



VII SIMPOSIO NACIONAL  
de ONCOLOGÍA de PRECISIÓN

Vigo, 20 y 21 de febrero de 2025

# ***LO MEJOR DE 2024 EN 20 DIAPOSITIVAS***

## Cáncer ginecológico

Luis Manso MD PhD

Head of Gynecologic Cancer Unit.

Medical Oncology Division  
12 de Octubre University Hospital.

# DISCLOSURE SLIDE

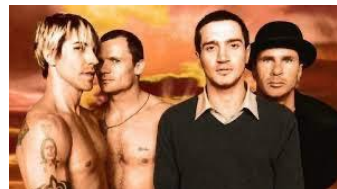
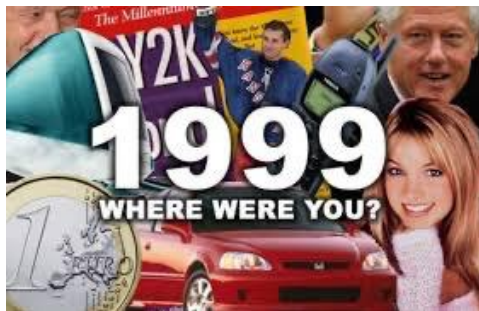
- Employment: Hospital Universitario 12 de Octubre
- Consultant or Advisory Roles: Lilly, GSK, Clovis, AstraZeneca, Roche, Novartis, Pfizer.
- Research Assistance: Tesaro-GSK
- Speaking Engagements: Lilly, Roche, AstraZeneca, Novartis, Pfizer, GSK, Clovis





## Cervical cancer

## MAJOR EVENTS 1999



"Californication"



Dreamcast  
Console



Baby one more time



# ENGOT-cx11/ GOG-3047/KEYNOTE-A18

## Key Eligibility Criteria

- FIGO 2014 stage IB2-IIIB (node-positive disease) or FIGO 2014 stage III-IVA (either node-positive or node-negative disease)
- RECIST 1.1 measurable or non-measurable disease
- Treatment naïve

R  
1:1  
N = 1060

Cisplatin 40 mg/m<sup>2</sup> QW for 5 cycles<sup>a</sup> + EBRT followed by brachytherapy + Pembrolizumab 200 mg Q3W for 5 cycles

Pembrolizumab 400 mg Q6W for 15 cycles

Cisplatin 40 mg/m<sup>2</sup> QW for 5 cycles<sup>a</sup> + EBRT followed by brachytherapy + Placebo Q3W for 5 cycles

Placebo Q6W for 15 cycles

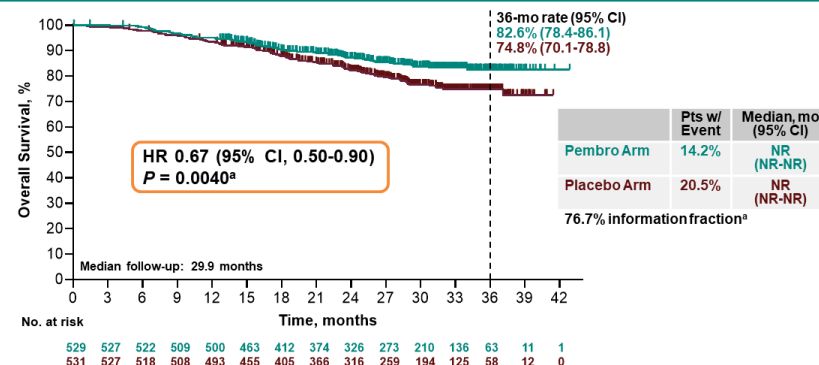
## Stratification Factors

- Planned EBRT type (IMRT or VMAT vs non-IMRT or non-VMAT)
- Stage at screening (stage IB2-IIIB N+ vs III-IVA)
- Planned total radiotherapy dose (<70 Gy vs ≥70 Gy [EQD2])

## End Points:

- Primary: PFS (per RECIST v1.1) by investigator or histopathologic confirmation and OS.
- Secondary: 24-month PFS, 36-month OS, ORR, patient-reported HRQoL, and safety

## Primary Endpoint: Overall Survival at IA2





## Endometrial cancer

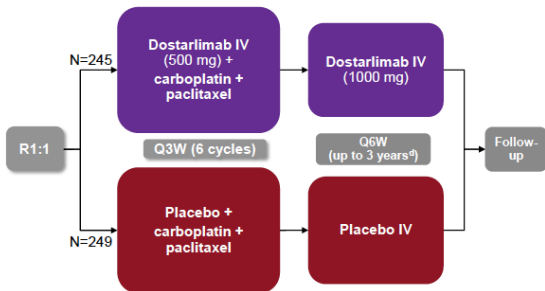


# ENGOT-EN6-NSGO/GOG-3031/RUBY (NCT03981796) Part 1



- Eligible patients**
- Stage III/IV disease or first recurrent EC\*
  - All histologies except sarcomas\*
  - Naïve to systemic anticancer therapy or had a recurrence or PD ≥6 months after completing systemic anticancer therapy

- Stratification**
- MMR/MSI status\*
  - Prior external pelvic radiotherapy
  - Disease status



## Primary endpoint

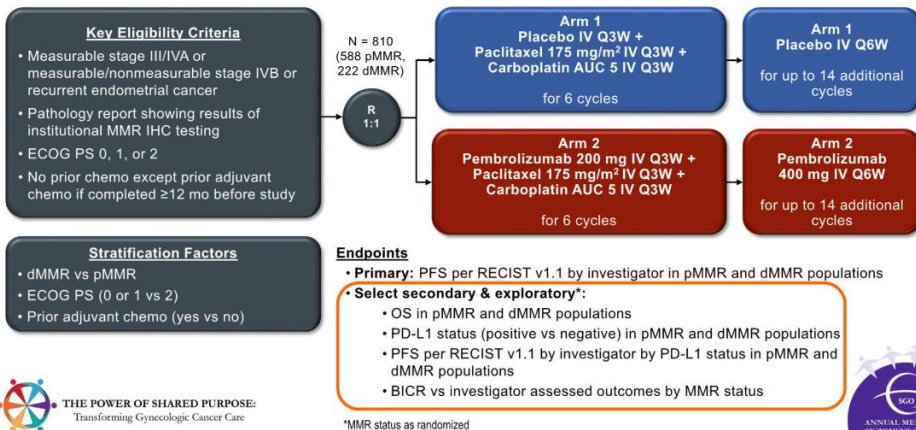
- PFS by INV\* (IA1)
- OS (IA1 & IA2)

