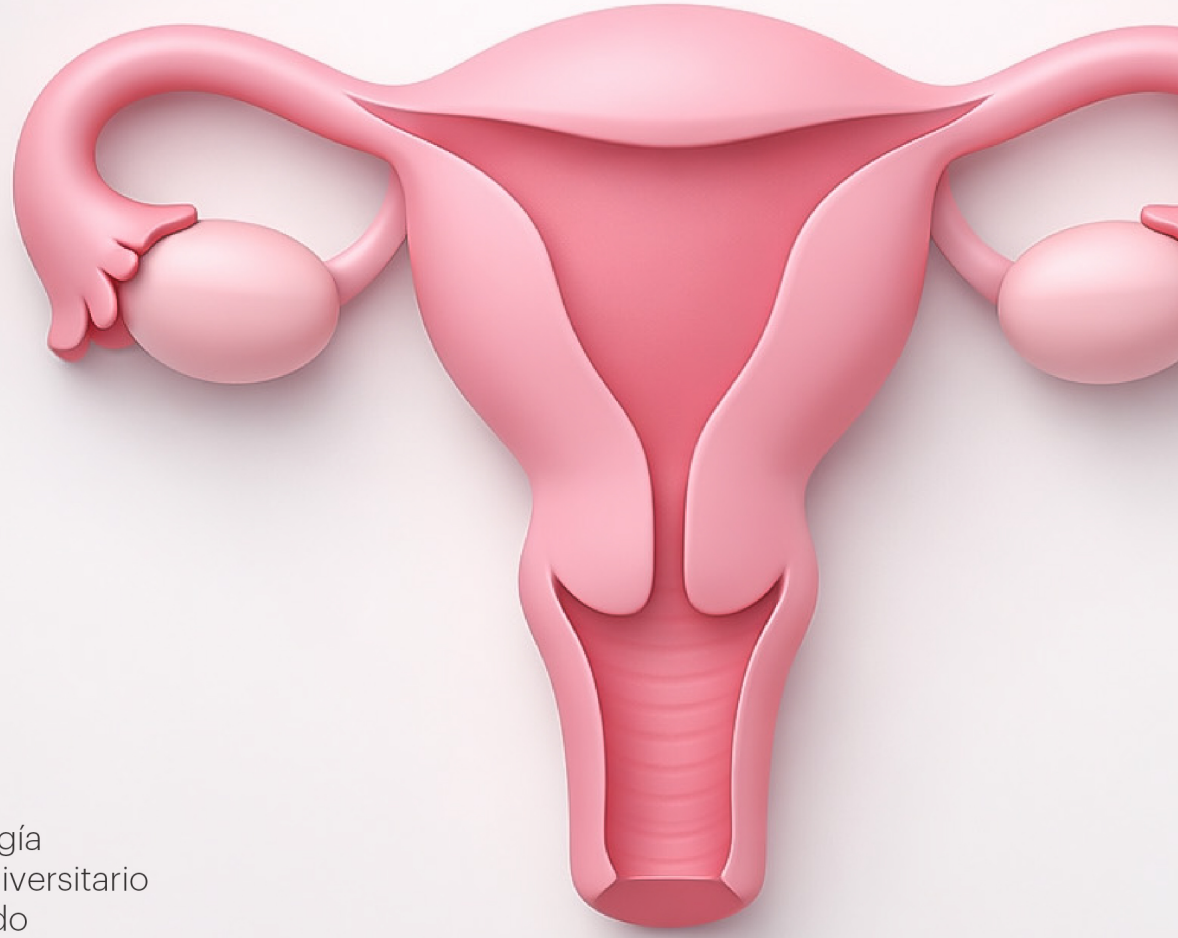
Organizado por
ASONMEC

4ª Jornada de Actualización en Cáncer Ginecológico

Bilbao · 20 – 21 de mayo 2026



Mantenimiento con iPARP: ¿Cuándo y cuál?

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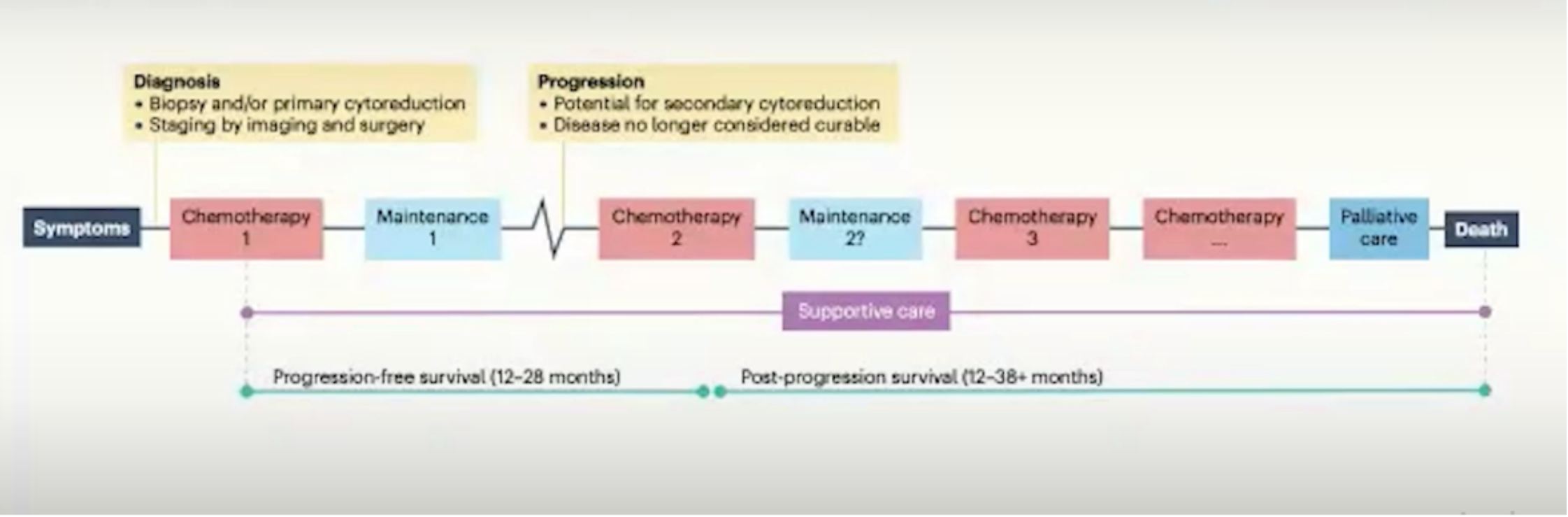
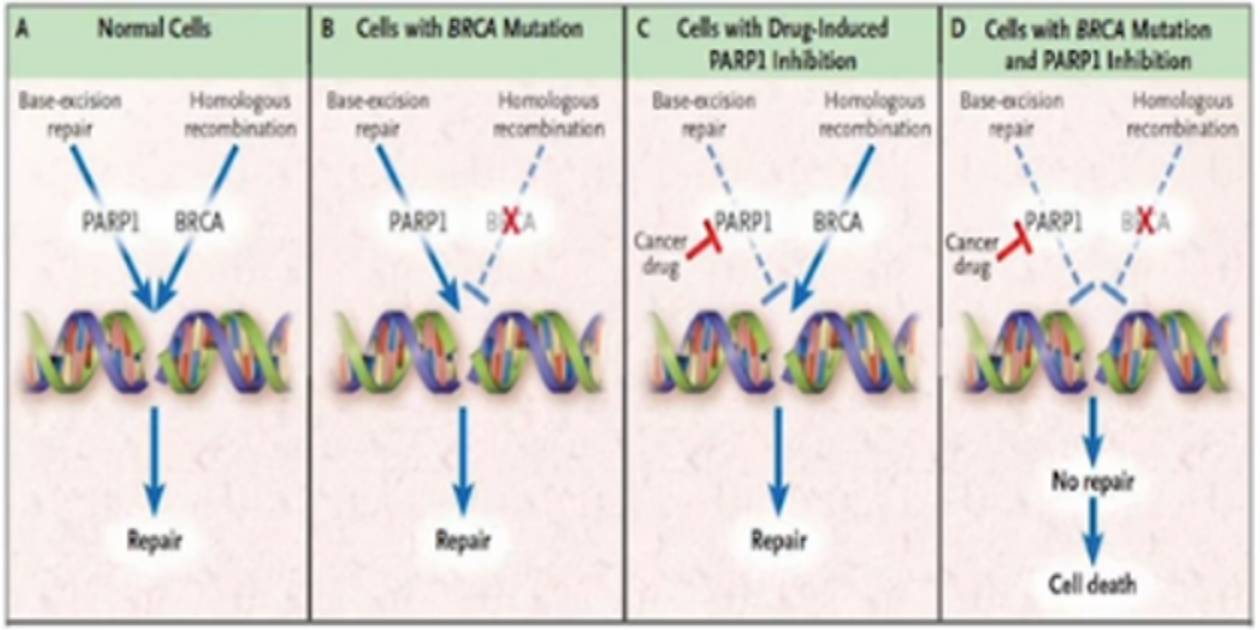
HISTORIA NATURAL DEL CÁNCER DE OVARIO



¿QUÉ SON LOS iPARP?

Letalidad sintética

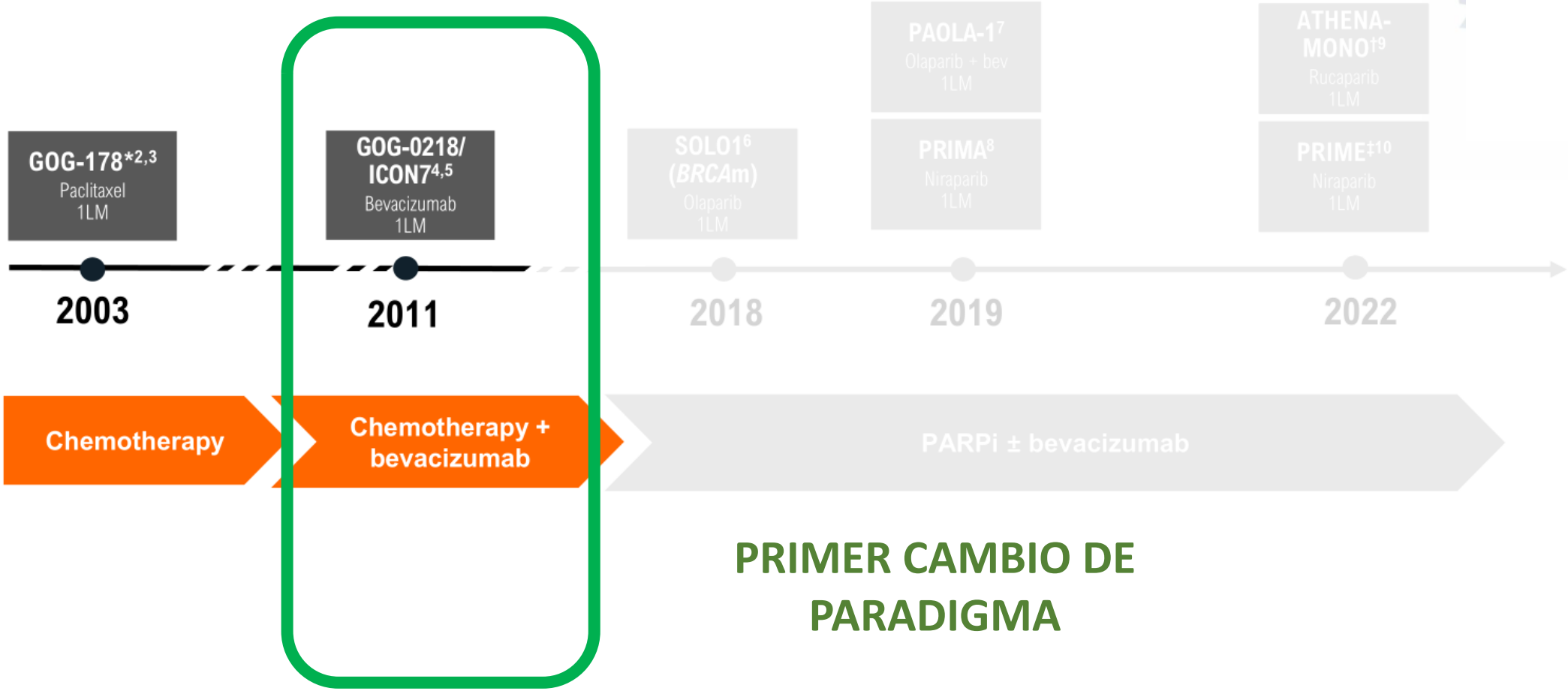


	Catalytic inhibition (IC50 nM)	Cytotoxicity (IC90 µM)	PARP-trapping potency (relative to olaparib set as 1)	Class
Veliparib	30	>50	<0.2	Class 1
Olaparib	6	4.5	1	Class 2
Rucaparib	21	3	1	Class 2
Niraparib	60	2.3	~2	Class 2
Talazoparib	4	0.04	~100	Class 2

Class 1: catalytic inhibition >> PARP trapping
Class 2: PARP trapping + catalytic inhibition:
Talazoparib >> Niraparib, Olaparib >> Veliparib

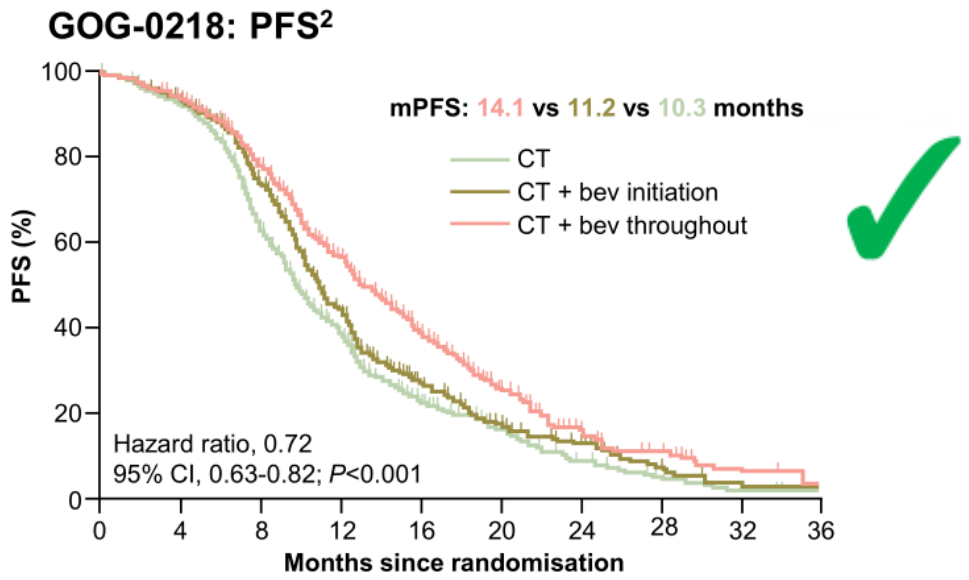
1. Las células tumorales presentan mutaciones en ADN
2. PARP es un complejo familiar enzimático que interviene en mecanismos reparadores de ADN
3. Las proteínas BRCA tienen papel fundamental en RH, reparando daños en el ADN
4. Los iPARP inhiben la actividad catalítica de PARP y "atrapan" a PARP
5. En las células con mutación BRCA, si inhibimos PARP, se crea efecto de letalidad sintética->muerte celular

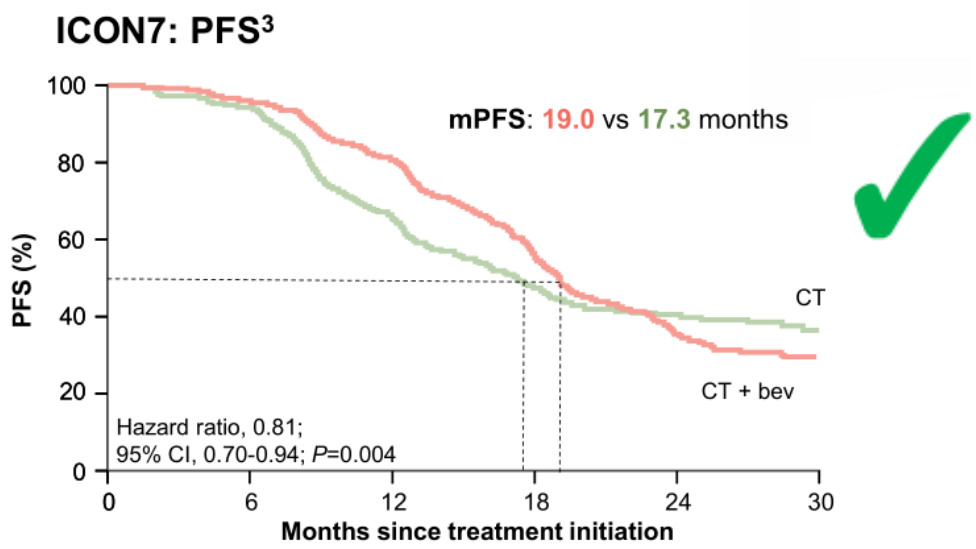
ERA PRE-iPARP



PRIMER CAMBIO DE PARADIGMA

Bevacizumab mantenimiento 1L: GOG 218/ICON7





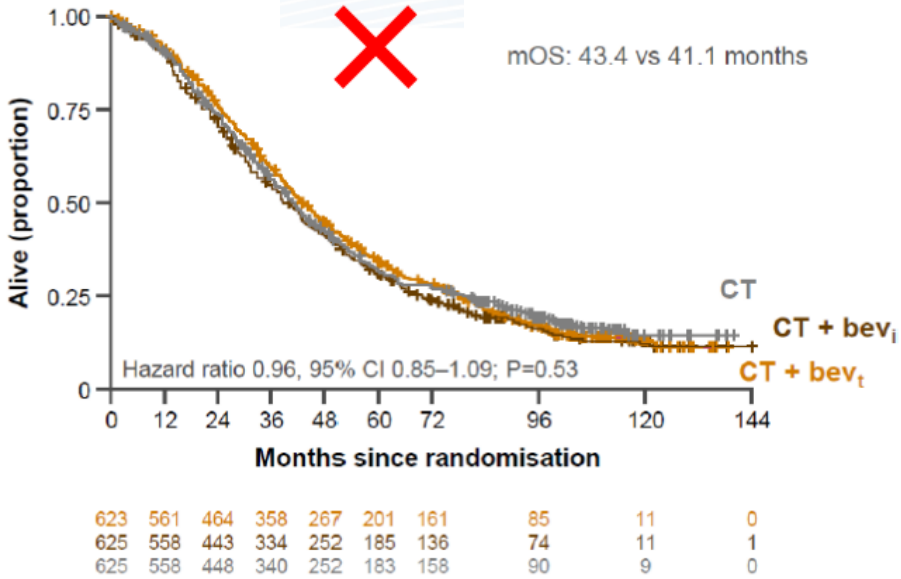
Tiempo medio (meses) de **PFS** con QT+Bv: **19** (ICON7)/**14.1** (GOG 218)

1.Babaier A, Ahmad A, AlHilli M, et al. Among patients with advanced ovarian carcinoma, who benefits from bevacizumab the most? *Ann Transl Med.* 2023;11(10):367. 2.Burger RA, Brady MF, Bookman MA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Engl J Med.* 2011;365(26):2473-83. 3.Perren TJ, Swart AM, Pfisterer J, et al. A phase 3 trial of bevacizumab in ovarian cancer. *N Engl J Med.* 2011;365(26):2484-96. 4. Pfisterer J, Joly F, Kristensen G, et al. Optimal Treatment Duration of Bevacizumab as Front-Line Therapy for Advanced Ovarian Cancer: AGO-OVAR 17 BOOST/GINECO OV118/ENGOT Ov-15 Open-Label Randomized Phase III Trial. *J Clin Oncol.* 2023;41(4):893-902.

