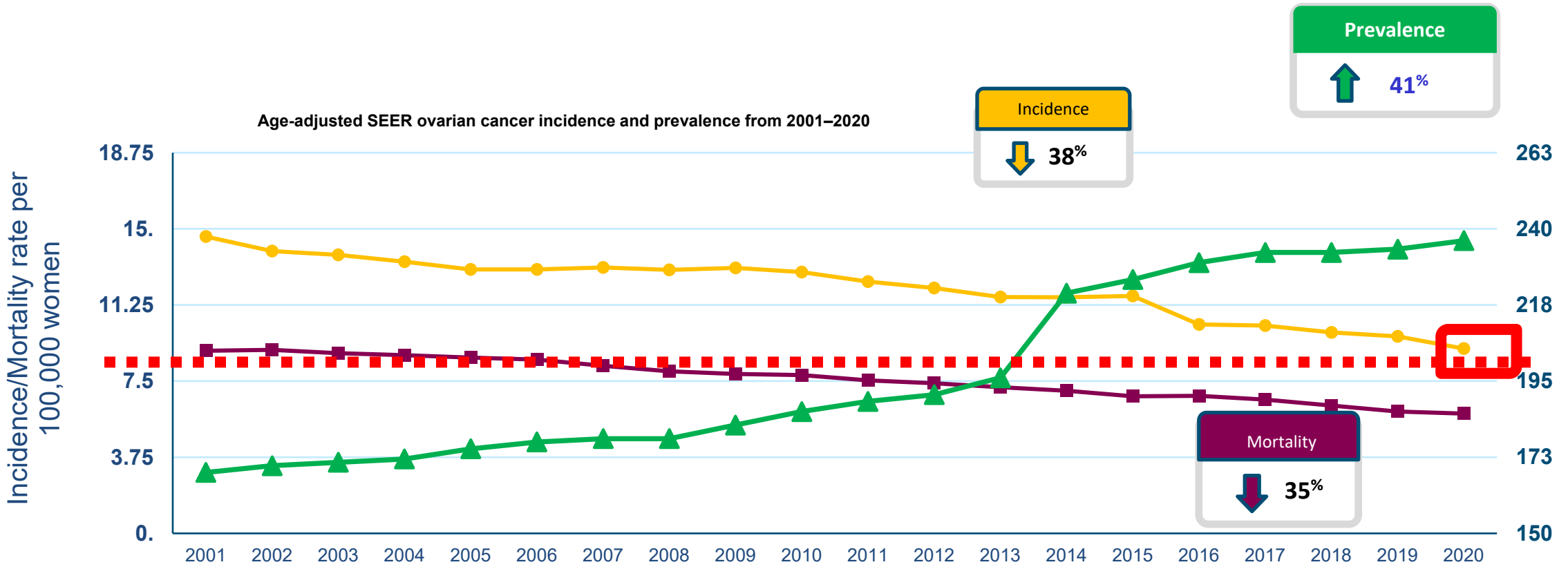
World Ovarian Cancer Rates



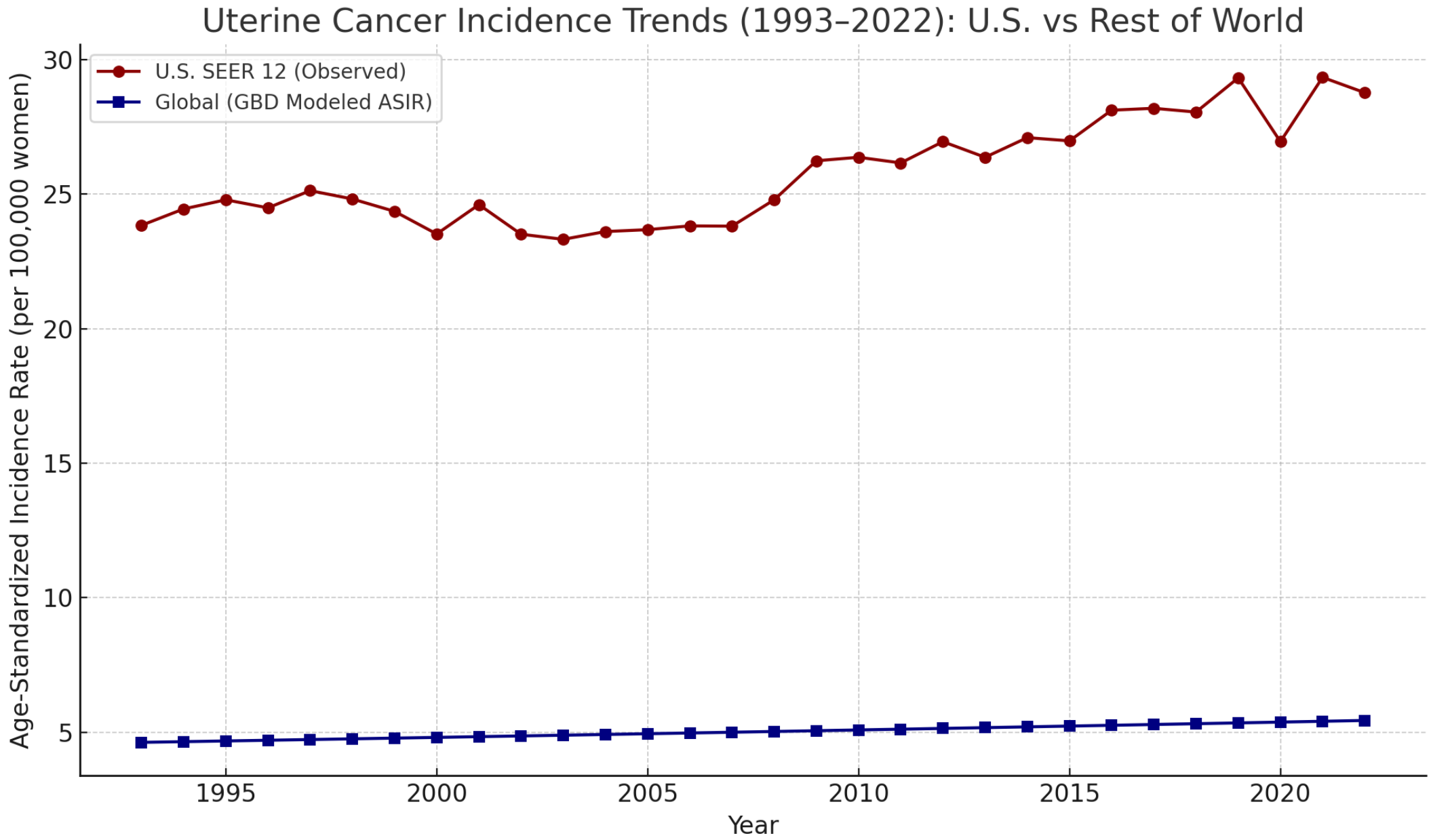
Ren Y, J Cancer Res Clin Oncol 151:225, 2025

