Clinical Trials 2023: Update and Highlights

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Disclosures

Consulting/advisory role: Merck, Seagen, AstraZeneca, Genmab, GSK, Aravive, Novocure, Alkermes, Genentech/Roche, Karyopharm, SutroBio, Immunogen, Mersana, BMS

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Endometrial Cancer 2023

66,200 new cases* | **13,030 deaths***

~2/3 of these will have early stage and low grade disease with excellent prognosis

~ 1/3 will have high grade or advanced stage/metastatic disease

Population of interest

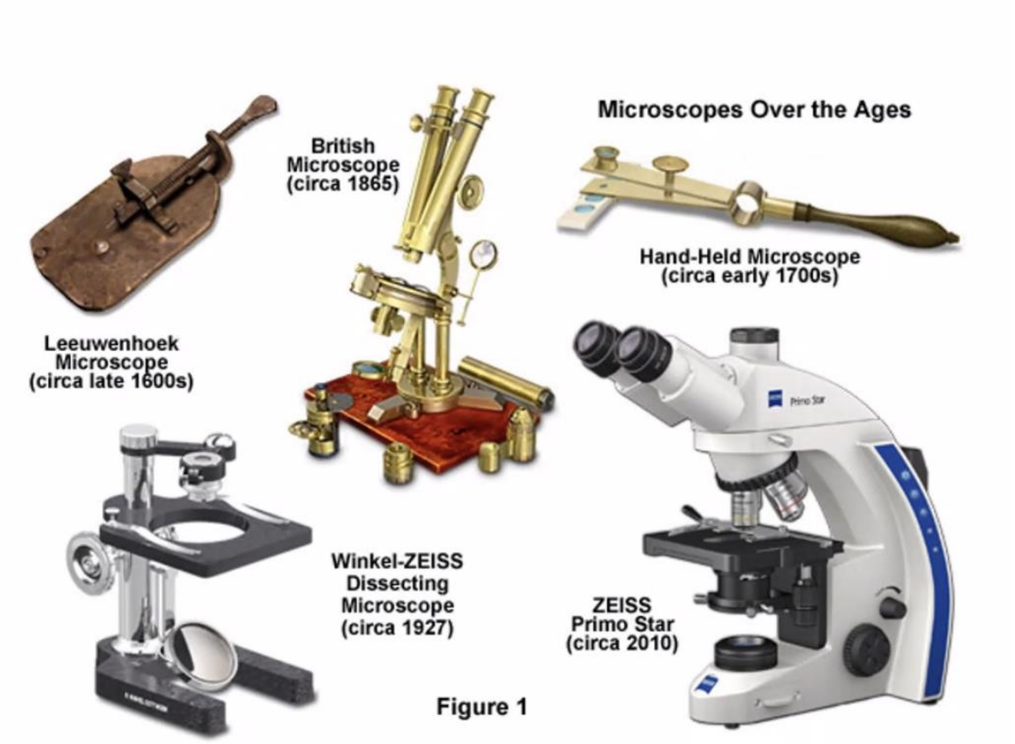
Increasing Incidence

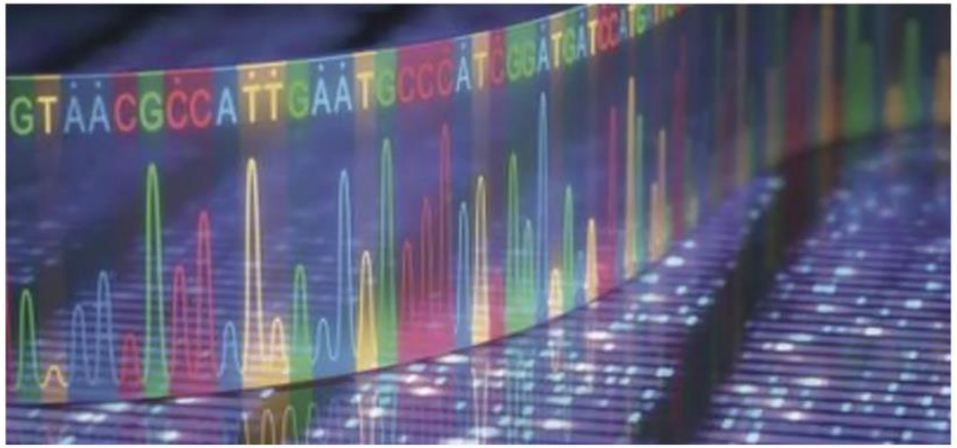
Increasing Mortality

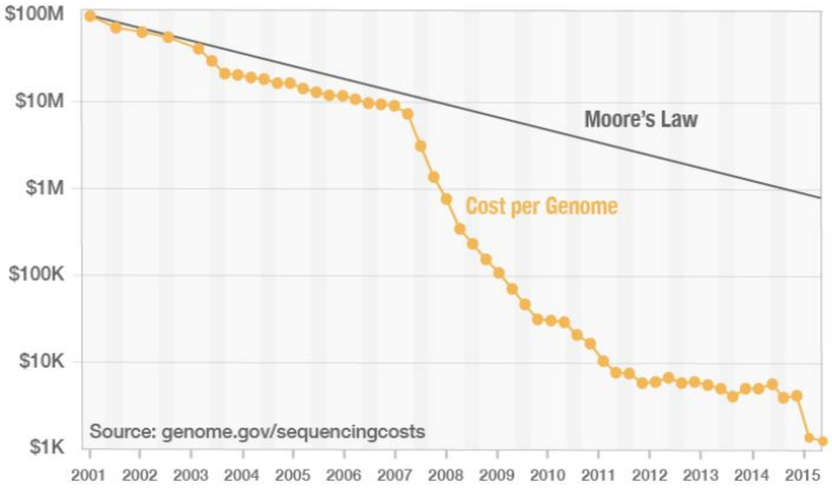
Anticipated to surpass ovarian cancer mortality in the coming years

Siegel et al. Cancer Statistics 2023
Cancer Facts & Figures 2023. American Cancer Society. Available at https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf. Accessed January 31, 2023.

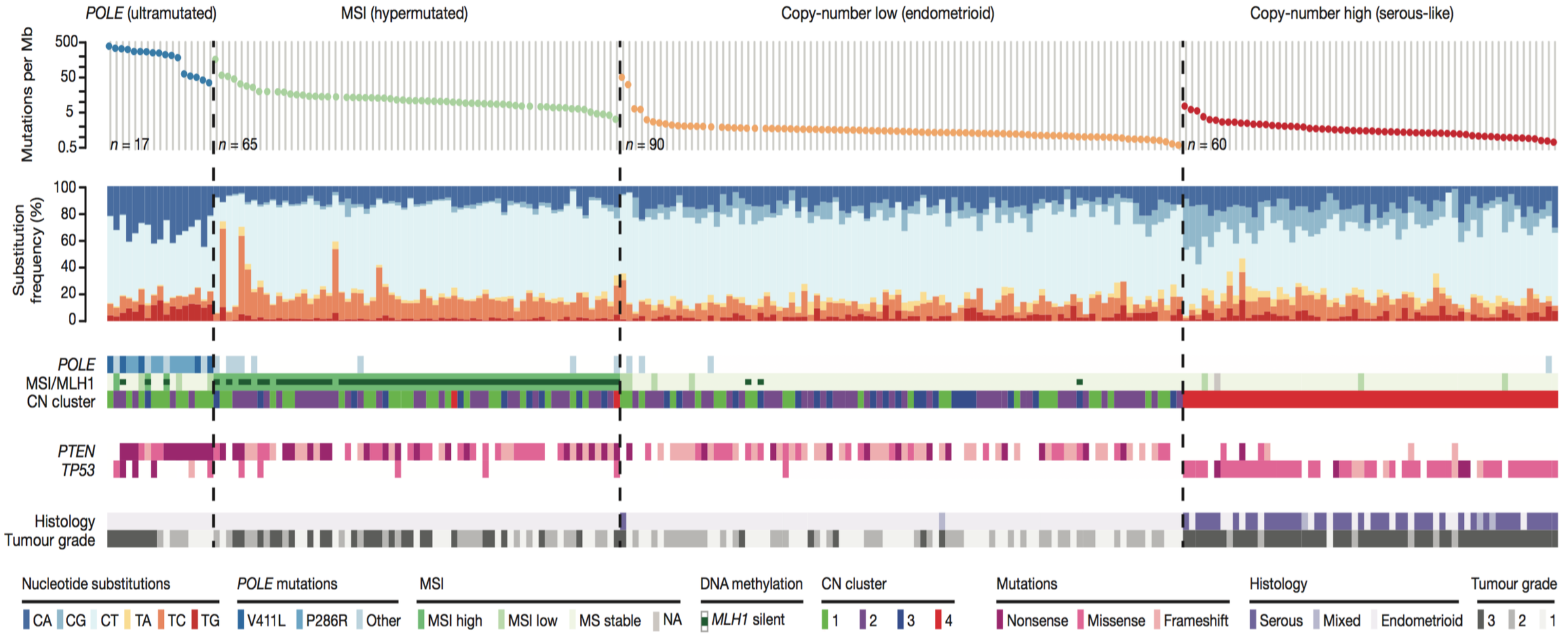
Endometrial Cancer: Moving from the Light Microscope to the Molecular Microscope







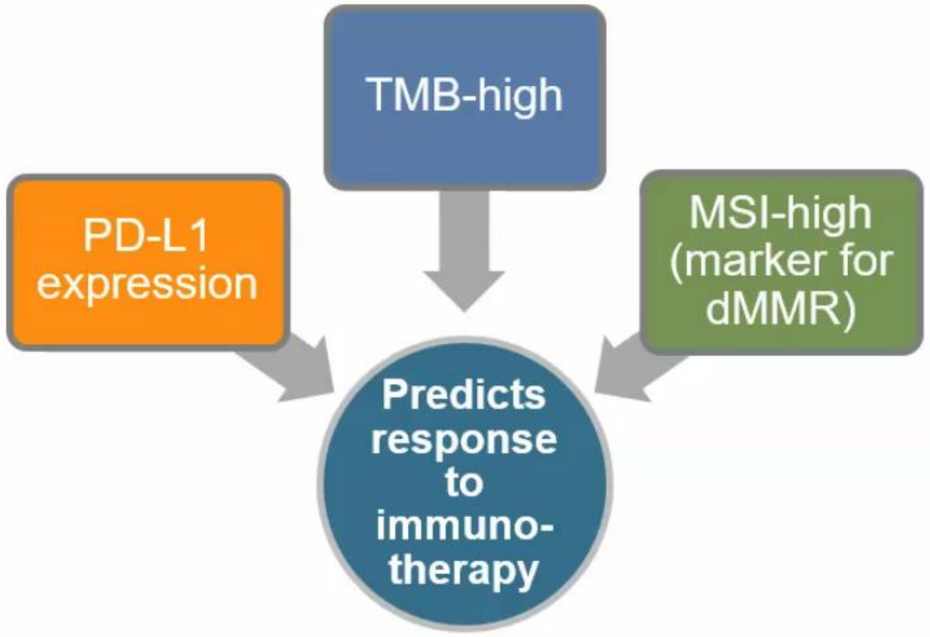
Endometrial Cancer: Molecular Characterization



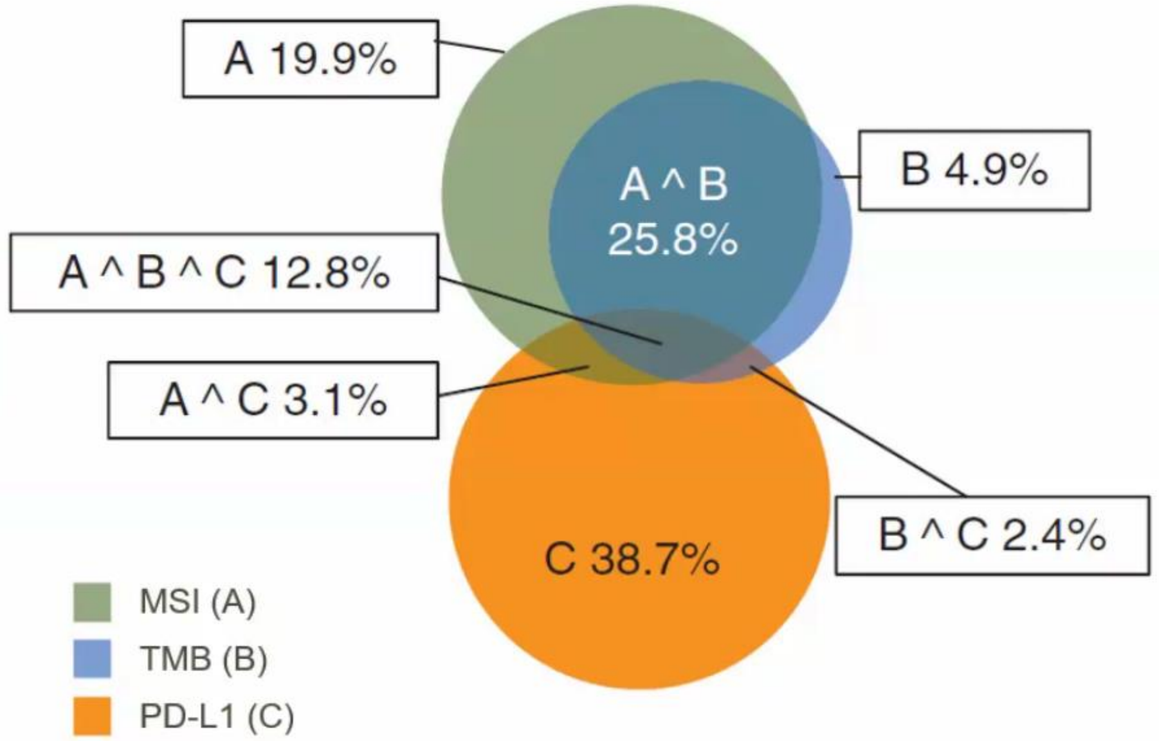
TCGA, Nature 2013

Relationship between PD-L1, TMB and MSI in Endometrial Cancer

Overlap between PD-L1 expression, TMB-high, and MSI-high varies across tumor types[1,2]

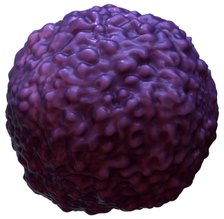


Relationship between MSI, TMB, and PD-L1 expression in EC*[1]



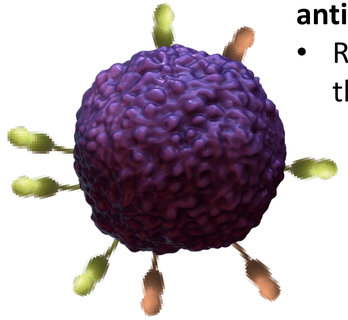
*Out of 4186 cases (100%) of solid tumors and generic cancer types.[1]
MMR, mismatch repair; MSI, microsatellite instability; PD-L1, programmed cell death ligand 1; TMB, tumor mutational burden.
1. Luchini C et al. *Ann Oncol.* 2019;30:1232-1243. **2.** Vanderwalde A et al. *Cancer Med.* 2018;7(3):746-756.

Rational for Combinatorial Approach with Chemotherapy + IO



Tumor cell death

- Immunogenic cell death
- Reduction of tumor cells producing immunosuppressive mediators



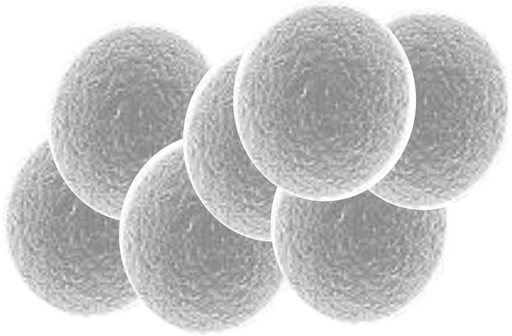
Increased expression of tumor antigens

- Recognized and targeted by the immune system

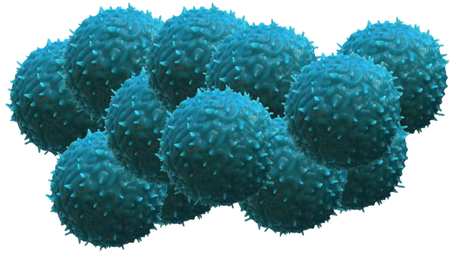
Anti-PD1

Chemo

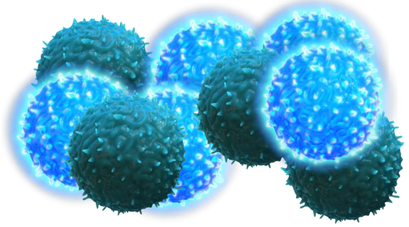
MDSC depletion



Treg depletion



Homeostatic proliferation of T cells



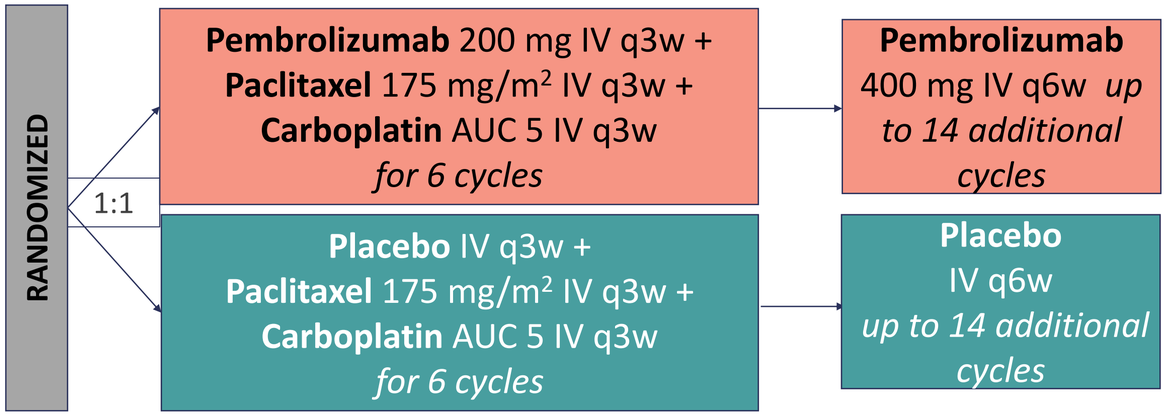
Chemo, chemotherapy; ICI, immune checkpoint inhibitors; IO, immunotherapy; MDSC, myeloid-derived suppressor cell; Treg, regulatory T cells.

1. Hato SV et al. *Clin Cancer Res.* 2014. 2. Chen Y et al. *Am J Cancer Res*. 2021. 3. Pfannenstiel T et al. *Cell Immunol*. 2010. 4. Sevko A et al. *J Immunol*. 2013.

NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC

Key Eligibility Criteria

- Measurable stage III/IVA or measurable/nonmeasurable stage IVB or recurrent EC
- MMR IHC testing
- ECOG PS 0-2
- No prior Chemo except adjuvant Chemo if completed ≥12 mo before study



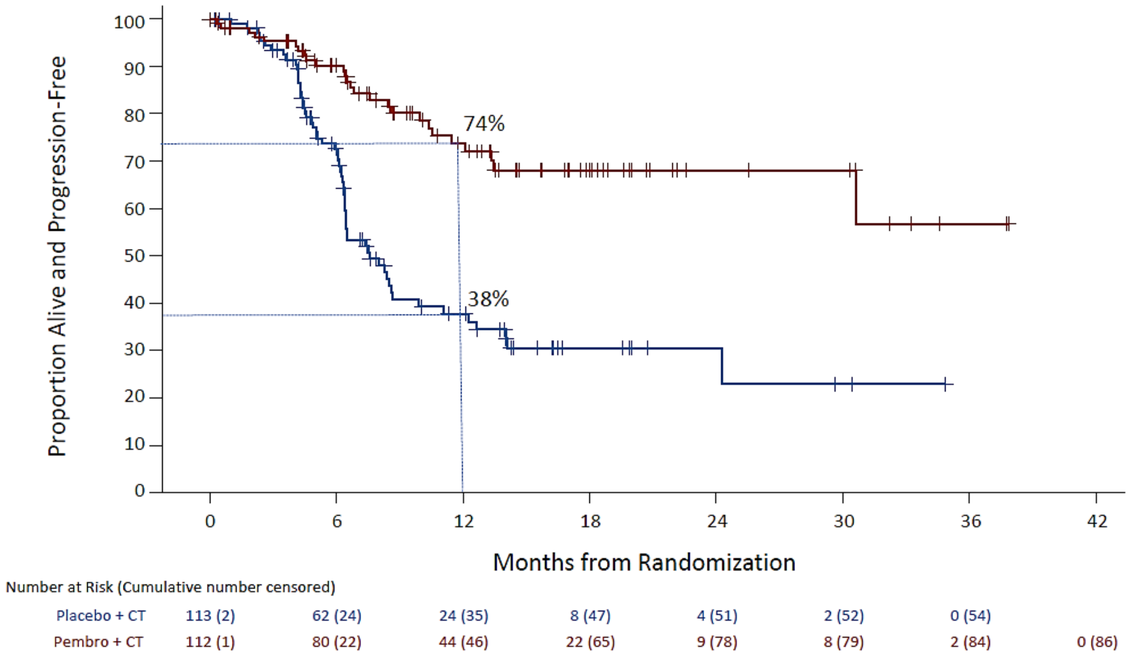
Stratified by MMR status (pMMR vs dMMR), ECOG status, and prior adjuvant Chemo

Primary endpoints: PFS per RECIST v1.1 by INV in pMMR and dMMR cohorts
Secondary endpoints: Safety, ORR/DOR, OS, PRO/QoL, concordance of MMR testing results

