IGCS 2023
Annual Global Meeting
SEOUL

IGCS 2023 Abstracts: Late-Breaking Oral Presentations

Late-breaking abstracts selected for oral and short oral presentations are included in the below sessions. The sessions will be recorded for on-demand viewing via the IGCS 360 Educational Portal.

Plenary 01: Oral Abstract Presentations
Sunday, November 5, 2023, 9:00 – 10:30 AM
Auditorium

Plenary 02: Changing the Landscape of Endometrial Cancer
Sunday, November 5, 2023, 4:30 – 5:30 PM
Auditorium

Plenary 03: Oral Abstract Presentations – Ovarian Cancer
Tuesday, November 7, 2023, 8:30 – 9:30 AM
Auditorium

Focused Plenary 02: Surgery
Monday, November 6, 2023, 5:50 – 6:50 PM
Grand Ballroom 101+102

Closing Session: The Development of Prognosis and Predictive Markers
Tuesday, November 7, 2023, 3:55 – 5:00 PM
Auditorium

PO004LBA / #1515 – Late-Breaking Abstract

EFFICACY AND SAFETY OF AVUTOMETINIB + DEFACTINIB IN RECURRENT LOW-GRADE SEROUS OVARIAN CANCER FOLLOWING PRIOR SYSTEMIC THERAPY

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

Rachel Grisham[1], Carol Aghajanian[1], Els Van Nieuwenhuysen[2], Manuel Rodrigues[3], Kari Ring[4], Alessandro Santin[5], Nicoletta Colombo[6], Emily Prendergast[7], Premal Thaker[8], Kathleen Moore[9], Erin Salinas[10], Isabelle Ray-Coquard[11], Hye Sook Chon[12], Peter Rose[13], Ana Oaknin[14], Andrew Clamp[15], Mitul Gandhi[16], Bradley Monk[17], Robert Holloway[18], Toon Van Gorp[19], Michel Fabbro[20], Christine Gennigens[21], Nicholas Wojtynek[22], Stephanie Lustgarten[23], Susana Banerjee[24]
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Introduction: Avutometinib is a novel small molecule RAF/MEK clamp. FAK activation is a resistance mechanism to RAF/MEK inhibition; defactinib, a small molecule FAK inhibitor, has shown synergistic antitumor activity with avutometinib. Avutometinib + defactinib demonstrated a 45% ORR and a mild to moderate, manageable/reversible safety profile in heavily pretreated (mLoT=4) recurrent LGSOC (KRAS mt + wt) (ENGOT-ov60/GOG-3052/RAMP 201, NCT04625270).

Methods: This post-hoc analysis of the phase 2 ENGOT-ov60/GOG-3052/RAMP 201 study in recurrent LGSOC (06Apr2023 data cutoff) was performed to assess efficacy (Part A; confirmed ORR via blinded independent central review) and safety (all treated patients) in the context of 1) lines of prior systemic therapy (1-3 LoT, ≥4 LoT) and 2) best response to most recent prior treatment in the metastatic/recurrent setting (PR/CR, no PR/CR; as assessed by treating investigator).

Results: In the combination arm, similar ORRs were observed in patients that were treated with 1-3 (5/11, 45.5%) and ≥4 LoT (8/18, 44.4%) (Table 1). Prior to enrollment in RAMP 201, only 2/23 (8.7%) patients responded to their last prior treatment, whereas the combination of avutometinib + defactinib yielded an ORR of 43.5% (10/23) in this subgroup (Table 2). The safety profiles of avutometinib + defactinib were similar in the less and more heavily pretreated subgroups, and both analyses were consistent with previously reported safety data. The majority of TRAEs were mild to moderate,

manageable/reversible.

Table 1. ORR by Number of Prior Therapies per Blinded Independent Central Review.

	Avutometinib			Avutometinib + Defactinib		
	1-3 LoT (n=16)	≥4 LoT (n=15)	Total (n=31)	1-3 LoT (n=11)	≥4 LoT (n=18)	Total (n=29)
Confirmed ORR, n (%)	2 (12.5)	1 (6.7)	3 (9.7)	5 (45.5)	8 (44.4)	13 (44.8)
CR, n (%)	1 (6.3)	0 (0)	1 (3.2)	0 (0)	0 (0)	0 (0)
PR, n (%)	1 (6.3)	1 (6.7)	2 (6.5)	5 (45.5)	8 (44.4)	13 (44.8)
Confirmed + Unconfirmed PR[a,b], n (%)	1 (6.3)	1 (6.7)	2 (6.5)	7 (63.6)	8 (44.4)	15 (51.7)
SD[b], n (%)	13 (81.3)	12 (80.0)	25 (80.7)	5 (45.5)	8 (40.4)	13 (41.8)
PD, n (%)	1 (6.3)	2 (12.5)	3 (9.7)	1 (9.1)	2 (11.1)	3 (10.34)
DCR[c], n (%)	15 (93.8)	13 (86.7)	28 (90.3)	10 (90.9)	16 (88.9)	26 (89.7)

Abbreviations: CR, complete response; DCR, disease control rate; LoT, lines of therapy; ORR, objective response rate; PR, progressive response; SD, stable disease.
[a]Includes any patient with unconfirmed PR.
[b]Includes patients with unconfirmed PR who have a chance to be confirmed at their next assessment.
[c]Disease control rate (SD + PR + CR) at 8 weeks.

Table 2. ORR by Best Response to Most Recent Prior Treatment in the Metastatic/Recurrent Setting per Blinded Independent Central Review.

	Avutometinib			Avutometinib + Defactinib		
	Best Response to Prior Tx: PR/CR (n=8)	Best Response to Prior Tx: No PR/CR (n=11)	Total (n=19)	Best Response to Prior Tx: PR/CR (n=2)	Best Response to Prior Tx: No PR/CR (n=21)	Total (n=23)
Confirmed ORR, n (%)	0 (0)	2 (18.2)	2 (10.5)	1 (50.0)	9 (42.9)	10 (43.5)
CR, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
PR, n (%)	0 (0)	2 (18.2)	2 (10.5)	1 (50.0)	9 (42.9)	10 (43.5)
Confirmed + Unconfirmed PR[a,b], n (%)	0	2 (18.2)	2 (10.5)	1 (50.0)	9 (42.9)	10 (43.5)
SD[b], n (%)	7 (87.5)	7 (63.6)	14 (73.7)	0 (0)	10 (47.6)	10 (43.5)
PD, n (%)	1 (12.5)	1 (9.1)	2 (10.5)	0 (0)	2 (9.5)	2 (8.7)
NE/Unknown, n (%)	0	1 (9.1)	1 (5.3)	1 (50.0)	0 (0)	1 (4.4)
DCR[c], n (%)	7 (87.5)	9 (81.8)	16 (84.2)	1 (50.0)	19 (90.5)	20 (87.0)

Abbreviations: CR, complete response; DCR, disease control rate; NE, non-evaluable; ORR, objective response rate; PR, progressive response; SD, stable disease; Tx, therapy.
[a]Includes any patient with unconfirmed PR.
[b]Includes patients with unconfirmed PR who have a chance to be confirmed at their next assessment.
[c]Disease control rate (SD + PR + CR) at 8 weeks.

Conclusion/Implications: Avutometinib + defactinib demonstrated robust efficacy (ORR) in recurrent LGSOC irrespective of the number of prior therapies, and for most of which, response to previous therapy was poor.