## Secondary endpoints

- PFS by BICR (IA1)
- PFS2 (IA1 & IA2)
- ORR (IA1)
- DOR (IA1)
- DCR (IA1)
- HRQOL/PRO (IA1)
- Safety (IA1 & IA2)

On-study imaging assessments were performed Q3W (±7 days) from the randomization date until week 25 (cycle 6), followed by Q6W (±7 days) until week 52. Subsequent tumor imaging was performed every 12 weeks (±7 days) until radiographic PD was documented by investigator assessment per RECIST v1.1 followed by one additional imaging 4-6 weeks later, or subsequent anticancer therapy was started, whichever occurred first. Thereafter, scans may have been performed per standard of care. \*Histologically confirmed proven advanced or recurrent EC; stage III/IV disease or first recurrent EC with low potential for cure by radiation therapy or surgery alone or in combination. \*Carcinosarcoma, clear cell, serous, or mixed histology permitted (must histology containing at least 10% carcinosarcoma, clear cell, or serous histology). \*Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used with local results were not available. For local determination of MMR/MSI status, IHC, next-generation sequencing, and polymerase chain reaction assays were accepted. For central determination of MMR/MSI status, IHC per Ventana MMR Plus panel was used. \*Treatment ends after 3 years, PD, toxicity, withdrawal consent, investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered following discussion between the sponsor and the investigator. \*The threshold for the primary endpoint was crossed at IA1. Therefore, IA1 was considered the final analysis for PFS. BICR: blinded independent central review; DCR, disease control rate; DOR, duration of response; EC, endometrial cancer; HRQOL, health-related quality of life; IA, interim assessment; IHC, immunohistochemistry; INV, investigator assessment; MMR, miss repair; MSI, microsatellite instability; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; Q6W, every 6 weeks; Q9W, every 9 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

## NRG-GY018/KEYNOTE-868 (NCT03914612): Randomized, Placebo-Controlled, Phase 3

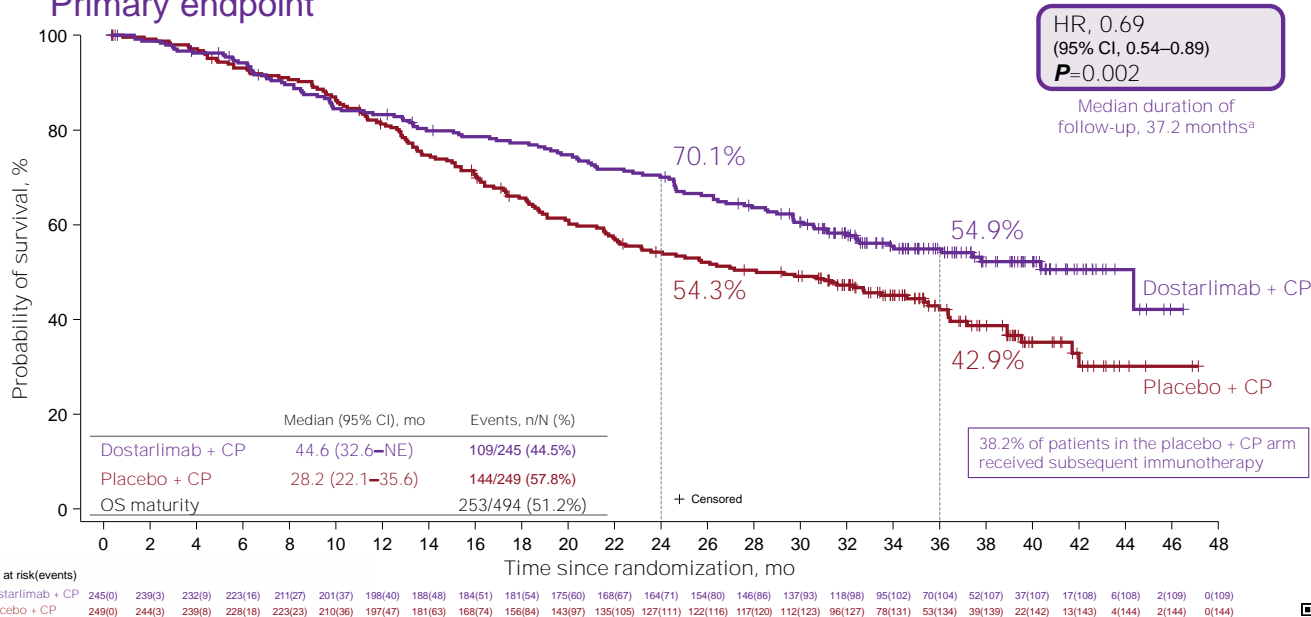




# ENGOT-EN6/GOG-3031/RUBY trial

## Statistically Significant OS Benefit in Overall Population

### Primary endpoint



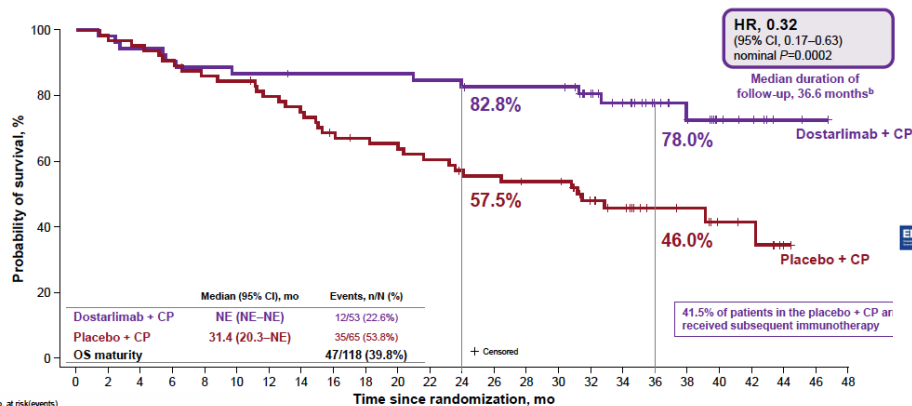
<sup>a</sup>Median expected duration of follow-up; range 31.0–49.5 months.  
CP, carboplatin-paclitaxel; HR, hazard ratio; NE, not estimable; OS, overall survival.



