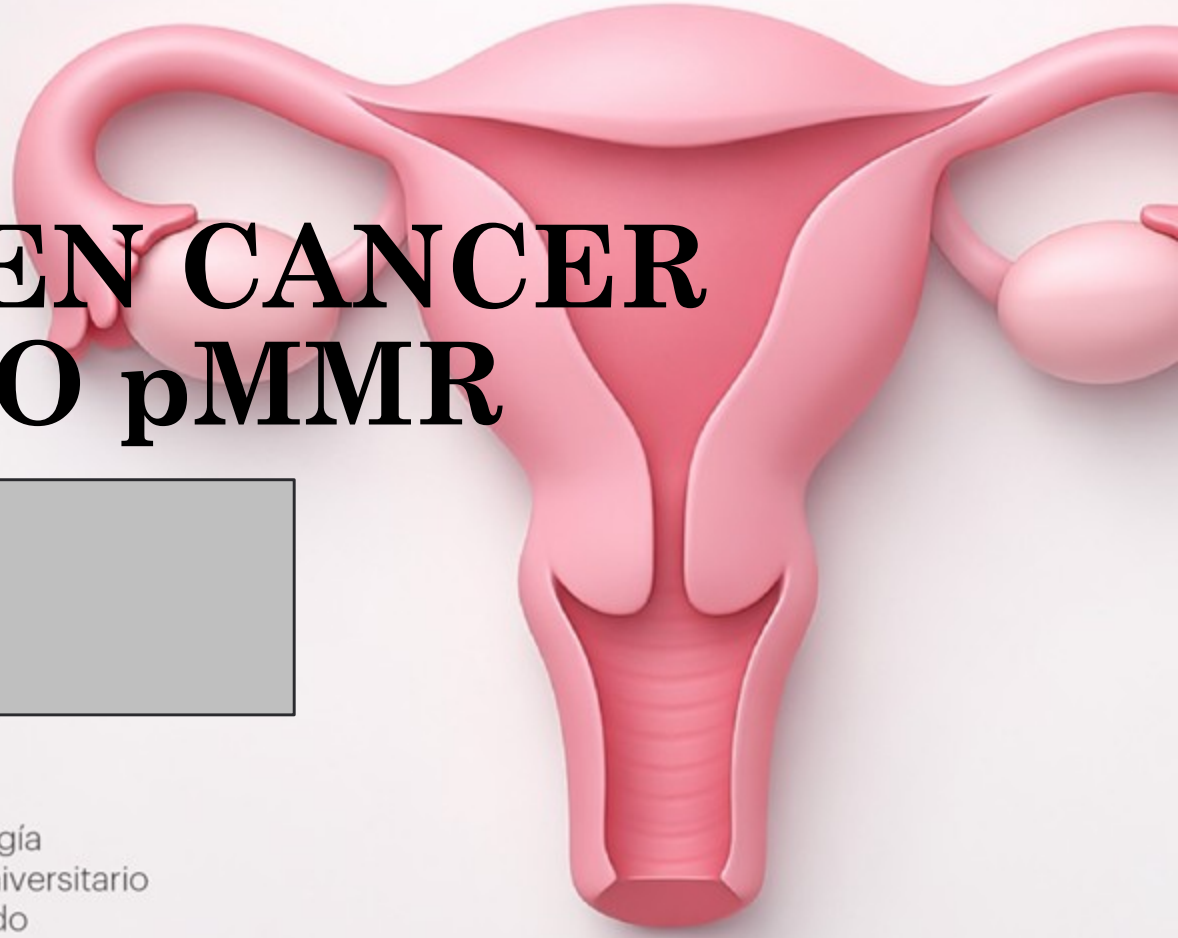
4ª Jornada de Actualización en Cáncer Ginecológico

Bilbao · 20 – 21 de mayo 2026

Organizado por ASONMEC

SECUENCIA DE TRATAMIENTO EN CANCER DE ENDOMETRIO pMMR



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20 de mayo 2026

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ÍNDICE

INTRODUCCIÓN

- El cáncer de endometrio es el **tumor ginecológico más frecuente.**

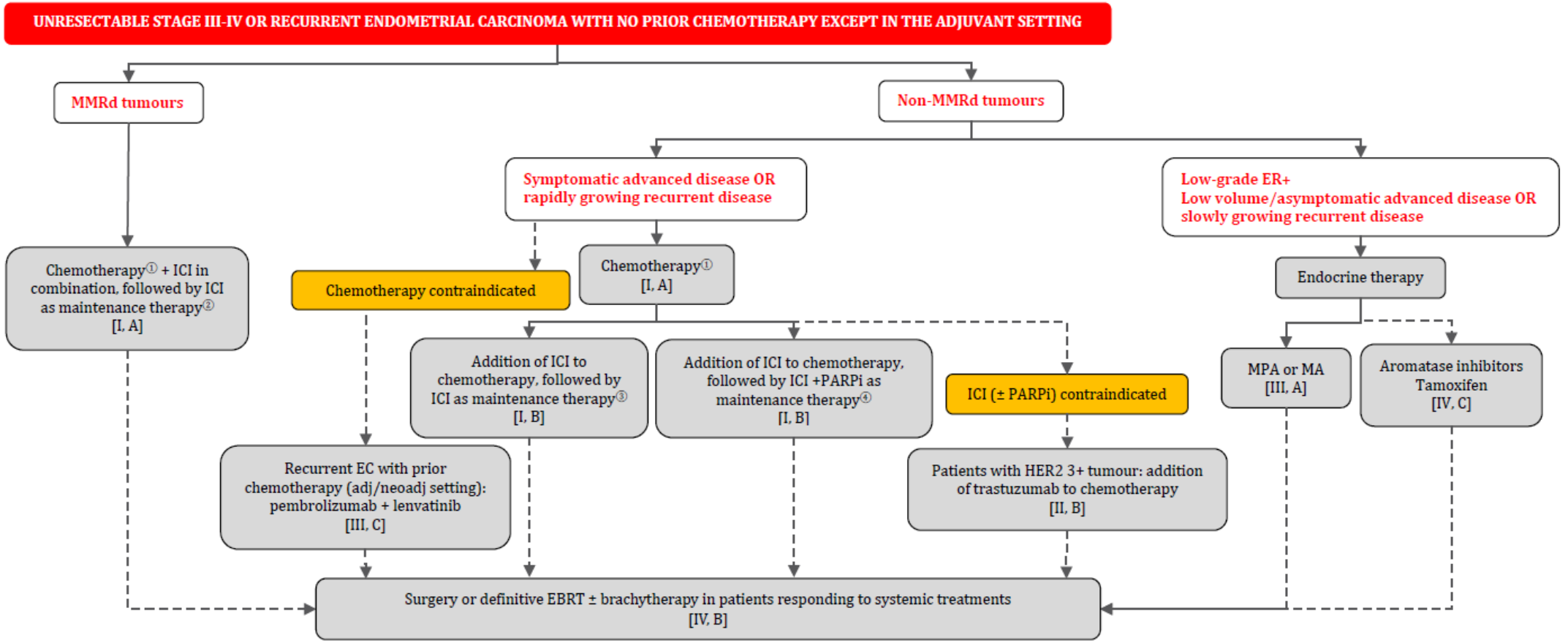
- Generalmente se detectan en estadíos tempranos (80%) y tienen un pronóstico excelente pero las pacientes diagnosticadas con **enfermedad avanzada** tienen una **supervivencia estimada a 5 años de un 17-20%.**

- **25-30% son dMMR/MSI-H**. >90% son esporadicos.

- Estadificación **FIGO 2023**

- **FR**: obesidad, HTA, hiperinsulinemia, nuliparidad, menarquia precoz, menopausia tardía, tamoxifeno, sdmes hereditarios.

4.8 Algorithm #8 - First line systemic therapy in unresectable stage III-IV or recurrent endometrial carcinoma with no prior chemotherapy except in the adjuvant setting (including patients with residual disease after surgery)



①The standard chemotherapy regimen is carboplatin + paclitaxel.

②Immune checkpoint inhibitor (ICI): dostarlimab or durvalumab or pembrolizumab (drugs in alphabetical order).

③ICI: dostarlimab or pembrolizumab.

④ICI + poly(ADP-ribose) polymerase inhibitor (PARPi): durvalumab + olaparib.

Adj/neoadj adjuvant/neoadjuvant; EBRT external beam radiotherapy; ER+ estrogen receptor positive; MA megestrol acetate; MMRd mismatch repair deficiency, MPA medroxyprogesterone acetate; non-MMRd non-mismatch repair deficiency; NSMP no~~n~~ specific molecular profile.

Supplement to: Concin N, Matias-Guiu X, Cibula D, et al. ESGO–ESTRO–ESP guidelines for the management of patients with endometrial carcinoma: update 2025. Lancet Oncol 2025; 26: e423–35


A
B

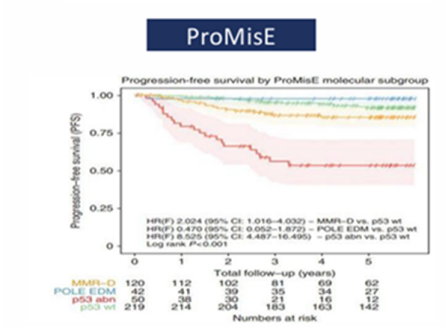
p MMR ….UNA ENTIDAD MUY HETEROGÉNEA

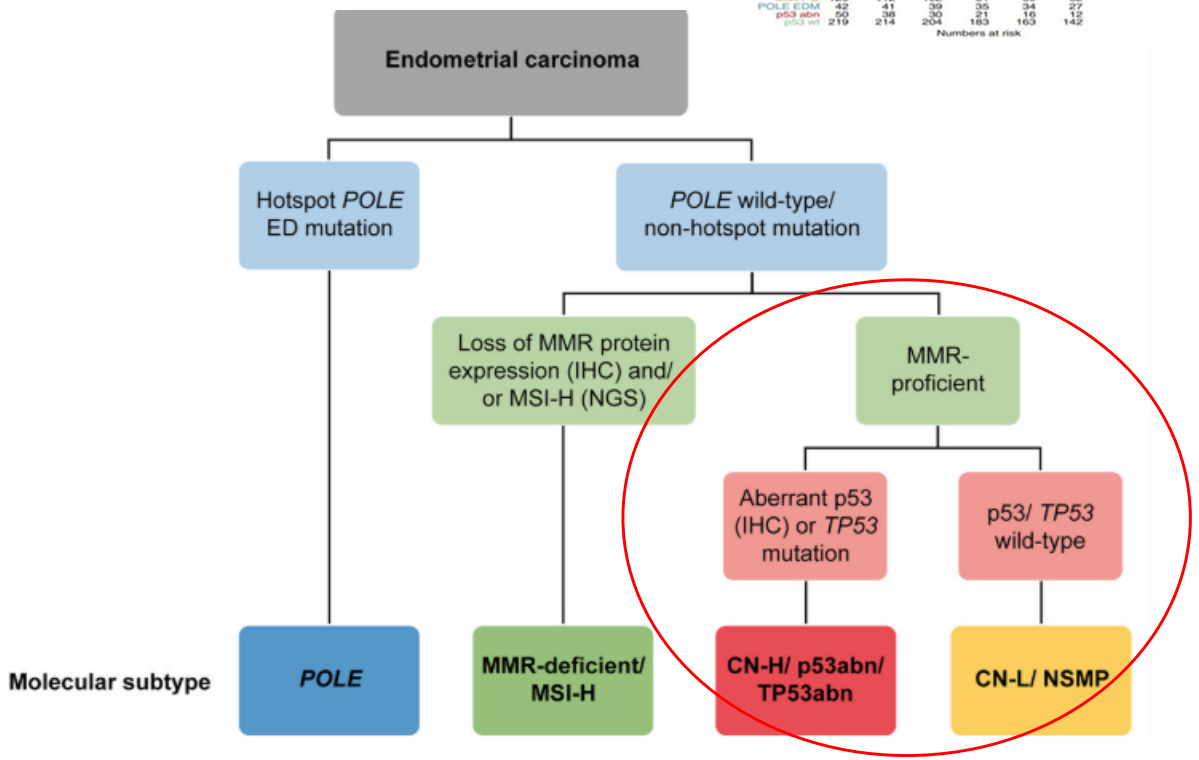
P53 ABNORMAL:

- **Subtipo de peor pronóstico**, 15% de los cánceres de endometrio pero supone el 50-70% de la mortalidad.
- Más agresivos y enfermedad más avanzada al diagnóstico
- Aprox 20% sobreexpresión de HER2
- Tiene un alto número de alteraciones somáticas.
- El p53 mutado es más frecuente en determinadas histologías: 93% seroso, 85% carcinosarcomas y 38% células claras.
- Se detecta por IHQ: mutado implica la sobreexpresión del p53 así como la ausencia de tinción del mismo.
- HRD es más prevalente en los tumores p53 mutados.

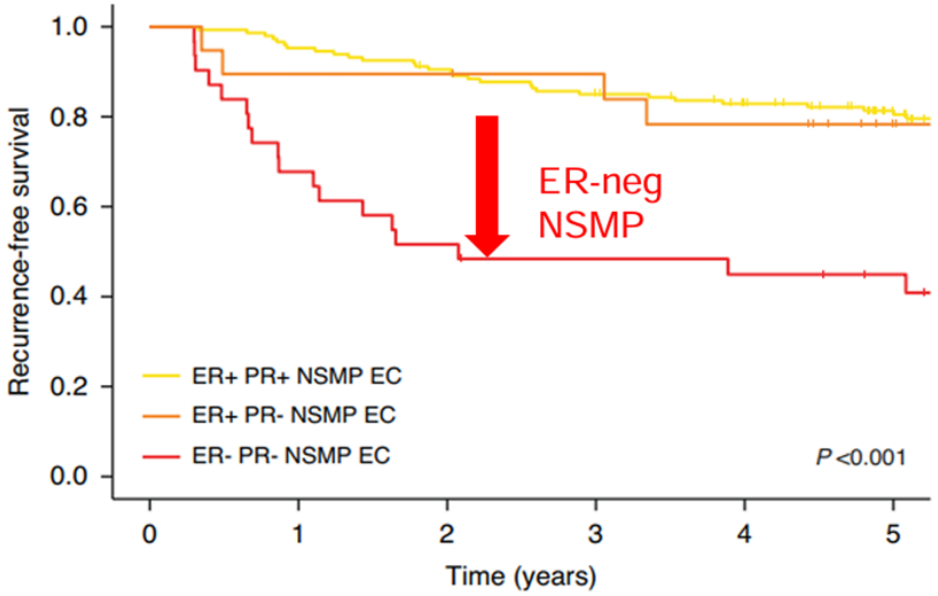
NSMP:

- Es un subgrupo muy heterogéneo, y el subgrupo más frecuente (50% aprox).
- Se caracterizan por p MMR, p53 wild type y ausencia de mutaciones en POLE y suelen expresar RH (con una expresión variable).
- Subtipo de pronóstico intermedio.
- Marcadores como L1CAM (sobreexpresión), negatividad de los RH, mutaciones en CTNNB1 o la amplificación del cromosoma 1q, se están proponiendo como marcadores para una mejor estratificación del riesgo del subtipo NSMP.