Patient Characteristics, n (%)		dMMR (n=225)		pMMR (n=588)	
		Pembro + CT (n=112)	Placebo + CT (n=113)	Pembro + CT (n=293)	Placebo + CT (n=295)
Median age (range), years		67 (38-81)	66 (37-85)	66 (31-93)	65 (29-90)
ECOG PS	0	72 (64.3)	73 (64.6)	196 (66.9)	198 (67.1)
	1	39 (34.8)	35 (31.0)	88 (30.0)	88 (29.8)
	2	1 (0.9)	5 (4.4)	9 (3.1)	9 (3.1)
Histology					
Clear cell		1 (0.9)	0	17 (5.8)	20 (6.8)
Endometrioid, G1		21 (18.8)	35 (31.0)	54 (18.4)	46 (15.6)
Endometrioid, G2		52 (46.4)	41 (36.3)	51 (17.4)	58 (19.7)
Endometrioid, G3		15 (13.4)	16 (14.2)	53 (18.1)	42 (14.2)
Serous		4 (3.6)	1 (0.9)	78 (26.6)	72 (24.4)
No prior chemotherapy		107 (95.5)	105 (92.9)	221 (75.4)	218 (73.9)

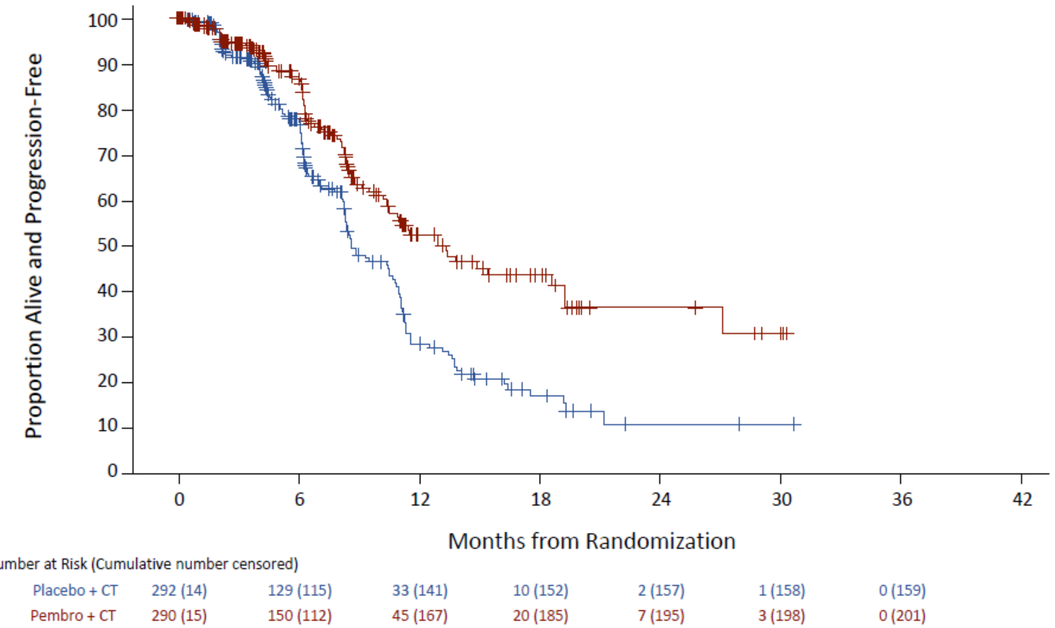
NRG GY018: Phase 3 Trial of Pembrolizumab + Chemo for Measurable Stage 3 or 4a, Stage 4b, or Recurrent EC – PFS

PFS per RECIST v1.1 in dMMR Population



	Events, n/N	Median (95% CI), mo	HR (stratified; 95% CI)
Pembro + CT	26/112	NR (30.6-NR)	**0.30 (0.19-0.48) P<0.00001**
Placebo + CT	59/113	7.6 (6.4-9.9)	

PFS per RECIST v1.1 in pMMR Population



	Events, n/N	Median (95% CI), mo	HR (stratified; 95% CI)
Pembro + CT	89/290	13.1 (10.5-18.8)	**0.54 (0.41-0.71) P<0.00001**
Placebo + CT	133/292	8.7 (8.4-10.7)	

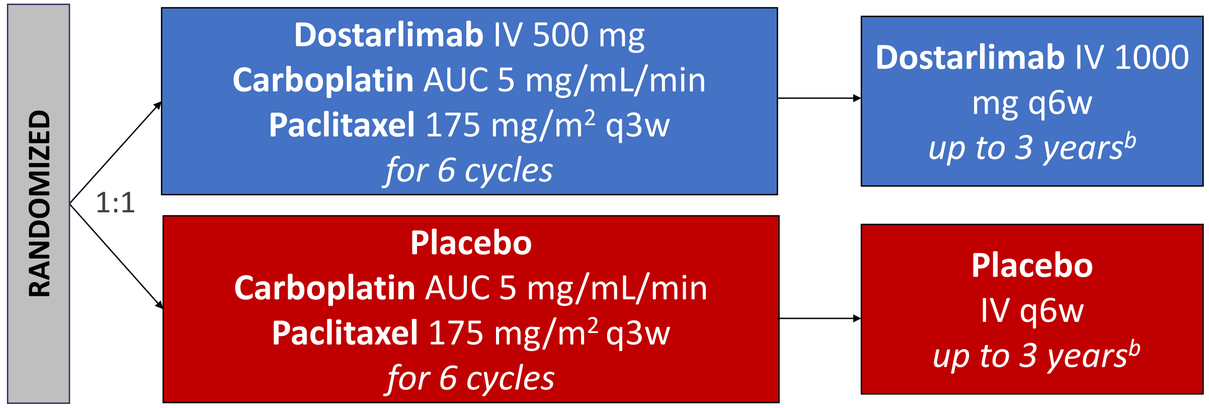
- **Median follow-up: 12 months for dMMR, 7.9 months for pMMR**

Data cutoff: December 16, 2022 for dMMR; December 6, 2022 for pMMR.
Eskander R, et al. N Eng J Med. March 2023

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC

Key Eligibility Criteria

- Histologically/cytologically proven stage III/IV or first recurrent EC
- Carcinosarcoma, clear cell, serous, or mixed histology permitted[a]
- ECOG PS 0-1
- Naive to systemic therapy or systemic anticancer therapy and had a recurrence or PD ≥6 months after completing treatment



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

Primary endpoints: PFS by INV, OS
Secondary endpoints: PFS by BICR, PFS2, ORR, DOR, DCR, HRQOL/PRO, safety

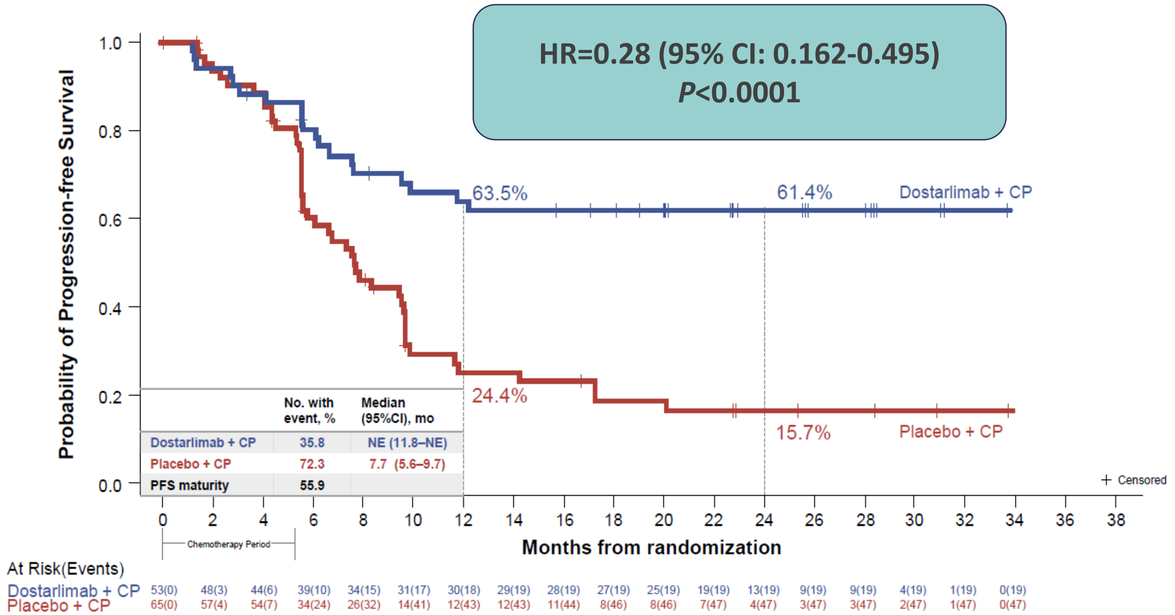
Patient Characteristics, n (%)		dMMR/MSI-H		Overall	
		Dostarlimab + CP (n=53)	Placebo + CP (n=65)	Dostarlimab + CP (n=245)	Placebo + CP (n=249)
Median age (range), years		61 (45-81)	66 (39-85)	64 (41-81)	65 (28-85)
ECOG PS	0	28 (53.8)	39 (60.0)	145 (60.2)	160 (65.0)
	1	24 (46.2)	26 (40.0)	96 (39.8)	86 (35.0)
Histology					
Clear cell		0	0	8 (3.3)	9 (3.6)
Carcinosarcoma		4 (7.5)	1 (1.5)	25 (10.2)	19 (7.6)
Endometrioid		44 (83.0)	56 (86.2)	134 (54.7)	136 (54.6)
Prior systemic therapy		7 (13.2)	10 (15.4)	48 (19.6)	52 (20.9)
Carboplatin/paclitaxel		4 (7.5)	6 (9.2)	36 (14.7)	39 (15.7)
Measurable disease at baseline		49 (92.5)	58 (89.2)	212 (86.5)	219 (88.0)

[a] Mixed histology containing at least 10% carcinosarcoma, clear cell, or serous histology. [b] Treatment ends after 3 years. [c] Patients were randomized based on either local or central MMR/MSI testing results. For local determination of MMR/MSI status, IHC, NGS, and PCR assays were accepted. For central determination of MMR/MSI status IHC per Ventana MMR RxDx Panel was used. Central testing was used when local results were not available.

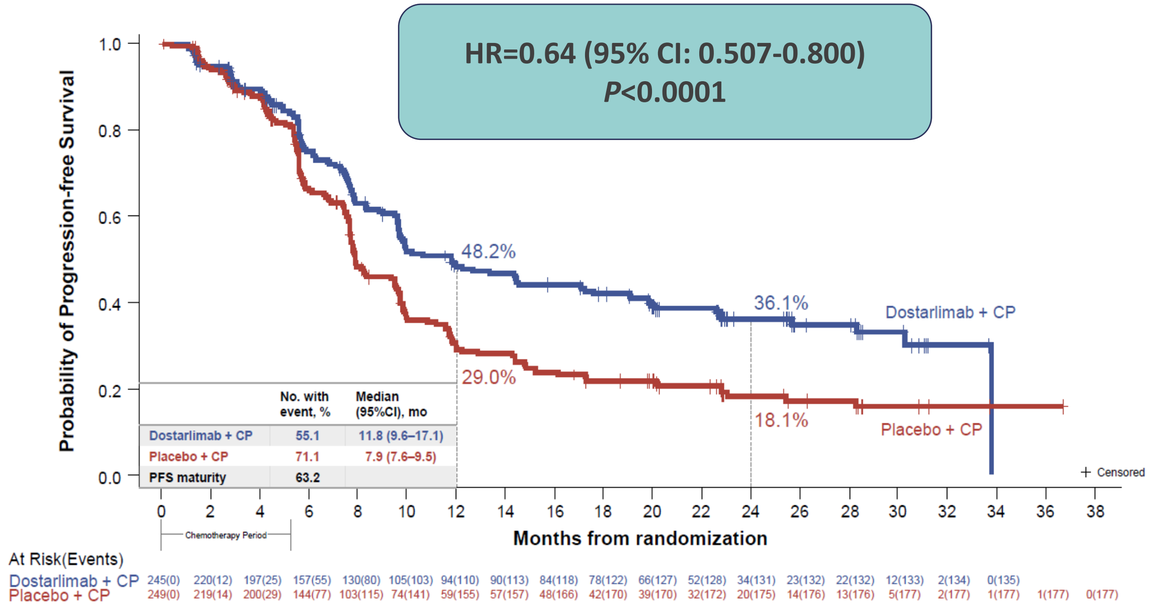
Mirza MR, et al. N Eng J Med March 2023.

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – PFS

PFS in dMMR/MSI-H Population



PFS in Overall Population

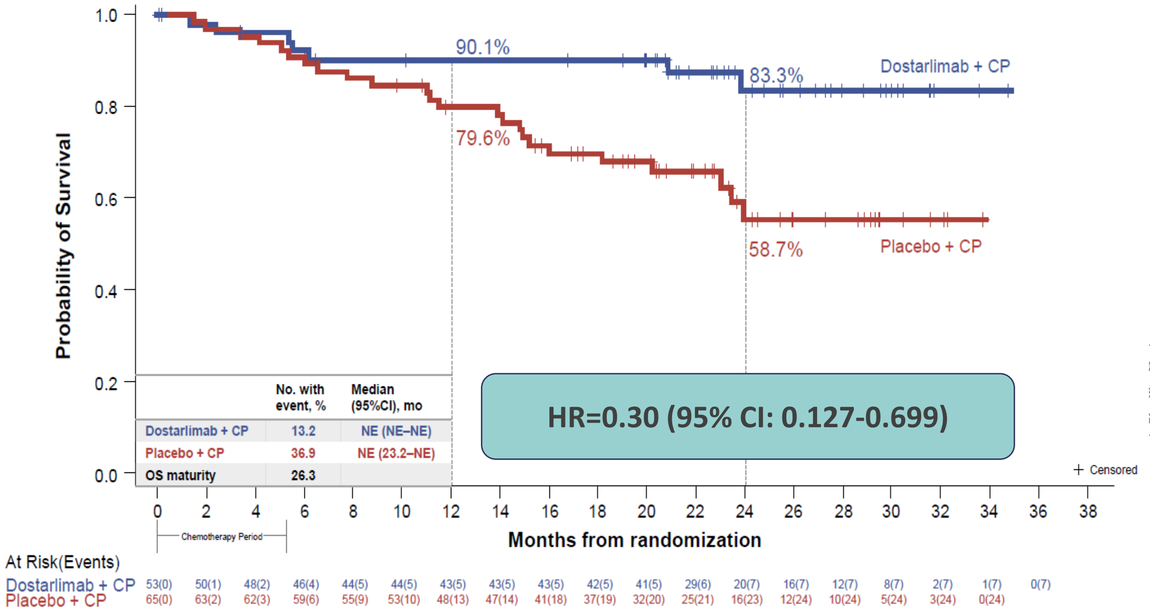


- Median duration of follow-up in the dMMR/MSI-H population was 24.79 months
- Median duration of follow-up in the overall population was 25.38 months

Data cutoff: September 28, 2022.
Mirza MR, et al. N Eng J Med March 2023

GOG-3031/RUBY: Phase 3 Trial of Dostarlimab + Chemo for Primary Advanced/Recurrent EC – OS

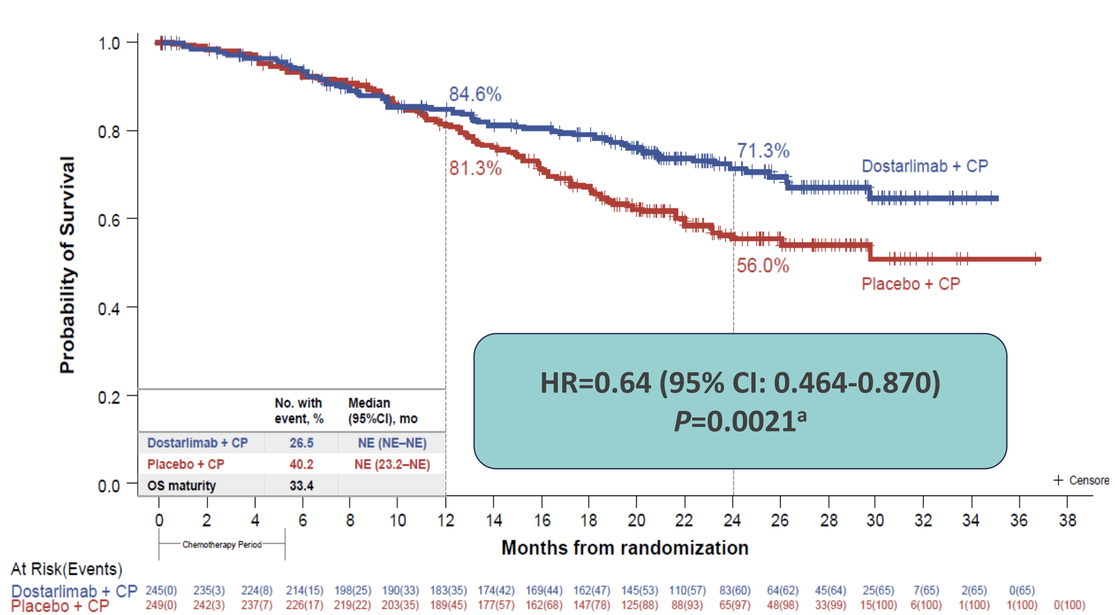
OS in dMMR/MSI-H Population



Received subsequent immunotherapy:

- **38.5% of patients on placebo arm**
- **15.1% of patients on dostarlimab arm**

OS in Overall Population (33% Maturity)



Received subsequent immunotherapy:

- **34.5% of patients on placebo arm**
- **15.5% of patients on dostarlimab arm**

Data cutoff: September 28, 2022. Median duration of follow-up in overall population was 25.38 months.

[a] $P \leq 0.00177$ required to declare statistical significance at first interim analysis.

Mirza MR, et al. N Eng J Med March 2023

Endometrial Cancer: 1L/Metastatic or Recurrent Disease

Setting	Trial Name	Study Intent	Update
Front-line, metastatic or recurrent **PI: Westin** **Co-PI: Moore** ***GOG led**	**GOG-3041/DUO-E**	A Randomised, Multicentre, Double-blind, Placebo-controlled, Phase III Study of First-line Carboplatin and Paclitaxel in Combination With Durvalumab, Followed by Maintenance Durvalumab With or Without Olaparib in Patients With Newly Diagnosed Advanced or Recurrent Endometrial Cancer	**Active, Not Recruiting**

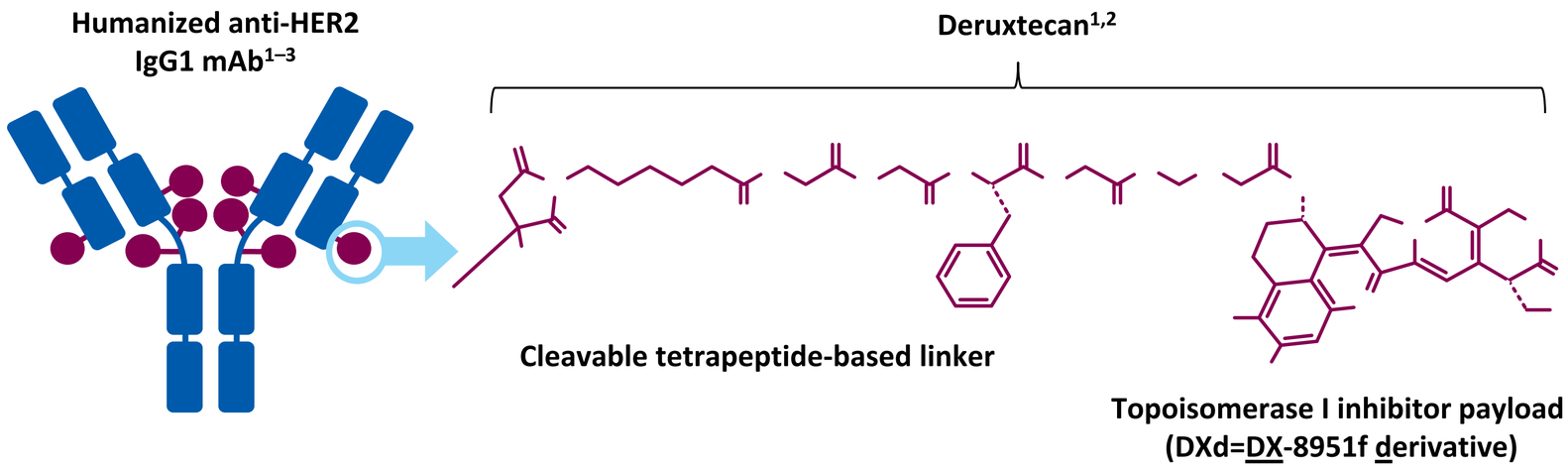
DUO-E is the first global Phase III trial of immunotherapy plus PARP inhibition to demonstrate clinical benefit in this setting

Positive high-level results from the DUO-E Phase III trial showed *Imfinzi* (durvalumab) in combination with platinum-based chemotherapy followed by either *Imfinzi* plus *Lynparza* (olaparib) or *Imfinzi* alone as maintenance therapy both demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to standard-of-care chemotherapy alone in patients with newly diagnosed advanced or recurrent endometrial cancer. There was a greater clinical benefit observed with the combination of *Imfinzi* and *Lynparza* as maintenance treatment.

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

T-DXd is an ADC with three components:

1. A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
2. A topoisomerase I inhibitor payload, an exatecan derivative
3. A tetrapeptide-based cleavable linker



[a]The clinical relevance of these features is under investigation.

ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; T-DXd, trastuzumab deruxtecan.

1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173–185. 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097–5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126–142.
4. Okamoto H, et al. *Xenobiotica*. 2020;50(10):1242–1250. 5. Nagai Y, et al. *Xenobiotica*. 2019;49(9):1086–1096.