PO005LBA / #1579 – Late-Breaking Abstract

A RANDOMIZED, PHASE II/III STUDY OF PEGYLATED-LIPOSOMAL-DOXORUBICIN AND ATEZOLIZUMAB (IND #134427) VERSUS PEGYLATED-LIPOSOMAL-DOXORUBICIN, BEVACIZUMAB AND ATEZOLIZUMAB VERSUS PEGYLATED-LIPOSOMAL-DOXORUBICIN AND BEVACIZUMAB IN PLATINUM-RESISTANT OVARIAN CANCER (NRG-GY009)

PLENARY 01: ORAL ABSTRACT PRESENTATIONS

Roisin O'Cearbhaill[1], Michael Sill[2], Hoa Duong[3], Steven Waggoner[4], Rachel Grisham[1], Floor Backes[5], Robert Mannel[6], Janos Tanyi[7], Matthew Powell[8], Cara Mathews[9], Sharad Ghamande[10], Leah Mcnally[11], Alexander Olawaiye[12], David Bender[13], Linda Duska[14], Heather Lankes[15], Dmitriy Zamarin[16], Russell Schilder[17], Michael Bookman[18], Carol Aghajanian[1]
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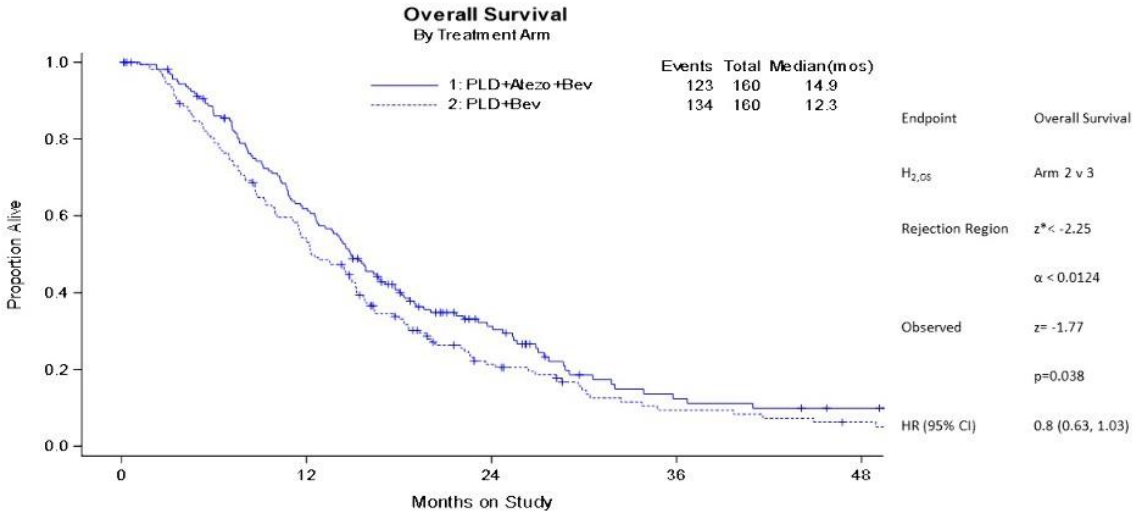
Introduction: In this multicentre randomized, phase II/III trial, we sought to examine if the 1) combination of anti-programmed death ligand 1 (PD-L1) monoclonal antibody atezolizumab (ATEZO) with pegylated-liposomal- doxorubicin (PLD) [Arm 1] and/or 2) addition of ATEZO to PLD and bevacizumab (BEV) [Arm 2] result in an improvement in survival for patients with platinum resistant ovarian cancer (PROC) compared to the standard PLD/BEV [Arm 3].

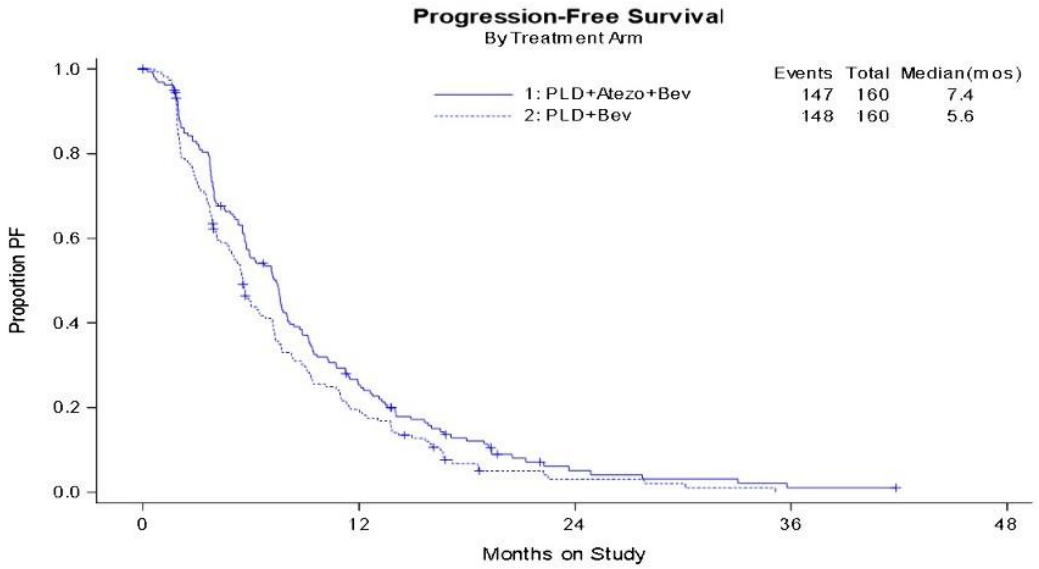
Methods: Patients were randomly assigned 1:1:1 to PLD/ATEZO, PLD/BEV/ATEZO or PLD/BEV (IV PLD 40mg/m^2 q4weeks; BEV 10mg/kg q2weeks; ATEZO 800mg q2weeks). Key eligibility: 1-2 prior lines of therapy (no PLD), ECOG 0-2, and RECIST measurable/evaluable PROC. No stratification by PD-L1 status. The phase II primary endpoint was PFS. The phase III coprimary endpoints were PFS/OS.

Results: From 05/2017-10/2021 444 patients with PROC were enrolled. The median age was 63yrs (35-86). All had received prior chemotherapy; 434 (97.7%) prior surgery and 9 (2%) prior biological therapy. At the phase III interim analysis Arm 1 (PLD/ATEZO) was discontinued for futility. The phase III OS/PFS analysis included accruals to Arms 2 (PLD/BEV/ATEZO) and 3 (PLD/BEV) from all phases. With median follow-up of 47 months, median PFS was 7.4 months and 5.6 months (HR 0.79 with 99.99% 1-sided CI 0.0-1.21), and median OS was 14.9 months and 12.3 months (HR 0.80; 98.78% 1-sided CI 0.00-1.06; 1-sided p=0.038) for Arms 2 and 3, respectively. Adverse events were as expected.

Conclusion/Implications: The addition of ATEZO to PLD/BEV did not result in a statistically significant longer OS than PLD/BEV in PROC. Subset analysis are planned to evaluate survival outcomes with high

PD-L1 expression (NRG-GY009/NCT02839707).