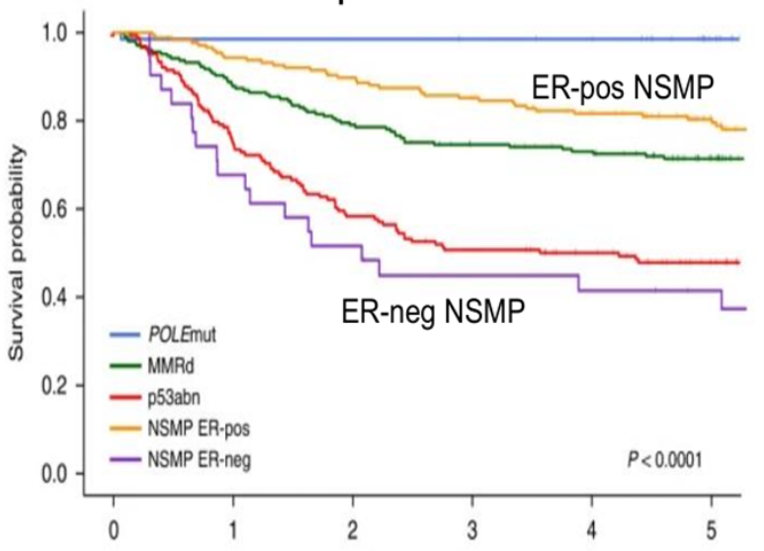




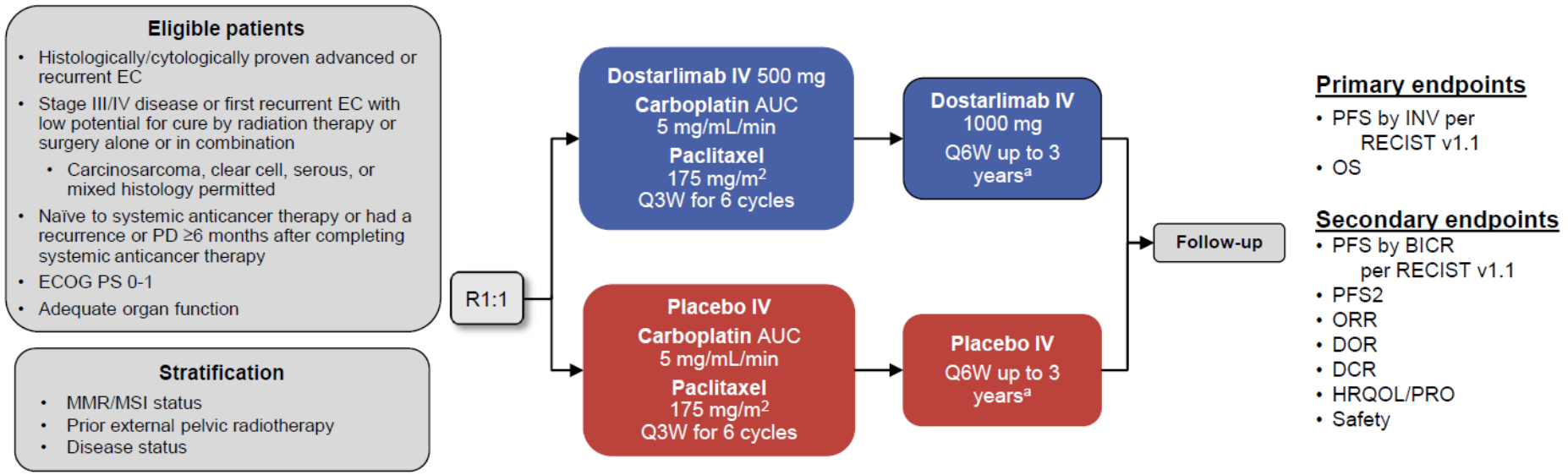
Within the NSMP subclass, ER-neg stand out

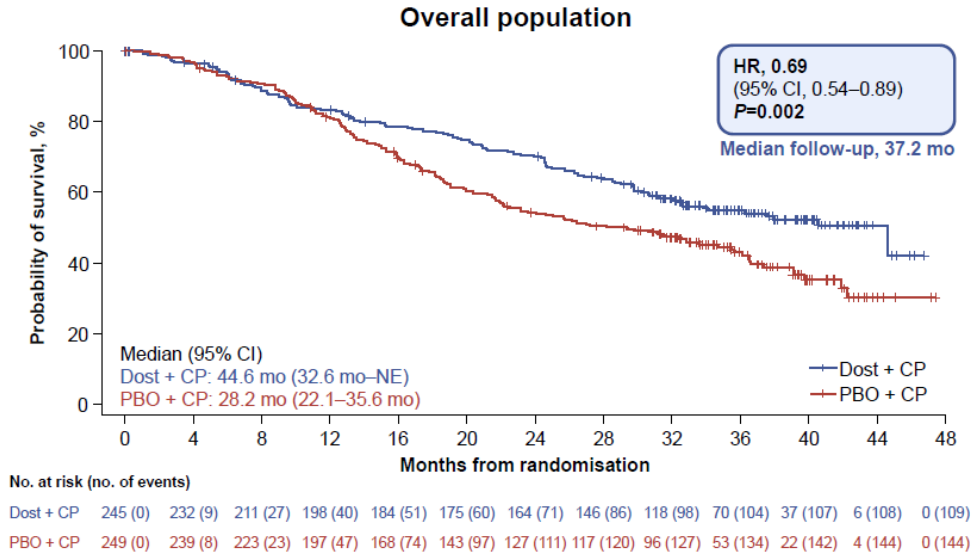


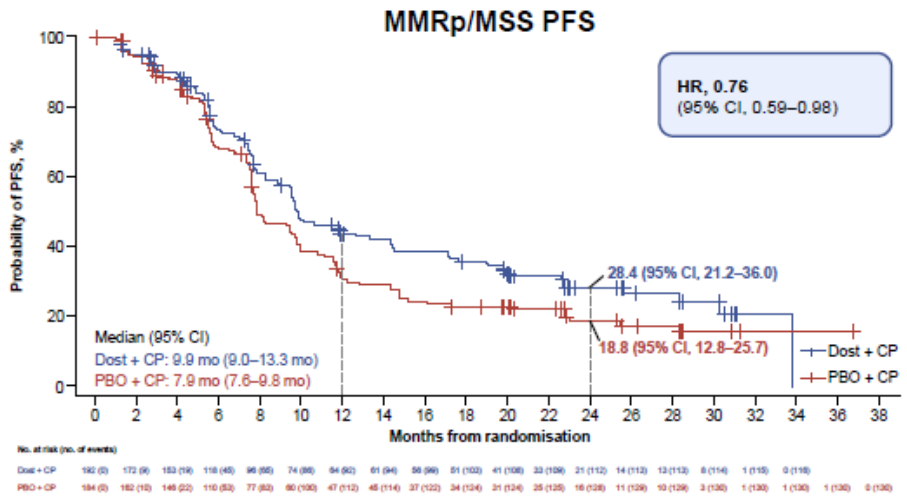
Within molecular classified EC, ER-neg NSMP behave like p53abn…

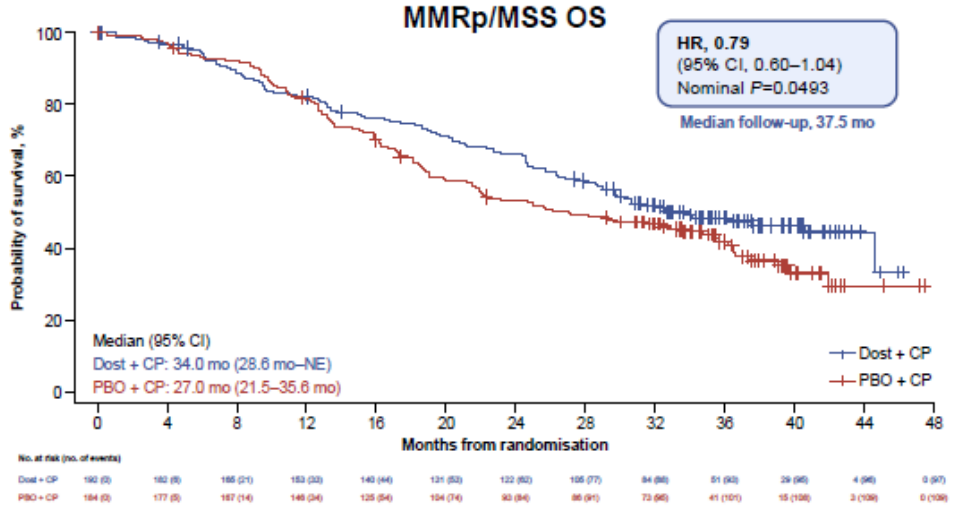


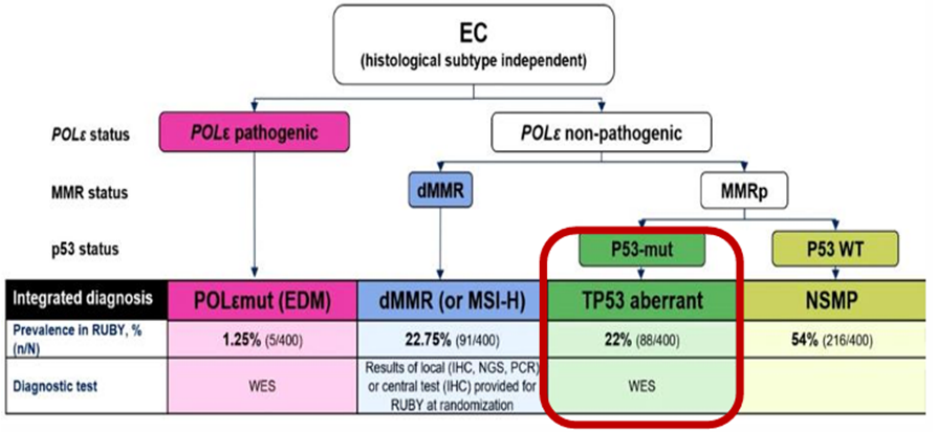
RUBY


Eligible patients
• Histologically/cytologically 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
• Naïve to systemic anticancer therapy or had a recurrence or PD ≥6 months after completing systemic anticancer therapy
• ECOG PS 0-1
• Adequate organ function
Stratification
• MMR/MSI status
• Prior external pelvic radiotherapy
• Disease status
R1:1
Dostarlimab IV 500 mg
Carboplatin AUC 5 mg/mL/min
Paclitaxel 175 mg/m2
Q3W for 6 cycles
Dostarlimab IV 1000 mg
Q6W up to 3 years[a]
Placebo IV
Carboplatin AUC 5 mg/mL/min
Paclitaxel 175 mg/m2
Q3W for 6 cycles
Placebo IV
Q6W up to 3 years[a]
Follow-up
Primary endpoints
• PFS by INV per RECIST v1.1
• OS
Secondary endpoints
• PFS by BICR per RECIST v1.1
• PFS2
• ORR
• DOR
• DCR
• HRQOL/PRO
• Safety

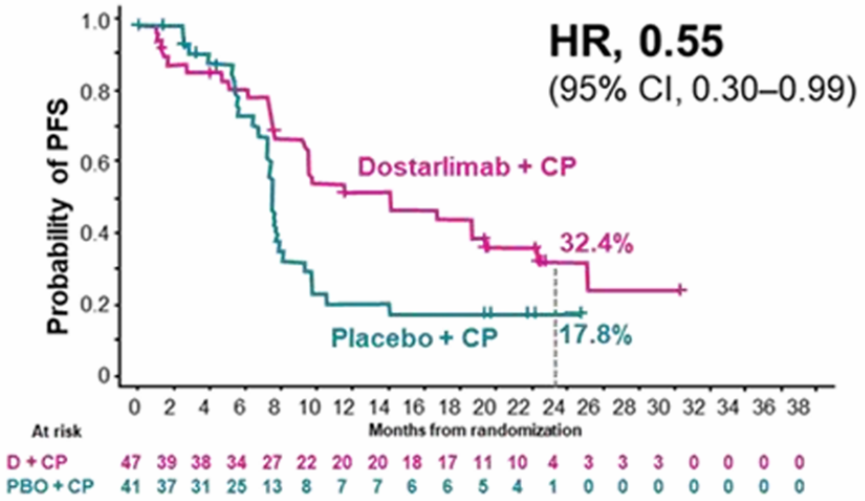

Overall population
HR, 0.69
(95% CI, 0.54–0.89)
P=0.002
Median follow-up, 37.2 mo
Probability of survival, %
Median (95% CI)
Dost + CP: 44.6 mo (32.6 mo–NE)
PBO + CP: 28.2 mo (22.1–35.6 mo)
Dost + CP
PBO + CP
Months from randomisation
No. at risk (no. of events)
Dost + CP 245 (0) 232 (9) 211 (27) 198 (40) 184 (51) 175 (60) 164 (71) 146 (86) 118 (98) 70 (104) 37 (107) 6 (108) 0 (109)
PBO + CP 249 (0) 239 (8) 223 (23) 197 (47) 168 (74) 143 (97) 127 (111) 117 (120) 96 (127) 53 (134) 22 (142) 4 (144) 0 (144)

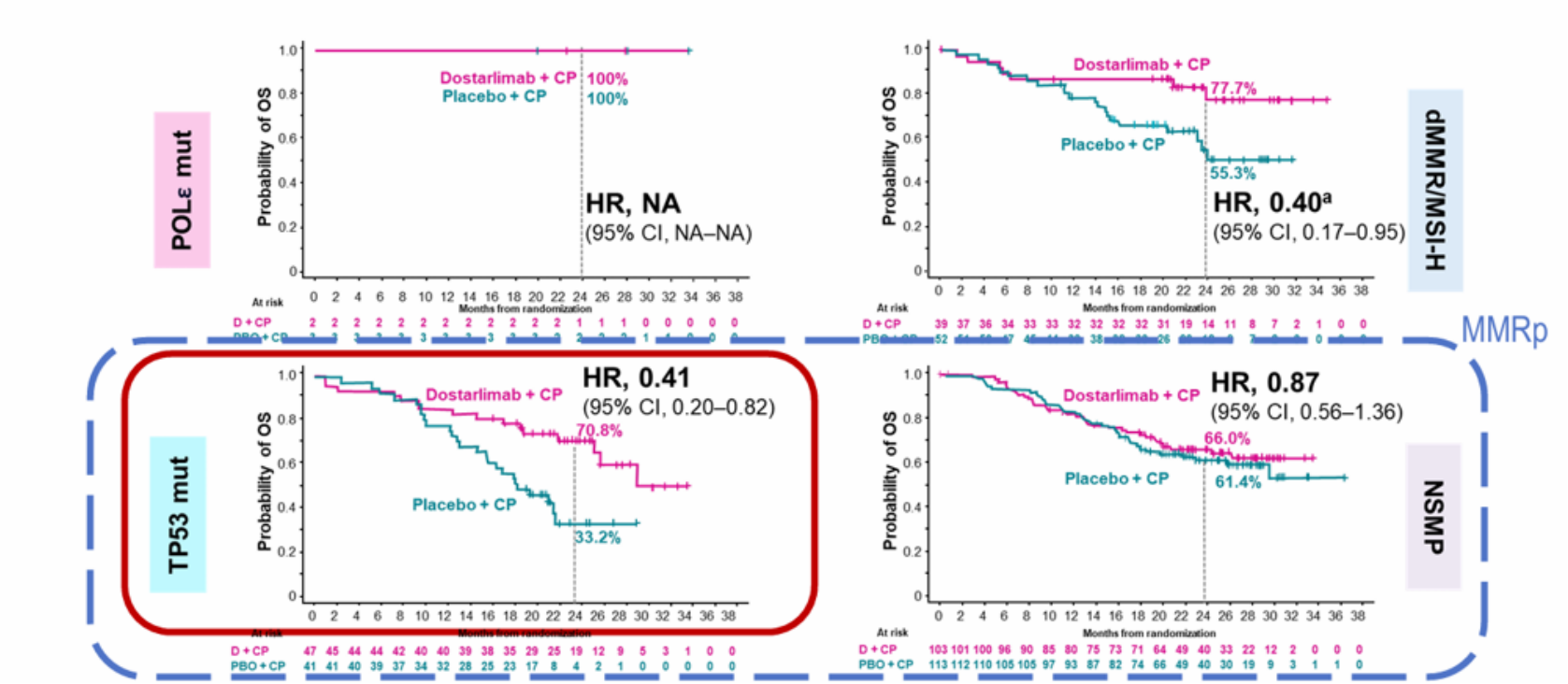

MMRp/MSS PFS
HR, 0.76
(95% CI, 0.59–0.98)
Probability of PFS, %
28.4 (95% CI, 21.2–36.0)
18.8 (95% CI, 12.8–25.7)
Median (95% CI)
Dost + CP: 9.9 mo (9.0–13.3 mo)
PBO + CP: 7.9 mo (7.6–9.8 mo)
Dost + CP
PBO + CP
Months from randomisation


