Beyond PRIMA: Evolving Evidence for Niraparib in 1L Ovarian Cancer Maintenance

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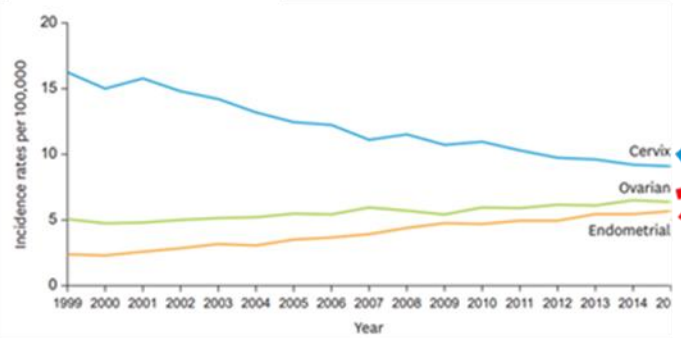
Disclosure

- ✓ I have no conflicts of interest to disclosure.



Introduction

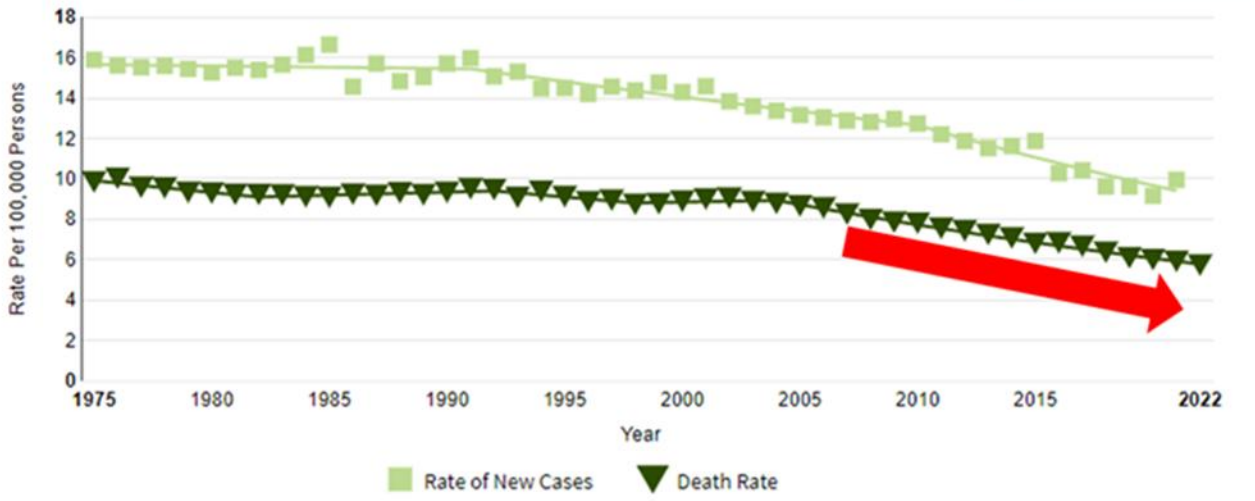
Cancer Incidence and Mortality in Korea 2025



Age-standardized incidence curves between 1999 and 2015 (Korea Central Cancer Registry)

Estimated new cancer cases during 2025 in Korea

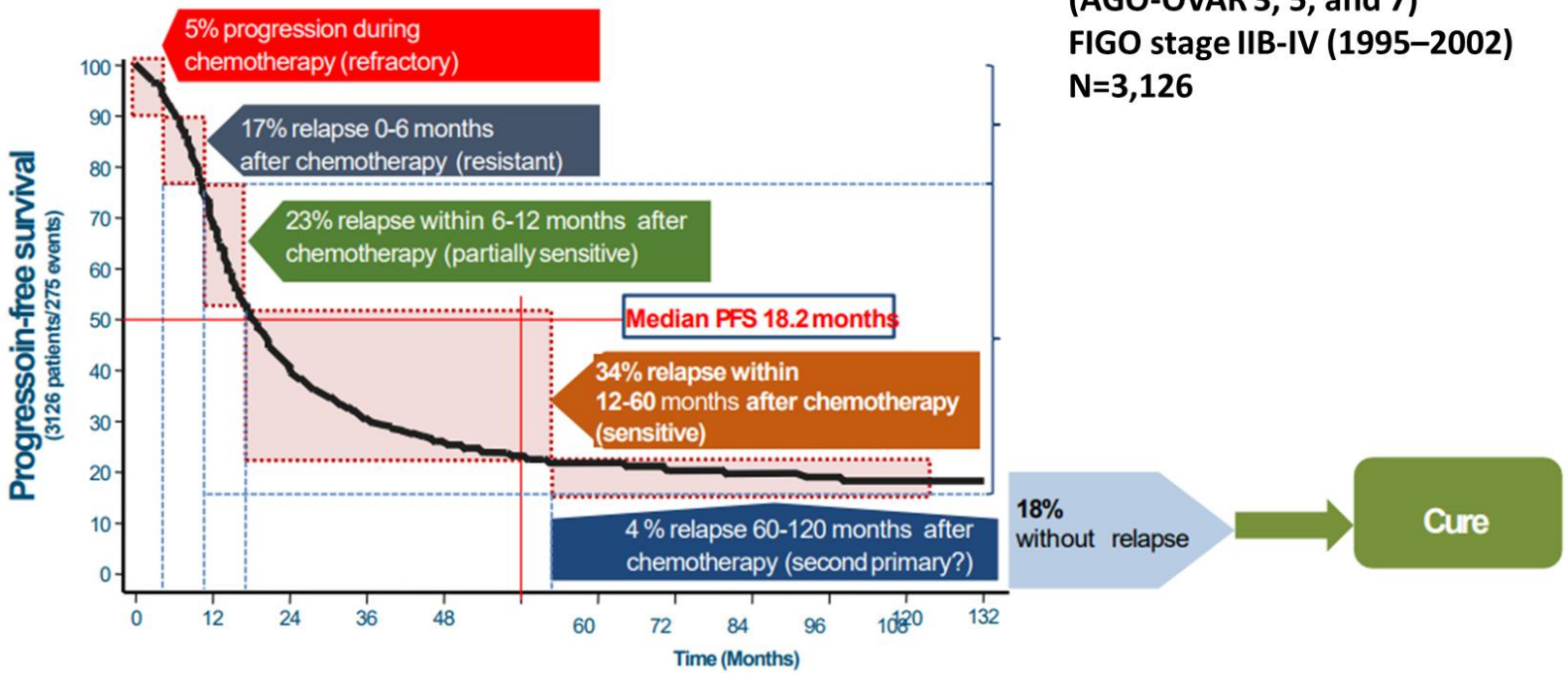
	N
Endometrial cancer	4,348
Ovarian cancer	3,580
Cervical cancer	2,521



New cases come from SEER 8. Deaths come from U.S. Mortality.
All Races, Females. Rates are Age-Adjusted.

Lim MC, et al. J Gynecol Oncol. 2019.
Jung KW, et al. Cancer Res Treat. 2025.

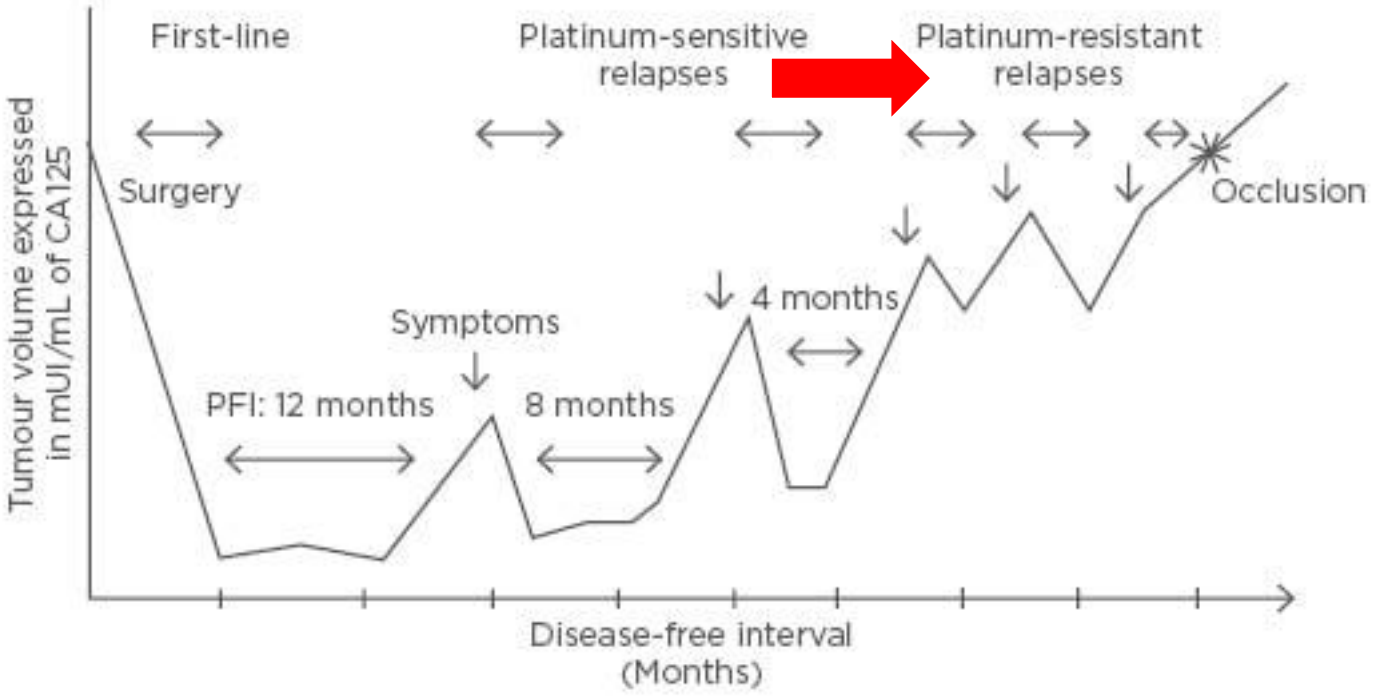
Ovarian cancer: Disease course



- ✓ **Individual patient data of 3 AGO phase III RCTs (AGO-OVAR 3, 5, and 7)**
  FIGO stage IIB-IV (1995–2002)
  N=3,126