Bevacizumab mantenimiento 1L: GOG 218/ICON7

GOG-0218: OS[1]

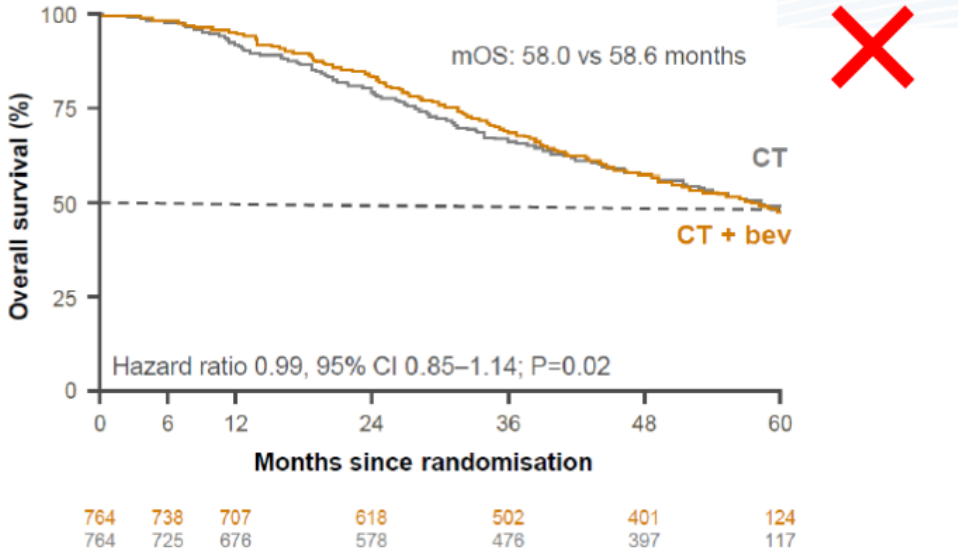
Overall survival – ITT population



Adaptado de Tewari KS. et al. *J Clin Oncol* 2019

ICON-7: OS[2]

Overall survival – ITT population



Adaptado de Oza AM, et al. *Lancet Oncol* 2015

1.Tewari KS, Java JJ, Salani R, et al. Final Overall Survival of a Randomized Trial of Bevacizumab for Primary Treatment of Ovarian Cancer. *J Clin Oncol*. 2019;37(26):2317-28. 2.Oza AM, Cook AD, Pfisterer J, et al. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. *Lancet Oncol*. 2015;16(8):928-36

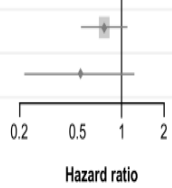
Mantenimiento Bevacizumab: GOG 218/ICON7

Estratificadas por estadio /enf residual
No por status BRCA/HRD

30% pacientes alto riesgo

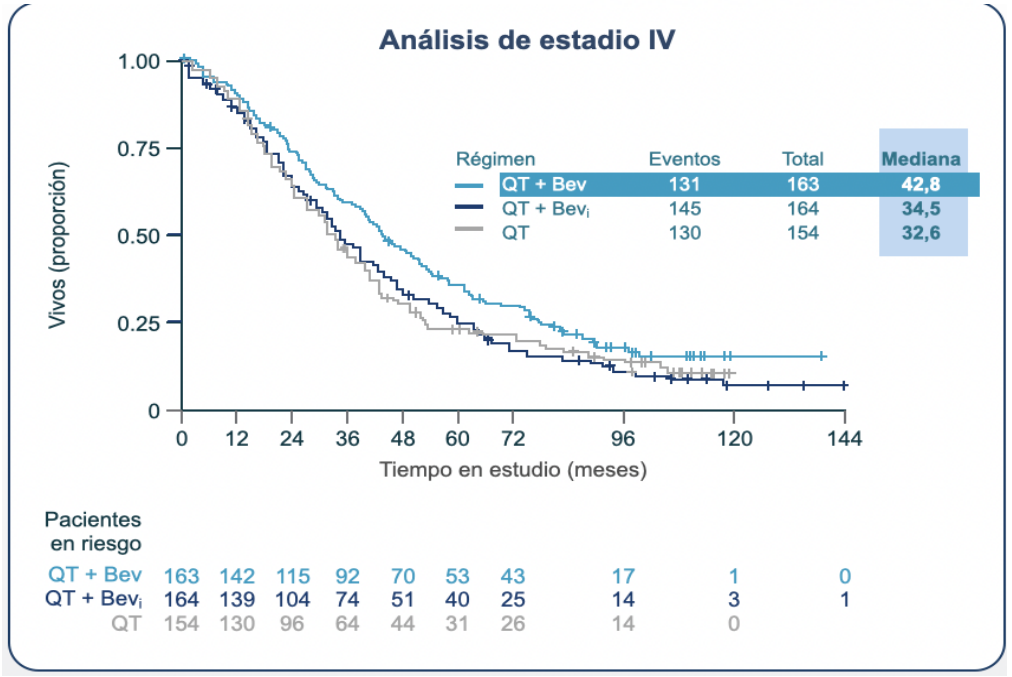
ICON-7 Overall survival

	Events (n)/patients (n)	Hazard ratio (95% CI)	Mean overall survival (months)		
			Bevacizumab	Control group	
All patients	714/1528	0.99 (0.85-1.14)	45.5 (44.2-46.7)	44.6 (43.2-45.9)	
Risk status					Interaction *p*=0.01
Non-high-risk patients	382/1026	1.14 (0.93-1.40)	48.4 (47.0-49.9)	49.7 (48.3-51.1)	
High-risk patients	332/502	0.78 (0.63-0.97)	39.3 (37.0-41.7)	34.5 (32.0-37.0)	
Disease stage					Trend *p*=0.004
Stage I,II, III (0 cm)	197/725	1.23 (0.93-1.62)	51.5 (49.9-53.0)	52.3 (50.8-53.8)	
Stage III (>0, ≤1 cm)	185/301	0.95 (0.71-1.26)	41.9 (39.1-44.7)	42.6 (39.8-45.4)	
Stage III (>1 cm)	194/290	0.84 (0.63-1.11)	40.2 (37.3-43.1)	36.1 (32.9-39.3)	
Stage IV	115/182	0.76 (0.53-1.10)	38.9 (34.9-42.9)	33.5 (29.0-37.9)	
Inoperable	23/30	0.52 (0.21-1.27)	34.5 (22.0-47.0)	24.9 (17.7-32.1)	



73,5% fueron **estadio III**
26,5% fueron **estadio IV**

GOG 218: Overall survival



Alto riesgo: estadío IV o estadios III con enfermedad residual > 1cm
Tiempo medio de OS (meses) en alto riesgo con QT+Beva: **39.3** (ICON7)/ **42.8** (GOG 218)

1.Monk BJ, Coleman RL, Fujiwara K, et al. Optimal bevacizumab treatment strategy in advanced ovarian cancer: A review. *Cancer Treat Rev*. 2025;137:102945. 2.Oza AM, Cook AD, Pfisterer J, et al. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. *Lancet Oncol*. 2015;16(8):928-36.

ERA POST-iPARP

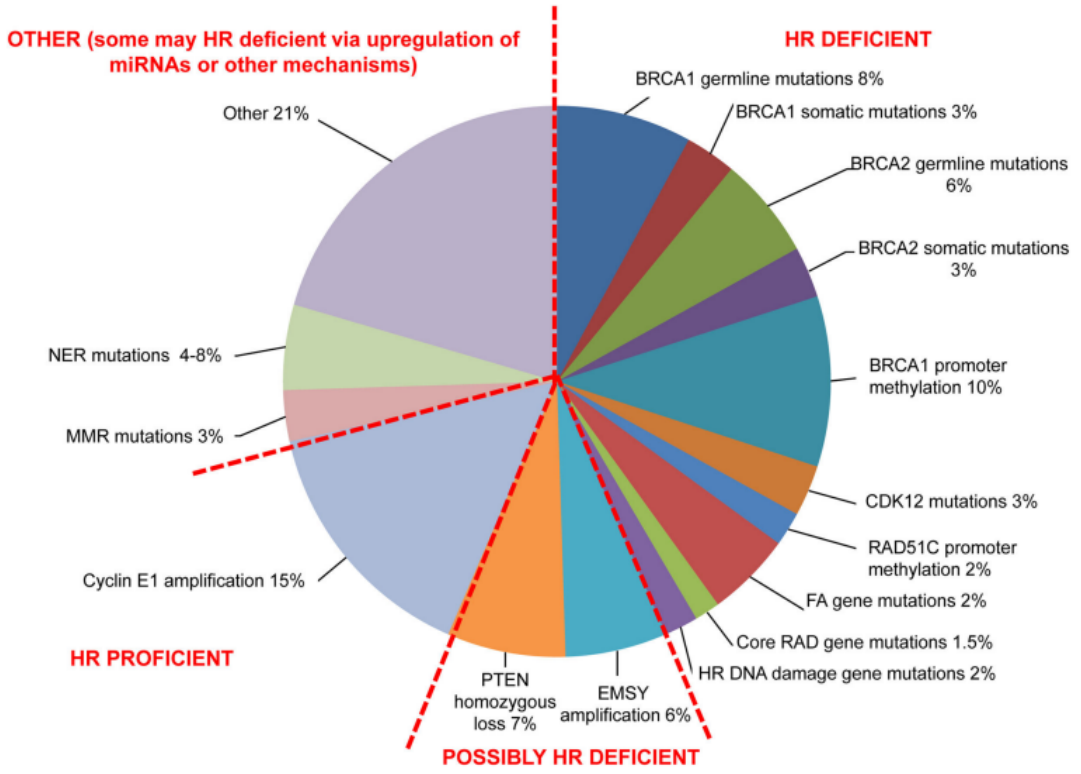
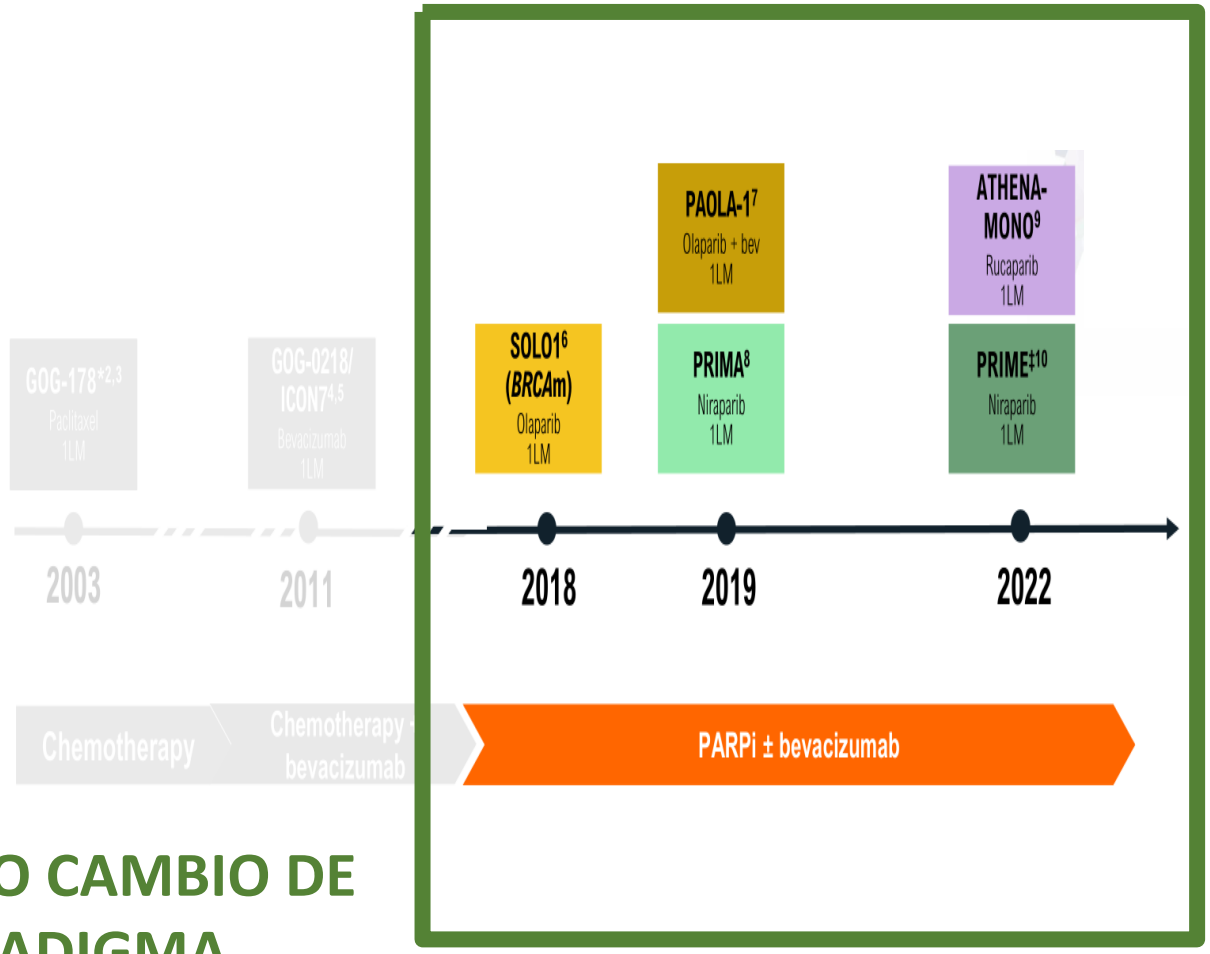


Figure 2. Approximately 50% of high grade serous EOC have alterations in HR repair genes



SEGUNDO CAMBIO DE PARADIGMA

Konstantinopoulos PA et al. Cancer Discov 2015

SEOM–GEICO clinical guideline on epithelial ovarian cancer (2023)

Jose Alejandro Perez-Fidalgo[1] · Fernando Gálvez-Montosa[2] · Eva María Guerra[3] · Ainhoa Madariaga[4] · Aranzazu Manzano[5] · Cristina Martin-Lorente[6] · Maria Jesús Rubio-Pérez[7] · Jesus Alarcón[8] · María Pilar Barretina-Ginesta[9] · Lydia Gaba[10]

MANAGEMENT OF ADVANCED STAGE OVARIAN CANCER (STAGE III OR IV)

Biopsy or laparoscopy (preferred) for histology and BRCA/HRD testing

Multidisciplinary committee: High probability to achieve complete cytoreduction		Multidisciplinary committee: Low probability to achieve complete cytoreduction
High grade	Low grade Low chemosensible histology	High grade
PRIMARY DEBULKING SURGERY AND STAGING Bilateral salpingo-oophorectomy Hysterectomy Omentectomy Abdominal cavity exploration Random biopsies of peritoneal surfaces Cytology peritoneal lavage Appendectomy if mucinous tumor		Carboplatin + Paclitaxel every 3 weeks for 3-4 cycles
Carboplatin + Paclitaxel +/-bevacizumab every 3 week for 6 cycles	Carboplatin + Paclitaxel +/-bevacizumab every 3 week for 6 cycles	INTERVAL DEBULKING SURGERY Bilateral salpingo-oophorectomy Hysterectomy Omentectomy Abdominal cavity exploration Random biopsies of peritoneal surfaces Cytology peritoneal lavage Appendectomy if mucinous tumor
Maintenance treatment: see options	Consider endocrine therapy (letrozole) for low grade serous	Carboplatin + Paclitaxel +/-bevacizumab every 3 week for 3 cycles
		Maintenance treatment: see options

Maintenance options for high grade serous or endometrioid AOC responding to platinum

BRCA 1/ 2 mut
- Olaparib
- Niraparib
- Rucaparib
- Olaparib+Bevacizumab*

HRD/BRCAwt
- Niraparib
- Rucaparib
- Olaparib+Bevacizumab*

HRP
- Niraparib
- Rucaparib
- Bevacizumab*

Guias ESMO 2026

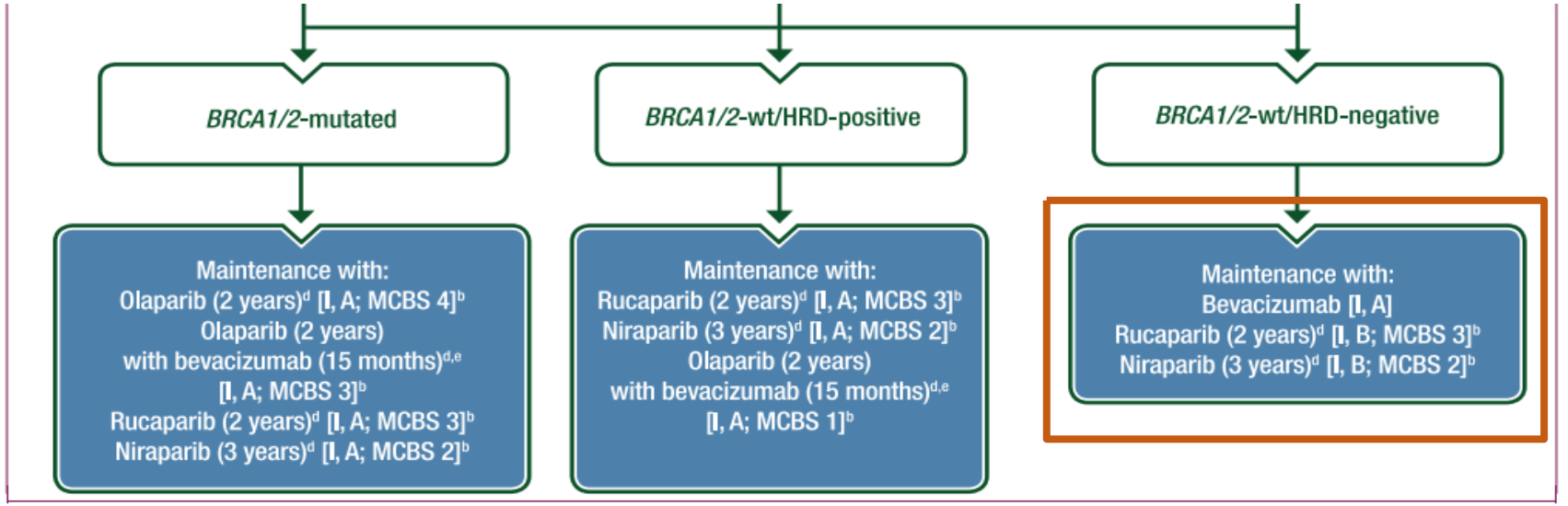


Figure 1. Management of advanced EOC (FIGO stage III-IV).
Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or combination of treatment modalities; white: other aspects of management and non-treatment aspects.
AUC, area under the curve; ChT, chemotherapy; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; ESCAT, ESMO Scale for Clinical Actionability of molecular Targets; FDA, Food and Drug Administration; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PARPi, poly (ADP-ribose) polymerase inhibitor; wt, wild type.
[a]ESCAT scores apply to alterations from genomic-driven analyses only. These scores have been defined by the guideline authors, assisted if needed by the ESMO Precision Medicine Working Group.[7]
[b]ESMO-MCBS v2.0[3] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms).
[d]Only when patients have complete or partial response to platinum or no evidence of disease. For patients without response to platinum, a PARPi is not indicated; these patients can be managed with bevacizumab maintenance if appropriate (mainly stable disease), or with second-line therapy if they have progressive disease (see Figure 3 in the original Clinical Practice Guideline[1]).
[e]Option for patients for whom bevacizumab was added to paclitaxel—carboplatin.

González-Martín A and Ledermann JA. ESMO Clinical Practice Guideline Express Update on the management of epithelial ovarian cancer. ESMO Open. 2026

PREMISA 1

Todas las pacientes con COA (III/IV) recibirán tratamiento mantenimiento

PREMISA 2

HRD+: Biomarcador predictivo de respuesta al platino/iPARP

PREMISA 3

Todas las pacientes HRD+/BRCAm (a priori) recibirán tratamiento con iPARP

SOLO1 | **PAOLA1** | **PRIMA** | **ATHENA-MONO**

CARACTERÍSTICAS COMUNES ENSAYOS iPARP+/-Beva:

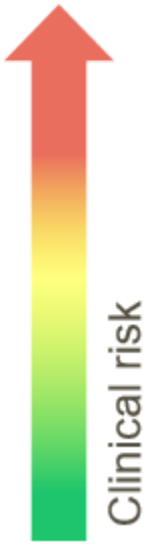
- Estadíos III y IV
- Histología: Ca epitelial de alto grado de ovario, trompa o primario peritoneal
- **Pacientes platino-sensibles (RC/RP/NEE**)
- Toda la población a estudio (salvo SOLO 1) y estratificadas por status molecular
- Mismo endpoint 1º (PFS) y 2º (OS, PFS2, TFST, TSST, seguridad, QoL)

SOLO1 | PAOLA1 | PRIMA | ATHENA-MONO

High-risk factors:*[1]

- Stage IV disease
- Visible residual disease or no surgery
- ICS/NACT or no surgery
- PR to chemotherapy[2]
- *BRCA*wt, *BRCA*nd, or missing

	Stage IV disease	Visible residual disease[†]	Neoadjuvant chemotherapy	PR to chemotherapy	*BRCA*wt
PRIMA[3-5]	35%	47%[‡]	67%	31%	70%[c]
PAOLA-1[6,7]	30%	40%	42%	27%[#]	70%
PRIME[8††]	28%	22%[§]	47%	18%	67%[°]
ATHENA-MONO[9]	25%	38%	51%	18%	79%
SOLO1[10,11]	17%	23%	35%	18%	0%



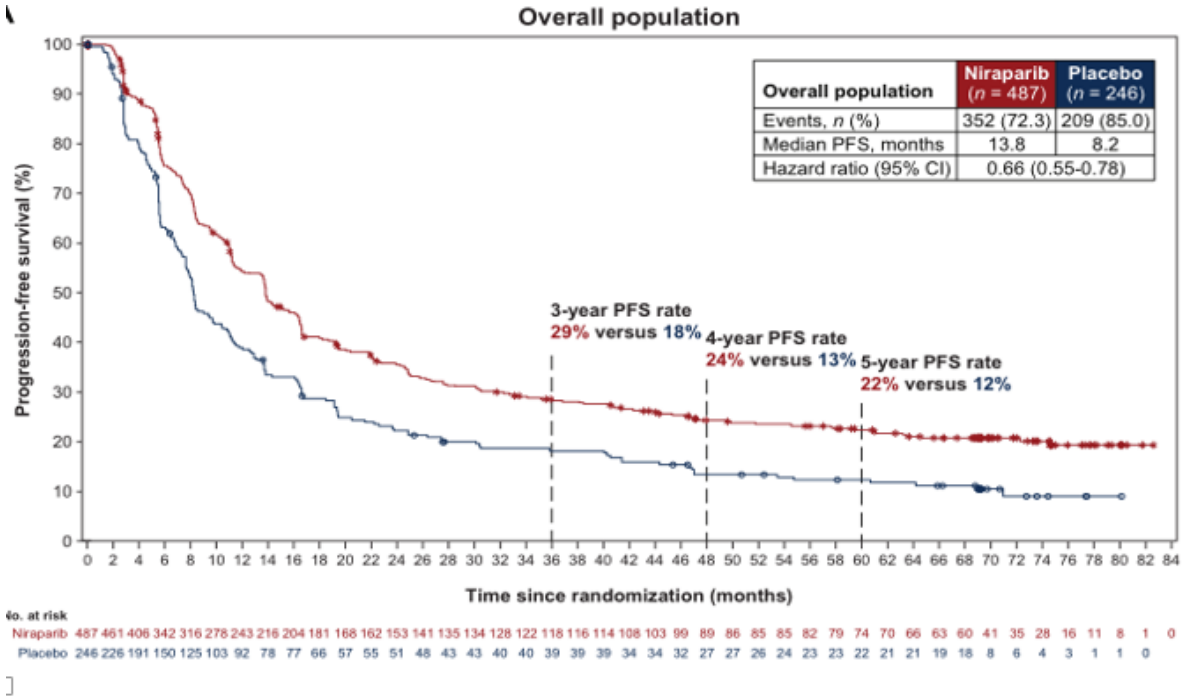
1Chase D, Perhanidis J, Gupta D, Kalilani L, Golembesky A, González-Martín A. Association of Multiple High-Risk Factors on Observed Outcomes in Real-World Patients With Advanced Ovarian Cancer Treated With First-Line Therapy. JCO Clinical Cancer Informatics. 2023;7:e2200189. 2. https://www.uptodate.com/contents/medical-treatment-for-relapsed-epithelial-ovarian-fallopian-tube-or-peritoneal-cancer-platinum-sensitive-disease#disclaimerContent; 3. González-Martín A, et al. N Engl J Med 2019;381:2391–402; 4. González-Martín A, et al. Presented at ESGO 2019, 2–5 Nov, Athens, Greece; 5. Braicu EI, et al. Presented at ESGO SoA 2020, 14–16 Dec (virtual); 6. Ray-Coquard I, et al. N Engl J Med 2019;381:2416–28; 7. Ray-Coquard I, et al. N Engl J Med 2019;381:2416–28 (Supplementary Appendix); 8. Li N, et al. Presented at SGO 2022, 18–21 Mar, Phoenix, AZ; 9. Monk BJ, et al. J Clin Oncol 2022;40:3952–64; 10. Moore K, et al. N Engl J Med 2018;379:2495–505; 11. Moore K, et al. N Engl J Med 2018;379:2495–505 (Supplementary Appendix).