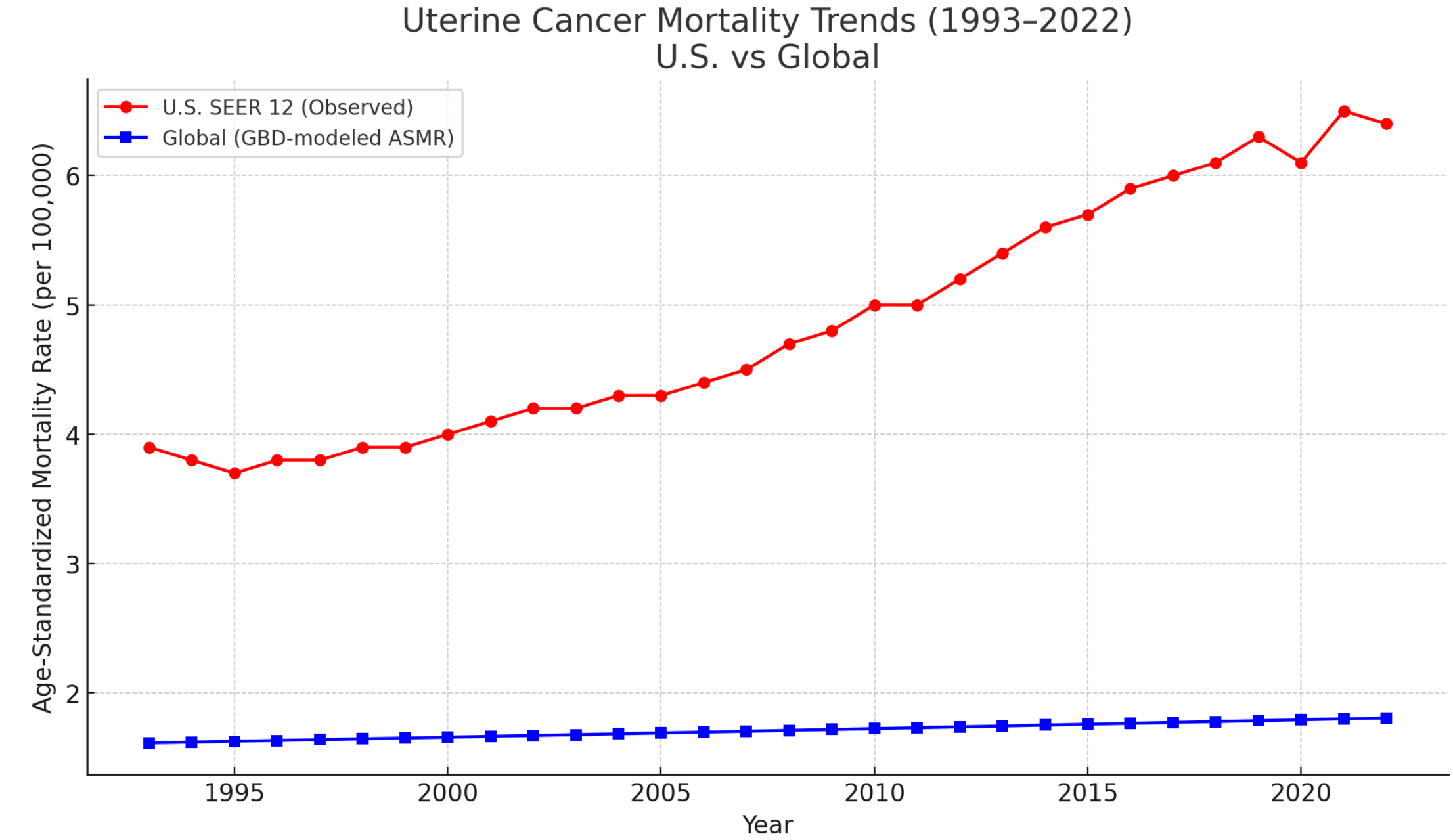

Ovarian cancer incidence (per 100,000 women)
United States vs World, 1995–2022
Incidence rate (per 100,000, age-standardized/adjusted)
14
13
12
11
10
9
8
7
1995
2000
2005
2010
2015
2020
Year
United States (age-adjusted)
World (age-standardized)

