19as Jornadas HITOS ONCOLÓGICOS: LO MEJOR DE 2024
MADRID 20 - 21 NOVIEMBRE 2024

Grandes cambios en el tratamiento del cáncer de ovario

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DISCLOSURE SLIDE

- Employment: Hosp. Univ. 12 de Octubre
- Consultant or Advisory Role: Lilly, GSK, Clovis, Astra-Zeneca, Roche, Novartis, Pfizer.
- Research Funding: Tesaro-GSK
- Speaking: Lilly, Roche, Astra-Zeneca, Novartis, Pfizer, GSK, Clovis

GRACIAS

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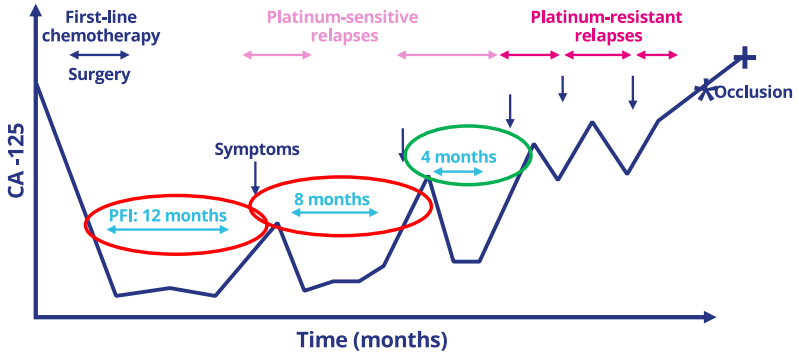
- Introduction.
- New first-line ovarian cancer data.
- Challenges in resistant/refractory ovarian cancer.
- Novel treatment pathways and combinations.
- Conclusions.

Advanced ovarian cancer: a "chronic" disease with multiple relapses

- **Ovarian cancer (OC) is the most lethal gynecologic cancer**
- **324.603 women were diagnosed worldwide with OC in 2022**
- **≥60% of newly diagnosed women will have advanced disease**
- **~70% of women relapse within 3 years of first-line treatment**
- **5-year survival for newly diagnosed advanced OC is about 30-50%**
- **There is a significant need for better treatment to improve outcomes for women with OC**

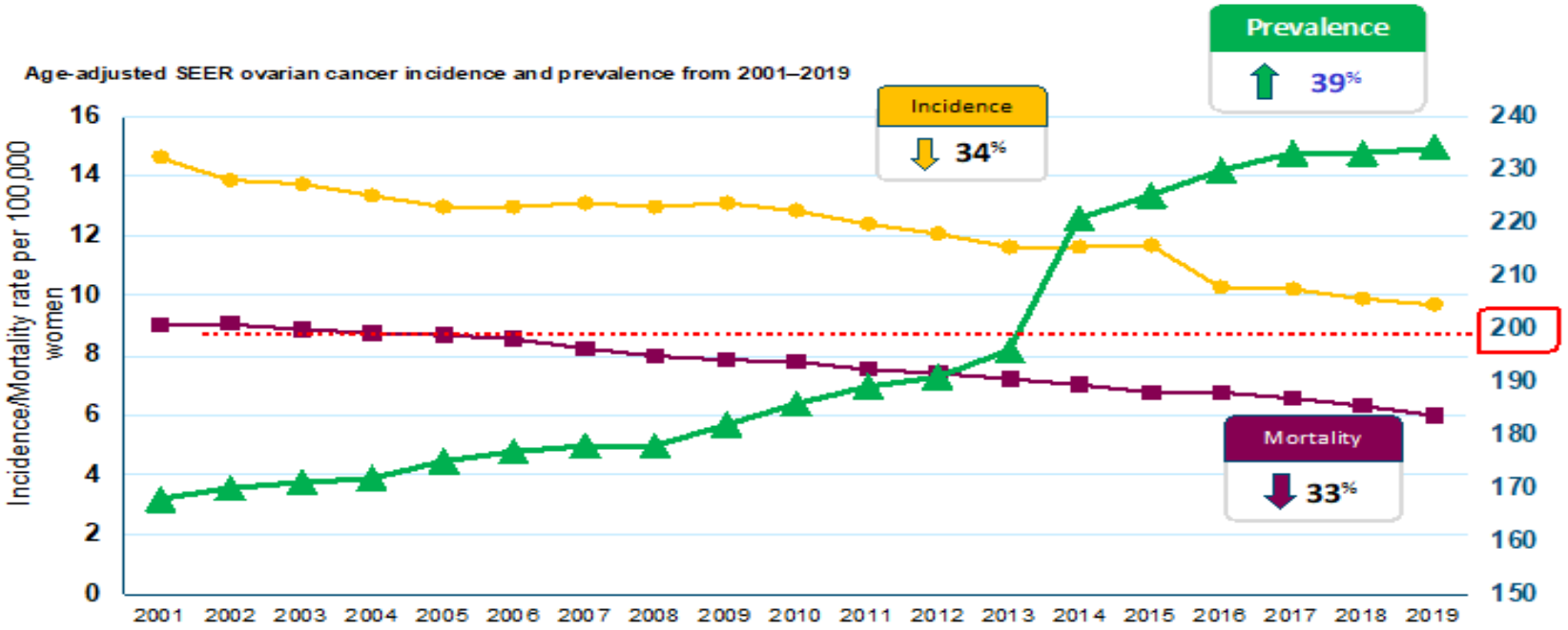


PFI: platinum-free interval or duration of disease control without chemotherapy.

Du Bois a, Pfisterer J. Zentralbl Gynakol. 2004;126:312-4.

Recent ovarian cancer epidemiology

Ovarian Cancer: Clinical Impact



https://seer.cancer.gov/statisticsnetwork/explorer/application.html?site=61&data_type=9&graph_type=2&compareBy=rate_type&chk_rate_type_1=1&chk_rate_type_2=2&chk_rate_type_3=3&hdn_sex=3&race=1&age_range=1&hdn_stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=0&advopt_display=2

Current ESMO 2023 guidelines

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

A. González-Martín[1], P. Harter[2], A. Leary[3], D. Lorusso[4,5], R. E. Miller[6,7], B. Pothuri[8], I. Ray-Coquard[9], D. S. P. Tan[10,11,12,13], E. Bellet[14], A. Oaknin[15] & J. A. Ledermann[16], on behalf of the ESMO Guidelines Committee*