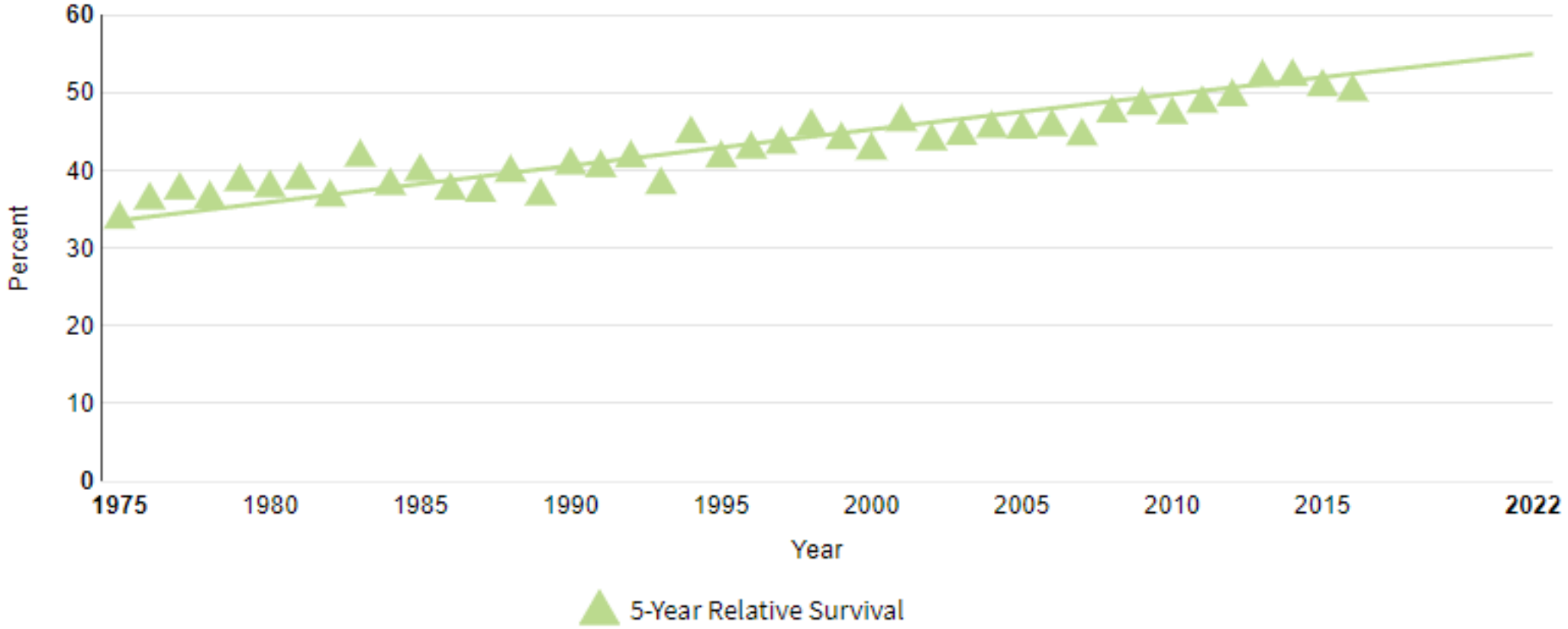
du Bois A, et al. Cancer J Clin. 2009.

Ovarian cancer: Disease course



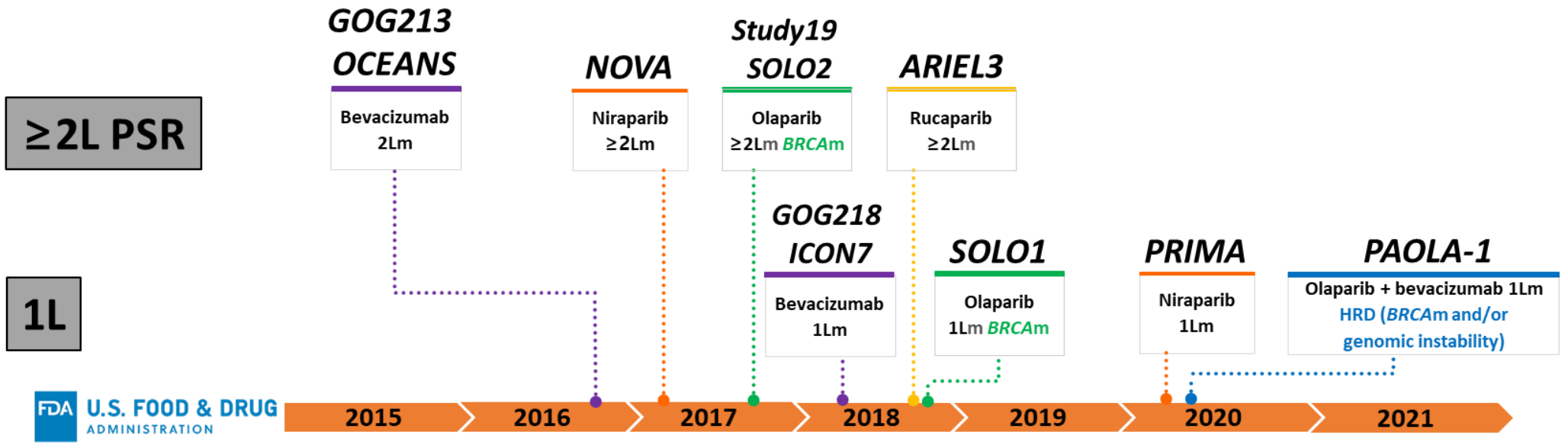
✓ As the disease relapses, treatment-free interval shortens…

Ovarian cancer: Improvement of survival



SEER 8 5-Year Relative Survival Percent from 1975–2016.

Recent advances in ovarian cancer management





Current practice guidelines

Initial treatment of ovarian cancer

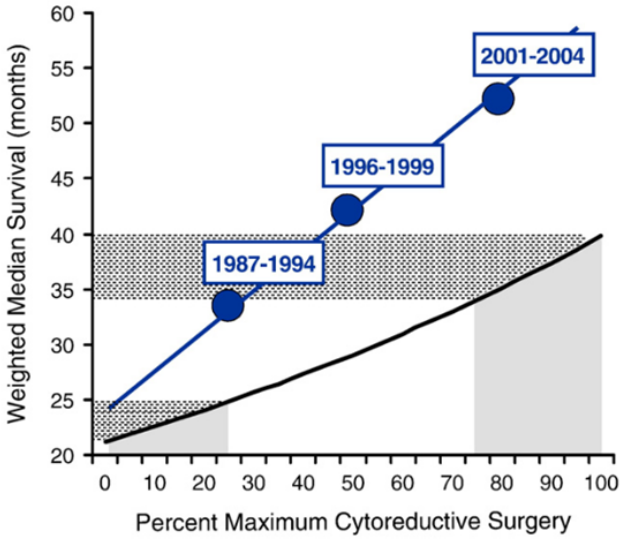
Cytoreductive surgery + **Platinum-based chemothreapy** + **Maintenance therapy**

"No residual tumor (R0)"

The most important prognostic factor

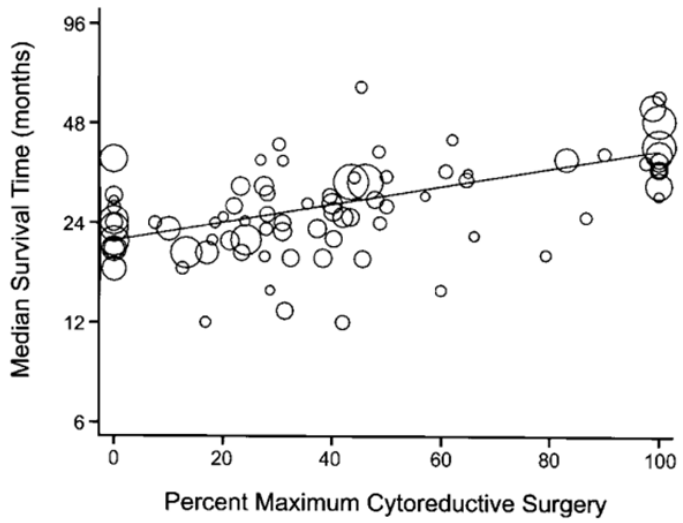
MSKCC

Chi DS, et al. Gynecol Oncol. 2009.



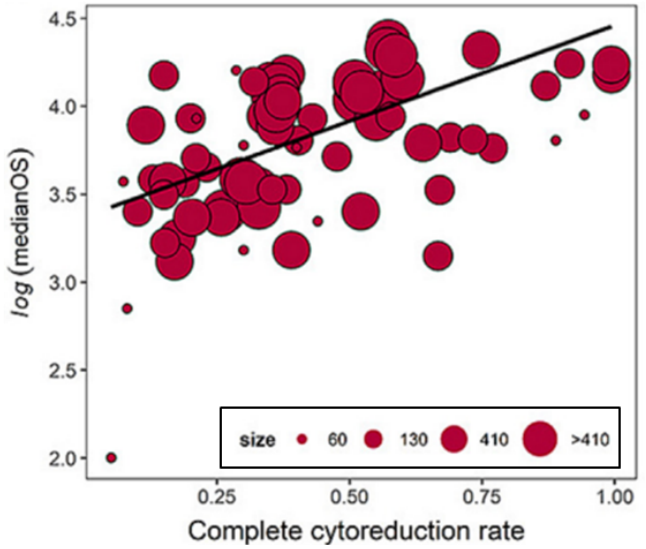
Old meta-analysis

Bristow RE, et al. J Clin Oncol. 2002.