Ovarian Cancer: Clinical Impact

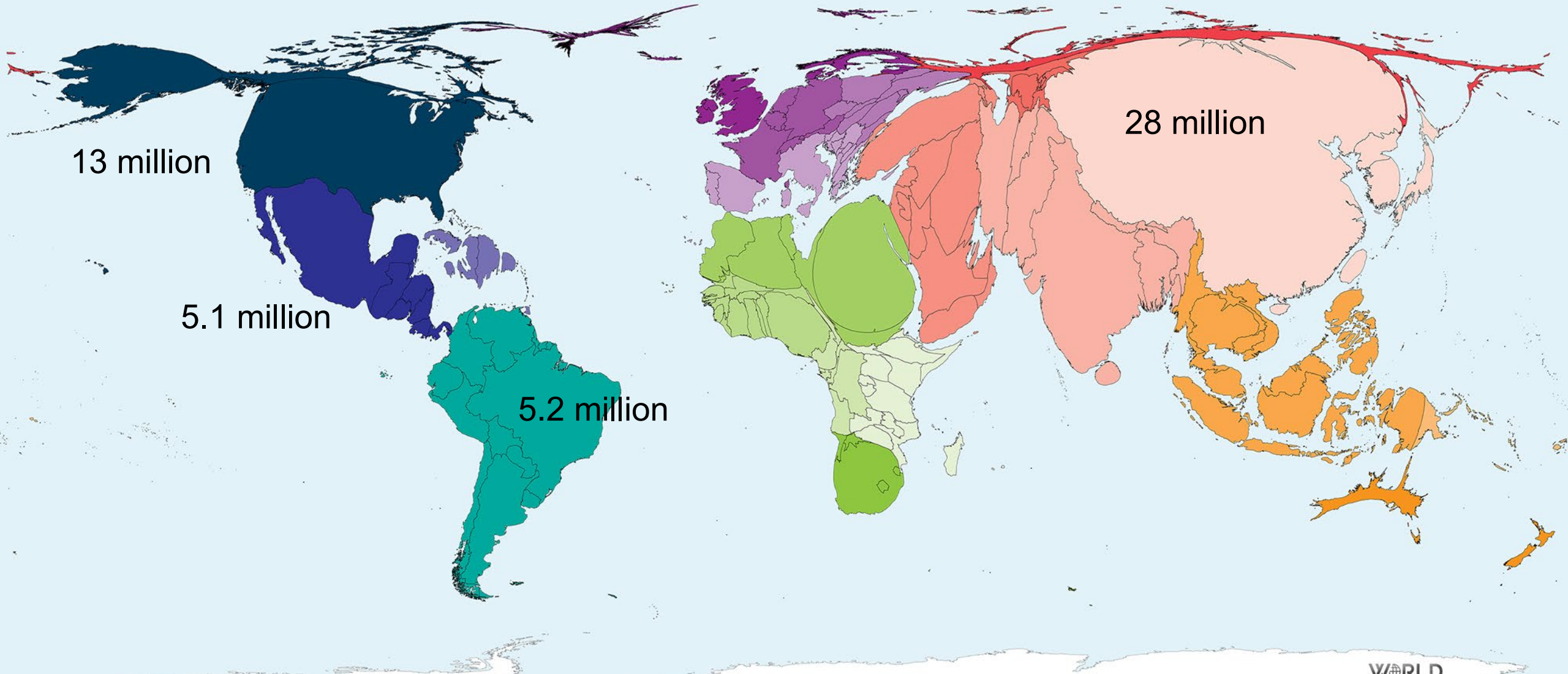


SEER=Surveillance, Epidemiology and End Results.
National Cancer Institute Surveillance, Epidemiology and End Results Program (SEER). SEER Cancer Statistics Review (CSR) 1975-2020 - Ovary. 2020; https://seer.cancer.gov/statistics-network/explorer/application.html?site=61&data_type=5&graph_type=11&compareBy=age_range&chk_age_range_1=1&chk_age_range_9=9&chk_age_range_141=141&chk_age_range_157=157&series=9&hdn_sex=3&advopt_compprev_y_axis_var=0&hdn_view=1#tableWrap; Accessed May 23, 2023

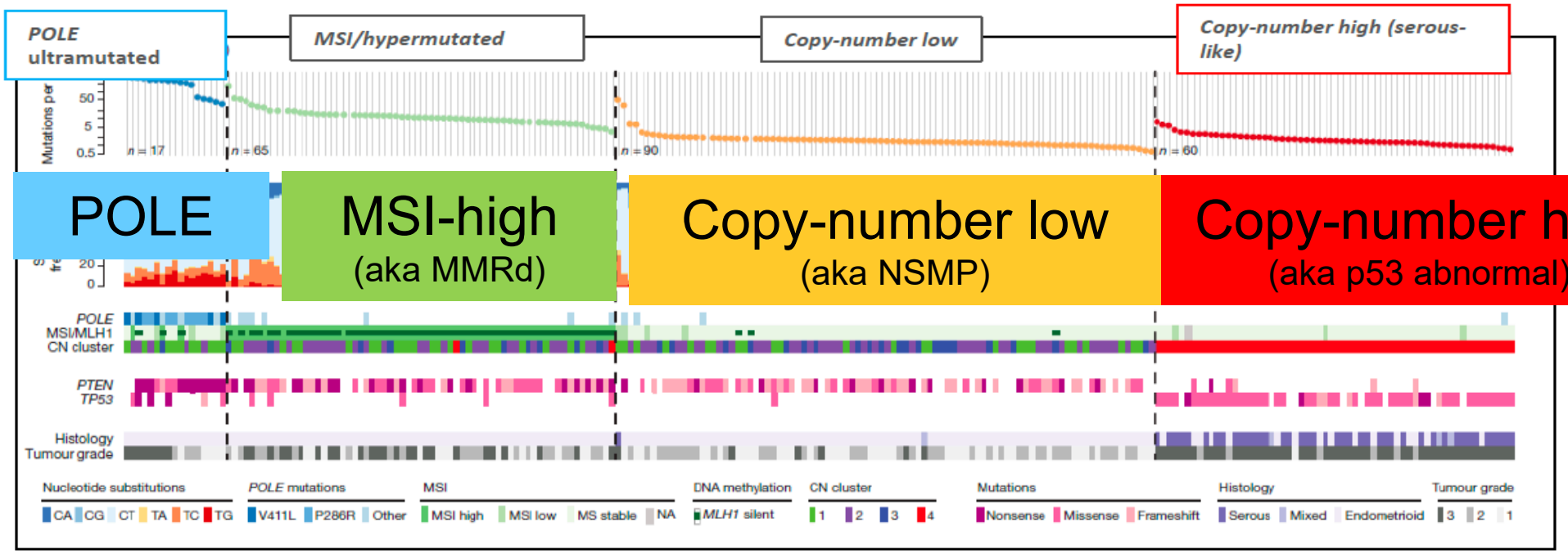

Uterine Cancer Incidence Trends (1993–2022): U.S. vs Rest of World
U.S. SEER 12 (Observed)
Global (GBD Modeled ASIR)
Age-Standardized Incidence Rate (per 100,000 women)
30
25
20
15
10
5
1995
2000
2005
2010
2015
2020
Year


Uterine Cancer Mortality Trends (1993–2022)
U.S. vs Global
U.S. SEER 12 (Observed)
Global (GBD-modeled ASMR)
Age-Standardized Mortality Rate (per 100,000)
2
3
4
5
6
1995
2000
2005
2010
2015
2020
Year