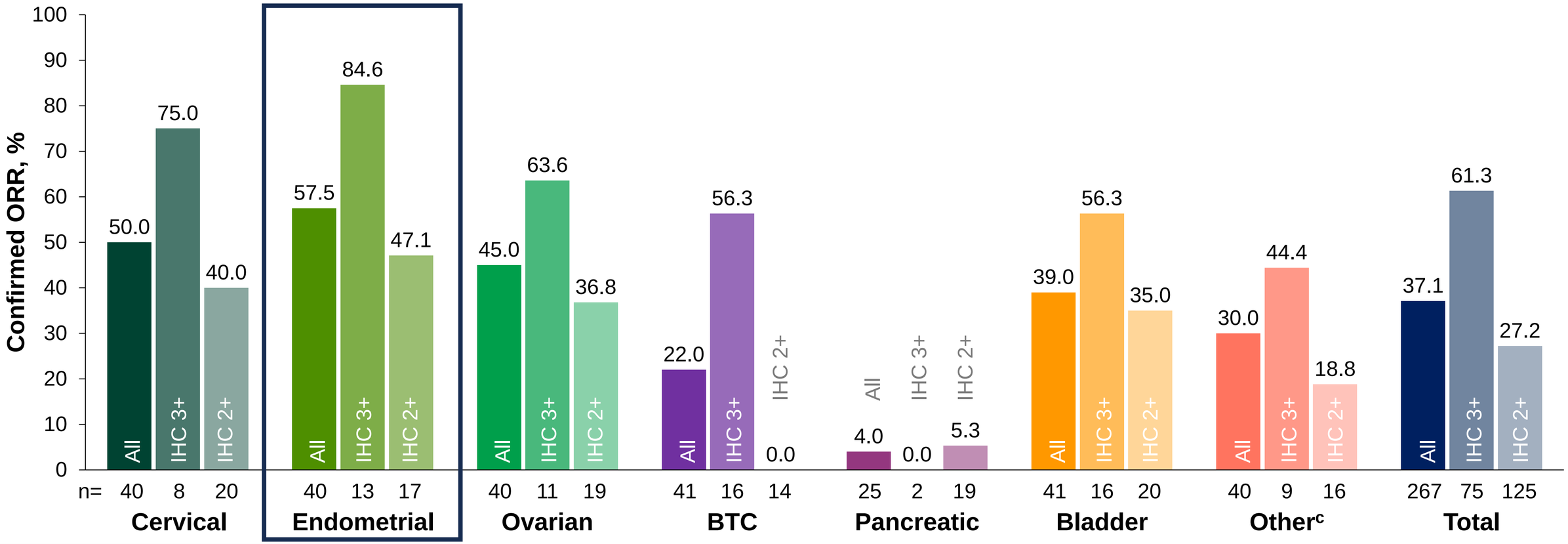
2023 ASCO ANNUAL MEETING

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

		Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)	BTC (n=41)	Pancreatic (n=25)	Bladder (n=41)	Other (n=40)	All patients (N=267)
Investigator assessment									
ORR, n (%)		**20 (50.0)**	**23 (57.5)**	**18 (45.0)**	**9 (22.0)**	**1 (4.0)**	**16 (39.0)**	**12 (30.0)**	**99 (37.1)**
Best overall response, n (%)	Complete response	2 (5.0)	7 (17.5)	4 (10.0)	1 (2.4)	0	1 (2.4)	0	15 (5.6)
	Partial response	18 (45.0)	16 (40.0)	14 (35.0)	8 (19.5)	1 (4.0)	15 (36.6)	12 (30.0)	84 (31.5)
	Stable disease	12 (30.0)	13 (32.5)	14 (35.0)	25 (61.0)	17 (68.0)	18 (43.9)	24 (60.0)	123 (46.1)
	PD	7 (17.5)	4 (10.0)	7 (17.5)	7 (17.1)	7 (28.0)	7 (17.1)	3 (7.5)	42 (15.7)
	Not evaluable	1 (2.5)	0	1 (2.5)	0	0	0	1 (2.5)	3 (1.1)
DCR[a] at 12 weeks, n (%)		27 (67.5)	32 (80.0)	28 (70.0)	27 (65.9)	9 (36.0)	29 (70.7)	30 (75.0)	182 (68.2)
Median DOR, months (95% CI)		9.8 (4.2–NE)	NR (9.9–NE)	11.3 (4.1–NE)	8.6 (2.1–NE)	NR	8.7 (4.3–11.8)	NR (4.1–NE)	11.8 (9.8–NE)
Independent central review: ORR, n (%)		16 (40.0)	21 (52.5)	17 (42.5)	11 (26.8)	3 (12.0)	17 (41.5)	13 (32.5)	98 (36.7)

2023 ASCO ANNUAL MEETING

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

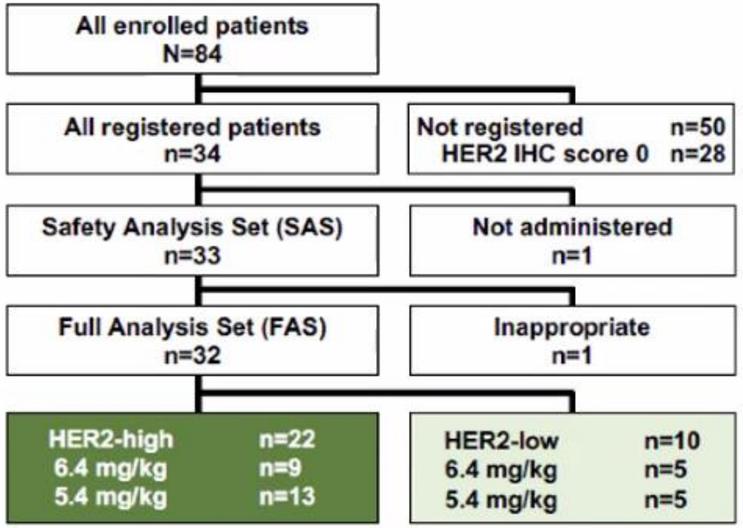


	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

T-DxD Efficacy in Uterine Carcinosarcoma

Patient Flow Diagram

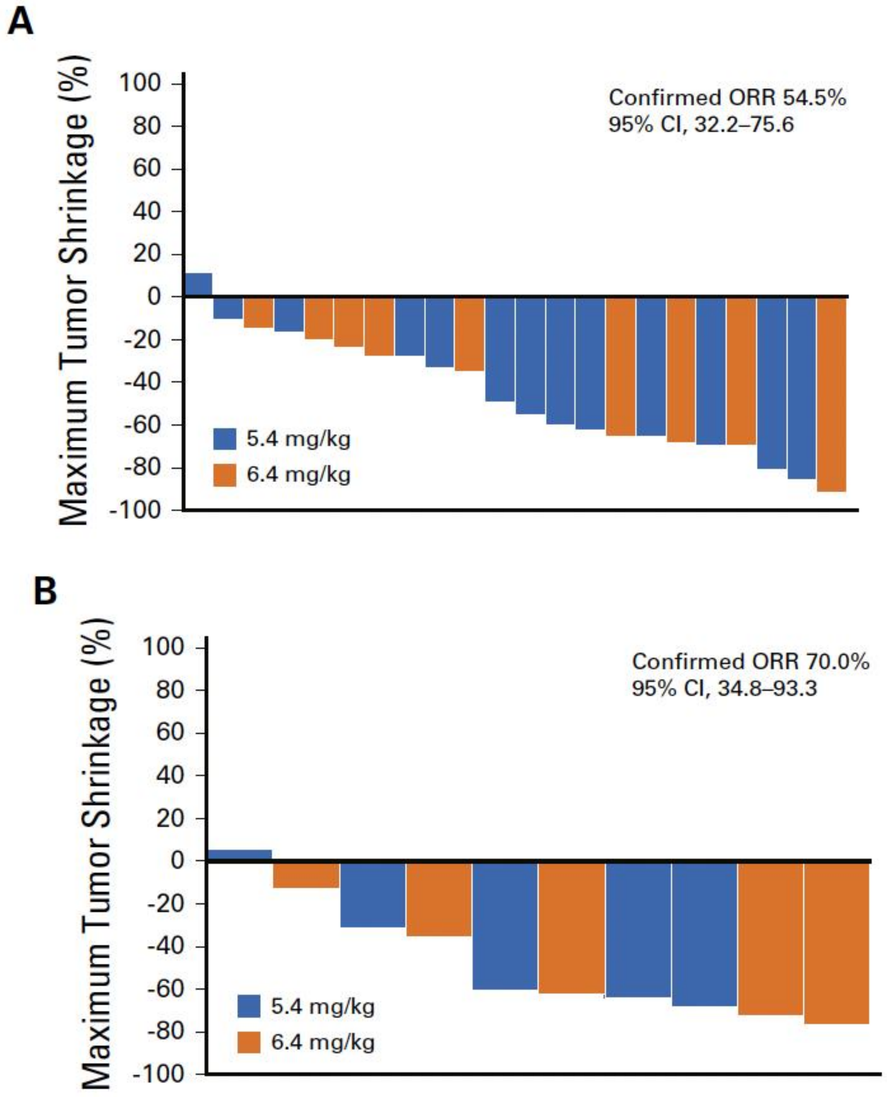
- Patients were enrolled from February 2018 to June 2020 at 7 institutions in Japan
- Data cut-off was done in December 2020
- Twenty-eight patients (33.3%) were excluded from registration due to HER2 IHC score 0
- One patient did not receive T-DXd due to progression of UCS
- One patient was excluded from FAS due to central review with no measurable target lesion



Patient Characteristics

HER2 IHC score (N=84)
0: 28 (33%), 1: 24 (29%)
2: 22 (26%), 3: 10 (12%)

		All (n=34)	(%)	FAS (n=32)	(%)
Age (years)		45- 81	65.5 (median)	45-81	64.5 (median)
PS (ECOG)	0	25	(73.5)	24	(75)
	1	9	(26.5)	8	(25)
HER2 (IHC)	1	11	(32.4)	10	(31.3)
	2	16	(47.1)	15	(46.9)
	3	7	(20.6)	7	(21.9)
HER2 (FISH)	Negative	26	(76.5)	24	(75)
	Positive	8	(23.5)	8	(25)
Prior regimens	1			17	(53.1)
	2			9	(28.1)
	≥ 3			6	(18.8)



Nishikawa et al. J Clin Oncol 2023

SYSTEMIC THERAPY FOR ENDOMETRIAL CARCINOMA

RECURRENT DISEASE[h,i]

First-Line Therapy for Recurrent Disease[i]	Second-Line or Subsequent Therapy
Preferred • Carboplatin/paclitaxel (category 1 for carcinosarcoma)[k,7] • Carboplatin/paclitaxel/pembrolizumab (except for carcinosarcoma) (category 1)[b,c,d,8] • Carboplatin/paclitaxel/dostarlimab-gxly (category 1)[c,d,e,9] • Carboplatin/paclitaxel/trastuzumab[d,g] (for HER2-positive uterine serous carcinoma)[d,10] • Carboplatin/paclitaxel/trastuzumab[d,g] (for HER2-positive carcinosarcoma)[f,10] **Other Recommended Regimens** • Carboplatin/docetaxel[l] • Carboplatin/paclitaxel/bevacizumab[d,m,11,12] **Useful in Certain Circumstances (Biomarker-directed therapy: after prior platinum-based therapy including neoadjuvant and adjuvant)** • MMR-proficient (pMMR) tumors ▸ Lenvatinib/pembrolizumab (category 1)[c,13] • TMB-H tumors[n] ▸ Pembrolizumab[c,14] • MSI-H/dMMR tumors[o] ▸ Pembrolizumab[c,15] ▸ Dostarlimab-gxly[c,16]	**Other Recommended Regimens** • Cisplatin/doxorubicin[17] • Cisplatin/doxorubicin/paclitaxel[p,14] • Cisplatin • Carboplatin • Doxorubicin • Liposomal doxorubicin • Paclitaxel[14] • Albumin-bound paclitaxel[q] • Topotecan • Bevacizumab[m,r,19] • Temsirolimus[20] • Cabozantinib • Docetaxel (category 2B) • Ifosfamide (for carcinosarcoma) • Ifosfamide/paclitaxel (for carcinosarcoma)[21] • Cisplatin/ifosfamide (for carcinosarcoma) **Useful in Certain Circumstances (Biomarker-directed therapy)** • pMMR tumors ▸ Lenvatinib/pembrolizumab (category 1)[c,13] • TMB-H tumors[n,12] ▸ Pembrolizumab[c] • MSI-H/dMMR tumors[o] ▸ Pembrolizumab[c,15] ▸ Dostarlimab-gxly[c,16] ▸ Avelumab[c] ▸ Nivolumab[c,22] • HER2-positive tumors (IHC 3+ or 2+) ▸ Fam-trastuzumab deruxetan[23] • *NTRK* gene fusion-positive tumors ▸ Larotrectinib ▸ Entrectinib

2023 ASCO ANNUAL MEETING

Preliminary results of a Phase II trial with Sacituzumab Govitecan (SG) in Patients with Recurrent Endometrial Carcinoma overexpressing Trop-2

Table 1. Demographics and clinical characteristics	SG (n = 21)
Median age at study entry, y (range)	63 (47-77)
Race, n (%)	
White	15 (71.4)
Black or African-American	0
Asian	2 (9.5)
Other	4 (19.0)
Histological/cytological diagnosis, n (%)	
Serous	10 (47.6)
Endometrioid	6 (28.6)
Carcinosarcoma	3 (14.3)
Other	2 (9.5)
Number of prior anticancer regimen, n (%)	
1-3	11 (52.4)
> 3	10 (47.6)
Median prior anticancer regimens, n (range)	3 (1-6)
Median follow up duration, m (IQR)	17 (7.6-35.2)

Table 2. Overall response rate and durable disease control	SG (n = 21) n (%)
Best overall response	
Confirmed complete response (CR)	1 (4.8)
Confirmed partial response (PR)	6 (28.5)
Stable disease	11 (47.6)
Progressive disease	3 (14.3)
Objective response rate (confirmed CR + PR)	7 (33.3)
Durable disease control (confirmed CR + PR + SD ≥ 6 months)	7 (35.0)*

*Out of 20 patients evaluable for durable disease control

Table 3. Most Common Treatment-Related Adverse Events	**Grade ≥ 3 (≥ 10% of patients)**
Neutropenia	9 (43%)
Fatigue	4 (19%)
Anemia	3 (14%)
Diarrhea	3 (14%)
Febrile neutropenia	2 (10%)

- **Median PFS was 5.7 months**
- **Median OS was 22.2 months**

Conclusions:

Sacituzumab govitecan shows encouraging clinical activity against **Trop-2** overexpressing **endometrial cancer** in stage 1 of an **open-label phase 2 trial**; stage 2 is now open/recruiting an all-comer population.

A. Santin, MD et al.
ASCO 2023 Poster #294

Evolution of Molecularly Directed Therapy in Endometrial Cancer

TP53

- Predictor of response to anti angiogenic therapy…
- **GOG-86P (bevacizumab):** PFS HR 0.48 vs 0.87 in mutant TP53 vs. wt TP53
- **EXPORT-EC (Selinexor)**
- **KRT-232 (Navtemadlin)**

DNA Damage Repair

- Potential opportunity in the mutant TP53 population
- **ADAGIO:** Adavosertib (WEE-1) single agent
  Median prior LOT = 3
  BICR ORR 26%
  Median PFS 2.8mo

Hormonal Therapies

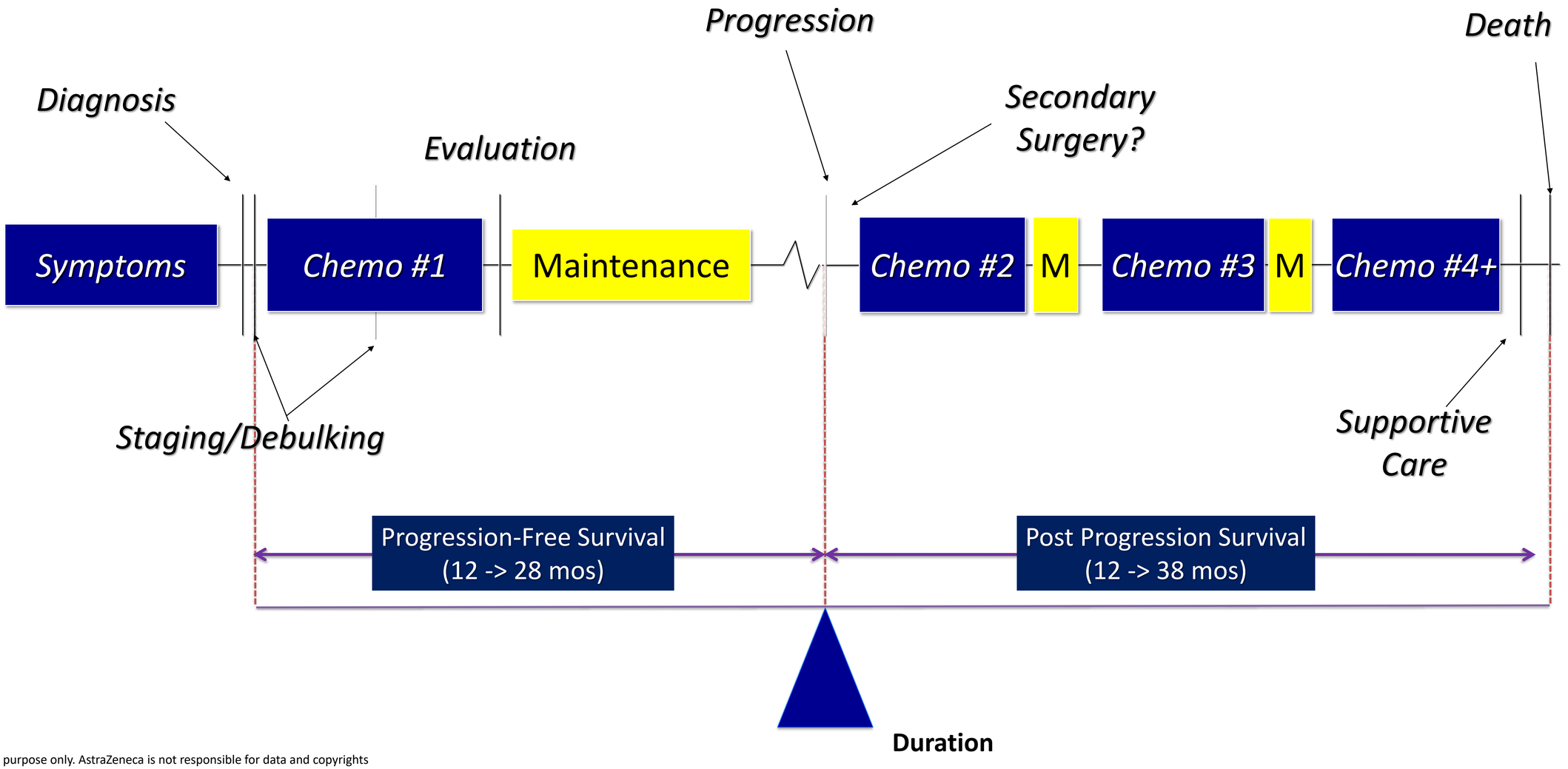
- ? Role in the copy number low wt TP53 population
- **PALEO Study:** Letrozole vs Palbocilcib + letrozole
  HR 0.56
  Median PFS 8.3 vs 3 mo
- **Letrozole + Abemaciclib:** ORR 30%

Aghajanian et al. J Clin Oncol. 2011; Leslie K. et al. Gyncol Oncol 2021; Nickles-Fader J Clin Oncol 2018; Nickles-Fader Clin Cancer Research 2020; Nishikawa et al. J Clin Oncol. 2023; Liu JF, et al. SGO 2023. Abstract 219; Mirza et al. ESMO 2020; P Konstantinopoulos et al. J Clin Oncol 2022;

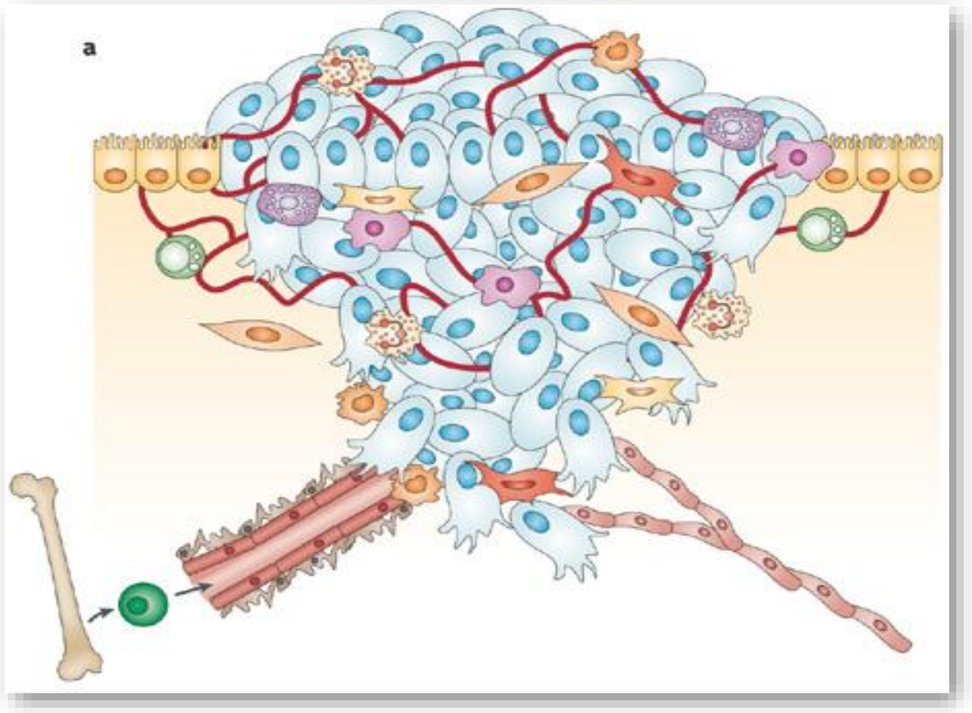
Endometrial Cancer: 1st line Metastatic/Recurrent (Results Pending)

Front-line, metastatic or recurrence	AtTEnd (NCT03603184)	Phase III Double-blind Randomized Placebo Controlled Trial of Atezolizumab in Combination With Paclitaxel and Carboplatin in Women With Advanced/Recurrent Endometrial Cancer	Active, not Recruiting
Front-line, metastatic or recurrence	GOG 3064/ ENGOT–en15/MK KN-C93 (NCT05173987)	1L dMMR platinum-doublet chemotherapy vs pembrolizumab (with formal cross over)	Recruiting
Front-line, metastatic or recurrence	LEAP-001 (NCT04865289)	1L platinum doublet chemotherapy vs lenvatinib + pembrolizumab	Active, not Recruiting

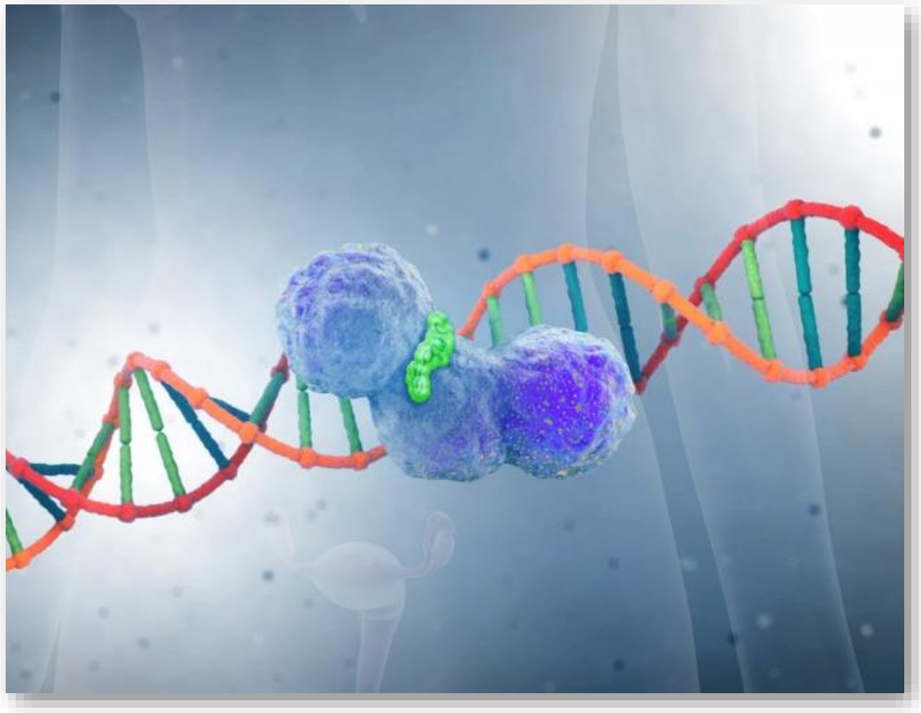
Ovarian Cancer: Natural History



Ovarian Cancer Differentiators



Anti-Angiogenesis



PARP inhibition

Joyce, J. A., & Pollard, J. W. (2009). Microenvironmental regulation of metastasis. Nature reviews cancer, 9(4), 239-252.