PO006LBA / #1520 – Late-Breaking Abstract

SELINEXOR MAINTENANCE FOR PATIENTS WITH TP53WT ADVANCED OR RECURRENT ENDOMETRIAL CANCER: LONG-TERM FOLLOW UP OF EFFICACY AND SAFETY SUBGROUP ANALYSIS OF THE ENGOT-EN5/GOG-3055/SIENDO STUDY

PLENARY 02: CHANGING THE LANDSCAPE OF ENDOMETRIAL CANCER

Giovanni Scambia[1], Ignace Vergote[2], Erika Hamilton[3], Jose Perez Fidalgo[4], Toon Van Gorp[5], Jalid Sehouli[6], Jaroslav Klat[7], Tally Levy[8], Stephen Welch[9], Debra Richardson[10], Eva Guerra Alía[11], Stéphanie Henry[12], Pauline Wimberger[13], David Miller[14], Jerónimo Martínez[15], Bradley Monk[16], Pratheek Kalyanapu[17], Mansoor Raza Mirza[18], Vicky Makker[19]
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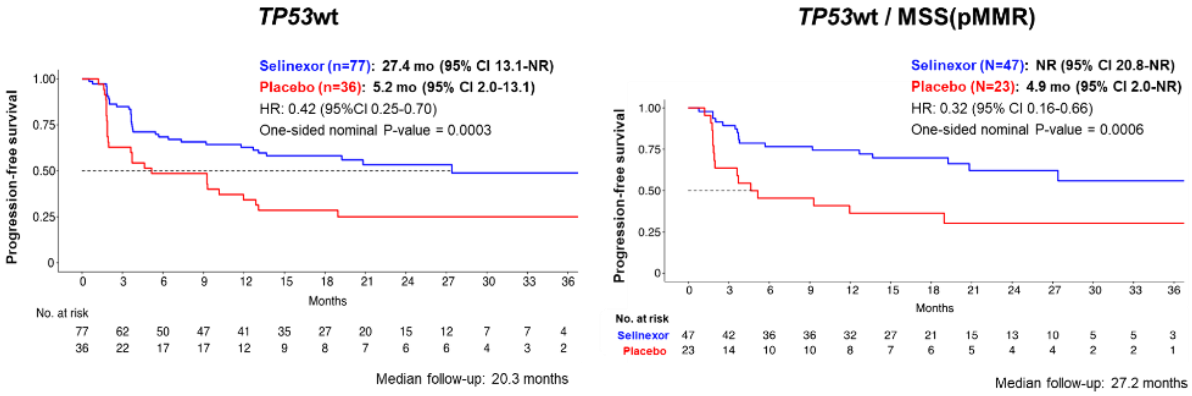
Introduction: Molecular characterization is important to inform treatment decisions for patients with endometrial cancer (EC). Wild type TP53 (TP53wt) is found in ~50% of advanced/recurrent EC and of those, ~70% are microsatellite stable (MSS/pMMR).

Methods: ENGOT-EN5/GOG-3055/SIENDO (NCT03555422) is a randomized double-blind, phase 3 trial evaluating selinexor vs placebo as a maintenance treatment for advanced/recurrent EC following response to prior systemic therapy. Here we report the updated efficacy and safety of a prespecified exploratory subgroup analysis of patients with TP53wt EC.

Results: 113 patients with TP53wt EC received selinexor (n=77) or placebo (n=36) as maintenance therapy. As of March 2023, the median follow-up was 25.3 months, and 26 patients remain on treatment. Median PFS (mPFS) was 27.4 months with selinexor vs 5.2 months with placebo (HR 0.42; 95% CI [0.25-0.70], nominal one-sided p=0.0003). PFS improvement was observed regardless of microsatellite instability status; in the TP53wt/MSS(pMMR) subgroup, the mPFS was not reached with selinexor vs 4.9 months with placebo. In patients with TP53wt, the most common adverse events (AEs) were nausea, vomiting, and diarrhea; most common grade ≥3 AEs were neutropenia, thrombocytopenia, and nausea; 16% of patients discontinued selinexor due to AEs. No grade 5 AEs occurred. No immune-related AEs were

observed.



Conclusion/Implications: TP53wt status may represent a robust predictive biomarker for selinexor efficacy in EC. Additionally, a strong PFS signal was observed in the TP53wt/MSS(pMMR) subgroup, a patient population with high unmet need. Both additional data and updated data will be presented at the conference.

PO007LBA / #1550 – Late-Breaking Abstract

EFFICACY AND SAFETY OF TRASTUZUMAB DERUXTECAN IN PATIENTS WITH HER2-EXPRESSING SOLID TUMORS: RESULTS FROM THE CERVICAL, ENDOMETRIAL, AND OVARIAN CANCER COHORTS OF THE DESTINY-PANTUMOR02 STUDY

PLENARY 02: CHANGING THE LANDSCAPE OF ENDOMETRIAL CANCER

Jung-Yun Lee[1], Vicky Makker[2,3], Luis Manso[4], Antonio González-Martín[5], Iwona Ługowska[6], Domenica Lorusso[7], Susana Banerjee[8], John Liao[9], Chien-Hsing Lu[10], Naiyarat Prasongsook[11], Bohuslav Melichar[12], Kai Chen[13], Robert Mcewen[14], Flavia Michelini[15], Soham Puvvada[14], Funda Meric-Bernstam[16], Ana Oaknin[17]
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Introduction: Trastuzumab deruxtecan (T-DXd) has demonstrated significant survival benefit for patients with HER2-expressing breast and gastric cancers. In DESTINY-PanTumor02, T-DXd demonstrated clinically meaningful response rates, progression-free survival (PFS), and overall survival (OS) in HER2-expressing tumors.

Methods: This open-label, Phase 2 study (NCT04482309) evaluated T-DXd (5.4 mg/kg Q3W) in patients across seven cohorts with HER2-expressing (immunohistochemistry [IHC] 3+/2+ by local [with retrospective central testing] or central testing) locally advanced/metastatic disease after ≥1 systemic treatment, or without alternative treatment. The primary endpoint was investigator-assessed confirmed objective response rate (ORR). Secondary endpoints included duration of response, PFS, OS, and safety. Exploratory endpoints included pharmacodynamic biomarkers.

Results: At data cutoff (June 2023), 120 patients in the endometrial, cervical, and ovarian cancer cohorts had received treatment (median follow-up [range]: 19.94 [0.8–31.1], 12.60 [0.9–31.0], and 13.13 [0.7–30.6] months, respectively). Overall, 80.8% received ≥2 prior lines of therapy. Table 1 shows efficacy outcomes by HER2 expression levels by cohort. Table 2 shows ORR by HER2 in situ hybridization (ISH) amplification and plasma *HER2* amplification by cohort. Grade (G)≥3 drug-related adverse events occurred in 54/120 (45.0%) patients; adjudicated treatment-related interstitial lung disease/pneumonitis occurred in 13/120 (10.8%) patients (n=12 G≤2; n=1 G5).

Conclusion/Implications: T-DXd demonstrated clinically meaningful benefit, including responses across HER2 expression levels and in ISH+ or plasma *ERBB2* amplified subgroups, and encouraging survival

outcomes in patients with gynecological tumors. Safety was consistent with the known profile. These data support T-DXd as a potential treatment for patients with gynecological HER2-expressing tumors who progressed on prior therapy.