Number of Obese Children



www.worldmapper.org



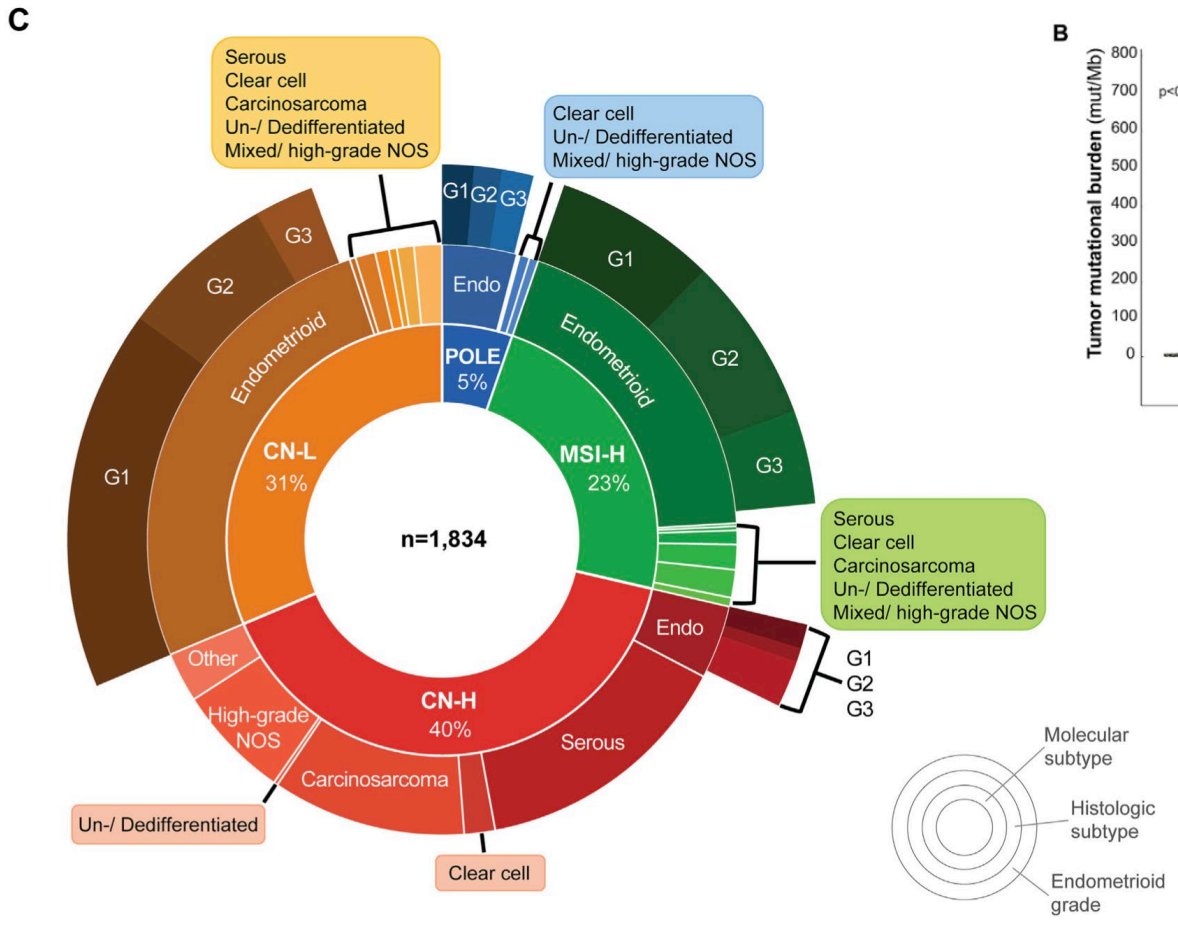
Mutational burden HIGH → LOW

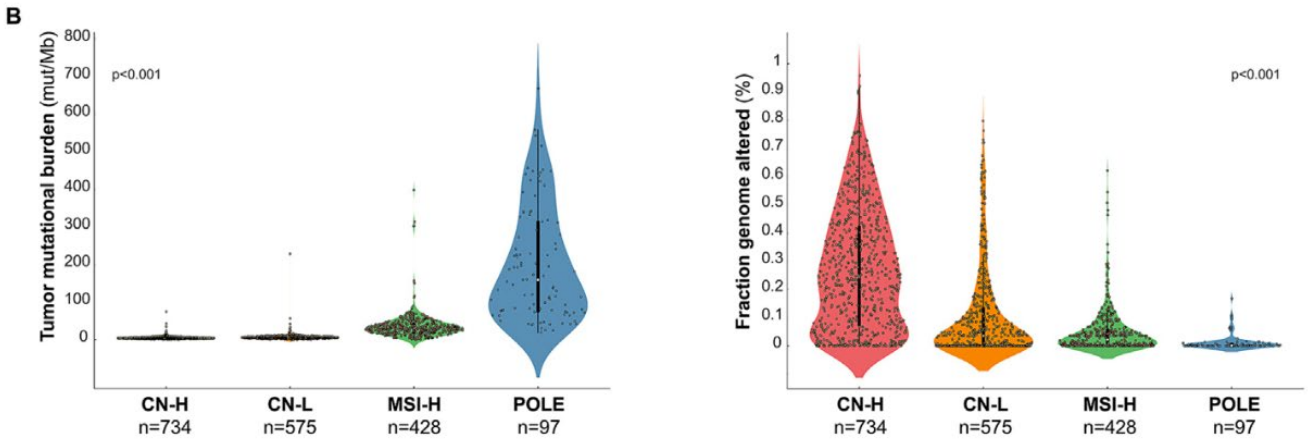
Somatic copy number alterations LOW ← HIGH

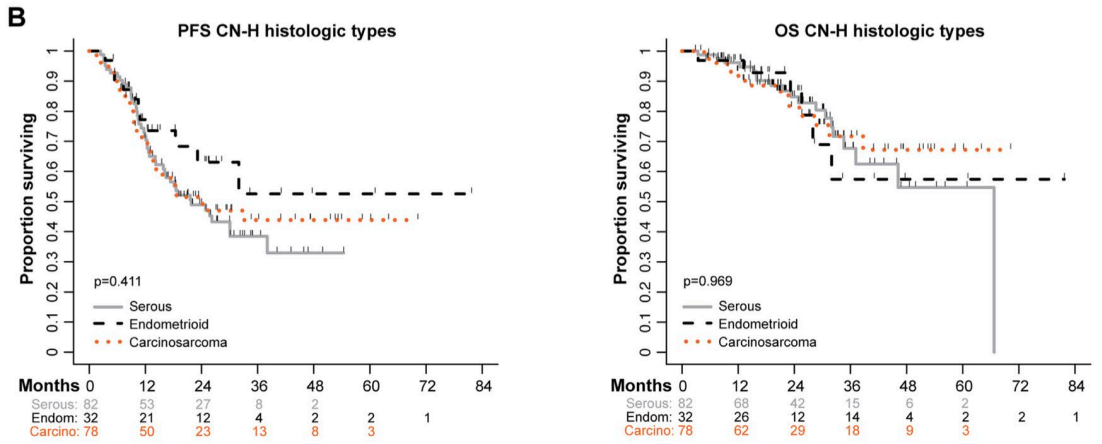
POLE	MSI-high	Copy-number low	Copy-number high
POLE (100%)	PTEN(88%)	PTEN (77%)	TP53 (92%)
PTEN(94%)	PIK3CA (54%)	PIK3CA (53%)	PIK3CA(47%)
	ARID1A (37%)	CTNNB1(52%)	FBXW7 (22%)
		ARID1A (33%)	PP2R1A (22%)
			PTEN (10%)