MMRp/MSS OS
HR, 0.79
(95% CI, 0.60–1.04)
Nominal P=0.0493
Median follow-up, 37.5 mo
Probability of survival, %
Median (95% CI)
Dost + CP: 34.0 mo (28.6 mo–NE)
PBO + CP: 27.0 mo (21.5–35.6 mo)
Dost + CP
PBO + CP
Months from randomisation



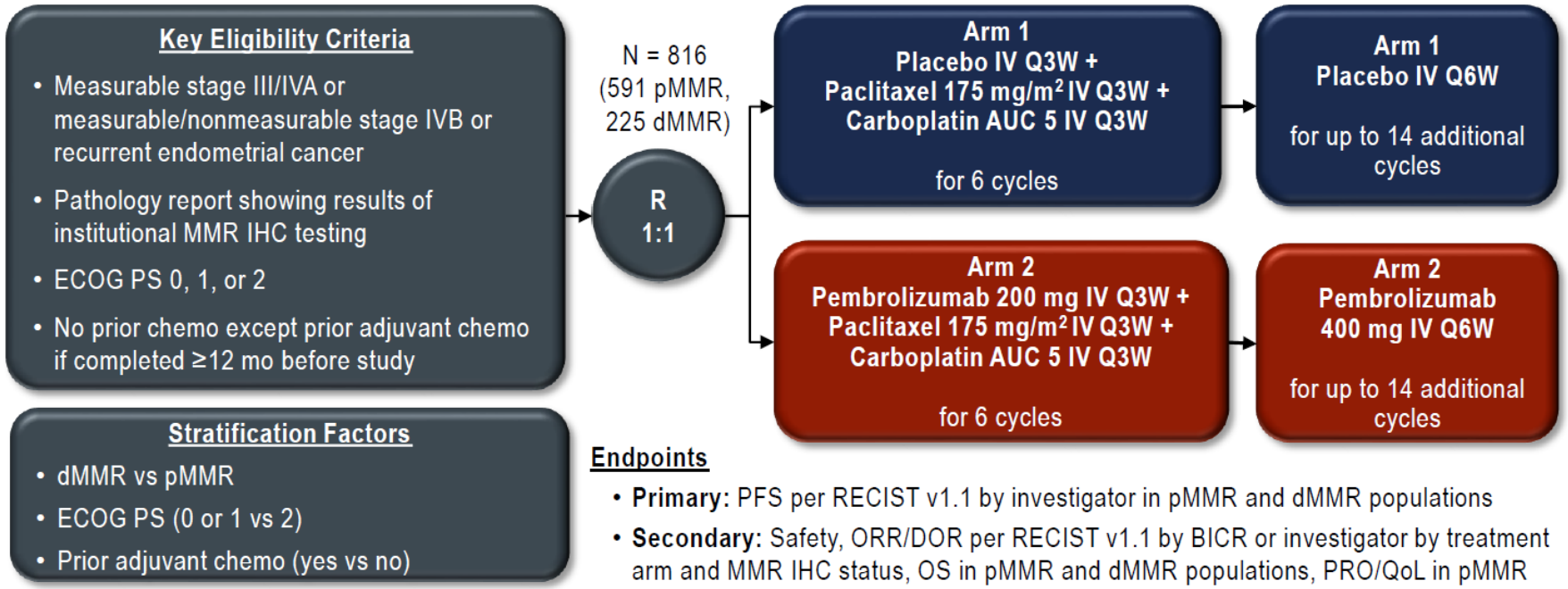
Integrated diagnosis	POLεmut (EDM)	dMMR (or MSI-H)	TP53 aberrant	NSMP
Prevalence in RUBY, % (n/N)	1.25% (5/400)	22.75% (91/400)	22% (88/400)	54% (216/400)
Diagnostic test	WES	Results of local (IHC, NGS, PCR) or central test (IHC) provided for RUBY at randomization	WES	




POLε mut
Probability of OS
Dostarlimab + CP
Placebo + CP
100%
100%
HR, NA
(95% CI, NA–NA)
At risk
D + CP 2 2 2 2 2 2 2 2 2 2 2 2 1 1 1 0 0 0 0 0 0
PBO + CP 3 3 3 3 3 3 3 3 3 3 3 3 2 2 2 1 1 1 0 0 0
Months from randomization
dMMR/MSI-H
Probability of OS
Dostarlimab + CP
Placebo + CP
77.7%
55.3%
HR, 0.40[a]
(95% CI, 0.17–0.95)
At risk
D + CP 39 37 36 34 33 33 32 32 32 32 31 19 14 11 8 7 2 1 0 0
PBO + CP 52 38 26 7 0 0
Months from randomization
MMRp
TP53 mut
Probability of OS
Dostarlimab + CP
Placebo + CP
70.8%
33.2%
HR, 0.41
(95% CI, 0.20–0.82)
At risk
D + CP 47 45 44 44 42 40 40 39 38 35 29 25 19 12 9 5 3 1 0 0
PBO + CP 41 41 40 39 37 34 32 28 25 23 17 8 4 2 1 0 0 0 0 0
Months from randomization
NSMP
Probability of OS
Dostarlimab + CP
Placebo + CP
66.0%
61.4%
HR, 0.87
(95% CI, 0.56–1.36)
At risk
D + CP 103 101 100 96 90 85 80 75 73 71 64 49 40 33 22 12 2 0 0 0
PBO + CP 113 112 110 105 105 97 93 87 82 74 66 49 40 30 19 9 3 1 1 0
Months from randomization

GY018

Study Design



Endpoints

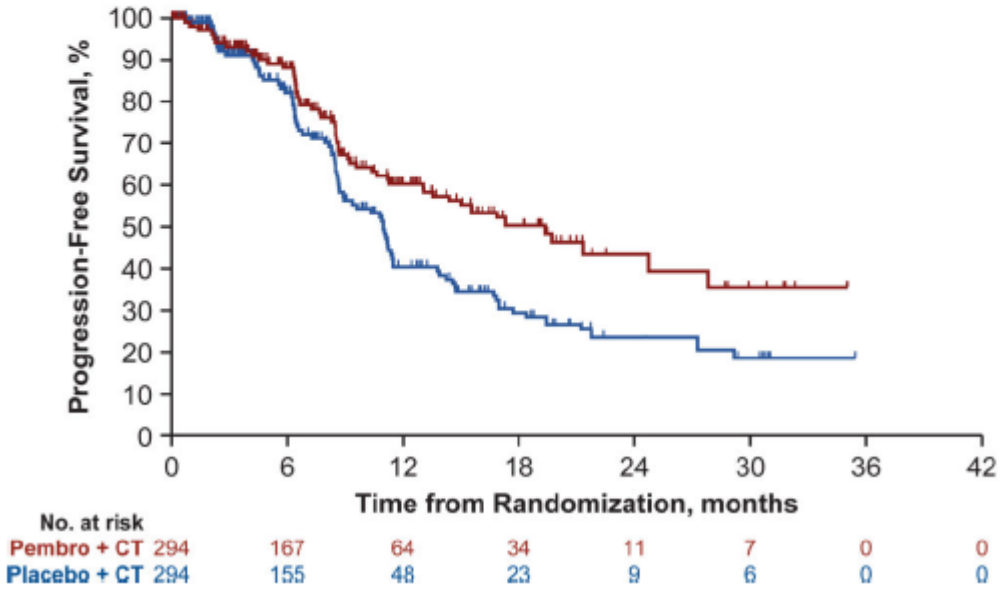
- **Primary:** PFS per RECIST v1.1 by investigator in pMMR and dMMR populations
- **Secondary:** Safety, ORR/DOR per RECIST v1.1 by BICR or investigator by treatment arm and MMR IHC status, OS in pMMR and dMMR populations, PRO/QoL in pMMR population, and concordance of MMR IHC testing at institution vs centralized

Median follow-up:

- IA1 data cutoff date of December 16, 2022: dMMR cohort, 12 months; pMMR cohort, 7.9 months
- **Current analysis data cutoff date of August 18, 2023**: dMMR cohort, 20.6 months; pMMR cohort, 15.8 months

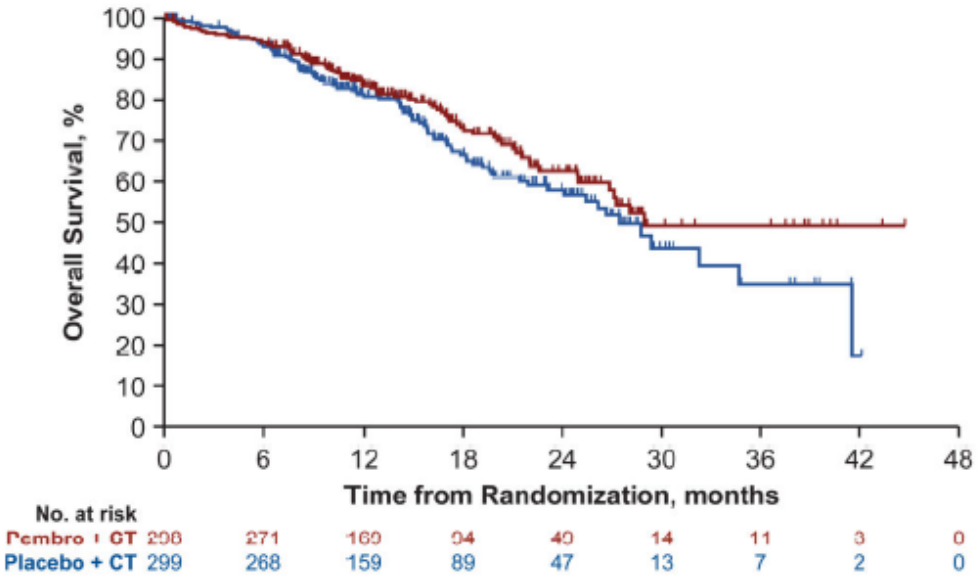
A)

	Events, n/N	Median PFS (95% CI), mo	HR (95% CI)[a], *P*-value[b]
Pembro + CT	85/294	19.5 (13.1–28.0)	**0.64 (0.49–0.85)**
Placebo + CT	122/294	11.0 (9.0–11.5)	***P* = 0.0008**

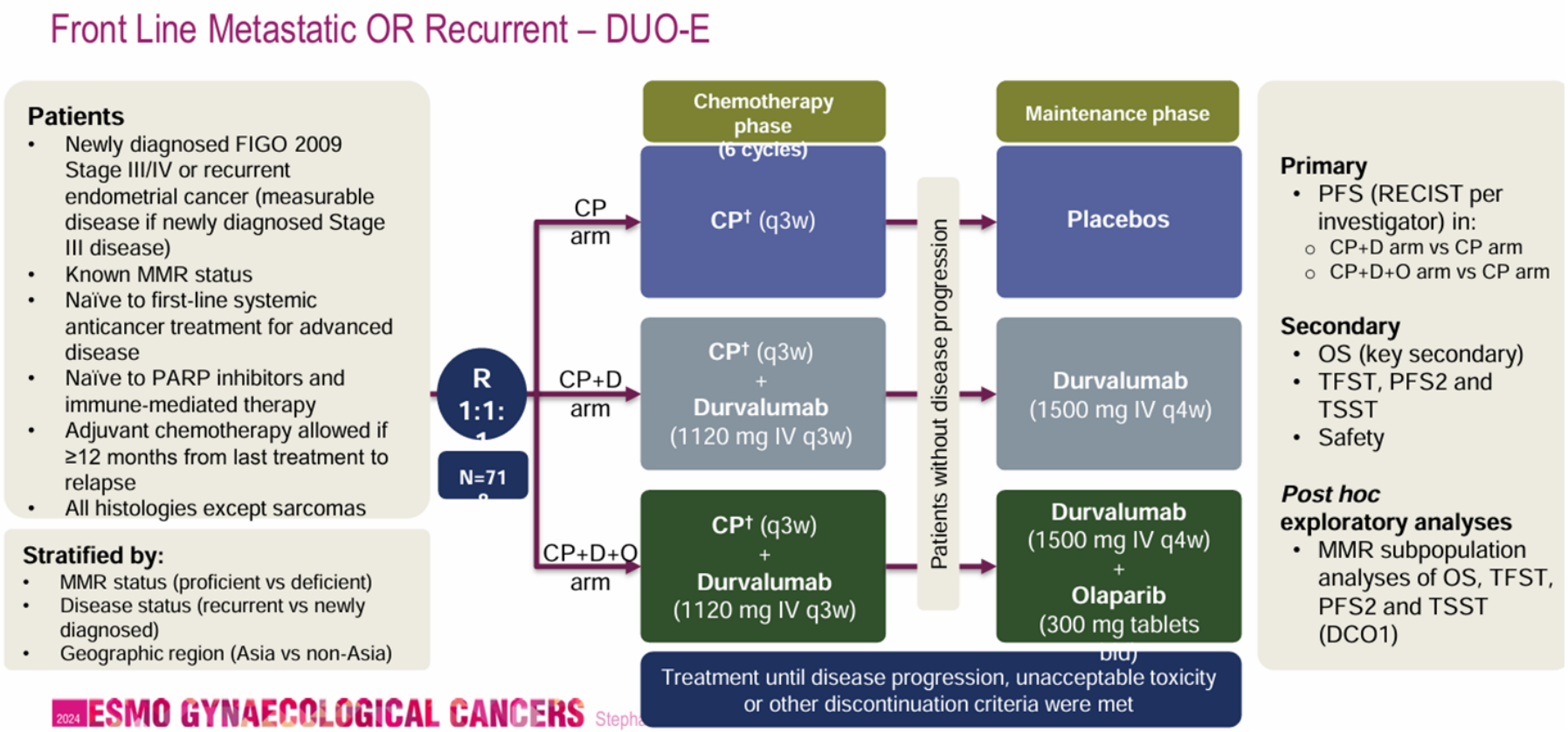


A)

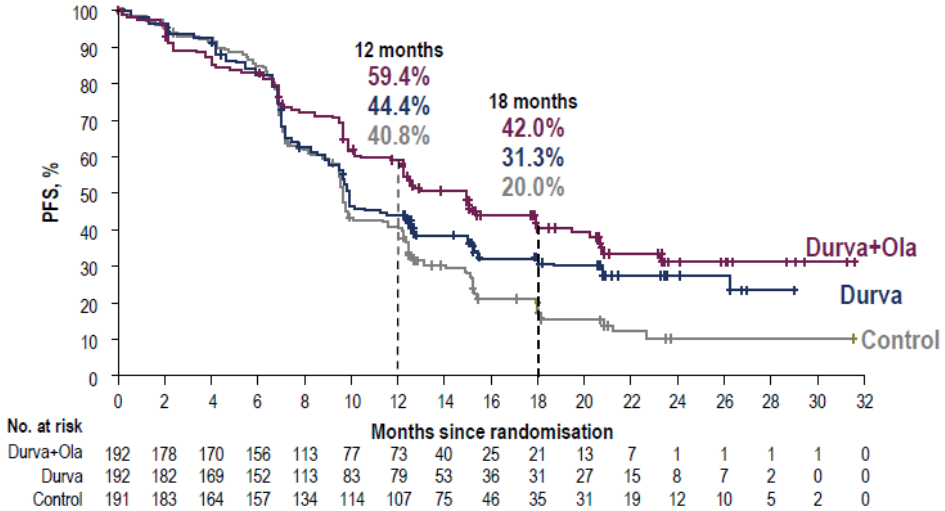
	Events, n/N	Follow-up Duration[a], median (range), mo	Median OS (95% CI), mo	HR (95% CI)[b], *P*-value[c]
Pembro + CT	77/298	15.7 (0.5–45.4)	28.9 (26.8–NR)	**0.80 (0.59–1.08)**
Placebo + CT	92/299	15.0 (0.9–45.6)	28.7 (24.0–34.6)	***P* = 0.0683**