TABLE 1

		N	ORR, % (95% CI)		Median DOR, months (95% CI)				Median PFS, months (95% CI)		Median OS, months (95% CI)
			INV	ICR	n	INV	n	ICR	INV	ICR	
Endometrial	All	40	57.5 (40.9, 73.0)	57.5 (40.9, 73.0)	23	NR (9.9, NE)	23	NR (9.9, NE)	11.1 (7.1, NE)	14.1 (7.3, NE)	26.0 (12.8, NE)
	IHC 3+	13	84.6 (54.6, 98.1)	76.9 (46.2, 95.0)	11	NR (9.6, NE)	10	NR (5.8, NE)	NR (7.3, NE)	NR (7.3, NE)	26.0 (18.9, NE)
	IHC 2+	17	47.1 (23.0, 72.2)	52.9 (27.8, 77.0)	8	18.2 (3.0, NE)	9	12.3 (3.0, NE)	8.5 (4.6, 15.1)	11.0 (4.6, 20.3)	16.4 (8.0, NE)
	IHC 1+	4	25.0 (0.6, 80.6)	25.0 (0.6, 80.6)	1	NR (NE, NE)	1	NR (NE, NE)	1.2 (0.8, NE)	1.2 (0.8, NE)	5.2 (0.8, NE)
	IHC 0	5	60.0 (14.7, 94.7)	60.0 (14.7, 94.7)	3	9.9 (2.8, NE)	3	NR (9.9, NE)	9.1 (2.6, NE)	11.1 (2.6, NE)	NR (4.2, NE)
	IHC unknown	1	0 (0.0, 97.5)	0 (0.0, 97.5)	0	-	0	-	NR (NE, NE)	NR (NE, NE)	21.7 (NE, NE)
Cervical	All	40	50.0 (33.8, 66.2)	37.5 (22.7, 54.2)	20	14.2 (4.1, NE)	15	15.6 (8.2, NE)	7.0 (4.2, 11.1)	9.7 (4.4, 16.8)	13.6 (11.1, NE)
	IHC 3+	8	75.0 (34.9, 96.8)	62.5 (24.5, 91.5)	6	NR (9.3, NE)	5	NR (9.3, NE)	NR (3.9, NE)	NR (2.9, NE)	NR (3.9, NE)
	IHC 2+	20	40.0 (19.1, 63.9)	20.0 (5.7, 43.7)	8	3.8 (2.8, NE)	4	8.2 (2.8, NE)	4.8 (2.7, 5.7)	4.4 (2.7, 7.6)	11.5 (5.1, NE)
	IHC 1+	8	50.0 (15.7, 84.3)	50.0 (15.7, 84.3)	4	14.2 (8.3, NE)	4	15.6 (8.5, NE)	11.1 (1.4, NE)	9.7 (1.4, NE)	NR (4.6, NE)
	IHC 0	4	50.0 (6.8, 93.2)	50.0 (6.8, 93.2)	2	NR (6.8, NE)	2	NR (NE, NE)	5.4 (1.3, NE)	NR (1.3, NE)	9.5 (2.6, NE)
Ovarian	All	40	45.0 (29.3, 61.5)	42.5 (27.0, 59.1)	18	11.3 (4.1, 22.1)	17	11.3 (4.2, NE)	5.9 (4.0, 8.3)	7.3 (4.4, 12.6)	13.2 (8.0, 17.7)
	IHC 3+	11	63.6 (30.8, 89.1)	72.7 (39.0, 94.0)	7	22.1 (4.2, NE)	8	NR (4.2, NE)	12.5 (3.1, NE)	7.4 (2.8, NE)	20.0 (3.8, NE)
	IHC 2+	19	36.8 (16.3, 61.6)	31.6 (12.6, 56.6)	7	11.3 (2.8, NE)	6	NR (4.1, NE)	4.1 (2.3, 12.6)	8.2 (2.2, NE)	13.0 (4.7, 21.9)
	IHC 1+	5	20.0 (0.5, 71.6)	20.0 (0.5, 71.6)	1	8.3 (NE, NE)	1	8.3 (NE, NE)	6.9 (0.7, NE)	7.3 (0.7, NE)	7.7 (0.7, NE)
	IHC 0	5	60.0 (14.7, 94.7)	40.0 (5.3, 85.3)	3	4.5 (2.6, NE)	2	10.4 (4.0, NE)	5.6 (1.3, NE)	6.3 (2.8, NE)	12.3 (6.2, NE)

HER2 status was assessed by central testing via HER2 HercepTest™ (Dako)
CI, confidence interval; DOR, duration of response; ICR, independent central review; IHC, immunohistochemistry; INV, investigator; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival

TABLE 2

			Responders/Total	ORR by INV, % (95% CI)
Endometrial	HER2 amp	ISH+	11/13	84.6 (54.6, 98.1)
		ISH-	9/20	45.0 (23.1, 68.5)
		Unknown	3/7	42.9 (9.9, 81.6)
	Plasma *HER2*amp*	*ERBB2* amplified	10/11	90.9 (58.7, 99.8)
		Not detected	13/29	44.8 (26.4, 64.3)
		Unknown†	0	0
Cervical	HER2 amp	ISH+	6/10	60.0 (26.2, 87.8)
		ISH-	12/26	46.2 (26.6, 66.6)
		Unknown	2/4	50.0 (6.8, 93.2)
	Plasma *HER2*amp*	*ERBB2* amplified	3/4	75.0 (19.4, 99.4)
		Not detected	16/35	45.7 (28.8, 63.4)
		Unknown†	1/1	100.0 (2.5, NE)
Ovarian	HER2 amp	ISH+	6/10	60.0 (26.2, 87.8)
		ISH-	9/25	36.0 (18.0, 57.5)
		Unknown	3/5	60.0 (14.7, 94.7)
	Plasma *HER2*amp*	*ERBB2* amplified	1/1	100.0 (2.5, NE)
		Not detected	15/37	40.5 (24.8, 57.9)
		Unknown†	2/2	100.0 (15.8, NE)

HER2 amplification was evaluated centrally using Ventana dual ISH on archival tissue and detected in baseline plasma ctDNA using Guardant Health OMNI assay; CI calculated using Clopper-Pearson method. *Focal amplification only. †Includes low shedders (no mutations detected, very low frequency mutations, or only variants of uncertain significance detected).
amp, amplification; CI, confidence interval; INV, investigator; ISH, in situ hybridization; NE, not evaluable; ORR, objective response rate

PO011LBA / #1512 – Late-Breaking Abstract

UBAMATAMAB (MUC16XCD3 BISPECIFIC ANTIBODY) WITH OR WITHOUT CEMIPLIMAB (ANTI-PD-1 ANTIBODY) IN RECURRENT OVARIAN CANCER: PHASE 1 CLINICAL AND BIOMARKER RESULTS

PLENARY 03: ORAL ABSTRACT PRESENTATIONS – OVARIAN CANCER

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Introduction: Ubamatamab (REGN4018; mucin16 [MUC16] x CD3 bispecific antibody) promotes T-cell-mediated killing of ovarian cancer (OC) cells in preclinical studies. This activity is enhanced by the anti-PD-1 antibody cemiplimab. We present first-in-human ubamatamab +/- cemiplimab dose escalation results in recurrent OC.

Methods: Patients with recurrent platinum-experienced OC received weekly intravenous ubamatamab 0.3–800mg after step-up dosing. Patients in combination cohorts received intravenous cemiplimab 350mg every 3 weeks beginning Day 29–36. Endpoints assessed safety (primary), clinical activity (secondary), and correlatives of tumor MUC16 immunohistochemistry and serum CA125 (exploratory).

Results: 109 patients (N=74 monotherapy/N=35 combination) were enrolled. Median number of prior therapies was 5 (range 1–17). Commonest treatment-related adverse events of any grade occurred in the first 4 weeks of treatment, including pain (75.2%; Grade 1-2 56.9%; Grade 3 18.3%) and cytokine release syndrome (72.5%; all Grade 1-2) (Table), with few of these events after addition of cemiplimab. In efficacy analyses (n=42 monotherapy/n=22 combination), ORR was 14.3%/18.2%, median duration of response was 13.7/8.3 months, and CA125 response (GCIG criteria) was 31.0%/22.7%. All patient tumors expressed MUC16 by immunohistochemistry. Responses with ubamatamab monotherapy were observed across a range of MUC16 expression levels. Response rates and PFS increased with increasing number and intensity of MUC16+ cells. CA125 response was associated with improved PFS (monotherapy: hazard ratio 0.35; 95% CI 0.17–0.72).