TCGA, Nature 497(7447):67, 2013 DOI:10.1038/nature12113

Histologic and Molecular Subtypes of Endometrial Cancer

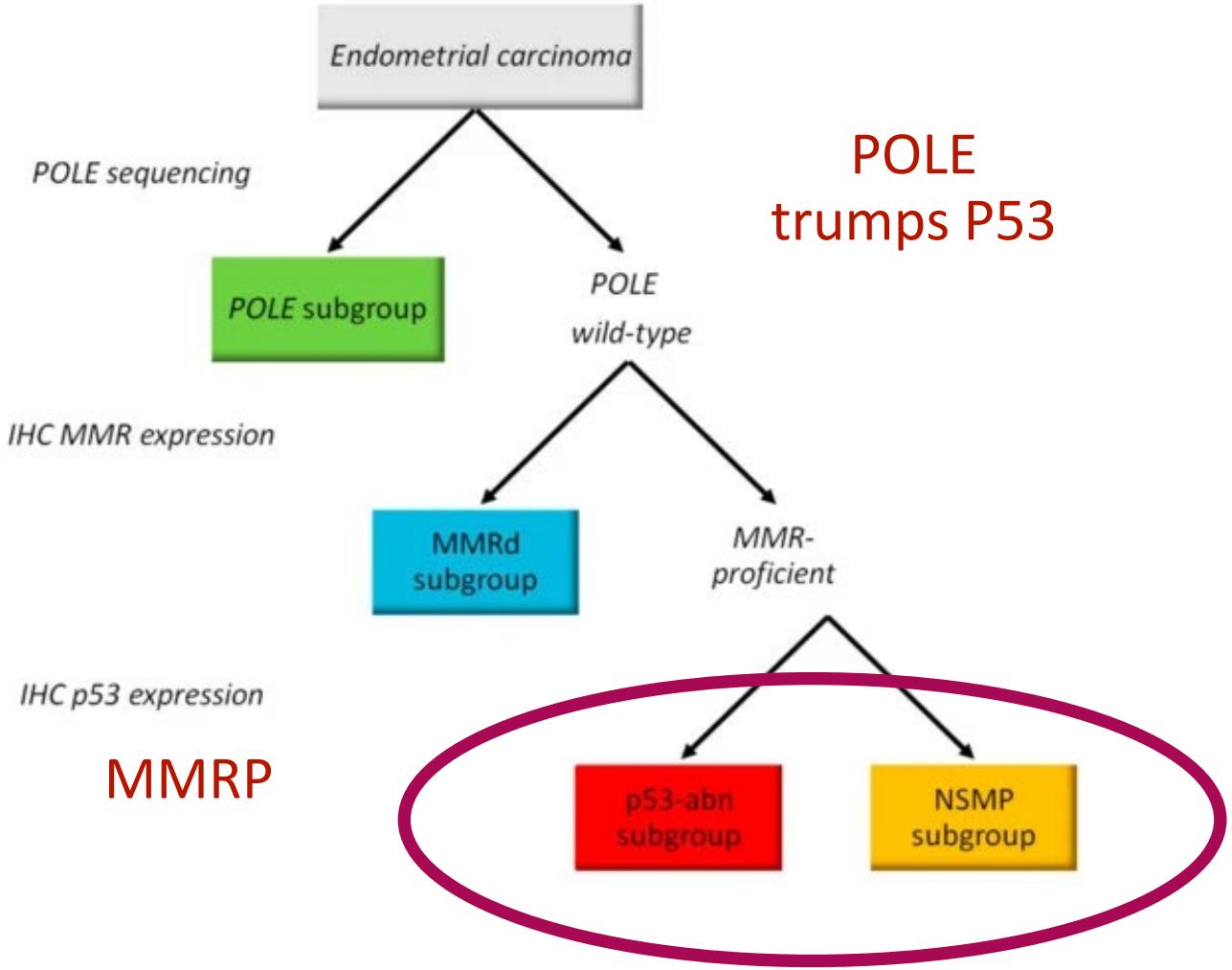






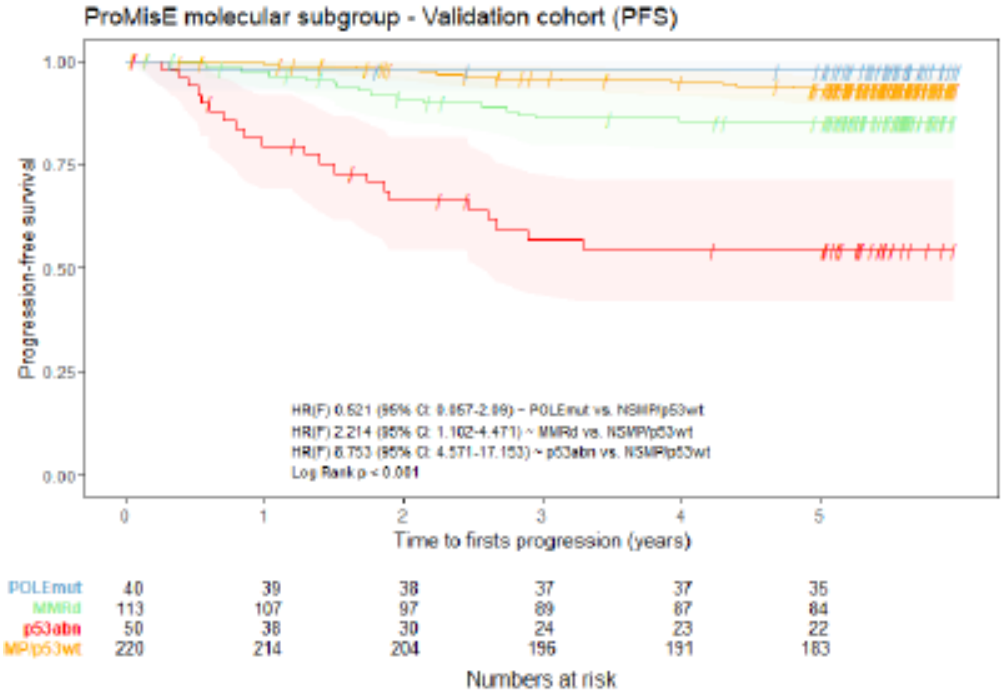
Rios-Doria, Gynecol Oncol 174:262, 2023

ProMisE (Proactive Molecular risk classifier for Endometrial cancer) Algorithm



POLE trumps P53

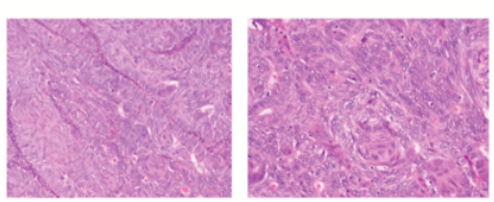
MMRP



92% concordant with NGS (some missed P53 abnml)