PRIMA

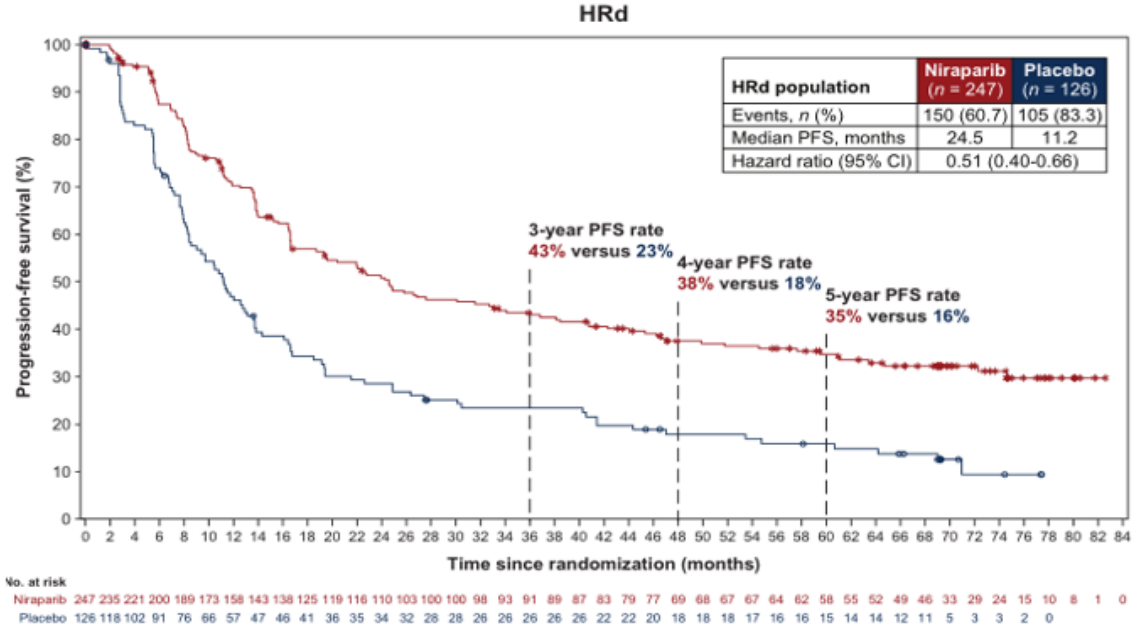
Pacientes HRD+/BRCAm

PFS

ITT



HRD+/BRCA



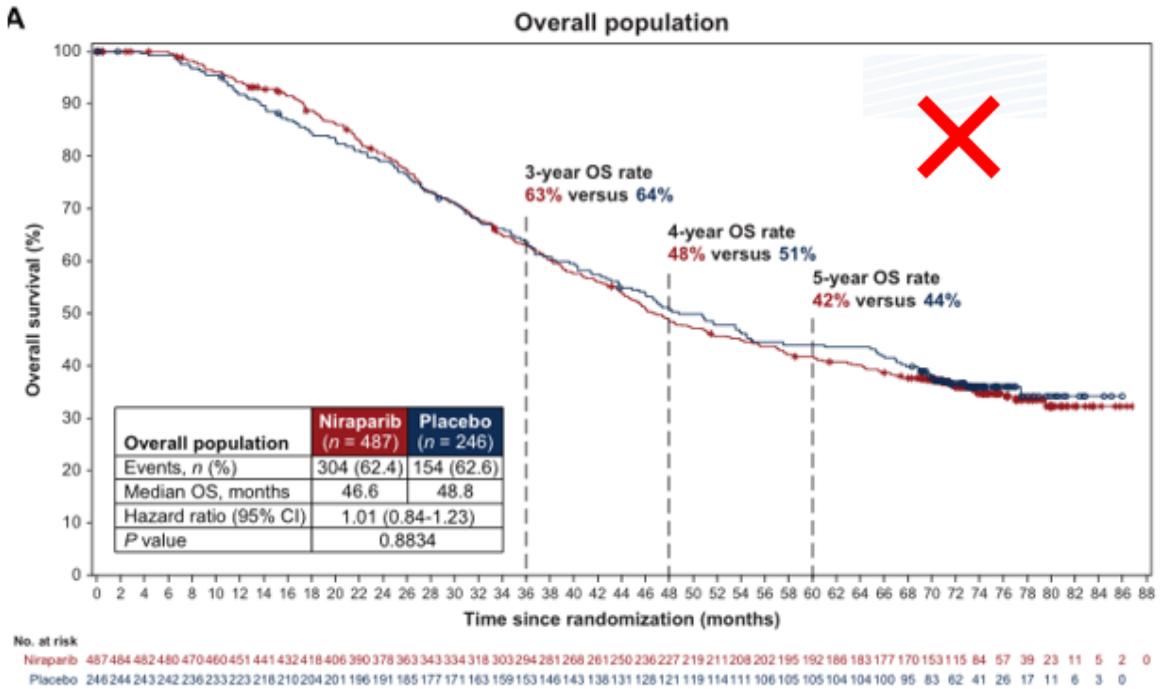
Monk BJ, Lorusso D et al. Ann Oncol.2024;35(11):981-92

PRIMA

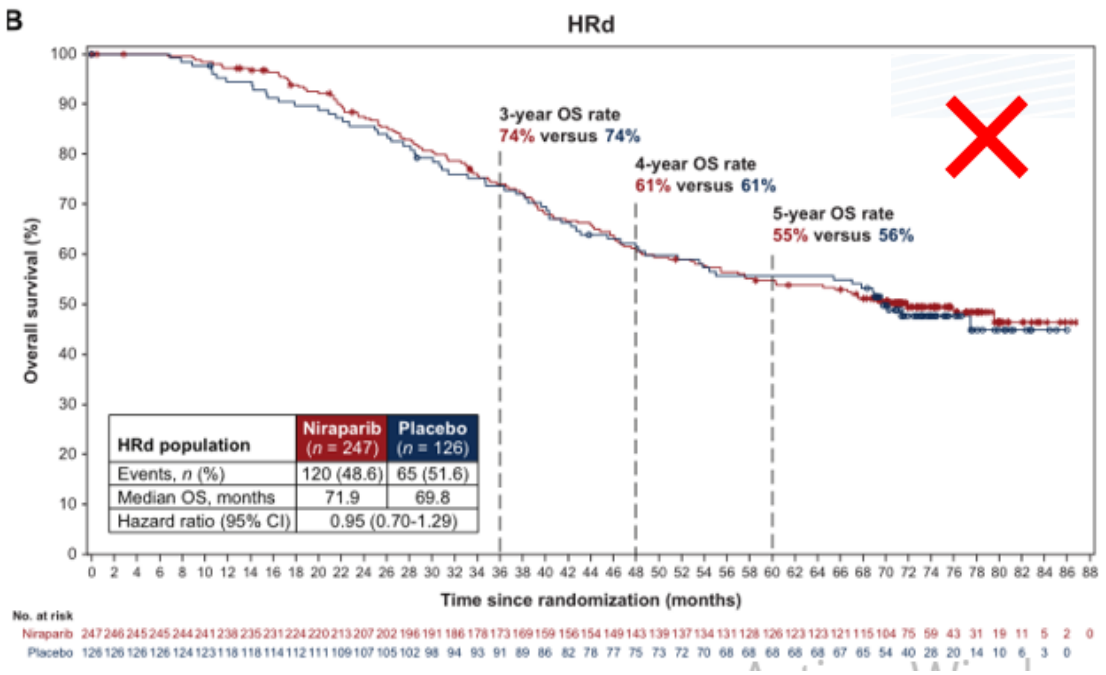
Pacientes HRD+/BRCAm

OS

ITT



HRD+/BRCA



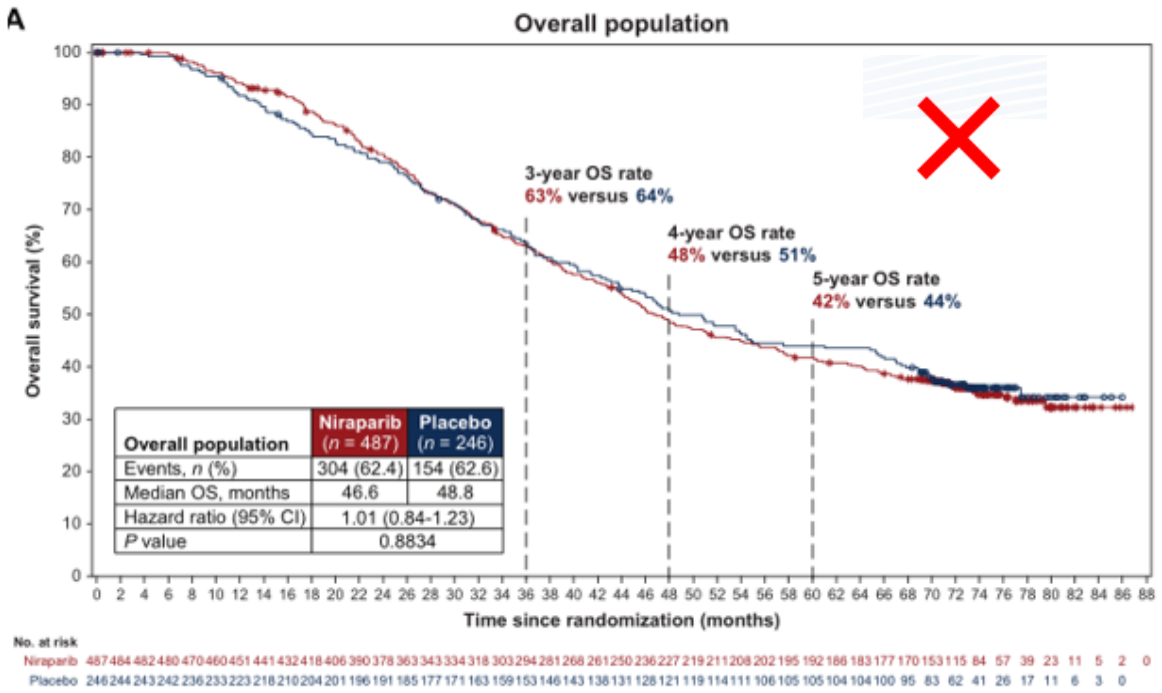
Monk BJ, Lorusso D et al. Ann Oncol.2024;35(11):981-92

PRIMA

Pacientes HRD+/BRCAm

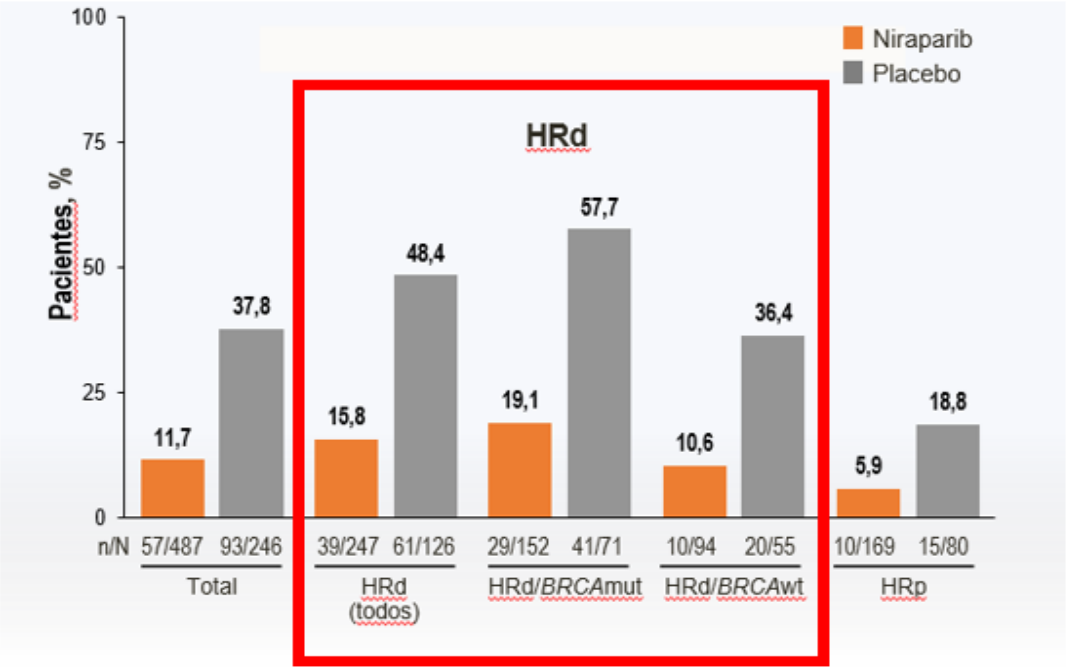
OS

ITT



Monk BJ, Lorusso D et al. Ann Oncol.2024;35(11):981-92

Tratamiento con iPARP posterior



Adaptado de González-Martín A, *et al.* Presentado en ESMO. 2024[1]

ATHENA-MONO

Pacientes HRD+/BRCAm

PFS

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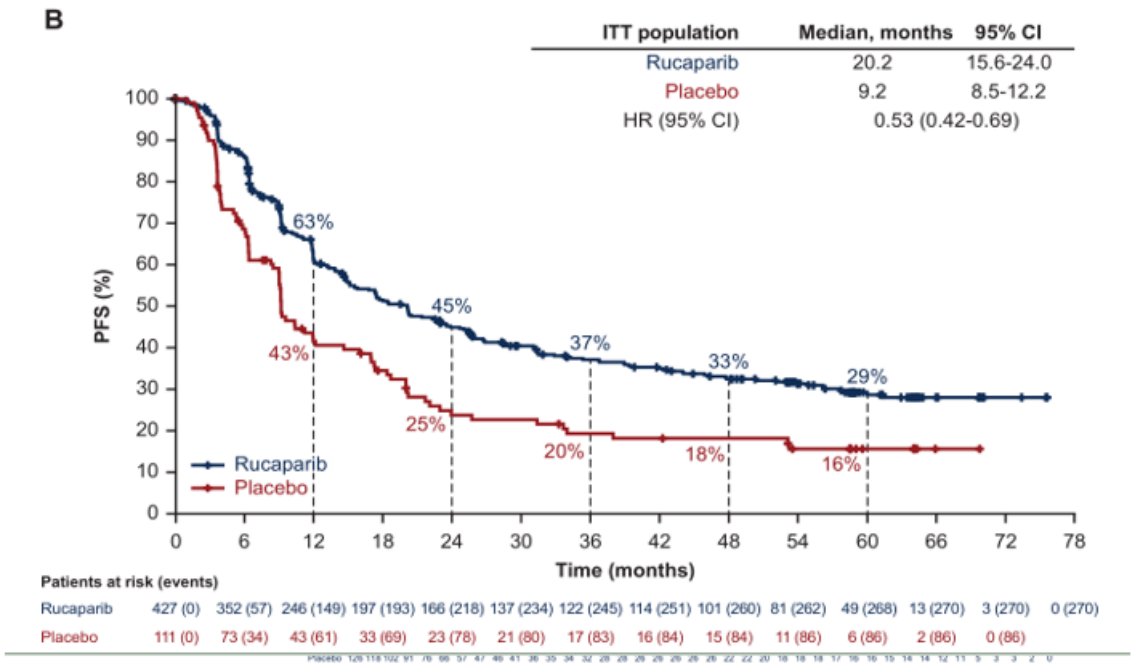
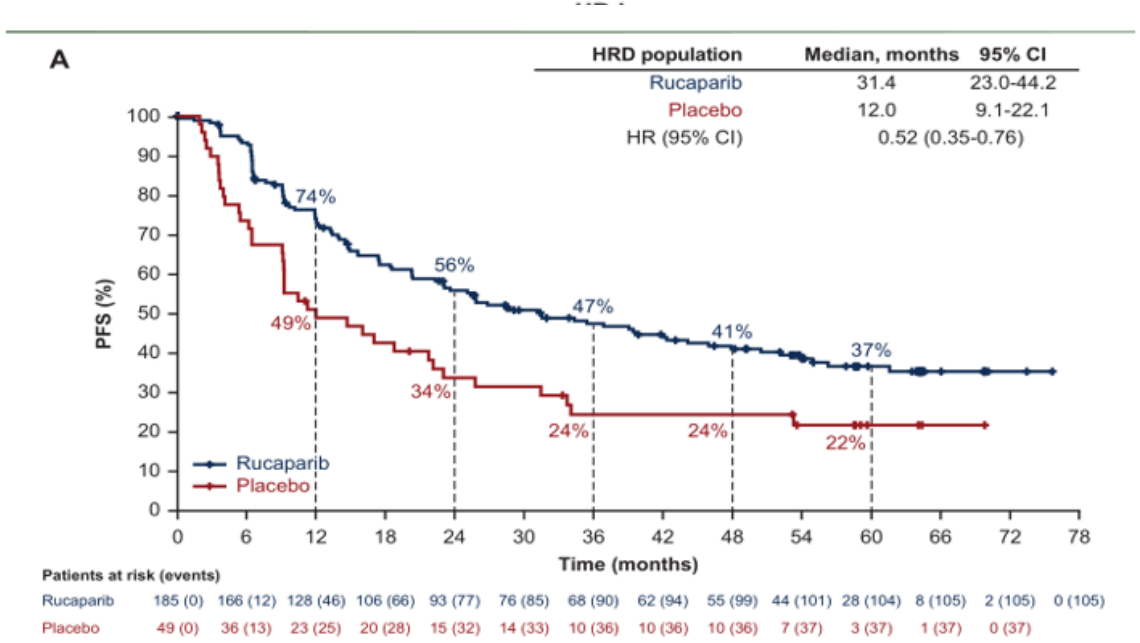


HRD+/BRCA

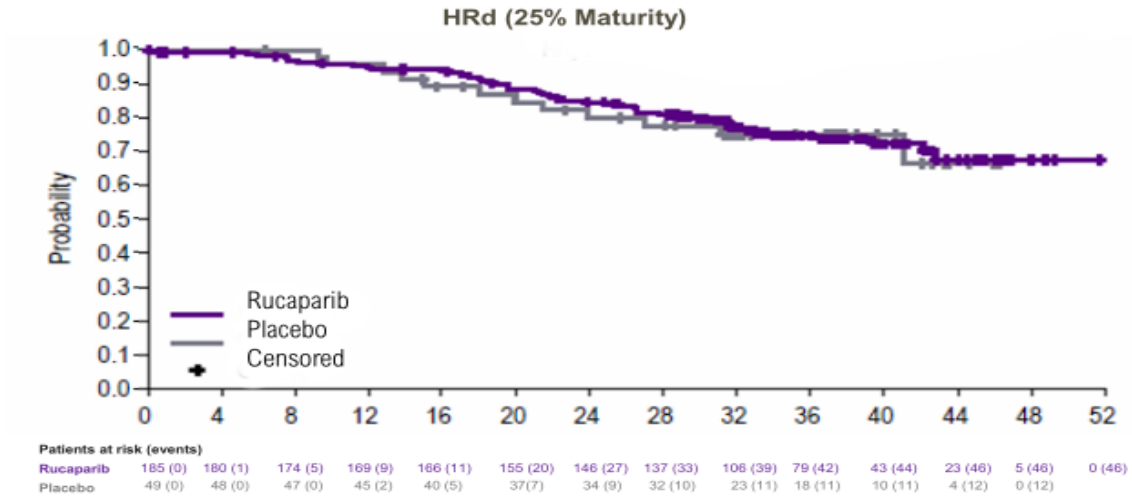


Kristeleit RS, Ghamande S, et al.. Ann Oncol. 2025

ATHENA-MONO

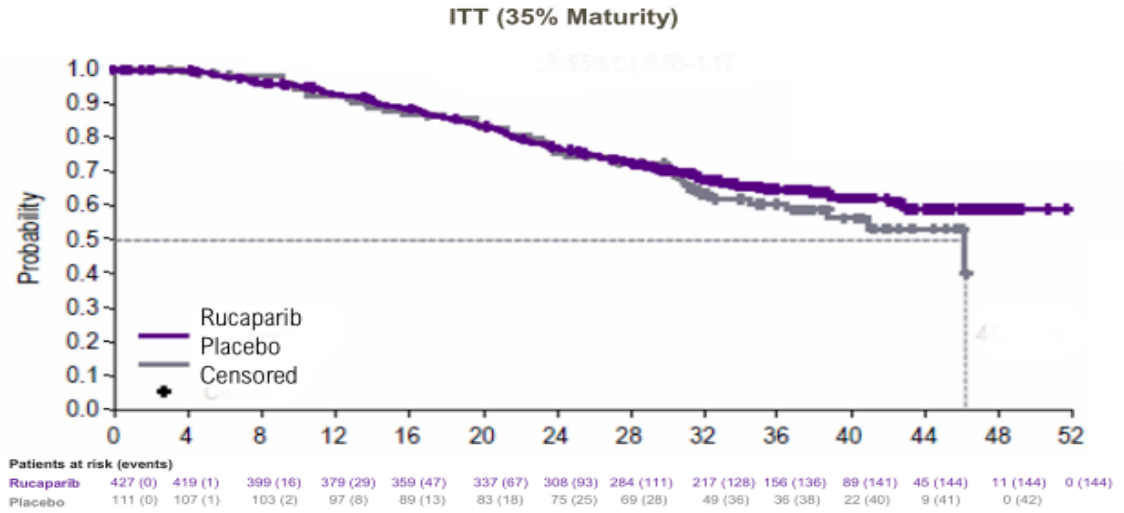
Pacientes HRD+/BRCAm

OS



	Events/N(%)	Median	95% CI	Range	12-mo Est	24-mo Est
Rucaparib	46/185 (24.9)	NR	NR-NR	0-52	0.95 (0.91-0.97)	0.85 (0.78 – 0.89)
Placebo	12/49 (24.5)	NR	41.0 - NR	0-46	0.96 (0.84 – 0.99)	0.80 (0.65 – 0.89)

HR 0.84; 95% CI 0.44- 1.58



Events/N(%)	Median	95% CI	Range	12-mo Est	24-mo Est
144/427 (33.7)	NR	NR-NR	0-52	0. 93 (0.90- 0.95)	0.77 (0.73 – 0.81)
42/111 (37.8)	46.2	34.6 - NR	0-46	0.92 (0.85 – 0.96)	0.76 (0.66 – 0.83)

HR 0.83; 95% CI 0.58- 1.17

1. Kristeleit RS, O´Mally DM, et al. Interim post-progression data and updated survival in patients with newly diagnosed advanced ovarian cancer in ATHENA-MONO. Presented at: SGO Annual Meeting; 2024 Mar; San Diego, CA. 2. Kristeleit RS, Ghamande S, et al.. Ann Oncol. 2025