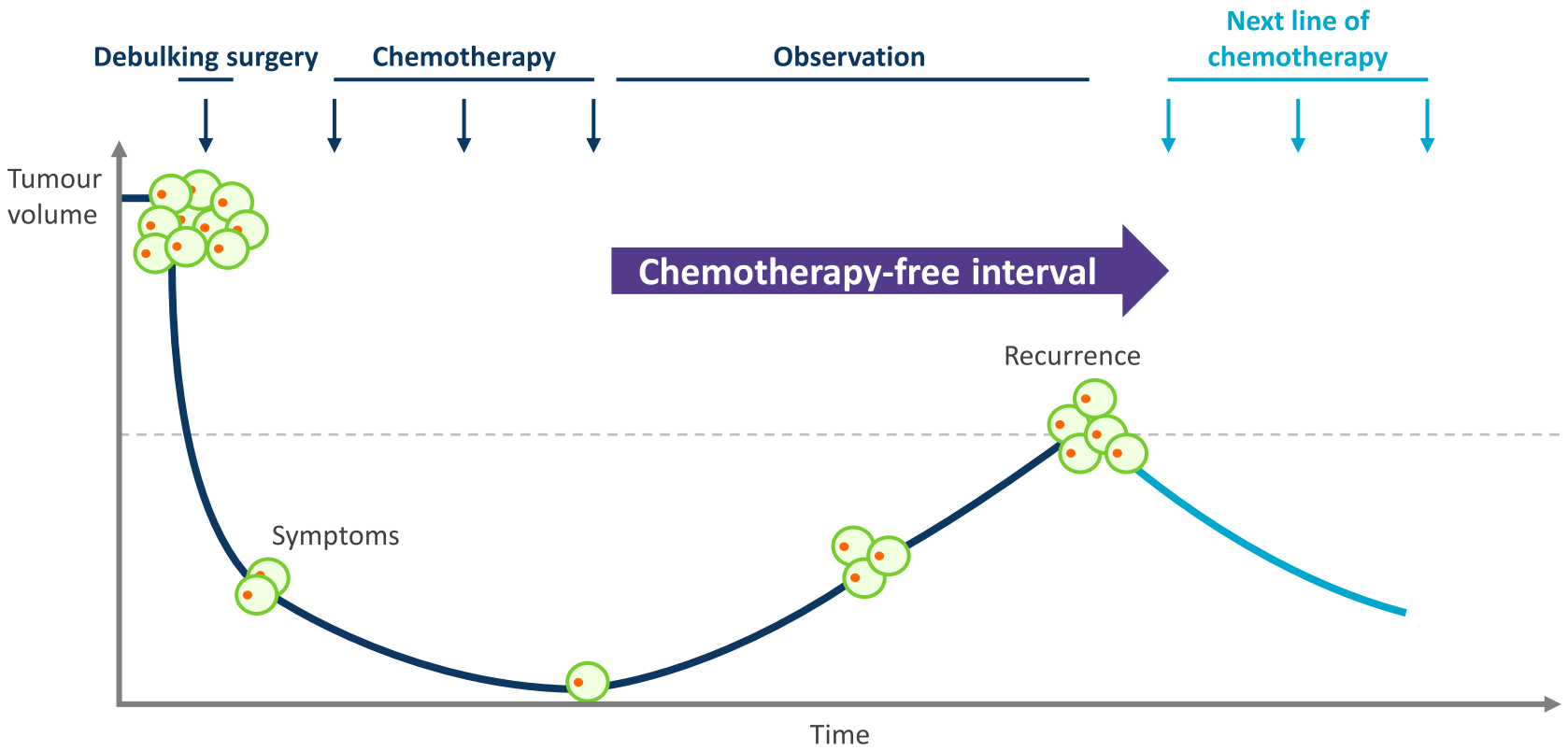
New meta-analysis

Kim JH, et al. Gynecol Oncol. 2023.



Maintenance therapy with PARPis have brought forward a paradigm shift, altering the natural course of disease in ovarian cancer by extending PFS

Management of OC:[1]

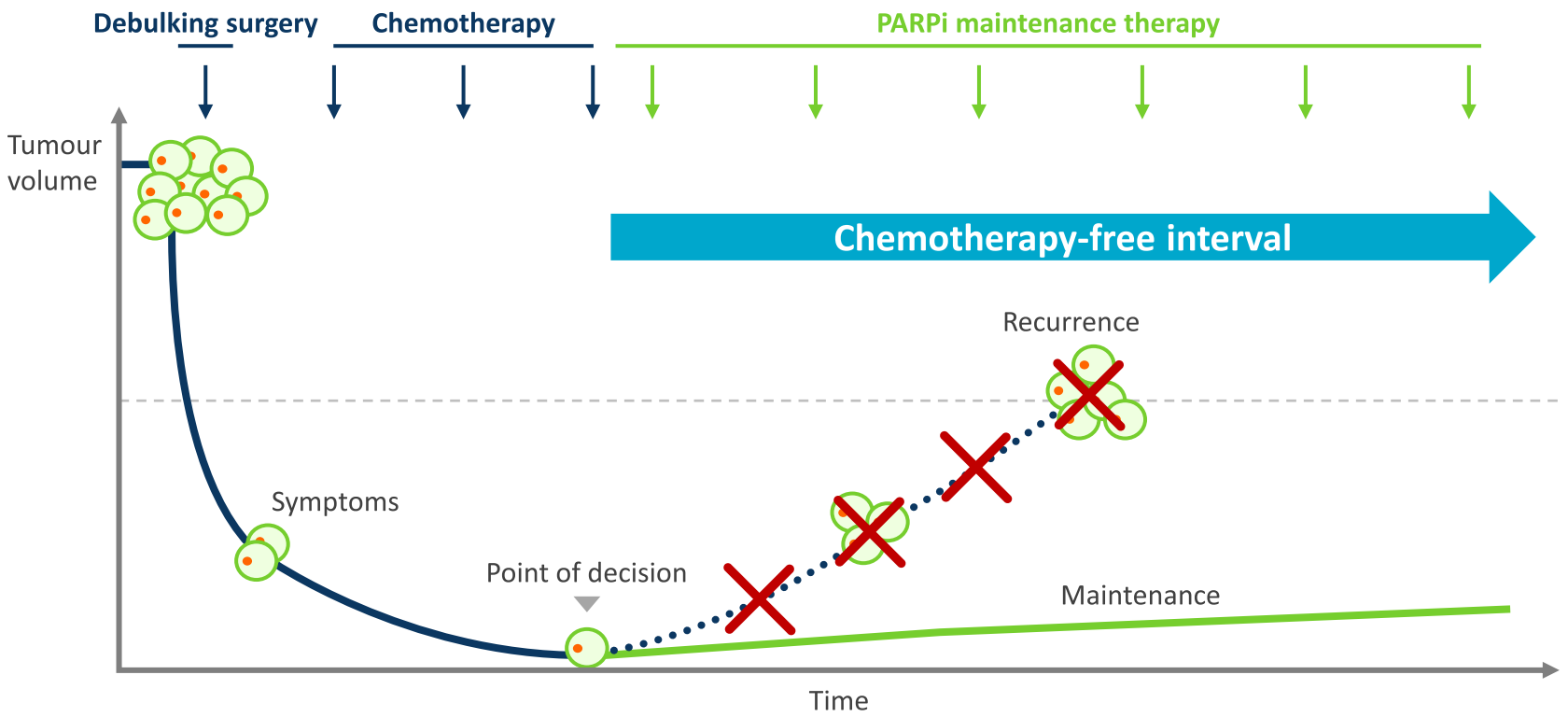


>70% of patients with advanced OC will recur within 3-5 years in the absence of 1L maintenance thearpy[2,3]

Figure is for illustrative purposes only.
1L, first-line; OC, ovarian cancer
1. DiSilvestro P, Alvarez Secord A. *Cancer Treat Rev* 2018;69:53-65. 2. Ledermann JA, *et al. Ann Oncol* 2013;24:vi24-vi32. 3. du Bois A, *et al. Cancer* 2009;115:1234-44.

Maintenance therapy with PARPis have brought forward a paradigm shift, altering the natural course of disease in ovarian cancer by extending PFS

Management of OC:[1]



Goals of Maintenance therapy

1. Prolong benefit following surgery and chemotherapy
2. Improve survival (PFS and hopefully OS)
3. Manageable toxicity and no negative effects on QoL

Figure is for illustrative purposes only.
OC, ovarian cancer; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PFS, progression-free survival; QoL, quality of life.
1. DiSilvestro P, Alvarez Secord *A. Cancer Treat Rev* 2018;69:53-65.

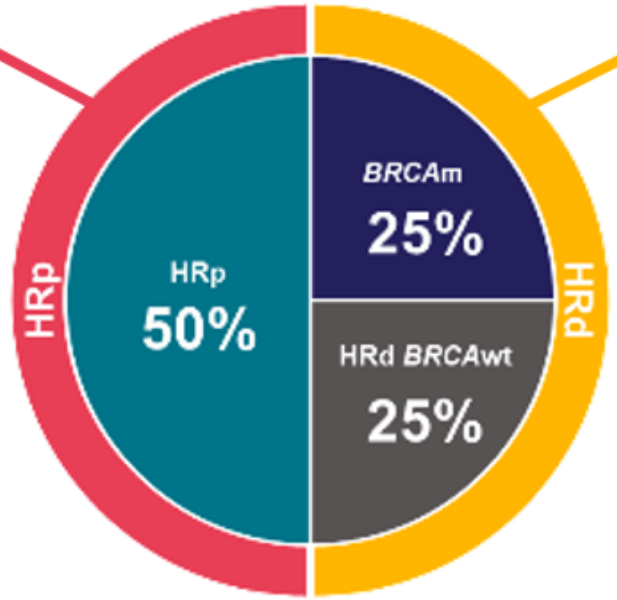
Approximately 50% of high-grade ovarian cancers are HRd[1]

Proportion of patients with genomic mutations in ovarian cancer[1]

HRp defined as "no detectable deficiency in DNA repair"[1]

In a meta-analysis of the studies PAOLA-1, PRIMA, SOLO-1 and VELIA, HRp was associated with higher risk of progression in patients treated with PARPi maintenance therapy[2]

- Risk of progression in HRp patients is 0.83 (95% CI: 0.67–1.03)
- Risk of progression in HRd patients is 0.39 (95% CI: 0.29–0.53)



HRD defined as "deficiency in DNA repair "[1]

HRD can arise from mutations in multiple components of the HR pathway, most frequently in *BRCA* genes[1–3]

- About 50% of patients with OC are HRd
- Within the group of patients with HRD, about half are *BRCA*m and half *BRCA*wt
- HRD is associated with good prognosis and response to PARPi and platinum-based therapies
- *BRCA*m is associated with even better prognosis and response to PARPi and platinum-based therapies

1. Konstantinopoulos PA, Ceccaldi R, Shapiro GI, *et al*. Cancer Discov. 2015;5(11):1137–1154.
2. Cheng H, Yang J, Liu H, *et al*. Arch Gynecol Obstet. 2021;304(2):285–296.
3. Ngoi NYL and Tan DSP. ESMO Open. 2021;6(3):100144.

Benefit from frontline PARPi maintenance therapy

Progression-free survival

	SOLO1	PAOLA-1	PRIMA	PRIME	ATHENA-MONO
PARPi	Olaparib	Olaparib	Niraparib	Niraparib	Rucaparib
Bevacizumab	No	Yes	No	No	No
Population	BRCAmut	All comers	All comers	All comers	All comers
HRD test	NA	MyChoice	MyChoice	BGI	Foundation-One
+++ *BRCA*mut	0.33 (0.25–0.43)	0.31* (0.20–0.47)	0.40* (0.27–0.62)	0.40* (0.23-0.68)	0.40* (0.21–0.75)
++ *BRCA*wt/HRd	-	0.43* (0.28-0.66)	0.50* (0.31-0.83)	0.58* (0.36-0.93)	0.58* (0.33-1.01)
+ *BRCA*wt/HRp	-	0.92* (0.72-1.17)	0.68* (0.49-0.94)	0.41* (0.25-0.65)	0.65* (0.45-0.95)

*exploratory

Moore, et al. N Engl J Med. 2018.
Ray-Coquard, et al. N Engl J Med. 2019.
González-Martín, et al. N Engl J Med. 2019.
Li, et al. SGO 2022.
Monk, et al. J Clin Oncol. 2022.