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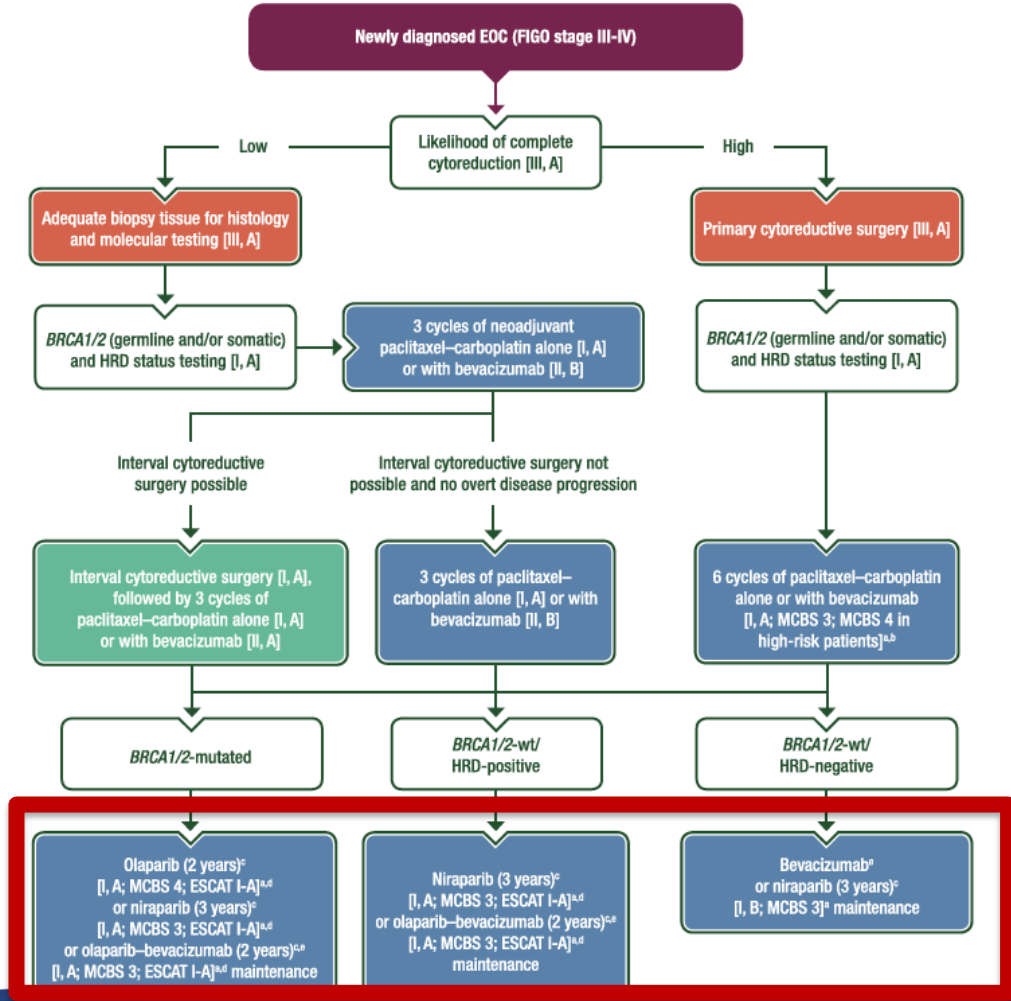
Available online 17 August 2023



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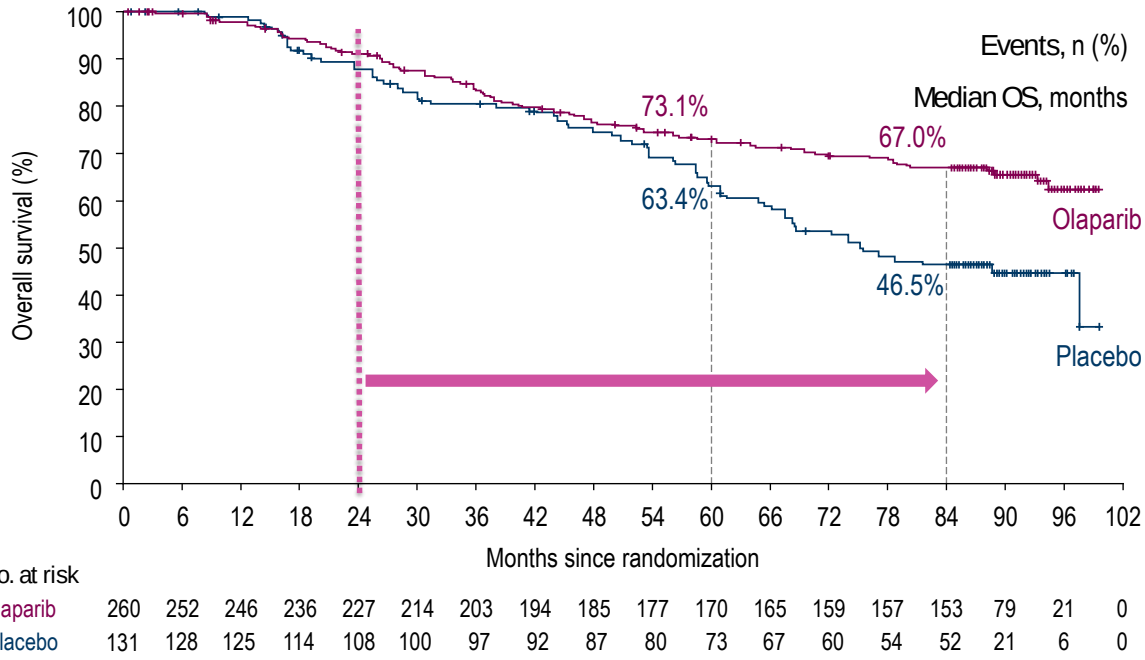
SOLO1 7 Year survival Analysis

Maintenance olaparib provided a clinically meaningful OS benefit



	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*		

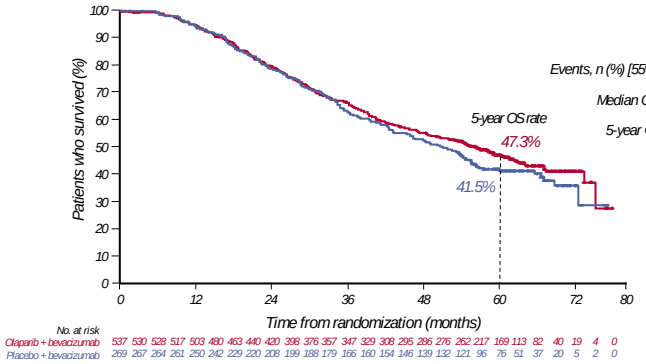
44.3% of patients in the placebo group received subsequent PARP inhibitor therapy, compared with 14.6% of patients in the olaparib group

*$P<0.0001$ required to declare statistical significance

PAOLA 1

Median FUP 61.9 months

OS analysis: ITT population



	Olaparib + bevacizumab (N=537)	Placebo + bevacizumab (N=269)
Events, n (%) [55% maturity]	288 (53.6)	158 (58.7)
Median OS, months	56.5	51.6
5-year OS rate, %	47.3	41.5

HR 0.92 (95% CI 0.76–1.12); P=0.4118

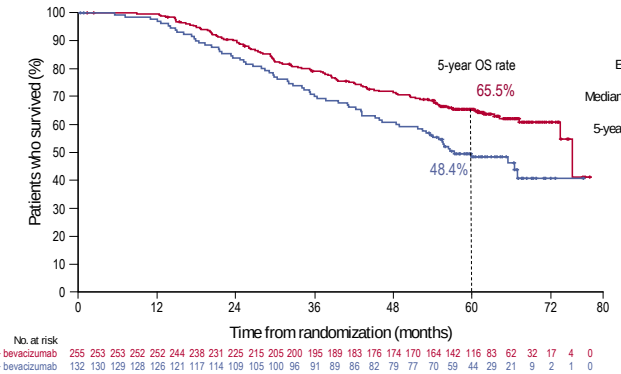
Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: 19.6% (105/537)
Placebo + bevacizumab: 45.7% (123/269)

Median time from first cycle of chemotherapy to randomization = 6 months

PARP, poly(ADP-ribose) polymerase.