Clearity Foundation. (2016, October 18). PARP inhibitor broadly active in ovarian cancer. Clearity Foundation.

Clinical trials with PARPi in front-line: Benefit across biomarkers

	SOLO-1[1]	PRIMA[2]	PAOLA-1[3]	ATHENA-MONO[4]	PRIME[5]
PARPi	Olaparib	Niraparib	Olaparib	Rucaparib	Niraparib
Bevacizumab	No	No	Yes	No	No
Population	BRCAmut	All comers	All comers	All comers	All comers (Chinese)
HRD test	NA	MyChoice	MyChoice	Foundation-One	BGI
+++ BRCAmut	0.33 (0.25–0.43)	0.40* (0.27–0.62)	0.31* (0.20–0.47)	0.31* (0.20–0.47)	0.40* (0.23-0.68)
++ BRCAwt/HRD+	-	0.50* (0.31-0.83)	0.43* (0.28-0.66)	0.58* (0.33-1.01)	0.58* (0.36-0.93)
+ BRCAwt/HRD-	-	0.68* (0.49-0.94)	1.0* (0.75-1.36)	0.65* (0.45-0.95)	0.41* (0.25-0.65)

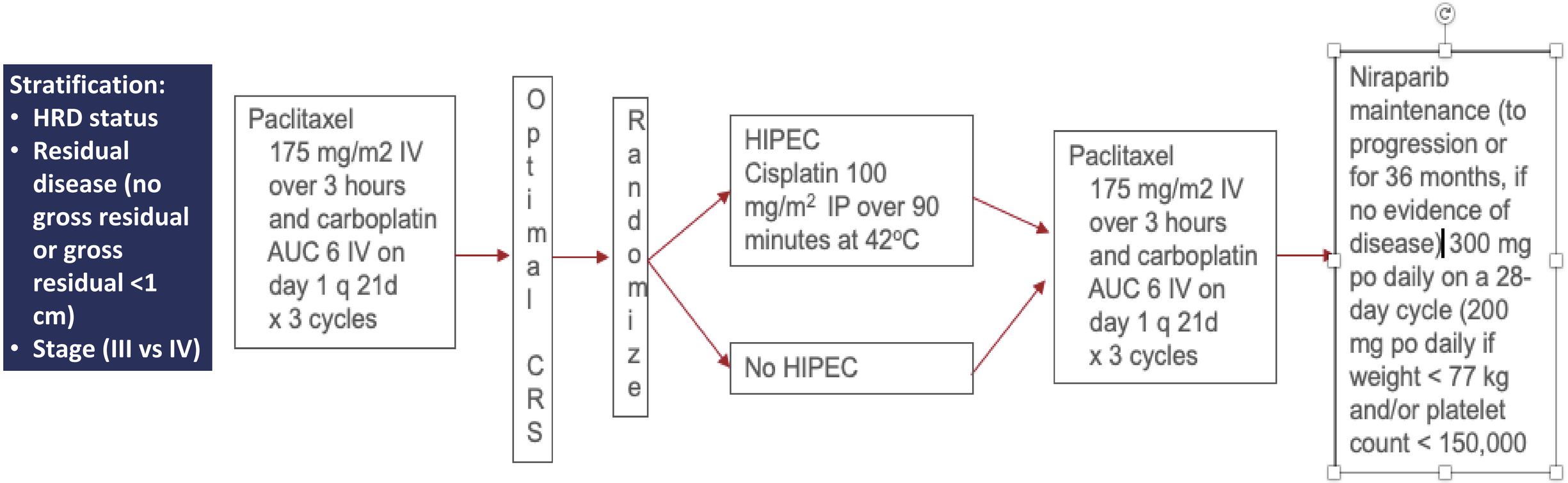
*exploratory

The aim of the table is not the cross-trial comparison

1. Moore. NEJM 2018; 2. Gonzalez-Martin. NEJM 20193; 3. Ray-Coquard. NEJM 2019; 4. Monk. J Clin Oncol 2022; 5. Li.SGO 2022

GOG-3068/HOTT

Ph III Randomized Trial of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) with Cisplatin versus no HIPEC at the Time of Optimal Interval Cytoreductive Surgery followed by Niraparib Maintenance in Patients with Newly Diagnosed Stage III and IV Ovarian, Primary Peritoneal, and Fallopian Tube Cancer (PI: Oliver Zivanovic, MD, Co-PI: Leslie Randall, MD)



NCT05659381

FLORA-5/QPT-ORE-005/GOG 3035

Randomized Trial of Oregovomab and Chemotherapy in Newly Diagnosed Stage III & IV Ovarian, Primary Peritoneal, and Fallopian Tube Cancer

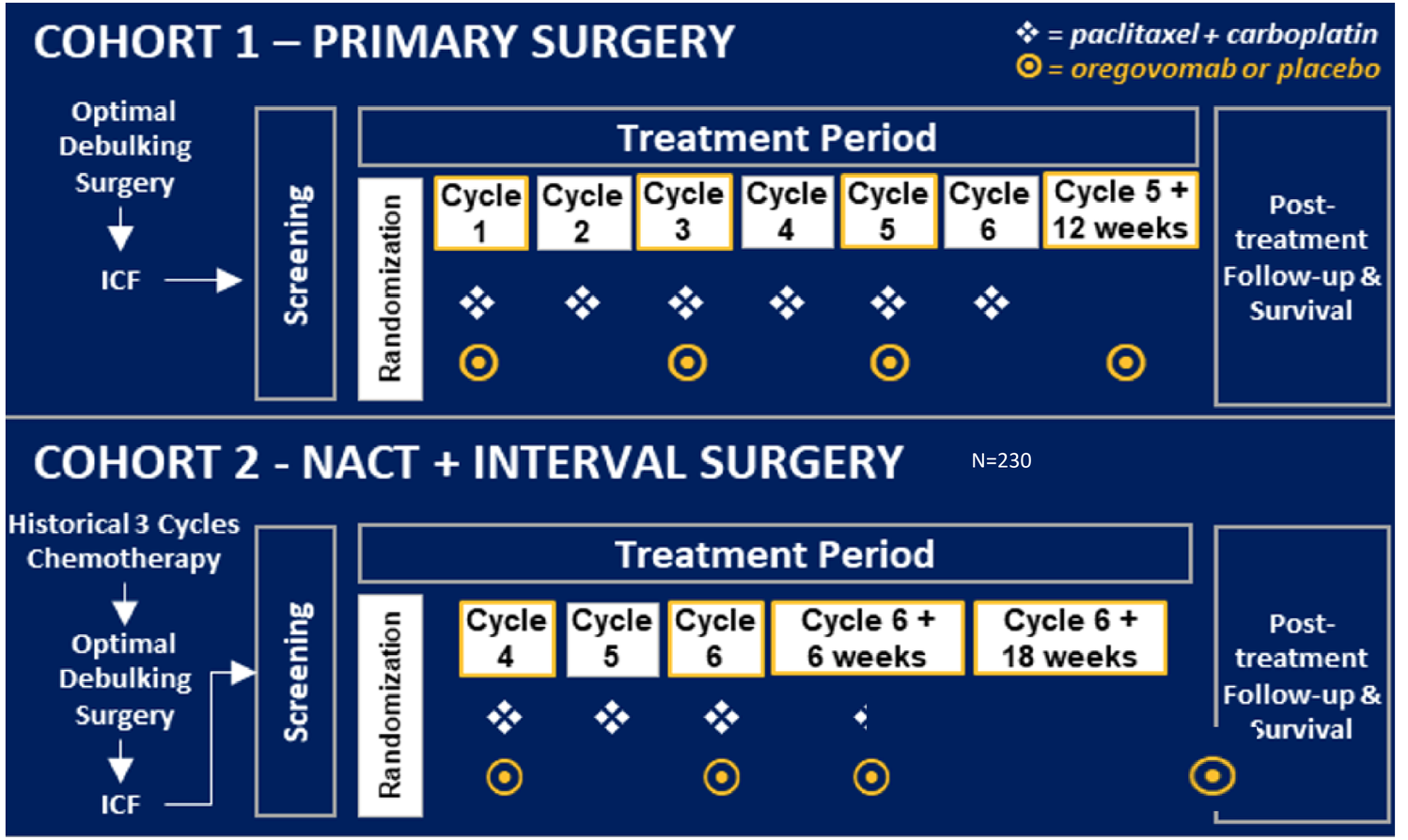
-Newly diagnosed stage III or IV epithelial ovarian, tubal, or peritoneal cancer

-BRCA wild-type

-ECOG PS 0-1

-Primary or interval cytoreductive surgery to R1 or R0

N=602



Primary endpoint: PFS – IA; Secondary endpoints: OS, Safety, QoL
Exploratory: iRECIST, TFST, TSST, PFS2, Biomarkers

Cohort	Total Screened	In Screening	Screening Failure	Total Randomized
Cohort 1	408	10	143	255
Cohort 2	239	6	56	177

N=432

NCT04498117

Global PI: Alvarez Secord A

Ovarian Cancer

Antibody Drug Conjugates ADCs

SORAYA

POSITIVE TOP-LINE RESULTS
POTENTIAL FOR ACCELERATED APPROVAL

SINGLE-ARM PIVOTAL TRIAL OF MIRVETUXIMAB IN FRα-HIGH PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER

INCLUSION CRITERIA

106 PATIENTS

- Platinum-resistant disease (PFI < 6 months)
- FRα-high only
- Prior bevacizumab required
- Prior PARPi allowed
- 1 to 3 prior lines allowed
- Patients with BRCA mutations allowed

PRIOR TREATMENT

51%
3 prior lines of therapy

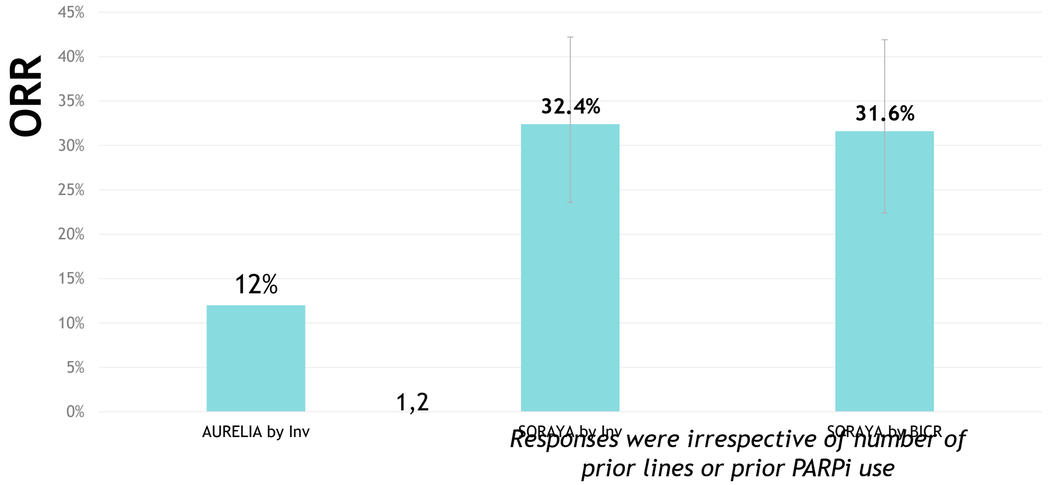
100%
Received prior bevacizumab

48%
Received prior PARPi

SAFETY AND TOLERABILITY

- Favorable tolerability data
- >700 patients treated to date
- The most common AEs were low-grade gastrointestinal and ocular events, including blurred vision, keratopathy, and nausea; 7% of patients discontinued due to treatment-related AEs, including one patient due to ocular AE

MET PRIMARY ENDPOINT



Responses were irrespective of number of prior lines or prior PARPi use

KEY SECONDARY ENDPOINT

5.9 months mDOR

By Investigator at Data Cutoff *(95% CI: 5.6, 7.7)*

Nearly half of responders still receiving mirvetuximab at data cutoff; with longer follow-up, ***mDOR could range from 5.7 to above 7 months***

FDA Accelerated Approval in November 2022

[1]AURELIA Study, JCO 2014, Pujade-Lauraine, E., et al.
[2]Disclaimer: These comparisons are not based on head-to-head clinical studies. The results from these two studies are not directly comparable and do not imply a clinical benefit of mirvetuximab over bevacizumab.
FRα: folate receptor alpha; PFI: platinum-free interval; PARPi: poly ADP-ribose polymerase inhibitor; BRCA: BReast CAncer gene; AE: adverse event; ORR: confirmed objective response rate Inv: Investigator; BICR: blinded independent central review; mDOR: median duration of response; BLA: Biologics License Application; FDA: US Food and Drug Administration

2023 ASCO® ANNUAL MEETING

Phase III MIRASOL (GOG 3045/ENGOT-ov55) Study: Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers with High Folate Receptor-Alpha (FRα) Expression

Kathleen N. Moore[1], Antoine Angelergues[2], Gottfried E. Konecny[3], Susana Banerjee[4], Sandro Pignata[5], Nicoletta Colombo[6], John Moroney[7], Casey Cosgrove[8], Jung-Yun Lee[9], Andrzej Roszak[10], Shani Breuer[11], Jacqueline Tromp[12], Diana Bello Roufai[13], Lucy Gilbert[14], Rowan Miller[15], Tashanna Myers[16], Yuemei Wang[17], Anna Berkenblit[17], Domenica Lorusso[18], Toon Van Gorp[19]

[1]Stephenson Cancer Center University of Oklahoma College of Medicine, Oklahoma City, OK, USA; [2]Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France; [3]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [4]The Royal Marsden NHS Foundation Trust - Royal Marsden Hospital, London, UK; [5]Istituto Nazionale Tumori- G. Pascale, Naples, Italy; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]The University of Chicago, Chicago, IL, USA; [8]The Ohio State University, Columbus, OH, USA; [9]Severance Hospital, Seoul, South Korea; [10]Wielkopolskie Centrum Onkologii, Poznan, Poland; [11]Hadassah Ein Kerem – Sharett, Jerusalem, Israel; [12]Amsterdam UMC, Amsterdam, The Netherlands; [13]Hopital Rene Huguenin, Institut Curie, Saint-Cloud, France; [14]McGill University Health Centre, Montreal, Canada; [15]University College London Hospital, London, UK; [16]Baystate Medical Center, Springfield, MA, USA; [17] ImmunoGen, Inc., Waltham, MA, USA; [18]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [19]University Hospital Leuven Leuven Cancer Institute, Leuven, Belgium

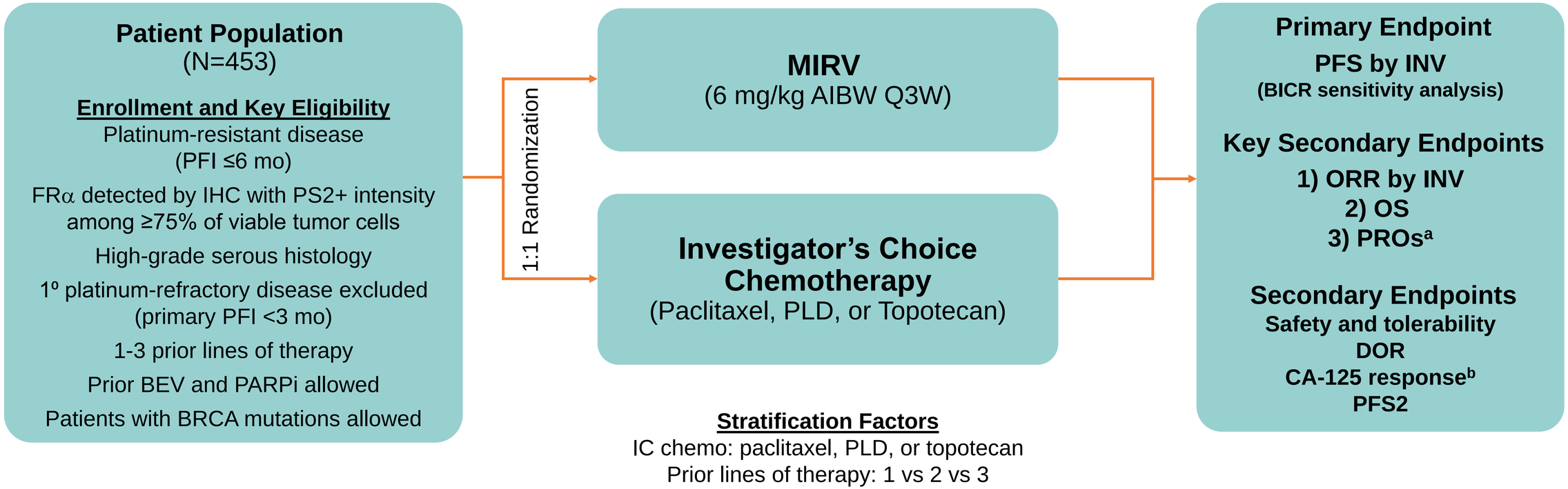
ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION® Transforming the standard of care™

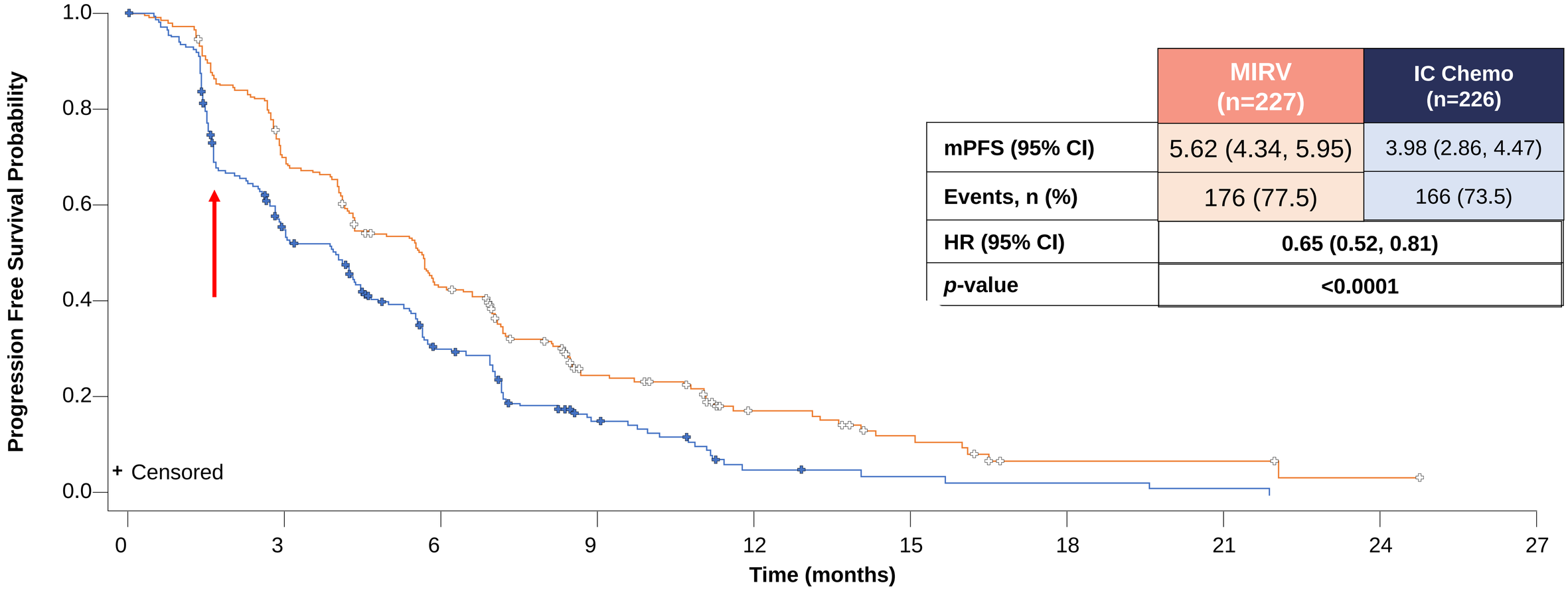
Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