Scan for slides

# ENGOT-EN6/GOG-3031/RUBY trial

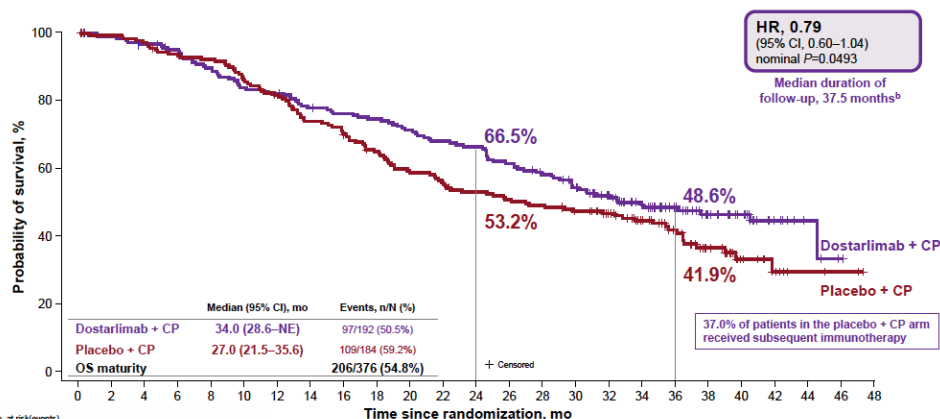
## Substantial OS Benefit in dMMR/MSI-H Population<sup>a</sup>



<sup>a</sup>Overall survival in the dMMR/MSI-H and MMRp/MSS populations was a prespecified exploratory endpoint. <sup>b</sup>Median expected duration of follow-up; range 31.0-48.7 months. CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability high; NE, not estimable; OS, overall survival.

ENGOT NSGO-CTU GOG FOUNDATION

## Clinically Meaningful OS Difference in MMRp/MSS Population<sup>a</sup>

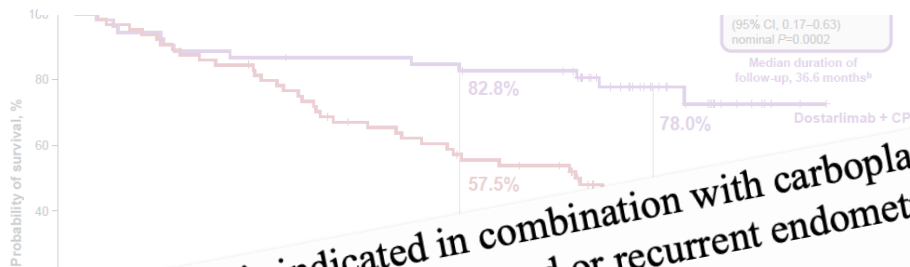


<sup>a</sup>Overall survival in the dMMR/MSI-H and MMRp/MSS populations was a prespecified exploratory endpoint. <sup>b</sup>Median expected duration of follow-up; range 31.2-48.5 months. CP, carboplatin-paclitaxel; HR, hazard ratio; MMRp, mismatch repair proficient; MSS, microsatellite stable; NE, not estimable; OS, overall survival.

ENGOT-EN6/COC-2024/DIARY trial

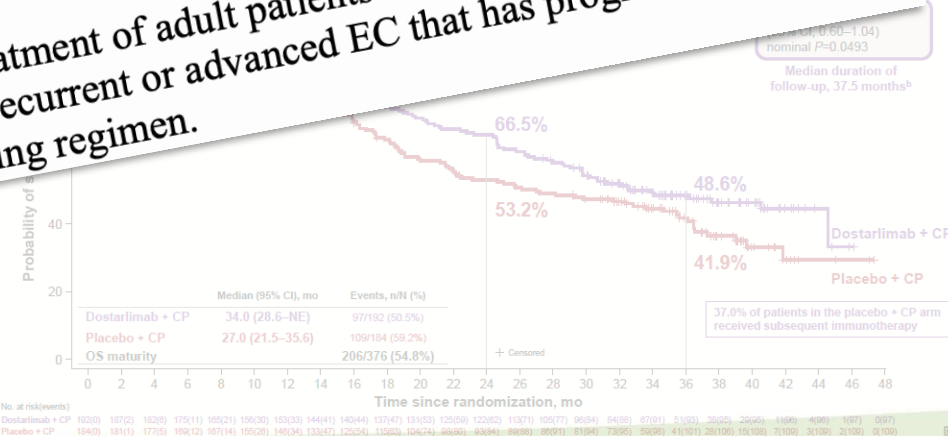
Date: 23 Jan 2025

## EMA Extension of Indications for Dostarlimab



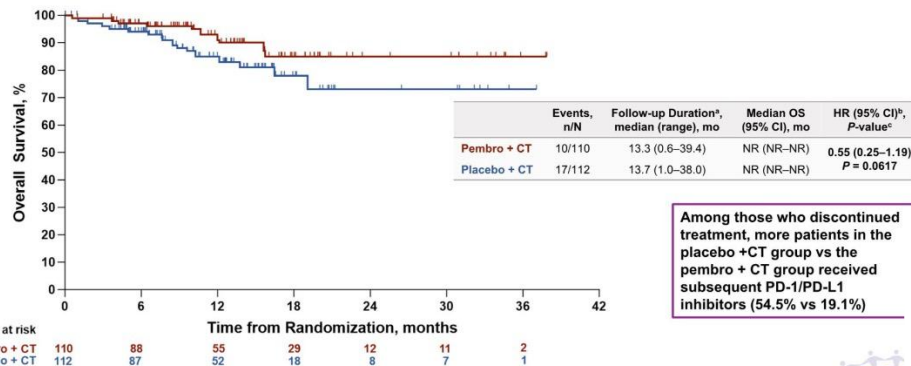
JEMPERLI is indicated in combination with carboplatin and paclitaxel for the first-line treatment of adult patients with primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy.

JEMPERLI is indicated as monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/ microsatellite instability-high (MSI-H) recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen.

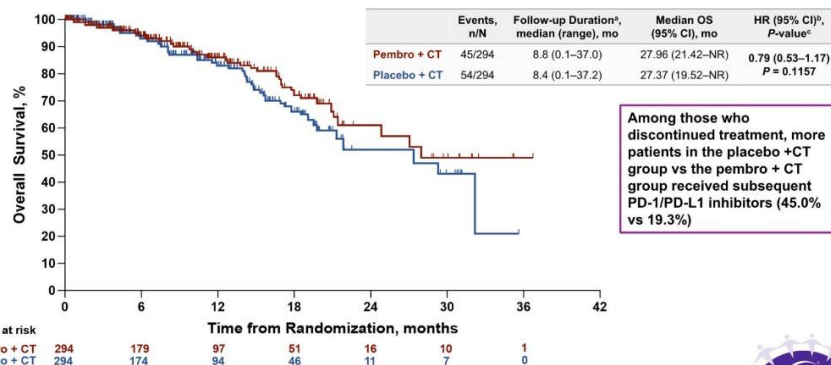


## NRG-GY018/KEYNOTE-868

### Favorable Trend in OS With Pembro + CT for dMMR EC OS Data Immature at IA (18.0% information fraction)



### Favorable Trend in OS With Pembro + CT for pMMR EC OS Data Immature at IA (27.2% information fraction)



THE POWER OF SHARED PURPOSE:  
Transforming Gynecologic Cancer Care

<sup>a</sup>Follow-up duration is defined as the time from randomization to the date of death or the database cutoff date if the participant is still alive.  
<sup>b</sup>Based on Cox regression model with Elfron's method of tie handling with treatment as a covariate stratified by prior chemotherapy.  
<sup>c</sup>One-sided P-value based on log-rank test stratified by prior chemotherapy.  
Database cutoff: Dec 16, 2022.