Isabelle Ray-Coquard

OS was prolonged in the HRD-positive subgroup



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	93 (36.5)	69 (52.3)
Median OS, months	75.2 (unstable)*	57.3
5-year OS rate, %	65.5	48.4

HR 0.62 (95% CI 0.45–0.85)

38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: 17.3% (44/255)
Placebo + bevacizumab: 50.8% (67/132)

Hospital Universitario 12 de Octubre

i+12 Instituto de Investigación Hospital 12 de Octubre

ESMO

ESMO ANNALS OF ONCOLOGY

ORIGINAL ARTICLE

Niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer: final overall survival results from the PRIMA/ENGOT-OV26/GOG-3012 trial☆

B. J. Monk[1,2*], M. P. Barretina-Ginesta[3,4], B. Pothuri[5,6], I. Vergote[6,7], W. Graybill[8], M. R. Mirza[9,10], C. C. McCormick[11], D. Lorusso[12,13], R. G. Moore[14], G. Freyer[15], R. E. O'Cearbhaill[16,17], F. Heitz[18,19,20], D. M. O'Malley[21], A. Redondo[22], M. S. Shahin[23], C. Vulsteke[24,25], W. H. Bradley[26], C. A. Haslund[27,28], D. M. Chase[29], C. Pisano[12,30], L. L. Holman[31], M. J. Rubio Pérez[4,32], P. DiSilvestro[33], L. Gaba[34], T. J. Herzog[35], I. Bruchim[36,37], N. Compton[38], L. Shtessel[39], I. A. Malinowska[40] & A. González-Martín[3,41]

Final overall survival in patients with newly diagnosed advanced ovarian cancer treated with niraparib first-line maintenance: results from PRIMA/ENGOT-OV26/GOG-3012

Presentation LBA29

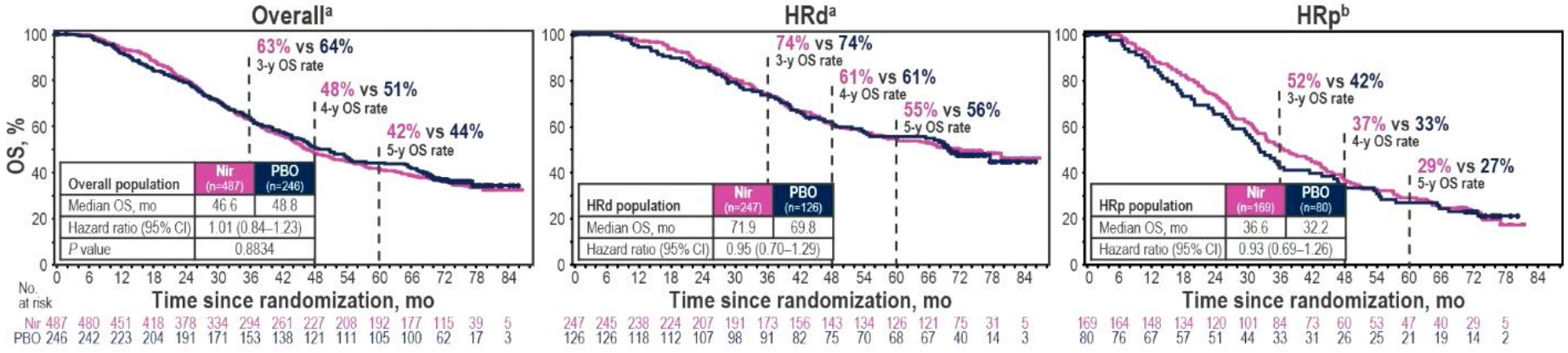
Antonio González-Martín,[1] Bhavana Pothuri,[2] Maria Pilar Barretina-Ginesta,[3] Whitney S. Graybill,[4] Ignace Vergote,[5] Colleen C. McCormick,[6] Mansoor R. Mirza,[7] Richard G. Moore,[8] Domenica Lorusso,[9] Roisin E. O'Cearbhaill,[10] Gilles Freyer,[11] David. M. O'Malley,[12] Florian Heitz,[13] Mark S. Shahin,[14] Ilan Bruchim,[15] William H. Bradley,[16] Natalie Compton,[17] Izabela A. Malinowska,[18] Andrés Redondo,[19] Bradley J. Monk[20]

[1]Medical Oncology Department, Translational Oncology Group, CIMA, Universidad de Navarra, Cancer Center Clínica Universidad de Navarra, and Grupo Español de Investigación en Cáncer ginecológicO (GEICO), Madrid, Spain; [2]Gynecologic Oncology Group (GOG) Foundation and Departments of Obstetrics/Gynecology and Medicine, Division of Gynecologic Oncology, Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [3]Medical Oncology Department, Institut Català d'Oncologia, Girona Biomedical Research Institute (IDIBGI-CERCA), Girona University, Girona, Spain, and GEICO, Spain; [4]Division of Gynecologic Oncology, Medical University of South Carolina, Charleston, SC, USA; [5]University Hospitals Leuven, Leuven Cancer Institute, and Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Leuven, Belgium; [6]Legacy Medical Group Gynecologic Oncology, Portland, OR, USA, when the analysis was conducted; present affiliation, John Hopkins Hospital, Baltimore, MD, USA; [7]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, and Nordic Society of Gynaecologic Oncology-Clinical Trial Unit, Copenhagen, Denmark; [8]Division of Gynecologic Oncology, Wilmot Cancer Institute, Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY, USA; [9]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Catholic University of Sacred Heart, and Multicenter Italian Trials in Ovarian Cancer (MITO), Rome, Italy, when the study (PRIMA) was conducted; present affiliation, Humanitas San Pio X, Milan, Humanitas University, Pieve Emanuele (Milan), Italy; [10]Department of Medicine, Memorial Sloan Kettering Cancer Center, and Weill Cornell Medical College, New York, NY, USA, and GOG Foundation; [11]Centre Hospitalier Lyon-Sud Hospices Civils de Lyon, Oullins-Pierre-Bénite, France; [12]The Ohio State University and James Comprehensive Cancer Center, Columbus, OH, USA; [13]Department of Gynecology and Gynecologic Oncology, Kliniken Essen-Mitte, Essen, Germany, and Department for Gynecology with the Center for the Oncologic Surgery Charité Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; [14]Hanjani Institute for Gynecologic Oncology, Abington Hospital–Jefferson Health, Asplundh Cancer Pavilion, Sidney Kimmel Medical College of Thomas Jefferson University, Willow Grove, PA, USA; [15]Gynecologic Oncology Department, Hillel Yaffe Medical Center, Hadera, Israel, Technion Institute of Technology, Haifa, Israel and Israeli Society of Gynecologic Oncology (ISGO); [16]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Medical College of Wisconsin, Milwaukee, WI, USA; [17]Compton Statistical Consulting Limited, Westerham, UK; [18]GSK, Waltham, MA, USA; [19]Hospital Universitario La Paz – IdiPAZ, Madrid, Spain; [20]GOG Foundation, Philadelphia, PA, USA; Florida Cancer Specialists and Research Institute, West Palm Beach, FL, USA.