Differences in study populations

High-risk factors:*[1]

- Stage IV disease
- Visible residual disease or no surgery
- IDS/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
PRMIA[3-5]	35%	47%‡	67%	31%	70%‡‡
PAOLA-1[6,7]	30%	40%	42%	27%††	70%
PRIME[8]	28%	22%§	47%	18%	67%§§
ATHENA-MONO[9]	25%	25%**	51%	18%	79%
SOLO1[10,11]	17%	24%	35%	18%	0%

CLINICAL RISK

1st Quartile | 2nd Quartile | 3rd Quartile | 4th Quartile

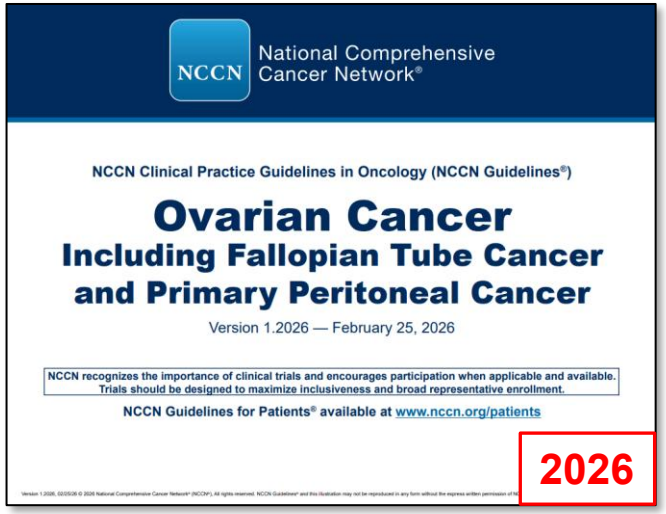
The colours are to indicate the proportion of 'higher-risk patients', where green represents the lowest proportion and red represents the highest population. ‡PRIMA did not include patients with stage III RO after PDS

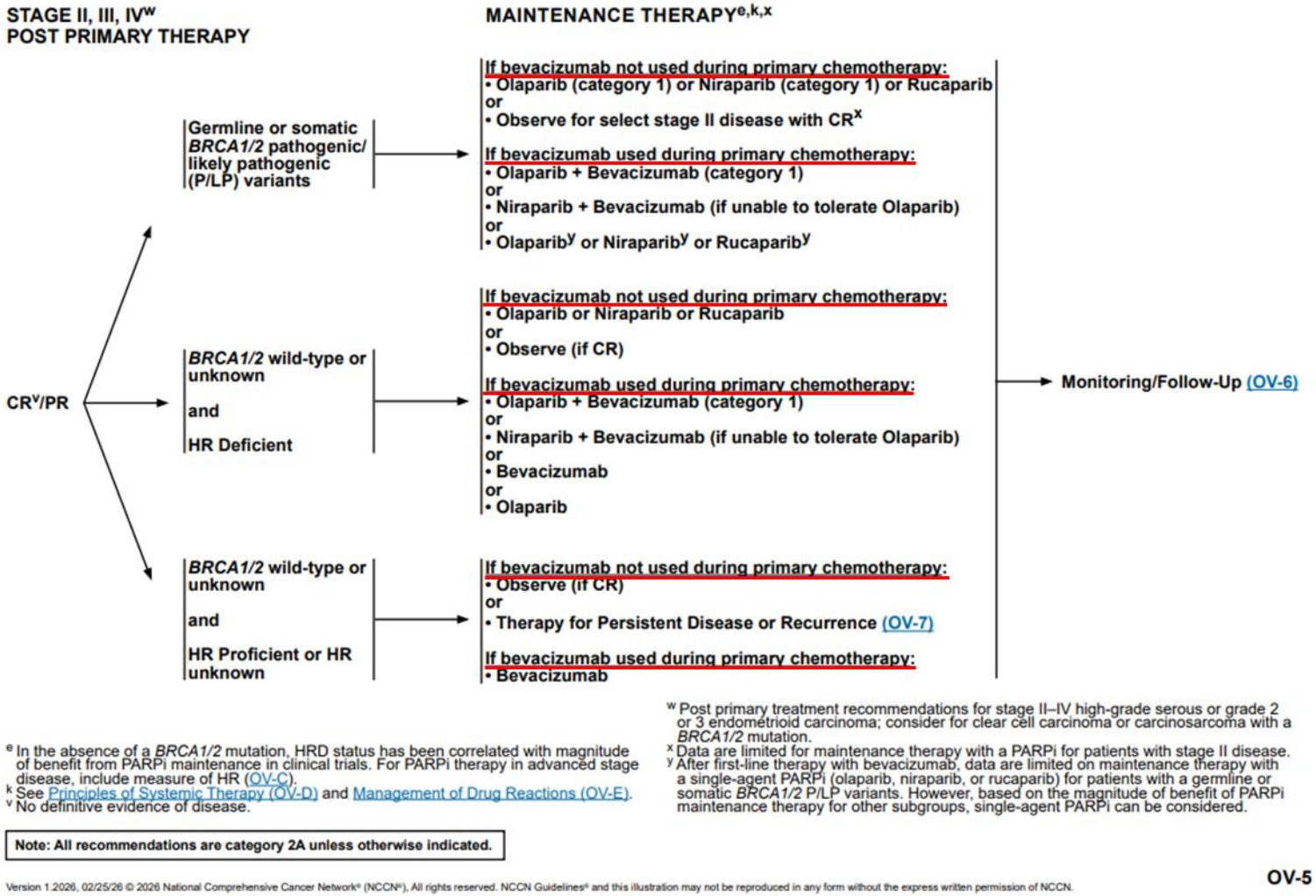
There are no completed direct head-to-head-trials of these products. These data are from different clinical trials, and since there are inherent limitations in cross-study comparisons, caution should be exercised in interpreting data. Theses data are for information purposes only and are not intended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

PRIME was sponsored by Zai Lab (Shanghai) Co., Ltd. *Classification based on known risk factors for progression of advanced OC: disease stage, therapy modality, visible residual disease surgery, and BRCA mutation status. †Includes patients who did not receive surgery. §R2 or missing (postoperative residual disease status). **visible disease after chemotherapy. ††Chemotherapy plus bevacizumab. BRCA, breast cancer gene; BRCAnd, BRCA status not determined. ‡‡Including BRCA not determined. §§Germline BRCAwt only. BRCAwt, BRCA wild-type; IDS, interval debulking surgery; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; PARPi, poly (ADP-ribose) polymerase inhibitor; PDS, primary debulking surgery; PR, partial response; R0, no residual disease; R2; >10 mm residual disease.

1. Chase DM., *et al*. presented at ESMO 2021.16-21 Sep (virtual). 2. www.uptodate.com/contents/medical-treatment-for-relapsed-epithelial-ovarian-fallopian-tube-or-peritoneal-cancer-platinum-sensitive-disease#disclaimerContent 3. González-Martin A, *et al. N Engl J Med* 2019:381:2391- 402. 4. González-Martin 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; https://doi.org/10.1200/JC0.22.01003. 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).

Current practice guidelines





1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) -Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Version 1. 2026

Current practice guidelines

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

SPECIAL ARTICLE

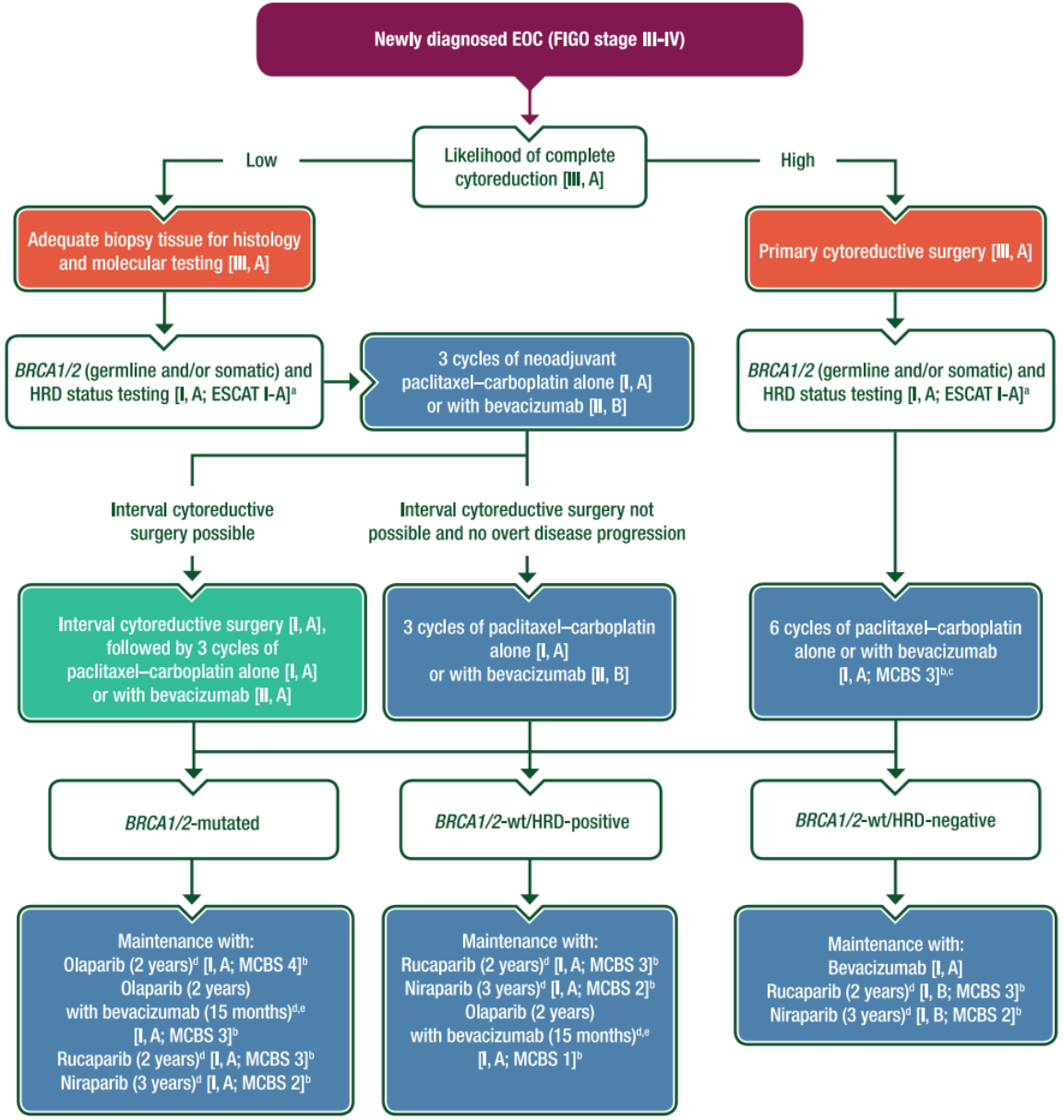
ESMO Clinical Practice Guideline Express Update on the management of epithelial ovarian cancer