Conclusion/Implications: Ubamatamab +/- cemiplimab demonstrated acceptable safety and evidence of clinical activity in heavily pretreated OC. An ongoing randomised Phase 2 study is evaluating ubamatamab alone and with

cemiplimab.

Table: Treatment-related TEAEs Occurring in >10% of Monotherapy and Combination Therapy Patients Combined During the First 4 Weeks of Treatment

	Ubamatamab and ubamatamab + cemiplimab combined (N=109)		
Preferred term, n (%)*	**All grades****	**Grade 1-2**	**Grade 3**
Pain†	75.2	56.9	18.3
Abdominal pain	65.1	49.5	15.6
Back pain	23.9	17.4	6.4
Non-cardiac chest pain	16.5	15.6	0.9
Cytokine release syndrome	72.5	72.5	0
Nausea	36.7	36.7	0
Fatigue	32.1	31.2	0.9
Vomiting	31.2	31.2	0
Ocular†	27.5	27.5	0
Dry eye	15.6	15.6	0
Conjunctivitis	10.1	10.1	0
Anemia	26.6	15.6	11.0
Infusion-related reaction	15.6	15.6	0
Pyrexia	13.8	13.8	0
Cough	12.8	12.8	0
Dyspnea	12.8	12.8	0
Headache	12.8	12.8	0

*A patient is counted only once (highest grade) for multiple occurences within a preferred term. **There were no Grade 4 or 5 events for the preferred terms reported here. †Sum of individual preferred term values may be greater than the total of the higher-level category value.
Abbreviations: TEAE: treatment-emergent adverse event.

PO012LBA / #1511 – Late-Breaking Abstract

FLAMES: RANDOMIZED PHASE 3 TRIAL OF MAINTENANCE SENAPARIB IN PATIENTS WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER

PLENARY 03: ORAL ABSTRACT PRESENTATIONS – OVARIAN CANCER

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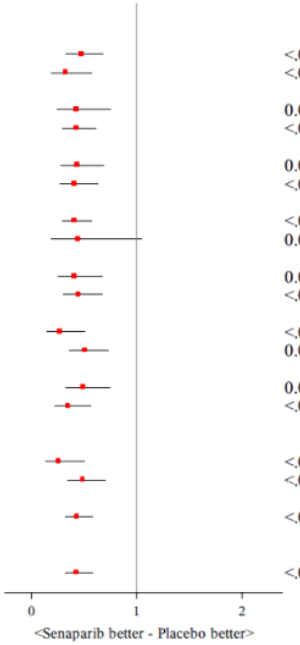
Introduction: FLAMES is a randomized, double-blind, placebo-controlled, phase 3 trial to evaluate efficacy and safety of senaparib as first line (1L) maintenance therapy in patients with newly diagnosed advanced ovarian cancer (OC).

Methods: Chinese patients with newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid OC who had achieved complete response (CR) or partial response (PR) to 1L platinum-based chemotherapy were randomized (2:1) to receive senaparib or placebo. Primary endpoint was progression-free survival (PFS) evaluated by BICR according to RECIST v1.1. A prespecified subgroup analysis was performed based on FIGO stage (III vs IV), BRCA mutation (positive vs negative), 1L treatment response (CR vs PR), neoadjuvant chemotherapy (yes vs no) and presence of residual disease after debulking surgery (yes vs no).

Results: 404 patients were randomized to receive senaparib vs placebo with a median follow up of 22.4 and 22.2 months, respectively. PFS was significantly increased in senaparib arm (HR 0.43, 95% CI 0.32-0.58, P < 0.0001) over placebo. All subgroup analysis demonstrated consistent treatment benefit (HR <0.50, P＜0.0001, Figure). Incidence rates of grade ≥3 adverse events (AEs) were 66.3 % vs 20.3%, respectively. The most common grade ≥3 AEs were anemia (29.3%) , thrombocytopenia (26.7%), and neutropenia (24.8%) after received senaparib. No new safety signals were identified among all subgroups.

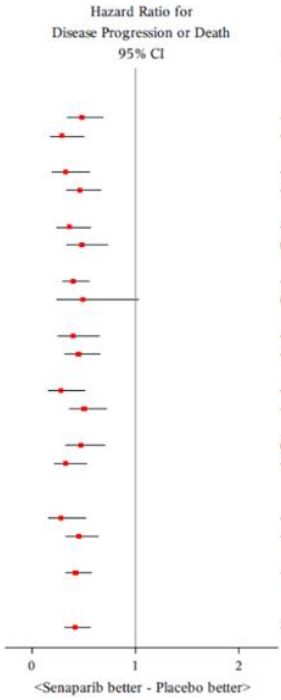
PFS per BICR ITT Population

Subgroup	Senaparib no. of patients with PD or death/total no.	Placebo no. of patients with PD or death/total no.	Senaparib VS. Placebo HR (95% CI)	P Value
FIGO stage at initial diagnosis				
III	59/186	59/98	0.48 (0.33, 0.68)	<.0001
IV	29/84	23/35	0.32 (0.18, 0.57)	<.0001
BRCA mutation				
Positive	29/94	23/44	0.43 (0.24, 0.76)	0.0026
Negative	59/177	59/89	0.43 (0.30, 0.61)	<.0001
No. of cycles of platinum-based chemotherapy				
6	42/128	37/61	0.44 (0.28, 0.69)	0.0002
7-9	43/139	45/72	0.41 (0.27, 0.63)	<.0001
Best response to platinum therapy				
Complete response	72/237	72/119	0.41 (0.30, 0.58)	<.0001
Partial response	16/34	10/14	0.45 (0.19, 1.05)	0.0575
ECOG score				
0	32/106	34/56	0.41 (0.25, 0.67)	0.0002
1	56/165	48/77	0.45 (0.30, 0.67)	<.0001
Age (year)				
< 50	18/65	26/36	0.27 (0.15, 0.51)	<.0001
>= 50	70/206	56/97	0.51 (0.36, 0.73)	0.0002
Neoadjuvant chemotherapy				
Yes	56/137	43/69	0.49 (0.32, 0.75)	0.0006
No	32/134	39/64	0.35 (0.22, 0.56)	<.0001
Presence of residual disease after debulking surgery performed before trial entry				
Yes	16/56	26/34	0.26 (0.13, 0.51)	<.0001
No	68/208	55/96	0.49 (0.34, 0.70)	<.0001
CA-125 level at baseline				
<= ULN	88/269	82/133	0.43 (0.32, 0.59)	<.0001
> ULN	0/2	0/0	N/A	
All patients	88/271	82/133	0.43 (0.32, 0.58)	<.0001



PFS per INV ITT Population

Subgroup	Senaparib no. of patients with PD or death/total no.	Placebo no. of patients with PD or death/total no.	Senaparib VS. Placebo HR (95% CI)	P Value
FIGO stage at initial diagnosis				
III	69/186	64/98	0.49 (0.35, 0.69)	<.0001
IV	33/84	29/35	0.30 (0.18, 0.51)	<.0001
BRCA mutation				
Positive	32/94	31/44	0.33 (0.20, 0.56)	<.0001
Negative	70/177	62/89	0.48 (0.34, 0.67)	<.0001
No. of cycles of platinum-based chemotherapy				
6	45/128	45/61	0.37 (0.24, 0.57)	<.0001
7-9	54/139	48/72	0.49 (0.33, 0.73)	0.0003
Best response to platinum therapy				
Complete response	80/237	80/119	0.41 (0.30, 0.56)	<.0001
Partial response	22/34	13/14	0.50 (0.24, 1.03)	0.0541
ECOG score				
0	36/106	38/56	0.41 (0.26, 0.65)	<.0001
1	66/165	55/77	0.46 (0.32, 0.66)	<.0001
Age (year)				
< 50	23/65	30/36	0.29 (0.17, 0.51)	<.0001
>= 50	79/206	63/97	0.52 (0.37, 0.72)	<.0001
Neoadjuvant chemotherapy				
Yes	66/137	49/69	0.48 (0.33, 0.71)	0.0002
No	36/134	44/64	0.34 (0.21, 0.53)	<.0001
Presence of residual disease after debulking surgery performed before trial entry				
Yes	22/56	29/34	0.29 (0.16, 0.52)	<.0001
No	77/208	63/96	0.46 (0.33, 0.65)	<.0001
CA-125 level at baseline				
<= ULN	102/269	93/133	0.43 (0.33, 0.57)	<.0001
> ULN	0/2	0/0	N/A	
All patients	102/271	93/133	0.43 (0.32, 0.57)	<.0001



Conclusion/Implications: Maintenance senaparib significantly improved PFS regardless of FIGO stage, 1L treatment response, surgical timing and residual disease status versus placebo in patients with newly diagnosed advanced OC.