Available online 14 September 2024

Final OS (62.5% maturity in overall population)

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

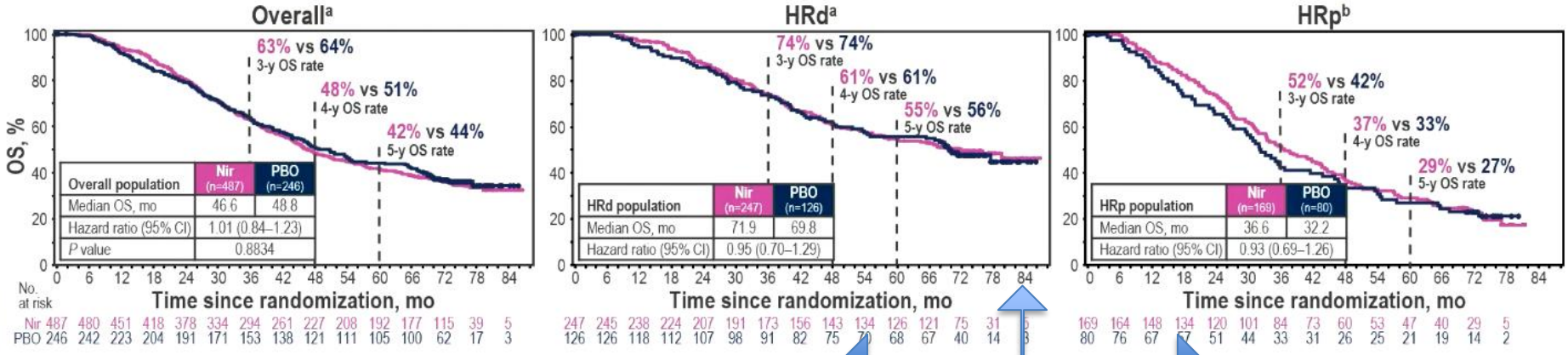


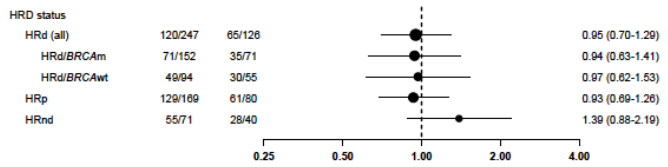
Available online 14 September 2024

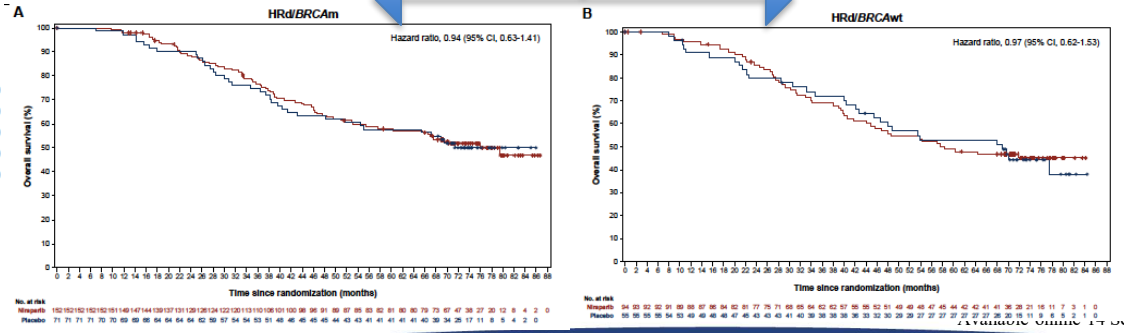
PRIMA

Final OS (62.5% maturity in overall population)

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

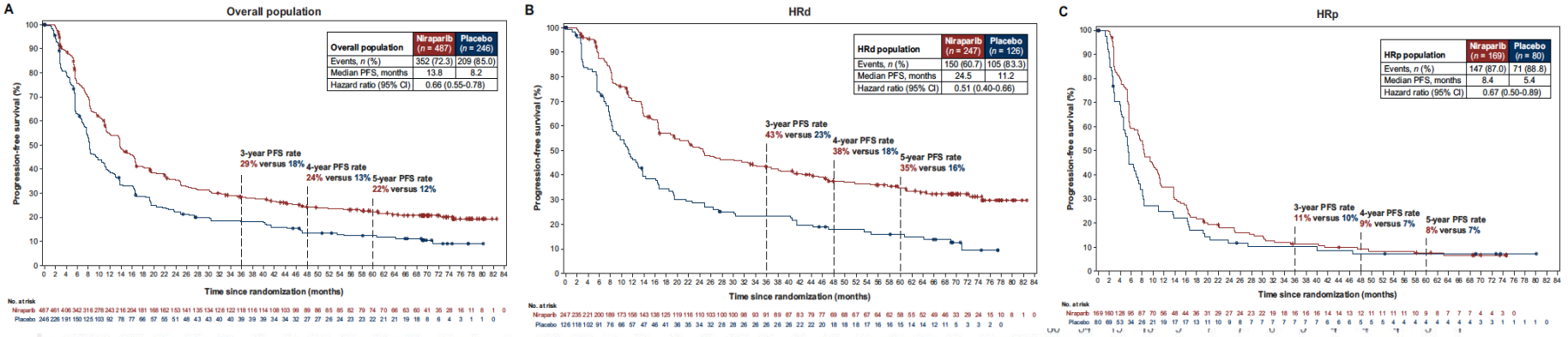






Updated long-term PFS (ad hoc, investigator-assessed)[a,b]

Niraparib PFS benefit sustained with additional follow-up in the overall and HRd populations

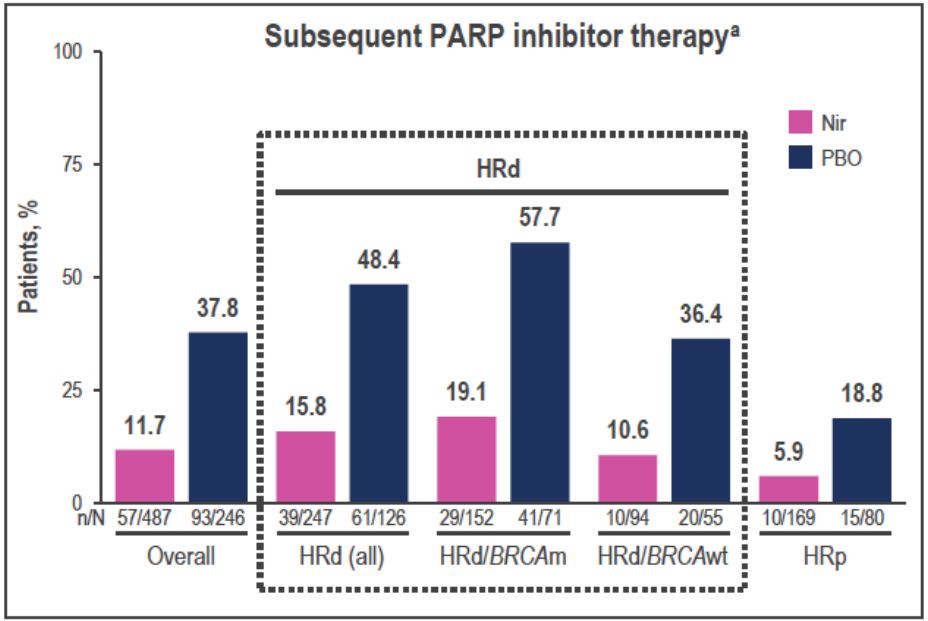


- Data cutoff date, 8 April 2024; median follow-up, 6.2 years
- Among patients alive at 5 years in the HRd population, patients who received niraparib were twice as likely to be progression free (35%) than patients who received placebo (16%)
- Delaying progression is critical to maintain health-related quality of life[1]