PAOLA 1

Pacientes HRD+/BRCAm

PFS

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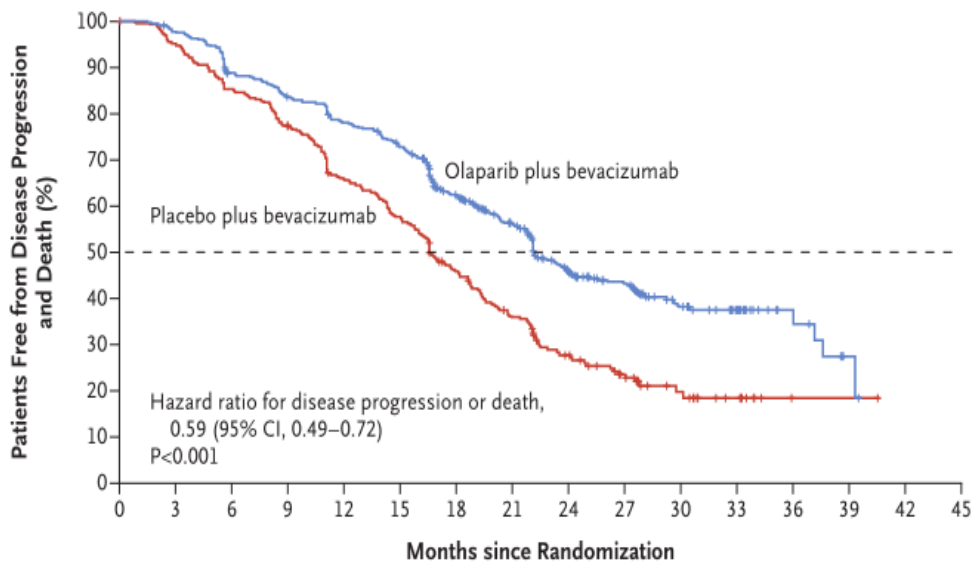
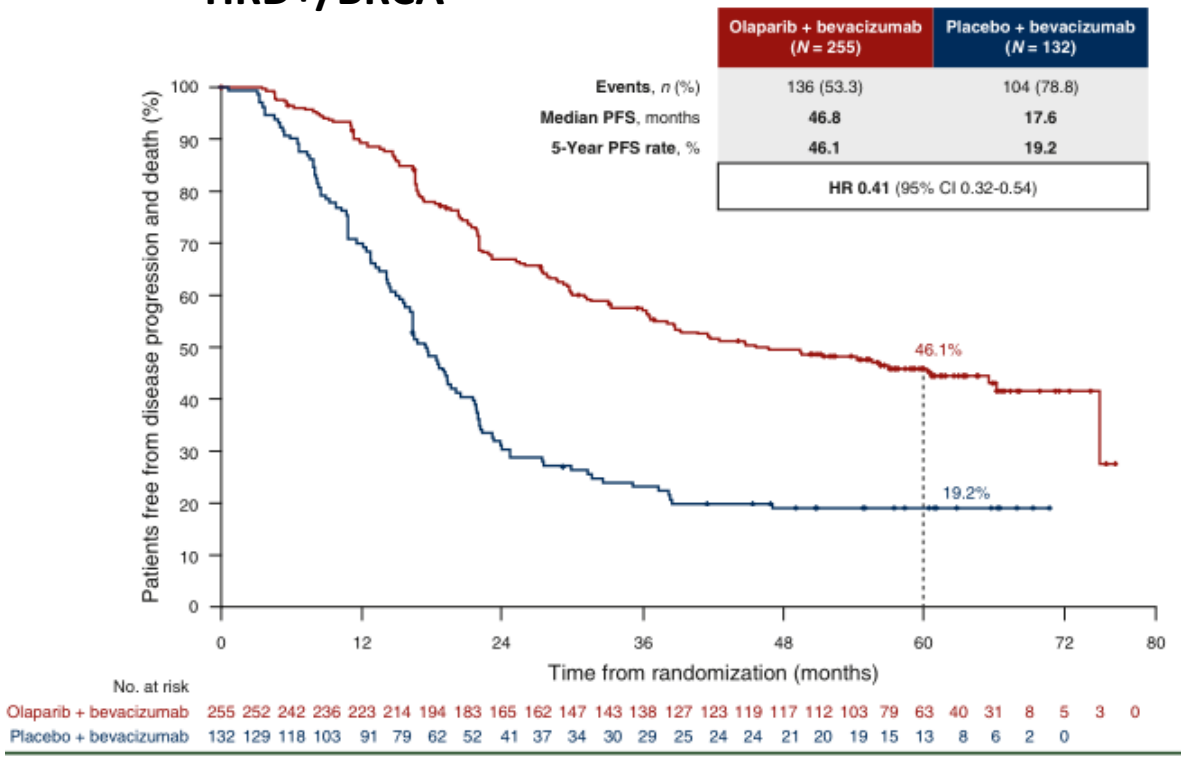


No. at Risk															
Olaparib plus bevacizumab	537	513	461	433	403	374	279	240	141	112	55	37	12	3	0
Placebo plus bevacizumab	269	252	226	205	172	151	109	83	50	35	15	9	1	1	0

HRD+/BRCA



No. at risk																									
Olaparib + bevacizumab	255	252	242	236	223	214	194	183	165	162	147	143	138	127	123	119	117	112	103	79	63	40	31	8	5	3	0
Placebo + bevacizumab	132	129	118	103	91	79	62	52	41	37	34	30	29	25	24	24	21	20	19	15	13	8	6	2	0		

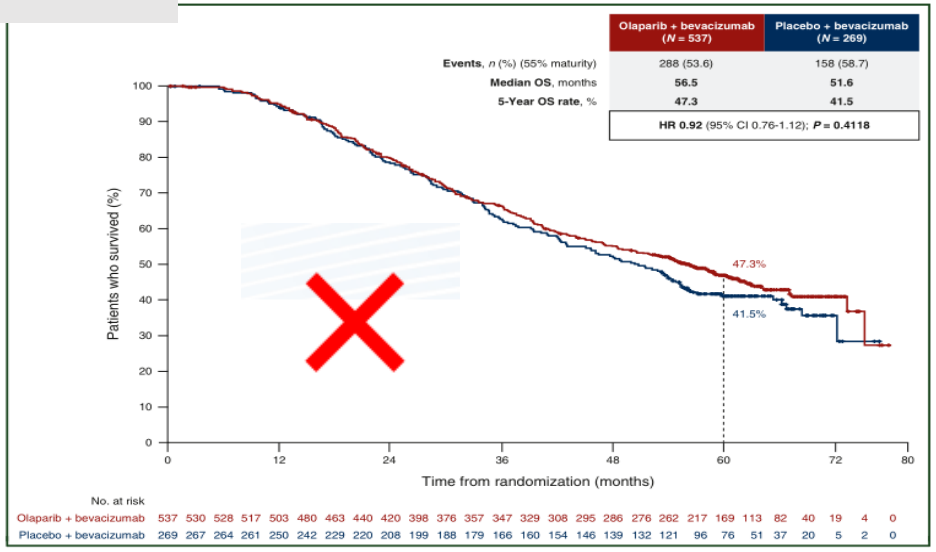
1. Ray-Coquard I, Pautier P, Pignata S, et al. N Engl J Med. 2019;381(25):2416-2428. 2. Ray-Coquard I et al. Annals of Oncology.2023;34(8):681-692

PAOLA 1

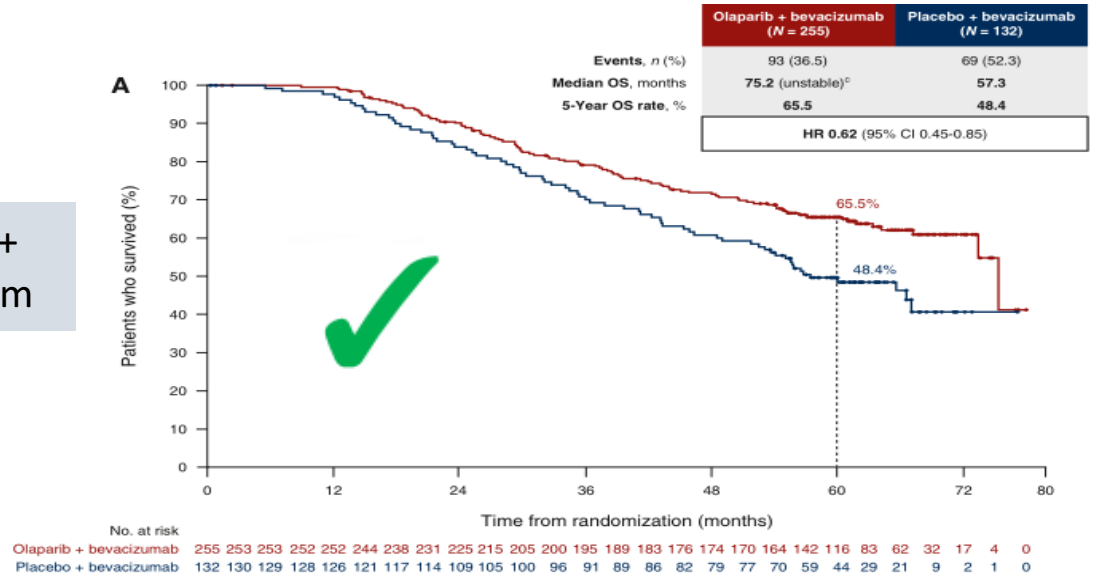
Pacientes HRD+/BRCAm

OS

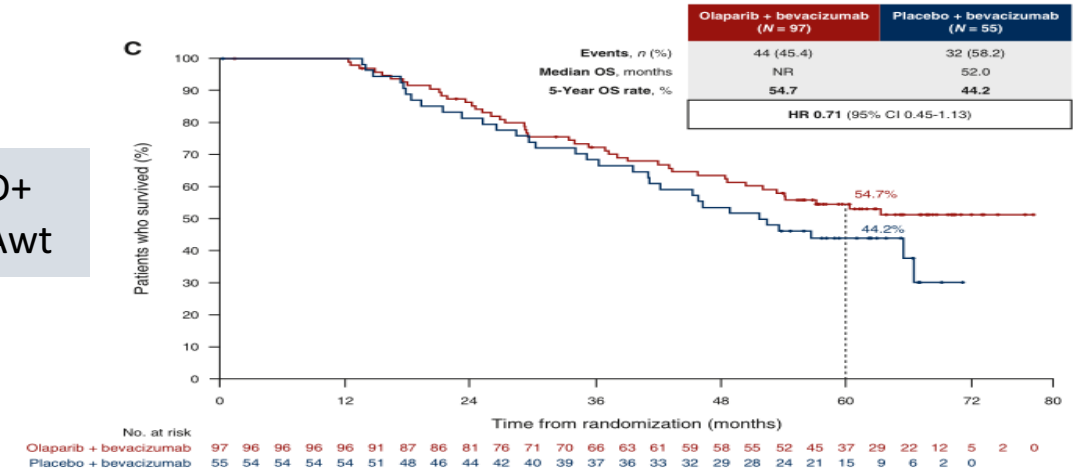
ITT



HRD+ BRCAm



HRD+ BRCAwt



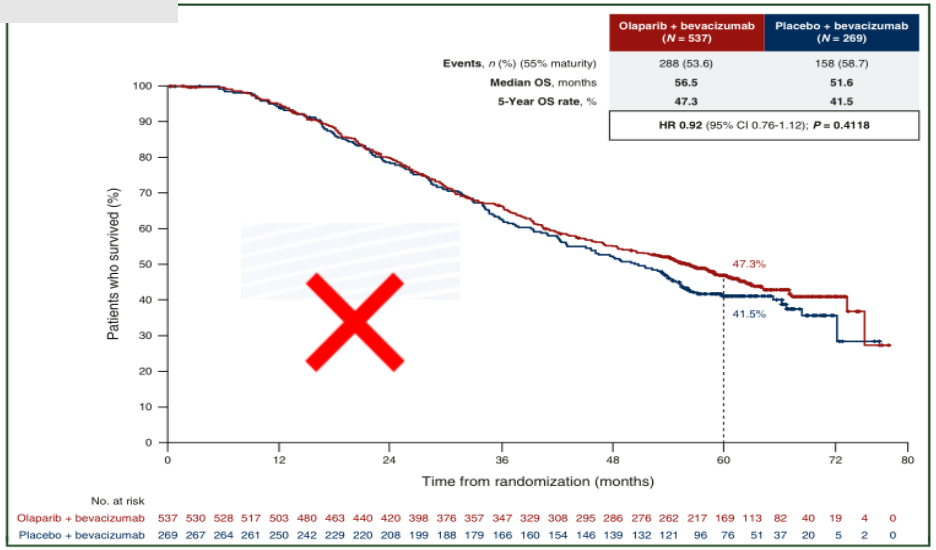
Ray-Coquard I et al. Annals of Oncology. 2023;34(8):681-692

PAOLA 1

Pacientes HRD+/BRCAm

OS

ITT



Patients receiving a PARP inhibitor during any subsequent treatment, %

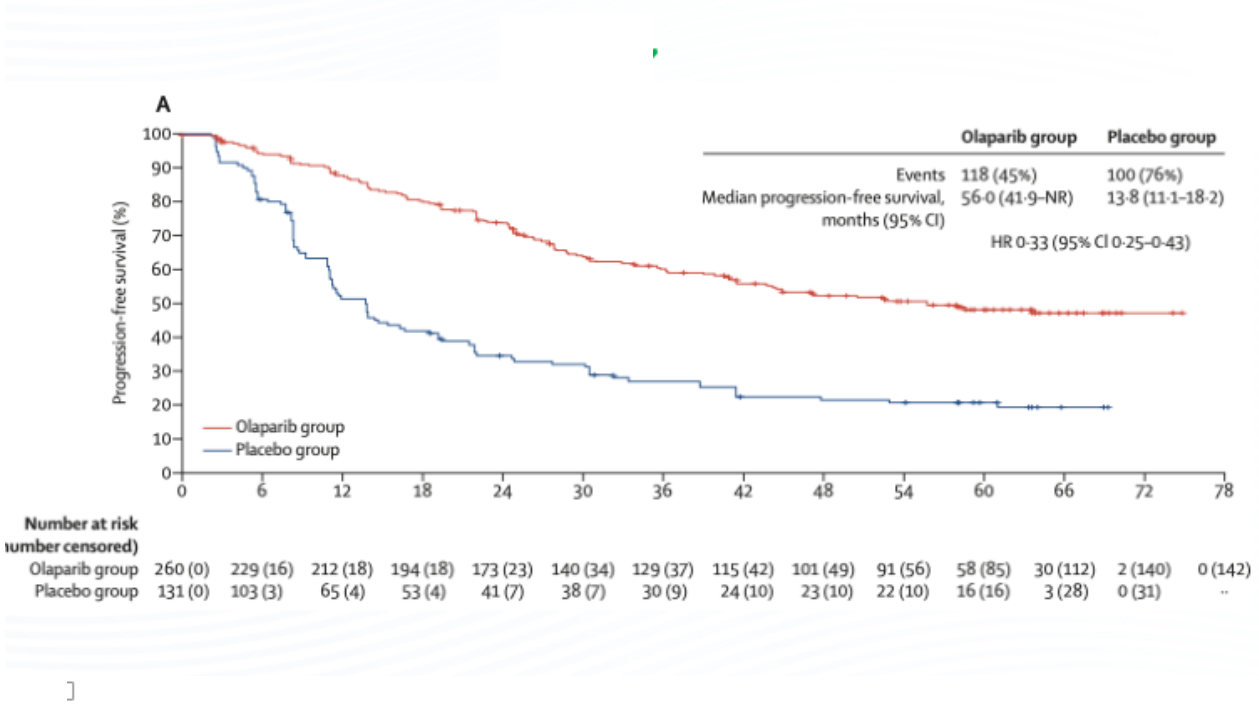
	Placebo	Olaparib
ITT	**>45%**	20%
HRD+	**>50%**	17%
HRD/BRCA wt	**42%**	9%
BRCAm	**55%**	24%

Ray-Coquard I et al. Annals of Oncology. 2023;34(8):681-692

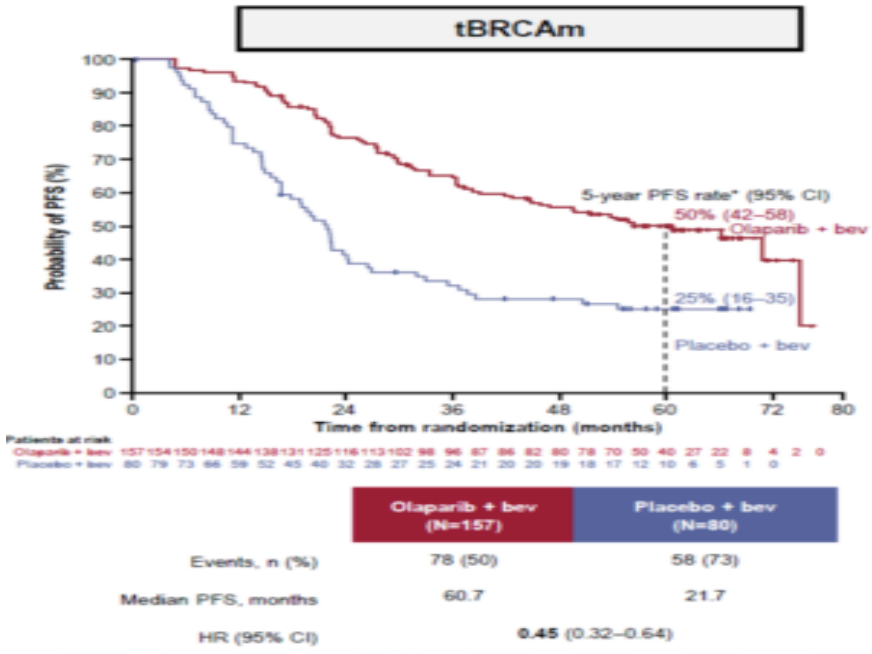
Pacientes BRCA EXCLUSIVAMENTE

PFS

SOLO 1



PAOLA 1



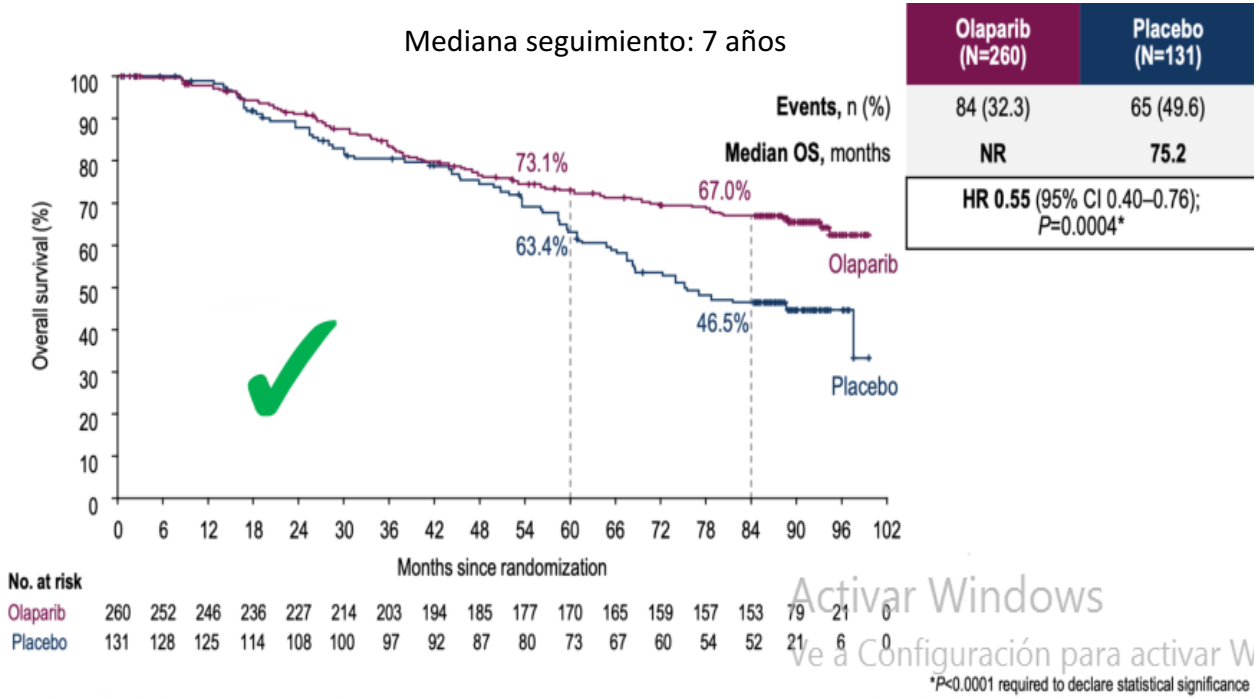
1. Banerjee S et al. Lancet Oncol 2021;22(12):1721–31. 2. Ray-Coquard I et al. Annals of Oncology. 2023;34(8):681-692

Pacientes BRCA EXCLUSIVAMENTE

OS

SOLO 1

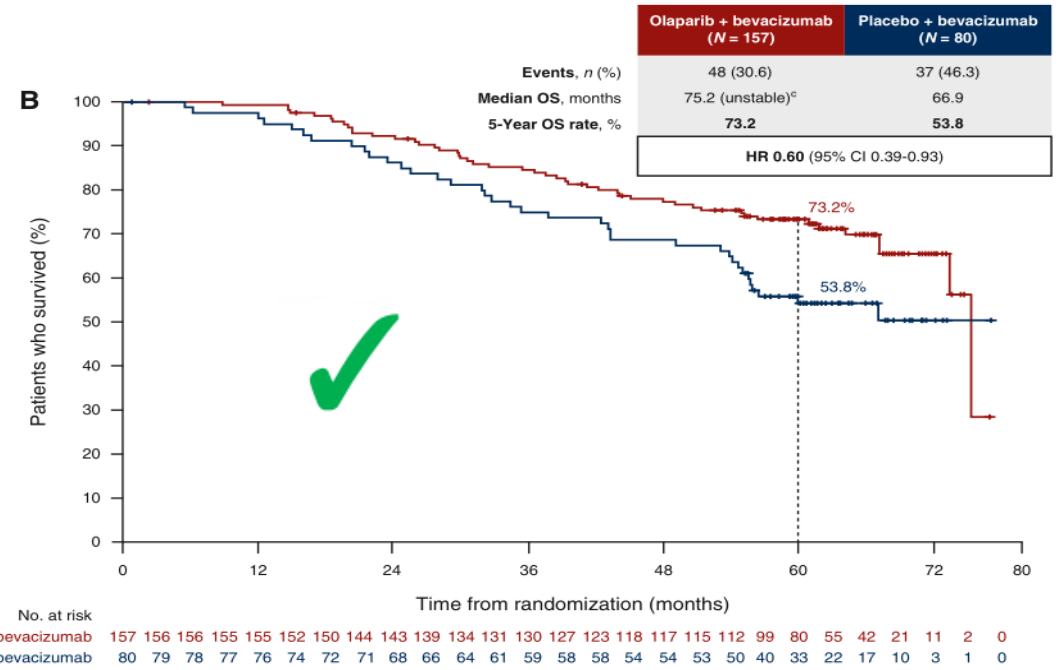
Mediana seguimiento: 7 años



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	84 (32.3)	65 (49.6)
Median OS, months	NR	75.2
HR 0.55 (95% CI 0.40–0.76); P=0.0004*		