A. González-Martín[1] & J. A. Ledermann[2], on behalf of the ESMO Guidelines Committee*

[1]Department of Medical Oncology and Program in Solid Tumors Cima-Universidad de Navarra, Cancer Center Clínica Universidad de Navarra, Madrid and Pamplona, Spain; [2]Department of Oncology, UCL Cancer Institute, University College London, London, UK

Available online 28 January 2026

2026



Current practice guidelines

ESGO2026 Congress
27th European Congress on Gynaecological Oncology
FEBRUARY 26–28 | 2026
COPENHAGEN | DENMARK

New ESGO Ovarian Cancer Guidelines: Practical Applications through Tumour Board Simulation and Updated Care Algorithms - part I

New ESGO Ovarian Cancer Guidelines: Practical Applications through Tumour Board Simulation and Updated Care Algorithms - part II

Primary treatment - Advanced stages

Maintenance therapy

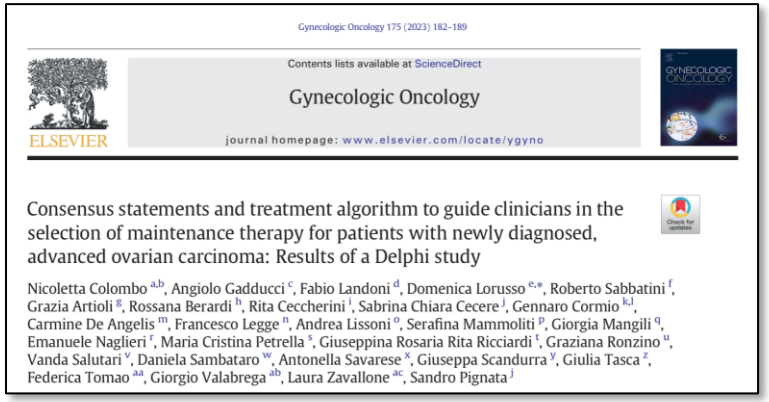
- The choice of treatment should be based on disease, molecular factors and clinical characteristics of the patient as well as patient preferences.
- For patients with BRCA1/2-mutated or BRCA1/2-wt/HRD-positive tumours, with no residual disease after surgery or a complete or partial response to first-line chemotherapy, maintenance treatment with PARP inhibitors, with or without bevacizumab, is recommended [I, A]:
  - For BRCA1/2-mutated: olaparib for 2 years, niraparib for 3 years, rucaparib 2 years or Olaparib-bevacizumab for 2 years (olaparib 2 years and total bevacizumab 15 months)
  - For BRCA1/2-wt/HRD-positive: niraparib for 3 year, rucaparib 2 years or olaparib-bevacizumab for 2 years (olaparib 2 years and total bevacizumab 15 months).

Primary treatment - Advanced stages

Maintenance therapy

- For patients with HRD-negative tumours, maintenance treatment is recommended [I, A]:
  - With either bevacizumab, irrespective of response to chemotherapy.
  - Or PARP inhibitors such as niraparib (for 3 years) or rucaparib (for 2 years) in patients with no evidence of disease, complete or partial response to platinum-paclitaxel first-line chemotherapy.
- For low-grade serous carcinoma, the following therapy options can be considered:
  - Bevacizumab for a maximum of 15 months [IV, B];
  - Endocrine therapy after first-line platinum-based chemotherapy [IV, B].

Current practice guidelines



Gynecologic Oncology 175 (2023) 182–189

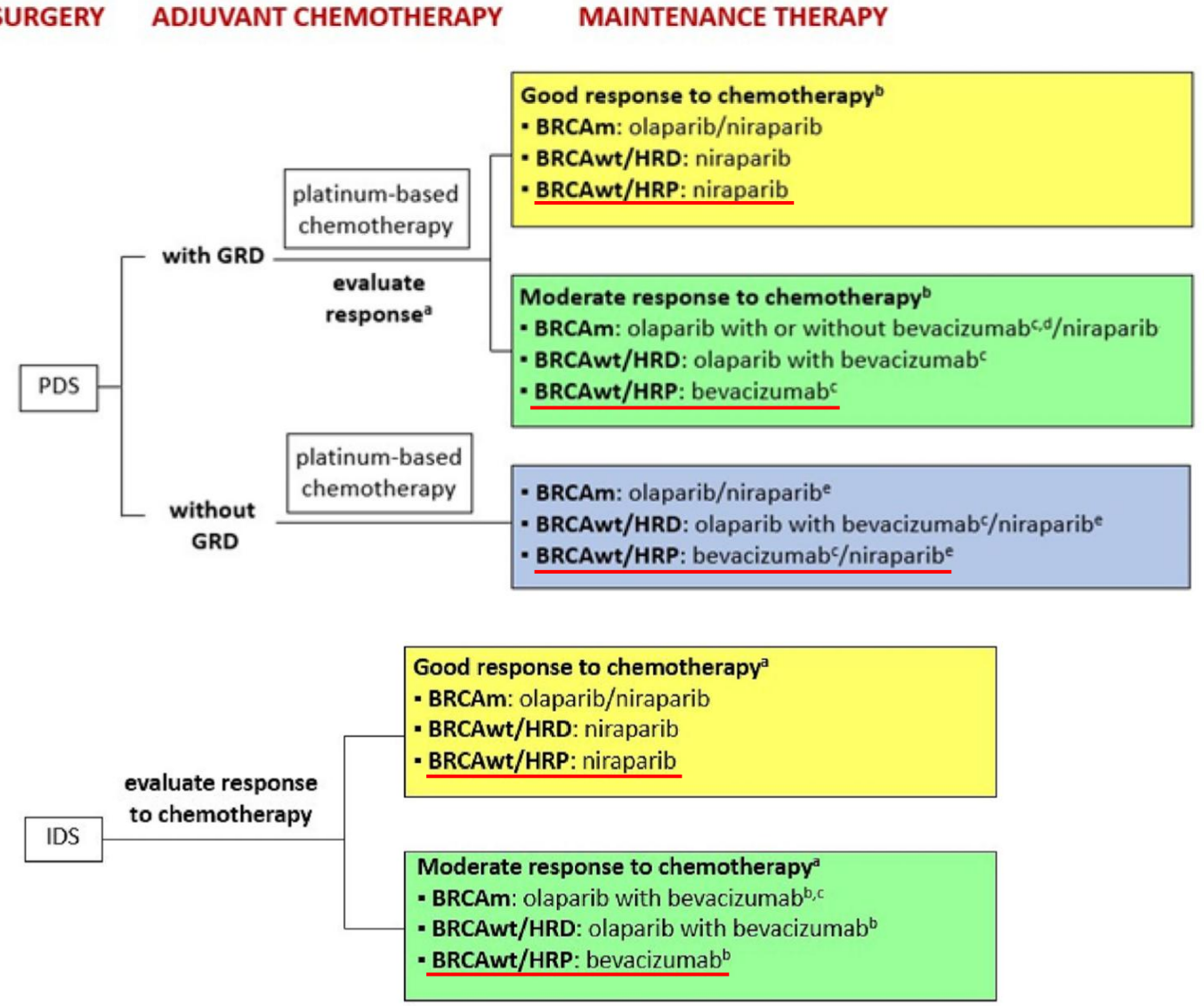
Contents lists available at ScienceDirect

Gynecologic Oncology

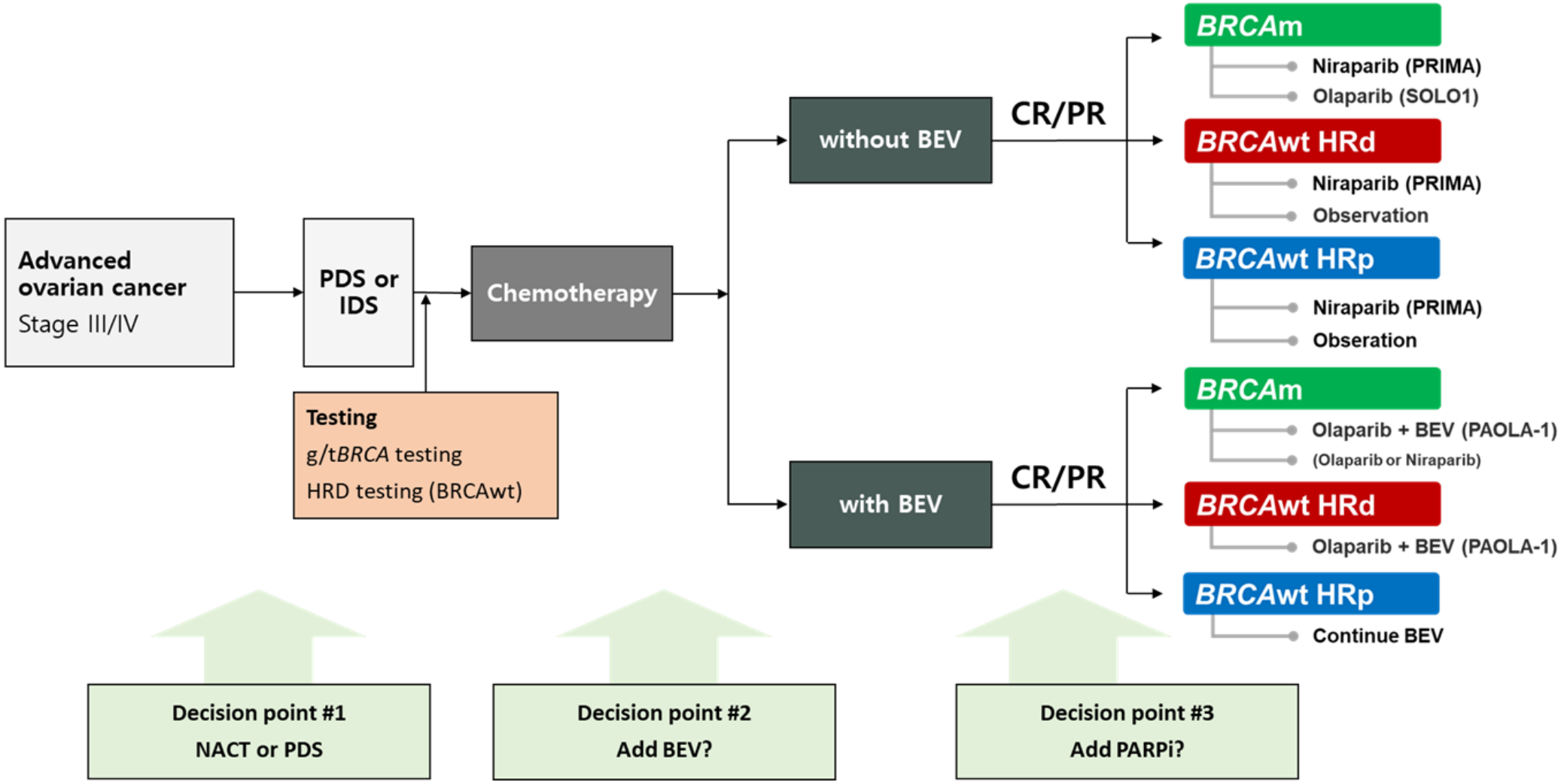
journal homepage: www.elsevier.com/locate/ygyno