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



Primary Endpoint: Progression-Free Survival by Investigator



	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**	

No. Participants at Risk

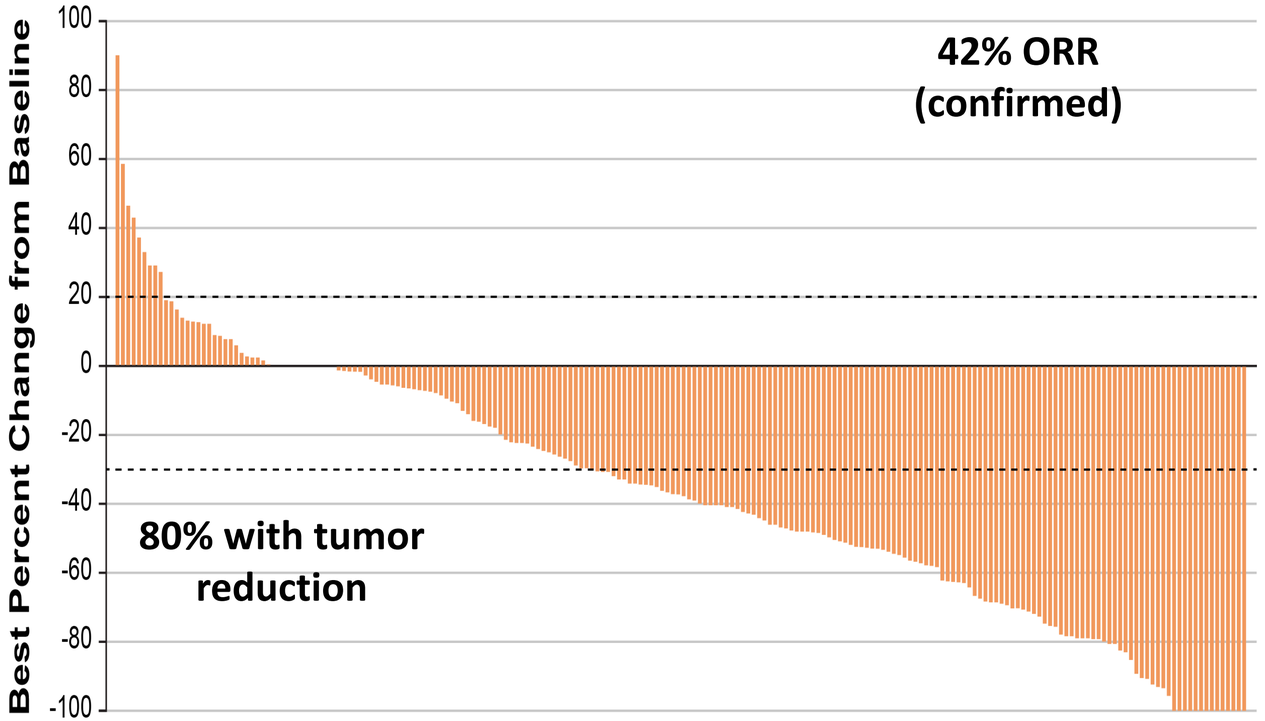
MIRV	227	151	89	38	18	10	3	3	1	0
IC Chemo	226	98	48	19	5	3	2	1	0	

Data cutoff: March 6, 2023

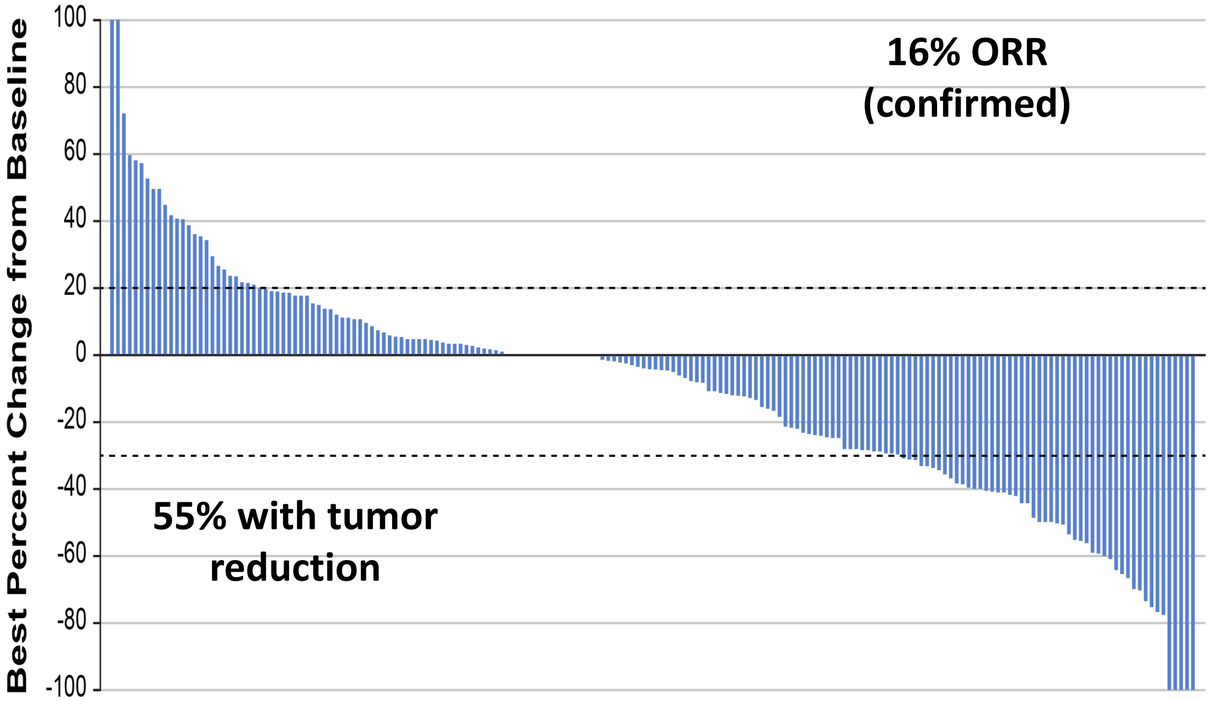
MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mPFS, median progression-free survival; CI, confidence interval; HR, hazard ratio.

Maximum Percentage Change in Target Lesion Size from Baseline by Investigator (N=453)

MIRV



IC Chemo

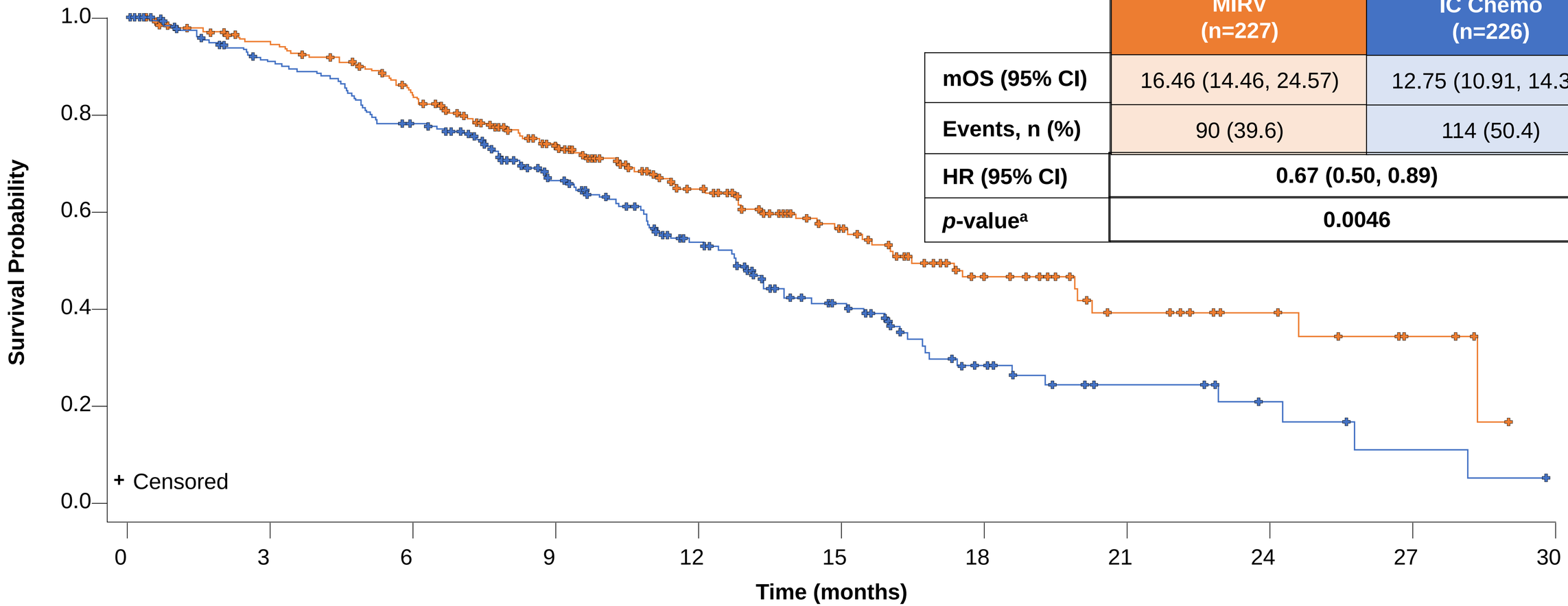


Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC chemo, investigator's choice chemotherapy; ORR, objective response rate.

Overall Survival

	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**	



No. Participants at Risk

MIRV	227	204	175	128	82	53	28	15	9	4	0
IC Chemo	226	185	157	107	68	39	18	9	5	2	0

Data cutoff: March 6, 2023; median follow-up time: 13.11 months

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.

[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

GLORIOSA

RANDOMIZED PHASE 3 TRIAL FOR MIRVETUXIMAB + BEVACIZUMAB MAINTENANCE IN FRα-HIGH PSOC PATIENTS

TARGET TIMELINES

- Open for Accrual
- Global trial
- POTENTIAL APPROVAL 2026

PRIMARY ENDPOINT

PFS

SECONDARY ENDPOINT

OS by BICR

ENROLLMENT AND KEY ELIGIBILITY

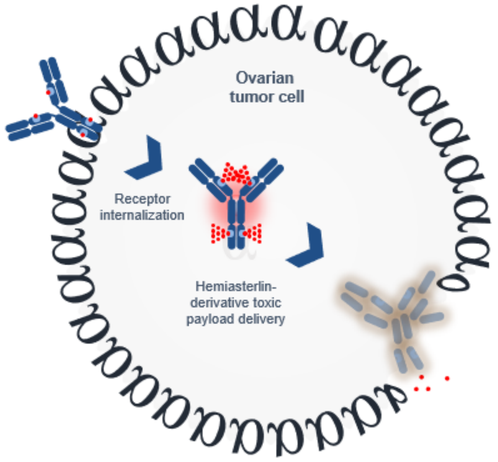
438 patients
Platinum-sensitive ovarian cancer
1 prior systemic treatment
Prior PARPi required if BRCA+
CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

PRIOR MIRV EXPERIENCE

Strong MIRV/BEV treatment efficacy and tolerability in > 120 patients
FRα high rPSOC, MIRV/BEV has an ORR of 69% and mPFS of 13.3 months

PFS (progression-free survival); BICR (blinded independent central review); OS (overall survival); CR (complete response); PR (partial response); SD (stable disease); BRCA (BReast CAncer gene); MIRV (mirvetuximab soravtansine); DOR: duration of response; ORR: overall response rate

STRO-002-GM1 (Luveltamab Tazevibulin) Phase 1 Dose Expansion Cohort



Luveltamab tazevibulin is a FolRα targeting antibody

NCT03748186

- Recurrent disease
  - Platinum resistant 1–3 prior regimens or platinum-sensitive 2–3 prior regimens
- Fresh or archival tissue required
- No mandate for FolRα expression
- At least 1 target lesion

R 1:1

Luveltamab 4.3 mg/kg Q3W n=23

Luveltamab 5.2 mg/kg Q3W n=21

- Primary endpoint: ORR by RECIST v1.1
- Secondary endpoints: Safety, PK, PFS, DOR

- FolRα expression retrospectively determined using IHC* on fresh or archival tissue required
- TPS is the percentage of cells stained positive at any intensity
  - Established in multiple approvals and tumor indications
  - Does not require differentiation between staining intensity
  - Simple and straightforward for pathology read
- **Enriched population defined as TPS >25%**
- **TPS >25% in 35/44 (80%) of all enrolled patients**

Patients enrolled unselected for FolRα N=44

FolRα >25% by TPS (TPS >25%) n=35

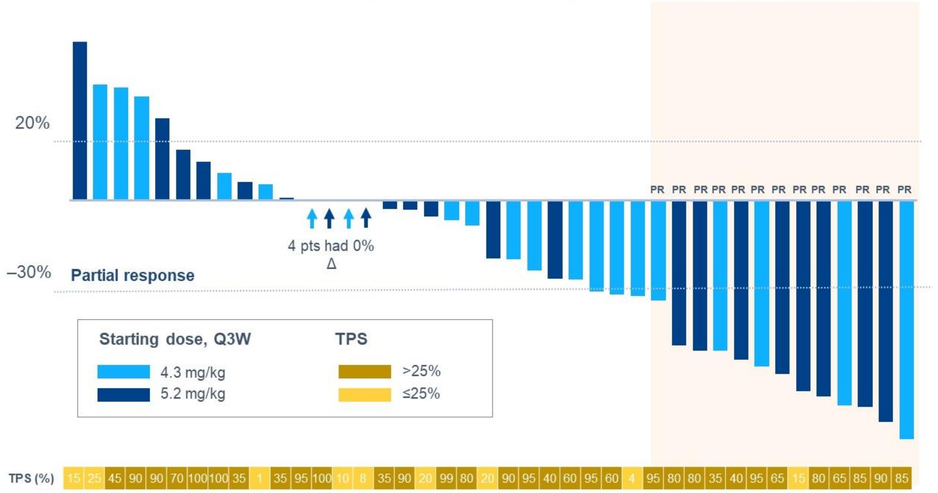
- **RECIST v1.1 evaluable** At least 1 post-baseline scan n=32
- **Not RECIST evaluable** Discontinued prior to receiving any post-baseline scan n=3†

FolRα ≤25% by TPS (TPS ≤25%) n=9

- **RECIST v1.1 evaluable** At least 1 post-baseline scan n=9
- **Not RECIST evaluable** Discontinued prior to receiving any post-baseline scan n=0

Efficacy

Maximum Reduction in Tumor Target Lesions in RECIST-Evaluable Patients (N=41)



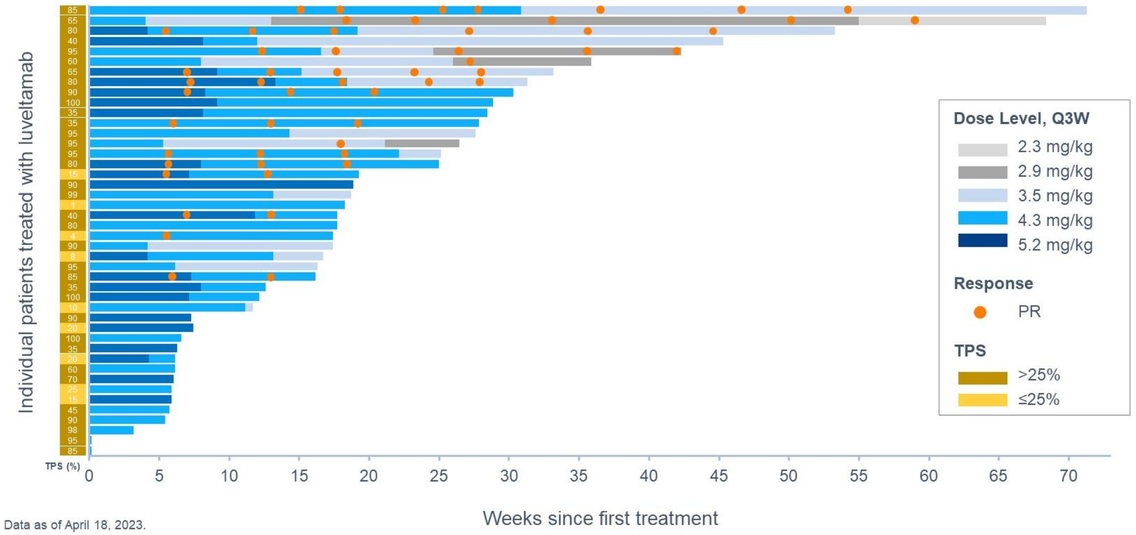
ORR: 31.7% in unselected pts

- 37.5% for FoLRα >25% by TPS

Disease control rate: 78% in unselected pts

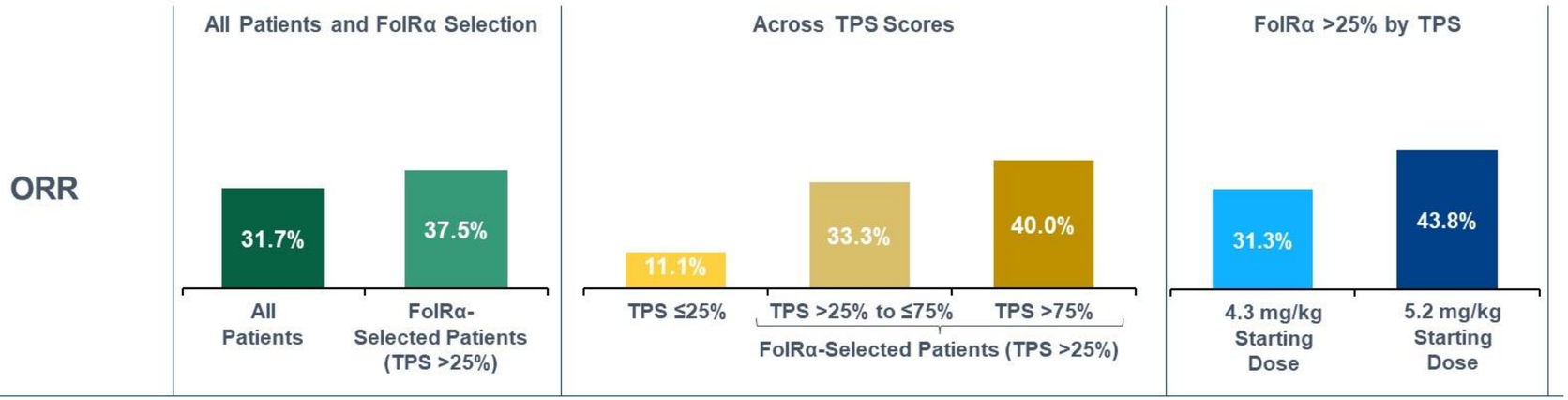
- 81% for FolRα >25% by TPS

Treatment Duration for Patients With at Least 1 Dose (N=44)



Data as of April 18, 2023.

Treatment Response in RECIST-Evaluable Patients (N=41)



RECIST-evaluable patients	N=41	n=32	n=9	n=12	n=20	n=16	n=16
PR	13	12	1	4	8	5	7
ORR (95% CI), %	**31.7 (18.1, 48.1)**	**37.5 (21.1, 56.3)**	**11.1 (0.3, 48.3)**	**33.3 (9.9, 65.1)**	**40.0 (19.1, 63.9)**	**31.3 (11.0, 58.7)**	**43.8 (19.8, 70.1)**

A Oaknin, et al.
ASCO 2023

2023 ASCO ANNUAL MEETING

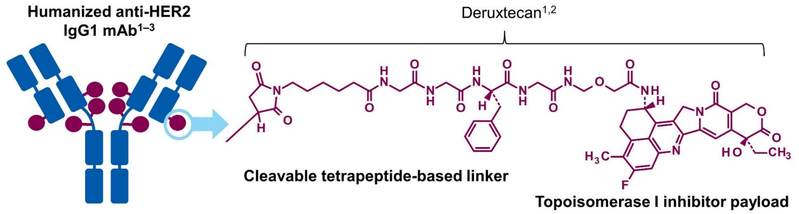
DESTINY-PanTumor02

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

Funda Meric-Bernstam

T-DXd is an ADC with three components:

1. A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
2. A topoisomerase I inhibitor payload, an exatecan derivative
3. A tetrapeptide-based cleavable linker



Seven Key Attributes[a,1–5]
Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug-to-antibody ratio ≈8
Payload with short systemic half-life
Stable linker payload
Tumor-selective cleavable linker
Bystander antitumor effect

[a]The clinical relevance of these features is under investigation.

ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; T-DXd, trastuzumab deruxtecan.
1. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173–185. 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097–5108. 3. Trail PA, et al. *Pharmacol Ther.* 2018;181:126–142.
4. Okamoto H, et al. *Xenobiotica.* 2020;50(10):1242–1250. 5. Nagai Y, et al. *Xenobiotica.* 2019;49(9):1086–1096.