*P<0.0001 required to declare statistical significance

PAOLA 1



	Olaparib + bevacizumab (N = 157)	Placebo + bevacizumab (N = 80)
Events, n (%)	48 (30.6)	37 (46.3)
Median OS, months	75.2 (unstable)[c]	66.9
5-Year OS rate, %	73.2	53.8
HR 0.60 (95% CI 0.39-0.93)		

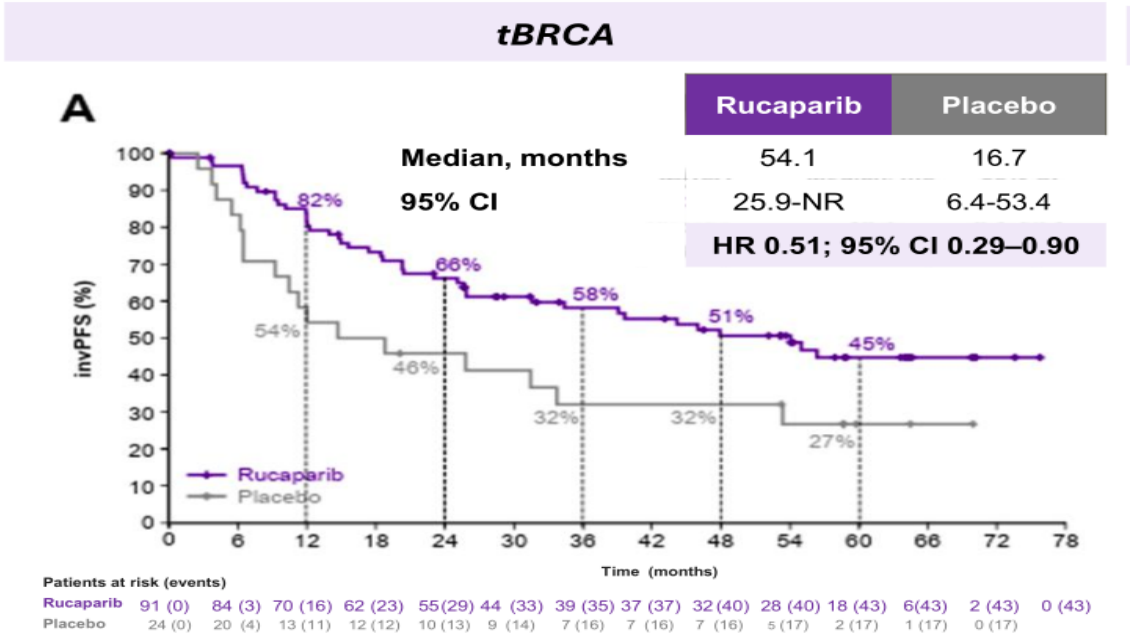
1. DiSilvestro P, Banerjee S et al. J Clin Oncol 2023;41(3): 609–17. 2. Ray-Coquard I et al. Annals of Oncology. 2023;34(8):681-692

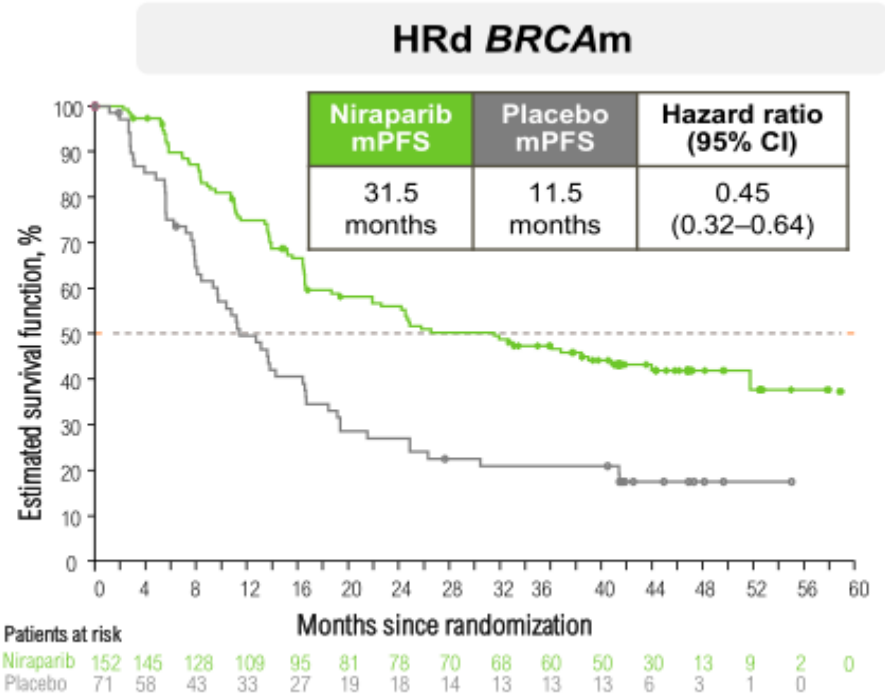
Pacientes BRCA EXCLUSIVAMENTE

ATHENA-MONO

PRIMA

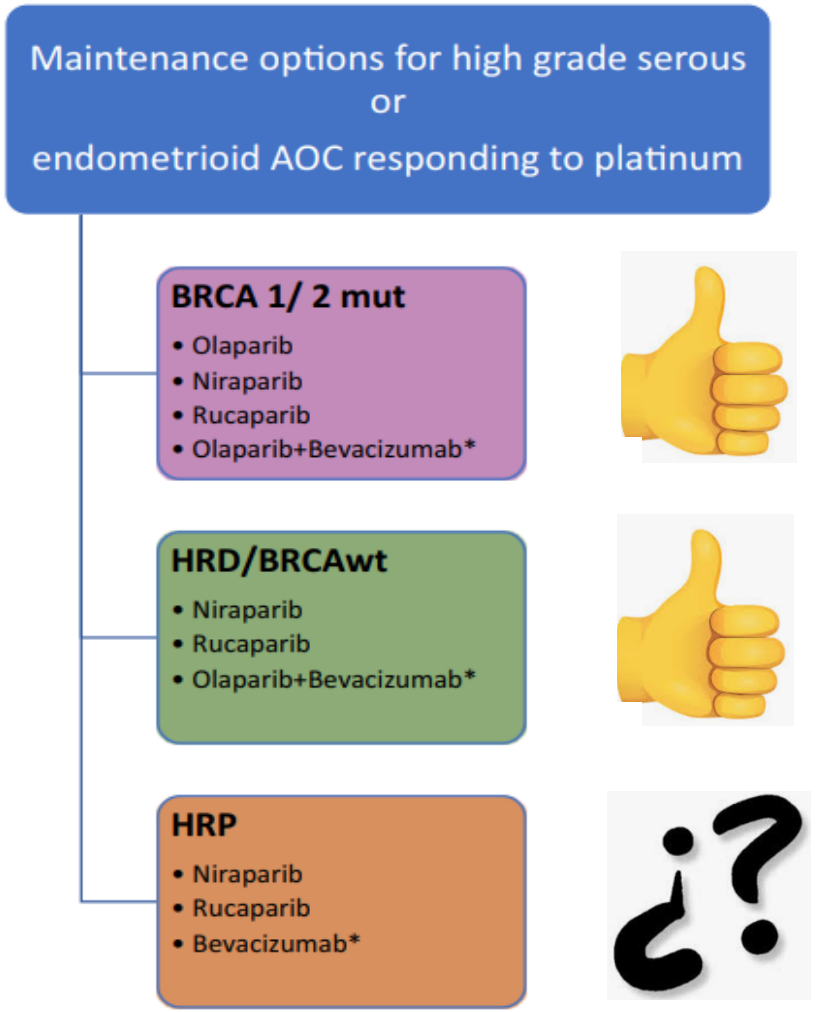
PFS





1. Kristeleit RS, Ghamande S, Lisyanskaya A, et al. Ann Oncol. 2025; Oct 18:S0923-7534(25)04950-6. 2. González-Martín A, Pothuri B, Vergote I, et al. Progression-free survival and safety at 3.5years of follow-up: results from the randomised phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib maintenance treatment in patients with newly diagnosed ovarian cancer. Eur J Cancer. 2023;189(112908):112908

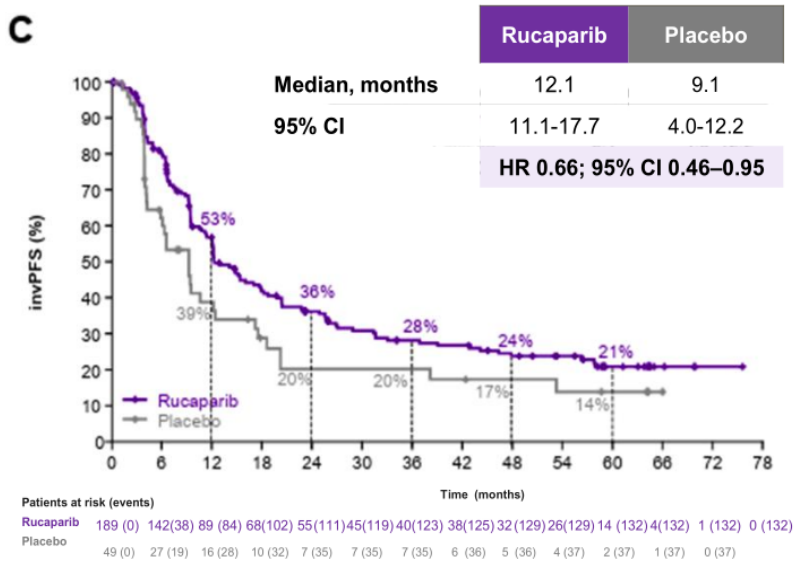
¿Cuándo realizar mantenimiento con iPARP?



Pacientes HRP

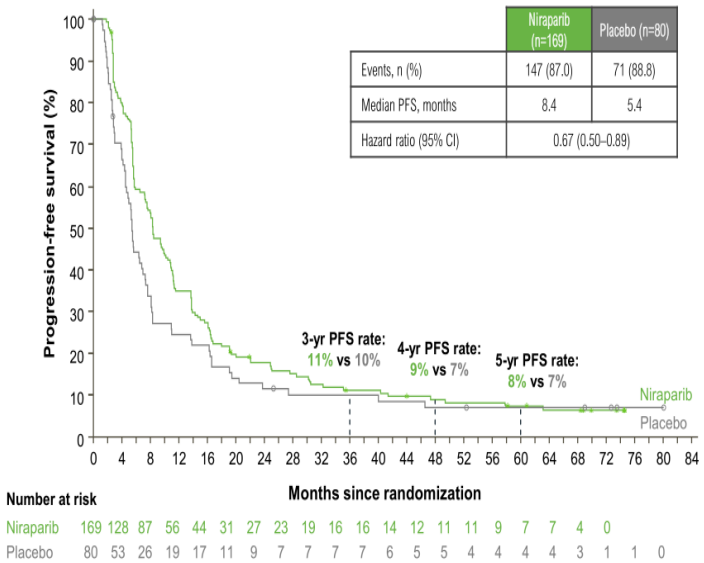
ATHENA-MONO

***BRCA* wild-type/LOH^{low}**

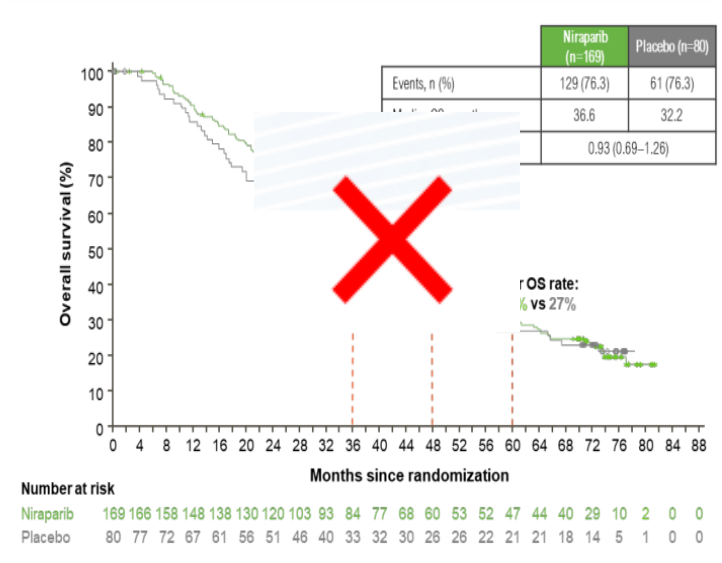


PRIMA

PFS in HRp



OS in HRp



Tiempo medio (meses) de **PFS** con Ruca/Nira: **12.1** (ATHENA-M)/**8.4** (PRIMA), HR: 0.66, 0.67, respectivamente

1. Kristeleit RS et al. Ann Oncol. 2025;Oct 18:S0923-7534 (25)04950-6. 2. Monk BJ, Lorusso D et al. Ann Oncol.2024;35(11):981-92

Pacientes HRP

PARPi alone

Bevacizumab

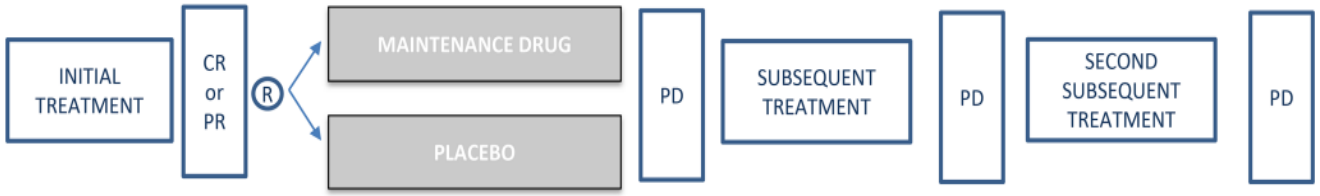
SI iPARP NO IMPACTA EN OS… ¿HAY IMPACTO DE OTROS ENDPOINT SECUNDARIOS?

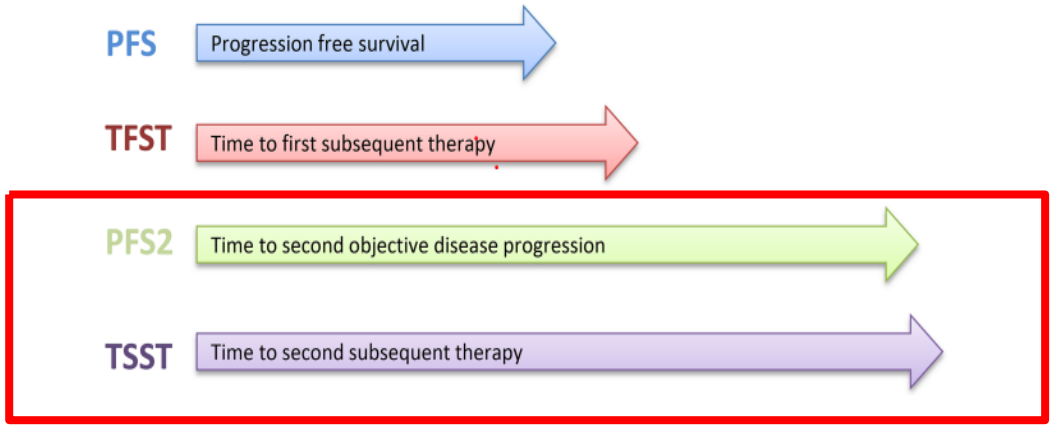
Review

Outcomes and endpoints of relevance in gynecologic cancer clinical trials

Ainhoa Madariaga [1], Rodrigo Sanchez-Bayona,[1] Fernanda G Herrera,[2] Pedro T Ramirez [3], Antonio González Martín [4]

Review





Other Time to Event Endpoints

Other time to event endpoints, including time from randomization to progression on the second-line therapy or death (progression-free survival two) and time to second subsequent therapy, can be used as secondary outcomes in phase III clinical trials (Figure 1).[41] These measures are important to support the hypothesis that the benefit provided by the increase in progression-free survival is maintained over time, and the disease remains controlled at a longer term.[41] In cases where it is not feasible to ensure regular disease reassessment until the time of second progression, time to second subsequent therapy should be used instead of progression-free survival two.

Regulatory agencies recommend that maintenance trials should report the impact in the subsequent line of therapy. Both progression-free survival two and time to second subsequent therapy have an important role in studies assessing maintenance strategies.[41] Prolonged administration of a treatment as maintenance may reduce the ability of patients to benefit from the same or similar agents; patients could develop cross-resistances and treatment-related toxicity that might decrease tolerance to subsequent therapy. Analysis of the benefit in time to second subsequent therapy could help to elucidate whether a statistically non-significant difference in overall survival might be real.[41]

Madariaga et al. Int J Gynecol Cancer. 2023 Mar 6;33(3):323-332.

SI iPARP NO IMPACTA EN OS… ¿HAY IMPACTO DE OTROS ENDPOINT SECUNDARIOS?

PFS2 ITT en PRIMA:
30,1 vs 27.6 HR 0.96 (0.79-1.17)
PFS2 HRP en PRIMA:
21.4 vs 18.1 HR 0.90 (0.66-1.23)

PRIMA

Monk BJ et al

Table S2. Time to first subsequent treatment and progression-free survival 2

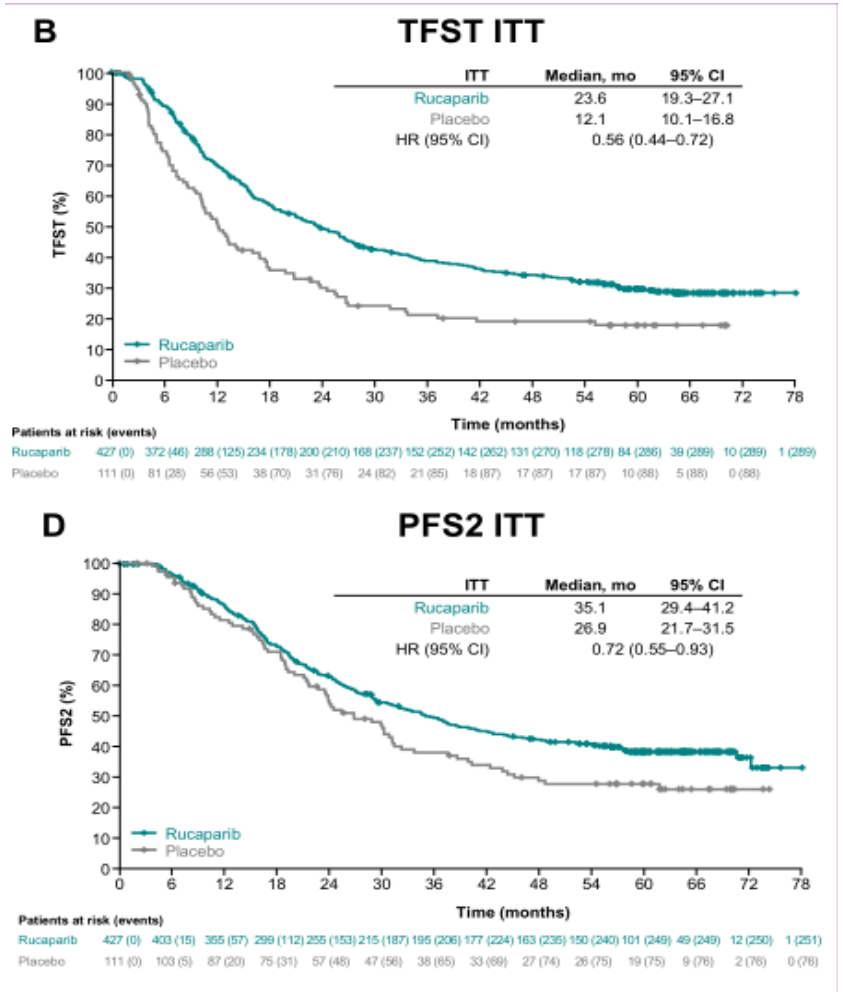
Prespecified secondary efficacy endpoint	Overall population		All HRd		HRd/*BRCA*m		HRd/*BRCA*wt		HRp	
	Niraparib (*n* = 487)	Placebo (*n* = 246)	Niraparib (*n* = 247)	Placebo (*n* = 126)	Niraparib (*n* = 152)	Placebo (*n* = 71)	Niraparib (*n* = 94)	Placebo (*n* = 55)	Niraparib (*n* = 169)	Placebo (*n* = 80)
TFST										
Median, months	17.0	12.0	26.9	13.9	34.3	14.9	22.5	12.9	11.6	7.9
Hazard ratio, 95% CI	0.74 (0.62-0.89)		0.55 (0.43-0.71)		0.45 (0.32-0.62)		0.76 (0.50-1.14)		0.88 (0.65-1.18)	
PFS2										
Median, months	30.1	27.6	43.4	39.3	46.6	46.5	38.0	34.1	21.4	18.1
Hazard ratio, 95% CI	0.96 (0.79-1.17)		0.87 (0.66-1.17)		0.90 (0.61-1.32)		0.88 (0.57-1.36)		0.90 (0.66-1.23)	

Hazard ratios and 95% CIs for HRd/*BRCA*wt and HRp were calculated using unstratified Cox proportional hazards models.