[a]At study start, patients were monitored for disease progression (CT/MRI) every 12 weeks (3 cycles); in August 2019, the protocol was amended to monitor patients who stayed on study treatment for more than 2 years for disease progression every 24 weeks (6 cycles).
[b]PFS hazard ratios and associated 95% CI calculated using stratified Cox proportional hazards model. For all analyses, stratification factors were those used in randomization. CT, computed tomography; HRd, homologous recombination deficient; HRp, homologous recombination proficient; MRI, magnetic resonance imaging; Nir, niraparib; PBO, placebo; PFS, progression-free survival. 1. Chase DM, et al. *Gynecol Oncol* 2022;166(3):494–502.

Available online 14 September 2024

Subsequent PARP inhibitor therapy



Subsequent PARP inhibitor use

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

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

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

Available online 14 September 2024

Recommendation

- Maintenance treatment with PARPis, with or without bevacizumab, is recommended for patients with tBRCAm or HRD positive tumours with no evidence of disease at the end of ChT or a complete or partial response to platinum paclitaxel first-line ChT [I, A].
- For BRCA1/2-wt/HRD-positive: niraparib for 3 years [ESMO-MCBS v1.1 score: 3; ESCAT score: I-A] or olaparib-bevacizumab for 2 years [ESMO-MCBS v1.1 score: 3; ESCAT score: I-A).
- **NB** recently Rucaparib for 2 years received full approval from EMA and can be considered as well

ATHENA-MONO

Recommendation

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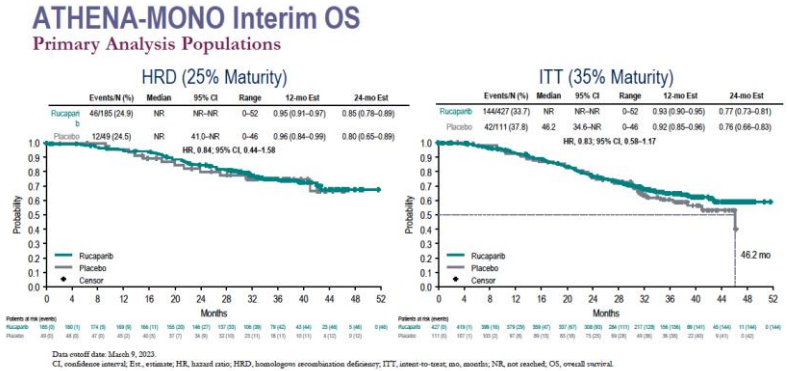

Data cutoff date: March 9, 2023.
CI, confidence interval; Est., estimate; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; mo, months; NR, not reached; OS, overall survival.

Rebecca Kristeleit SGO 2024

AEs of special interest MDS/AML/LA

		Primary PFS analysis		Intermediate analysis		Final OS analysis	
		PARPi arm	Placebo +/- bevacizumab	PARPi arm	Placebo +/- bevacizumab	PARPi arm	Placebo +/- bevacizumab
PAOLA1	MDS/AML/AA, n (%)	6 (1.1)	1 (0.4)	7 (1.3)	4 (1.5)	9 (1.7%)	6 (2.2%)
	New primary malignancies, n (%)*	7 (1.3%)	3 (1.1%)	13 (2.4%)	5 (1.9%)	22 (4.1%)	8 (3.0%)
SOLO1	MDS/AML/AA, n (%)	3 (1.2)	0	3 (1)	0 (0)	4 (1.5%)	1 (0.8%)
	New primary malignancies, n (%)*	5 (1.9)	3 (2.3)	7 (3)	5 (4)	14 (5.4%)	8 (6.2%)
PRIMA	MDS/AML/AA, n (%)	1(0.2%)	0 (0)	6 (1.2%)	3 (1.2%)	11 (2.3%)	4 (1.6%)
	New primary malignancies, n (%)*	NR	NR	NR	NR	NR	NR
ATHENA	MDS/AML/AA, n (%)	2 (0.4%)	0 (0)	4 (0.8%)	NR	NR	NR
	New primary malignancies, n (%)*	NR	NR	NR	NR	NR	NR

AE, adverse event; AML, acute myeloid leukaemia; MDS, myelodysplastic syndrome.

Ray-Coquard I *et al.N Engl J Med* 2019;381:2416–28; 2. K Moore NEJM 2019, S BarnerjeeS, et al ESMO 2020, P Di Silvestro JCO 2022, González-Martín A *et al*. *Eur J Cancer*2022;174:221–31, Ray-Coquard et al ANN ONCOL 2023, A Martin Gonzales NEJM 2019, ESMO 2022 Monk et al Ann Oncol 2024, B Monk JCO 2022.