Kommoss, Ann Oncol, 2018

The Conundrum



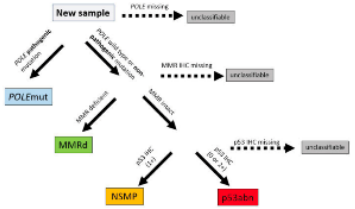
Endometrial Biopsy or Curettage

↓

Pathology + Molecular Classification

↓

Impact surgical decision /staging



*POLE*mut

- Early ~90% → De-escalation e.g., surgery only
- Advanced ~10% → ? De-escalation ? Radiation only

Clinicopathologic and molecular parameters; e.g., LVI, grade, myoinvasion, L1CAM do not add prognostic or predictive stratification

Adjuvant Clincal Trials

PORTEC-4a (de-escalation)
RAINBO Blue (de-escalation)
TAPER (de-escalation)

MMRd

Adjuvant Radiation
? No additional benefit from chemotherapy

- Loss of MSH6, MSH2, PMS2 → Hereditary Cancer Referral → Consider ICB
- Loss of MLH1
  - Not Methylated → Hereditary Cancer Referral → Consider ICB
  - Methylated → ? Less response to ICB ? Pembro + Lenvat

Further stratified by MLH1 and immune profile?

Adjuvant Clincal Trials

NRG GY 020 (+ICB; pembrolizumab)
RAINBO Green (+ICB; durvalumab)
ADELE Trial (+ICB; tislelizumab)

NSMP

Additional Stratification

- LVI
- Grade
- ER/PR
- L1CAM?
- *CTNNB1?*
- Immune, e.g., CD8?

- Highly Favourable
  - De-escalation
  - Vault brachy
  - Endocrine therapy
- Unfavourable
  - ?Chemo RT
  - ? Pembro + Lenvat

Clinicopathologic parameters do add prognostic and possible predictive stratification

Adjuvant Clincal Trials

RAINBO Orange (+endocrine therapy)
TAPER (de-escalation)

p53abn

- Stage IA No myoinvasion → ?Surgery only, ?Vault brachy, ?ChemoRT
- Stage IA with myoinvasion/Stage IB+ → Significant benefit from chemotherapy
  - HRD (20-25%) PARPi
  - HER2 (20-25%) Anti-HER2 Rx
  - CCNE1 (20-30%) Wee1-i
  - Pembro + Lenvat (50% response in serous)

Aggressive tumors regardless of grade and histotype

Molecular parameters for predictive stratification

Adjuvant Clincal Trials

RAINBO Red (+PARPi; olaparib)
CAN-STAMP (+PARPi; niraparib)
NRG GY 026 (+HER2; trastuzumab/pertuzumab)

Jamieson A…McAlpine J, Caner 128(15):2853, 2022

Number of Research Papers on Endometrial Cancer from Africa over a 10 year period

Fig. 2 Geographic Distribution of Prospective Endometrial Cancer Research within Africa. The map represents individual countries only and does not clearly illustrate some of the smaller African countries

Can remote mentoring help?

*Anakwenze, C.P., Ewongwo, A., Onyewadume, L. et al. A systematic review of endometrial cancer clinical research in Africa. Infect Agents Cancer **19**, 2 (2024). https://doi.org/10.1186/s13027-023-00563-2*

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International Difference in Ovarian Cancer Care

- Global survey of 1,059 physicians in 115 countries
  - 46% High income
  - 29% Middle income
  - 25% Low income

