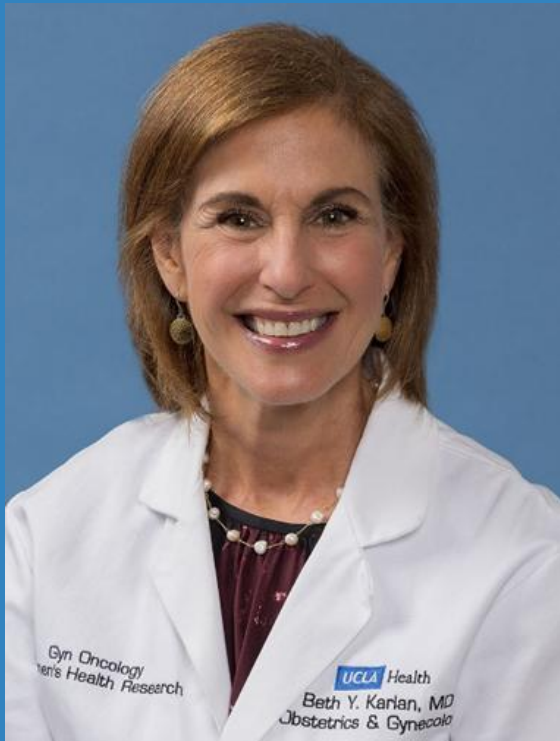


Sharsheret The Jewish Breast & Ovarian Cancer Community

Ovarian Cancer 2026: Progress, Prevention, and Possibilities



Beth Y. Karlan, MD

Nancy Marks Endowed Chair in Women's Health Research
Professor and Vice Chair, Obstetrics and Gynecology
Director, Cancer Population Genetics
UCLA-Jonsson Comprehensive Cancer Center
David Geffen School of Medicine at UCLA

Outline for this evening's talk and discussion

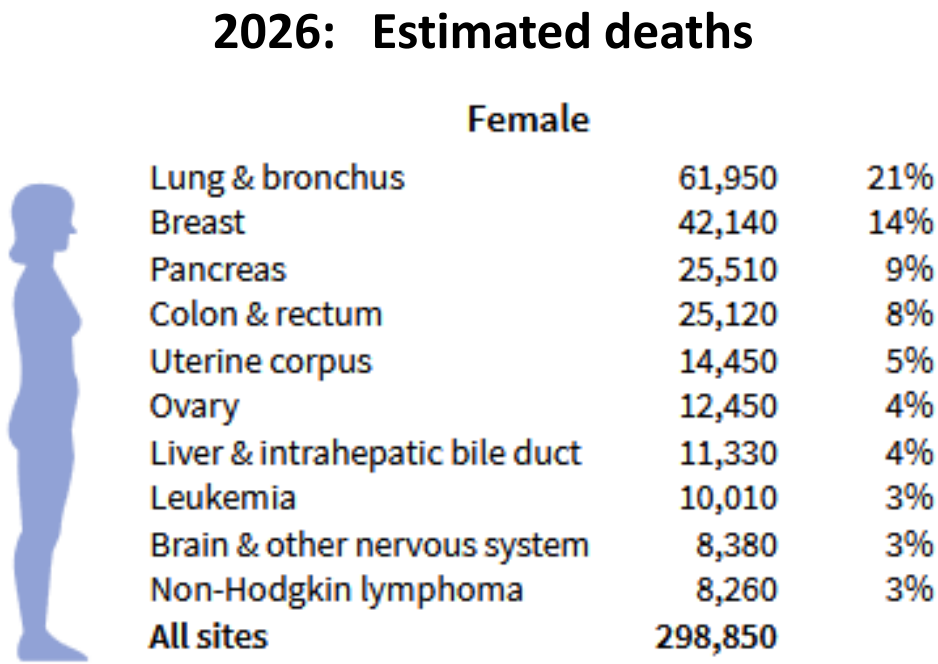
- 2026 Numbers and trends
- Pathology subtypes and clinical implications
- Treatment updates:
 - Current standard of care
 - HIPEC
 - Genetics and PARPs and molecular testing
- Antibody drug conjugates and what's on the horizon
- Survivorship
- Salpingectomy and prevention

Ovarian Cancer Statistics 2026

21,010 new cases
(19,680 in 2024)

12,450 estimated deaths
(12,740 in 2024)

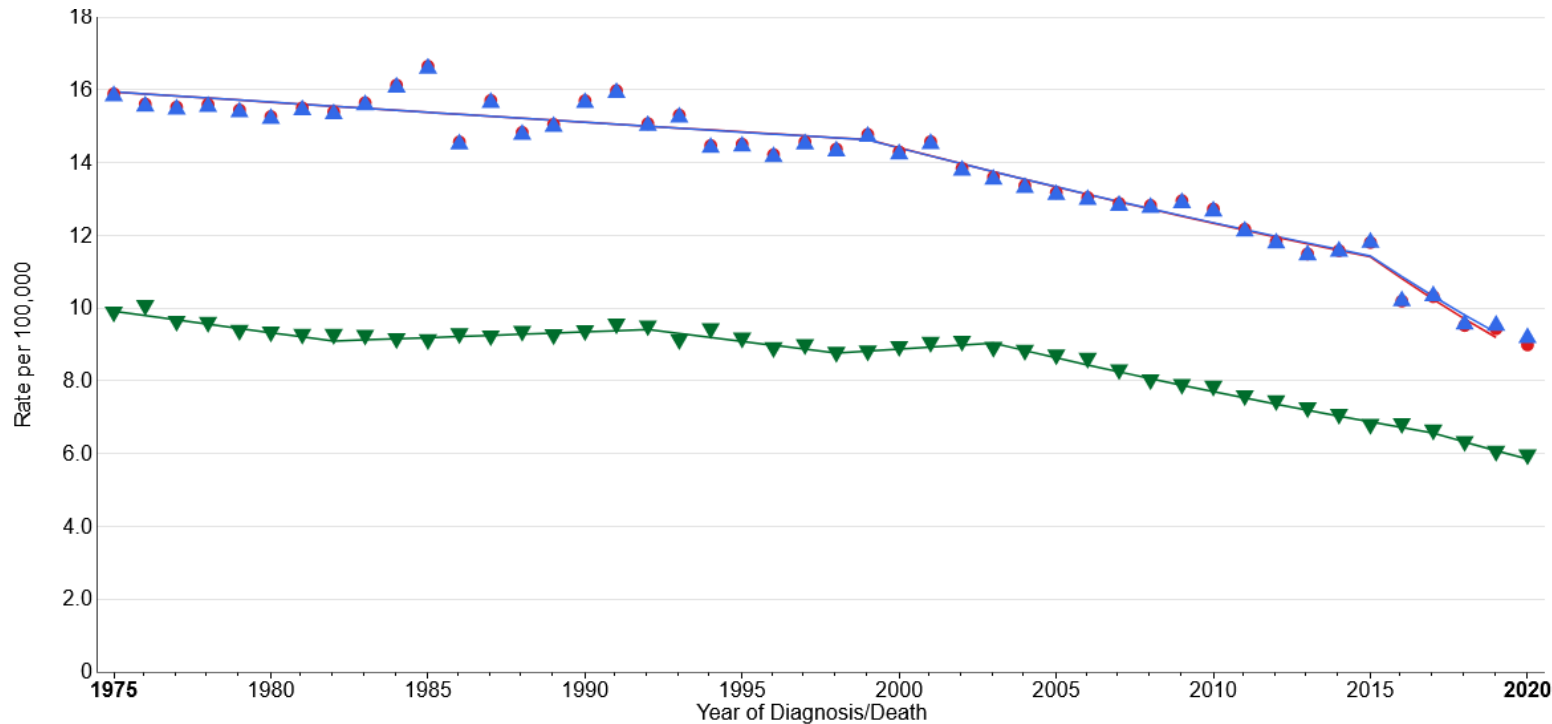
Survival is improving:
more women are living
longer and living better



Age at Prevalence	Number of people alive with cancer
All Ages	238,484
Ages < 50	32,504
Ages 50-64	72,993
Ages 65+	132,987

The good news: Both incidence and mortality are decreasing

Long-term trends in SEER incidence and mortality



Incidence down due to:

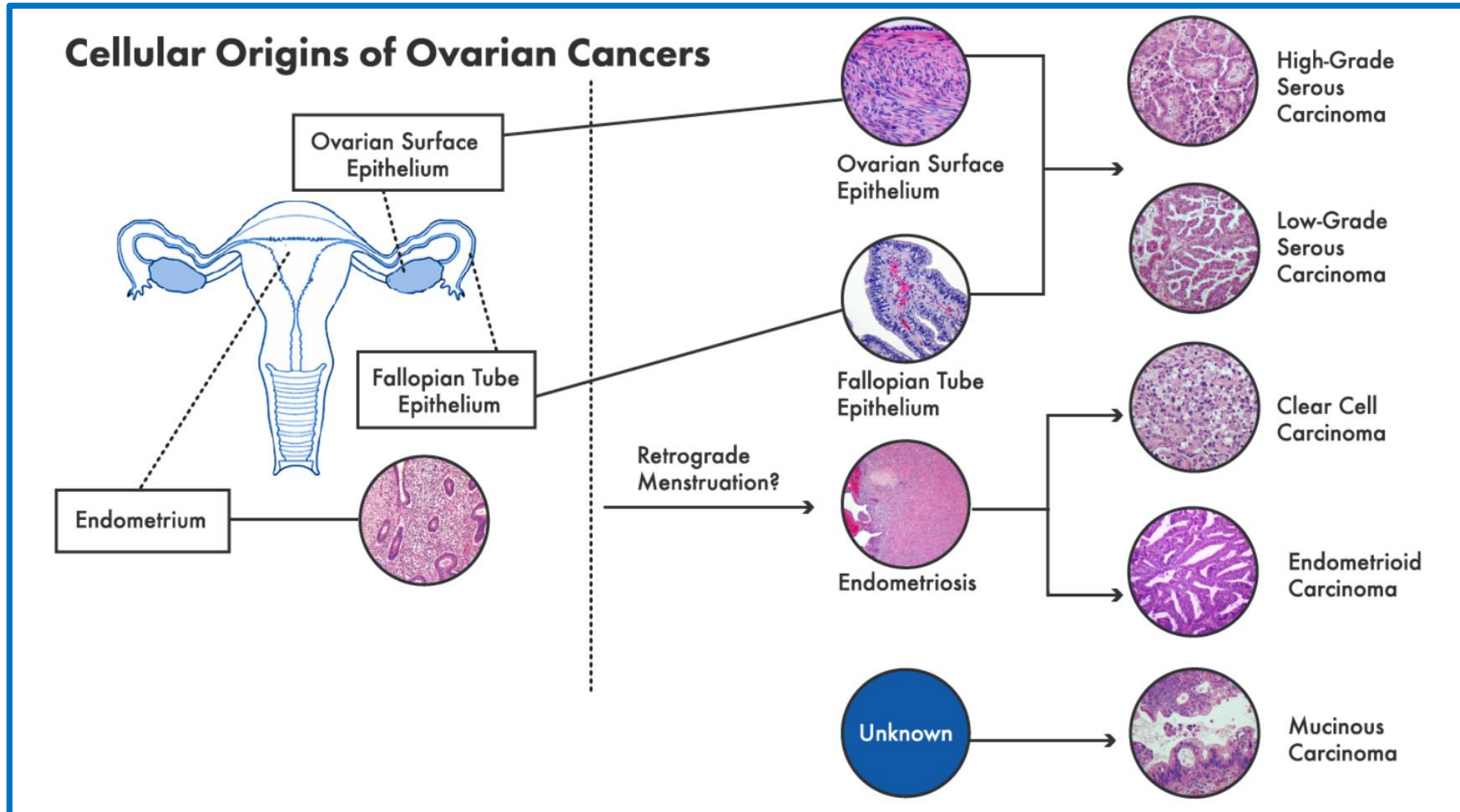
- OCP use increased in 1970s/80s
- Genetic testing & RRSO
- Opportunistic salpingectomy.