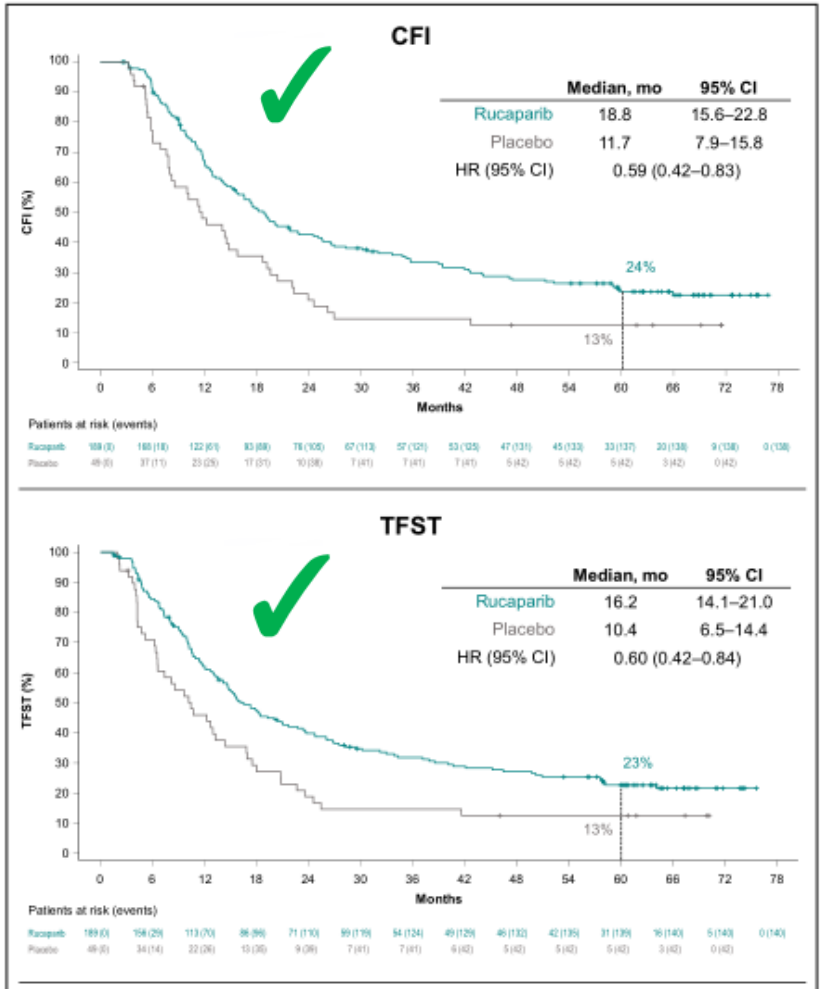
*BRCA*m, *BRCA*-mutated; *BRCA*wt, *BRCA* wild-type; CI, confidence interval; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PFS2, progression-free survival 2; TFST, time to first subsequent treatment.

ATHENA-MONO

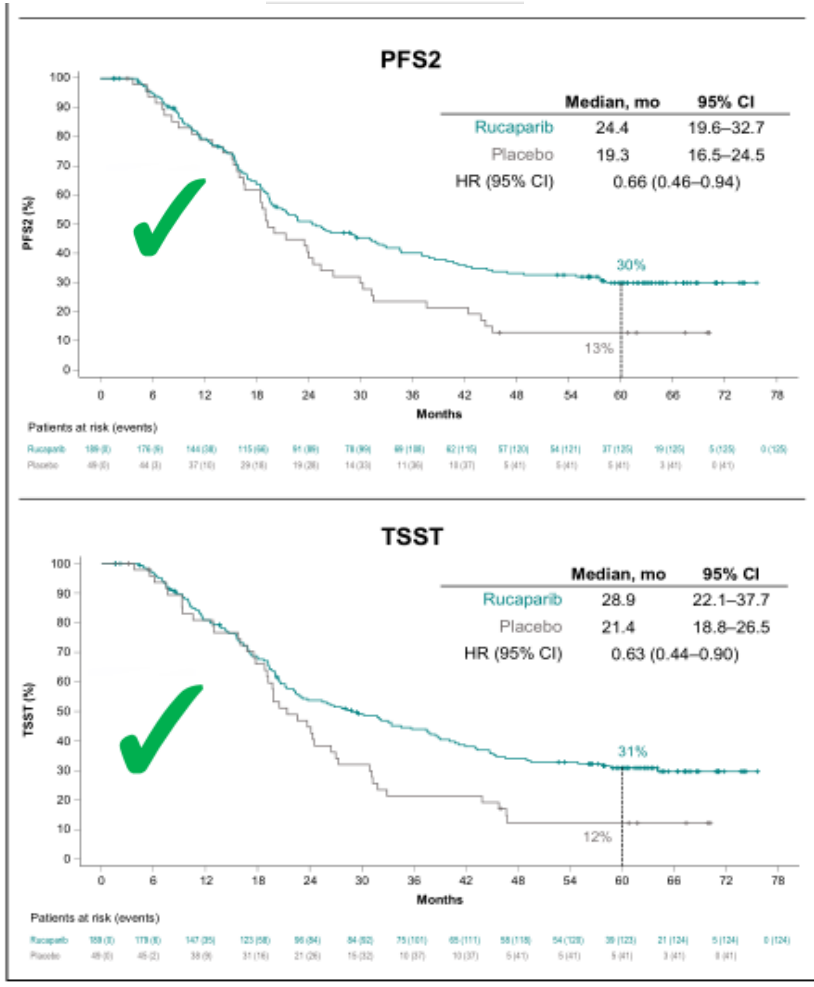
SI iPARP NO IMPACTA EN OS… ¿HAY IMPACTO DE OTROS ENDPOINT SECUNDARIOS?



HRD-negative



HRD-negative



1.Kristeleit RS, Ghamande S et al Poster ESMO 2025. 2. Zagouri F, Diaz JP et al. Poster ESGO2026

LIMITACIONES DEL TEST HRD

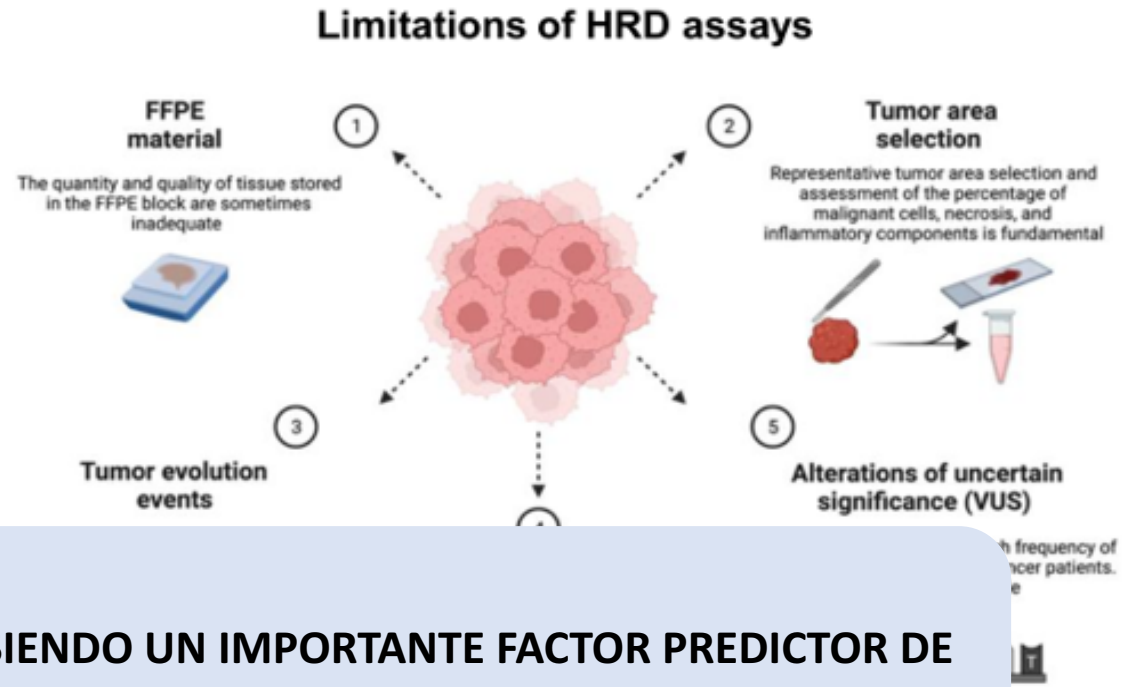
Argumentos

Definición dicotómica.

Calidad de la muestra.

Heterogeneidad intratumoral.

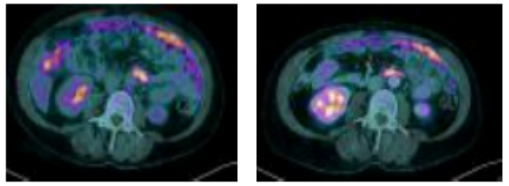
Diferentes punt



LA RESPUESTA AL PLATINO SIGUE SIENDO UN IMPORTANTE FACTOR PREDICTOR DE RESPUESTA A LOS iPARP, ESPECIALMENTE EN LAS PACIENTES HRP

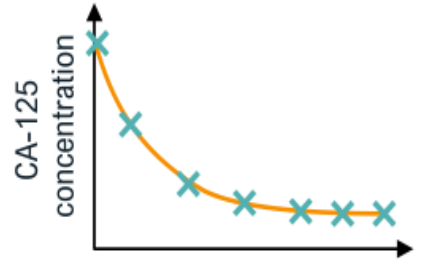
¿CÓMO MEDIR LA PLATINO-SENSIBILIDAD?

Radiological (RECIST)[2]

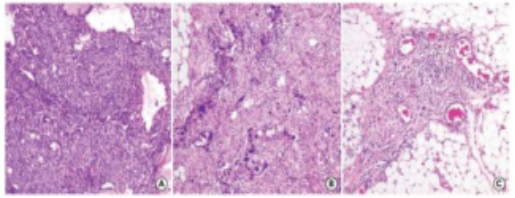


Baseline After 3 cycles

Biochemical CA-125 (KELIM)[4]



Pathological (CRS)[6]



CRS1: No or minimal tumor response

CRS2: Appreciable tumor response amid viable tumor that is readily identifiable

CRS3: Complete or near-complete response with no residual tumor

Symptomatic response[8]

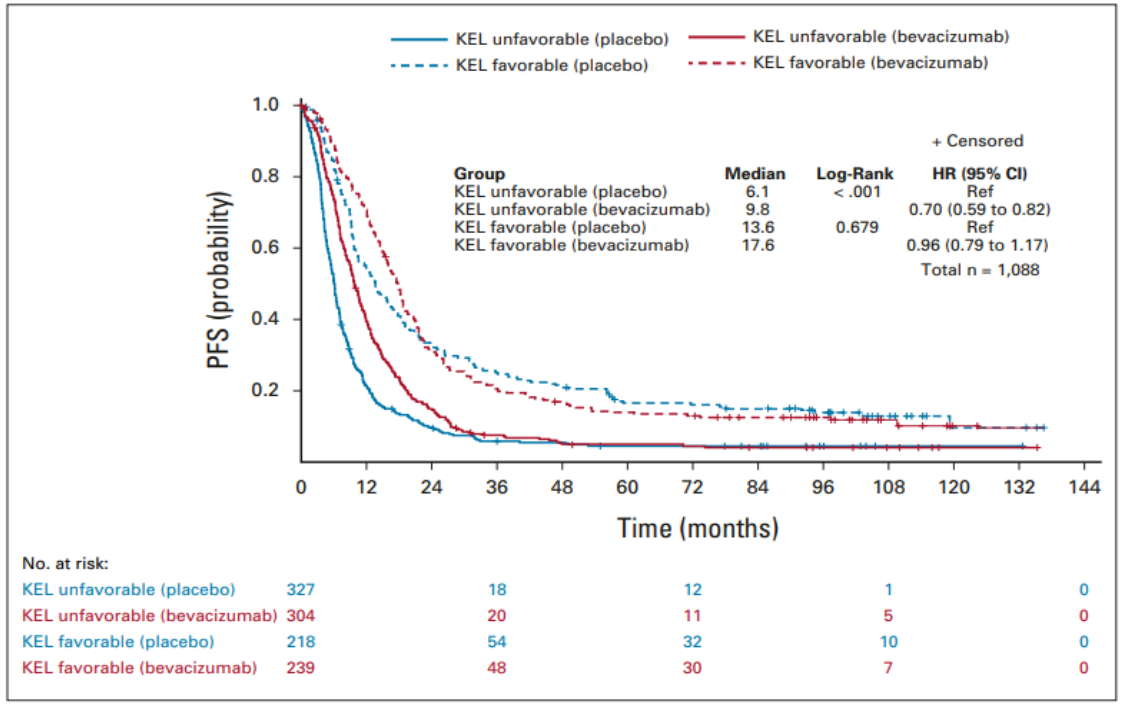
- Radiológica: **RECIST**
- Bioquímica: **KELIM** (mide la cinética de eliminación del CA 125)
- Patológica: **CRS** (exámen histológico del omento tras NACT)
- **Clínica** (ascitis, dolor abdominal, disnea, suboclusión…)

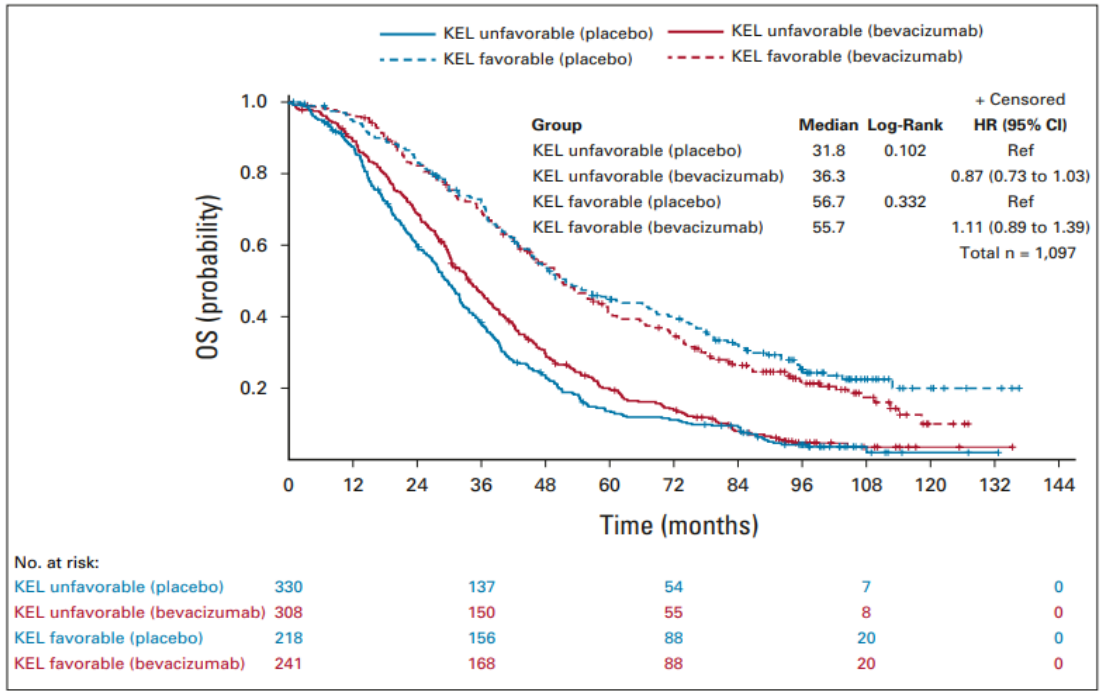
KELIM DEFINE BENEFICIO A BEVACIZUMAB

Identification of Patients With Ovarian Cancer Experiencing the Highest Benefit From Bevacizumab in the First-Line Setting on the Basis of Their Tumor-Intrinsic Chemosensitivity (KELIM): The GOG-0218 Validation Study

No impacto de BEVA en Kelim FAVORABLE

SI en alto riesgo y Kelim DESFAVORABLE (PFS y OS)





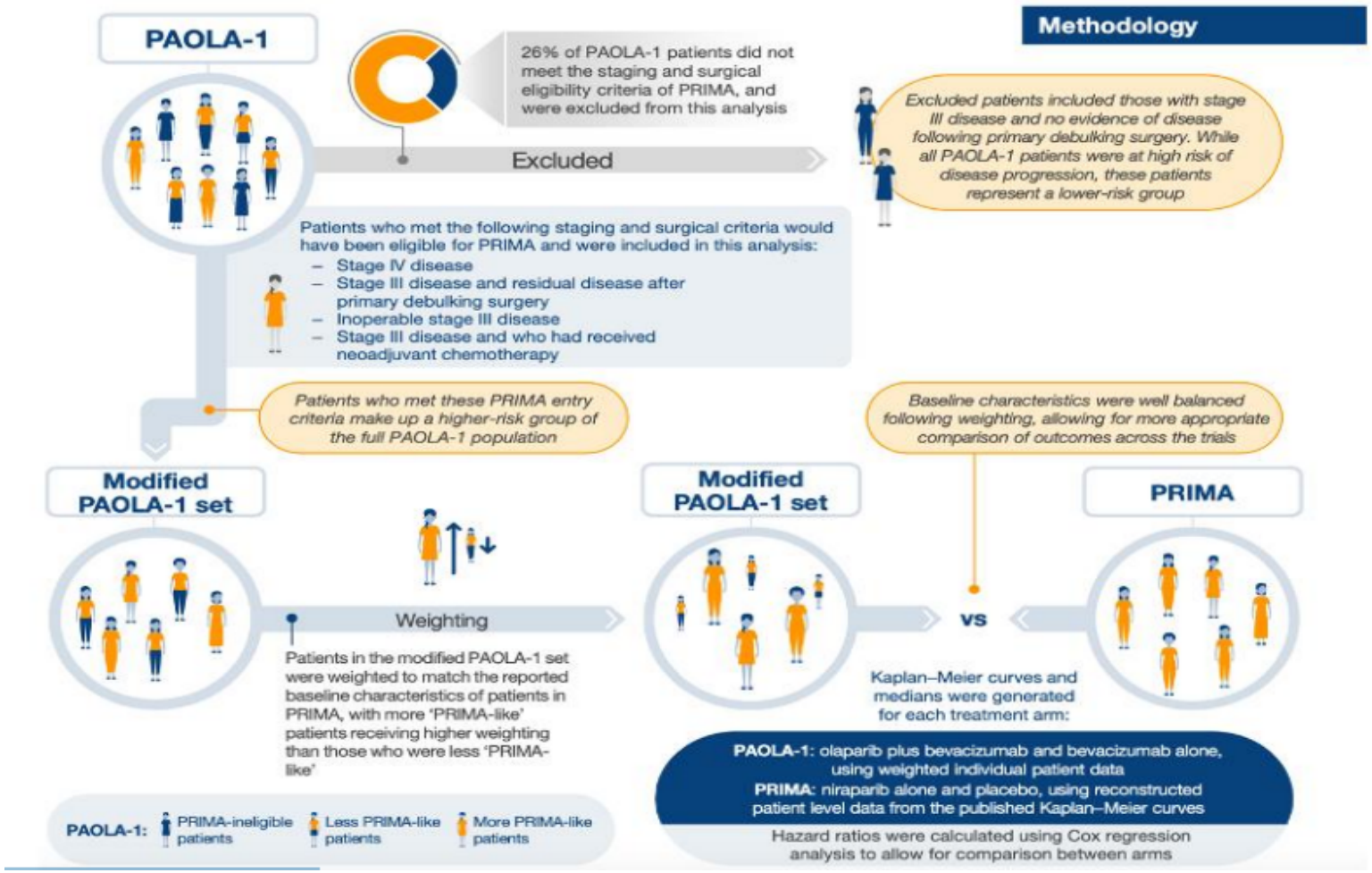
You B, *et al.* J Clin Oncol. 2022;40(34):3965–3974.

COMPARACIONES INDIRECTAS ENTRE ESTUDIOS

COMPARACIONES INDIRECTAS ENTRE ESTUDIOS

Population-adjusted indirect treatment comparison of maintenance PARP inhibitor with or without bevacizumab *versus* bevacizumab alone in women with newly diagnosed advanced ovarian cancer

Robert Hettle, Charles McCrea, Chee Khoon Lee and Richard Davidson



Hettle R, et al. Ther Adv Med Oncol. 2021

COMPARACIONES INDIRECTAS ENTRE ESTUDIOS

Population-adjusted indirect treatment comparison of maintenance PARP inhibitor with or without bevacizumab *versus* bevacizumab alone in women with newly diagnosed advanced ovarian cancer

Robert Hettle, Charles McCrea, Chee Khoon Lee and Richard Davidson

Niraparib vs placebo:
Beneficio a favor de NIRA en todos los subgrupos.

Niraparib vs Beva:
SI beneficio de Nira en HRD+
NO diferencias en pacientes HRP/no seleccionadas

Unadjusted-anchored ITC of PFS for niraparib versus bevacizumab in the HRD-negative population

	Hazard ratio (95% confidence interval)		
Comparison	HRD-negative	Biomarker-unselected (including HRD-negative, HRD-positive and HRD-unknown/missing)*	HRD-positive*
Placebo plus bevacizumab *versus* placebo	0.55 (0.43–0.70)†	0.55 (0.43–0.70)	0.58 (0.41–0.83)
Niraparib *versus* placebo	0.68 (0.49–0.94)‡	0.59 (0.47–0.74)	0.41 (0.29–0.58)
Niraparib *versus* placebo plus bevacizumab	1.24 (0.82–1.86)§	1.07 (0.87–1.32)	0.70 (0.51–0.97)

Hettle R, et al. Ther Adv Med Oncol. 2021

COMPARACIONES INDIRECTAS ENTRE ESTUDIOS

Systematic Review

Comparative Analysis of Maintenance Treatments in Patients with Newly Diagnosed Advanced Ovarian Cancer After First-Line Platinum-Based Regimens

Lorenzo Gasperoni [1], Luca Cancanelli [2,3], Andrea Ossato [3,4], Luna Del Bono [5], Stefano Vecchia [6], Caterina Fontanella [7], Vera Damuzzo [2,3] and Andrea Messori [8,9,*]

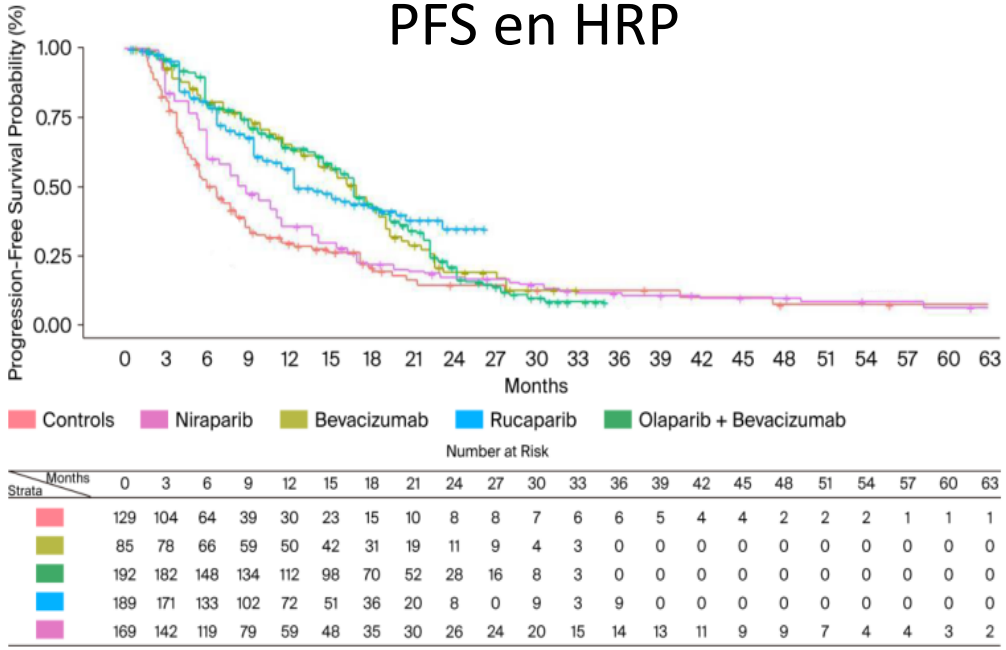
Comparación indirecta a partir de los resultados obtenidos en los estudios **(SOLO1, PRIMA, PAOLA1, ATHENA, FLAMES**).
Objetivo primario PFS

Dos conclusiones principales en HRP:

- La adicción de Olaparib a Beva no aporta beneficio respecto a Beva en monoterapia.