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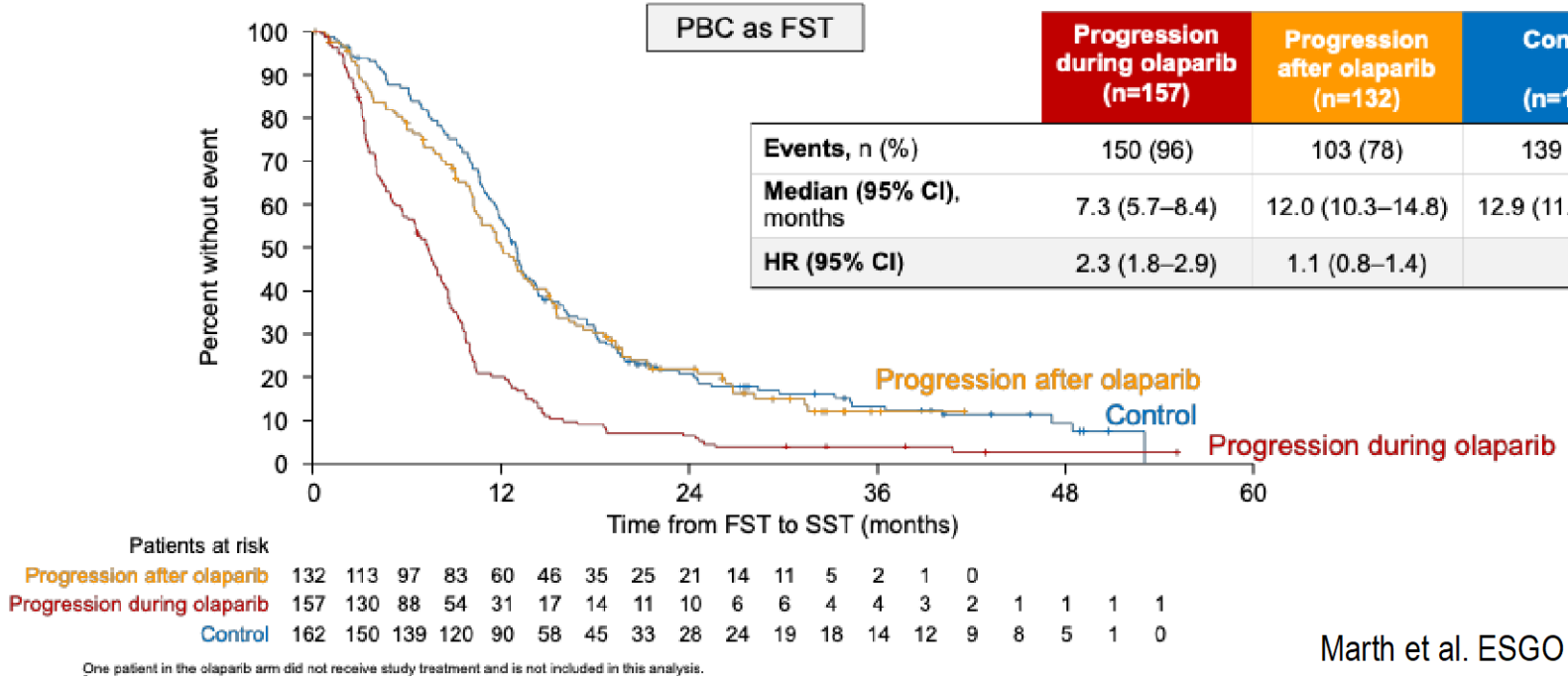
POST-PARPI SPACE

Efficacy of chemotherapy appears to be reduced after progression on PARPi in the retrospective post hoc exploratory analysis of PAOLA-1



	Progression during olaparib (n=157)	Progression after olaparib (n=132)	Control (n=162)
Events, n (%)	150 (96)	103 (78)	139 (86)
Median (95% CI), months	7.3 (5.7–8.4)	12.0 (10.3–14.8)	12.9 (11.8–14.1)
HR (95% CI)	2.3 (1.8–2.9)	1.1 (0.8–1.4)	

One patient in the olaparib arm did not receive study treatment and is not included in this analysis.

Marth et al. ESGO 2023

Harter P. et al. Ann Oncol. 2024 Nov 9

Mirvetuximab soravtansine (MIRV)

MIRASOL (NCT04209855) – Study Design[1,2]

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

Patient Population
(N=453)

Enrollment and Key Eligibility
Platinum-resistant disease
(PFI ≤6 mo)

FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells

High-grade serous histology

1º platinum-refractory disease excluded (primary PFI <3 mo)

1-3 prior lines of therapy

Prior BEV and PARPi allowed

Patients with BRCA mutations allowed

1:1 Randomization

Treatment Regimen-Experimental

MIRV
(6 mg/kg AIBW Q3W)

Treatment Regimen-Control

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

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

Primary Endpoint
PFS by INV
(BICR sensitivity analysis)

Key Secondary Endpoints
1) ORR by INV
2) OS
3) PROs[a]

Secondary Endpoints
Safety and tolerability
DOR
CA-125 response[b]
PFS2

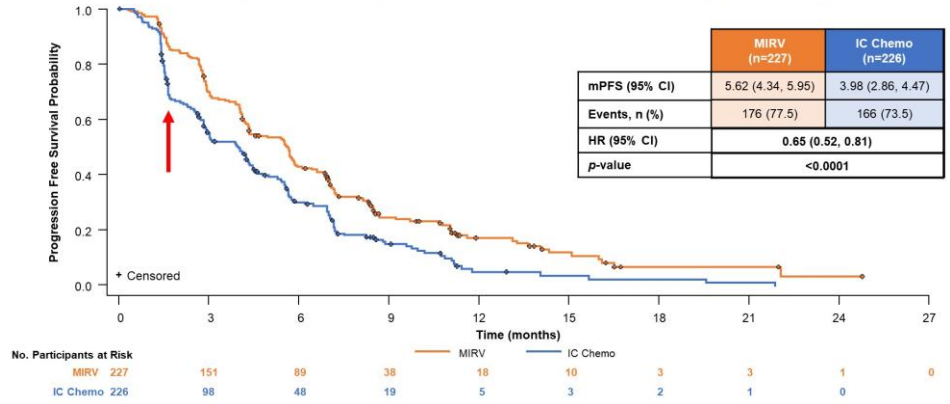
Enrolled patients: 62% prior Bevacizumab, 55% prior PARPi

Moore et al. NEJM 2023; Konecny GE SGO 2024

Mirvetuximab soravtansine (MIRV)

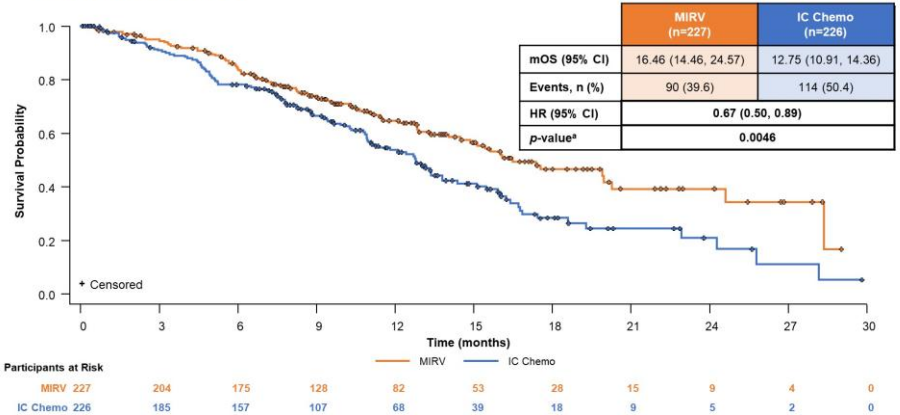
MIRASOL randomized phase III trial

Primary Endpoint: Progression-Free Survival by Investigator



	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
Events, n (%)	176 (77.5)	166 (73.5)
HR (95% CI)	0.65 (0.52, 0.81)	
p-value	<0.0001	