Mortality down due to:

- Better treatment
- Individualized approaches
- Improved medical medical/surgical care

Ovarian cancer is not one disease. Most don't begin at the ovary.

Different cells of origin. Different genetics. Different biologies. Different therapies.



Advanced ovarian cancer management: Standard of care 2026

Primary debulking surgery (PDS) and interval debulking surgery (IDS) after neoadjuvant chemotherapy (NACT) have equivalent survival outcomes

- Decision for PDS v NACT should be made by gyn onc
- Fewer surgical complications after NACT/IDS
- Most important to get to no visible residual disease (R0)
- HIPEC should be considered at time of IDS
- Germline and somatic testing (including HRD) should be universally offered
- Carboplatin and paclitaxel x 6 cycles IV +/- bev + bev maintenance
- PARP inhibitor maintenance +/- bev is standard of care for *BRCAm*/HRD stage III/IV cancers

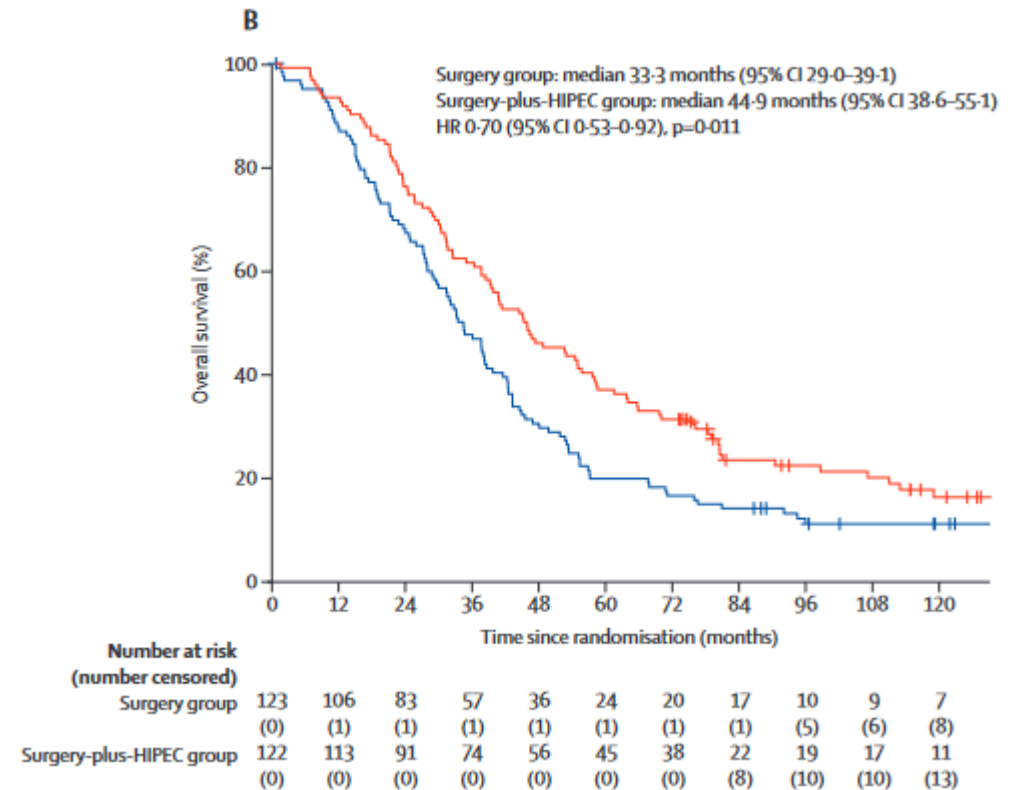
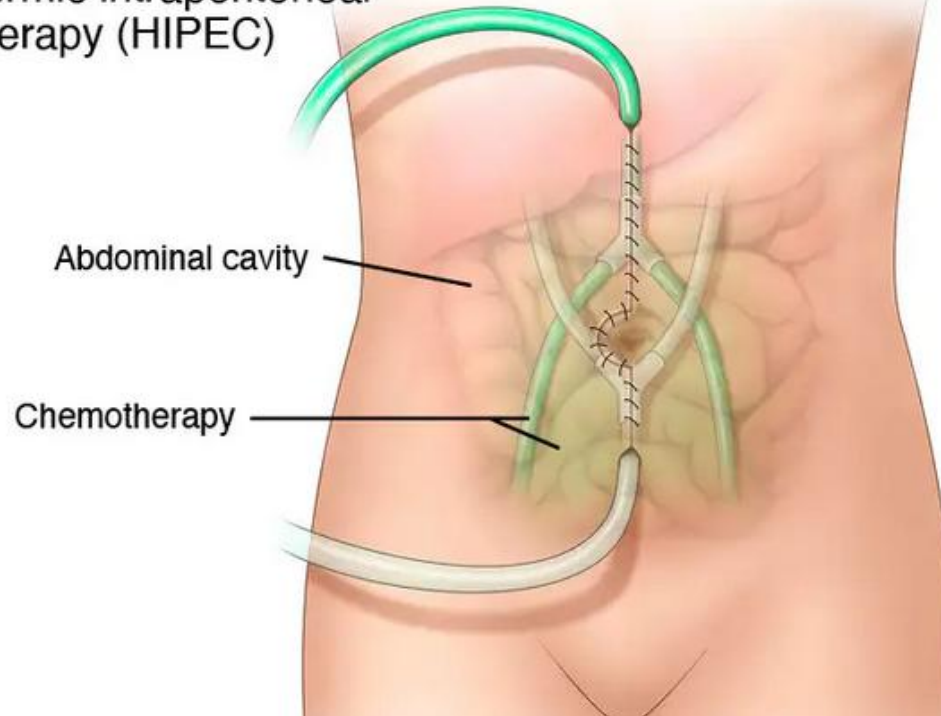
Cliby WA, Gyn Onc 2015, Wright et al Gyn Onc 2016, Konstantinopoulos/Matulonis, Nature Medicine 2023, Coleridge 2021, Clamp et al, Lancet 2019, Lancet Onc 2022, Bladgen et al, Lancet Onc 2020, Vergote et al Lancet Onc 2019, Ray-Coquard Int J of Cancer 2020, Ledermann et al Lancet 2016; SGO 2020, ESMO 2020, JCO 2021, Lancet Oncology 2021, Harter ASCO 2023, Gyn Onc 2023; NEJM 2006, Lancet Onc 2023

HIPEC improves overall survival in advanced ovarian cancer

OVHIPEC-1 trial. Phase 3 RCT. NACT/IDS +/- HIPEC

- 10 year follow up demonstrated long term survival benefit

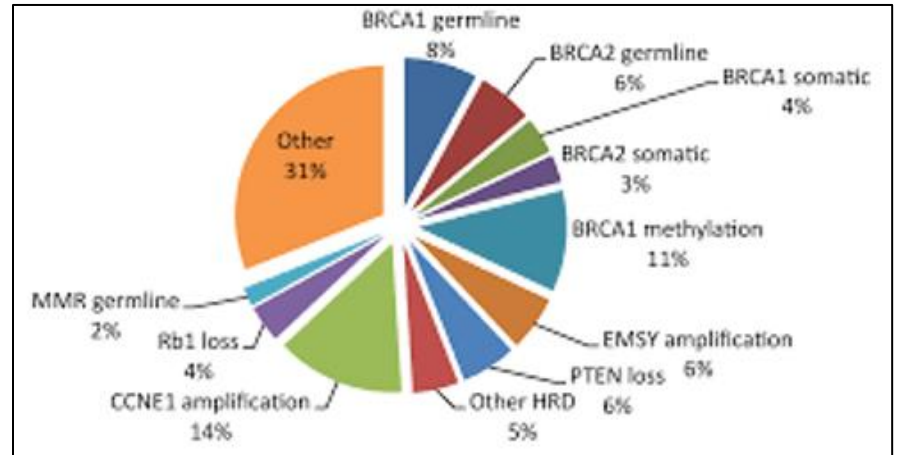
Hyperthermic intraperitoneal chemotherapy (HIPEC)



- ~20% ovarian cancer patients carry an inherited mutation:
 - 65-85% are due to BRCA1 and BRCA2.
 - 15-35% to RAD51C, RAD51D, PALB2, BRIP1 and MMR genes
- Since 2010, NCCN guidelines have recommended universal genetic testing for all ovarian cancer patients...yet <50% of patients are getting tested
- Not testing leads to missed opportunities for targeted therapies and interventions for second cancer prevention
- Missed opportunities cascade testing of family members and primary prevention for at-risk relatives