SO015LBA / #1261 – Late-Breaking Abstract

IDENTIFYING A SAFE ALGORITHM FOR SENTINEL LYMPH NODE MAPPING IN HIGH-RISK ENDOMETRIAL CANCER; THE SENTIREC ENDO STUDY.

FOCUSED PLENARY 02: SURGERY

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Introduction: Sentinel lymph node (SLN) mapping is suggested to be a safe staging method for women with high-risk endometrial cancer (EC). However, approximately 20-45% of women have failed mapping, leaving a need for consensus on the choice of the surgical algorithm in case of non-mapping. We aimed to assess the safety of SLN-mapping algorithms in women with high-risk EC.

Methods: We undertook a national prospective diagnostic accuracy study of SLN-mapping in women with high-risk EC from March 2017- January 2023. A power calculation was based on the negative predictive value (NPV). Women underwent SLN-mapping, pelvic (PLD) and paraaortic (PALND) lymph node dissection besides removal of any FDG/PET–positive lymph nodes.

Results: We included 216 women; 170 women underwent SLN mapping, PLD and PALND and were included in the analyses. 42/170 (24.7%) had nodal metastasis. The algorithm SLN+PLD in case of failed mapping demonstrated a sensitivity of 88% (95% CI 74-96) and an NPV of 96% (95% CI 91-99). The sensitivity increased to 93% (95% CI 81-99) and the NPV to 98% (95% CI 93-100) if PLD was combined with removal of any PET-positive lymph nodes regardless of mapping. PLD+PALND in non-mapping cases achieved a sensitivity of 95% (95% CI 84-99), NPV 98% (95% CI 95-100).

Conclusion/Implications: SLN-mapping is a safe staging procedure in women with high-risk EC if strictly adhering to a surgical algorithm, including removal of any PET-positive lymph nodes independent of location and PLD in failed mapping cases. PLD+PALND obtain similar accuracy in case of failed mapping if FDG/PET-CT is not available.

SO019LBA / #875 – Late-Breaking Abstract

MOLECULAR FEATURES PREDICTS OUTCOMES IN MULTICENTRIC INTERNATIONAL STUDY OF CHEMORADIATION AND MRI BASED IMAGE GUIDED BRACHYTHERAPY FOR CERVICAL CANCER (EMBRACE):FINAL ANALYSIS FROM BIOEMBRACE-I.

CLOSING SESSION: THE DEVELOPMENT OF PROGNOSIS AND PREDICTIVE MARKERS

Supriya Chopra[1], Nanda Horeweg[2], Kedar Deodhar[3], Santosh Menon[3], Tynisha Rafael[4], Venkatesh Pai[1], Katja Jordanova[4], Lucia Rijstenberg[5], Sadhana Kannan[6], Barbara Šegedin[7], Fleur Huang[8], Kjersti Bruheim[9], Margarita Pérez-Mosso Pérez-Mosso[10], Bhavana Rai[11], Li Tee Tan[12], Maximilian Schmid[13], Kari Tanderup[14], Richard Pötter[13], Tjalling Bosse[15], Remi Nout[16]
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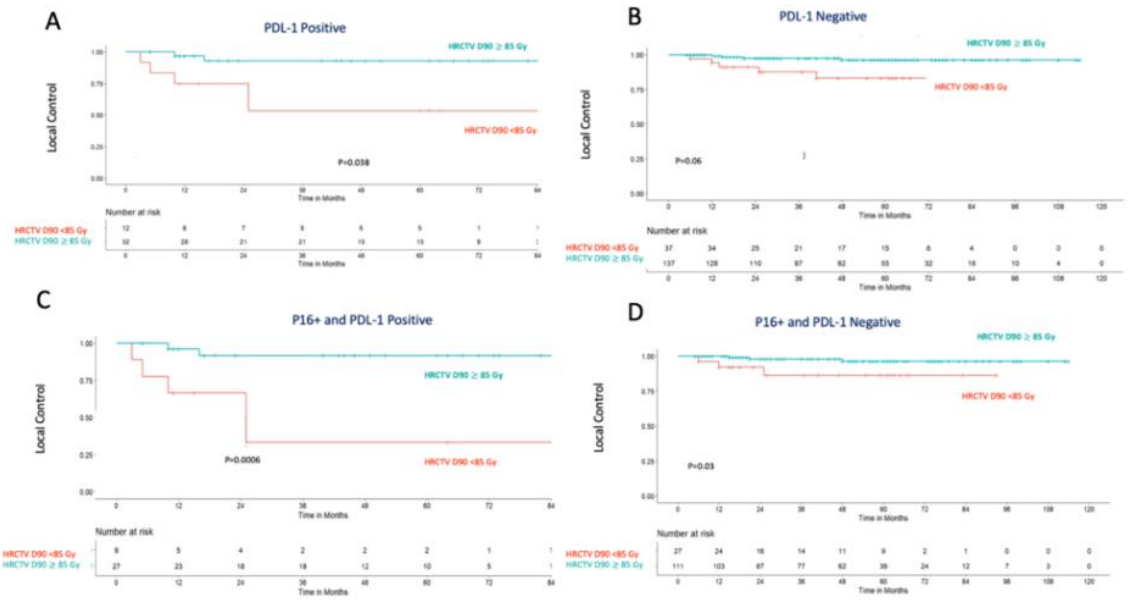
Introduction: BIOEMBRACE-I was designed to investigate biomarkers of response and disease control in patients treated with chemo-radiation and MRI guided brachytherapy (BT) for cervix cancer.

Methods: Between 2018-2021, eight EMBRACE-I sites contributed tumor tissue for immunohistochemistry (p16, PD-L1 and L1CAM). Biomarkers and clinicopathological factors (FIGO stage, nodal status, histology, necrosis on MR) were used to determine predictors of poor response (high-risk clinical target volume (HRCTV>40cc) at BT and 5-year local, pelvic control and disease-free survival (DFS). Interaction between p16, PDL-1, radiotherapy dose (HRCTV D90) and local control was investigated. Univariate and multivariable analysis (MVA) was performed.

Results: Two hundred sixty-four patients were included. The median D90 was 89 (86-95) Gy. P16, PD-L1>1% and L1CAM>10% expression was noted in 81.4%, 17% and 17.4% respectively. P16 -ve status (OR 2.4 (1-5.7), p=0.04), necrosis on MRI (OR=2.1(1.1-4.3), p<0.02) independently predicted for HRCTV-BT >40cc in addition to FIGO stage and tumor width. PD-L1>1% was associated with reduced local (82% vs. 94%, p=0.02) and pelvic control (79% vs 89%, p=0.02). HRCTV D90 <85Gy was associated with inferior 5-year local control in p16+ patients especially if PDL-1 was co-expressed (Fig 1). On MVA, PD-L1>1% was the only independent predictive factor for 5-year local event (HR 3.3, p=0.04) and L1CAM for pelvic event (HR 5.5 (1.3-23.3), p =0.02) (Table 1).