Consensus statements and treatment algorithm to guide clinicians in the selection of maintenance therapy for patients with newly diagnosed, advanced ovarian carcinoma: Results of a Delphi study

Nicoletta Colombo [a,b], Angiolo Gadducci [c], Fabio Landoni [d], Domenica Lorusso [e,*], Roberto Sabbatini [f], Grazia Artioli [g], Rossana Berardi [h], Rita Ceccherini [i], Sabrina Chiara Cecere [j], Gennaro Cormio [k,l], Carmine De Angelis [m], Francesco Legge [n], Andrea Lissoni [o], Serafina Mammoliti [p], Giorgia Mangili [q], Emanuele Naglieri [r], Maria Cristina Petrella [s], Giuseppina Rosaria Rita Ricciardi [t], Graziana Ronzino [u], Vanda Salutari [v], Daniela Sambataro [w], Antonella Savarese [x], Giuseppa Scandurra [y], Giulia Tasca [z], Federica Tomao [aa], Giorgio Valabrega [ab], Laura Zavallone [ac], Sandro Pignata [j]



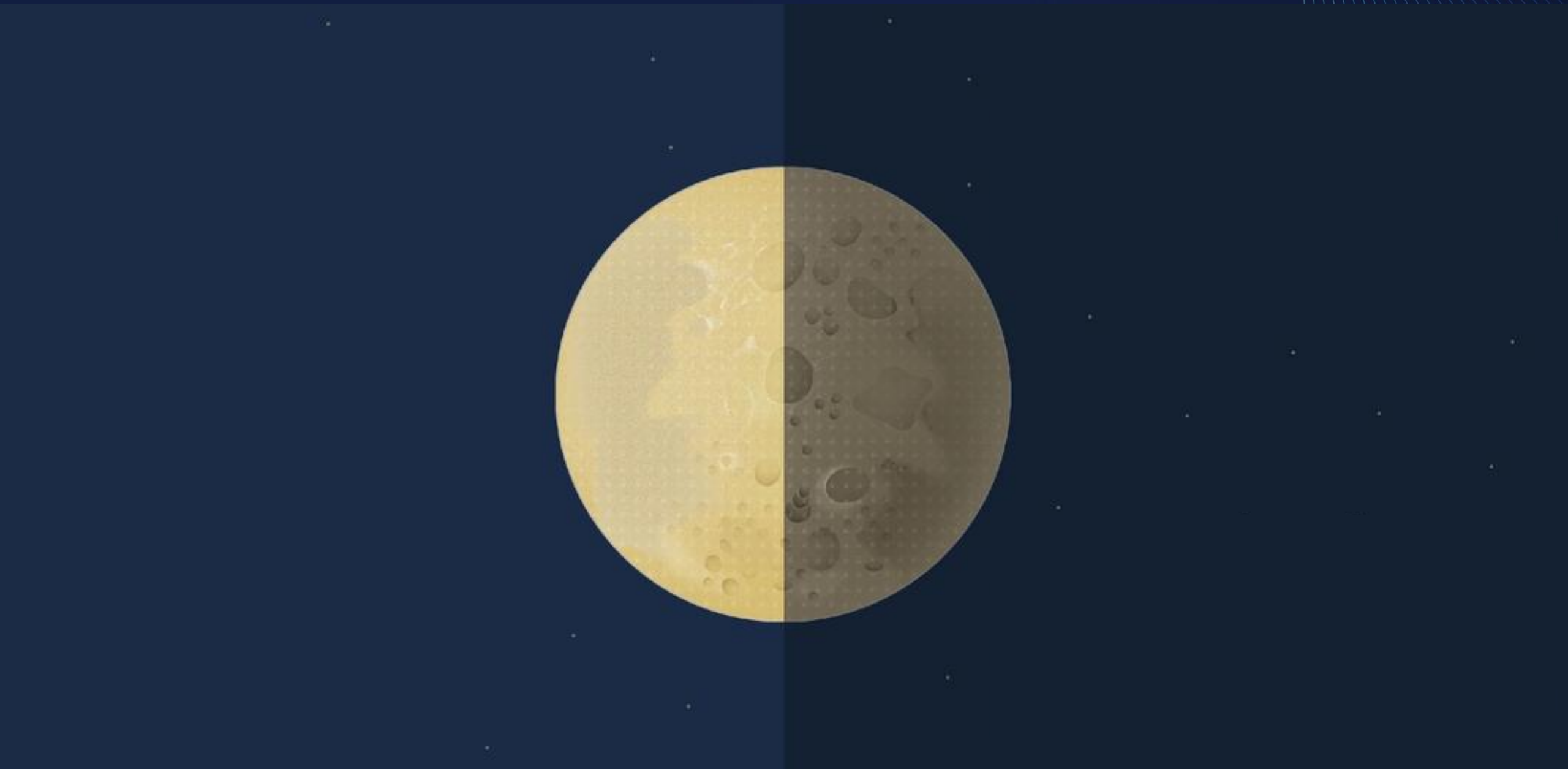
Ovarian cancer treatment algorithms



NCCN, ESMO, and ASCO guidelines

✓ The choice of treatment should be based on the distribution of disease, response to chemotherapy, and the patient's clinical characteristics.

HRD-negative = HR proficient = “The Dark Side of the Moon”

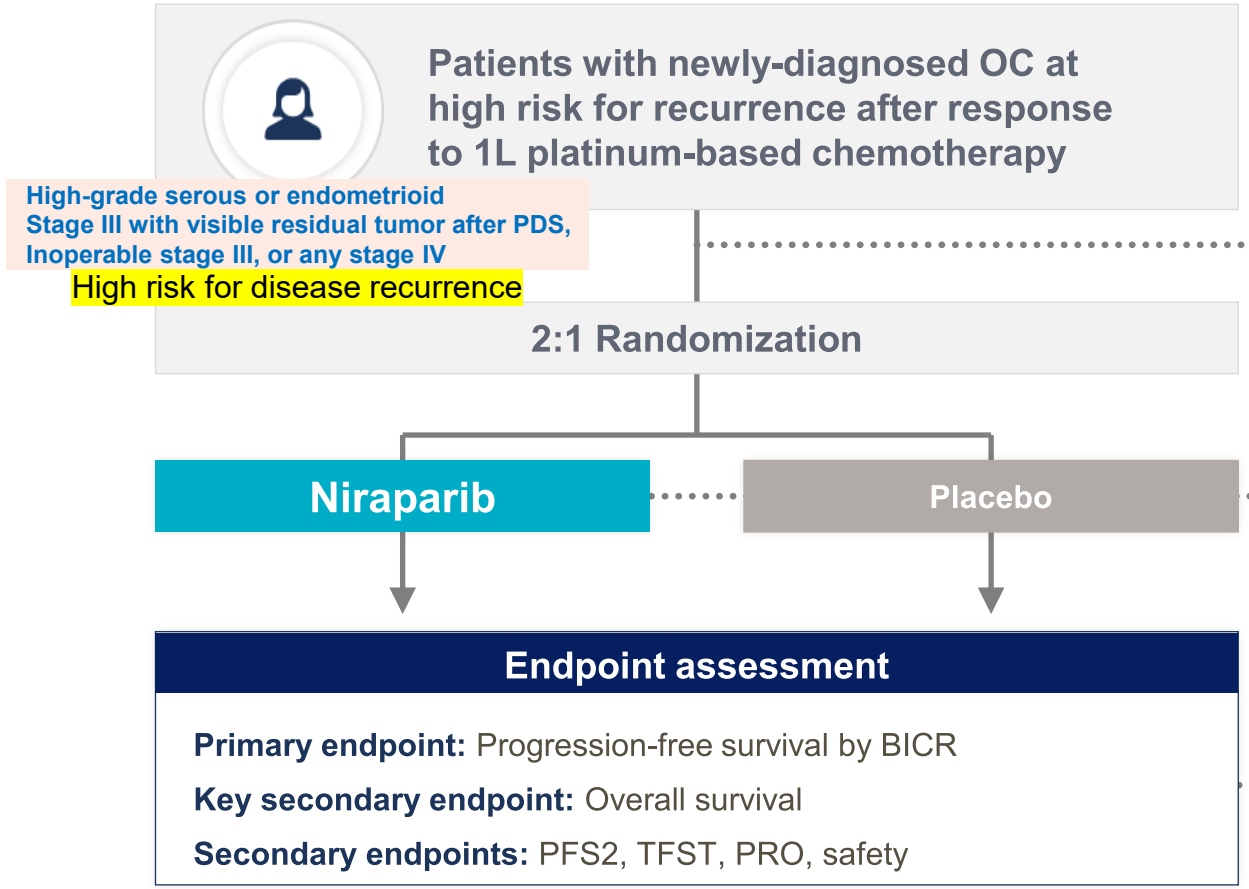




PRIMA

PRIMA study

- **PRIMA was a landmark Phase III trial in advanced ovarian cancer**



Endpoint assessment

Primary endpoint: Progression-free survival by BICR

Key secondary endpoint: Overall survival

Secondary endpoints: PFS2, TFST, PRO, safety

Stratification Factors

- NACT administered: Yes or no
- Best response to first platinum therapy: CR or PR
- Tissue homologous recombination test status: deficient or proficient/not-determined

Protocol Amendment, November 2017

- Body weight ≥77 kg and platelets ≥150,000/μL started with 300 mg QD
- Body weight <77 kg and/or platelets <150,000/μL started with 200 mg QD

Hierarchical PFS Testing

- **Patients with homologous recombination-deficient tumors**, followed by the **overall population**
- Statistical assumption: a hazard ratio benefit in PFS of
  - 0.50 in homologous recombination-deficient patients
  - 0.65 in the overall population
- >90% statistical power and one-sided type I error of 0.025

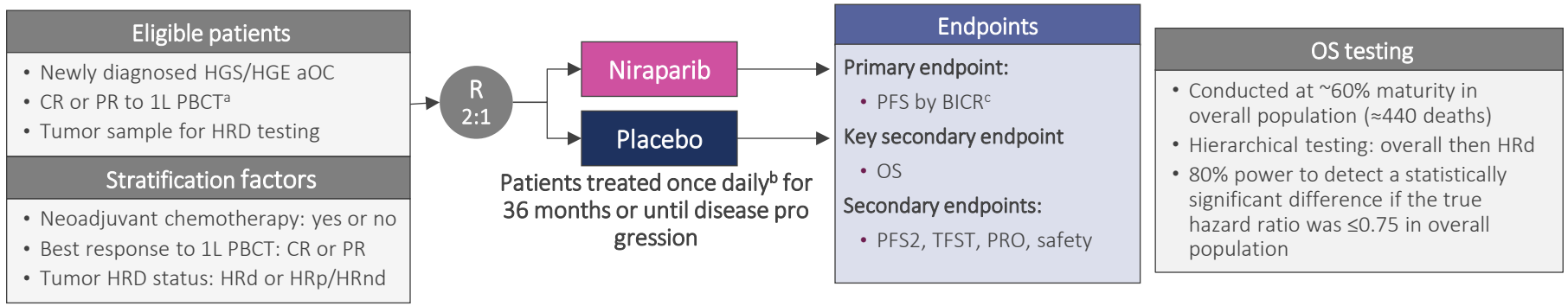
1L first-line BICR blinded independent central review CR complete response NACT neoadjuvant chemotherapy OC ovarian cancer OS overall survival PFS2 progression-free survival 2 PR partial response PRO patient-reported outcomes TFST time to first subsequent therapy.