DUO-E


Front Line Metastatic OR Recurrent – DUO-E
Patients
Newly diagnosed FIGO 2009 Stage III/IV or recurrent endometrial cancer (measurable disease if newly diagnosed Stage III disease)
Known MMR status
Naïve to first-line systemic anticancer treatment for advanced disease
Naïve to PARP inhibitors and immune-mediated therapy
Adjuvant chemotherapy allowed if ≥12 months from last treatment to relapse
All histologies except sarcomas
Stratified by:
MMR status (proficient vs deficient)
Disease status (recurrent vs newly diagnosed)
Geographic region (Asia vs non-Asia)
R 1:1:
N=71
CP arm
CP+D arm
CP+D+O arm
Chemotherapy phase (6 cycles)
CP† (q3w)
CP† (q3w) + Durvalumab (1120 mg IV q3w)
CP† (q3w) + Durvalumab (1120 mg IV q3w)
Patients without disease progression
Maintenance phase
Placebos
Durvalumab (1500 mg IV q4w)
Durvalumab (1500 mg IV q4w) + Olaparib (300 mg tablets
Treatment until disease progression, unacceptable toxicity or other discontinuation criteria were met
Primary
PFS (RECIST per investigator) in:
CP+D arm vs CP arm
CP+D+O arm vs CP arm
Secondary
OS (key secondary)
TFST, PFS2 and TSST
Safety
Post hoc exploratory analyses
MMR subpopulation analyses of OS, TFST, PFS2 and TSST (DCO1)
2024 ESMO GYNAECOLOGICAL CANCERS

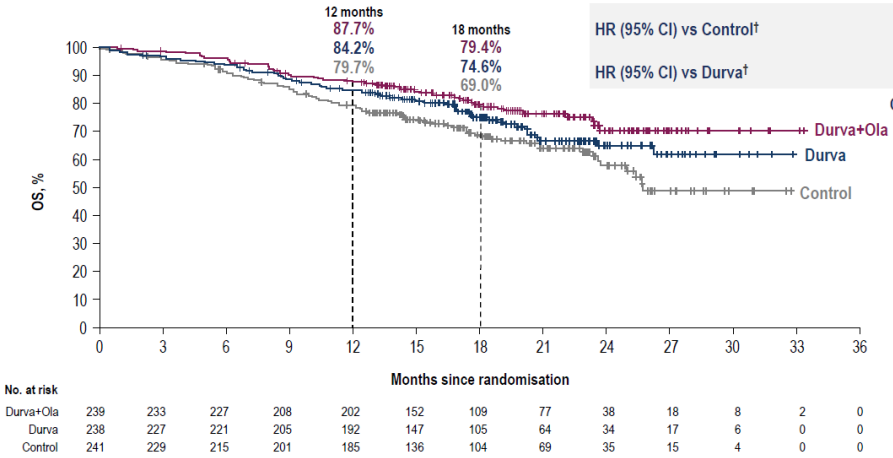
pMMR (80% of population)



	Control (N=192)	Durva (N=192)	Durva+Ola (N=191)
Events, n (%)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS (95% CI),* months	9.7 (9.2–10.1)	9.9 (9.4–12.5)	15.0 (12.4–18.0)
HR (95% CI) vs Control†		**0.77 (0.60–0.97)**	**0.57 (0.44–0.73)**
HR (95% CI) vs Durva†			**0.76 (0.59–0.99)**

OS: ITT population

Secondary endpoint; interim analysis

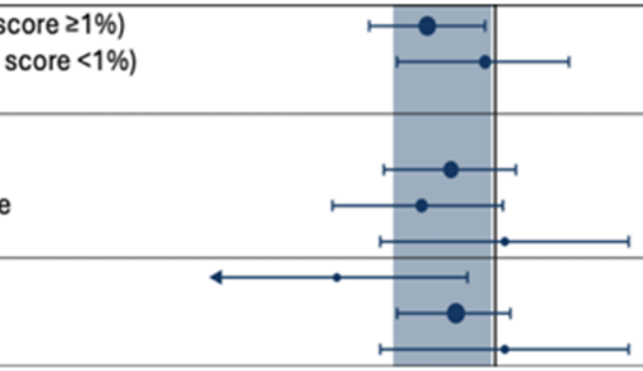


	Control (N=241)	Durva (N=238)	Durva+Ola (N=239)
Events, n (%)	82 (34.0)	65 (27.3)	52 (21.8)
Median OS (95% CI),* months	25.9 (23.9–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs Control†		**0.77** (0.56–1.07); *P*=0.120	**0.59** (0.42–0.83); *P*=0.003
HR (95% CI) vs Durva†			**0.77** (0.53–1.10)

Overall data maturity 27.7%

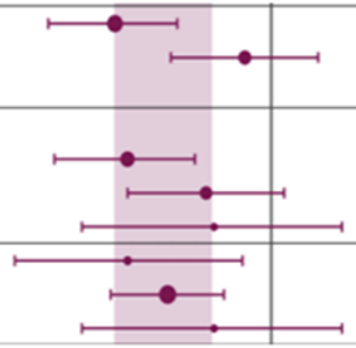
CP + durvalumab vs CP

PD-L1 expression*	Positive (TAP score ≥1%)	**0.71 (0.53–0.95)**
	Negative (TAP score <1%)	**0.95 (0.61–1.45)**
	Unknown‖	**NC (NC–NC)****
***POLE*m and *TP53*m status†,‡**	*POLE*m	**NC (NC–NC)****
	*TP53*m	**0.80 (0.57–1.11)**
	TP53 wild-type	**0.69 (0.44–1.04)**
	Unknown‖	**1.05 (0.56–1.96)**
HRRm status†,§	HRRm	**0.45 (0.23–0.87)**
	Non-HRRm	**0.82 (0.61–1.08)**
	Unknown‖	**1.05 (0.56–1.96)**



CP + durvalumab + olaparib vs CP

PD-L1 expression*	Positive (TAP score ≥1%)	**0.44 (0.31–0.61)**
	Negative (TAP score <1%)	**0.87 (0.59–1.28)**
	Unknown‖	**NC (NC–NC)****
***POLE*m and *TP53*m status†,‡**	*POLE*m	**NC (NC–NC)****
	*TP53*m	**0.47 (0.32–0.67)**
	TP53 wild-type	**0.71 (0.47–1.07)**
	Unknown‖	**0.74 (0.37–1.45)**
HRRm status†,§	HRRm	**0.47 (0.26–0.86)**
	Non-HRRm	**0.58 (0.43–0.78)**
	Unknown‖	**0.74 (0.37–1.45)**

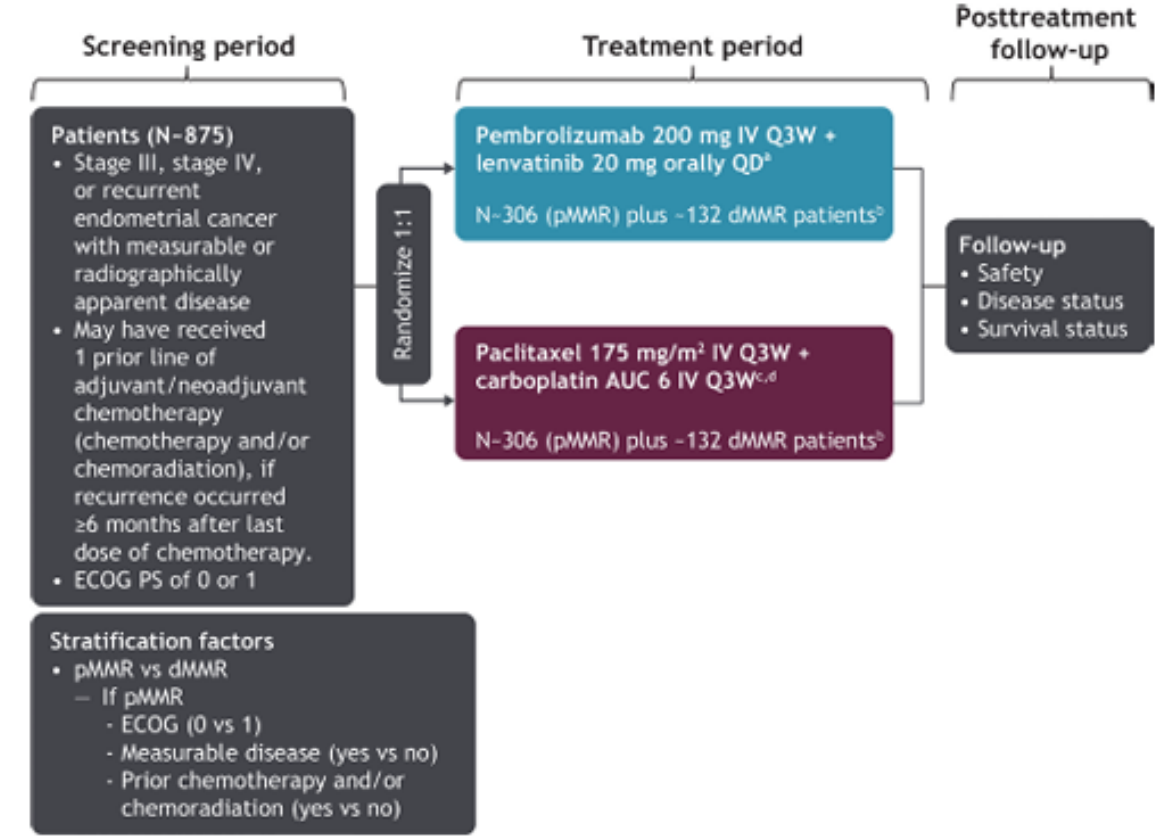


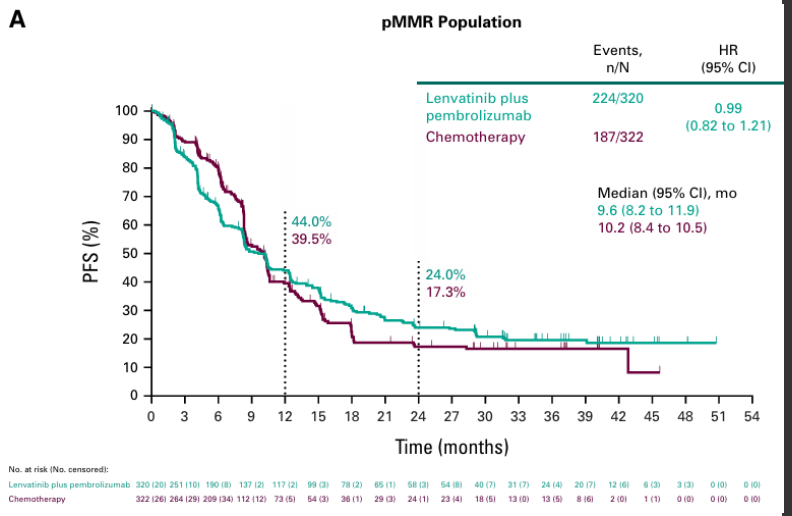
DIFERENCIAS EN LOS CRITERIOS DE INCLUSIÓN

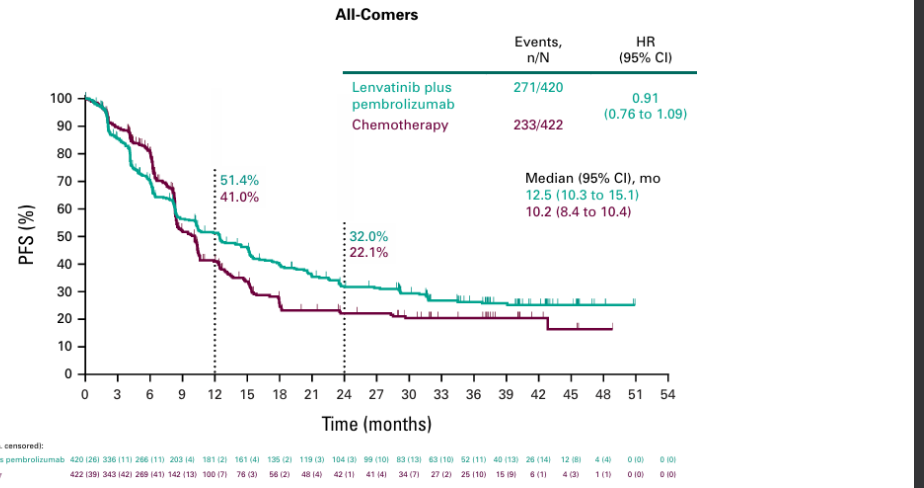
	GY018	RUBY	DUO-E
Carcinosarcoma	no	si	si
Tiempo desde QT ady/neoady	> 12m	> 6m	> 12 m
Duración mantenimiento	2 años	3 años	Hasta PD o toxicidad inaceptable

LEAP 001

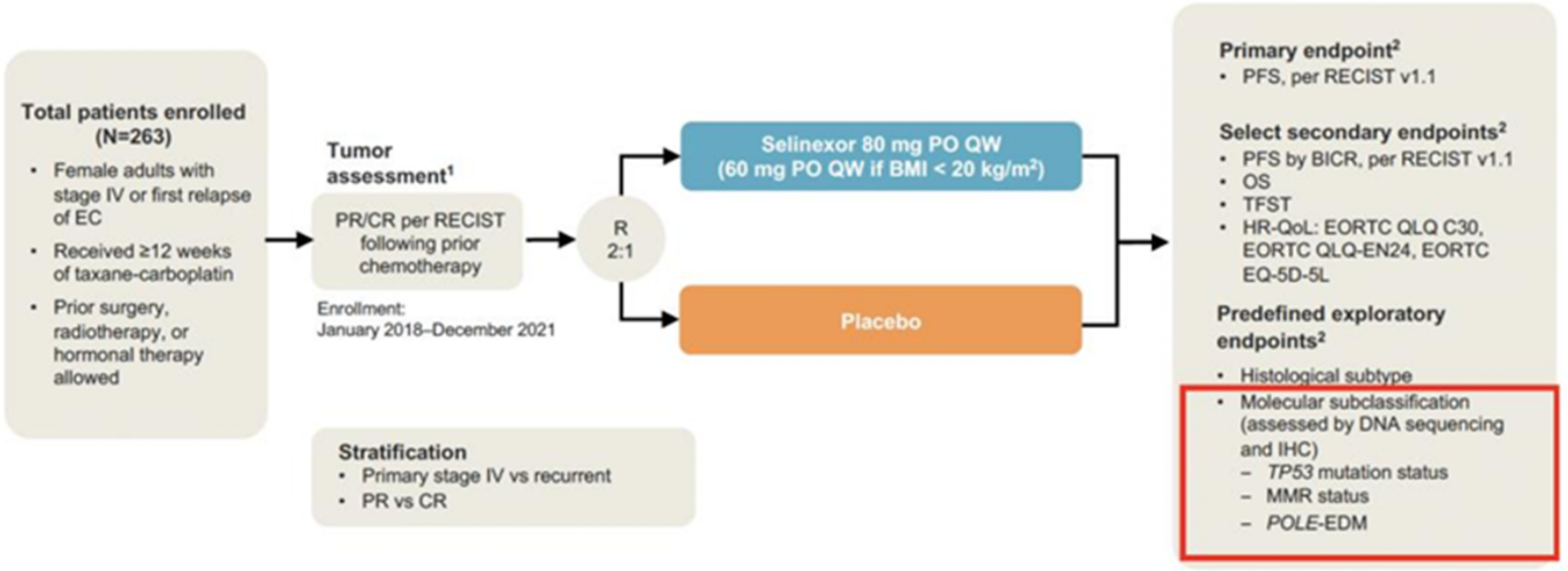
ENSAYO NEGATIVO







ENGOT-EN5/GOG-3055/SIENDO (NCT03555422): A Randomized Double-Blind, Phase 3 Trial of Maintenance With Selinexor/Placebo After Combination Chemotherapy for Patients With Advanced or Recurrent Endometrial Cancer[1,2]