- NO diferencias significativas en PFS entre iPARP y BEVA

PFS en HRP



Gasperoni L, et al. Cancers 2025, 17, 3714

CAMBIO EN LOS PATRONES DE RECAÍDA

ESTUDIO RWE Italia

Patterns of disease distribution and treatment at recurrence

373 PATIENTS Treated with **1L PARPi monotherapy maintenance**

167 PATIENTS **Experienced a recurrence** at the DCO with a median follow-up of 38 months

44.9%
Experienced relapse with **<5 lesions** visualized on [18F]-FDG-PET-CT.

41.2%
Received **local treatment**
- 28 SCS
- 18 SBRT

53.7%
Continued PARPi treatment
- Median duration of extended PARPi administration was **~7 months** (95% CI 3.7-10.3 months)
- No significant difference were seen between radiotherapy and surgery groups.

Oportunidad para **tratamientos LOCALES** (cirugía vs SBRT), aumentar la supervivencia y alargar la terapia de mantenimiento con iPARP.

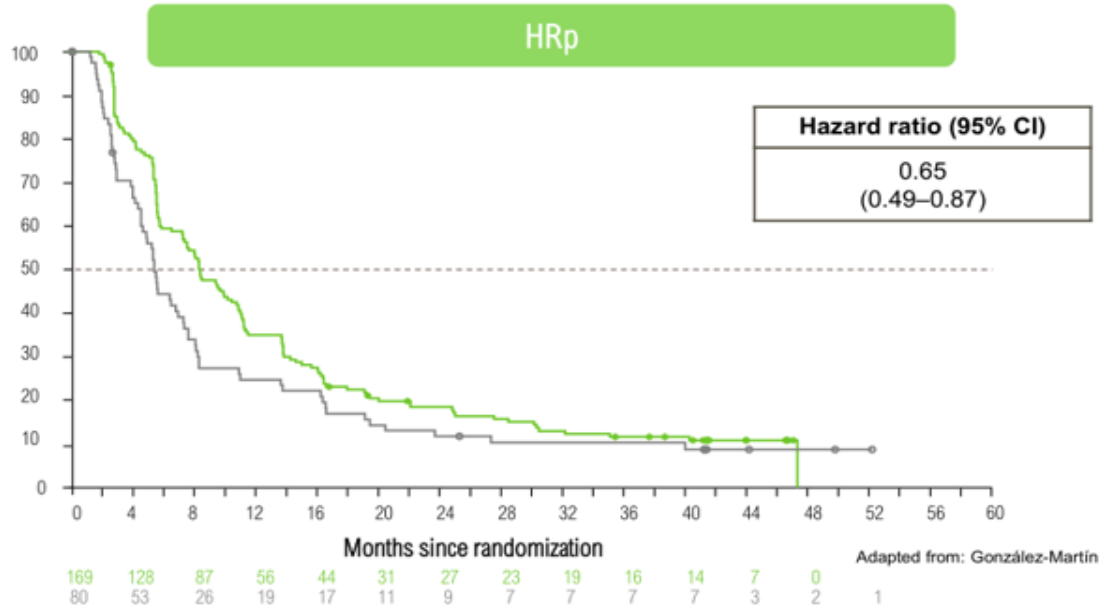
Loverro M, et al. ESMO Open. 2025, Kamrava M, GynOncol, 2024

ESTUDIO PRIMA

	Overall (n=190)	Biomarker status				Disease stage at diagnosis		Type of cytoreductive surgery	
		*BRCA*m (n=44)	*BRCA*wt (n=138)	HRd (n=77)	HRp (n=80)	III (n=119)	IV (n=71)	Primary (n=59)	Interval (n=131)
Median number of new lesions, n (IQR)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–2.5)	2.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–2.0)	1.0 (1.0–2.0)
Number of new lesions, n (%)									
1	96 (50.5)	23 (52.3)	70 (50.7)	40 (51.9)	38 (47.5)	54 (45.4)	42 (59.2)	27 (45.8)	69 (52.7)
2	53 (27.9)	12 (27.3)	37 (26.8)	20 (26.0)	22 (27.5)	37 (31.1)	16 (22.5)	18 (30.5)	35 (26.7)
3	28 (14.7)	5 (11.4)	22 (15.9)	10 (13.0)	16 (20.0)	17 (14.3)	11 (15.5)	8 (13.6)	20 (15.3)
4	9 (4.7)	1 (2.3)	8 (5.8)	4 (5.2)	3 (3.8)	7 (5.9)	2 (2.8)	2 (3.4)	7 (5.3)
5	3 (1.6)	2 (4.5)	1 (0.7)	2 (2.6)	1 (1.3)	3 (2.5)	0	3 (5.1)	0
>5	1 (0.5)	1 (2.3)	0	1 (1.3)	0	1 (0.8)	0	1 (1.7)	0
Location of new lesions, n (%)									
Peritoneum	57 (30.0)	9 (20.5)	48 (34.8)	19 (24.7)	31 (38.8)	35 (29.4)	22 (31.0)	20 (33.9)	37 (28.2)
Lymph nodes	50 (26.3)	11 (25.0)	39 (28.3)	24 (31.2)	20 (25.0)	31 (26.1)	19 (26.8)	20 (33.9)	30 (22.9)
Liver	39 (20.5)	8 (18.2)	28 (20.3)	10 (13.0)	22 (27.5)	27 (22.7)	12 (16.9)	11 (18.6)	28 (21.4)
Other[a]	35 (18.4)	11 (25.0)	21 (15.2)	16 (20.8)	12 (15.0)	23 (19.3)	12 (16.9)	8 (13.6)	27 (20.6)
Pelvis	25 (13.2)	5 (11.4)	18 (13.0)	9 (11.7)	14 (17.5)	19 (16.0)	6 (8.5)	7 (11.9)	18 (13.7)

La mayoría de las pacientes **(93%)** tenía entre **1-3 lesiones** en la primera recaída, con un 50% de las pacientes con 1 única lesión

¿El NO recibir un iPARP en primera línea en la enfermedad HRP una pérdida de oportunidad?



Adapted from: González-Martín A, et al. Eur J Cancer. 2023

Why move PARPi to 1L?

1. The first line may be the only opportunity patients have to receive a PARPi.[2]
2. First-line treatment can prolong the platinum-free interval and increase the likelihood of cure.[3,4]
3. **Safety:** The incidence of MDS/AML with PARPi was described as <2.4% in first-line clinical trials and 1.7-8.0% in relapsed clinical trials.[4,5-9]

Approximately **42% of patients** will never benefit from PARPi activity if they miss their opportunity in the first line. The risk of missing the PARPi benefit in the treatment algorithm is **even higher** in the subgroup of BRCAwt/HRD and **HRP** patients.[2]

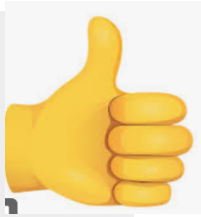
These prespecified subgroup analyses were not sufficiently powered to detect a statistically significant treatment effect; therefore, the results should be interpreted with caution.*Those relapses that occurred during the first 6 months after completion of the last cycle of platinum-based chemotherapy were considered platinum-resistant. Platinum-resistant patients could not receive PARPi-based therapy. **From the placebo arm.

1.Banerjee SN, Lord CJ. First-line PARP inhibition in ovarian cancer – standard of care for all? Nat Rev Clin Oncol. 2020;17(3):136-7. 2.Caruso G, Tomao F, Parma G, et al. Poly (ADP-ribose) polymerase inhibitors (PARPi) in ovarian cancer: lessons learned and future directions. Int J Gynecol Cancer. 2023;33(4):431-43 3. Gupta S, Nag S, Aggarwal S, et al. Maintenance therapy for recurrent epithelial ovarian cancer: current therapies and future perspectives – a review. J Ovarian Res. 2019;12:103. 4. González-Martín A, Pothuri B, Vergote I, et al. Progression-free survival and safety at 3.5 years of follow-up: results from the randomised phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib maintenance treatment in patients with newly diagnosed ovarian cancer. Eur J Cancer. 2023;189:112908. 5.González-Martín A, Pothuri B, Vergote I, et al. Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. 2019;381(25):2391-402. 6.Moore K, Colombo N, Scambia G, et al. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. 2018;379(26):2495-505.7. Monk BJ, Lorusso D, Fujiwara K, et al. A Randomized, Phase III Trial to Evaluate Rucaparib Monotherapy as Maintenance Treatment in Patients With Newly Diagnosed Ovarian Cancer (ATHENA-MONO/GOG-3020/ENGOT-ov45). J Clin Oncol. 2022;40(34):3952-64. 8. Del Campo JM, Birrer M, Fujiwara K, et al. Niraparib Maintenance Therapy in Patients With Recurrent Ovarian Cancer After a Partial Response to the Last Platinum-Based Chemotherapy in the ENGOT-OV16/NOVA Trial. J Clin Oncol. 2019;37(32):2968-73. 9.Poveda A, Floquet A, Ledermann JA, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a final analysis of a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Oncol. 2021;22(5):620-31.

A FAVOR BEVACIZUMAB

- ❑ Beneficio en PFS
- ❑ No beneficio en OS salvo pacientes alto riesgo
- ❑ Kelim desfavorable y alto riesgo
- ❑ Comparaciones indirectas entre estudios

A FAVOR iPARP



- ❑ Beneficio en PFS
- ❑ No beneficio en OS
- ❑ PFS2 positiva para Rucaparib (no para Niraparib)
- ❑ Limitaciones del test HRD
- ❑ Kelim favorable
- ❑ Comparaciones indirectas entre estudios
- ❑ Cambio en el patrón de recidivas
- ❑ Pérdida de oportunidad

DESEMPATE

Ongoing trials will allow a direct comparison of 1L PARPi with and without bevacizumab

NIRVANA-1[5]	AGO-OVAR 28[6]	MITO25[7]
Niraparib ± bevacizumab as maintenance after complete cytoreduction	Niraparib vs niraparib + bevacizumab as maintenance after platinum + bevacizumab	Chemotherapy ± bevacizumab followed by rucaparib maintenance ± bevacizumab or bevacizumab alone

¿QUÉ DEBEMOS TENER EN CUENTA AL ELEGIR UN TRATAMIENTO?

Table 1:

Absorption, distribution, metabolism, and excretion of poly (ADP-ribose) polymerase (PARP) inhibitors

	Enzymes used for metabolism	Effect of PARP inhibitors on other drugs	Effect of other drugs on PARP inhibitors	Effect on renal and hepatic uptake transporters	Pharmacokinetics	Effect with food
Rucaparib[14,27,28]	Is metabolised predominantly by CYP2D6, and by CYP1A2 and CYP3A4 to a lesser extent	Reversibly inhibits CYP1A2, CYP2C19,CYP2C9, and CYP3A; increased area under the curve (ie, total drug exposure overtime) of caffeine, midazolam, warfarin, omeprazole, and digoxin *[29]	No known clinically significant effect	Inhibits MATE1 and MATE2-K (potent effect), and 0CT1 (moderate effect)	Mean half-life=17 h; median time to maximal concentration=1·9 h	Coadministration of a high-fat meal delayed Tmax by 2·5 h and increased area under the curve by 38%, although between-subject variability of the area under the curve and maximum concentration were the same in high-fat intake and fasting groups
Olaparib[30–32]	Is metabolised primarily by CYP3A4	Induces CYP2B6 and inhibits CYP3A *[31]	CYP3A inhibitors increased area under the curve (ie, total drug exposure overtime) in 170% (strong effect) or 121% (moderate effect); CYP3A inducers decreased area under the curve in 87% (strong effect) or 60% (moderate effect)	Inhibits 0ATP1B1, OCT1, OCT2, OAT3, MATE1, and MATE2-K	Mean half-life=14·9 h (tablet) or 11·9 hours (capsule); median time to maximal concentration=1·5 h	Coadministration of a high-fat meal delayedTmax by 2·5 h but did not alter the extent of olaparib absorption
Niraparib[24,33, 34]	Is metabolised by carboxylesterase-catalysed amide hydrolysis (primarily hepatic metabolism)	Has negligible effect on CYP450 enzymest *[33]	No formal drug interaction studies have been performed with niraparib	No known interaction with the major hepatic or renal transporters	Mean half-life=~36 h; median time to maximal concentration=3 h	Coadministration of a high-fat meal did not affect the pharmacokinetics

* Data from clinical studies.

LaFargue CJ et al. Lancet Oncol . 2019 January ; 20(1): e15–e28

	PRIMA Niraparib (n:484)	SOLO 1 Olaparib (n:260)	ATHENA-MONO Rucaparib (n: 427)
Any TEAE, n(%)	99	99	97
Grade≥3 TEAE	73	40	61
Any serious TEAE	27	21	NR
TEAE leading to PARPi treatment discontinuacion	14	12	12
TEAE leading to dose reduction	71	29	49
TEAE leading to treatment interruption	80	53	61

There are no completed direct head-to-head trials of these products. These data are from different clinical trials, and since there are inherent limitations in cross-study comparisons, caution should be exercised in interpreting these data. These data are for information purposes only and are not intended to imply or infer the noninferiority or superiority of either product, in terms of efficacy or safety.

†1. González-Martín A et al. Eur J Cancer. 2023;189:112908. 2. Li N et al. JAMA Oncol. 2023:9:1230-7. 3. DiSilvestro P et al. J Clin Oncol. 2023;41:609-617. 4. González-Martín A et al. Eur J Cancer. 2022; 172:221-231 (Supplementary Appendix).
5. Monk BJ et al. J Clin Oncol. 2022;40:3952-3964. 6. Caruso G et al. Int J Gynecol Cancer. 2023;33:1448–1457.

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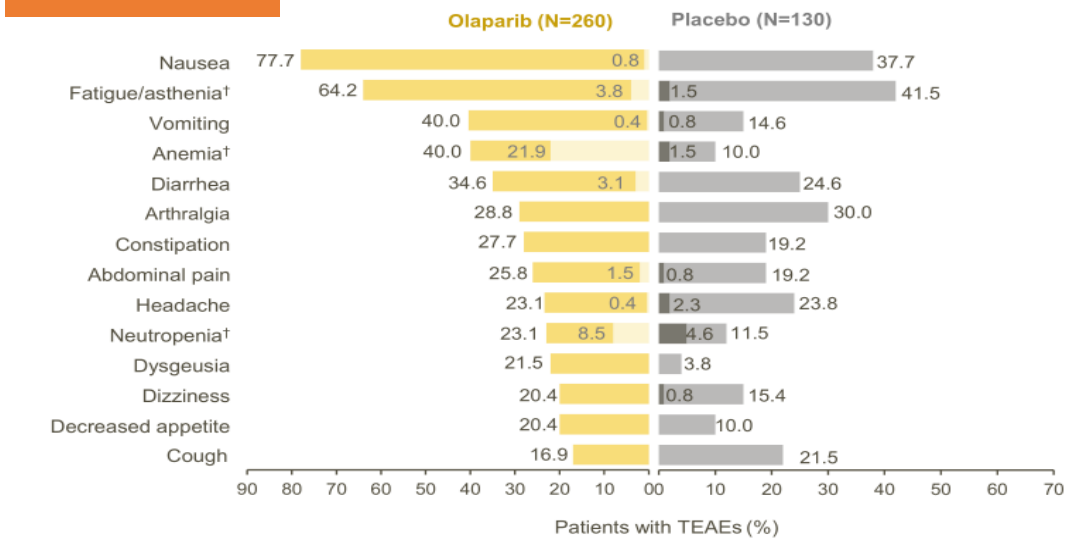
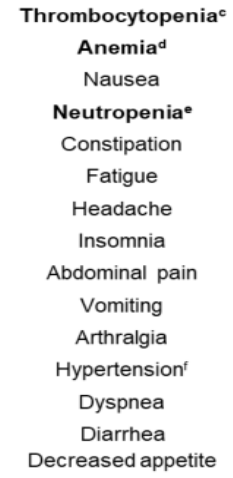
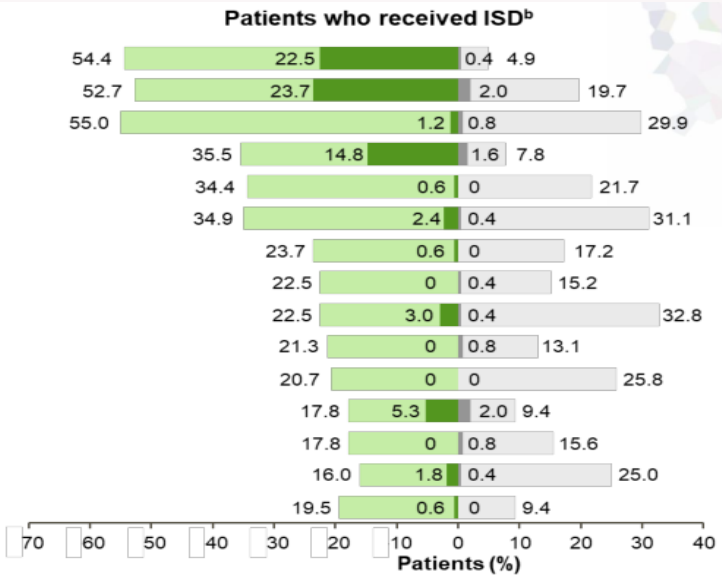
SOLO 1

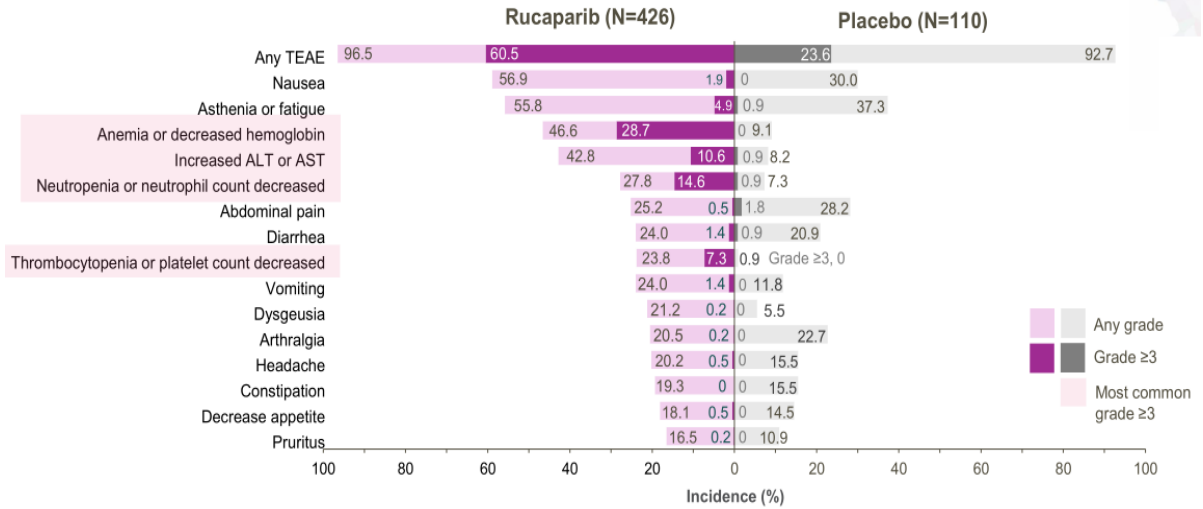




PRIMA ISD



ATHENA-MONO



	OLAPARIB	NIRAPARIB IDS	RUCAPARIB
Anemia, %	40	52	46
Neutropenia,%	23	35	27.8
Trombopenia,%	11	54	23.8
N/V%	78/40	55/21	57/23.5
Diarrea,%	34.6	16	24
Estreñimiento, %	27.7	34	19
Fatiga,%	64	34.9	55.8
HTA,%		18	
↑AST/ALT,%			42

DiSilvestro P, et al.Presented at ESMO 2022; 9–13 Sep; Paris, France. O´Malley DM et al. ASCO Annual Meeting June, 2024;Chicago.Monk BJ et al. Ann Oncol.2024;35:981-92

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REVIEW ARTICLE

Journal of Clinical Pharmacy and Therapeutics · WILEY

Haematologic toxicities with PARP inhibitors in cancer patients: an up-to-date meta-analysis of 29 randomized controlled trials

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Funding information
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Abstract

What is known and ob
emerged as one of the n
cancer. Haematologic t
tors. We conducted a m
PARP inhibitors in canc
Study design: PubMed
till September 2020. Th
tients treated with PARI
performed.
Results: Twenty-nine R
ysis suggests that the
grade anaemia (RR, 2.3
95% CI, 1.38–2.07; $p <$
$p < 0.00001$). The use
grade anaemia (RR, 3.0
95% CI, 1.33–2.07; $p <$
$p < 0.00001$). Anaemia
included PARP inhibitor
Combination treatment
pared to those receiving
What is new and concl
hibitors was associated

KEYWORDS
cancer, haematologic toxic

Exploring and comparing advers
inhibitors

Christopher J LaFargue*, **Graziela Z Dal Molin**
Department of Gynecologic Oncology and Repro
Molin MD, Prof A K Sood MD, Prof R LColeman
Sood), and Center for RNA Interference and Nor
Texas MD Anderson Cancer Center, Houston, T

Abstract

Ovarian cancer remains one of the most challeng
as poly (ADP-ribose) polymerase (PARP) inhibit
treatments for ovarian cancer, particularly in wor
without a functional homologous recombination
characteristic of PARP inhibitors is their mechan
basis of their inherent deficiencies while seeming
health-care providers might assume a low toxicit
action, PARP inhibitors are not completely benig
profile. Further complicating this situation, three
the US Food and Drug Administration since 201
individual toxicity profiles. The diversity of adve
of drug underscores the importance of having a c
decision making when treating patients. This Re
associated with each PARP inhibitor, both in mo
drugs, with a particular focus on potential manag
Although the excitement surrounding P ARP inh
understanding of all associated toxicities is impe
clinical benefit.