Overall Survival



	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value[a]	0.0046	

↑ **ORR**: MIRV 42% vs Chemo 16%

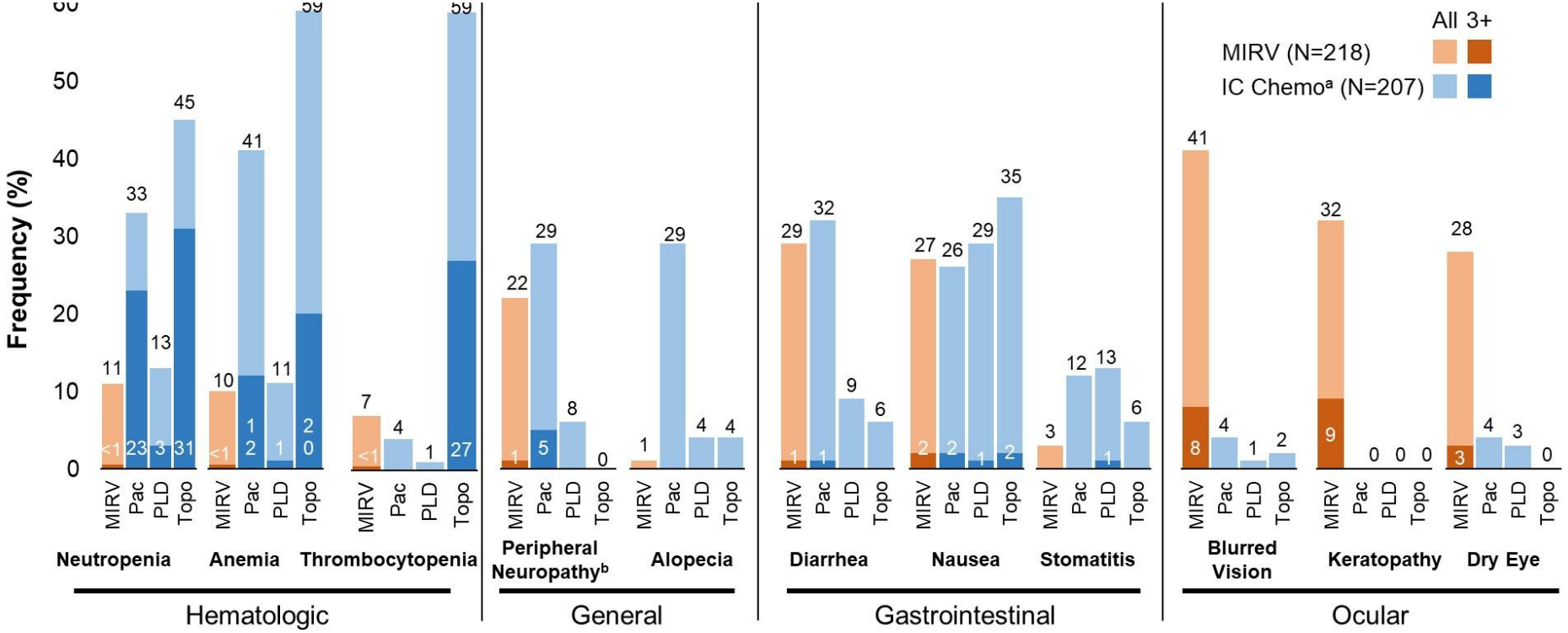
Improved QoL (EORTC QLQ-OV28 GI scale, overall) in the MIRV arm

Efficacy regardless of prior Bevacizumab and PARPi

Moore et al. NEJM 2023; Konecny GE SGO 2024

Mirvetuximab soravtansine (MIRV)

MIRASOL randomized phase III trial: Treatment emergent AEs



Moore et al. NEJM 2023; Konecny GE SGO 2024

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Antigens exploited for ADC development in OC[1]

Reported expression in OC	60–100%	70%	5–60%	55–100%	80–90%	95%	25–100%	70–90%

Some ADCs may only demonstrate efficacy in higher expression levels of the target antigen.[2,3]

1. Chelariu-RaicuA, et al. IntJ GynecolCancer. 2023 2. Moore KN, et al. European Society for Medical Oncology (ESMO) Annual Meeting. 2019; Presentation 992O. 3. Meric-BernstamF, et al. J ClinOncol. 2024.

Targeting Trop2 in Ovarian Cancer: ESMO 2024- First Data Disclosures for TROP2 ADCs

	Sacituzumab tirumotecan (MK-2870) 5mg/kg D1, D15 N=35 (PROC)	Datopotamab deruxtecan N=26 (PROC)	SHR A1921[2] Q 21 day dosing 3.0mg/kg (N=26) Day 1, 8 2.0mg/kg (N=20)
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1- deruxtecan	Topoisomerase 1 (proprietary SHR9265)
DAR	7.4	4	4
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker
Trial	NCT06049212	NCT05489211	NCT05765032
Prior PARPi	NR	51.4%	65.4% 50.0%
Prior Bev	NR	71.4%	76% 60.0%
ORR (PROC)	37.1% (PROC)	34.6% (95% CI 17.2- 55.7)	42.3% (95% CI 23.4-63.1) 58.8% (95% CI 32.9-81.6)
DOR (PROC)	5.3 months (2.1, 24.4+)	5.6 months (2.9-NC)	9.9 months (4.5-NC) 6.3 months (3.0-NC)
mPFS	6.0 months (95% CI 3.9-7.3) (inclusive of PSOC)	5.6 months (inclusive of PSOC)	7.9 (4.2-NR) 6.9 (4.2- 9.6)

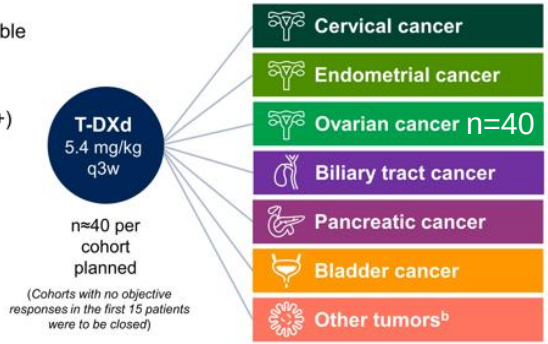
Wang

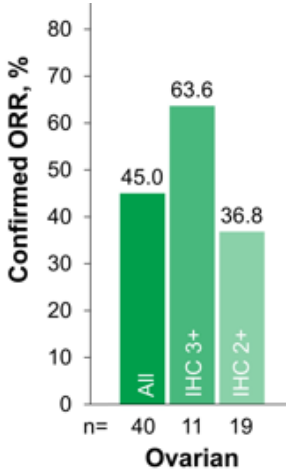
Targeting Trop2 in Ovarian Cancer: Context with other ADCs in PROC

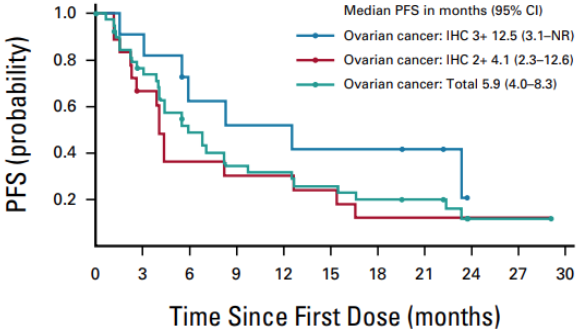
	Sacituzumab tirumotecan 5mg/kg D1, D15 N=35 (PROC)	Datopotamab deruxtecan N=26 (PROC)	SHR A1921[2] Q 21 day dosing 3.0mg/kg (N=26) Day 1, 8 2.0mg/kg (N=20)	Raludotatug deruxtecan Q21 day dosing (N=45)
Target	TROP2	TROP2	TROP2	CDH6
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1-Deruxtecan	Topoisomerase 1 (proprietary SHR9265)	Topoisomerase 1-Deruxtecan
DAR	7.4	4	4	8
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker	Cleavable tetrapeptide based linker
Trial	NCT06049212	NCT05489211	NCT05765032	NCT04707248
ORR (PROC)	37.1%	34.6% (95% CI 17.2-55.7)	42.3% (95% CI 23.4-63.1) 58.8% (95% CI 32.9-81.6)	48.6% (95% CI 31.9-65.6)
DOR (PROC)	5.3 months (2.1, 24.4+)	5.6 months (2.9-NC)	9.9 months (4.5-NC) 6.3 months (3.0-NC)	11.2 months (95%CI 3.1-NE)
mPFS	6.0 months (95% CI 3.9-7.3)	5.6 months (inclusive of PSOC)	7.9 (4.2-NR) 6.9 (4.2- 9.6)	8.1 months (95% CI 5.3-NE)