BICR, blinded independent central review; CR, complete response; EDM, exonuclease domain mutation; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, Quality of Life Questionnaire EuroQol-5 Dimensions-5 Levels; HR-QoL, health-related quality of life; MMR, mismatch repair; OS, overall survival; PD, progressive disease; PO, by mouth; POLE, polymerase epsilon; PR, partial response; PRO, patient-reported outcome; QLQ, quality of life questionnaire; QW, once weekly; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; TFST, time to first subsequent therapy

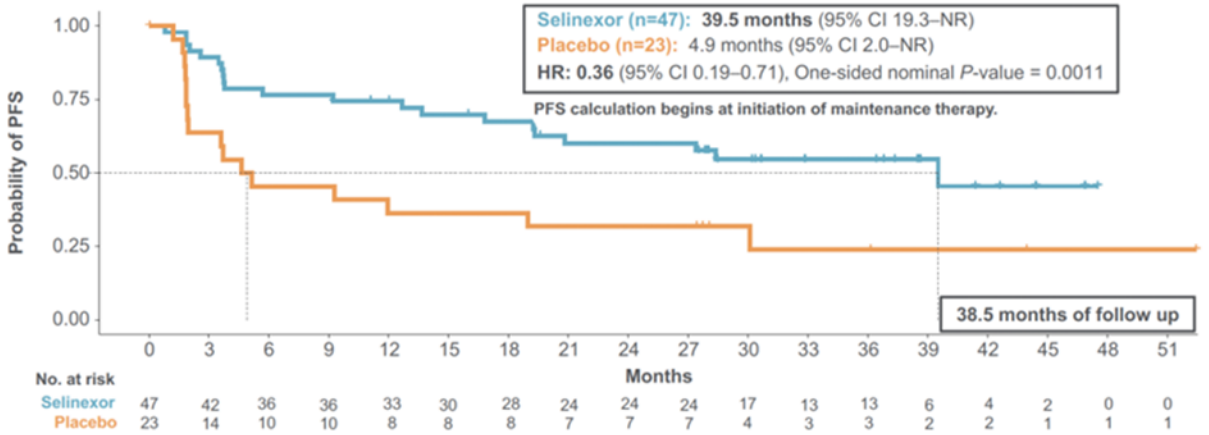
1. ClinicalTrials.gov. NCT03555422. https://www.clinicaltrials.gov/study/NCT03555422?term=NCT03555422. Accessed April 1 2024. **2.** Vergote I, *et al.* Presentation at: European Society for Medical Oncology Virtual Plenary; March 17-18, 2022; Abstract VP2-2022.
Primary study results previously published in Vergote I, et *al J Clin Oncol.* 2023;41(35):5400-5410.

ENGOT GOG FOUNDATION

Long-term mPFS of 28.4 Months in *TP53*wt Subgroup

Data cutoff date: April 1, 2024
HR, hazard ratio; NR, not reached.
*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53* mutant, n=29).

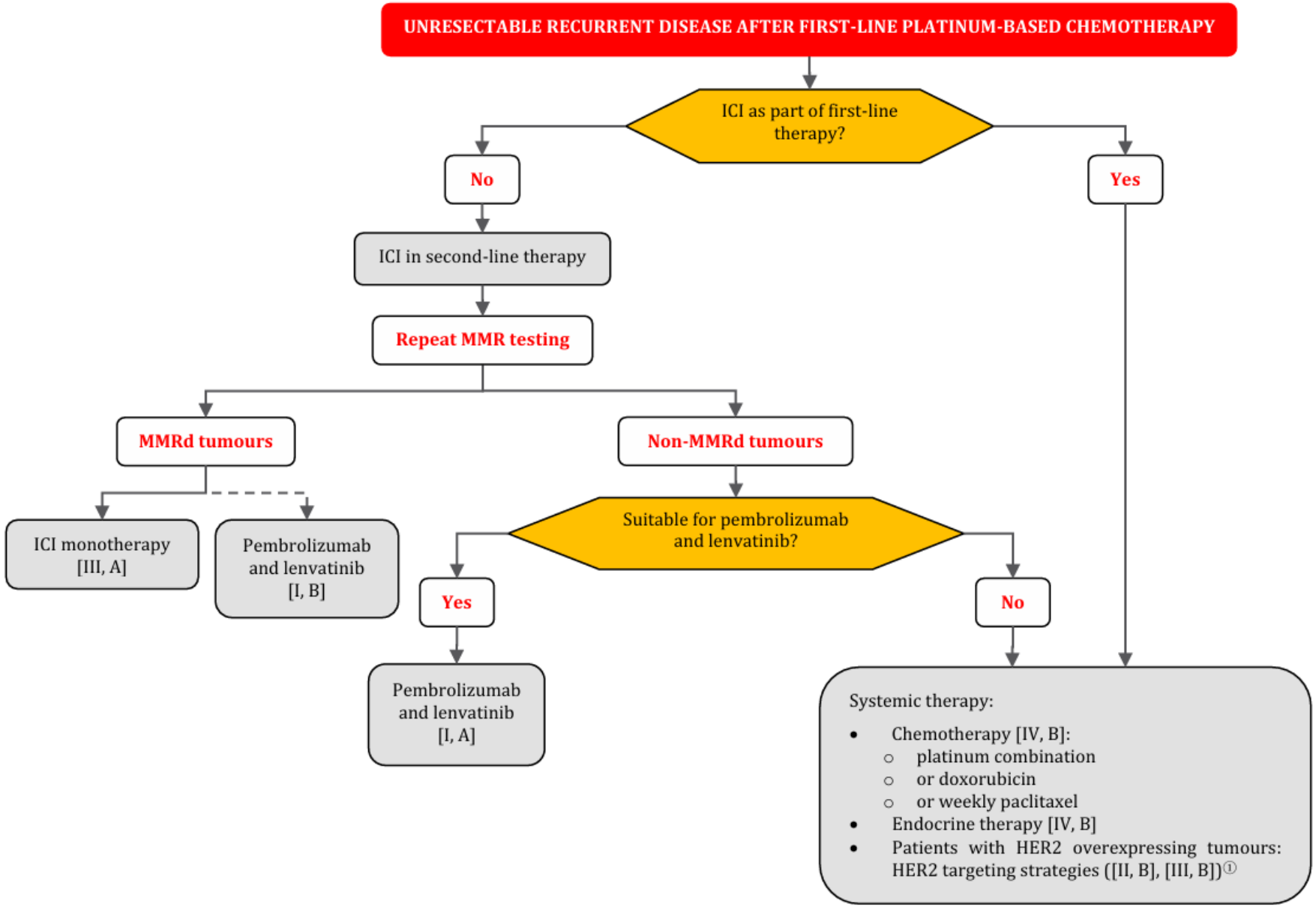
Long-term mPFS of 39.5 Months in *TP53*wt/pMMR* Subgroup



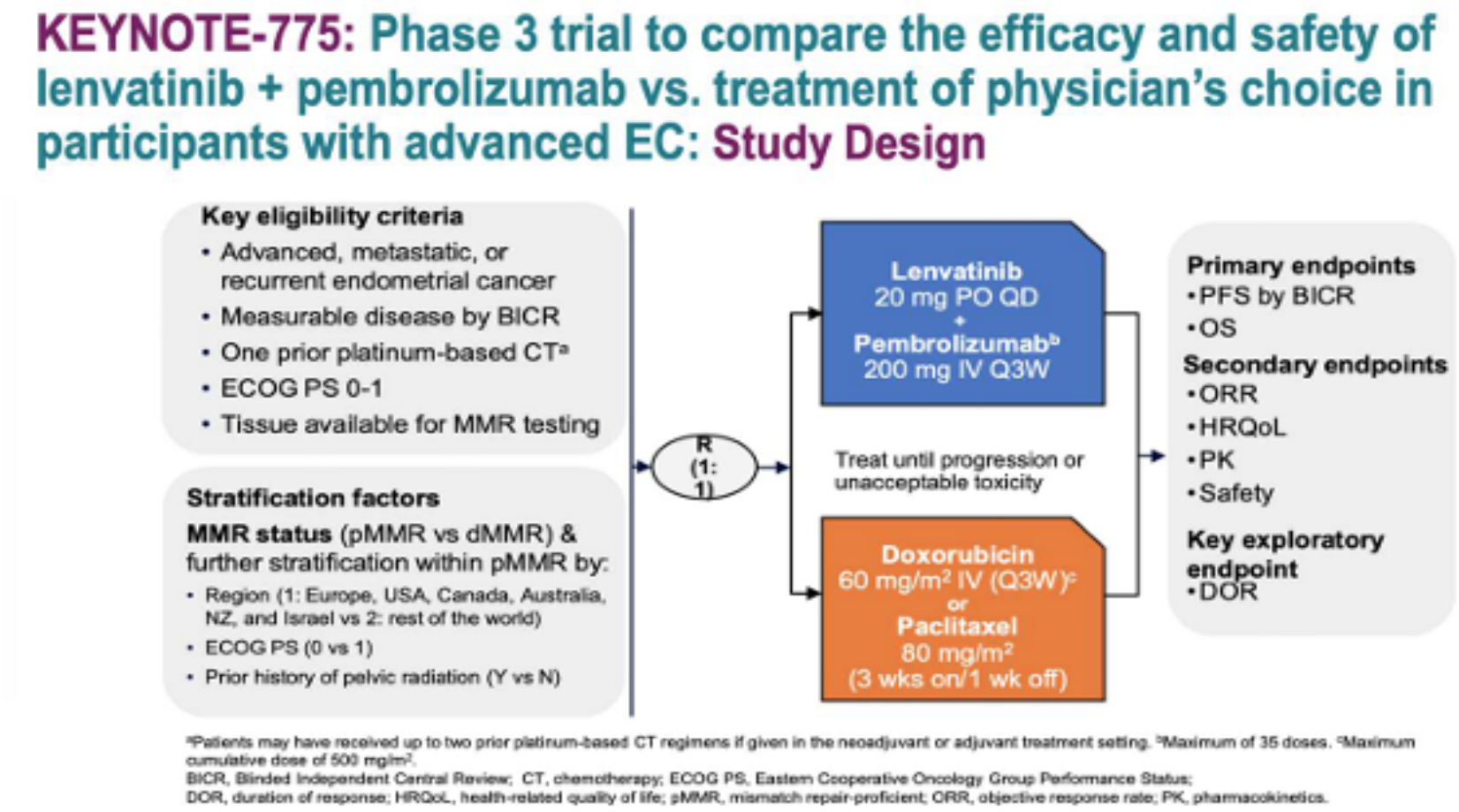
Data cutoff date: April 1, 2024
*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97; pMMR, n=164) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53*wt mutant, n=29; pMMR, n=20).

- **IMPORTANCIA del subtipo molecular** a la hora de elegir tratamiento, sabemos que no todo pMMR es igual, tienen diferente comportamiento, pronóstico así como respuesta a los tratamientos.

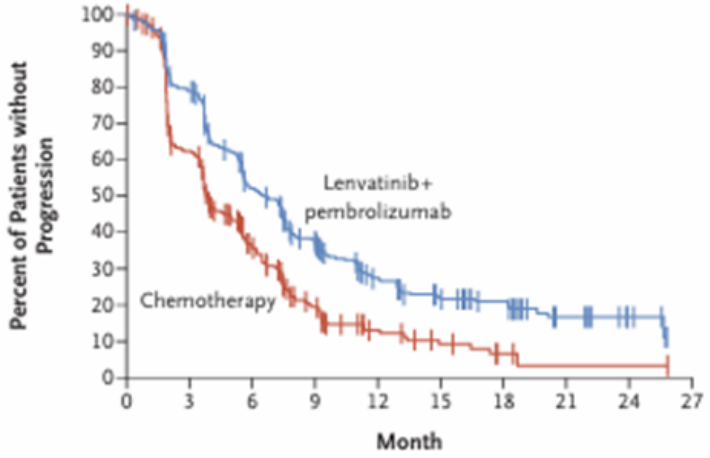
- Pero en RESUMEN: el nuevo SOC en Cancer de Endometrio avanzado o metastásico en 1º línea es la combinación de quimioterapia basada en platino junto con Inmunoterapia (salvo excepciones)


UNRESECTABLE RECURRENT DISEASE AFTER FIRST-LINE PLATINUM-BASED CHEMOTHERAPY
ICI as part of first-line therapy?
No
Yes
ICI in second-line therapy
Repeat MMR testing
MMRd tumours
Non-MMRd tumours
ICI monotherapy [III, A]
Pembrolizumab and lenvatinib [I, B]
Suitable for pembrolizumab and lenvatinib?
Yes
No
Pembrolizumab and lenvatinib [I, A]
Systemic therapy:
Chemotherapy [IV, B]:
platinum combination
or doxorubicin
or weekly paclitaxel
Endocrine therapy [IV, B]
Patients with HER2 overexpressing tumours: HER2 targeting strategies ([II, B], [III, B])①

KEYNOTE 775


KEYNOTE-775: Phase 3 trial to compare the efficacy and safety of lenvatinib + pembrolizumab vs. treatment of physician's choice in participants with advanced EC: Study Design
Key eligibility criteria
• Advanced, metastatic, or recurrent endometrial cancer
• Measurable disease by BICR
• One prior platinum-based CT[a]
• ECOG PS 0-1
• Tissue available for MMR testing
Stratification factors
MMR status (pMMR vs dMMR) & further stratification within pMMR by:
• Region (1: Europe, USA, Canada, Australia, NZ, and Israel vs 2: rest of the world)
• ECOG PS (0 vs 1)
• Prior history of pelvic radiation (Y vs N)
R (1:1)
Lenvatinib 20 mg PO QD + Pembrolizumab[b] 200 mg IV Q3W
Treat until progression or unacceptable toxicity
Doxorubicin 60 mg/m² IV (Q3W)[c] or Paclitaxel 80 mg/m² (3 wks on/1 wk off)
Primary endpoints
•PFS by BICR
•OS
Secondary endpoints
•ORR
•HRQoL
•PK
•Safety
Key exploratory endpoint
•DOR
[a]Patients may have received up to two prior platinum-based CT regimens if given in the neoadjuvant or adjuvant treatment setting. [b]Maximum of 35 doses. [c]Maximum cumulative dose of 500 mg/m².
BICR, Blinded Independent Central Review; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; DOR, duration of response; HRQoL, health-related quality of life; pMMR, mismatch repair-proficient; ORR, objective response rate; PK, pharmacokinetics.