THE POWER OF SHARED PURPOSE:  
Transforming Gynecologic Cancer Care

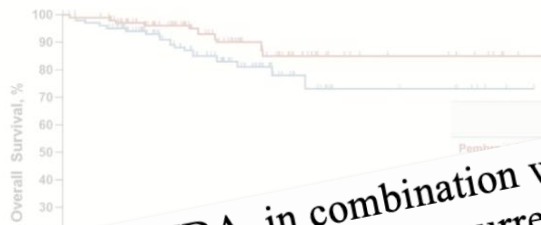
<sup>a</sup>Follow-up duration is defined as the time from randomization to the date of death or the database cutoff date if the participant is still alive.  
<sup>b</sup>Based on Cox regression model with Elfron's method of tie handling with treatment as a covariate stratified by prior chemotherapy.  
<sup>c</sup>One-sided P-value based on log-rank test stratified by prior chemotherapy.  
Database cutoff: Dec 6, 2022.



NDC\_GV012/KEYNOTE\_262

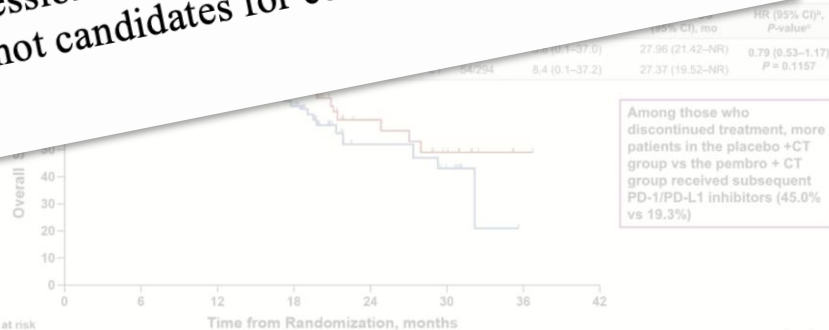
Date: 07 Oct 2024

## EMA Extension of Indications for Pembrolizumab



KEYTRUDA, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of primary advanced or recurrent endometrial carcinoma in adults who are candidates for systemic therapy.

KEYTRUDA, in combination with lenvatinib, is indicated for the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.



Among those who discontinued treatment, more patients in the placebo + CT group vs the pembro + CT group received subsequent PD-1/PD-L1 inhibitors (45.0% vs 19.3%)

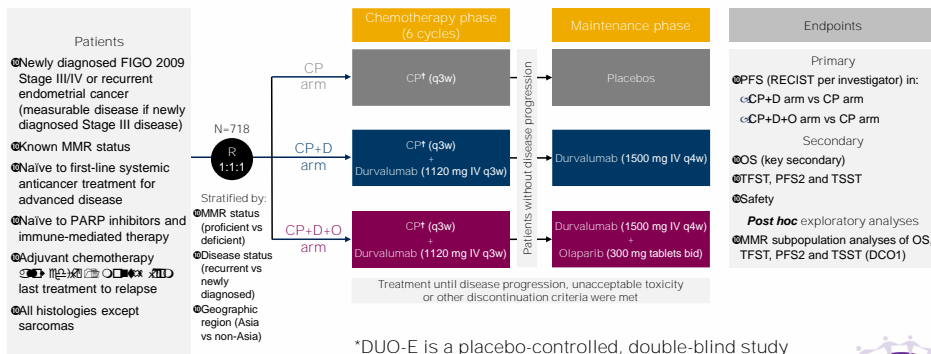


THE POWER OF SHARED PURPOSE:  
Transforming Oncologic Clinical Trials

\*Follow-up duration is defined as the time from randomization to the date of death or the database cutoff date if the participant is still alive.  
\*Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy.  
\*One-sided P-value based on log-rank test stratified by prior chemotherapy.  
Database cutoff: Dec 02, 2023.



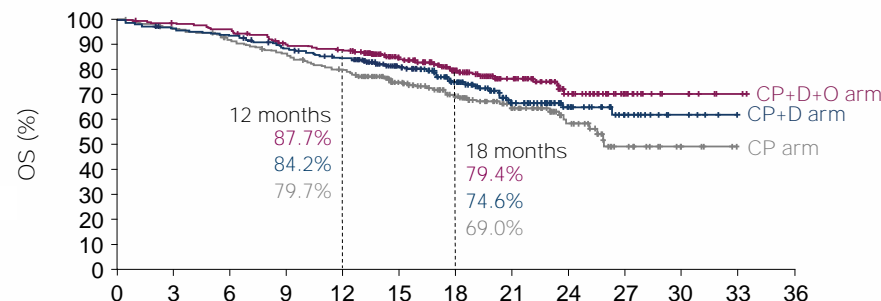
## DUO-E study



\*Six cycles of carboplatin at an area under the concentration-time curve of 5 or 6 mg•h/Limin and paclitaxel 175 mg/m<sup>2</sup>, bid, twice daily; CP, carboplatin/paclitaxel; D, durvalumab; DCO1, data cut-off 1; FIGO, International Federation of Gynaecology and Obstetrics; IV, intravenously; O, olaparib; q3(4)w, every 3(4) weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.