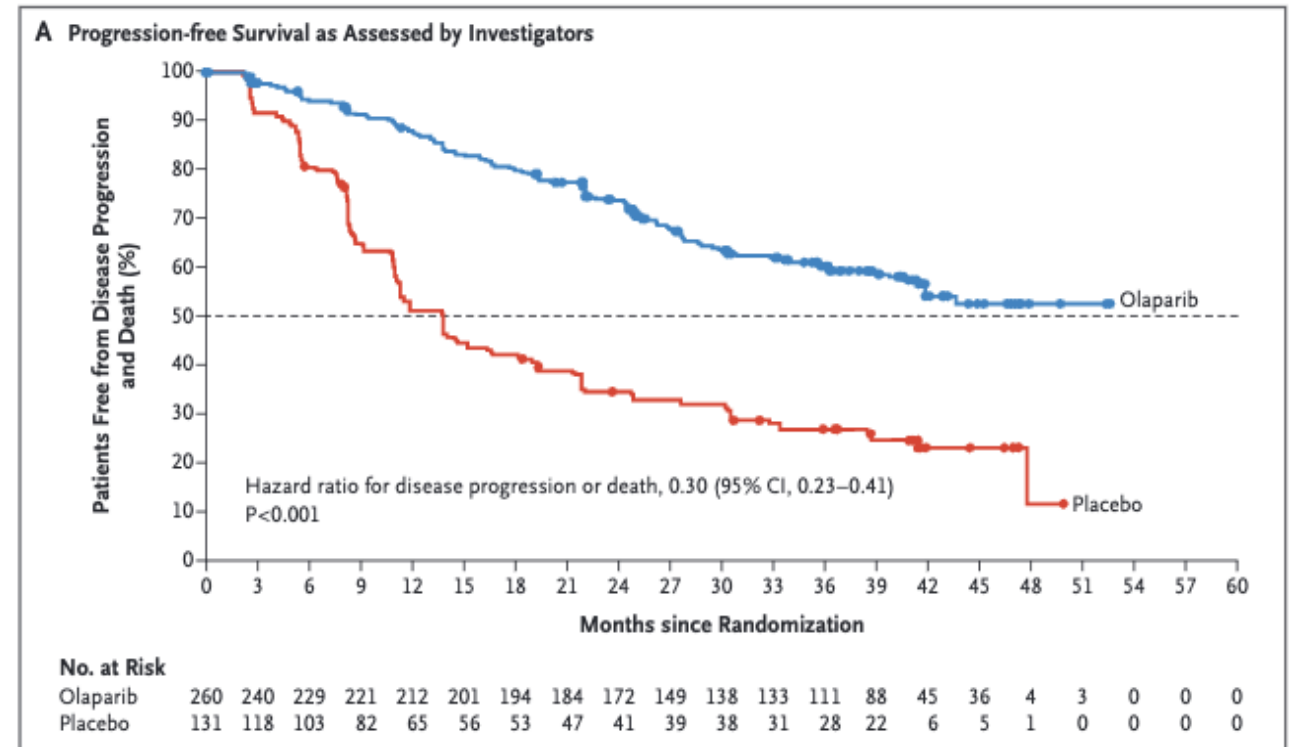
Genetics can improve ovarian cancer survival

Over 50% of ovarian cancers are susceptible to PARP inhibition due to deficient DNA damage repair (germline, somatic, and epigenetic changes)



- PARPi maintenance significantly prolongs survival, especially when tumors lose DNA damage repair proficiency
- Tumors with MMR gene deficiencies benefit from immunotherapy treatment
- Growing list of targeted agents with pathway-specific, organ-agnostic efficacy that further adds to survival benefit has driven paired tumor/normal tissue NGS testing.

- SOLO1 Landmark Trial
 - Maintenance Olaparib following surgery and adjuvant platinum/paclitaxel in *BRCA* carriers
- 70% lower risk of progression/death at 5 years (HR= 0.30, $P<0.001$)
- Genetic testing can improve ovarian cancer survival



Moore, et al. NEJM; 2018.

Molecular testing is the basis for precision oncology



Over 17,000 genes have been associated with a cancer diagnosis

Germline versus somatic mutations

Inherited cancer susceptibility vs tumor molecular profiling

Somatic DNA changes

Acquired over a person's lifetime in single cells

Can lead to cancer

Can NOT be inherited



Germline DNA changes

Present in every cell of the body including egg and sperm

Can increase cancer susceptibility

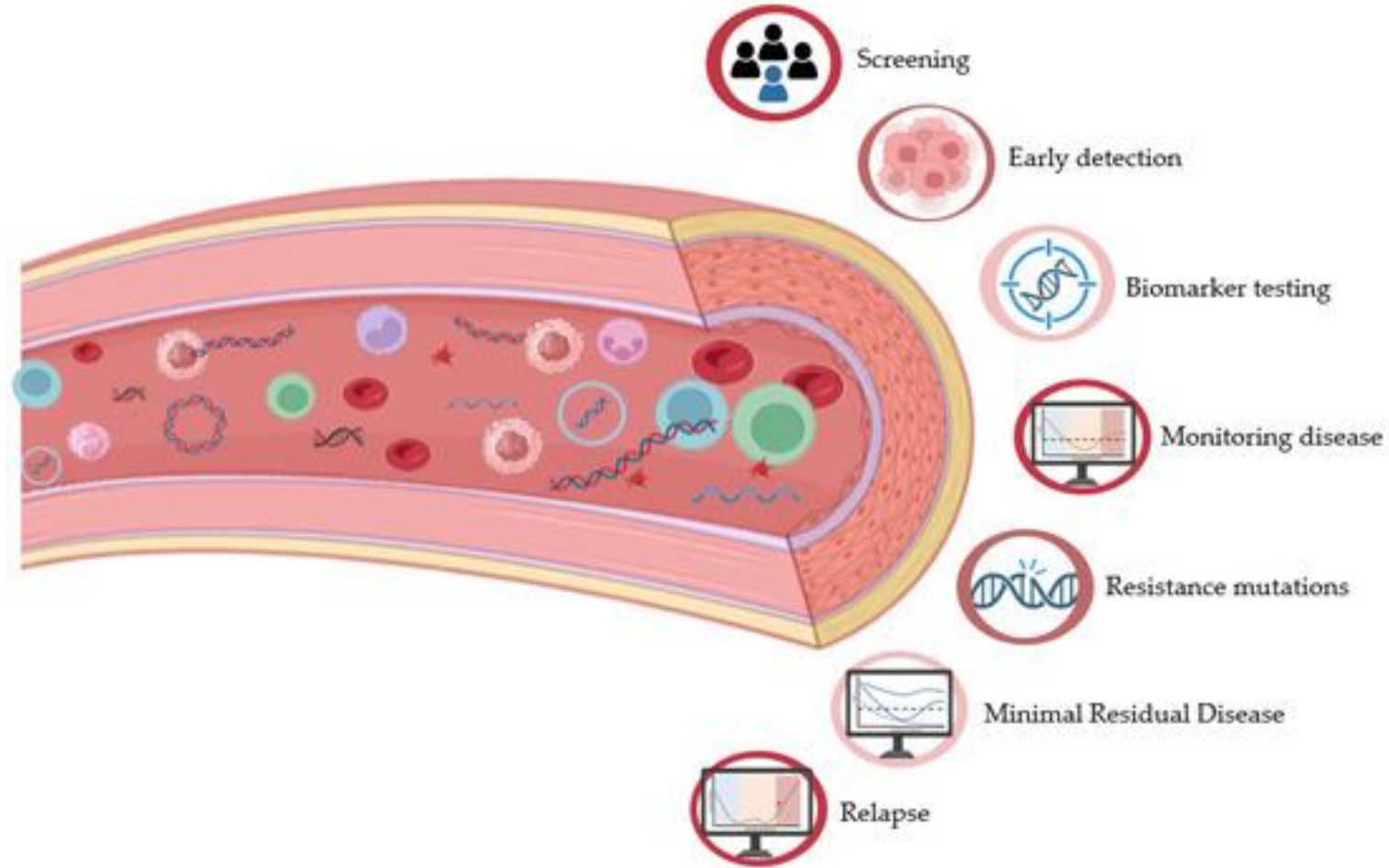


Can be inherited

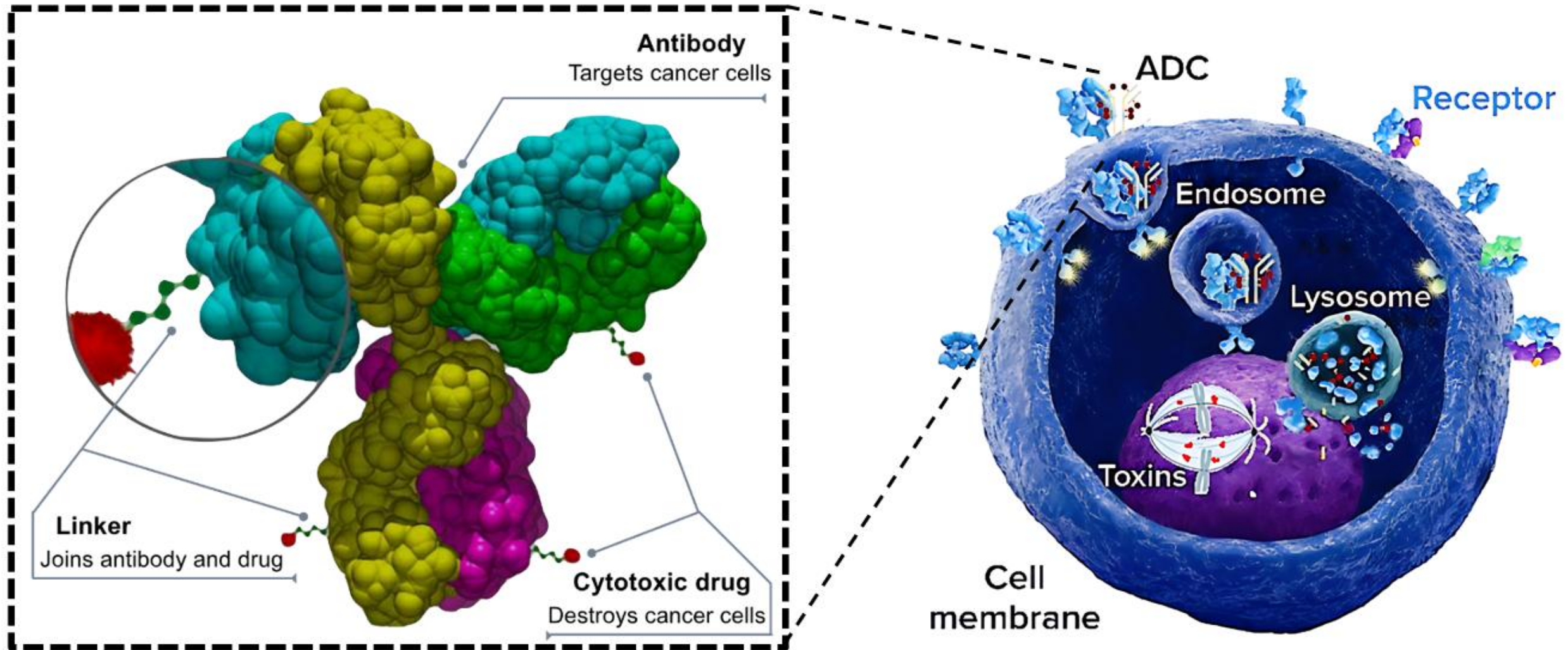


Liquid biopsy applications in cancer care

- Tumor cells and DNA are routinely shed into blood
- Can find one cancer cell among million healthy cells or trace amounts of ctDNA.
- Can be used to identify specific mutations and guide targeted therapy
- Can detection of unique ctDNA fragments for minimal residual disease surveillance
- Early detection on the horizon.