	Poo response at Brachytherapy High risk Clinical target volume > 40 cc	Local Control	Regional Control	Pelvic Control	Disease Free Survival
Smoker vs Non Smoker	32% vs. 28.5% P=0.57	94% vs 88% P=0.16	85.5% vs 87.7% P=0.60	83.2% vs 88.2% P=0.33	56.8% vs 67.9% P=0.09
Histological Subtype Squamous vs Adeno	32.7% vs. 28.6%	94% vs 86% P=0.08	86% vs.93% P=0.27	89% vs 79% P=0.18	68.4% vs 54.6% P=0.25
FIGO 2009 stage I-II vs III-IV	17% vs. 52% P=0.0001	91% vs 96% p=0.14	89% vs 85% P=0.35	86.6% vs 88.9% P=0.78	65.5% vs 62.5% P=0.27
Node Positive vs Negative	32.7% vs. 25% P=0.17	91% vs 94% P=0.91	83% vs 93% P=0.01	85% vs 90% P=0.22	59.5% vs 74.4% P=0.01
Tumor Width>/=5 cm vs.< 5 cm	46%vs. 13% P<0.001	90.7% vs. 92.8% P=0.44	84.% vs 90.7% P=0.08	85.6% vs 88.9% P=0.34	60.9% vs 67.5% P=0.45
P16 positive vs. negative	27.2% vs. 45.5% P=0.03	93% vs 92% P=0.77	86% vs. 96% P=0.12	86.5% vs 89.6% P=0.60	64.1% vs 69.6% P=0.77
L1CAM<50% vs. >50%	28.4% vs. 40% P=0.57	92.8% vs. 80% p=0.14	88% vs 40% P=0.0001	87.6% vs 53.3% P=0.008	66.3% vs 40.2% P=0.06
Necrosis on MRI Yes vs. No	46.2% vs. 23.9% P=0.001	92.8% vs 923% P=0.87	86% vs 88% P=0. 52	88% vs 87% P=0.88	64.8% vs 65.9% P=0.70
PDL1 positive vs. Negative	26.7% vs. 29.5% P=0.87	82% vs 94% P=0.02	86% vs 89% P=0.33	79% vs 89% P=0.05	62% vs 62% P=0.36
Multivariable Analysis	P16 –ve OR:2.4 (1.0-5.7) p=0.04 Tumor width OR 3.2 (1.6-6.3)p<0.001 FIGO stage OR 3.9 (2-7.4) p<0.001 Necrosis on MRI OR 2.1 (1.1-4.3)p<0.02	PDL1+>1% HR 3.3 (0.69-16), p-0.04	Node positive HR 2.9(1.1-7.2), p=0.01 L1CAM (HR 8.6 (2.5-28.7) p<0.001	LI CAM HR=5.5 (1.3-23.3), p=0.02	Node Positive HR =1.7 (1-2.6) P=0.01

Conclusion/Implications: P16 -ve status and necrosis on MRI independently predict for poor response to EBRT (HRCTV-BT >40cc) and PD-L1 and L1CAM independently predict local and pelvic control suggesting impact of molecular features on radiotherapy response.Further validation is planned in EMBRACE-II.

SO023LBA / #1384 – Late-Breaking Abstract

PROGNOSTIC PERFORMANCE OF THE 2023 FIGO STAGING SCHEMA FOR ENDOMETRIAL CANCER

CLOSING SESSION: THE DEVELOPMENT OF PROGNOSIS AND PREDICTIVE MARKERS

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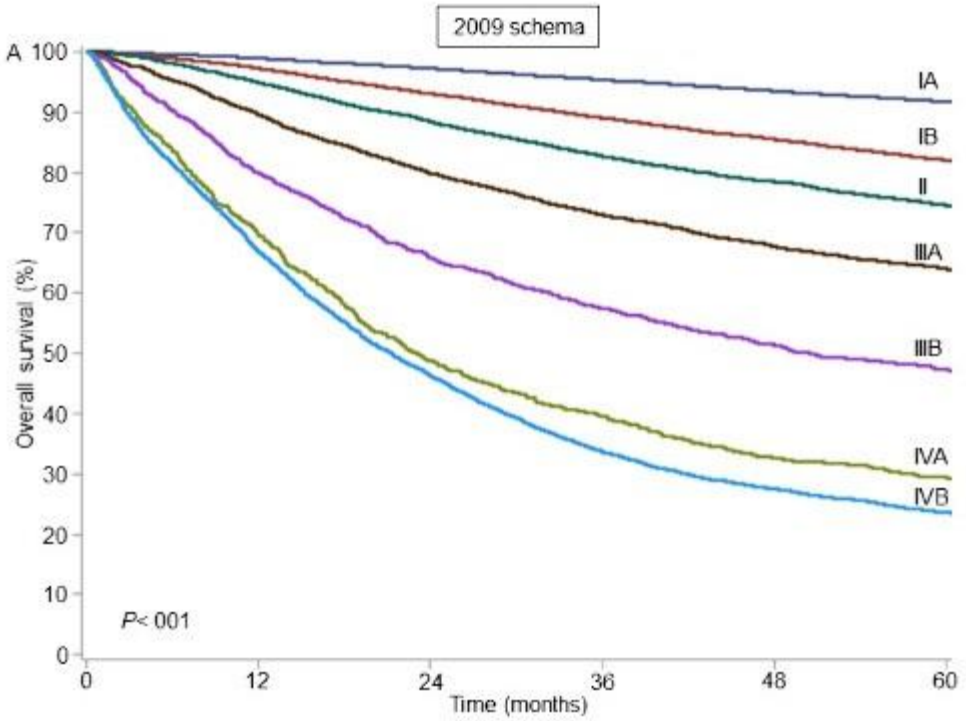
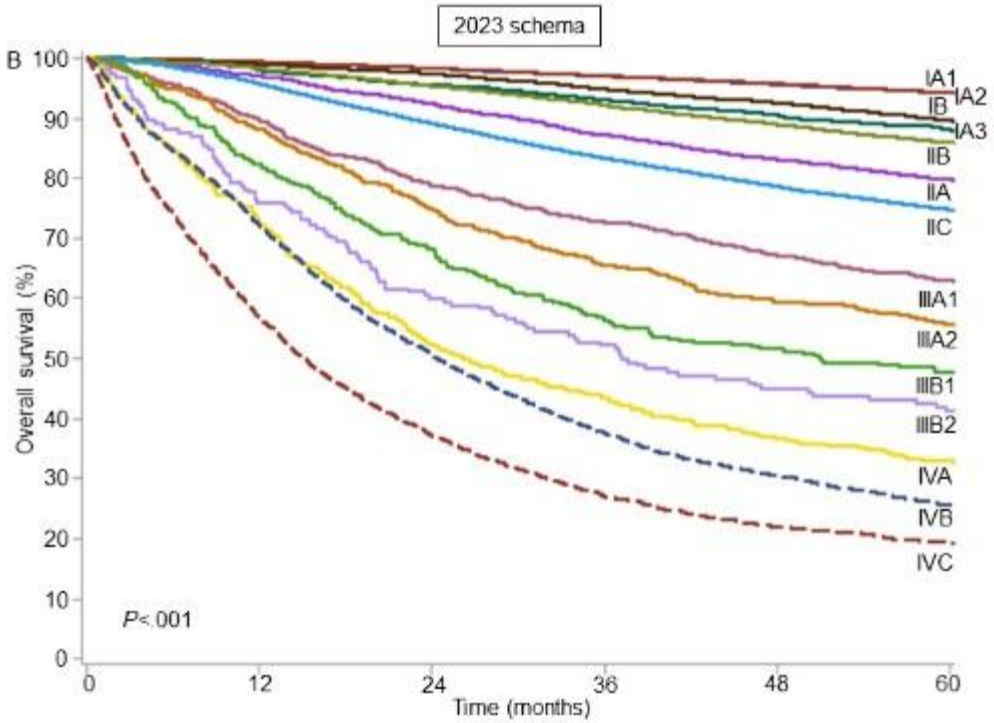
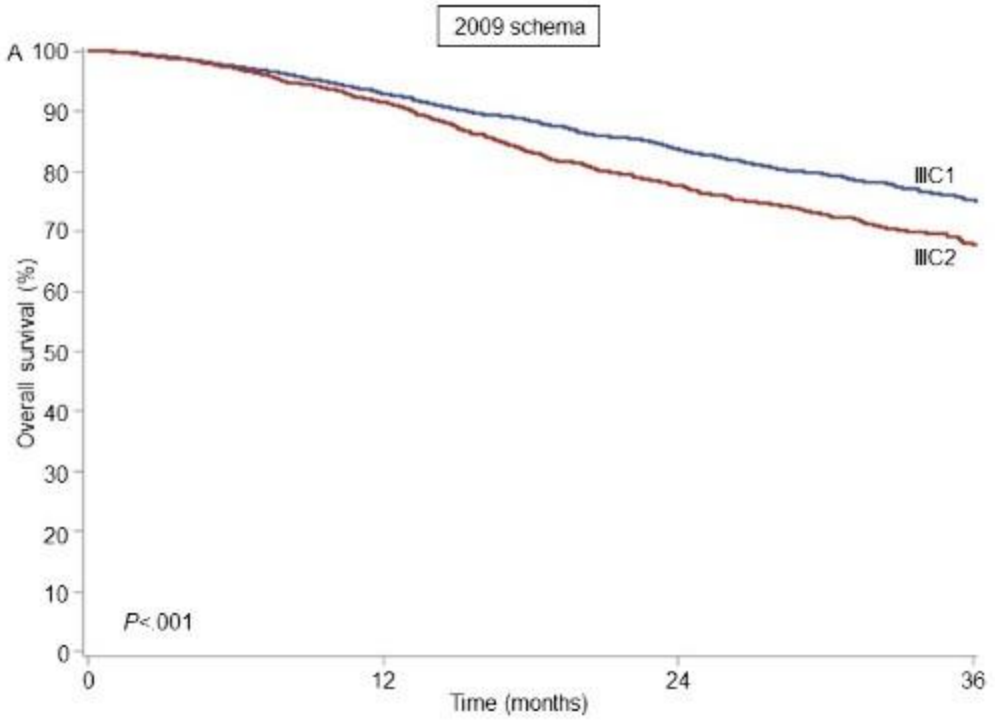
Introduction: This study examined prognostic performance of the 2023 FIGO endometrial cancer staging schema.