## OS: Secondary endpoint; prespecified interim analysis



No. at risk

	239	233	227	208	202	152	109	77	38	18	8	2	0
CP+D+O	239	233	227	208	202	152	109	77	38	18	8	2	0
CP+D	238	227	221	205	192	147	105	64	34	17	6	0	0
CP	241	229	215	201	185	136	104	69	35	15	4	0	0

	CP arm (N=241)	CP+D arm (N=238)	CP+D+O arm (N=239)
Events, n (%)	82 (34.0)	65 (27.3)	52 (21.8)
Median OS (95% CI), months	25.9 (23.9–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm†		0.77 (0.56–1.07); P=0.120	0.59 (0.42–0.83); P=0.003
HR (95% CI) vs CP+D arm†			0.77 (0.53–1.10)

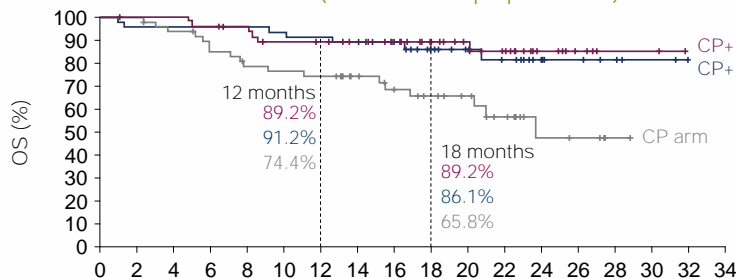
Overall data maturity: 27.7%

DU

# MMR subpopulations: OS

*Post hoc* exploratory analyses

dMMR (20% of ITT population)

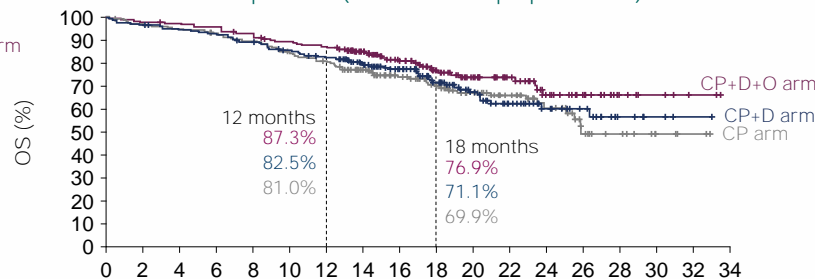


No. at risk	CP arm (n=49)	CP+D arm (n=46)	CP+D+O arm (n=48)
CP+D+O	48	47	47
CP+D	46	44	44
CP	49	49	45

	CP arm (n=49)	CP+D arm (n=46)	CP+D+O arm (n=48)
Events, n (%)	18 (36.7)	7 (15.2)	6 (12.5)
Median OS (95% CI), months	23.7 (16.9–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm*		0.34 (0.13–0.79)	0.28 (0.10–0.68)
HR (95% CI) vs CP+D arm*			0.84 (0.27–2.52)

Overall data maturity: 21.7%

pMMR (80% of ITT population)



No. at risk	CP arm (n=192)	CP+D arm (n=192)	CP+D+O arm (n=191)
CP+D+O	191	187	185
CP+D	192	187	180
CP	192	185	181

	CP arm (n=192)	CP+D arm (n=192)	CP+D+O arm (n=191)
Events, n (%)	64 (33.3)	58 (30.2)	46 (24.1)
Median OS (95% CI), months	25.9 (25.1–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm*		0.91 (0.64–1.30)	0.69 (0.47–1.00)
HR (95% CI) vs CP+D arm*			0.75 (0.51–1.11)

Overall data maturity: 29.2%



**THE POWER OF SHARED PURPOSE:**  
Transforming Gynecologic Cancer Care

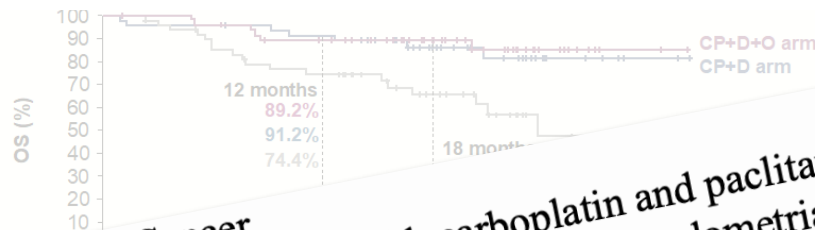
DCO: April 12, 2023. For the dMMR subpopulation, median duration of follow-up for OS was 18.4 (CP), 19.1 (CP+D) and 19.9 months (CP+D+O) in censored patients; for the pMMR subpopulation, median duration of follow-up was 18.6 (CP), 18.2 (CP+D) and 18.4 months (CP+D+O) in censored patients. MMR status was evaluated using the Ventana MMR immunohistochemistry panel. OS rates were estimated by the Kaplan–Meier method. \*HRs and CIs were estimated from an unstratified Cox proportional hazards model.





Date: 02 Aug 2024

## EMA Extension of Indications for Durvalumab



**Endometrial Cancer**  
IMFINZI in combination with carboplatin and paclitaxel is indicated for the first-line treatment of adults with primary advanced or recurrent endometrial cancer who are candidates for systemic therapy, followed by maintenance treatment with:

- IMFINZI as monotherapy in endometrial cancer that is mismatch repair deficient (dMMR)
- IMFINZI in combination with olaparib in endometrial cancer that is mismatch repair proficient (pMMR).

	CP+D arm (n=192)	CP+D arm (n=191)	CP+D+O arm (n=191)
Median OS (95% CI), months	25.9 (25.1–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs CP arm*		0.91 (0.64–1.30)	0.69 (0.47–1.00)
HR (95% CI) vs CP+D arm*			0.75 (0.51–1.11)

Overall data maturity: 21.7%

Overall data maturity: 29.2%



THE POWER OF SHARED PURPOSE:  
Transforming Gynecologic Cancer Care

DCO: April 12, 2023. For the dMMR subpopulation, median duration of follow-up for OS was 18.4 (CP), 19.1 (CP+D) and 19.9 months (CP+D+O) in censored patients; for the pMMR subpopulation, median duration of follow-up was 18.6 (CP), 18.2 (CP+D) and 18.4 months (CP+D+O) in censored patients. MMR status was evaluated using the Ventana MMR immunohistochemistry panel. OS rates were estimated by the Kaplan-Meier method. \*HRs and CIs were estimated from an unstratified Cox proportional hazards model.



# VII SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

## ENGOT-en11/GOG-3053/KEYNOTE-B21 Study Design

### Key Eligibility Criteria

- Newly diagnosed EC or carcinosarcoma
- Curative surgery with no residual disease
- At high risk for recurrence:
  - FIGO (2009) surgical stage I/II, non-endometrioid with myometrial invasion
  - FIGO (2009) surgical stage I/II with myometrial invasion of any histology with known aberrant p53 expression or TP53 mutation
  - FIGO (2009) surgical stage III/IVA of any histology
- No prior radiation or systemic therapy (including neoadjuvant) for EC

### Stratification Factors

- MMR status (pMMR vs dMMR), and within pMMR stratum:
  - Planned radiation (chemo-EBRT vs EBRT vs no EBRT)
  - Histology (endometrioid vs non-endometrioid)
  - FIGO (2009) surgical stage (I/II vs III/IVA)

R 1:1  
N=1095

### Stage 1

Carboplatin (AUC 5 or 6) +  
paclitaxel 175 mg/m<sup>2</sup>  
(Q3W, 4 or 6 cycles)