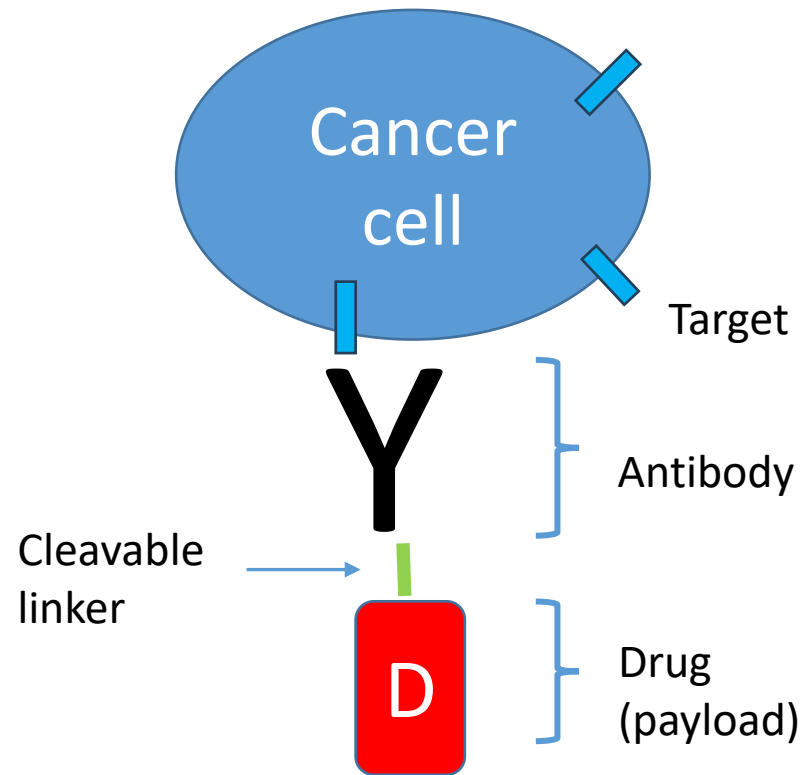


New kid on the block: Antibody-Drug Conjugates (ADCs)



ADC “Smart bombs” to attack ovarian cancer

Ovarian Cancer Targets with ADCs in clinical trial:



Folate Receptor alpha

HER2

Napi-2B

CDH6

B7H4

B7H3

TROP2

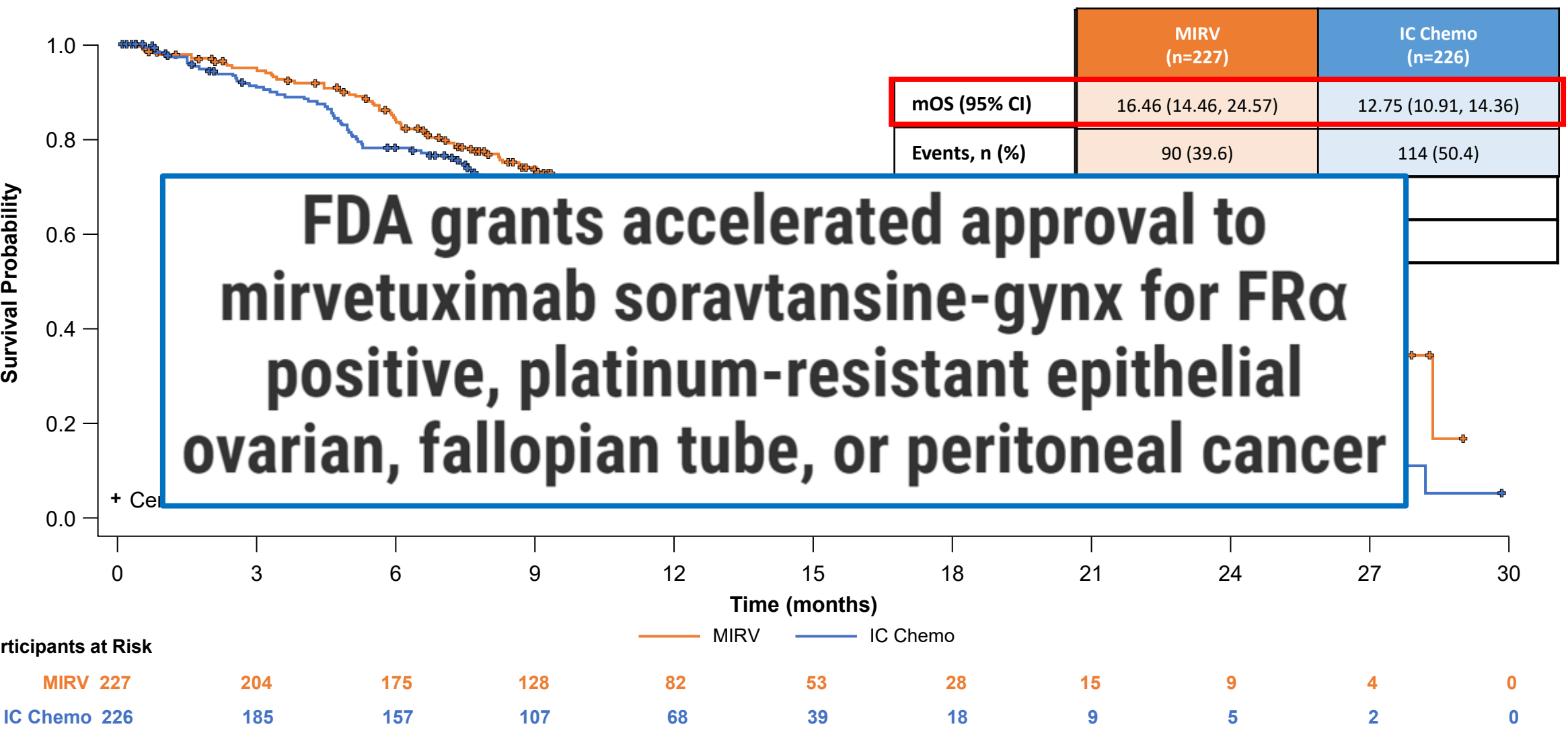
Mesothelin

Claudin-6

Mirvetuximab soravtansine-gynx

- Mirvetuximab is an antibody-drug conjugate (ADC) comprised of:
 - FR α -binding antibody
 - Cleavable linker
 - Maytansinoid DM4 payload, a potent tubulin-targeting agent
 - Drug Antibody Ratio (DAR): 3.4
- FR α (folate receptor 1 (FOLR1)): limited expression on normal tissues but is elevated in 80-90% ovarian cancers
- Lessons learned in development:
 - Need to optimize companion diagnostic: 1st Phase III of mirvetuximab (FORWARD I) was negative.
 - FOLR1 assay changed, cut-off increased in follow-up clinical trials
 - Use Adjusted Ideal Body Weight
 - SORAYA (single arm trial) , MIRASOL (confirmatory randomized phase III RCT)

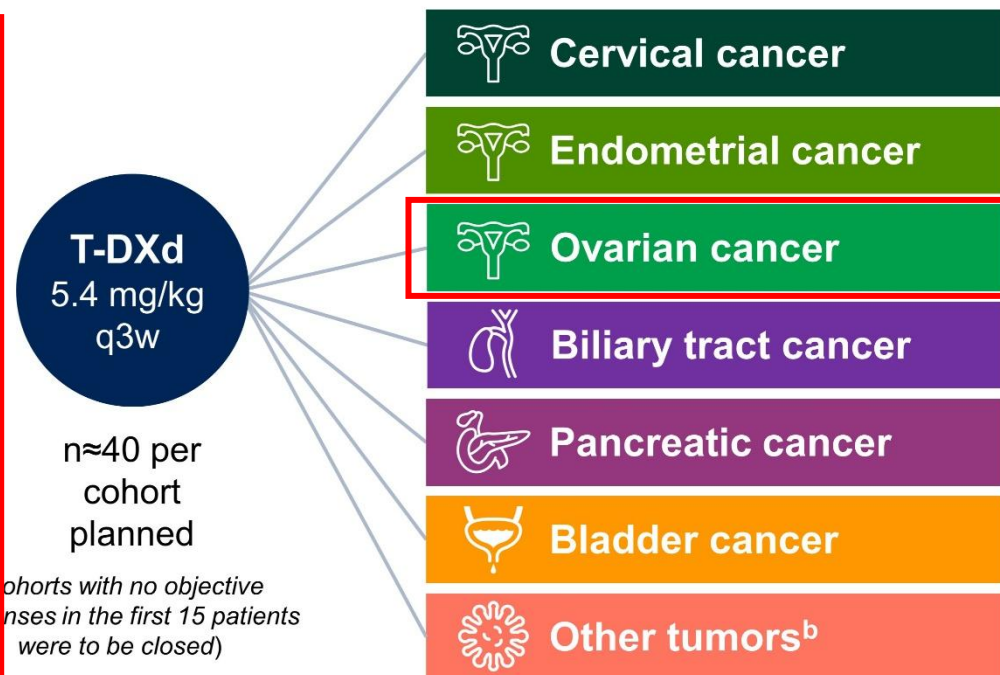
Overall Survival in MIRASOL Clinical Trial (Elahere)



DESTINY-PanTumor02: A Phase 2 Study of T-DXd for HER2-Expressing Solid Tumors

An open-label, multicenter study (NCT04482309)

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
 - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines¹)^a
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1



Primary endpoint

- Confirmed ORR (investigator)^c

Secondary endpoints

- DOR^c
- DCR^c
- PFS^c
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

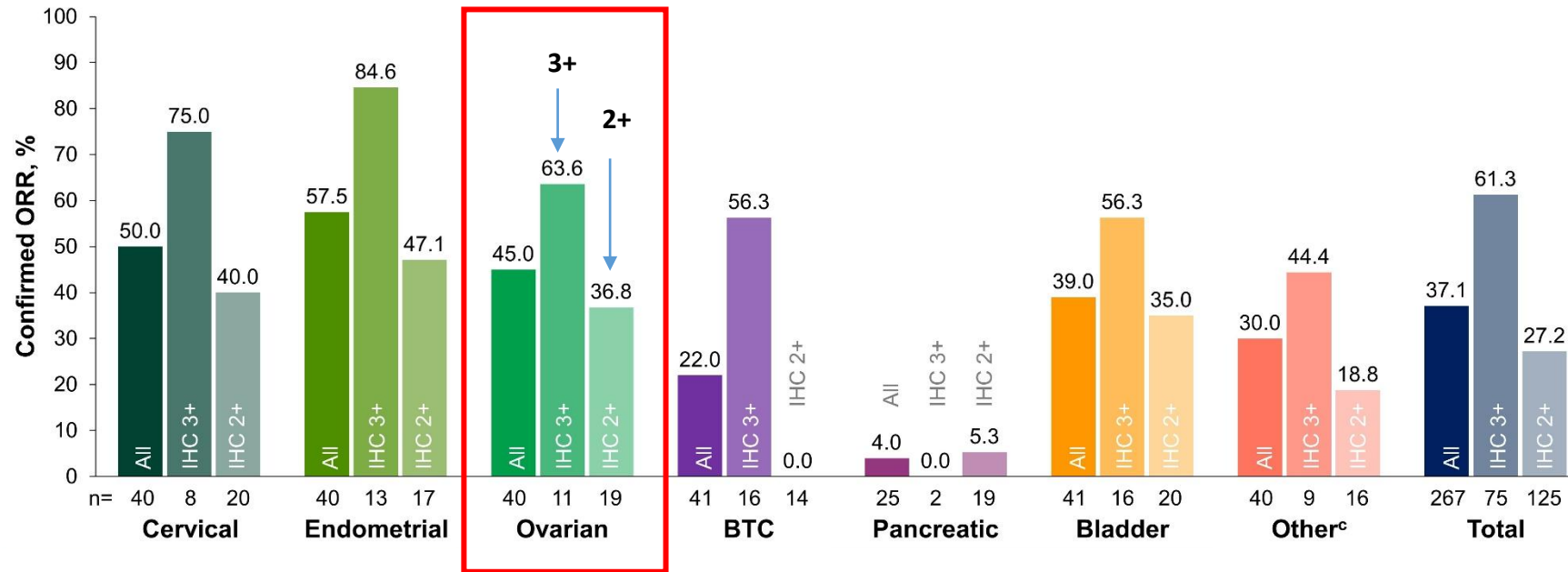
^aPatients were eligible for either test. All patients were centrally confirmed. ^bPatients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.