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

T-DXd
5.4 mg/kg
q3w

n≈40 per cohort planned

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

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

Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

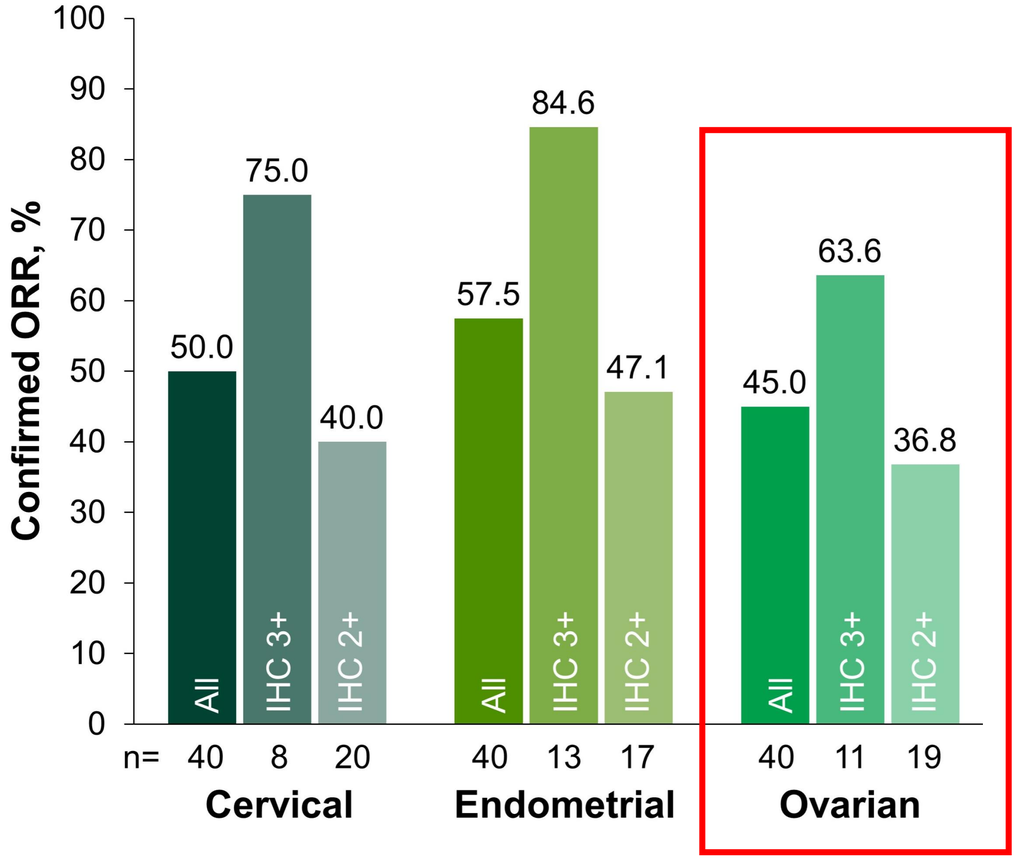
- DOR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

Efficacy

		Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)
Investigator assessment				
ORR, n (%)		**20 (50.0)**	**23 (57.5)**	**18 (45.0)**
Best overall response, n (%)	Complete response	2 (5.0)	7 (17.5)	4 (10.0)
	Partial response	18 (45.0)	16 (40.0)	14 (35.0)
	Stable disease	12 (30.0)	13 (32.5)	14 (35.0)
	PD	7 (17.5)	4 (10.0)	7 (17.5)
	Not evaluable	1 (2.5)	0	1 (2.5)
DCR[a] at 12 weeks, n (%)		27 (67.5)	32 (80.0)	28 (70.0)
Median DOR, months (95% CI)		9.8 (4.2–NE)	NR (9.9–NE)	11.3 (4.1–NE)
Independent central review: ORR, n (%)		16 (40.0)	21 (52.5)	17 (42.5)

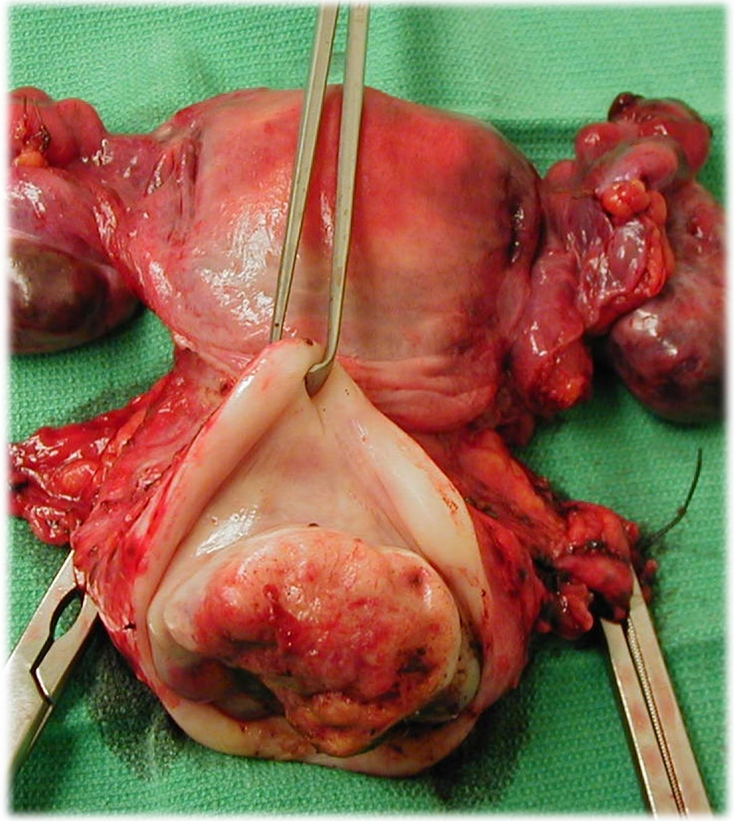


	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

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.

PRESENTED BY: Funda Meric-Bernstam, MD

Innovations in Cervix Cancer Management



- Used to treat cervical cancers with invasion >3 mm but confined to the cervix and vagina <4 cm (stage IA2-IB2)

- Removal of parametrium and upper vagina

Are we too radical?

Parametrial Invasion

A "low-risk" group?

Series	Year	Stage	Tumor size (cm)	DOI (mm)	(-) LVSI	(-) PLN	N	N (+) parametria	% (+) parametria
Kinney	1995	IA2 - IB1	<=2		X		83	0	0
Covens	2002	IA1(LVSI) - IB1	<=2	<=10		X	536	3	0.6
Wright	2007	IA1(LVSI) - IB1	<2		X	X	270	1	0.4
Frumovitz	2009	IA1(LVSI) - IB1	<2		X		125	0	0
Kim	2010	IB1	<=4	<=5			140	0	0
Klat	2012	IA2-IB1	<2	any	any	X	63	0	0
Gemer	2013	I-IIA	<=2	any	X	X	107	0	0
Total							**1324**	**4**	**0.3**

Acceptable Alternatives for Stage IA2 and IB1 Cervical Cancer

- Radical trachelectomy (or cone) and nodes (Fertility sparing)
- Intracavitary brachytherapy and pelvic RT + chemo
- Simple hysterectomy and nodes?
- Laparoscopic radical hysterectomy and nodes?
- Robotic radical hysterectomy and nodes?

CONCERV Trial

"Low-risk" Stage IA2-IB1

Prospective

2009-2019

IA2-IB1 cervical SCC/Adeno

Tumor <2cm

DOI <10mm; No LVSI

Cone with negative margins

Fertility desiring: PLND (n=44)

Not desiring fertility: Simple hyst + PLND (n=56)

N=100

MIS approach: 96 (96%)

Residual in hyst: 1/56 (1.8%)

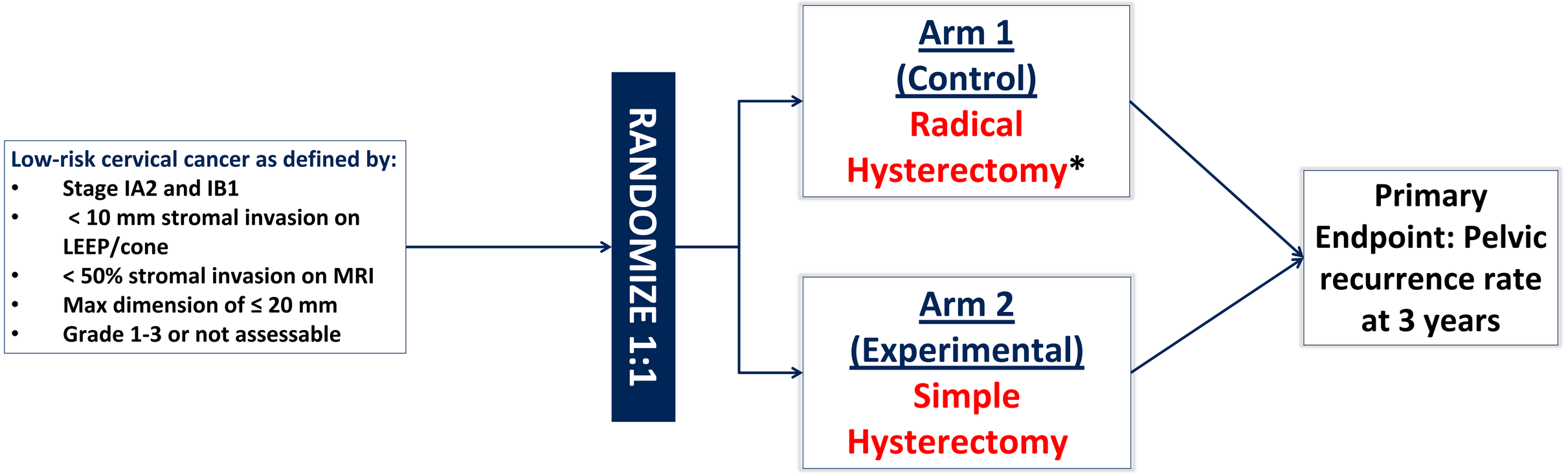
Med F/U=36 months

5% positive nodes

2-year recurrence rate : 3.5%

Schmeler K, et al. IJGC 2021

SHAPE Trial Schema

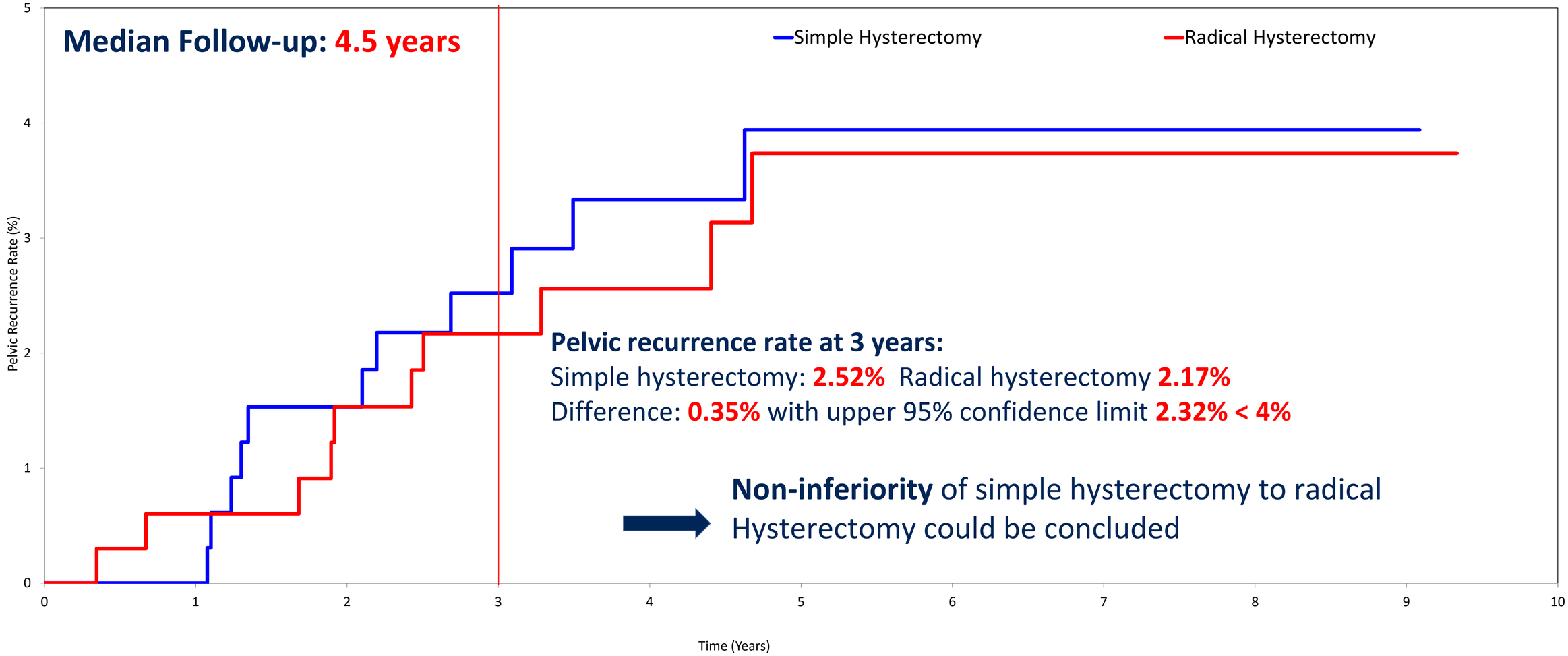


Secondary Endpoints

- Pelvic relapse free survival (PRFS)
- Extra pelvic relapse free survival (EPRFS)
- Relapse free survival (RFS)
- Overall Survival (OS)
- Rates of sentinel node detection, parametrial involvement, involved surgical margins, positive pelvic nodes
- Patient reported outcomes

***Regardless of treatment assignment, surgery will include pelvic lymph node dissection with optional sentinel lymph node (SN) mapping. If SN mapping is to be done, the mode is optional, but the laparoscopic approach is preferred**

Pelvic Recurrence Rate (ITT)



Simple	350	328	311	273	204	133	61	31	14	4	0
Radical	350	329	315	286	208	132	66	31	16	2	0

The NEW ENGLAND JOURNAL of MEDICINE

LACC Trial

Primary outcome

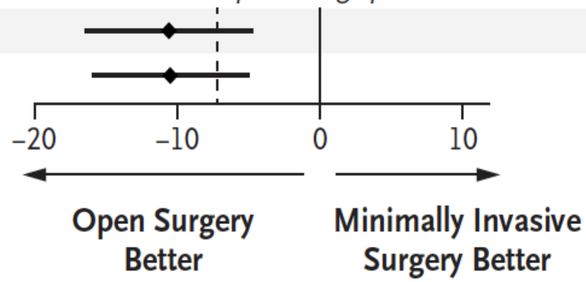
ORIGINAL ARTICLE

Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer

Pedro T. Ramirez, M.D., Michael Frumovitz, M.D., Rene Pareja, M.D., Aldo Lopez, M.D., Marcelo Vieira, M.D., Reitan Ribeiro, M.D., Alessandro Buda, M.D., Xiaojian Yan, M.D., Yao Shuzhong, M.D., Naven Chetty, M.D., David Isla, M.D., Mariano Tamura, M.D., Tao Zhu, M.D., Kristy P. Robledo, Ph.D., Val Gebski, M.Stat., Rebecca Asher, M.Sc., Vanessa Behan, B.S.N., James L. Nicklin, M.D., Robert L. Coleman, M.D., and Andreas Obermair, M.D.

A

Population	Disease-free Survival Rate at 4.5 Yr (95% CI)		Difference (95% CI)	P Value for Noninferiority
	Minimally Invasive Surgery	Open Surgery		
	percent		*percentage points*	
Intention-to-treat population	86.0 (79.7–90.4)	96.5 (92.7–98.4)		0.87
Per-protocol population	87.1 (81.0–91.3)	97.6 (94.1–99.0)		0.88



Median F/U = 2.5 years (0-6.3)

Information at 4.5 years = 59.7% of the cases

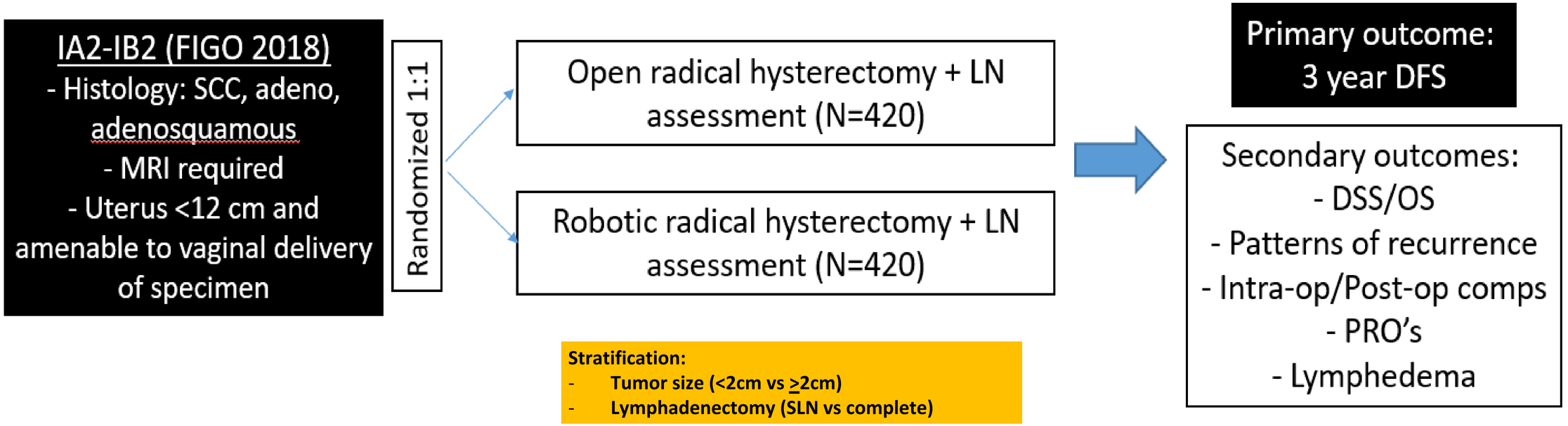
Final power = 84%

Disease-free survival at 4.5 years was lower with minimally invasive surgery - 86% vs 96.5%

Ramirez PT, et al. N Engl J Med 2018;379:1895-1904

GOG-3043/ROCC

A Randomized Controlled Trial of Robotic versus Open Radical Hysterectomy for Early-Stage Cervical Cancer



N= 840

Primary Endpoint = DFS

PI: Bixel, K, Leitao, M, Randall L

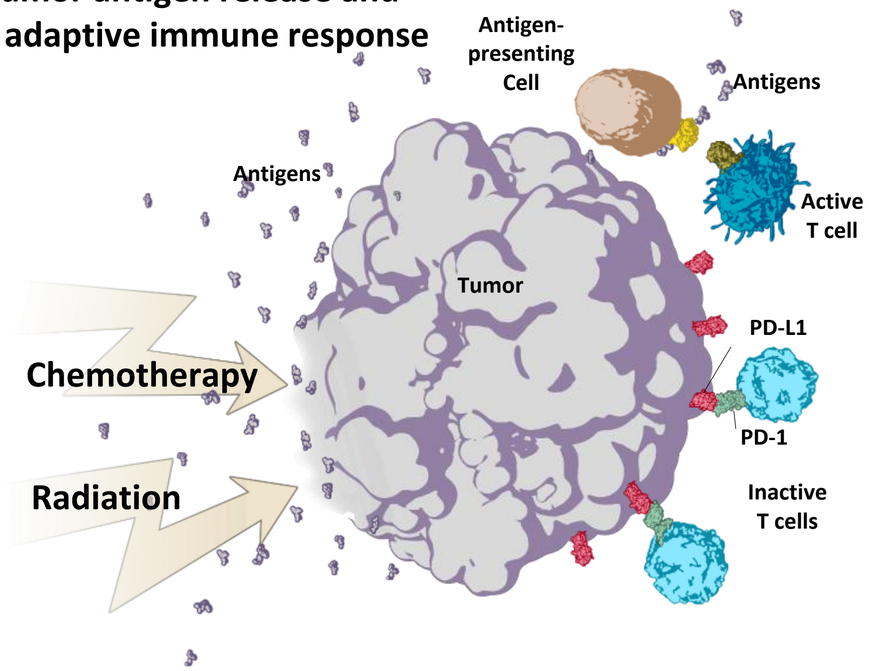
NCT04831580

Checkpoint Inhibitor (Cpi) Mechanism of Action with Chemoradiation

CHEMORADIATION

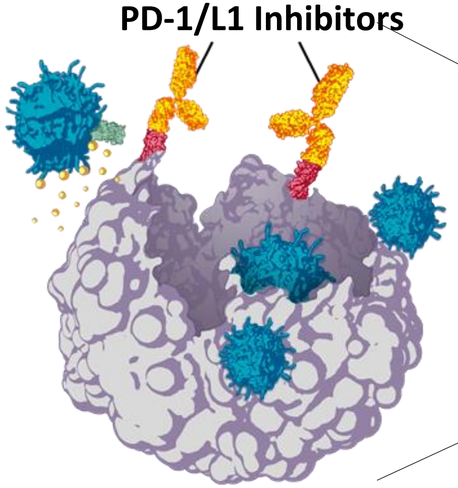
Chemoradiation induces tumor antigen release and an adaptive immune response

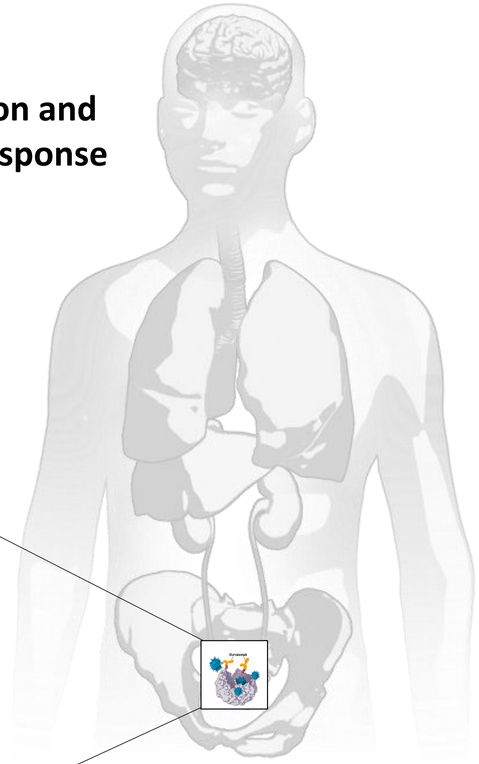
PD-L1 overexpression leads to immune cell evasion