Pembrolizumab  
200 mg Q3W (6 cycles)

Carboplatin (AUC 5 or 6) +  
paclitaxel 175 mg/m<sup>2</sup>  
(Q3W, 4 or 6 cycles)

Placebo  
Q3W (6 cycles)

### Stage 2

± radiotherapy  
± cisplatin

Pembrolizumab  
400 mg Q6W (6 cycles)

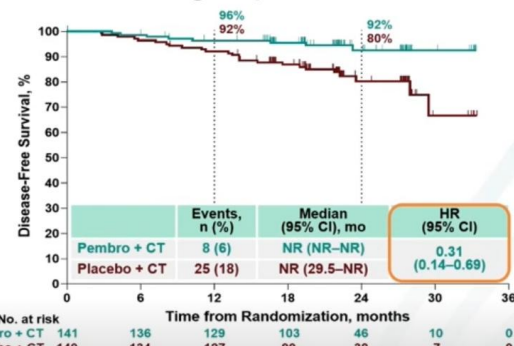
± radiotherapy  
± cisplatin

Placebo  
Q6W (6 cycles)

### Dual Primary Endpoints

- DFS as assessed radiographically by the investigator or by histopathologic confirmation
- OS (not mature at this interim analysis)

## Pembrolizumab Plus Chemotherapy Improved DFS<sup>a</sup> per Investigator in dMMR Subgroup



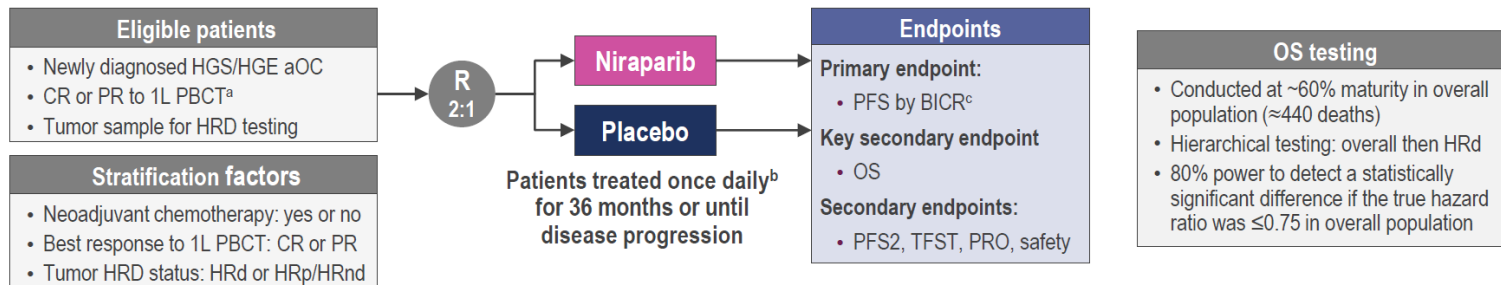
<sup>a</sup>DFS was defined as the time from randomization to local or distant recurrence of EC (assessed radiographically by the investigator or by histopathologic confirmation) or death from any cause. Data cutoff date: March 4, 2024.



## Ovarian cancer

# PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib 1L maintenance

Phase 3 PRIMA trial enrolled patients with newly diagnosed aOC at a high risk for disease recurrence

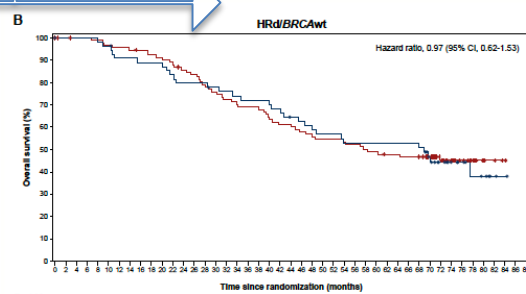
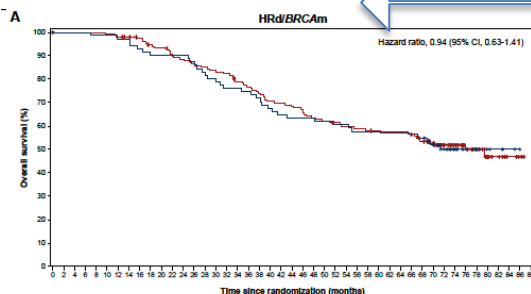
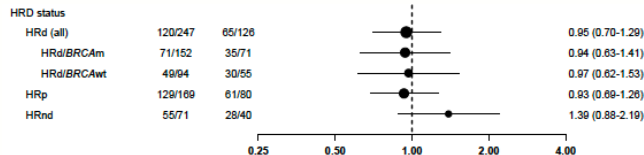
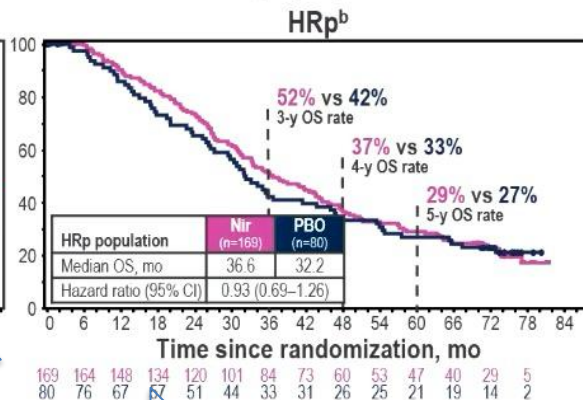
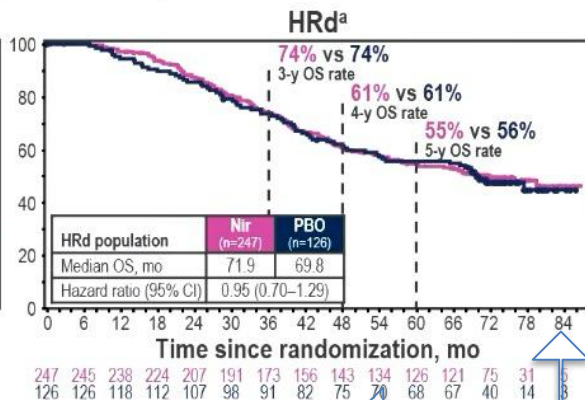
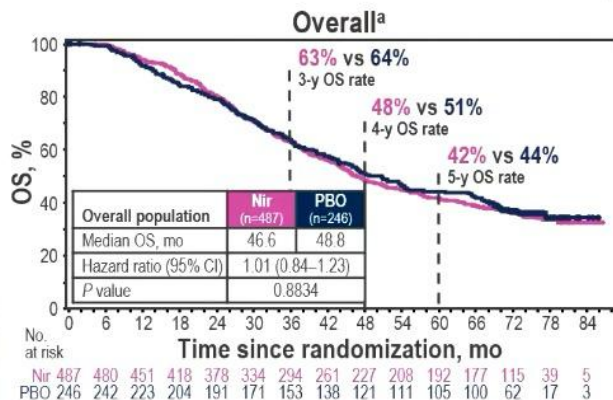