Drug Design, Development and Therapy

Open Access Full Text Article

Risk of selected gastrointestinal t
associated with poly (ADP-ribose
(PARP) inhibitors in the treatmen
cancer: a meta-analysis of publishe

This article was published in the following Dove Press journal
Drug Design, Development and Therapy

Yongping Liu
Jun Meng
Guichan Wang

Department of Gynecology, Obstetrics, Yuhuangding Hospital, Yantai, Shandong Province, People's Republic of China

Aims: We aimed to comprehensively assess th
with poly (ADP-ribose) polymerase inhibitors
patients.
Materials and methods: We searched sever
ies included prospective Phase II and III trials o
(olaparib, veliparib, niraparib and rucaparib), de
and constipation. Summary incidence, relative ris
ing fixed- or random-effects models.
Results: A total of 2,286 ovarian cancer patients
results showed that summary incidences of all-g
patients were nausea 68.8% (95% CI, 63.5%–73.6
diarrhea 25.3% (95% CI, 21.2%–29.8%), and con
RRs of all-grade nausea, vomiting, diarrhea, an
$P<0.001$), 2.12 (95% CI: 1.75–2.58; $P<0.001$),
(95% CI: 0.88–1.80; $P=0.21$); respectively. While, the RRs of high-grade nausea, vomiting, diarrhea, and constipation were 3.74 (95% CI: 1.50–9.36; $P=0.005$), 2.81 (95% CI: 1.17–6.74; $P=0.02$), 0.56 (95% CI: 0.22–1.43; $P=0.23$), 0.92 (95% CI: 0.34–2.49, $P=0.87$); respectively.
Conclusion: Our study suggests that the risk of all-grade gastrointestinal toxicities associated with PARPis, excepting constipation, is significantly increased in ovarian cancer patients. And the use of PARPis significantly increased the risk of developing high-grade nausea and vomiting, but not for diarrhea and constipation. Close clinical monitoring is recommended when administering these drugs.

Keywords: poly (ADP-ribose) polymerase inhibitors, gastrointestinal toxicities, clinical trials, meta-analysis, targeted agents, gynaecological tumors, systematic review

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https://doi.org/10.1007/s10555-025-10283-1

REVIEW

Hematological toxicity of parp inhibitors in solid tumors: a systematic review and safety meta-analysis

Brigida Anna Maiorano[1] · Martina Catalano[2] · Mauro Francesco Pio Maiorano[3] · Alessio Signori[4] · Vera Loizzi[3] · Gennaro Cormio[3] · Michele Reni[1,5] · Giandomenico Roviello[2] · Andrea Necchi[1,5]

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Abstract
Poly (ADP-ribose) polymerase (PARP) inhibitors (PARPis) are effective agents in different tumor types. A typical class of adverse events (AEs) associated with these agents, often leadin
ment, is hematological toxicity. In our systematic review and s
of all grades and ≥ grade (G) 3 hematological AEs, including a
leukemia (AML)/myelodysplastic syndrome (MDS) due to PA
with solid tumors. This systematic review and meta-analysis foll
and Meta-Analysis (PRISMA) statement. We systematically sea
American Society of Clinical Oncology, and the European Soci
clinical trials (RCTs) concerning the use of PARPis in patients wi
calculated risk ratios (RRs) for all-grade and ≥ G3 AEs of PARP
Anemia was the most common all-grade (49.2%) and ≥ G3 AE (2
the risk of developing all grades of anemia (RR = 2.15, p < 0.0
cytopenia (RR = 2.59, p < 0.00001) compared to non-PARPis.
(RR = 5.43, p < 0.00001), neutropenia (RR = 1.70, p = 0.002), an
PARPis did not increase the risk of AML/MDS (p = 0.86). PAR
other treatments in solid tumors. Clinicians should be aware of
use in the next year in different tumor types.

Keywords PARP inhibitors · Hematological toxicity · Solid tumo
MCRPC · Ovarian cancer · Breast cancer · Prostate cancer

Giandomenico Roviello and Andrea Necchi share the last authorship.

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cancers · MDPI

Systematic Review

Comparative Analysis of Maintenance Treatments in Patients with Newly Diagnosed Advanced Ovarian Cancer After First-Line Platinum-Based Regimens

Lorenzo Gasperoni [1], Luca Cancanelli [2,3], Andrea Ossato [3,4], Luna Del Bono [5], Stefano Vecchia [6], Caterina Fontanella [7], Vera Damuzzo [2,3] and Andrea Messori [8,9,*]

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Simple Summary

Poly (ADP-ribose) polymerase inhibitors (PARPi) are standard first-line maintenance therapy in advanced ovarian cancer, but their benefit is strongly influenced by BRCA status and homologous recombination deficiency (HRD), and no direct head-to-head trials exist. We performed an indirect comparison using reconstructed individual patient data from Kaplan–Meier curves of phase III studies (SOLO1, PRIMA, PAOLA1, ATHENA, FLAMES). The primary endpoint was progression-free survival (PFS), while overall survival (OS) was exploratory. Subgroups were BRCA−mutated (BRCA+), BRCA−/HRD+, and BRCA−/HRD−. Safety was assessed through a network meta-analysis of adverse events. In BRCA+ patients, the largest PFS benefit was observed with olaparib plus bevacizumab, followed by olaparib monotherapy, while niraparib performed worse. In BRCA−/HRD+ disease, olaparib plus bevacizumab outperformed niraparib and rucaparib, with restricted mean survival time gains of 3–4 months. In BRCA−/HRD− patients, PARPi yielded only modest benefits, showing no advantage over bevacizumab alone. Exploratory OS analysis confirmed durable survival with olaparib in BRCA+ but not in other subgroups. Regarding safety, olaparib demonstrated the most favorable hematologic profile, whereas niraparib was linked to higher rates of severe anemia, thrombocytopenia, and neutropenia, although it showed lower gastrointestinal toxicity and fatigue. In conclusion, PARPi efficacy is highly dependent on BRCA and HRD status: olaparib-based regimens provide the greatest clinical advantage with manageable safety in BRCA+ and HRD+ disease, while their value in HRD-negative ovarian cancer remains limited.

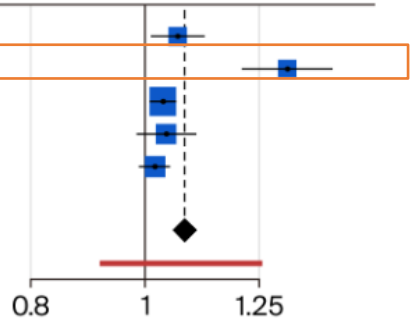
Comparación indirecta de los resultados obtenidos en los estudios fase III **SOLO1, PRIMA, PAOLA1, ATHENA, FLAMES**.

Perfil de seguridad menos favorable para Niraparib. Con mayor toxicidad G≥3

Toxicidad cualquier grado

(A)

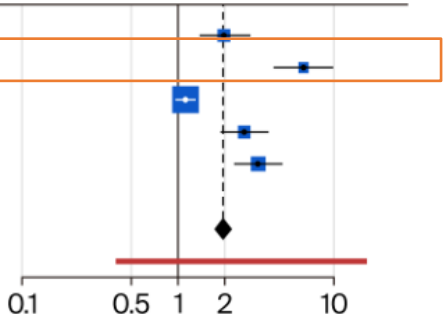
Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	256	260	120	130	16.3%	1.07 [1.01, 1.12]
PRIMA	160	169	175	244	14.6%	1.32 [1.21, 1.44]
PAOLA1	531	535	256	267	34.8%	1.04 [1.01, 1.06]
ATHENA	411	425	102	110	16.5%	104 [0.99, 1.10]
FLATES	269	270	130	133	17.8%	1.02 [0.99, 1.05]



Toxicidad severa G≥3

(B)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	103	260	26	130	11.2%	1.98 [1.36, 2.88]
PRIMA	93	169	21	244	5.5%	6.39 [4.16, 9.84]
PAOLA1	306	535	137	267	58.9%	1.11 [0.97, 1.28]
ATHENA	257	425	25	110	12.8%	2.66 [1.87, 3.79]
FLATES	179	270	27	133	11.7%	3.27 [2.31, 4.62]



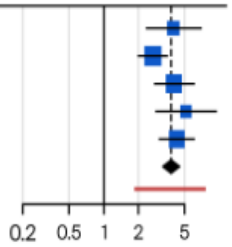
Gasperoni L, et al. Cancers 2025

- **Las toxicidades hematológicas son las más frecuentes** (anemia y trombocitopenia)
- **Olaparib** demostró un perfil de toxicidad hematológica más favorable (neutropenia y trombopenia) que Nira y Ruca.

Anemia

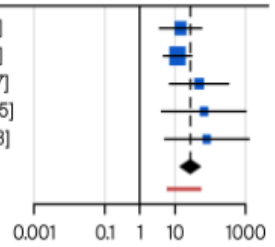
(A)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	104	260	13	130	12.2%	4.00 [2.34, 6.84]
PRIMA	89	169	48	244	27.7%	2.68 [2.00, 3.58]
PAOLA1	219	535	27	267	25.4%	4.05 [2.79, 5.87]
ATHENA	198	425	10	110	11.2%	5.12 [2.81, 9.33]
FLATES	218	270	25	133	23.6%	4.30 [3.00, 6.14]



(B)

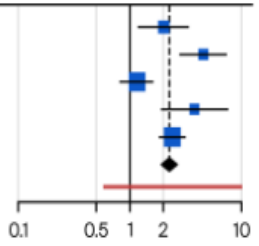
Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	57	260	2	130	27.9%	14.25 [3.53, 57.45]
PRIMA	40	169	5	244	42.8%	11.55 [4.66, 28.66]
PAOLA1	94	535	1	267	14.0%	46.91 [6.58, 334.67]
ATHENA	122	425	0	110	8.3%	63.84 [4.00, 1018.35]
FLATES	79	270	0	133	7.0%	78.62 [4.91, 1258.18]



Neutropenia

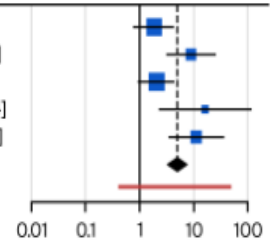
(C)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	60	260	15	130	12.5%	2.00 [1.18, 3.38]
PRIMA	60	169	19	244	9.7%	4.56 [2.83, 7.35]
PAOLA1	98	535	42	267	34.9%	1.16 [0.84, 1.62]
ATHENA	118	425	8	110	7.9%	3.82 [1.93, 7.57]
FLATES	206	270	42	133	35.0%	2.42 [1.87, 3.13]



(D)

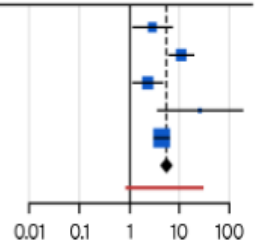
Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	22	260	6	130	29.0%	1.83 [0.76, 4.41]
PRIMA	25	169	4	244	11.9%	9.02 [3.20, 25.46]
PAOLA1	33	535	8	267	38.7%	2.06 [0.96, 4.39]
ATHENA	62	425	1	110	5.8%	16.05 [2.25, 114.44]
FLATES	67	270	3	133	14.6%	11.00 [3.53, 34.32]



Trombocitopenia

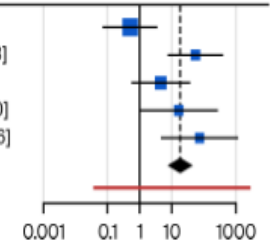
(E)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	29	260	5	130	11.5%	2.90 [1.15, 7.32]
PRIMA	92	169	12	244	16.9%	11.07 [6.27, 19.55]
PAOLA1	42	535	9	267	20.6%	2.33 [1.15, 4.71]
ATHENA	101	425	1	110	2.7%	26.14 [3.69, 185.30]
FLATES	189	270	21	133	48.3%	4.43 [2.97, 6.61]



(F)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	2	260	2	130	42.5%	0.50 [0.07, 3.51]
PRIMA	38	169	1	244	13.0%	54.86 [7.61, 395.73]
PAOLA1	9	535	1	267	21.2%	4.49 [0.57, 35.27]
ATHENA	30	425	0	110	12.6%	15.89 [0.98, 257.90]
FLATES	72	270	0	133	10.7%	71.70 [4.48, 1148.36]



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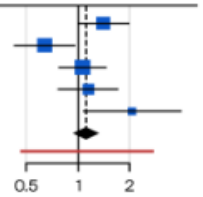
- **Toxicidad GI es menos frecuente** que la hematológica.
- **Niraparib** demostró un perfil más favorable para la toxicidad digestiva y la fatiga/astenia respecto a Ola y Ruca.

Diarrea

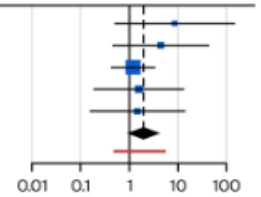
(A)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	90	260	32	130	20.9%	1.41 [1.00, 1.98]
PRIMA	27	169	61	244	24.5%	0.64 [0.42, 0.96]
PAOLA1	98	535	46	267	30.1%	1.06 [0.77, 1.46]
ATHENA	102	425	23	110	17.9%	1.15 [0.77, 1.71]
FLATES	42	270	10	133	6.6%	2.07 [1.07, 3.99]



(B)

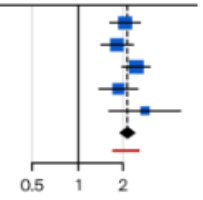
Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	8	260	0	130	6.0%	8.53 [0.50, 146.69]
PRIMA	3	169	1	244	7.4%	4.33 [0.45, 41.29]
PAOLA1	12	535	5	267	60.2%	1.20 [0.43, 3.36]
ATHENA	6	425	1	110	14.3%	1.55 [0.19, 12.77]
FLATES	3	270	1	133	12.1%	1.48 [0.16, 14.07]



Náuseas

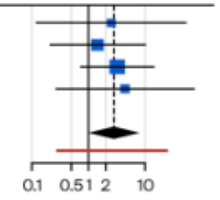
(C)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	202	260	49	130	24.0%	2.06 [1.64, 2.60]
PRIMA	93	169	73	244	21.9%	1.84 [1.45, 2.33]
PAOLA1	285	535	58	267	28.4%	2.45 [1.93, 3.12]
ATHENA	239	425	33	110	19.3%	1.87 [1.39, 2.52]
FLATES	74	270	13	133	6.4%	2.80 [1.62, 4.87]



(D)

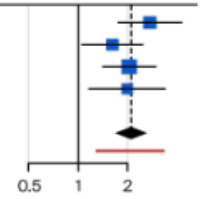
Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	2	260	0	130	11.6%	2.51 [0.12, 51.89]
PRIMA	2	169	2	244	28.4%	1.44 [0.21, 10.15]
PAOLA1	13	535	2	267	46.3%	3.24 [0.74, 14.27]
ATHENA	8	425	0	110	13.8%	4.43 [0.26, 76.16]
FLATES	0	270	0	133	0.0%	



Vómitos

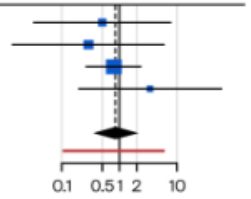
(E)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	104	260	19	130	22.9%	2.74 [1.76, 4.26]
PRIMA	36	169	32	244	23.6%	1.62 [1.05, 2.51]
PAOLA1	119	535	29	267	34.9%	2.05 [1.40, 2.99]
ATHENA	100	425	13	110	18.6%	1.99 [1.40, 3.41]



(F)

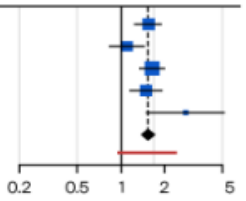
Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	1	260	1	130	12.3%	0.50 [0.03, 7.93]
PRIMA	0	169	2	244	18.9%	0.29 [0.01, 5.97]
PAOLA1	8	535	5	267	61.5%	0.80 [0.26, 2.42]
ATHENA	6	425	0	110	7.3%	3.39 [0.19, 59.67]



Fatiga

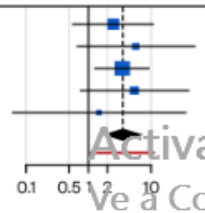
(G)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	167	260	54	130	21.9%	1.55 [1.24, 1.93]
PRIMA	59	169	76	244	18.9%	1.12 [0.85, 1.48]
PAOLA1	284	535	86	267	34.9%	1.65 [1.36, 2.00]
ATHENA	237	425	41	110	19.8%	1.50 [1.16, 1.93]
FLATES	63	270	11	133	4.5%	2.82 [1.54, 5.17]



(H)

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio MH, Fixed, 95% CI
SOLO1	10	260	2	130	24.1%	2.50 [0.56, 11.24]
PRIMA	4	169	1	244	7.4%	5.78 [0.65, 51.22]
PAOLA1	28	535	4	267	48.2%	3.49 [1.24, 9.86]
ATHENA	21	425	1	110	14.3%	5.44 [0.74, 39.97]
FLATES	1	270	0	133	6.0%	1.48 [0.06, 36.17]



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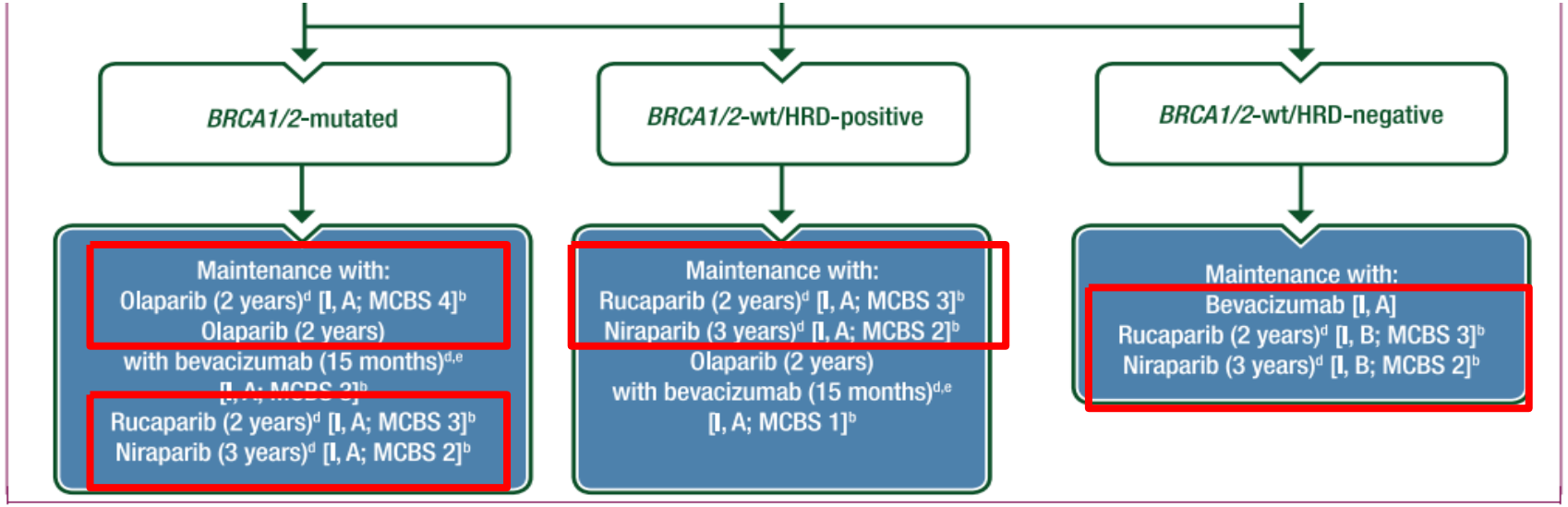

Figure 1. Management of advanced EOC (FIGO stage III-IV).
Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or combination of treatment modalities; white: other aspects of management and non-treatment aspects.
AUC, area under the curve; ChT, chemotherapy; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; ESCAT, ESMO Scale for Clinical Actionability of molecular Targets; FDA, Food and Drug Administration; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PARPi, poly (ADP-ribose) polymerase inhibitor; wt, wild type.
[a]ESCAT scores apply to alterations from genomic-driven analyses only. These scores have been defined by the guideline authors, assisted if needed by the ESMO Precision Medicine Working Group.[7]
[b]ESMO-MCBS v2.0[3] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms).
[c]Weekly ChT with paclitaxel (60 mg/m^2)—carboplatin (AUC 2) can be an alternative in frail patients [I, B].
[d]Only when patients have complete or partial response to platinum or no evidence of disease. For patients without response to platinum, a PARPi is not indicated; these patients can be managed with bevacizumab maintenance if appropriate (mainly stable disease), or with second-line therapy if they have progressive disease (see Figure 3 in the original Clinical Practice Guideline[1]).
[e]Option for patients for whom bevacizumab was added to paclitaxel—carboplatin.

González-Martín A and Ledermann JA. ESMO Clinical Practice Guideline Express Update on the management of epithelial ovarian cancer. ESMO Open. 2026

Mantenimiento con iPARP: ¿Cuándo y cuál?

BRCAm: SI
HRD/BRCAwt: SI
HRP: pacientes seleccionadas

- Tenemos 3 iPARP disponibles como 1L de mantenimiento en COA.
- Todos ellos han demostrado eficacia pero con diferente perfil de toxicidad.
- A la hora de seleccionar un tratamiento u otro hemos de tener en cuenta factores individualizados de cada paciente.
- Es muy importante tener en cuenta las comorbilidades, las posibles interacciones con los tratamientos concomitantes y la toxicidad residual post-quimioterapia.
- Necesitamos biomarcadores que nos ayuden a seleccionar qué pacientes se van a beneficiar más del tratamiento.

GRACIAS

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