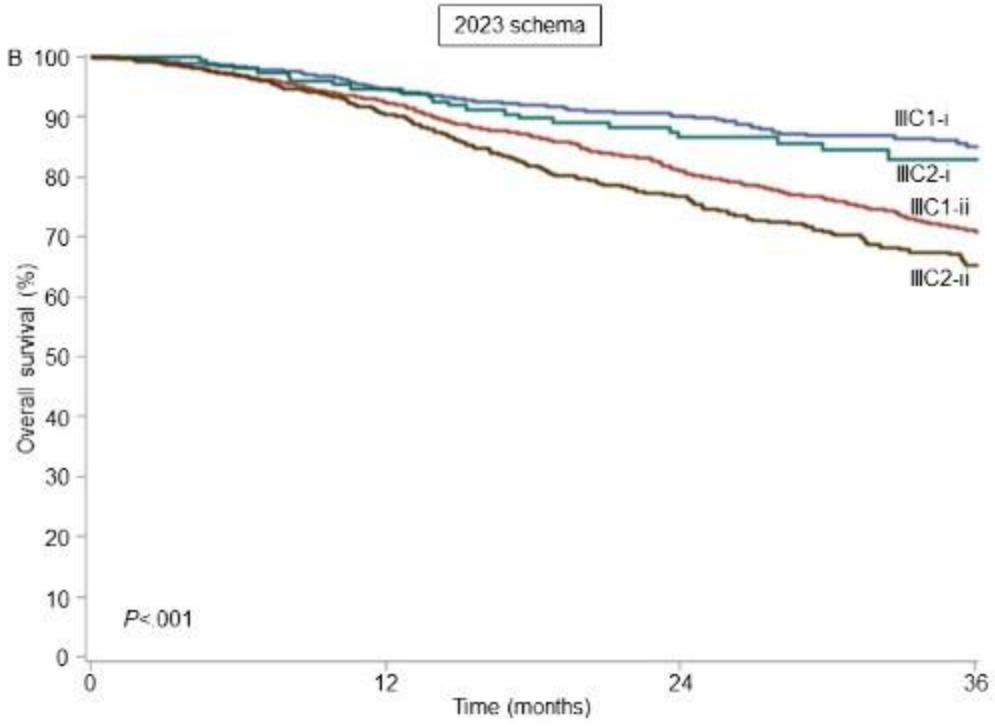
Methods: The National Cancer Database was retrospectively queried to examine 129,146 patients with stage I-IV endometrial cancer per the 2009 FIGO schema. Overall survival (OS) per the 2023 FIGO schema was assessed (Figures 1-2).


2009 schema
A
Overall survival (%)
100
90
80
70
60
50
40
30
20
10
0
IA
IB
II
IIIA
IIIB
IVA
IVB
P< 001
0
12
24
36
48
60
Time (months)


2023 schema
B
Overall survival (%)
100
90
80
70
60
50
40
30
20
10
0
IA1
IA2
IB
IA3
IIB
IIA
IIC
IIIA1
IIIA2
IIIB1
IIIB2
IVA
IVB
IVC
P<.001
0
12
24
36
48
60
Time (months)

Results:





In the 2009 schema, the inter-stage difference in 5-year OS rate was 68.2% (91.4% for IA and 23.4% for IVB; this widened to 74.9% in the 2023 schema (94.1% for IA1 and 19.2% for IVC). In the 2023 schema, 5-year OS rate of IIC was more than 10%-point lower compared to that of IA-IB (74.7% vs 88.0-94.4%). In the 2009 schema, 5-year OS rate of IIIA was 63.9%; this was greater segregated to 88.0% for IA3, 62.9% for IIIA1, and 55.7% for IIIA2 in the 2023 schema. This 5-year OS rate of new IA3 was comparable to IB in the 2023 schema (88.0% vs 89.5%). In the 2023 schema, irrespective to nodal metastatic sites, 3-year

OS rates were similar in micrometastasis (IIIC1-i vs IIIC2-i, 84.9% vs 82.9%) but not in macrometastasis (IIIC1-ii vs IIIC2-ii, 71.1% vs 65.2%). In the 2009 schema, the 5-year OS rate of IVB was 23.4%; this was segregated to 25.4% for IVB and 19.2% for IVC in the 2023 schema.

Conclusion/Implications: The 2023 FIGO endometrial cancer staging schema is a major revision from the 2009 FIGO schema. Almost doubled enriched sub-stages based on detailed anatomical metastatic site and incorporation of histological information enable more robust prognostication.