A pMMR Population

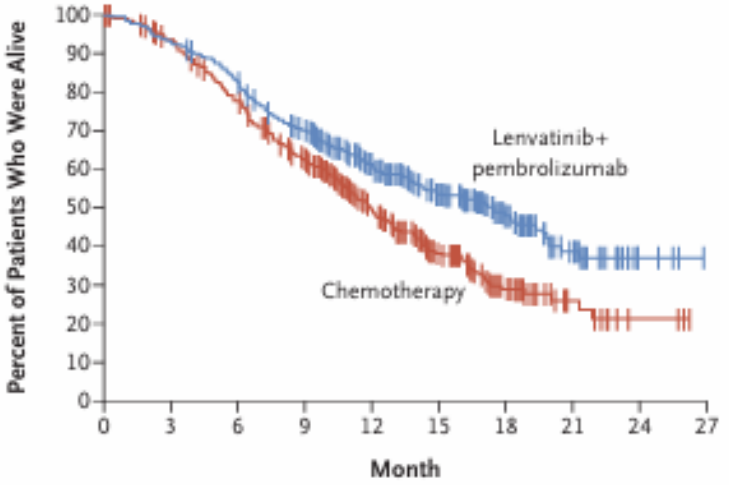


	Median Progression-free Survival (95% CI)
	mo
Lenvatinib+ Pembrolizumab	6.6 (5.6–7.4)
Chemotherapy	3.8 (3.6–5.0)

Hazard ratio for progression or death, 0.60 (95% CI, 0.50–0.72)
P<0.001

No. at Risk										
Lenvatinib+pembrolizumab	346	264	165	112	60	39	30	12	5	0
Chemotherapy	351	177	83	37	15	8	3	1	1	0

A pMMR Population

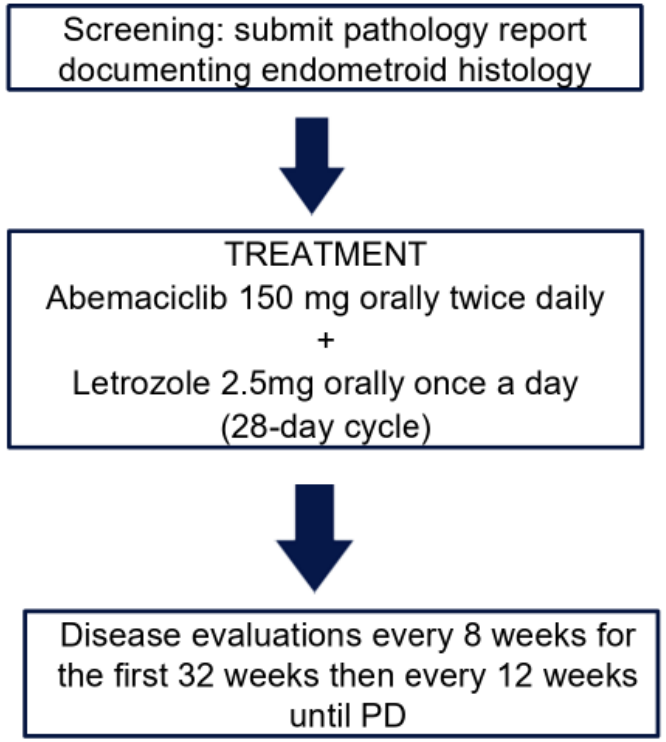


	Median Overall Survival (95% CI)
	mo
Lenvatinib+ Pembrolizumab	17.4 (14.2–19.9)
Chemotherapy	12.0 (10.8–13.3)

Hazard ratio for death, 0.68 (95% CI, 0.56–0.84)
P<0.001

No. at Risk										
Lenvatinib+pembrolizumab	346	322	285	232	160	109	62	28	5	0
Chemotherapy	351	319	262	201	120	70	33	11	3	0

Phase II Study of Abemaciclib Plus Letrozole in Advanced or Recurrent Endometrioid Endometrial Carcinoma: A GOG Partners Trial (GOG 3039)



KEY ELIGIBILITY

- Advanced (FIGO 2014 III or IV) or recurrent endometrial cancer not likely to be cured by surgery or radiotherapy
- ECOG performance status of 0-1
- Must have endometrioid histology, any grade
- Must have measurable disease by RECIST v1.1
- Allows for prior chemo in adjuvant setting for Stage I-III; chemo for Stage IV disease permitted if patient without evidence disease and 6-month PFS since completion of chemo before recurrence detected

Primary Endpoint: PFS at 6 months

Secondary endpoint: Objective response rate (ORR)
PFS & Overall survival (OS),Toxicity

Phase II Study of Abemaciclib Plus Letrozole in Advanced or Recurrent Endometrioid Endometrial Carcinoma: A GOG Partners Trial (GOG 3039)

Baseline Patient Characteristics

		N	(%)
Race	Asian	1	(2%)
	Black or African American	3	(5.9%)
	White	44	(86.3%)
	Other	3	(5.9%)
Ethnicity	Hispanic	6	(11.8%)
	Non-Hispanic	45	(88.2%)
Performance Status	0	30	(58.8%)
	1	21	(41.2%)
Grade	1-2	46	(90.2%)
	3	5	(9.8%)
Stage (FIGO 2014)	I	30	(58.8%)
	II-III	17	(33.3%)
	IV	4	(7.8%)
Prior Chemotherapy	Chemotherapy +/- Radiation therapy	30	(58.8%)
	No prior chemotherapy	21	(41.2%)
Prior Lines of Therapy	0*	19	(37.3%)
	1-2	32	(62.7%)

6-month PFS rate 56.9%

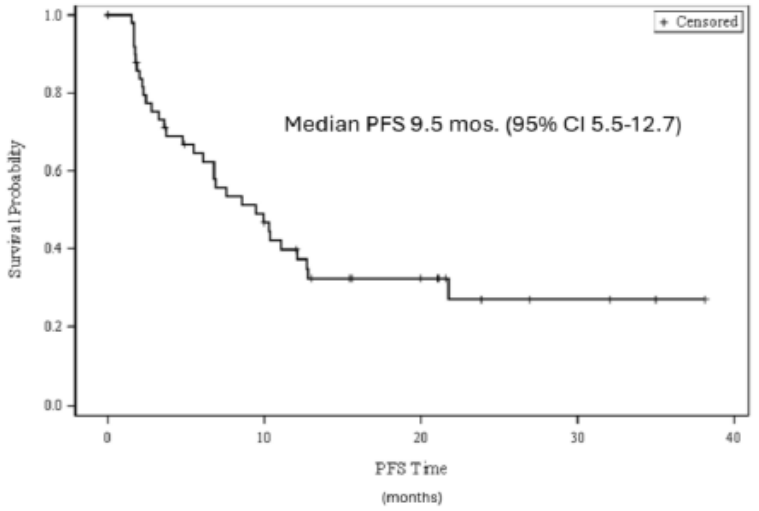
Prior chemotherapy

6-month PFS 46.7%
Stage 1= 29.4% / Stage 2= 69.2%

Chemotherapy-naive

6-month PFS 71.4%
Stage 1= 70.0% / Stage 2= 72.7%

Overall Progression Free Survival



A randomized phase II trial of everolimus and letrozole or hormonal therapy in women with advanced, persistent or recurrent endometrial carcinoma

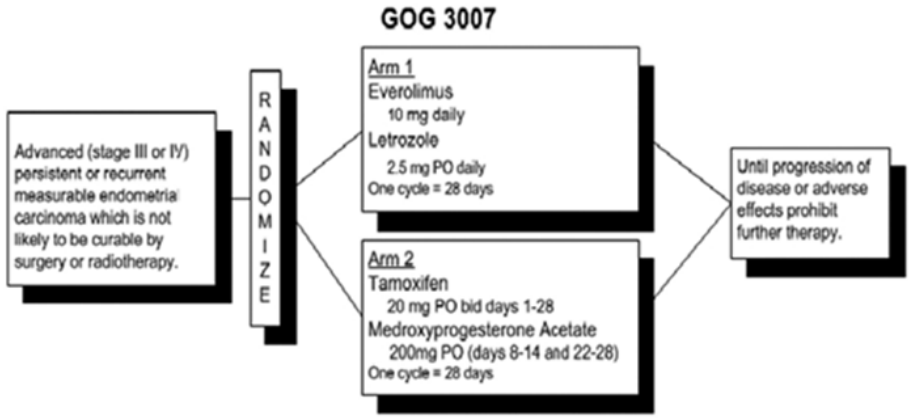


Fig. 1. Schema.

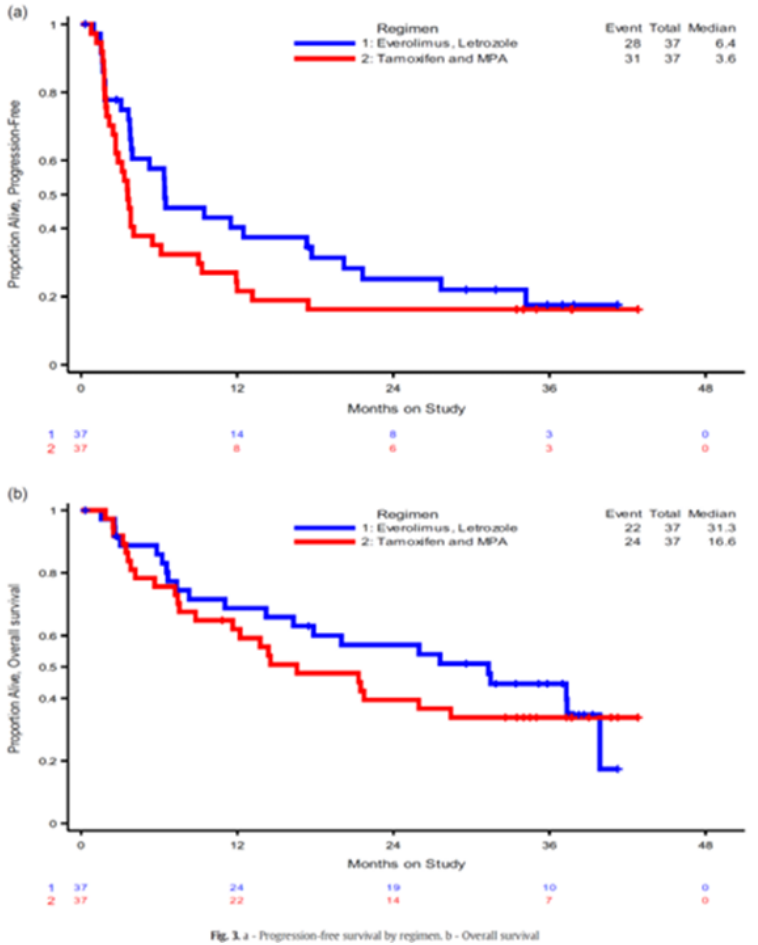


Fig. 3. a - Progression-free survival by regimen. b - Overall survival

ENGOT model A, sponsor NSGO-CTU, NCT02730429

- Measurable/evaluable endometrial cancer
- Primary stage 4 or relapsed disease
- ≥1 prior systemic therapy
- ER+ (≥10%) endometrioid adenocarcinoma
- ECOG PS 0/1
- No prior endocrine therapy except MPA and megestrol acetate
- No prior CDK inhibitor

Stratification:
- No. of prior lines (primary advanced disease vs 1st relapse vs ≥2 relapses)
- Measurable vs evaluable disease per RECIST
- Prior use of MPA/megestrol acetate

1:1 randomisation

Placebo 125 mg days 1–21
Letrozole 2.5 mg days 1–28

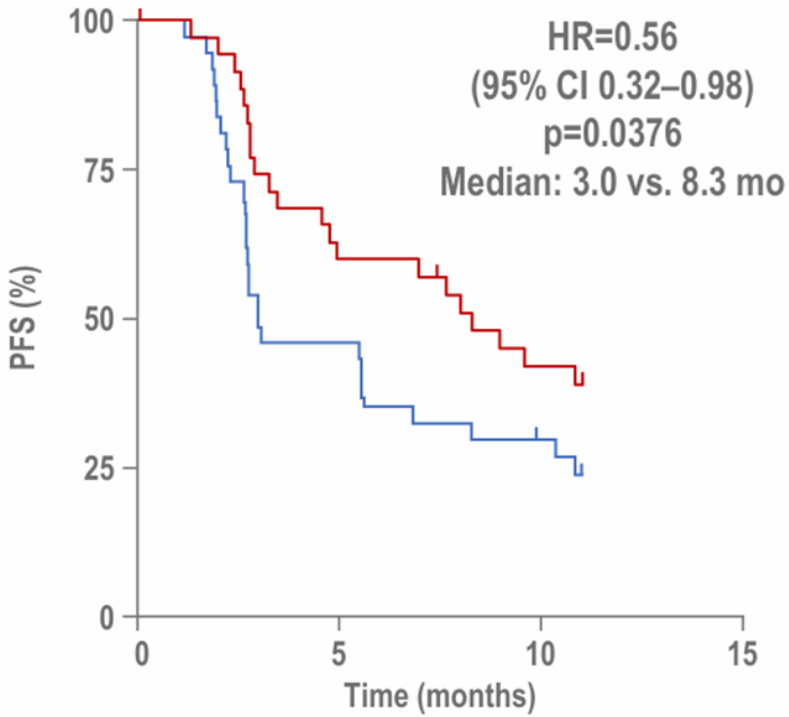
Repeated every 28 days until progression

Palbociclib 125 mg days 1–21
Letrozole 2.5 mg days 1–28

Primary endpoint: Investigator-assessed PFS (target HR 0.625, 80% power, 15% 1-sided α)
Secondary endpoints:
- PFS in subgroups
- Objective response rate, disease control rate, PFS2, overall survival
- PROs
- Safety and tolerability

HR = hazard ratio; MPA = medroxyprogesterone acetate; PROs = patient-reported outcomes