1. González-Martín A et al. Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med 2019;381:2391-402

PRIMA study

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

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



Key risk characteristics of PRIMA population[1,2]

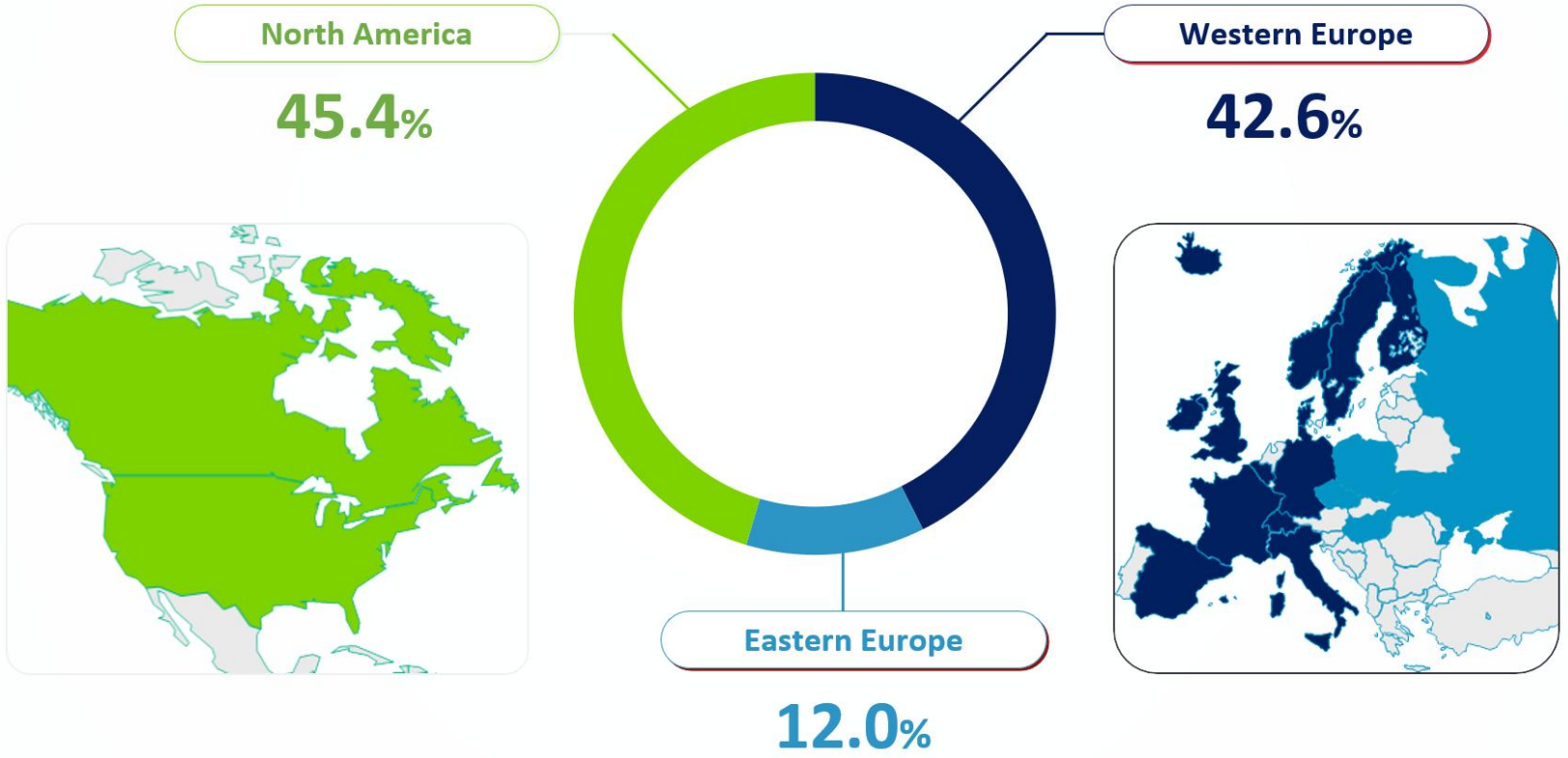
Disease stage		Residual disease		Tumor HRD/*BRCA* status	
35.1%	stage IV disease at diagnosis	>99%	stage III disease at diagnosis with residual disease after primary debulking surgery	50.9%	HRd
Initial treatment				30.4%	HRd/*BRCA*m
66.7%	received neoadjuvant chemotherapy	47.5%	postoperative visible residual disease or no debulking surgery	34.0%	HRp
30.6%	achieved partial response to 1L PBCT				

PRIMA/ENGOT-OV26/GOG-3012 trial (NCT02655016). aPatients must have either had CA-125 in the normal range or a ≥90% decrease in CA-125 during 1L treatment that was stable for at least 7 days. At baseline, 7.1% of the overall population had CA-125 above the upper limit of normal. bAt study start, all patients received a fixed starting dose of 300 mg once daily. Subsequently, the protocol was updated to use an individualized starting dose adjusted according to baseline body weight/platelet count. cPrimary endpoint of PFS by BICR assessed by hierarchical testing, first in patients with HRd tumors and then in the overall population. 1L, first-line; aOC, advanced ovarian cancer; BICR, blinded independent central review; BRCAm, BRCA-mutated; CA-125, cancer antigen 125; CR, complete response; HGE, high-grade endometrioid; HGS, high-grade serous; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRnd, homologous recombination status not determined; HRp, homologous recombination proficient; OS, overall survival; PBCT, platinum-based chemotherapy; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; PRO, patient-reported outcomes; TFST, time to first subsequent therapy.

1. González-Martín A, et al. N Engl J Med. 2019;381(25):2391–2402. 2. O'Cearbhaill RE, et al. Gynecol Oncol. 2022;166(1):36–43.

PRIMA study

Global Phase 3 Study Conducted in 20 countries at 181 sites



PRIMA/ENGOT-OV26/GOG-3012 trial (NCT02655016). aPatients must have either had CA-125 in the normal range or a ≥90% decrease in CA-125 during 1L treatment that was stable for at least 7 days. At baseline, 7.1% of the overall population had CA-125 above the upper limit of normal. bAt study start, all patients received a fixed starting dose of 300 mg once daily. Subsequently, the protocol was updated to use an individualized starting dose adjusted according to baseline body weight/platelet count. cPrimary endpoint of PFS by BICR assessed by hierarchical testing, first in patients with HRd tumors and then in the overall population. 1L, first-line; aOC, advanced ovarian cancer; BICR, blinded independent central review; BRCAm, BRCA-mutated; CA-125, cancer antigen 125; CR, complete response; HGE, high-grade endometrioid; HGS, high-grade serous; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRnd, homologous recombination status not determined; HRp, homologous recombination proficient; OS, overall survival; PBCT, platinum-based chemotherapy; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; PRO, patient-reported outcomes; TFST, time to first subsequent therapy.

1. González-Martín A, et al. N Engl J Med. 2019;381(25):2391–2402. 2. O'Cearbhaill RE, et al. Gynecol Oncol. 2022;166(1):36–43.

PRIMA study

- **Patient Characteristics and Baseline Demographics**[1,2]

Characteristic	Niraparib (n=487)	Placebo (n=246)
Age, median (range), years	**62 (32-85)**	62 (33-88)
Stage at initial diagnosis, n (%)		
III	**318 (65.3)**	158 (64.2)
IV	**169 (34.7)**	88 (35.8)
Prior NACT, n (%)		
Yes	**322 (66.1)**	167 (67.9)
No	**165 (33.9)**	79 (32.1)
Best response to platinum-based CT, n (%)		
CR	**337 (69.2)**	172 (70.0)
PR	**150 (30.8)**	74 (30.0)
Homologous recombination test status, n (%)		
HRd	**247 (50.7)**	126 (51.2)
*BRCA*mut	**152 (31.2)**	71 (28.9)
*BRCA*wt	**95 (19.5)**	55 (22.4)
HRp	**169 (34.7)**	80 (32.5)
HRnd	**71 (14.6)**	40 (16.3)

Overall (n=733)