GOG FOUNDATION® Transforming the standard of care

GOG PARTNERS

Algera M, Int J Gyncol Cancer 33:1612, 2023

Responses to Survey on Ovarian Cancer Care

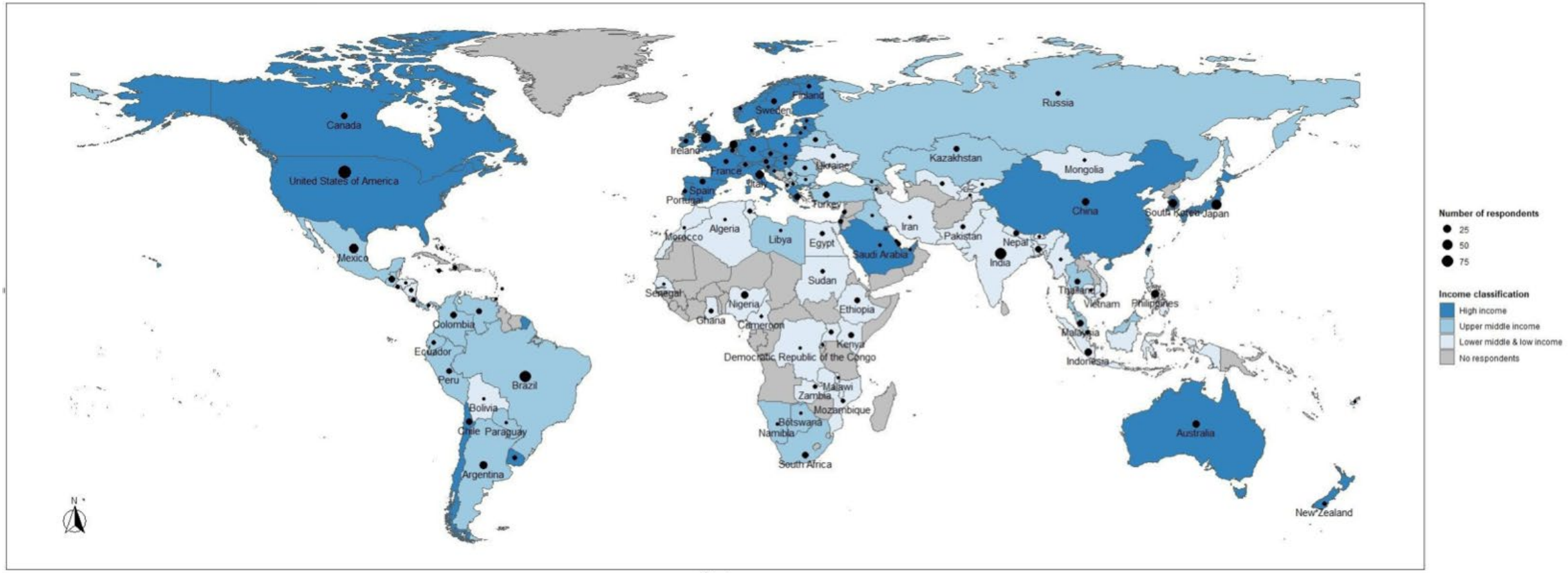
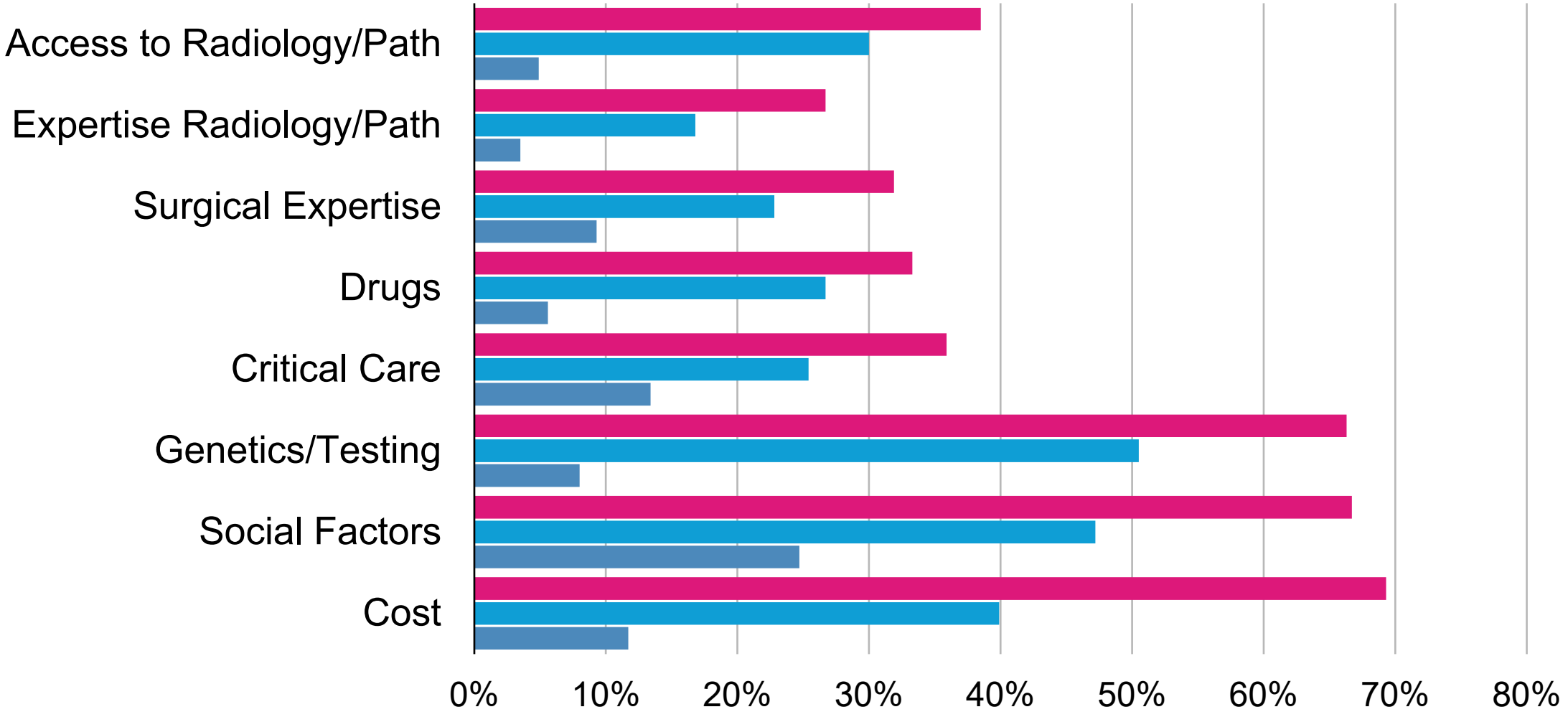


Figure 1 Global Equality in Ovarian Cancer Care Survey: number of responses per country.