Key risk characteristics of PRIMA population <sup>1,2</sup>		
Disease stage	Residual disease	Tumor HRD/BRCA status
35.1% stage IV disease at diagnosis	>99% stage III disease at diagnosis with residual disease after primary debulking surgery	50.9% HRd
Initial treatment		30.4% HRd/BRCAm
66.7% received neoadjuvant chemotherapy	47.5% postoperative visible residual disease or no debulking surgery	34.0% HRp
30.6% achieved partial response to 1L PBCT		

PRIMA/ENGOT-OV26/GOG-3012 trial (NCT02655016). <sup>a</sup>Patients must have either had CA-125 in the normal range or a ≥90% decrease in CA-125 during 1L treatment that was stable for at least 7 days. At baseline, 7.1% of the overall population had CA-125 above the upper limit of normal. <sup>b</sup>At study start, all patients received a fixed starting dose of 300 mg once daily. Subsequently, the protocol was updated to use an individualized starting dose adjusted according to baseline body weight/platelet count. <sup>c</sup>Primary endpoint of PFS by BICR assessed by hierarchical testing, first in patients with HRd tumors and then in the overall population. 1L, first-line; aOC, advanced ovarian cancer; BICR, blinded independent central review; BRCAm, BRCA-mutated; CA-125, cancer antigen 125; CR, complete response; HGE, high-grade endometrioid; HGS, high-grade serous; HRd, homologous recombination deficiency; HRnd, homologous recombination deficient; HRp, homologous recombination proficient; OS, overall survival; PBCT, platinum-based chemotherapy; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; PRO, patient-reported outcomes; TFST, time to first subsequent therapy. 1. González-Martín A, et al. *N Engl J Med*. 2019;381(25):2391–2402. 2. O’Cearbhaill RE, et al. *Gynecol Oncol*. 2022;166(1):36–43.

# Final OS (62.5% maturity in overall population)

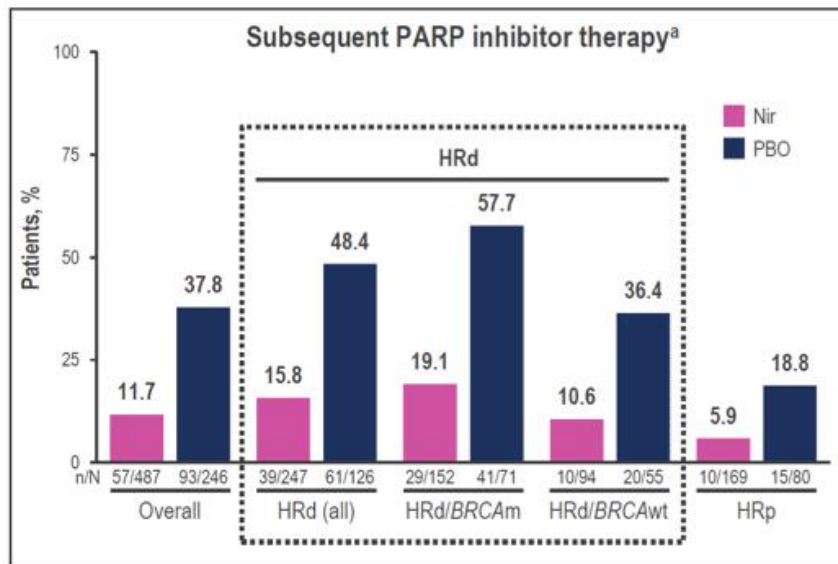
No difference in OS between niraparib and placebo arms in the overall, HRd, and HRp populations





## Subsequent PARP inhibitor therapy

3-fold higher subsequent PARP inhibitor use in placebo arm than niraparib arm across populations



### Subsequent PARP inhibitor use

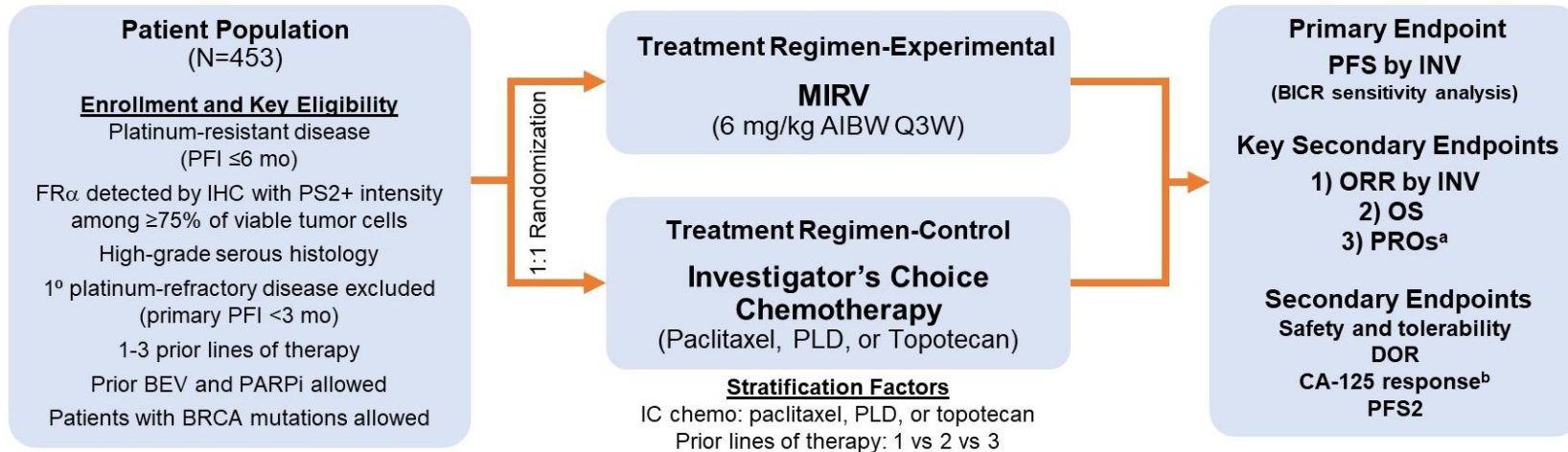
- Most predominant in HRd population, with highest use in HRd/*BRCAm* population
- Most patients initiated in the 2L setting

Any subsequent PARP inhibitor by treatment line, % <sup>a</sup>	Overall		HRd	
	Nir (n=487)	PBO (n=246)	Nir (n=247)	PBO (n=126)
Any treatment line	11.7	37.8	15.8	48.4
2L	8.2	30.5	13.0	37.3
3L+	3.5	7.3	2.8	11.1

<sup>a</sup>Percentages calculated out of the total number of patients in each population, not the number of patients who experienced disease progression. 2L, second-line; 3L+, third-line and beyond; *BRCAm*, *BRCA*-mutated; *BRCAw*, *BRCA* wild-type; HRd, homologous recombination deficient; HRp, homologous recombination proficient; Nir, niraparib; PARP, poly(ADP-ribose) polymerase; PBO, placebo.