^cInvestigator-assessed per Response Evaluation Criteria In Solid Tumors version 1.1.

2L, second-line; ASCO, American Society of Clinical Oncology; DCR, disease control rate; CAP, College of American Pathologists; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.

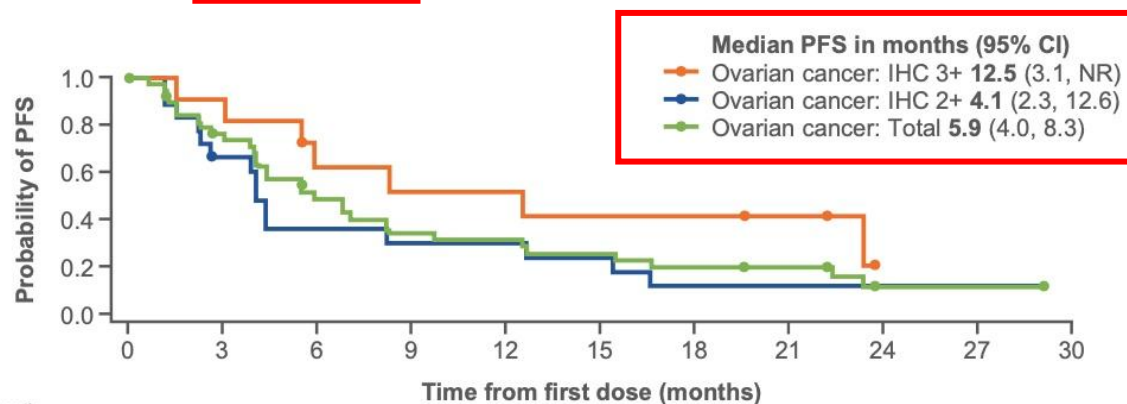
1. Hofmann M, et al. *Histopathology* 2008;52(7):797–805.

Objective Response Rate by HER2 status



2024:
Accelerated
FDA approval
for **HER2 3+
IHC** regardless
of cancer type

2024:
NCCN ovarian
cancer guidelines
adopted 2B rec
for **2+ HER2 IHC**



Number at risk, month

Ovarian cancer: IHC 3+	11	10	6	5	5	4	4	3	0		
Ovarian cancer: IHC 2+	19	11	6	5	5	4	2	2	1	1	0
Ovarian cancer: Total	40	28	17	12	11	9	7	6	1	1	0

ASCO 2023, ESMO 2023

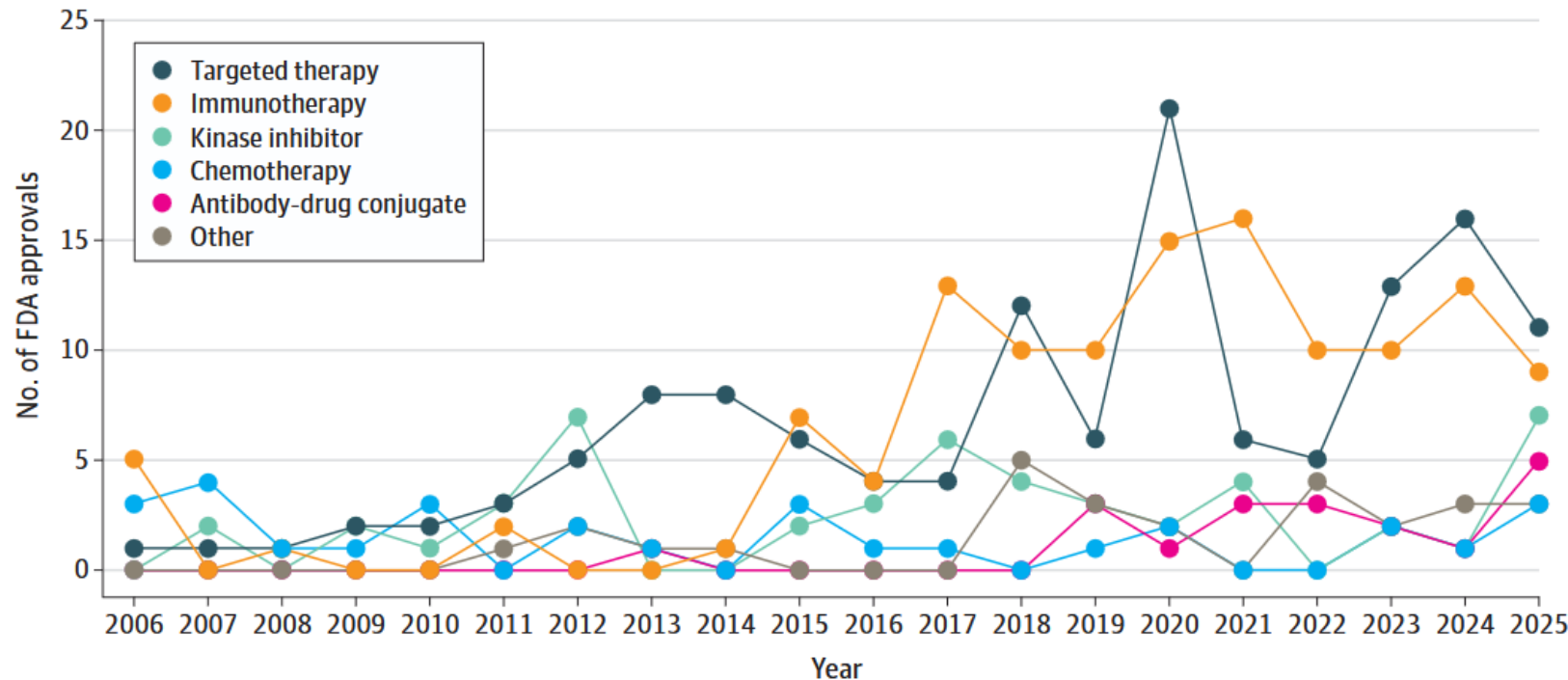
Phase 2/3 ongoing or planned ADC studies in ovarian cancer

Line of therapy	Phase of trial	Year launched	ADC	Trial name	Trial design	NCT#	Data readout
1 st line	III	not yet	Trastuzumab Deruxtecan (HER2)	ENGOT-ov89/DESTINY-OV-01	Maintenance HER2+	NCT06819007	
	III	not yet	Sacituzumab tirumotecan; Sac-TMT (TROP-2)	ENGOT-ov85/MK-2870-021	1 st line HRP	none yet (planned)	
2 nd line platinum sensitive	III	not yet	Sac-TMT (TROP-2)	ENGOT-ov-84/GEICO141/MK-2870-022	2 nd line Platinum sens	none yet (planned)	
	III	2022	Mirvetuximab (FOLR1)	GLORIOSA	Mirvetuximab/bev vs bev alone, as maintenance	NCT05445778	March 2027 PFS
Platinum resistant	II/III	2023	Luveltamab tazevibulin (FOLR1)	ENGOTov79/GEICO134-O/STRO-002-GM3 (REFRaME-01)	2-4 previous lines, FR α +	NCT05870748	Aug 2027: PFS, ORR
	II/III	2024	Raludotatug-DXd (CDH6)	REJOICE-Ovarian01	2-4 previous lines, high grade	NCT06619236	Dec 2027: PFS, ORR
	III	2024	Rinatabart sesutecan (FOLR1)	ENGOT-ov86/GEICO152-O/RAINFOL-OV2	2 line + lines	NCT06619236	Feb 2027: PFS

US FDA Cancer Medicine Approvals 2006-2025

Over the last 20 years, FDA approved 385 unique indications for medicines to treat solid tumors: 40% novel new drugs, 60% supplemental new indications

A Approvals by drug type



“Other” includes hormone therapy, cell therapies, immunomodulatory drugs and radiopharmaceuticals

FDA Approvals in Ovarian Cancer

An uneven history, with a recent acceleration in new approvals:



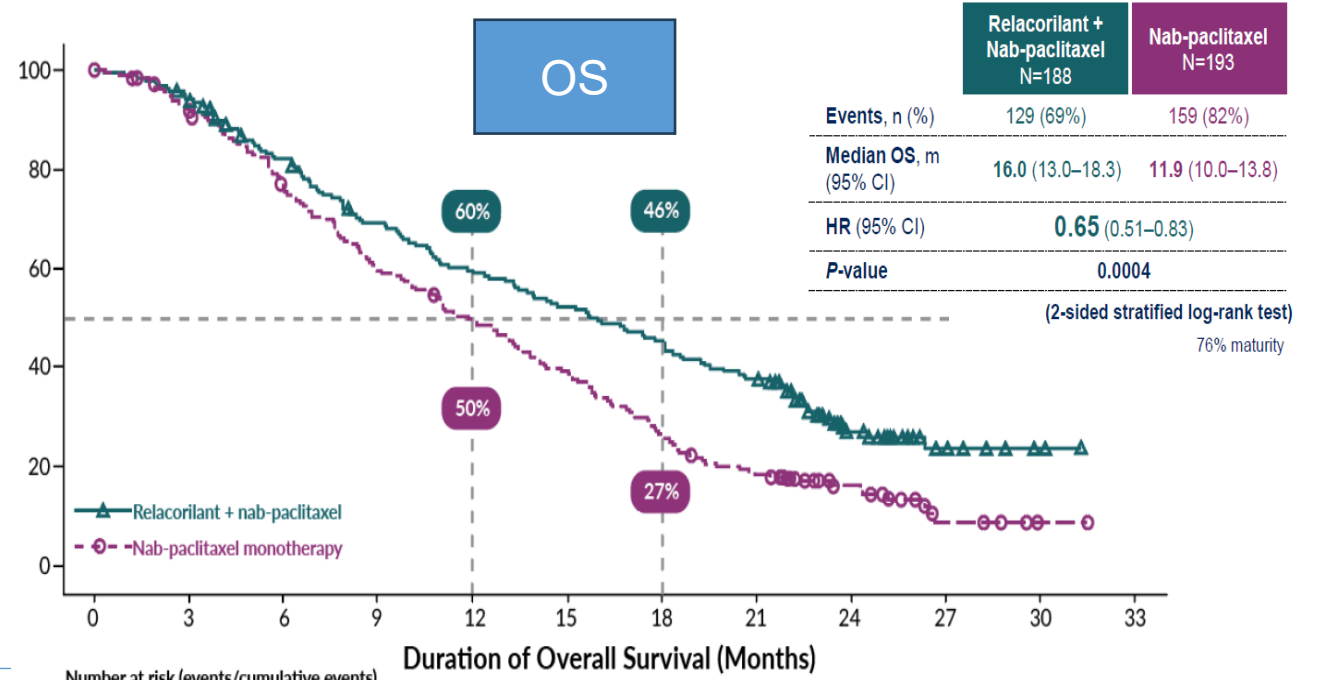
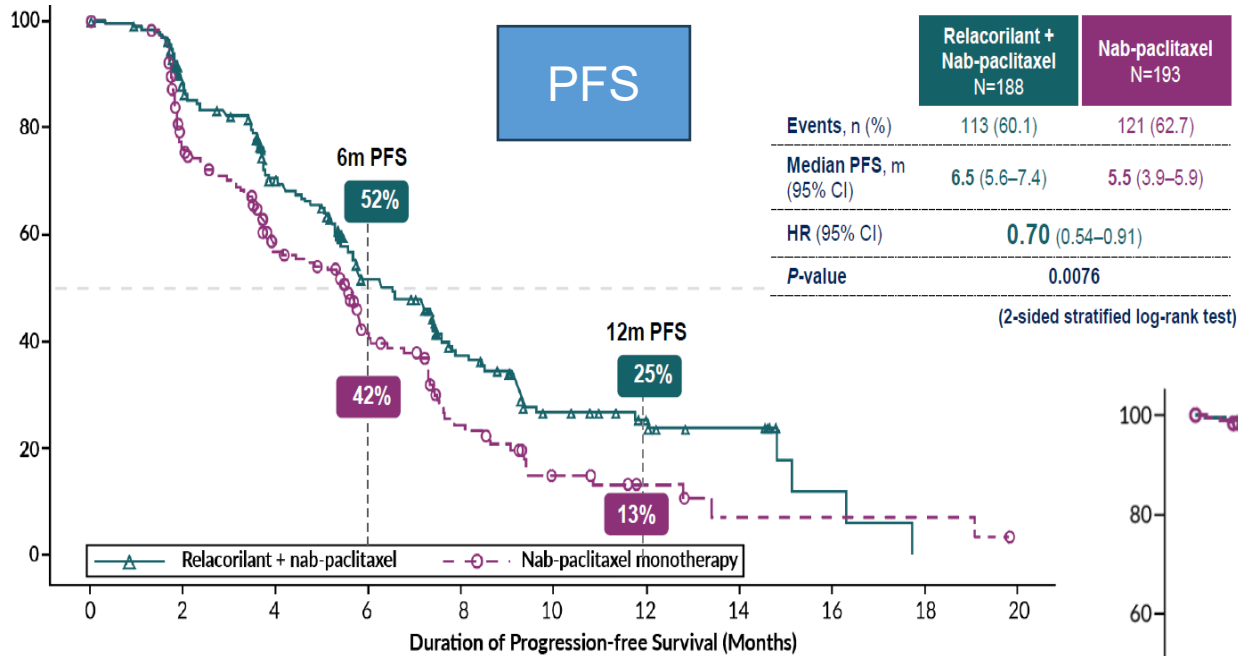
RECENT HISTORY AND EVEN BRIGHTER PATH AHEAD

PARP era → biomarker-selected ADCs → targeted combinations + immunotherapy

Recent progress has been especially notable in biomarker-defined therapies and approaches to platinum-resistant disease.

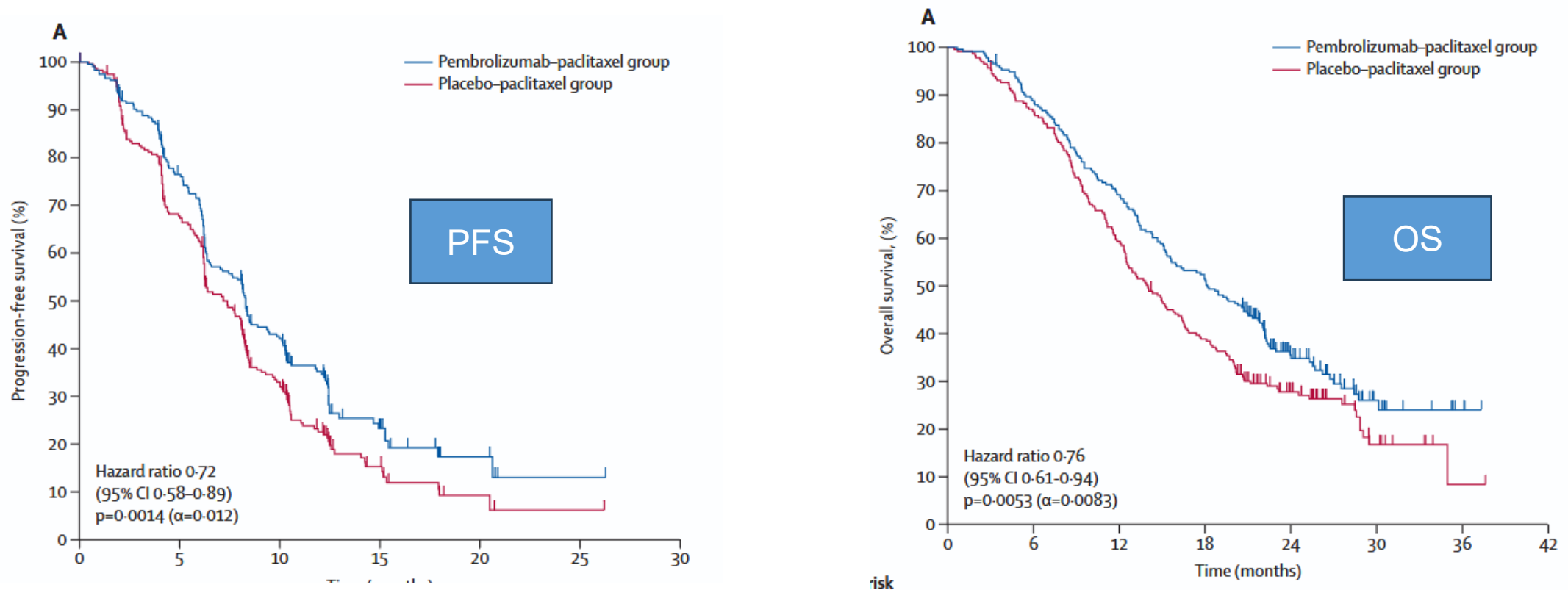
2026 FDA approvals for Platinum-resistant ovarian cancer

ROSELLA Trial: Nab-Paclitaxel +/- Recorilant



2026 FDA approvals for Platinum-resistant ovarian cancer

KEYNOTE-B96 Trial*: Pembrolizumab + weekly Paclitaxel +/- Bevacizumab

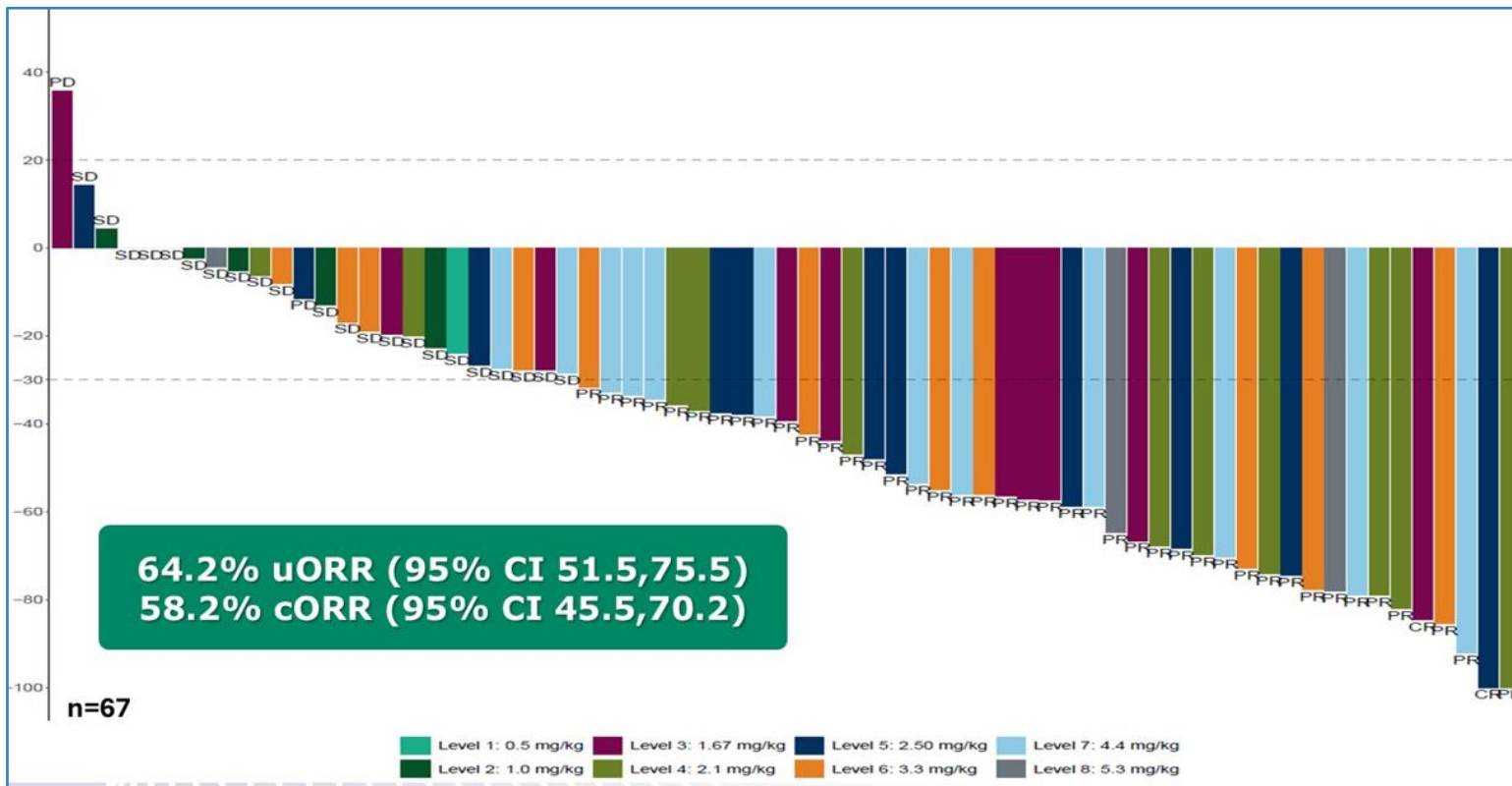


*Biomarker driven: CPS $\geq$ 1

Emerging Targets and Therapies: NaPi2b

NAPISTAR 1-01: Results of phase 1 dose escalation of monotherapy with TUB-040, a novel NaPi2b-targeting exatecan ADC, in patients (pts) with platinum-resistant ovarian cancer (PROC)

Toon Van Gorp, Jalid Sehouli, Debra L. Richardson, Rebecca Kristeleit, Shiraj Sen, Juergen Wolf, Valentina Boni, Alexander Spira, Alexander Starodub, Björn Hock, Charles S. Fuchs, Yariv Houvras, Ines Vasconcelos, Antonio Gonzalez-Martin.