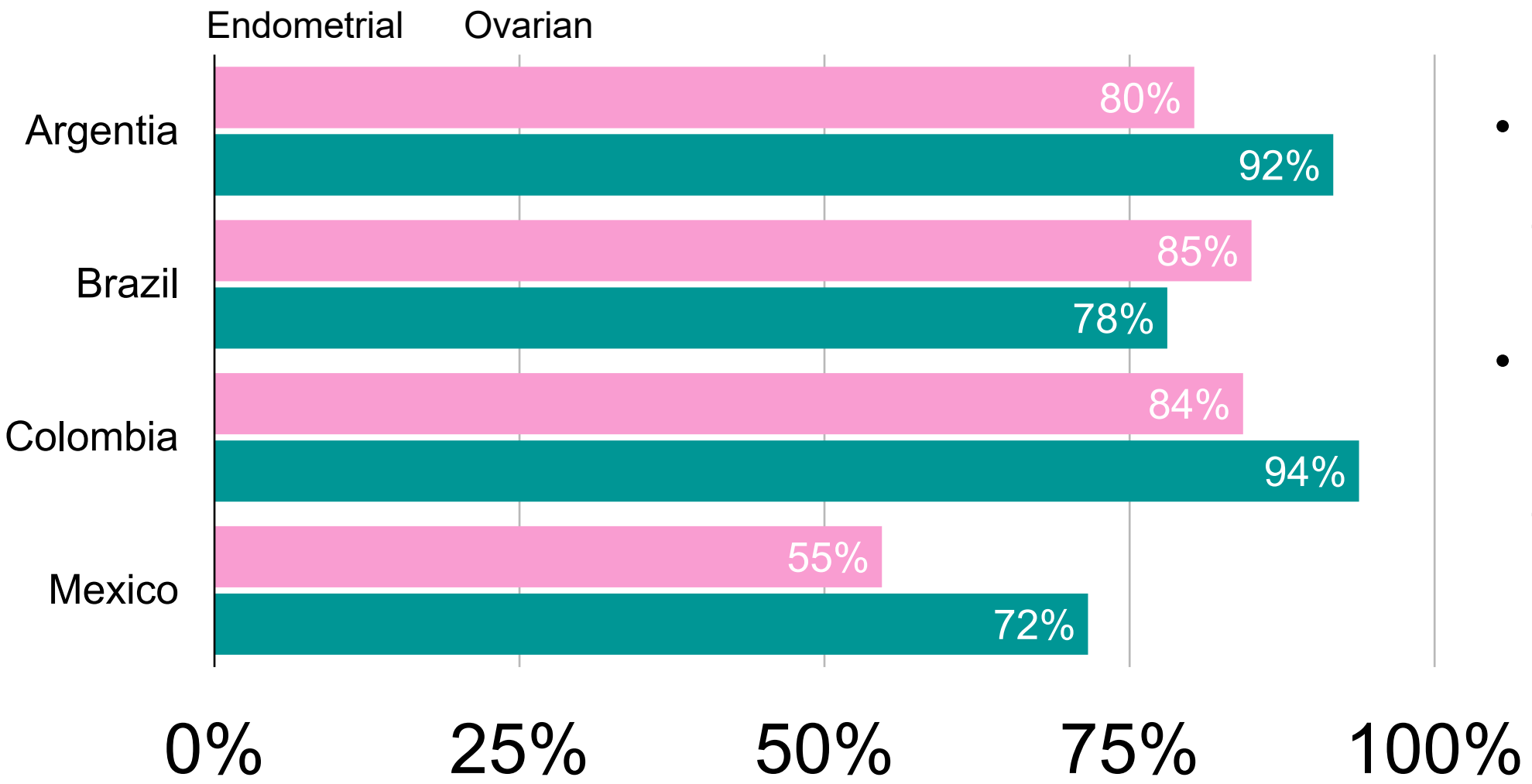
Algera M, Int J Gyncol Cancer 33:1612, 2023

Reported Challenges



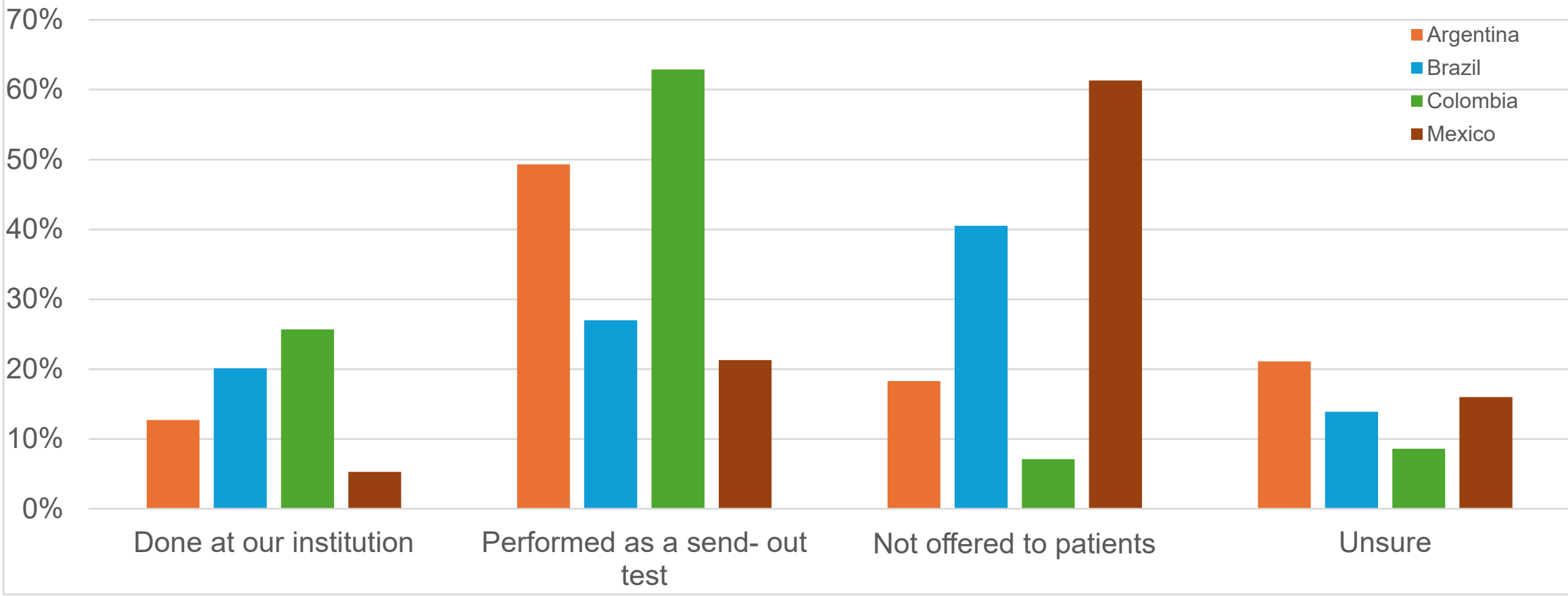
Algera M, Int J Gyncol Cancer 33:1612, 2023

IGCS Survey Report: Patterns of Care, Biomarker Testing, and Educational Needs in Gynecologic Cancers Across Latin America



- 5%-26% perform POLε testing in-house
- 10-25% perform in-house HRD testing

Indicate how your institution performs or offers somatic NGS for endometrial cancer patients? (check all that apply)



A Call to Action!

https://igcs.org/wp-content/uploads/2024/06/Global-Call-to-Action-Reducing-Disparities-Uterine-Cancer.pdf?utm_source=chatgpt.com

Atrium Health

Wake Forest University School of Medicine

IGCS Call to Action

- Raise Awareness of the Disease and Symptoms
- Prevention
  - Includes prevention such as weight control/exercise
- Overcome barriers to diagnosis
- Improve access to treatment
  - Gyn Oncology surgical training
  - State of the art radiation therapy
  - Access to molecular testing and genetics
  - Systemic therapies including access to immunotherapy
  - Fertility sparing therapies
  - Support diversity in research
  - Access to clinical trials

Interactive Panel Discussion: Emerging Targets, Real-World Decision Making

All Faculty

Summary & Closing Remarks

All Faculty

Thank You

View this symposium as part of the IGCS on-demand program following the meeting

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