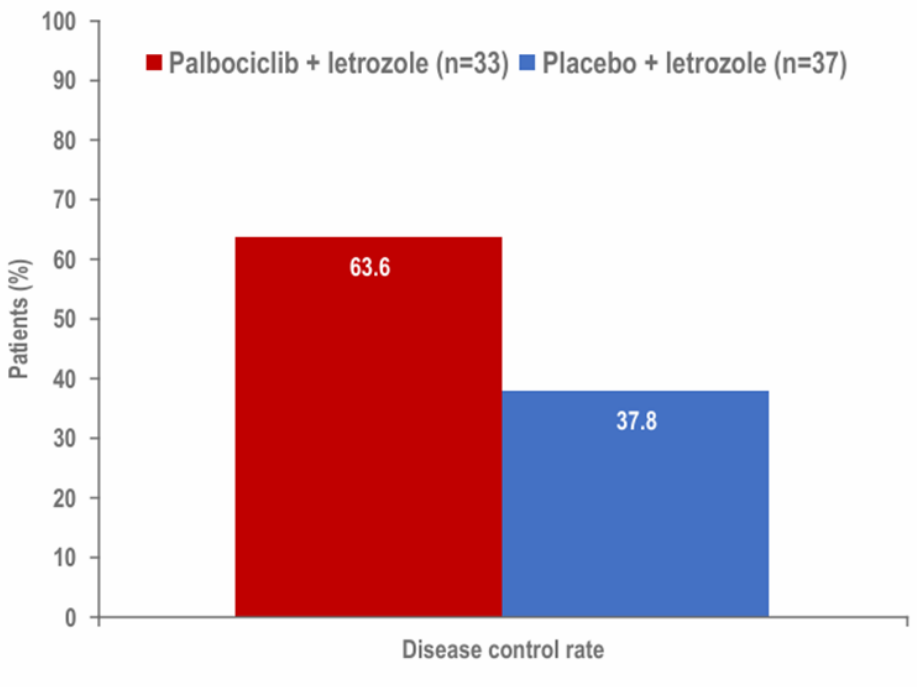
Primary endpoint: PFS



Number at risk

Palbociclib + letrozole	36	21	14
Placebo + letrozole	37	17	10

Secondary endpoint: Disease control rate*



CI = confidence interval; HR = hazard ratio

* = at 24 weeks


BACK
TO THE FUTURE
JCPenney

ADC

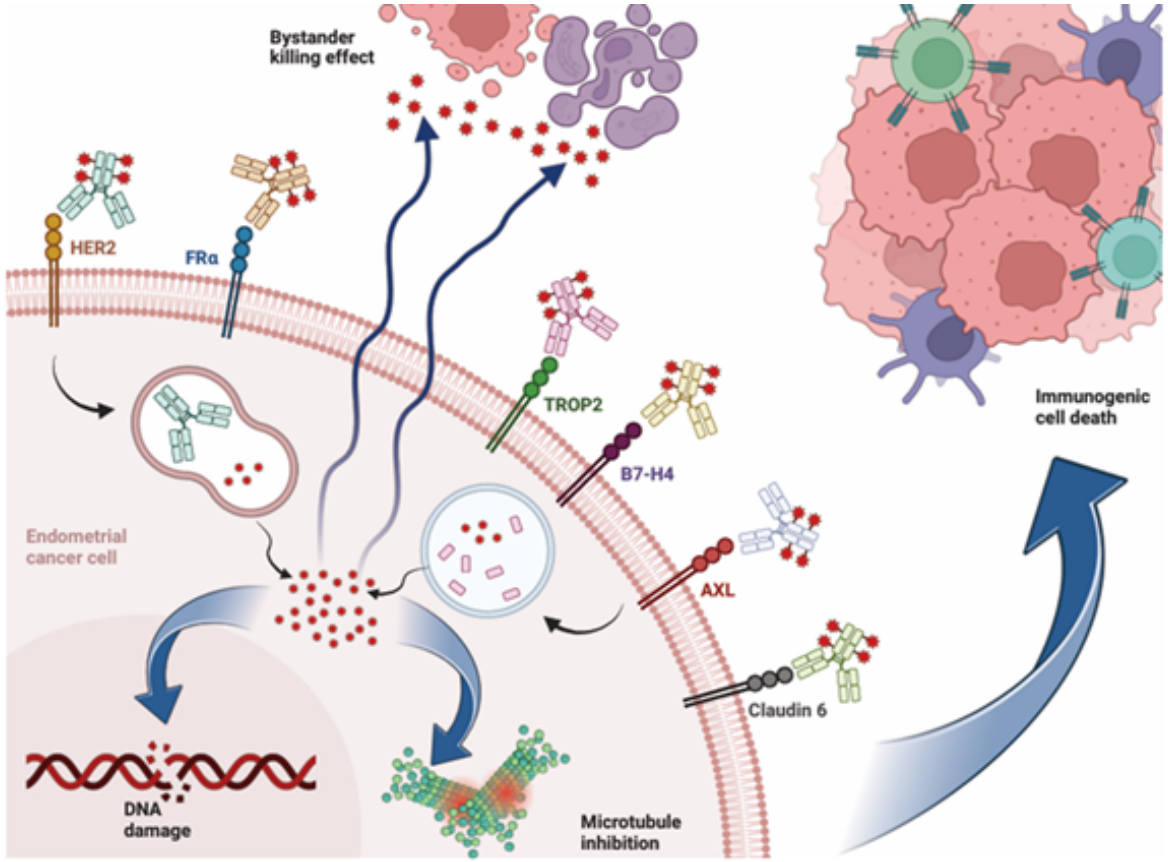


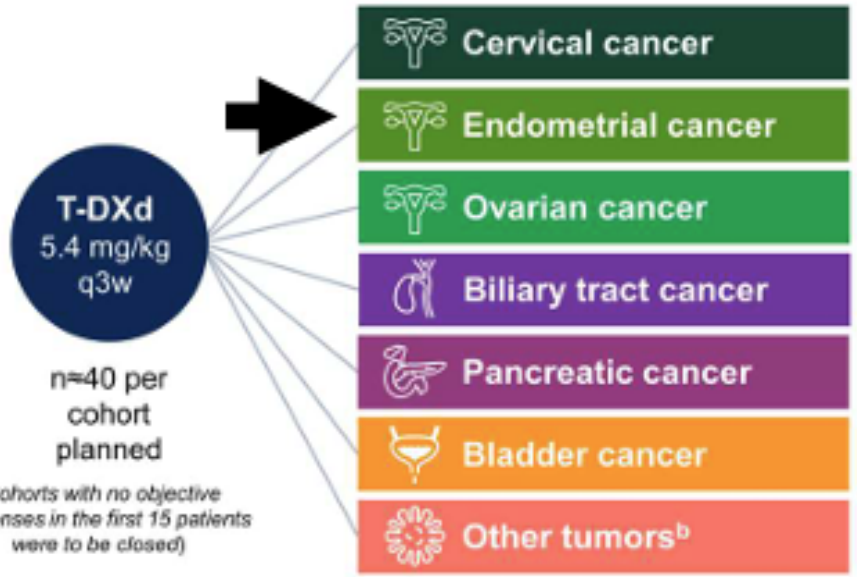
Figure 1 Mechanism of action of antibody-drug conjugates and promising targets in endometrial cancer. FRα, folate receptor alpha; HER2, human epidermal growth factor receptor 2; TROP2, trophoblast cell-surface antigen-2.

Target	Drug	Payload	Mechanism of Action	Linker	DAR
TROP2	Sacituzumab Tirumotecn (MK-2870)	Proprietary belotecan derivative	Inhibition of topoisomerase I	sulfonyl pyrimidine-CL2A-carbonate	7.4
	Sacituzumab Govitecan (IMMU-132)	SN-38 (irinotecan metabolite)	Inhibition of topoisomerase I	Acid cleavable	7.5
	Datopotomab Deruxtecan (Dato-Dxd)	Deruxtecan	Inhibition of topoisomerase I	Cleavable tetrapeptide-based linker	~4
B7H4	AZD8205	MMAE (monomethyl auristatin E)	Inhibition of topoisomerase I	Val-ala peptide linker with a PEG8 spacer	8
	GSK 5733584 / HS-20089	Exatecan derivative	Inhibition of topoisomerase I	Protease Cleavable	6
	SGN-B7H4V	MMAE	Multimodal	Protease-cleavable mc-vc linker	4
	XMT-1660	AF-HPA/AF	Inhibition of tubulin polymerization	Polymer scaffold (cleavable)	6
HER2	Trastuzumab Deruxtecan (DS-8201a)	Deruxtecan	Inhibition of topoisomerase I	Peptide-based (enzime cleavable)	8
	Trastuzumab Duocarmazine (SYD985)	Duocarmycin	DNA alkylation	Mb-Val-Cit-PABC	2.7
	DB-1303/BNT323	P1003	Inhibition of topoisomerase I	cleavable maleimide tetrapeptide-based	8
FRα	Mirvetuximab Soravtansine (IMGN853)	DM4	Inhibition of tubulin polymerization	Cleavable	3.5
	Luveltamab Tazevibulin (STRO-002)	SC239 (Hemiasterlin)	Inhibition of tubulin polymerization	Valine-citruline (cleavable)	4
	Farletuzumab Ecteribulin (MORAb-202)	Eribulin mesylate	Inhibition of microtubules	Valine-citruline (cleavable)	4
	Rinatabart sesutecan (Rina-S)	Exatecan	Inhibition of topoisomerase I	cleavable hydrophilic	8
	LY4170156	Exatecan	Inhibition of topoisomerase I	*cleavable polysarcosine (PSAR*	8

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



Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

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

Data cut-off for analysis:

- Nov 16, 2022

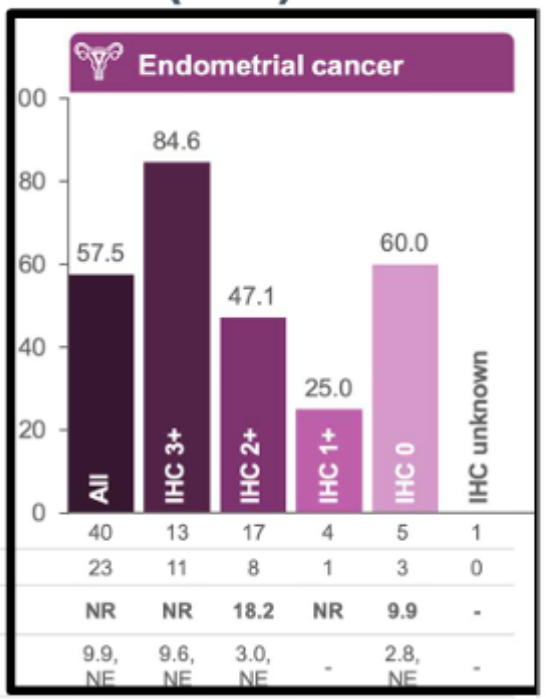
- 77% enrollment by local assessment
- Central conformation: IHC 1+ or 0= 20% (N=55)

ORR and DOR (INV)*

Eficacia en cánceres ginecológicos HER-2 IHC 3+ e IHC 2+

Endometrial Cancer

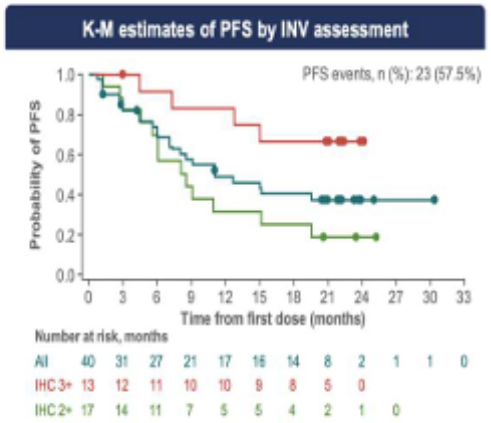
- Asian 25%
- Prior 2L 45%
- Prior ≥3L 32,5%
- Prior Her-2 tto 22,5%



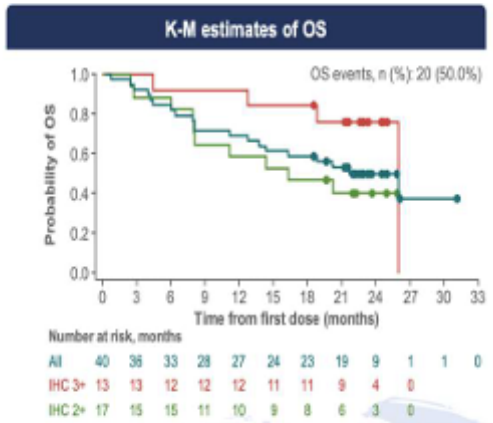
	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	IHC unknown
Total n in subgroup	40	13	17	4	5	1
n of responders	23	11	8	1	3	0
Median DOR, months†	NR	NR	18.2	NR	9.9	-
95% CI‡	9.9, NE	9.6, NE	3.0, NE	-	2.8, NE	-

HER2 status by central testing
*Similar ORR and DOR results were reported by retrospective independent central review; †median DOR repo
CI, confidence interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, im

Endometrial cancer: PFS and OS by HER2 status



	n	Median PFS, months (95% CI) INV	ICR
All	40	11.1 (7.1, NE)	14.1 (7.3, NE)
IHC 3+	13	NR (7.3, NE)	NR (7.3, NE)
IHC 2+	17	8.5 (4.6, 15.1)	11.0 (4.6, 20.3)
IHC 1+	4	1.2 (0.8, NE)	1.2 (0.8, NE)
IHC 0	5	9.1 (2.6, NE)	11.1 (2.6, NE)
IHC unknown	1	NR (-)	NR (-)



	n	Median OS, months (95% CI)
All	40	26.0 (12.8, NE)
IHC 3+	13	26.0 (18.9, NE)
IHC 2+	17	16.4 (8.0, NE)
IHC 1+	4	5.2 (0.8, NE)
IHC 0	5	NR (4.2, NE)
IHC unknown	1	21.7 (-)

Circle indicates a censored observation. CI, confidence interval; HER2, human epidermal growth factor receptor 2; ICR, independent central review; IHC, immunohistochemistry; INV, investigator; K-M, Kaplan-Meier; NE, not evaluable; NR, not reached; OS, overall survival; PFS, progression-free survival

- Larga duración de respuesta en respondedores.

These data suggest that T-DXd is a potential treatment for patients with these gynecologic HER2-expressing tumors who have disease progression on prior therapy

Check for updates

Efficacy and Safety of Sacituzumab Govitecan in Patients With Advanced Solid Tumors (TROPiCS-03): Analysis in Patients With Advanced Endometrial Cancer

TABLE 1. Baseline Demographics and Clinical Characteristics

Characteristic	SG (N = 41)
Age at study entry, years, median (range)	68 (44-83)
Race, No. (%)	
White	21 (51)
Black or African-American	1 (2)
Asian	8 (20)
Other	5 (12)
Not reported	6 (15)
ECOG performance status, No. (%)	
0	18 (44)
1	23 (56)
Microsatellite instability high, No. (%)	
Yes[a]	8 (20)
No	32 (78)
Not available	1 (2)
Histologic/cytologic diagnosis, No. (%)	
Serous	17 (42)
Endometrioid	20 (49)
Others	4 (10)
No. of previous anticancer regimen, No. (%)	
1	3 (7)
2	13 (32)
3	16 (39)
>3	9 (22)
Previous anticancer regimens, median (range)	3 (1-6)
Previous anticancer therapy type, No. (%)	
Chemotherapy	41 (100)
Hormonal therapy	5 (12)
Immunotherapy	35 (85)
Targeted agents	26 (63)
Other	1 (2)
Chemotherapy + IO,[b] No. (%)	35 (85)
Trop-2 expression	
Median H-score (range)	115 (0-245)

Variable	All Patients (N = 41)
ORR (confirmed CR + PR), No. (%)	9 (22)
95% CI	11 to 38
Best overall response, No. (%)	
Confirmed CR	0
Confirmed PR	9 (22)
SD	18 (44)
PD	8 (20)
NE	2 (5)
Not assessed[a]	4 (10)
Clinical benefit rate (confirmed CR + PR + SD ≥6 months), No. (%)	13 (32)
95% CI	18-48
Time to response, months[b,c]	
Median (range)	2.8 (1.4-5.8)
DOR, months[b,d]	
Median (95% CI)	8.8 (2.8 to NE)

Alessandro D. Santin et al ;J Clin Oncol 42:3421-3429,2024

Study of Sacituzumab Govitecan Versus Treatment of Physician's Choice in Participants With Endometrial Cancer After Platinum-Based Chemotherapy and Immunotherapy (ASCENT-GYN-01/GOG-3104/ENGOT-en26)

Key Eligibility Criteria

- Recurrent, advanced or metastatic endometrial carcinoma
- Histologically confirmed diagnosis of epithelial endometrial carcinoma, including carcinosarcoma
- Prior treatment with platinum-based chemotherapy and anti-PD-(L)1 therapy
  - These agents may have been received separately/ sequentially or in combination and in any setting
  - For pts who are ineligible for anti-PD-(L)1 therapy due to comorbidities, or if anti-PD-(L)1 agents are not available as standard of care in any line of treatment according to local standards, prior treatment with an anti-PD-(L)1 agent is not required
- Up to 3 prior lines of systemic therapy, with no more than 2 prior lines in the recurrent or advanced setting
  - Hormonal or hormonal-based therapies do not count as a line of therapy
- ECOG PS 0-1

N=520

R 1:1

Arm A: Sacituzumab Govitecan (SG)
10 mg/kg IV
Days 1 and 8, every 21 days

Arm B: Treatment of Physician's Choice (TPC)
Doxorubicin 60 mg/m² IV on Day 1, every 21 days, or
Paclitaxel 80 mg/m² IV on Days 1, 8, and 15, every 28 days

Stratification Factors

- # of Prior lines of systemic therapy in any setting (≤ 2 vs 3)
- Prior Anti-PD-(L)1 therapy (yes vs no)
- Histology (endometrioid vs non-endometrioid)

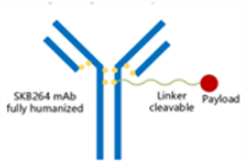
Key Study Endpoints

Primary Endpoint:
- PFS by BICR

Key Secondary Endpoints:
- OS
- ORR by BICR
- Change from baseline and TTdD in Physical Function as assessed by EORTC-QLQ-C30

Secondary Endpoints:
- PFS by INV
- ORR by INV
- DOR, CBR by BICR and INV
- Safety
- Change from baseline in GHS/QoL as assessed by EORTC-QLQ-C30

Safety and Efiicacy of Sacituzumab Tirumotecan (sac-TMT) in Patients with Previously Treated Advanced Endometrial and Ovarian Cancer from a Phase 2 Study



Cohort 8: Advanced EC (N=44)

Key inclusion criteria

- Received at least 1 prior line of platinum-based therapy
- Prior anti-PD-1/L1 therapy required for MSI-H/dMMR patients
- ECOG PS 0 or 1

sac-TMT (SKB264/MK-2870)

5 mg/kg, Q2W

→ Until disease progression, unacceptable toxicity or withdrawal of consent →

Primary endpoints

- ORR (RECIST v1.1 by investigator)

Secondary endpoints

- PFS, DoR, OS
- Safety

Tumor assessment:

- Once every 8 weeks for the first 12 months, and every 12 weeks thereafter.