## MIRASOL (NCT04209855) – Study Design<sup>1,2</sup>

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



Enrolled patients: 62% prior Bevacizumab, 55% prior PARPi



## MIRASOL (NCT04200855) – Study Design 1.2

Date: 14 nov 2024

### EMA Recommends Granting a Marketing Authorisation for Mirvetuximab Soravtansine

ELAHERE as monotherapy is indicated for the treatment of adult patients with folate receptor- $\alpha$  (FR $\alpha$ ) positive, platinum-resistant high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens (see section 4.2).

#### Patient Population (N=453)

##### Enrollment and Key Eligibility

Platinum-resistant disease  
(PFI  $\leq 6$  mo)

FR $\alpha$  detected by IHC with  $\geq 75\%$   
among  $\geq 75\%$

#### Treatment Regimen

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

##### Stratification Factors

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

#### Secondary Endpoints

- 1) ORR by INV
- 2) OS
- 3) PROs<sup>a</sup>

#### Secondary Endpoints

Safety and tolerability  
DOR  
CA-125 response<sup>b</sup>  
PFS2

Enrolled patients: 62% prior Bevacizumab, 55% prior PARPi



## Pantumor Gyn

## DESTINY-PanTumor02

# Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: biomarker and subgroup analyses from the cervical, endometrial, and ovarian cancer cohorts of the DESTINY-PanTumor02 study

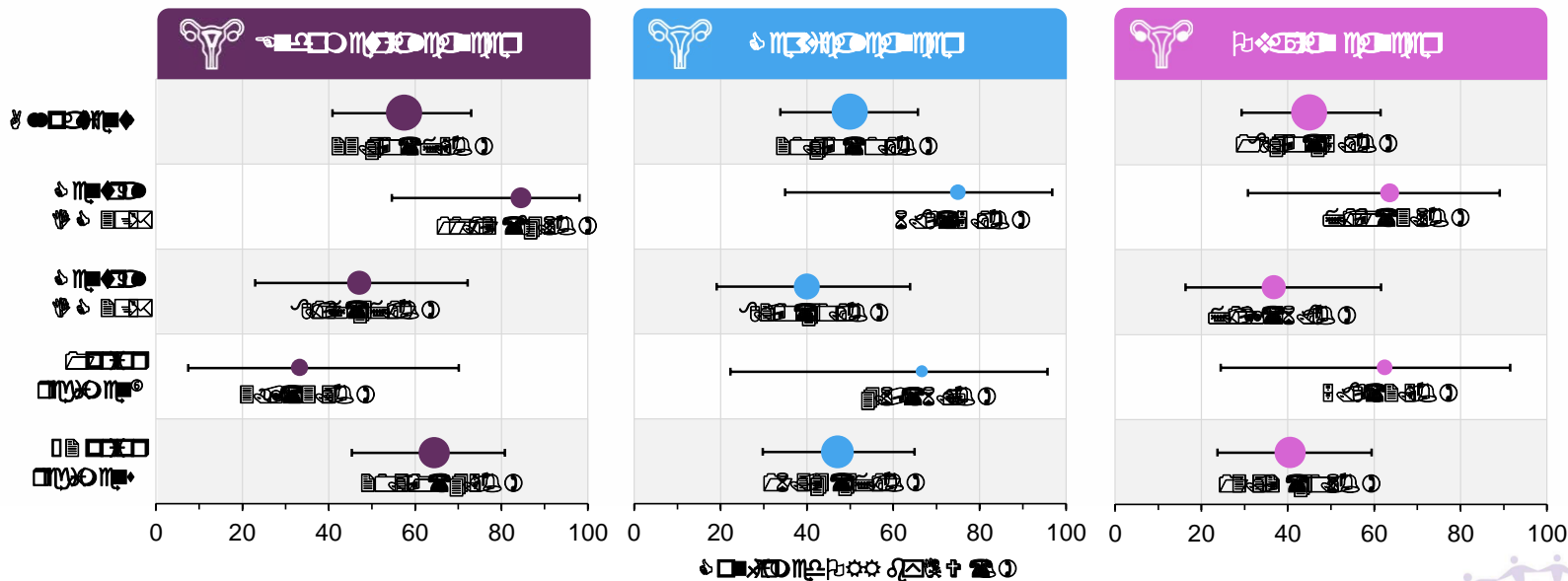
Vicky Makker,<sup>1,2</sup> Ana Oaknin, Luis Manso, Antonio González-Martín, Iwona Ługowska, Funda Meric-Bernstam, Domenica Lorusso, Susana Banerjee, John B Liao, Salvatore Siena, Chien-Hsing Lu, Naiyarat Prasongsook, Bohuslav Melichar, Anitra Fielding, Lindsey Jung, Soham Puvvada, Flavia Micheline, Jung-Yun Lee

<sup>1</sup>Gynecologic Medical Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY, US

<sup>2</sup>Department of Medicine, Weill Cornell Medical College, New York, NY, US

2024 SGO Annual Meeting on Women's Cancer | 16 March 2024, 08:30–09:45 PST





**THE POWER OF SHARED PURPOSE:**  
Transforming Gynecologic Cancer Care

\*In patients with IHC 1+/0/unknown by central testing, responses were observed in 4/10 patients with endometrial cancer, 6/12 patients with cervical cancer, and 4/10 patients with ovarian cancer; †one patient with endometrial cancer was reported to have received no prior regimens  
IHC, immunohistochemistry; INV, investigator; ORR, objective response rate



# CONCLUSIONS

- **Pembrolizumab** in addition to **chemoradiotherapy** as a **new standard of care** for LACC.
- **Immune checkpoint inhibitors** should be incorporated to first line Chemo in patients with advanced/recurrent endometrial cancer.
- No difference in OS between **niraparib** and placebo arms in overall population and by HRD status.
- **T-DXd** demonstrated clinically meaningful ORRs in heavily pre-treated patients with HER2-expressing endometrial, cervical, and ovarian tumors.