CHECKPOINT INHIBITOR

Cpi reverses immune suppression and leads to a systemic antitumor response





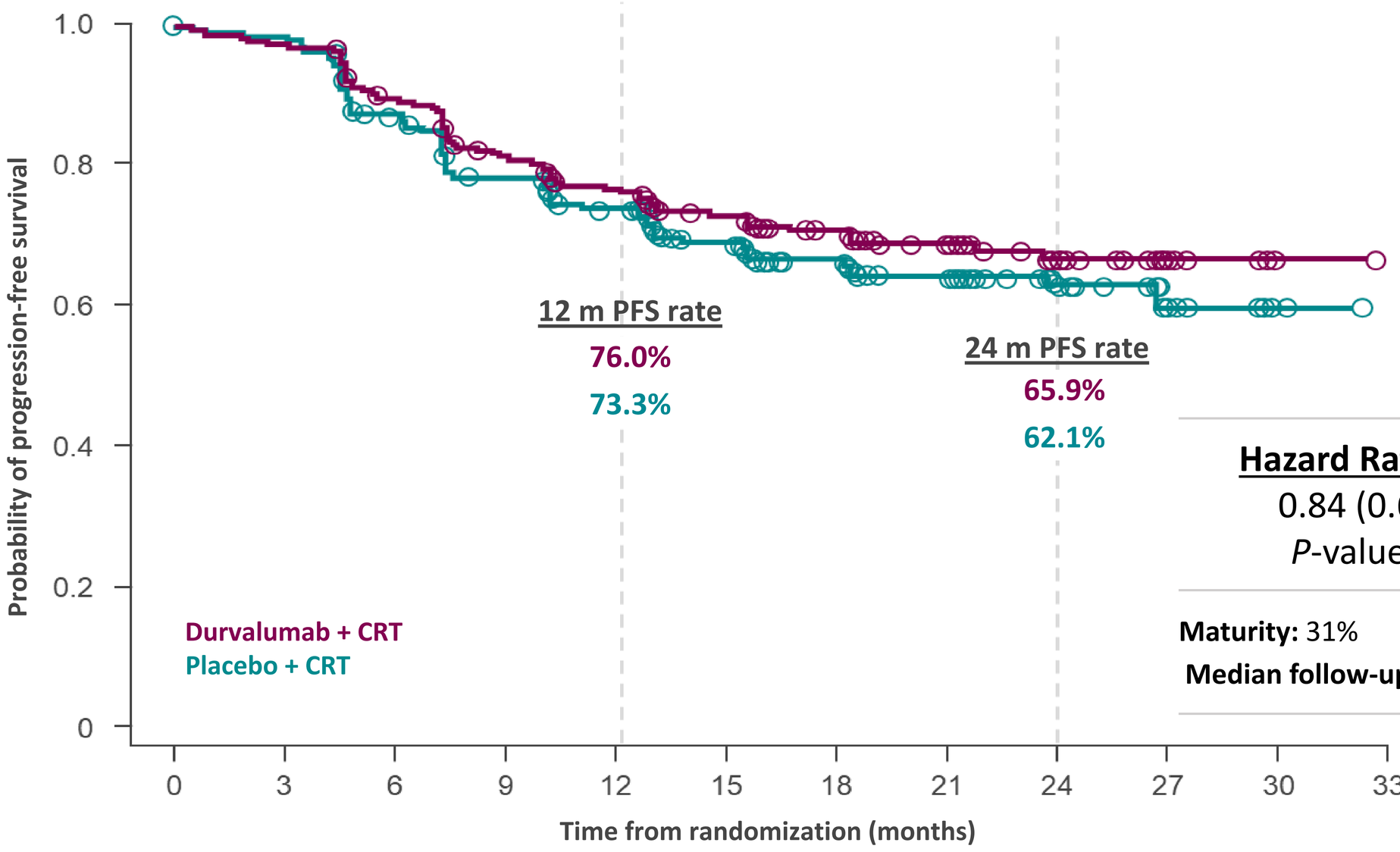
Deng L, et al. *J Clin Invest.* 2014;124:687-695; Dovedi SJ, et al. *Cancer Res.* 2014;74:5458-5468; Chacon JA, et al. *Vaccines (Basel).* 2016;4:E43;
Formenti SC, Demaria S. *J Natl Cancer Inst.* 2013;105:256-265; Funaki S, et al. *Oncol Rep.* 2017;38:2277-2284; Antonia SJ, et al. *N Engl J Med.* 2017;377:1919-1929.

Randomized Phase III ICI Trials in the Locally-advanced Setting

Frontline ICI trial	Population	Agent (n)	Design	Primary endpoint(s)
CALLA (NCT03830866)	•FIGO 2009 IB2-IIB node+ •IIIA-IVA any nodal status •Measurable RECIST v1.1 •ECOG PS: 0-1	Durva (714)	2 arm 1:1 CRT control 24 months	•PFS
ENGOT cx11/GOG 3047/ KEYNOTE-A18 (NCT04221945)	•FIGO 2009 IB2-IIB node+ •IIIA-IVA any nodal status •Measurable RECIST v1.1 •ECOG PS: 0-1	Pembro (980)	2 arm 1:1 CRT control 24 months	•PFS •OS

CRT, chemoradiotherapy; durva, durvalumab; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Gynecology and Obstetrics; ICI, immune checkpoint inhibitor; OS, overall survival; pembro, pembrolizumab; RECIST, Response Evaluation Criteria in Solid Tumours

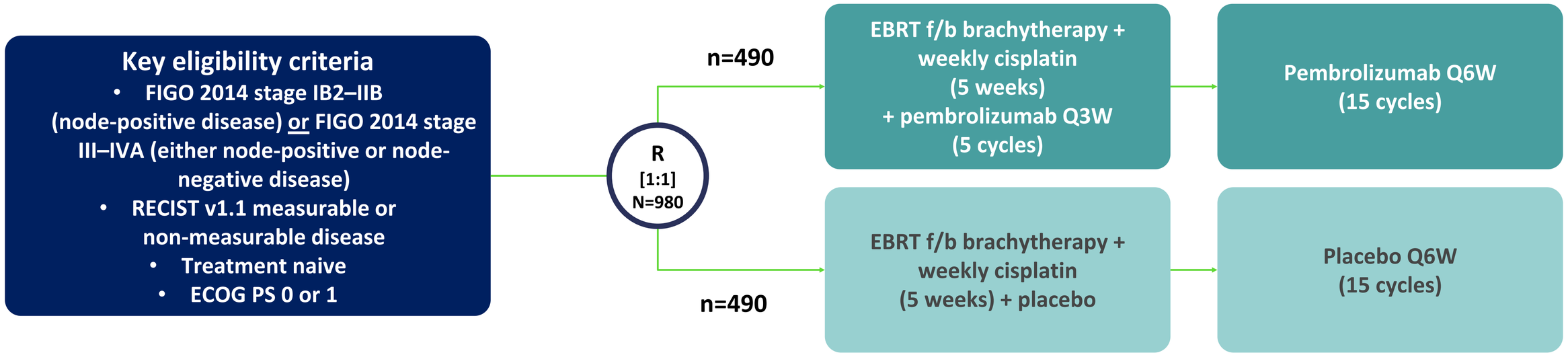
CALLA: Primary Endpoint: Progression-Free Survival



Hazard Ratio (95% CI)
0.84 (0.65–1.08)
P-value = 0.174

Maturity: 31%
Median follow-up: 18.5 m vs 18.4 m

ENGOT-CX11/GOG 3047/KEYNOTE-A18



Stratification factors

- IMRT or VMAT versus non-IMRT and non-VMAT
- Stage at initial diagnosis of cervical cancer (FIGO 2014 Stage IB2–IIB [node-positive disease] vs FIGO 2014 Stage III–IVA [either node-positive or node-negative disease])
- Planned total radiotherapy dose (EBRT + brachytherapy dose) of <70 Gy vs ≥70 Gy

Endpoints

- Dual primary: PFS, OS

ENGOT-CX11/GOG 3047/KEYNOTE-A18

Merck Announces Phase 3 KEYNOTE-A18 Trial Met Primary Endpoint of Progression-Free Survival (PFS) in Patients With Newly Diagnosed High-Risk Locally Advanced Cervical Cancer

Save

July 19, 2023 6:45 am ET

KEYTRUDA® (pembrolizumab) plus concurrent chemoradiotherapy demonstrated statistically significant and clinically meaningful improvement in PFS versus concurrent chemoradiotherapy alone in these patients

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study

Key Eligibility Criteria

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy (prior radiotherapy and chemoradiotherapy permitted)
- ECOG PS 0 or 1

Stratification Factors

- Metastatic disease at diagnosis (yes vs no)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)
- Planned bevacizumab use (yes vs no)

R
1:1

Pembrolizumab 200 mg IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

Placebo IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

End Points

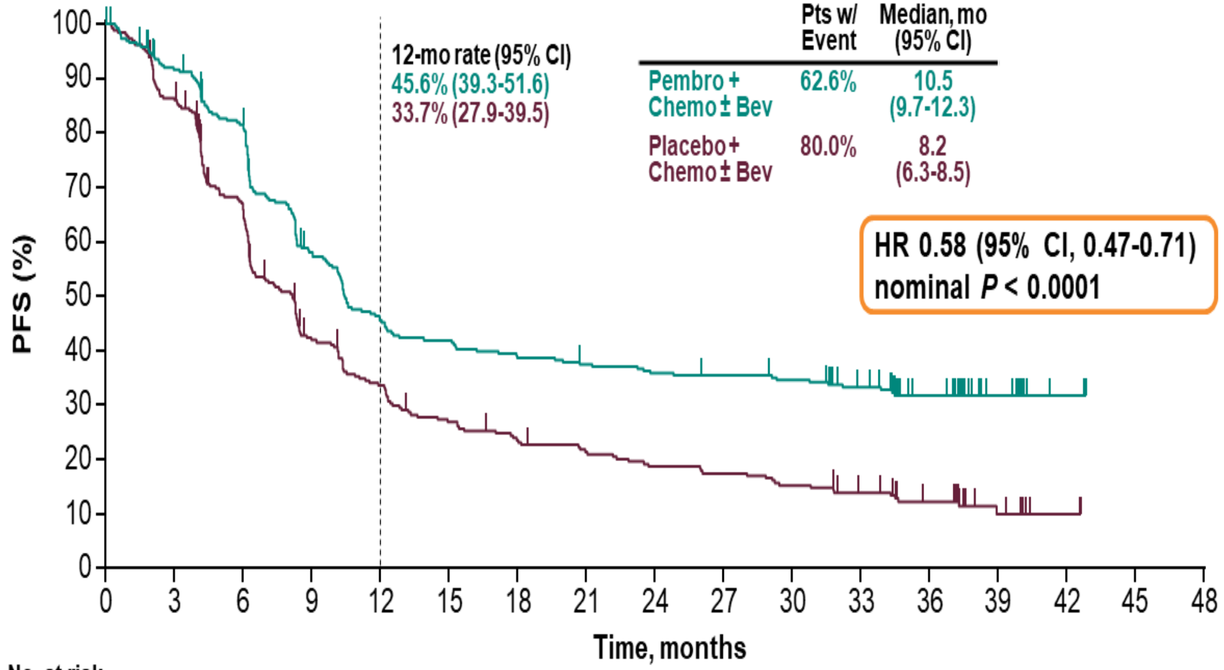
- **Dual primary:** OS and PFS per RECIST v1.1 by investigator
- **Secondary:** ORR, DOR, 12-mo PFS, and safety

[a]Paclitaxel: 175 mg/m^2. Cisplatin: cisplatin 50 mg/m^2. Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation. CPS, combined positive score (number of PD-L1–staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of viable tumor cells, multiplied by 100). KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

KN-826 Final PFS and OS

B Monk KN826 ASCO 2023

Protocol-Specified Final PFS: PD-L1 CPS ≥1 Population



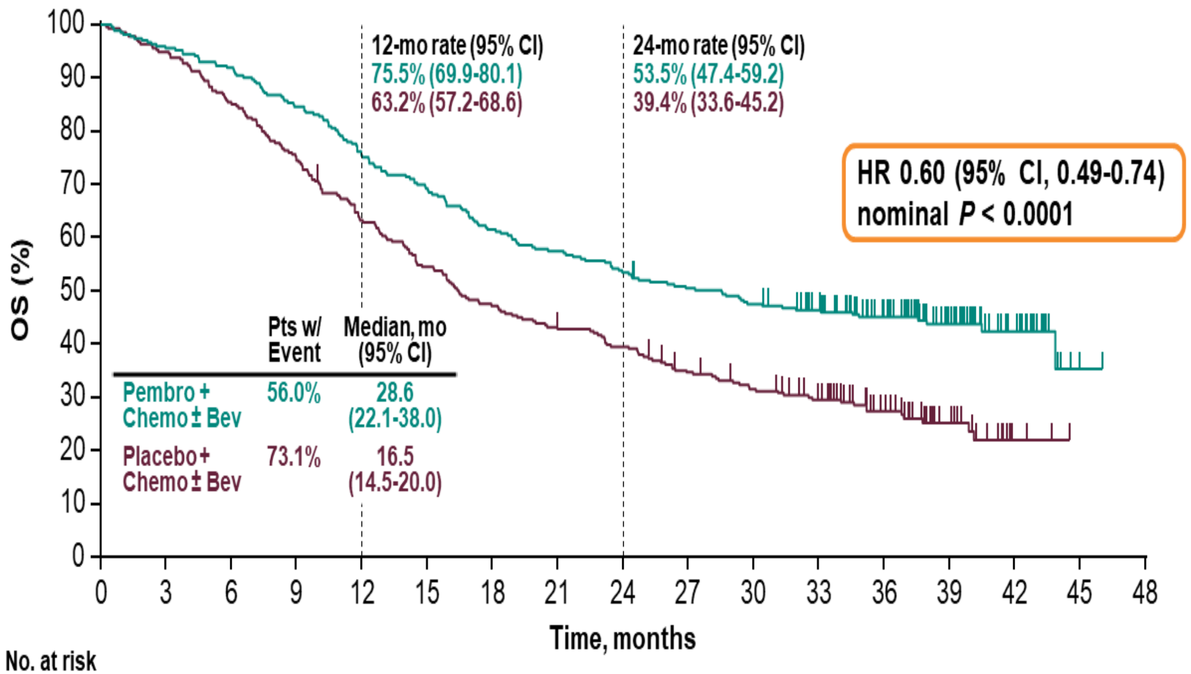
No. at risk

273	238	208	144	113	104	97	92	88	86	83	70	46	25	6	0	0
275	229	170	103	81	64	55	49	43	40	35	28	18	7	2	0	0

Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

B Monk KN826 ASCO 2023

Protocol-Specified Final OS: PD-L1 CPS ≥1 Population

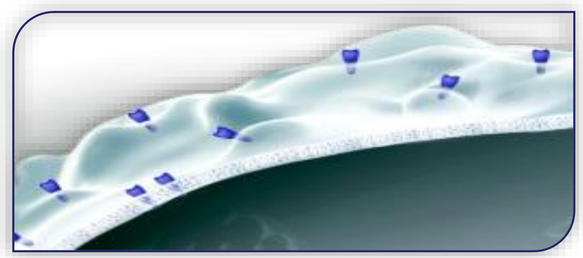


No. at risk

273	261	251	231	206	189	168	157	146	136	128	116	90	52	22	2	0
275	261	235	207	173	149	129	117	107	91	81	68	45	24	3	0	0

cutoff date: October 3, 2022.

Tisotumab Vedotin



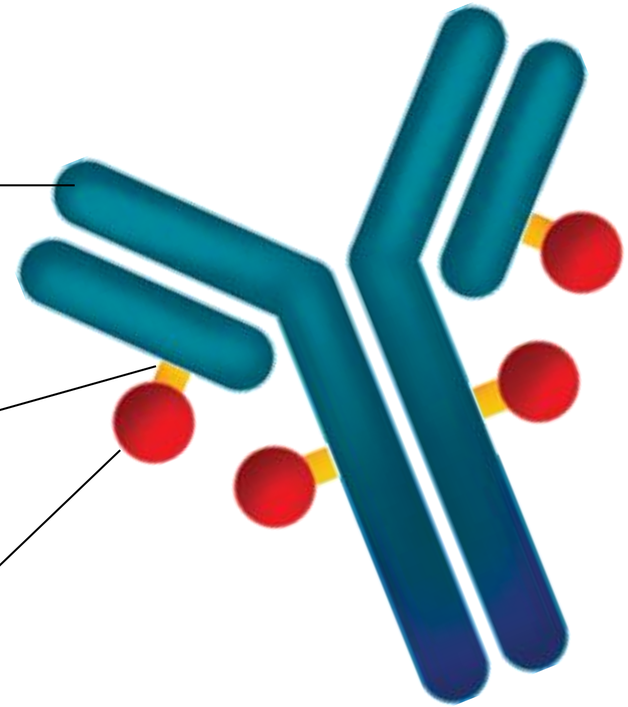
Tissue Factor (TF)

- Transmembrane protein – main physiological initiator of coagulation[1]
    - Role in oncogenesis includes angiogenesis, cell adhesion, motility, and cell survival[2]
- Highly expressed in many solid tumors, including cervical, ovarian, pancreatic, SCCHN, NSCLC, and others[3-8]
- Expression associated with poor clinical outcomes, tumor initiation, progression, angiogenesis, and metastasis[2]

Fully human mAb
Targets tissue factor

Linker
Protease-cleavable val-citrulline maleimidocaproyl linker
Conjugated to monoclonal antibody via cysteine residues

Cytotoxic payload
Monomethyl auristatin E (MMAE), a microtubule-disrupting agent
Drug-to-antibody ratio of approximately 4:1



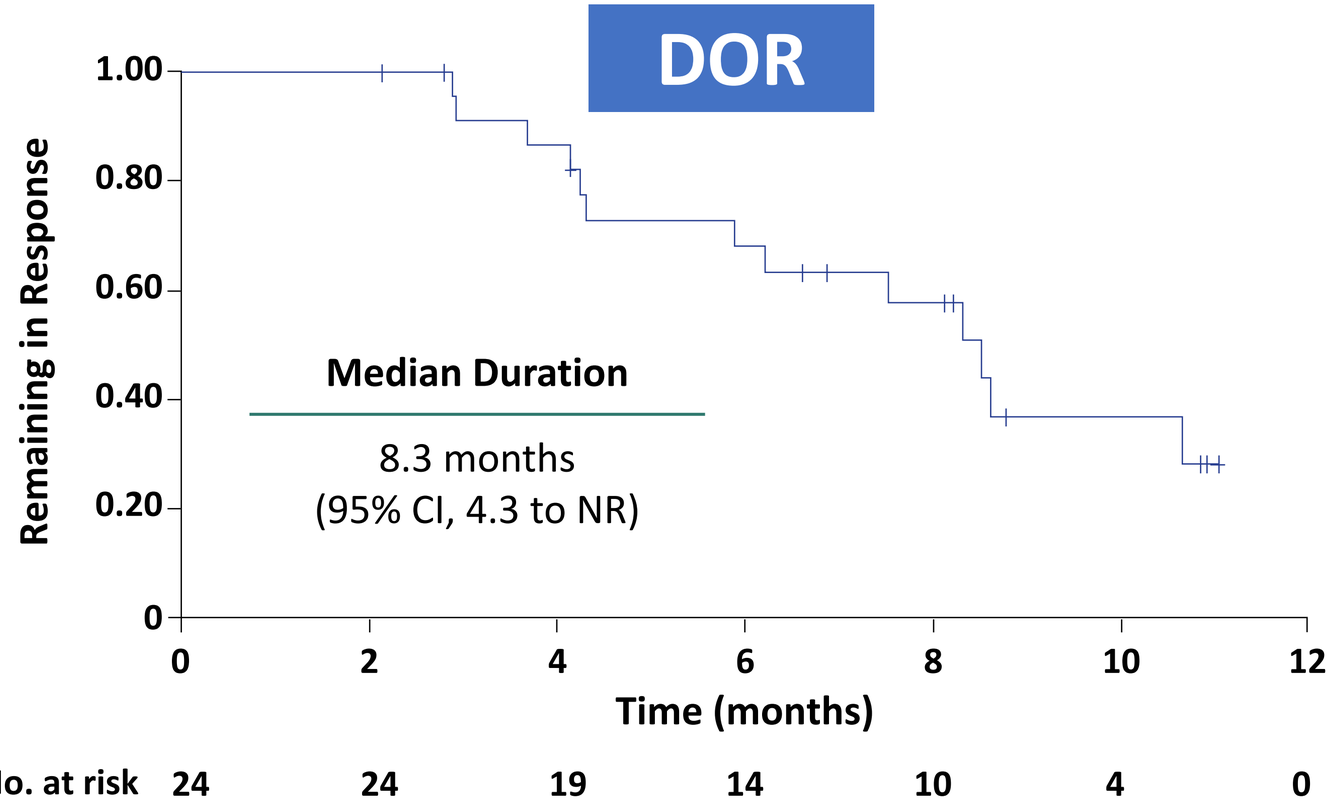
The human anti-TF antibody of TV inhibits tumor proliferation pathways with minimal impact on clotting cascade

Drug: Antibody ~ 4

1. Versteeg, H. H. (2015, October). Tissue factor: old and new links with cancer biology. In Seminars in Thrombosis and Hemostasis (Vol. 41, No. 07, pp. 747-755). Thieme Medical Publishers.
2. van den Berg, Y. W., Osanto, S., Reitsma, P. H., & Versteeg, H. H. (2012). The relationship between tissue factor and cancer progression: insights from bench and bedside. Blood, The Journal of the American Society of Hematology, 119(4), 924-932.
3. Chu, A. J. (2011). Tissue factor, blood coagulation, and beyond: an overview. International journal of inflammation, 2011.
4. Förster, Y., Meye, A., Albrecht, S., & Schwenzer, B. (2006). Tissue factor and tumor: clinical and laboratory aspects. Clinica Chimica Acta, 364(1-2), 12-21.
5. Cocco, E., Varughese, J., Buza, N., Bellone, S., Glasgow, M., Bellone, M., ... & Santin, A. D. (2011). Expression of Tissue factor in Adenocarcinoma and Squamous Cell Carcinoma of the Uterine Cervix: Implications for immunotherapy with hI-con1, a factor VII-IgGF c chimeric protein targeting tissue factor. BMC cancer, 11, 1-10.
6. Ruf, W., Disse, J., CARNEIRO-LOBO, T. C., Yokota, N., & Schaffner, F. (2011). Tissue factor and cell signalling in cancer progression and thrombosis. Journal of Thrombosis and Haemostasis, 9, 306-315.
7. Jacobs, B., Zhang, X., Gaughan, J. P., & Bromberg, M. (2012). Association of tissue factor expression in squamous cell head and neck carcinomas with well-differentiated tumors.
8. Coleman, R. L., Lorusso, D., Gennigens, C., González-Martín, A., Randall, L., Cibula, D., ... & Bhatia, S. (2021). Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. The Lancet Oncology, 22(5), 609-619.