Danbo Wang, MD, PhD et al. Presented at ESMO 2024

Baseline Characteristics in Endometrial Cancer cohort

Category	EC (N = 44)
Median age (range), years	58 (40, 73)
ECOG PS, % (n)	
0	31.8 (14)
1	68.2 (30)
Tumor histology, % (n)	
Endometrioid	54.5 (24)
Non-endometroid	31.8 (14)
Carcinosarcoma	6.8 (3)
Unknown/Not tested	6.8 (3)
MMR/MSI status, % (n)	
dMMR/MSI-H	2.3 (1)
pMMR/MSS or MSI-L	70.5 (31)
Unknown/Not tested	27.3 (12)
TROP2 IHC H-score,[a] % (n)	
>200	27.3 (12)
≤200	63.6 (28)
Prior lines of systemic therapy, % (n)	
1	47.7 (21)
≥2	52.3 (23)
Prior IO therapy, % (n)	
Yes	36.4 (16)
No	63.6 (28)

EC cohort: 44 patients enrolled and followed for ≥17 weeks.
22 (50.0%) remained on sac-TMT as of data cutoff date.
Median follow-up was 7.2 months

	EC (N = 44)[a]
ORR, % (n/N)	**34.1 (15/44)[b]**
Confirmed ORR	27.3 (12/44)
Subgroups	
TROP2 H-score >200	41.7 (5/12)
Prior IO	37.5 (6/16)
DCR, % (n/N)	**75.0 (33/44)**
PR	34.1 (15/44)
SD	40.9 (18/44)
DoR	
Median (range), months	5.7 (3.8, 7.4+)
PFS	
Median (95% CI), months	5.7 (3.7, 9.4)

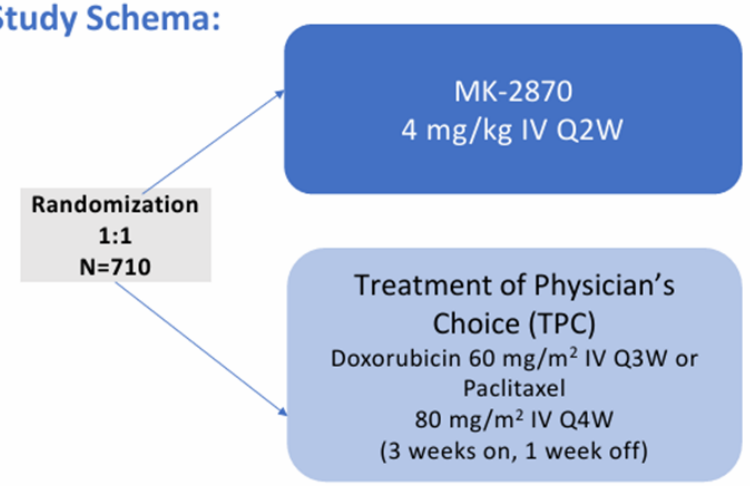
MK-2870-005/ENGOT-en23/GOG-3095/TroFuse-005

A Phase 3, Randomized, Active-controlled, Open-label, Multicenter Study to Compare the Efficacy and Safety of MK-2870 Monotherapy Versus Treatment of Physician's Choice in Participants With Endometrial Cancer Who Have Received Prior Platinum-Based Chemotherapy and Immunotherapy"

Key Eligibility Criteria:

- ✓ Histologically-confirmed endometrial cancer
- ✓ Radiologically apparent measurable or non-measurable disease
- ✓ Prior platinum exposure AND prior anti-PD-1/PD-L1 exposure (given separately or in combination), in any setting

Study Schema:



Dual Primary Endpoints

- PFS* (BICR)
- OS

Secondary Endpoints

- ORR
- DOR
- QoL
- Safety/Tolerability

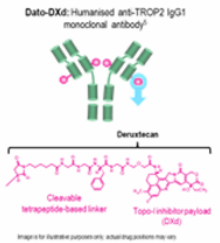
Stratification:

- ❖ MMR (deficient MMR or proficient MMR)
- ❖ TROP2 expression (high or low/negative), per immunohistochemistry (IHC)
- ❖ Prior lines of therapy (≤ 2 or 3)
- ❖ Disease status at baseline per RECIST 1.1 as assessed by BICR (measurable vs non-measurable)

***Futility Analysis for PFS is planned to ensure a minimal threshold of efficacy is being met early in the conduct of the study**

NCT06132958

Datopotamab deruxtecan (Dato-DXd) in patients with Ovarian or Endometrial Cancer: Results from the Phase 2 TROPION-PanTumor03 Study: Study Design



A Phase 2, open-label, global study (NCT05489211) evaluating Dato-DXd as monotherapy and in combination with various anticancer agents across several tumour types

Here, we present results of Dato-DXd monotherapy in the endometrial cancer cohorts

Endometrial cancer (TROP2 expression unselected)

- Advanced/metastatic endometrial carcinoma
- All histologies (except sarcoma)
- ECOG PS 0 or 1
- Progressed on ≥1 line of platinum chemotherapy but no more than 2 lines of therapy for advanced or metastatic disease

N=35

Dato-DXd† 6 mg/kg IV Q3W

N=40

Endpoints

Primary

- ORR by investigator per RECIST v1.1
- Safety & tolerability

Secondary

- PFS, DoR, DCR by investigator
- PK and immunogenicity

Exploratory

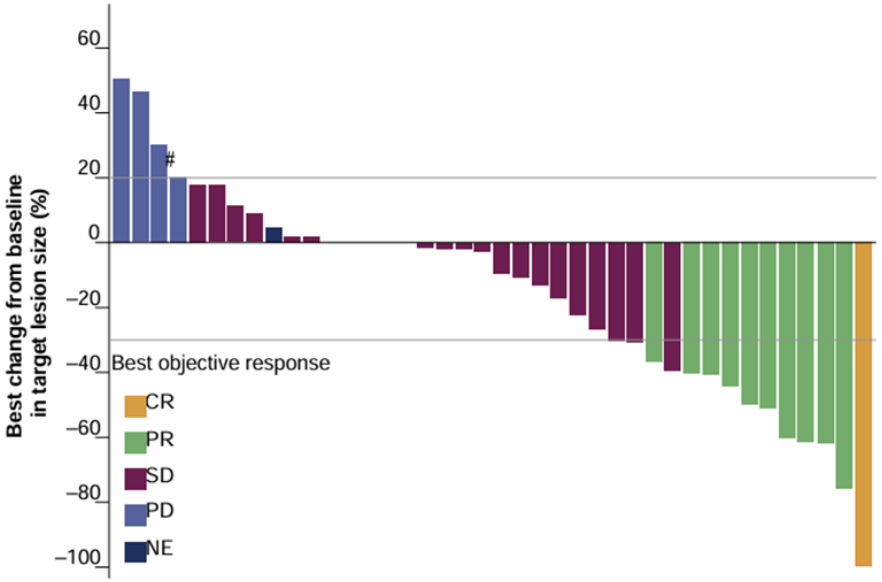
- OS
- Biomarker analyses

Oaknin A. et al. Presented at ESMO 2024

- As of June 14, 2024, median duration of follow-up* was 13.6 months (range 2.1–19.6) in the endometrial cohort

	Endometrial (N=40)
Confirmed ORR, % (95% CI)	27.5 (14.6–43.9)
Best overall response, n (%)	
CR	1 (2.5)
PR	10 (25.0)
SD†	23 (57.5)
PD‡	5 (12.5)
NE§	1 (2.5)
Median time to response, months (range)	2.8 (1.4–4.2)
Median DoR, months (95% CI)	16.4 (7.1–NC)
DCR at 12 weeks,‖ % (80% CI)	57.5 (46.1–68.3)
Median PFS, months (95% CI)	6.3 (2.8–NC)

Waterfall plot: best change from baseline in target lesion size¶

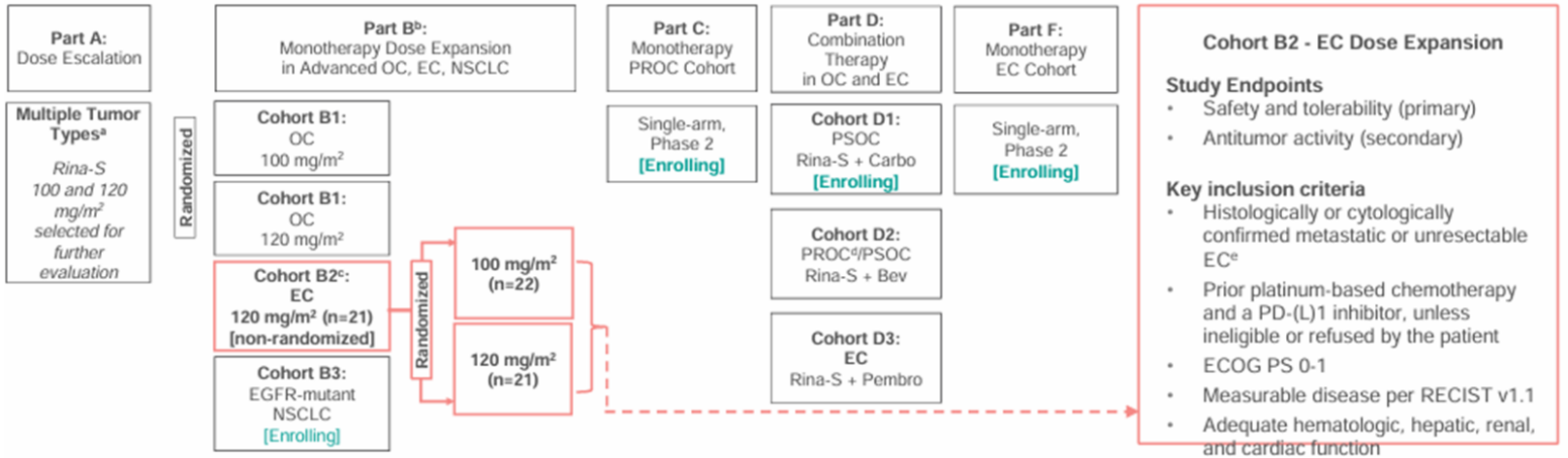


Oaknin A. et al. Presented at ESMO 2024

RAINFOL™-01 study (GCT1184-01)

Objective: To evaluate efficacy and safety of Rina-S in patients with advanced or recurrent endometrial cancer (a/r EC) from dose-expansion cohort B2 of the phase 1/2 RAINFOL™-01 study (NCT05579366)

RAINFOL-01: Rina-S Phase 1/2 Study (NCT05579366)



Ira Winer et al. Presented at ASCO 2025

	Rina-S 100 mg/m² (n=22)	Rina-S 120 mg/m² (n=34)[f]
Median on-study follow-up[b], months (95% CI)	7.7 (7.2-8.4)	9.8 (7.9-11.8)
Confirmed ORR[e], % (95% CI)	50.0 (28.2-71.8)	47.1 (29.8-64.9)
Confirmed response, n (%)		
CR	2 (9.1)	0
PR	9 (40.9)	16 (47.1)
SD	11 (50.0)	13 (38.2)
NE	0	1 (2.9)
DCR, % (95% CI)	100 (84.6-100.0)	85.3 (68.9-95.0)

BLUESTAR[1] first-in-human study : Safety and Preliminary Efficacy of P-Sam in patients with a/r Endometrial Cancer:

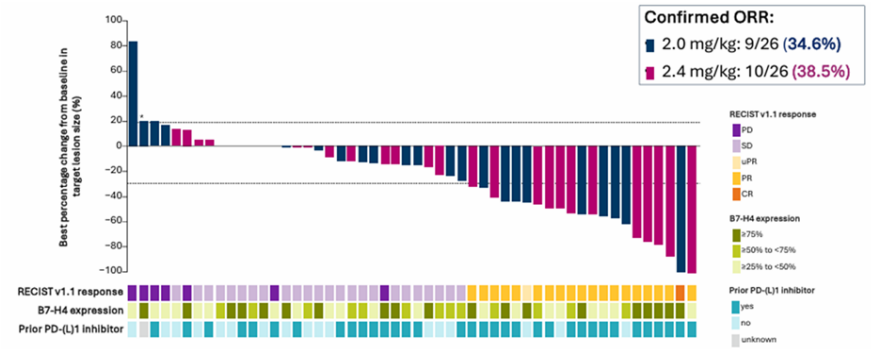
Key inclusion criteria:

- Patients aged ≥18 years
- ECOG PS 0 or 1
- Advanced or metastatic EC
- **B7-H4–positive tumor as measured by IHC**
- Measurable disease per RECIST v1.1
- Progressed after available SOC therapy
- No prior treatment with TOP1i

	P-Sam	
	2.0 mg/kg n=30	2.4 mg/kg n=35
Median age (range), years	62.0 (52–78)	65.0 (47–81)
Race, n (%)		
White	17 (56.7)	24 (68.6)
Asian	10 (33.3)	8 (22.9)
Other*	3 (10.0)	3 (8.6)
ECOG PS 0 / 1, n (%)	15 (50.0) / 15 (50.0)	20 (57.1) / 15 (42.9)
Median number of prior treatment regimens (range)	1.0 (1–2)	1.5 (1–5)
Prior platinum, n (%)	29 (96.7)	32 (91.4)
Prior PD-(L)1 inhibitor, n (%)	19 (63.3)	22 (62.9)
Histology type, n (%)		
Endometrioid	7 (23.3)	12 (34.3)
Serous	7 (23.3)	5 (14.3)
Carcinosarcoma	5 (16.7)	4 (11.4)
Clear cell	2 (6.7)	0
Other†	9 (30.0)	14 (40.0)
% tumor cells expressing B7-H4, median	67.5	55.0

Stéphanie Gaillard et al. Presented at SGO 2025

[1]clinicaltrials.gov/study/NCT05123482.



BEHOLD-1:

A 2-part, open-label, global, Phase 1 study with randomized dose optimization

Eligibility criteria

- Aged ≥18 years
- Histologically confirmed advanced solid tumor
- ECOG PS 0–2
- ≥1 measurable target lesion (RECIST v1.1)
- No prior B7-H4 therapy

Phase 1B only:

- PROC*: 1–3 prior LOT
- EC†: 1–3 prior LOT
- No prior TOPi

Phase 1A: Dose Escalation

Advanced solid tumors

7.2 mg/kg Q3W

5.8 mg/kg Q3W

4.8 mg/kg Q3W

2.8 mg/kg Q3W

Phase 1A: Main findings

- N=44 patients; DCO July 1, 2025
- MTD was not reached
- MAD was determined as 5.8 mg/kg Q3W

Scan QR code for more Phase 1A data

Phase 1B: Dose Expansion/Optimization

PROC

R 1:1:1

- 2.8 mg/kg Q3W, (n~30–50)
- 4.8 mg/kg Q3W, (n~30–50)
- 5.8 mg/kg Q3W, (n~30–50)

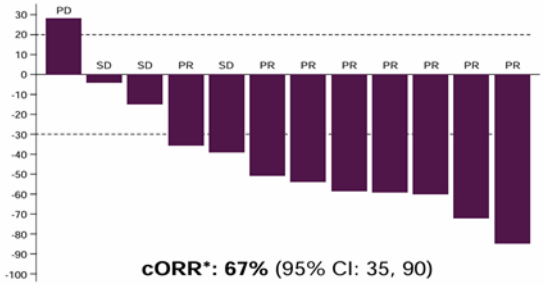
Recurrent/advanced EC

R 1:1

- 2.8 mg/kg Q3W, (n~30–50)
- 4.8 mg/kg Q3W, (n~30–50)

Expansion at recommended dose informed by totality of data

Mo-Rez 4.8 mg/kg (N=12)



cORR*: 67% (95% CI: 35, 90)

CONCLUSIONES

- En p MMR el SOC en 1º línea es la combinación de CBDCA-paclitaxel con ICI ,….PERO el subtipo molecular es MUY IMPORTANTE para la elección del tratamiento de las pacientes (diferente comportamiento, pronóstico y respuesta a los tratamientos).
- En 2º línea:
- * No tratadas previamente con ICI: Lenvatinib-Pembrolizumab.
- * Si ICI previo: EC /QT /ANTIHER2/ ADC
- La terapia hormonal es un tratamiento a tener en cuenta en pacientes con enfermedad de bajo volumen, de lento crecimiento, pacientes con comorbilidad,…etc
- BUSQUEDA NECESARIA de BIOMARCADORES, sobretodo para ayudarnos a estratificar mejor estos tumores y desarrollo de nuevas terapias.

GRACIAS