Destiny Pantumor-02: Phase II T-DXd multi-tumour

- 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







ORR 45% (4 CR, 14 PR), response duration 11.3m (4.1–NR)

FDA accelerated approval for HER2 IHC 3+

Meric-Bernstam et al. JCO 2024

Mirvetuximab Soravtansine (MIRV) in Recurrent Platinum-Sensitive Ovarian Cancer (PSOC) with High Folate Receptor-Alpha (FRα) Expression: Results From the Phase II PICCOLO Trial

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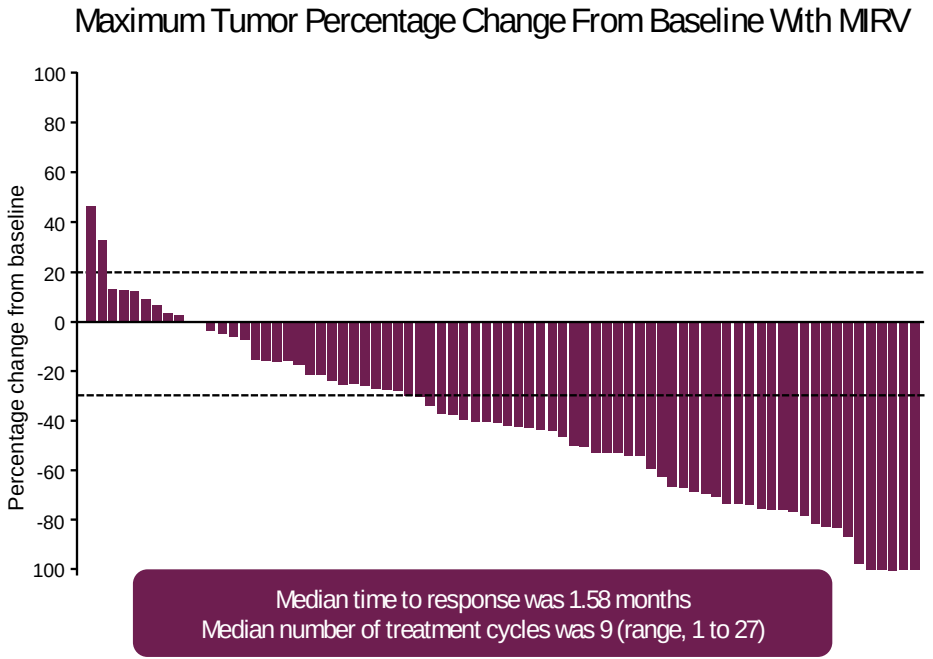
Angeles Alvarez Secord, MD, MHSc

Barcelona, Spain, 15 September 2024

Investigator-Assessed Efficacy Measures



Primary Endpoint	N=79
ORR, n (%) 95% CI	41 (51.9) 40.4-63.3
Best overall response, n (%)	
CR	6 (7.6)
PR	35 (44.3)
SD	29 (36.7)
PD	7 (8.9)
Not evaluable	2 (2.5)

Secondary Endpoints	
Median DOR[a]	n=41
Months (95% CI)	8.25 (5.55-10.78)
Median PFS	N=79
Months (95% CI)	6.93 (5.85-9.59)
CA-125 response[b]	n=47
n (%)	35 (74.5)
95% CI	59.7-86.1

Data cutoff: January 17, 2024.

[a]Calculated among participants who had a complete or partial response. [b]Analysis performed on the CA-125–evaluable population.

CA-125, cancer antigen 125; CI, confidence interval; CR, complete response; DOR, duration of response; MIRV, mirvetuximab soravtansine-gynx; ORR, objective response rate; PFS, progression-free survival; PD, progressive disease; PR, partial response; SD, stable disease.

Baseline Demographics and Characteristics

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Characteristics	N=79
Age, median (range), years	66 (41-84)
Race, n (%)	
White	65 (82.3)
Black or African American	4 (5.1)
Asian	1 (1.3)
Not reported	8 (10.1)
Other	1 (1.3)
Number of prior lines of systemic therapy, n (%)	
1-2[a]	49 (62.0)
[illegible]	30 (37.9)
Prior exposure to taxanes, n (%)	
Yes	77 (97.5)
Exposed in multiple lines	20 (25.3)
No	2 (2.5)

Characteristics	N=79
Prior exposure to PARPi[b],n (%)	
Yes	64 (81.0)
Progression[c]	59 (74.7)
No progression	5 (6.3)
No	12 (15.2)
Prior exposure to bevacizumab, n (%)	
Yes	51 (64.6)
No	28 (35.4)
Most recent platinum-free interval (months)[d], n (%)	
[illegible]	43 (54.4)
>12	34 (43.0)

Of the 302 patients screened, 124 (44%) had ≥75%≥2+ FRα tumor expression

PARPi resistance (75% of participants)

ORR by PARPi Exposure Subgroup

Total population ORR: 51.9% (95% CI, 40.4-63.3)

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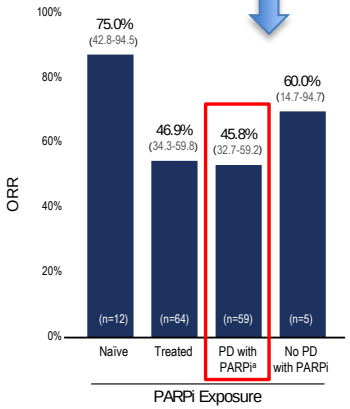

Exposure to PARPis	Median DOR months (95% CI)
Naïve	8.8 (3.5-NR)
Treated	8.3 (5.5-10.8)
PD with PARPi[a]	7.3 (5.0-10.8)
No PD with PARPi	8.4 (7.0-NR)

CONCLUSIONS

- Maintenance therapy with PARP inhibitors in front line has changed the natural history of patients with HGSOC.
- All PARPi reported a clinically meaningful improvement of the PFS in *tBRCA/HRD*+ and an overall survival benefice considering SOLO1 & PAOLA-1 trial.
- HRp population remains the worse prognosis population where new options need to be explored.
- Overall survival is a complex endpoint to reach in 1st line.
- Efficacy of first subsequent platinum-based therapy may be influenced by prior PARPi but prospective and confirmatory data are needed.
- MIRASOL phase III trial demonstrated that MIRV improved PFS, OS, QoL, compared to single agent chemo, in PlatR ovarian cancer.
- ADCs are among the most promising agents across gynaecologic cancers:
  candidates? (role of biomarkers); setting ?(treatment or maintenance); **duration?**; **sequence? (mechanism of resistance)**; **best combo?.**