Antitumor Activity by IRC Assessment

	N=101
Confirmed ORR (95% CI),[a] %	**24 (15.9–33.3)**
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)
PD, n (%)	24 (24)
Not evaluable, n (%)	4 (4)
Disease control rate (95% CI),[b] %	72 (62.5–80.7)
Median duration of response (95% CI), mo	**8.3 (4.2–NR)**
Median time to response (range), mo	1.4 (1.1–5.1)



Data cutoff: February 06, 2020.

CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PD, disease progression; PR, partial response; SD, stable disease.

[a] Based on the Clopper-Pearson method. [b] Patients with a confirmed response (CR or PR confirmed at least 4 weeks later) or SD (as measured at least 5 weeks after the first dose of tisotumab vedotin). [c] Median duration of follow-up: 10.0 months. + indicates a change greater than 100%. Colored bars represent the best overall confirmed response. CR, PR, SD, and PD were based on RECIST v1.1 as evaluated by IRC.

Coleman, R. L., Lorusso, D., Gennigens, C., González-Martín, A., Randall, L., Cibula, D., ... & Bhatia, S. (2021). Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. The Lancet Oncology, 22(5), 609-619.

FDA Grants Accelerated Approval to Tisotumab Vedotin in Recurrent Or Metastatic Cervical Cancer

September 20, 2021
Audrey Sternberg

Tisotumab vedotin may now be used to treat patients with recurrent or metastatic cervical cancer after the FDA's decision to grant the agent an accelerated approval.

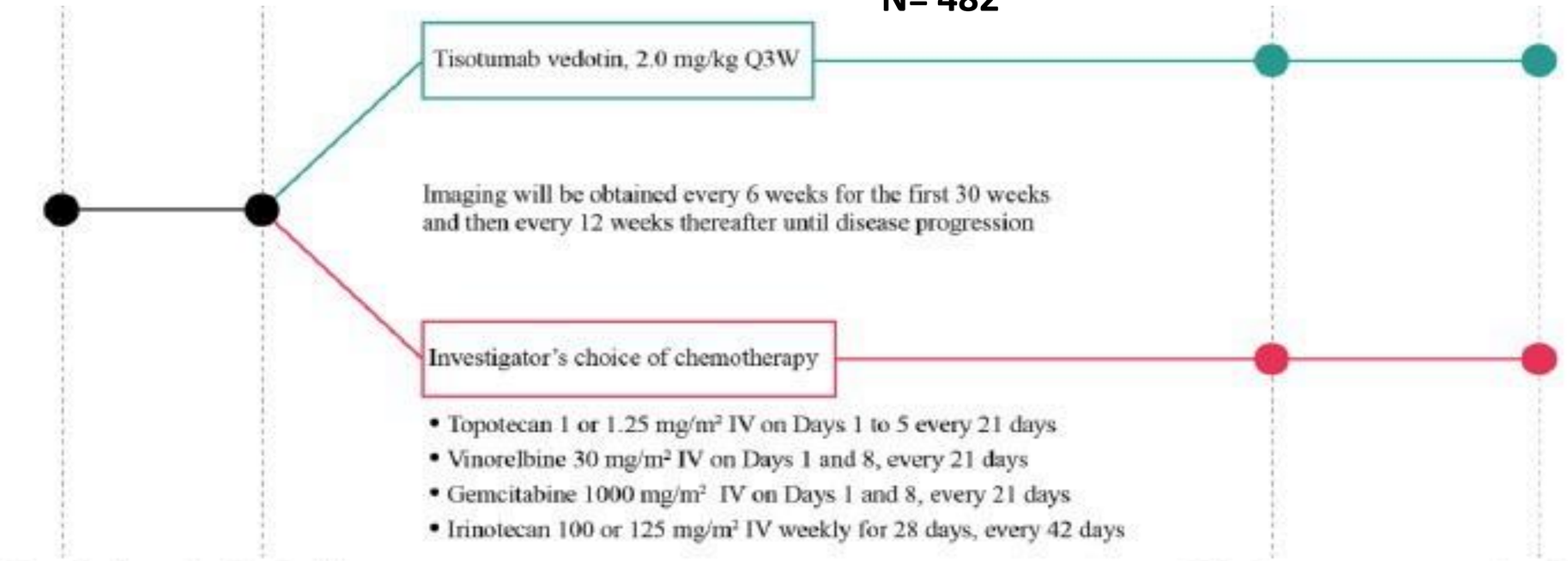
Accelerated approval has been granted to tisotumab vedotin-tftc for the treatment of patients with recurrent or metastatic cervical cancer following disease progression on or after chemotherapy, according the companies responsible for developing the agent.

The decision from the agency is supported by data from the single-arm phase 2 innovaTV 204 trial (NCT03438396) of tisotumab vedotin which resulted in a 24% (95% CI, 15.9%-33.3%) confirmed overall response rate by independent review committee in previously treated, recurrent or metastatic cervical cancer.

Sternberg, A. (2021, September 21). FDA Grants Accelerated Approval to Tisotumab Vedotin in Recurrent Or Metastatic Cervical Cancer. Cancer Network.

GOG-3057/InnovaTV 301: Schema

N= 482



Stratification Factors
ECOG Performance Status (0 vs 1)
Prior bevacizumab administration (yes vs no)
Region (US; EU; Other)
Prior anti-PD-1 or PD-L1 administration (yes vs no)

*The proportion of participants who have not received prior bevacizumab in combination with chemotherapy as 1L treatment will be capped at 50%.

** Some AESIs may be followed longer than 30 days until resolution, improvement, or stabilization.

Primary Endpoint = OS

Tisotumab Vedotin vs Chemotherapy in Recurrent or Metastatic Cervical Cancer (innovaTV 301) - ClinicalTrials.gov Identifier: NCT04697628. ClinicalTrials.gov. (n.d.).

innovaTV 301 - Tisotumab Vedotin vs Chemotherapy in Recurrent or Metastatic Cervical Cancer. Larvol. (2021, April 28).

ENGOT-Cx8/GOG 3024/InnovaTV 205: Dose Expansion

Phase 1b: Dose Escalation

- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Acceptable safety profile
- ✓ Encouraging anti-tumor activity

Phase 2: Dose Expansion

Datacut for all dose expansion arms reported here: 28 Feb, 2022

1L TV + pembro[b]	No prior systemic therapy for r/mCC	N=33 Median f/u: 18.8 mos	TV 2.0 mg/kg IV (Q3W) + pembro 200 mg IV (Q3W)
2L/3L TV + pembro[b]	r/mCC with disease progression on/after 1–2 prior systemic therapies	N=35 Median f/u: 15.0 mos	TV 2.0 mg/kg IV (Q3W) + pembro 200 mg IV (Q3W)
1L TV + carbo	No prior systemic therapy for r/mCC	N=33 Median f/u: 14.6 mos	TV 2.0 mg/kg IV (Q3W) + carbo AUC 5 IV (Q3W)

Primary endpoint:
Objective response rate[a] per RECIST v1.1

Secondary endpoints:
- AEs and laboratory parameters
- Duration of response
- Time to response
- Progression free survival
- Overall survival

1L TV + pembro in patients with r/mCC: First disclosure

2L/3L TV + pembro & 1L TV + carbo: Updated with longer follow-up

[a] Tumor response assessed every 6 weeks. [b] Pembro will be administered up to 35 cycles, approximately 2 years.

f/u, follow-up; r/mCC, recurrent or metastatic cervical cancer; TV, tisotumab vedotin.

Vergote I et al. 2022. Abstract TPS5603.

2023 ASCO ANNUAL MEETING

DESTINY-PanTumor02

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

Funda Meric-Bernstam

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

June 5, 2023

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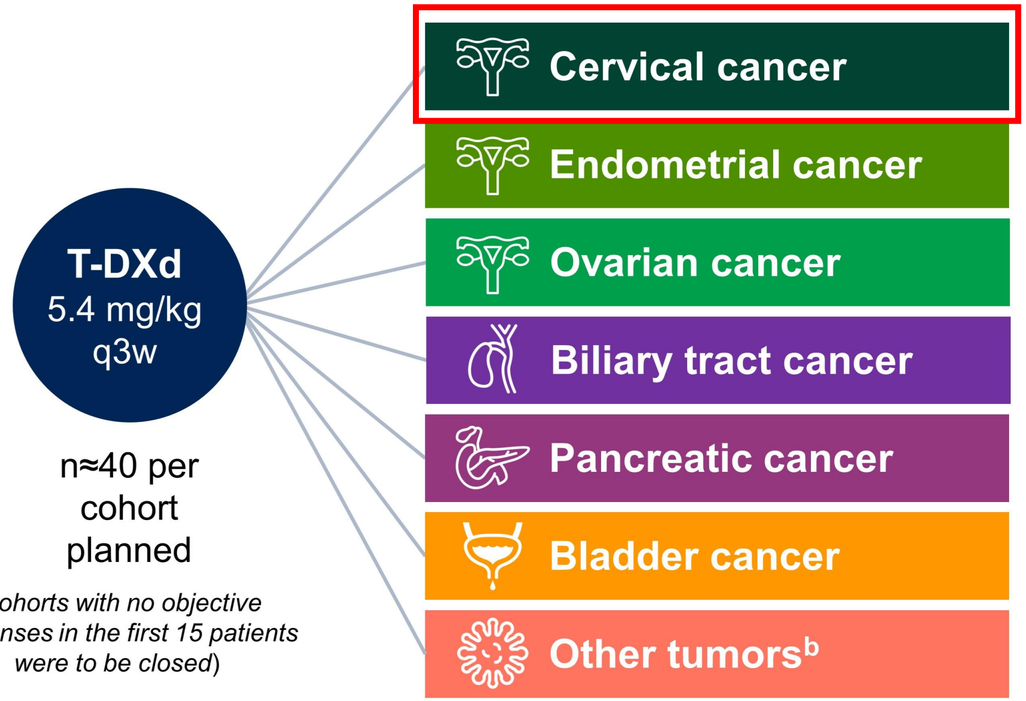
On behalf of the DESTINY-PanTumor02 investigators

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 guidelines[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1



n≈40 per cohort planned

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

Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

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

Data cut-off for analysis:

- Nov 16, 2022

[a]Patients were eligible for either test. All patients were centrally confirmed. [b]Patients 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.
[c]Investigator-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.

PRESENTED BY: Funda Meric-Bernstam, MD

Cervical Cancer Cohort (N=40): Efficacy T-Dxd

Investigator Assessment	
ORR N (%)	20 (50.0)
CR	2 (5.0)
PR	18 (45.0)
SD	11 (27.5)
PD	7 (17.5)
Not evaluable	1 (2.5)
DCR	27 (67.5)
Median DOR, month (95% CI)	9.8 (4.2- NR)
Independent Central Review ORR N (%)	16 (40)

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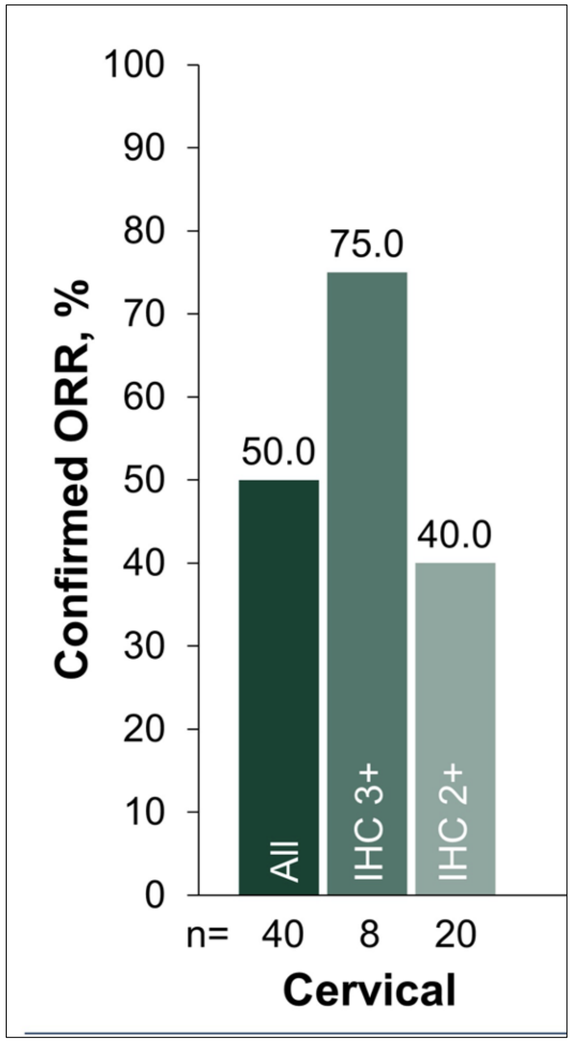
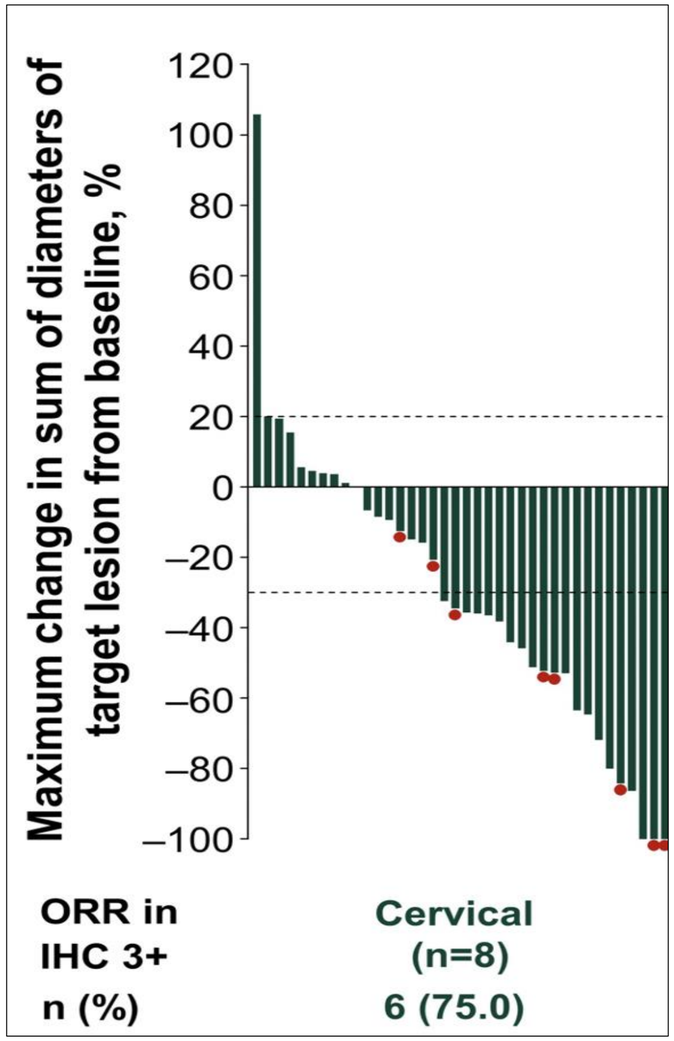
T-Dxd Efficacy by HER2 status in Cervical Cancer





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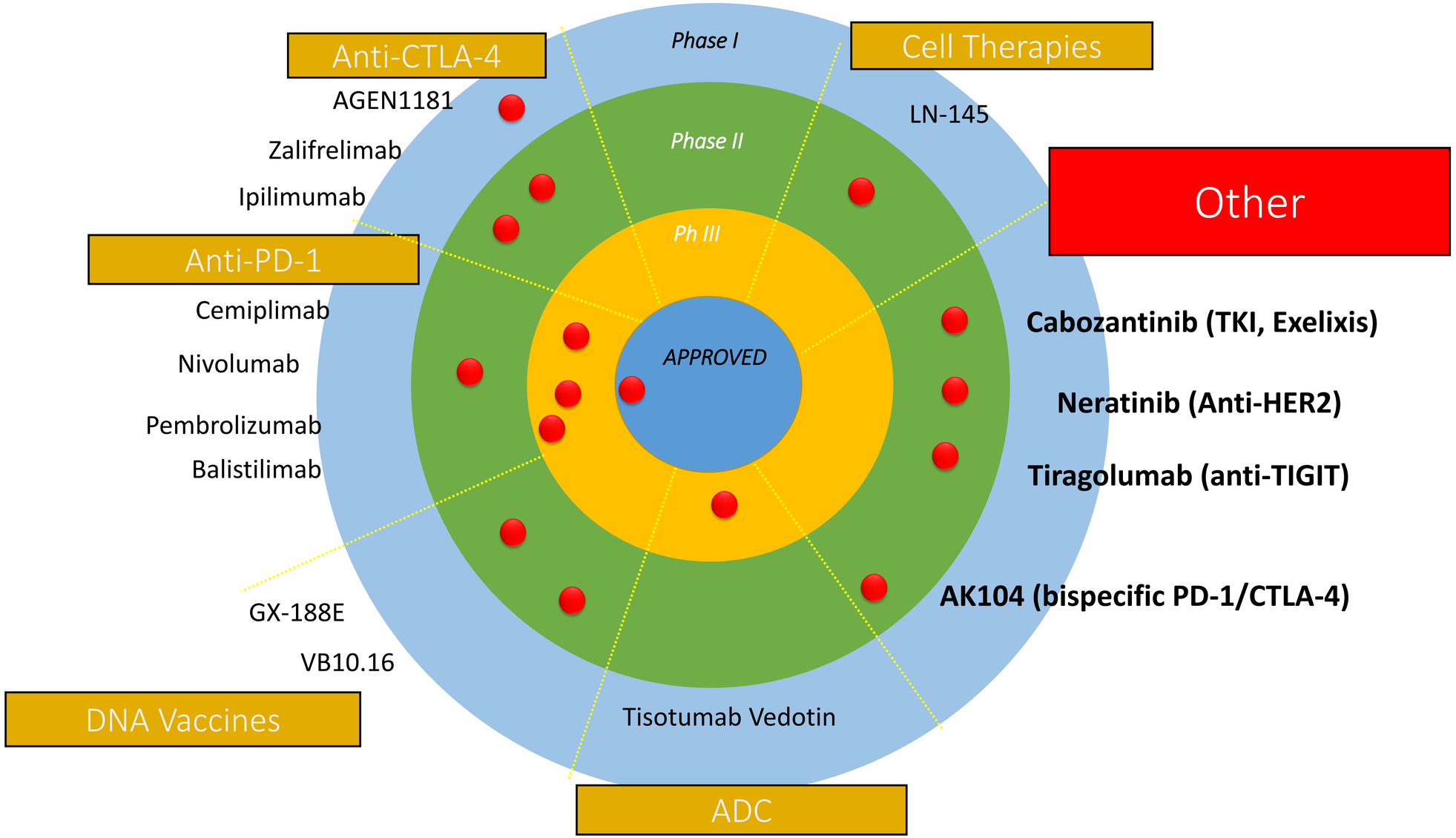
SYSTEMIC THERAPY FOR CERVICAL CANCER[a]

Squamous Cell Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma		
Chemoradiation[b]	**Recurrent or Metastatic Disease**	
	First-line Therapy[b,d]	**Second-line or Subsequent Therapy[i]**
Preferred Regimens • Cisplatin • Carboplatin if patient is cisplatin intolerant **Other Recommended Regimens[c] (if cisplatin and carboplatin are unavailable)** • Capecitabine/mitomycin[1] • Gemcitabine[2] • Paclitaxel[3,4]	**Preferred Regimens** • PD-L1–positive tumors ▸ Pembrolizumab + cisplatin/paclitaxel ± bevacizumab (category 1)[e,f,g,h,5] ▸ Pembrolizumab + carboplatin/paclitaxel ± bevacizumab (category 1)[e,f,g,h,5] • Cisplatin/paclitaxel/bevacizumab[e,h,6] (category 1) • Carboplatin/paclitaxel/bevacizumab[e,h] **Other Recommended Regimens** • Cisplatin/paclitaxel (category 1)[7,8] • Carboplatin/paclitaxel[9,10] (category 1 for patients who have received prior cisplatin therapy) • Topotecan/paclitaxel/bevacizumab[e,h,6,11] (category 1) • Topotecan/paclitaxel[11] • Cisplatin/topotecan[11] • Cisplatin[8] • Carboplatin[12,13]	**Preferred Regimens** • Pembrolizumab for TMB-H tumors[f,j] or PD-L1–positive[g] or MSI-H/dMMR tumors[f,14] • Tisotumab vedotin-tftv[15] • Cemiplimab[f,16] **Other Recommended Regimens** • Bevacizumab[e] • Paclitaxel[13,17] • Albumin-bound paclitaxel • Docetaxel • Fluorouracil • Gemcitabine • Pemetrexed • Topotecan • Vinorelbine • Irinotecan **Useful in Certain Circumstances** • PD-L1–positive tumors ▸ Nivolumab[f,g,18] • HER2-positive tumors (IHC 3+ or 2+) ▸ Fam-trastuzumab deruxtecan-nxki[19] • RET gene fusion-positive tumors ▸ Selpercatinib • *NTRK* gene fusion-positive tumors ▸ Larotrectinib ▸ Entrectinib


Anti-CTLA-4
AGEN1181
Zalifrelimab
Ipilimumab
Anti-PD-1
Cemiplimab
Nivolumab
Pembrolizumab
Balistilimab
DNA Vaccines
GX-188E
VB10.16
ADC
Tisotumab Vedotin
Cell Therapies
LN-145
Other
Cabozantinib (TKI, Exelixis)
Neratinib (Anti-HER2)
Tiragolumab (anti-TIGIT)
AK104 (bispecific PD-1/CTLA-4)
Phase I
Phase II
Ph III
APPROVED

Summary

- Clinical trial activity in gynecologic cancers is robust and meaningful
- New targets, strategies, and agents are rapidly entering the clinical domain
- Importance of clinical trial is evident in that through success/failure we define the new standards of care – increasing the efficacy/toxicity differential
- Thanks to all who have inquired about or participate in the investigative process

Thank You!!!

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