NaPi2b: Sodium-dependent phosphate transport protein. Maintains phosphate balance in cells.

Overexpressed in 90% HGSC

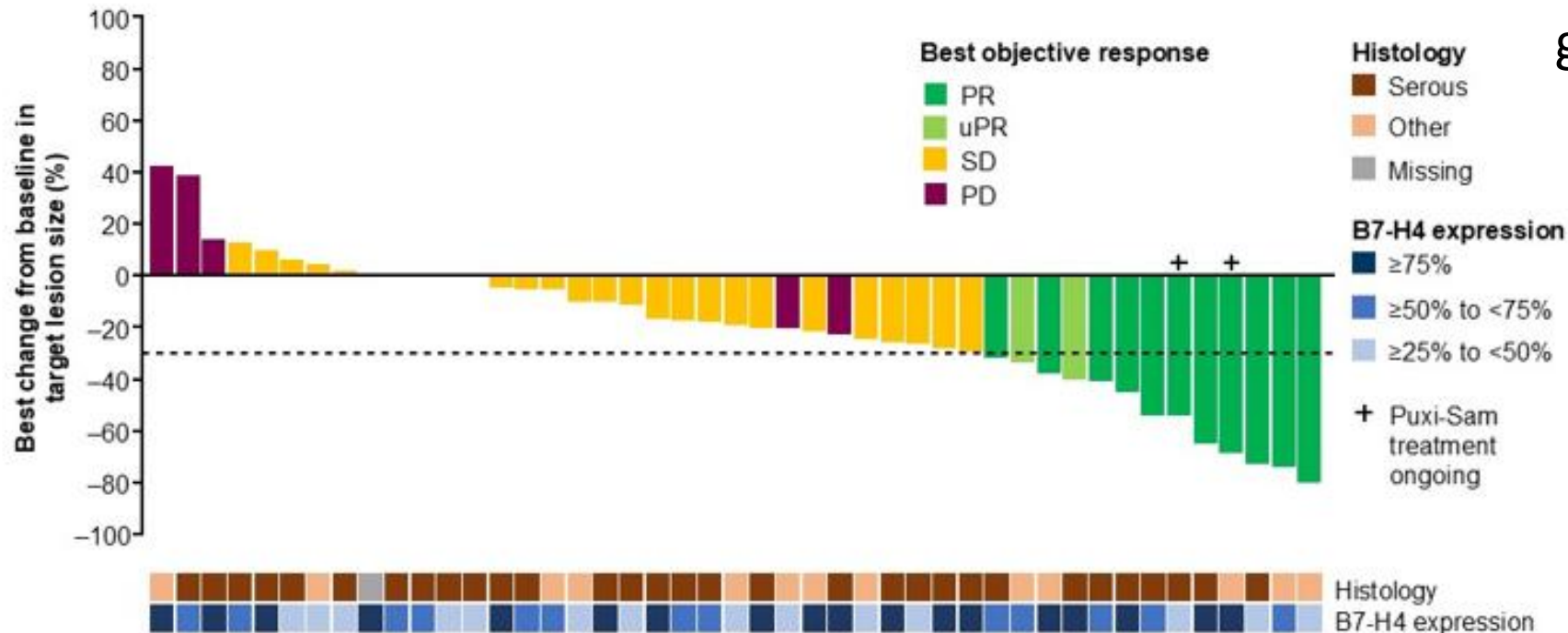
Older ADCs discontinued due to toxicity and modest response.

Emerging Targets and Therapies: B7-H4

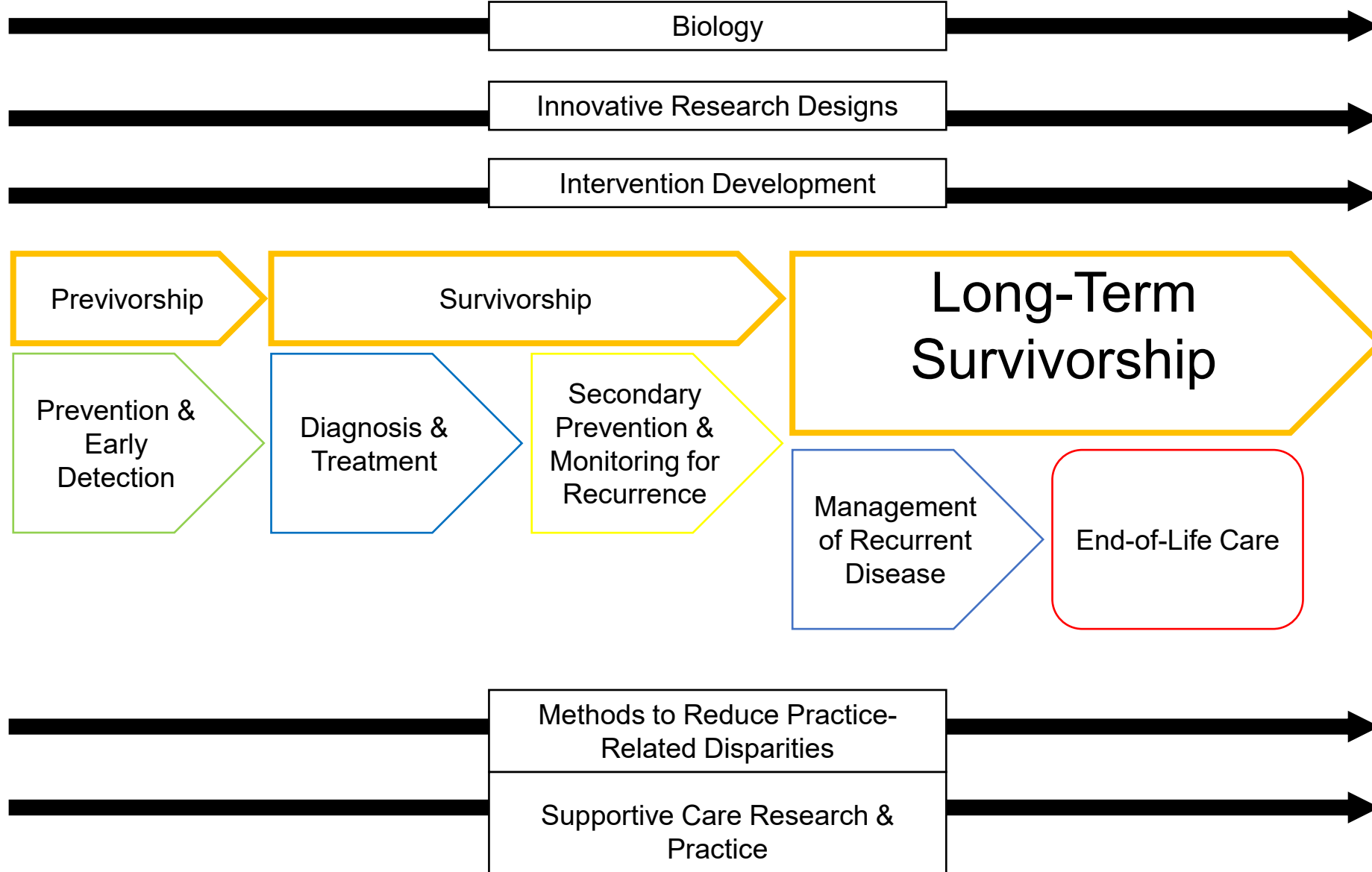
Updated safety and efficacy of puxitug samrotecan (Puxi-Sam, AZD8205) in patients with endometrial cancer (EC) or ovarian cancer (OC): Phase 1/2a BLUESTAR study

Linda Mileskin,¹ Stephanie Gaillard,² Robin Guo,³ Yoichi Naito,⁴ Karen Finkelstein,⁵ Anna V Tinker,⁶ R Wendel Naumann,⁷ Gun Min Kim,⁸ Toon Van Gorp,⁹ Marloes van Dongen,¹⁰ Thatthan Suksombooncharoen,¹¹ Tatsunori Shimoi,¹² Wang Jing,¹³ Joo Ern Ang,¹⁴ Theresa Proia,¹⁵ Sarah Cross,¹⁶ Chris Gibbs,¹⁶ Mohamed Zaid,¹⁵ Andreea Varga,¹⁶ Funda Meric-Bernstam¹⁷

B7-H4 puts a brake on immune response. Cancer cells overexpress B7-H4 and creates a shield allowing them to evade T-cells and can drive tumor growth and metastasis



Continuum of Ovarian Cancer Care and Research



Ovarian cancer survivorship



**Sharsheret 5th Annual
West Coast Dash
Sunday October 25, 2026
Playa Del Rey, CA**

Ovarian cancer survivorship plans: an important standard of care

Issues including:

- Menopause symptom management
- Sexual health
- Fatigue
- Peripheral neuropathy
- Lymphedema
- Cognitive complaints
- Anxiety, depression, PTSD
- Accelerated aging
- Financial toxicities

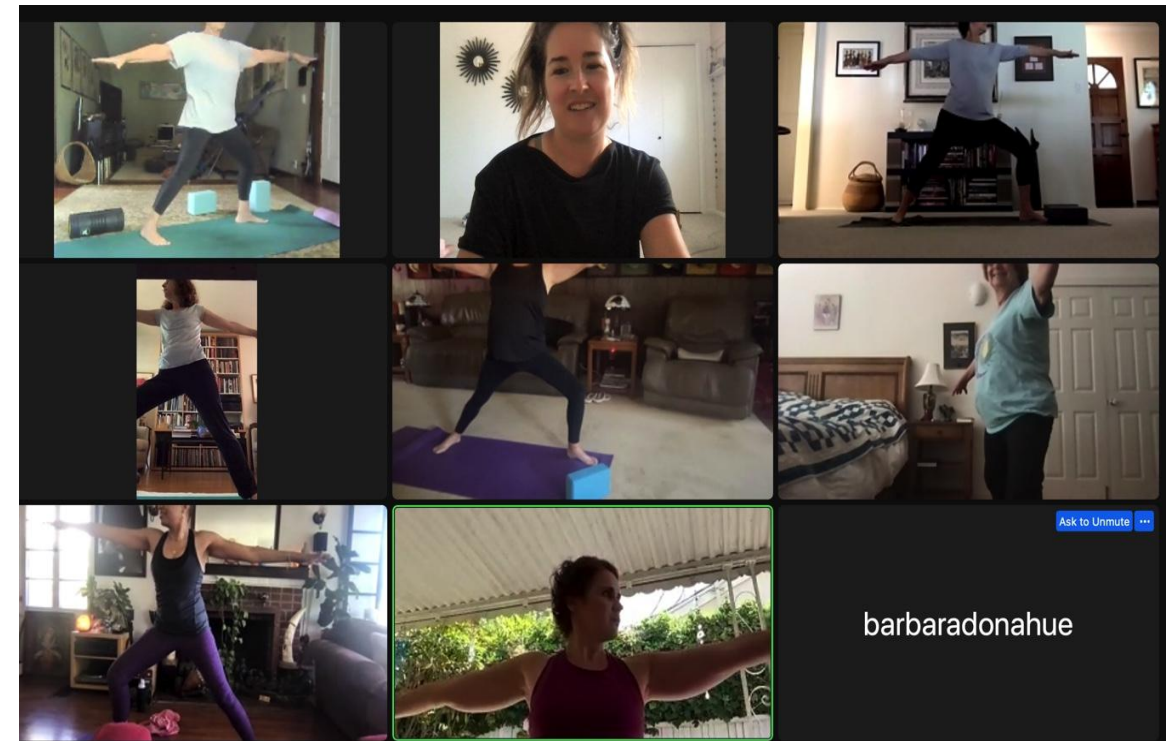
Actions:

- Healthy lifestyle, stress reduction
- Physical activity, yoga/Tai-chi
- Healthy diet
- Genetic testing
- Second cancer prevention
- **Launch new subspecialty of survivorship clinicians**
- Clinical trials to define evidence-based approaches to mitigate symptoms and improve quality of life

Integrative Care is part of cutting-edge cancer care

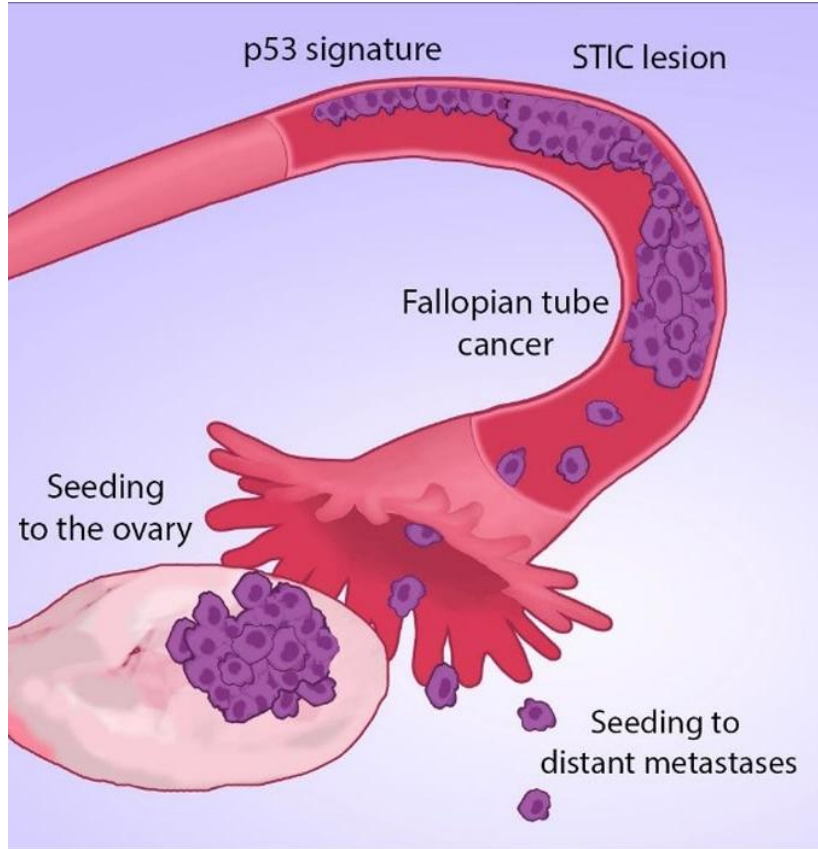
- Yoga can improve fatigue, pain, anxiety, depression, sleep, enhance immune system, improve balance and mobility, help with weight loss and bone health.
- 8 wk class, 8-10 pts/session
 - Less stiffness, improved balance
 - Improved brain fog, mood, sleep
 - Less anxiety, depression

UCLA Gyn Cancer Yoga Class



An ounce of
prevention
is Worth a pound
of cure.

Most ovarian cancers begin in the fallopian tube



Shifted current focus from screening to prevention

- Risk reduction surgery is the most effective way to reduce mortality
- Use of SEE-FIM protocol to interrogate tubal pathology and identify STIC lesions
- When a STIC lesion is found, the subsequent risk of HGSC is ~10% at 5yrs and ~25% at 10 yrs

Opened new avenues for prevention and interception research

The next prevention horizon: Opportunistic Salpingectomy (OS)

Impact of OS on serous ovarian cancer incidence

- Salpingectomy replaced tubal ligation and routinely performed at time of hysterectomy
- Follow up experience from 2008-2017 in BC, Canada

	Person Years	Ovarian Cancer Events
Opportunistic Salpingectomy	189,101	<5
NO Opportunistic Salpingectomy	370,133	21

HR = 0.22 (0.05, 0.95)

80% Reduction in Serous Ovarian Cancer

JAMA Netw Open
Published Online: February 2, 2026
2026;9;(2):e2557267.
doi:10.1001/jamanetworkopen.2025.57267

New ovarian cancer prevention guidance



- ACOG Clinical Practice Update 2026
- Endorsed by ACS, SGO, ESMO
 - OB/GYN should remove FT at time of hysterectomies
 - When childbearing complete, OB/GYN should offer OS at time of other gyn surgeries, including cesarean sections
 - OS should replace tubal ligation
 - OB/GYNs should support colleagues in counseling re: OS at time of non-gyn surgeries

The next prevention horizon: Bridging the implementation gap



- Broader awareness of effectiveness of OS among women and providers
- Wider access and availability of OS at time of abdominal surgeries
- Improve understanding and reduce mistrust

- Cancer risk estimates for *gBRCA* carriers

	Breast (Female)	Breast (Male)	Ovary	Pancreas	Prostate
<i>BRCA1</i>	>60%	0.2-1.2%	39- 58 %	<5%	7-26%
<i>BRCA2</i>	>60%	1.8-7.1%	13-29 %	5-10%	19-61%
General Population	13.3%	0.12%	1.3%	1.7%	13%

NCCN Guidelines: BOPP. 2026

Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate

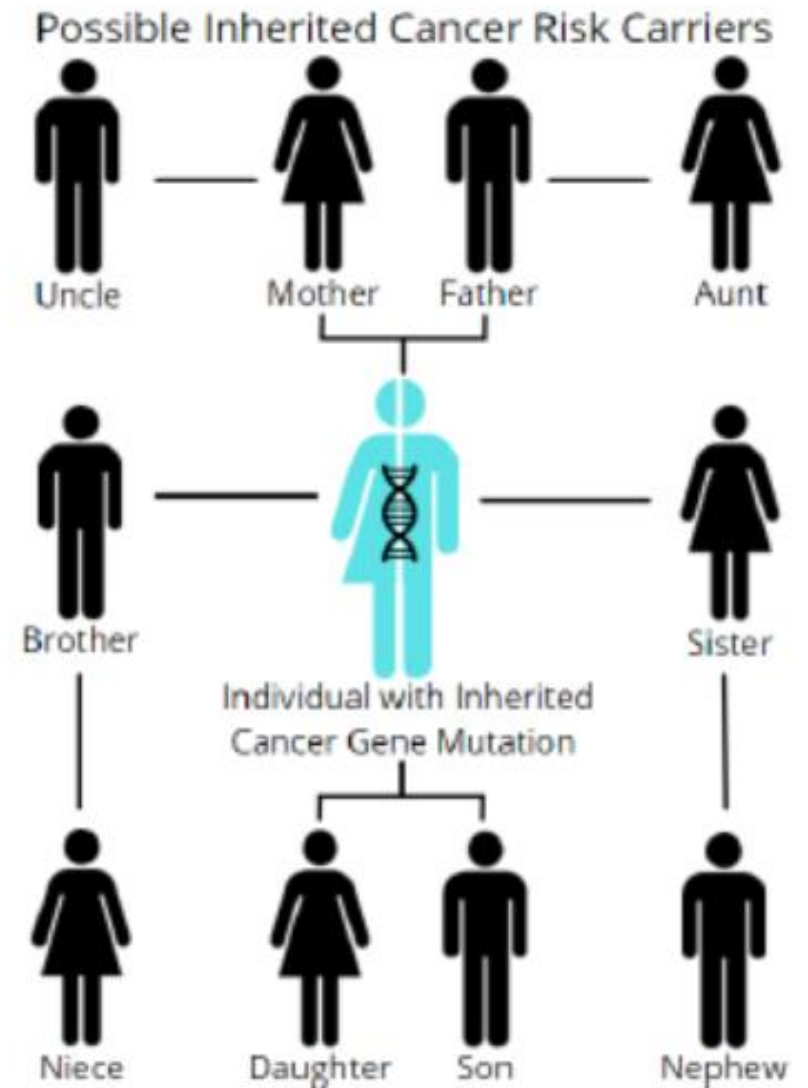
Version 3.2025 — March 6, 2025

NCCN.org

- RRSO recommended: 35-40 yo BRCA1, 40-45 yo BRCA2
- No effective screening tests at this time
- Salpingectomy (with delayed oophorectomy) should be discussed in context of patient's reproductive plans as interim step before oophorectomy

- Cascade testing is the extension of genetic counseling and testing to blood relatives of individuals found to have a pathogenic variant in a gene predisposing them to cancer.
- Cascade testing provides an opportunity for population-wide cancer prevention and control
- Cascade genetic testing for hereditary cancer risk is an underutilized tool for cancer prevention.
- Greatest return on investment for genetic counseling is in the application of cancer early detection and prevention interventions in these high-risk populations

- Cascade testing provides an opportunity for population-wide cancer prevention and control
- Extension of genetic testing to blood relatives of individuals with a mutation a hereditary cancer gene
- Greatest return on investment for genetic testing to identify at-risk individuals
- Cascade testing is underutilized!
 - ~50-70% patients tell their relatives and <50% relatives get genetic testing.



A teal-colored ribbon is tied in a loop on the left side of the image, with the ends trailing off towards the bottom right. The background is a light beige color with a subtle, repeating pattern of small teal dots.

TALK. EDUCATE. ADVOCATE. LIVE.

SEPTEMBER IS
OVARIAN CANCER
AWARENESS MONTH

Ovarian cancer call to action

- We've pushed the survival curve rightward, but almost all patients experience multiple recurrences and better survivorship care plans are needed
- Tumors are platinum sensitive at diagnosis, but emergence of resistance is almost universal and new treatments are urgently needed
- New drug approvals are great, but better insurance coverage needed
- Improve access and number of clinical trials as well as innovative designs
- Facilitate pathways to assure guideline concordant care and help eliminate inequities
- Implement efforts to broaden genetic testing, cascade testing, and primary prevention
- Increase research funding to ensure pipeline of clinical trialists, scientists, and new discoveries

Thank you for your attention



SHARSHERET

The Jewish Breast & Ovarian Cancer Community

**SHANA TOVA!
MAY YOU HAVE A YEAR
FULL OF JOY, LOVE
& HAPPINESS!
5787
WE'RE READY FOR YOU!**