23.1% with stage III with residual disease post-PDS

66.7% received NACT

35.0% Stage IV ovarian cancer

30.5% achieved a PR to 1L CT

50.9% had HRd tumors

30.4% had *BRCA*mut tumors included in HRd

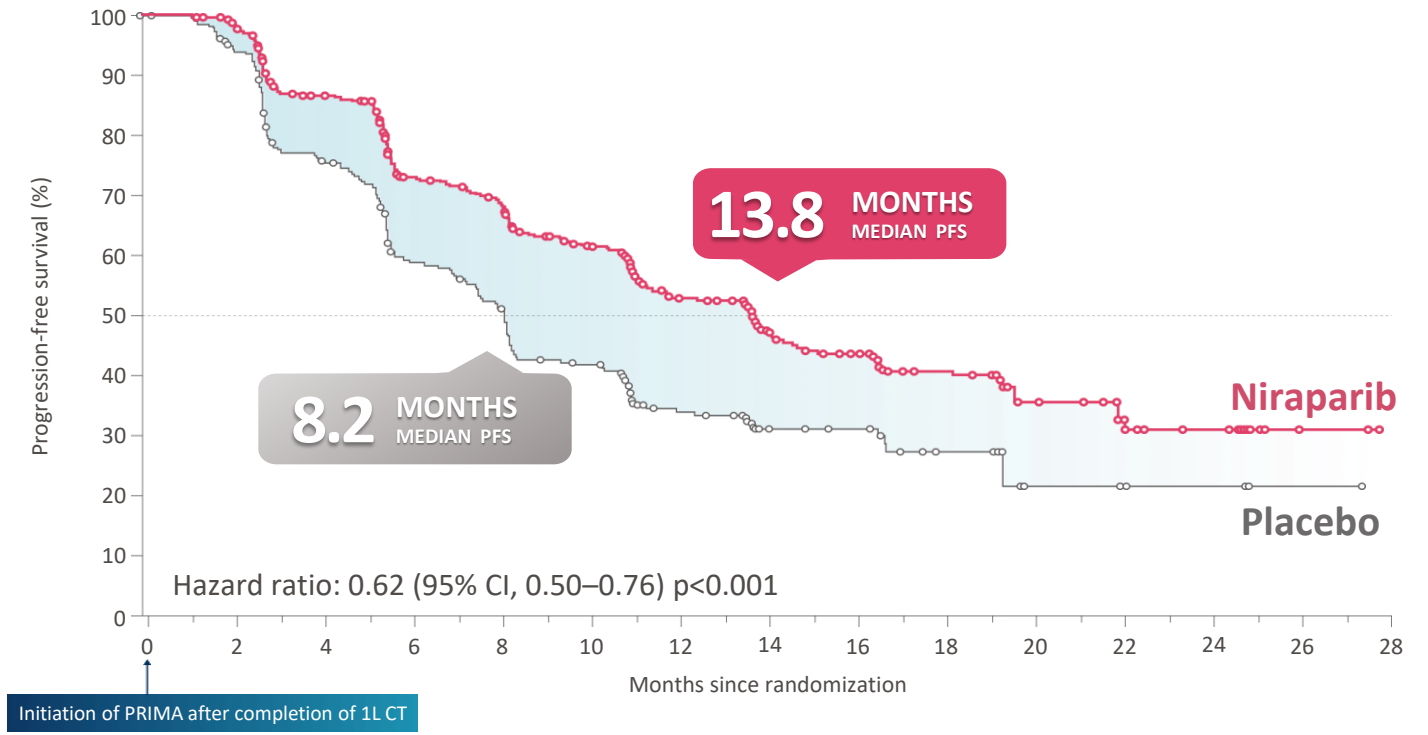
1L first-line **CR** complete response **CT** chemotherapy **HRd** homologous recombination deficient **HRp** homologous recombination proficient **HRnd** homologous recombination not determined **mut** mutation **NACT** neoadjuvant chemotherapy **PDS** primary debulking surgery **PR** partial response **wt** wild-type.

References 1. González-Martín A, *et al.*, Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. *N Engl J Med.* 2019 Dec 19;381(25):2391-2402. **2.** PRIMA CSR

PRIMA study

- **Primary Endpoint: PFS Benefit in the Overall Population**

PFS in the overall population (N=733)[1]



Niraparib	487	454	385	312	295	253	167	111	94	58	29	21	13	4	0
Placebo	246	226	177	133	117	90	60	32	29	17	6	6	4	1	0

Sensitivity analysis of PFS by the investigator was similar to and supported the BICR analysis

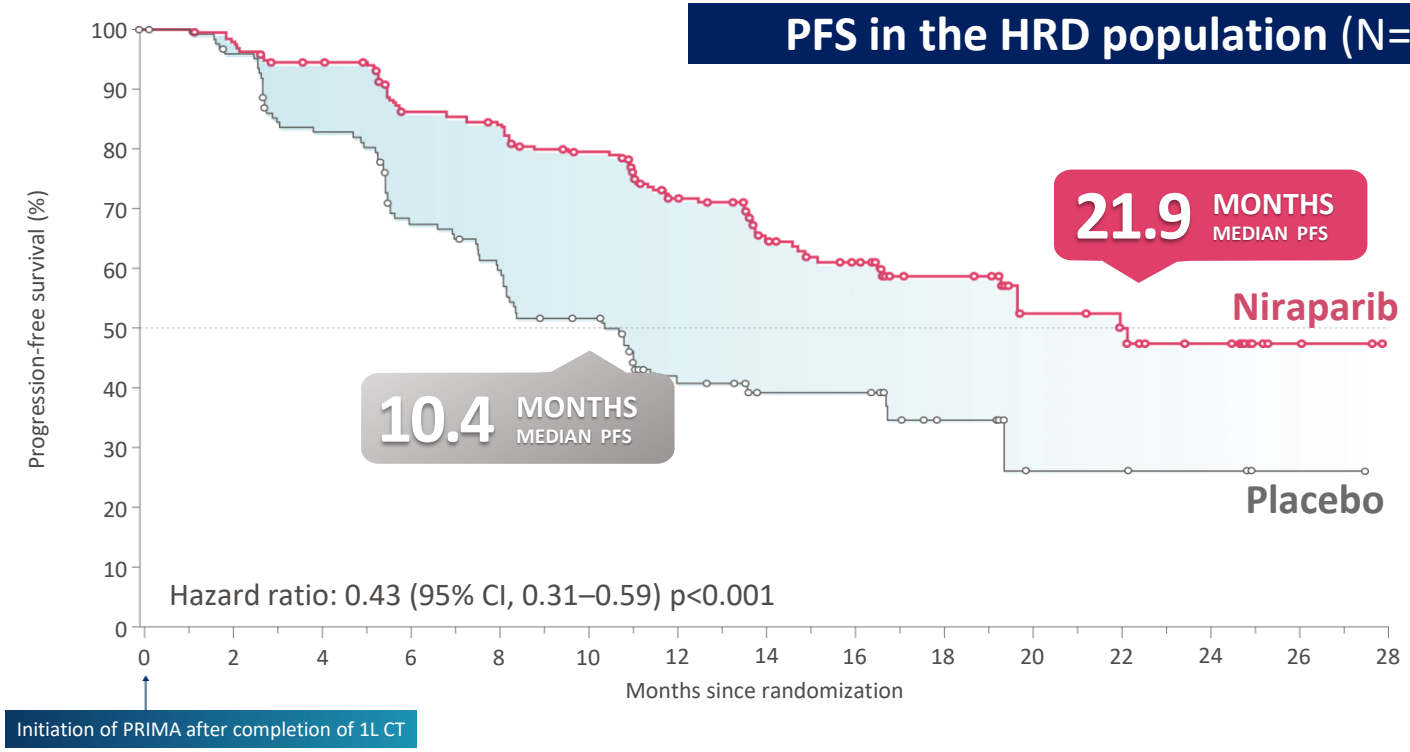
38% reduction
in hazard for progression or death with niraparib

	Niraparib (n=487)	Placebo (n=246)
Median PFS (Months)	**13.8**	8.2
Hazard Ratio (95% CI)	**0.62** (0.50-0.76)	
P value	*p*<0.001	

PRIMA study

- **Primary Endpoint: PFS Benefit in the HR-deficient Population**

PFS in the HRD population (N=373)[1]



Niraparib	**247**	**231**	**215**	**189**	**184**	**168**	**111**	**76**	**66**	**42**	**22**	**19**	**13**	**4**	**0**
Placebo	126	117	99	79	70	57	34	21	21	11	5	5	4	1	0

57% reduction
in hazard for progression or death with niraparib

	Niraparib (n=247)	Placebo (n=126)
Median PFS (Months)	**21.9**	10.4
Hazard Ratio (95% CI)	**0.43** (0.31-0.59)	
P value	*p*<0.001	

1L first-line **BICR** blinded independent central review **CI** confidence interval **CT** chemotherapy **HR** homologous recombination **NE** not estimable **PD** progressive disease **PFS** progression-free survival.

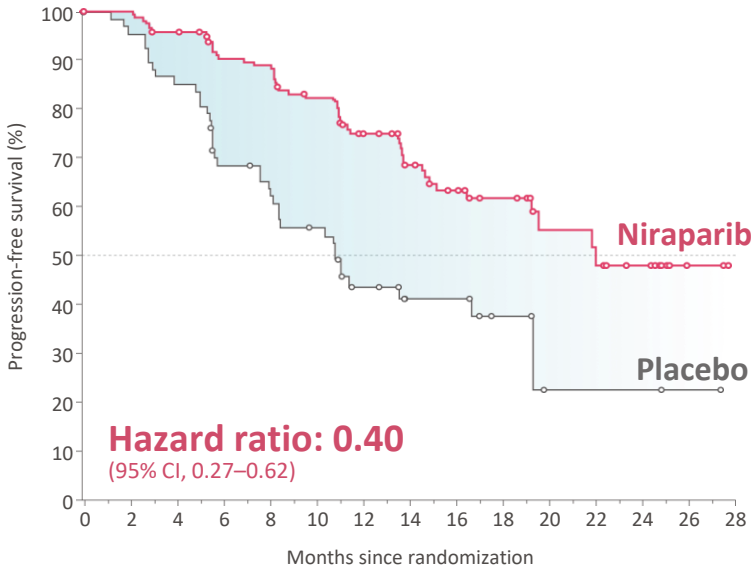
Reference 1. González-Martín A *et al.* Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. *N Engl J Med* 2019;381:2391-402

PRIMA study

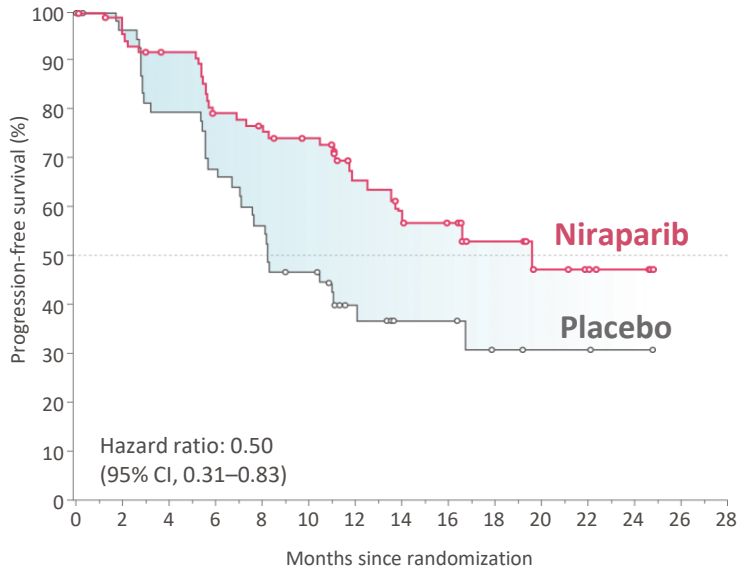
PFS in Biomarker Subgroups

Homologous Recombination Status

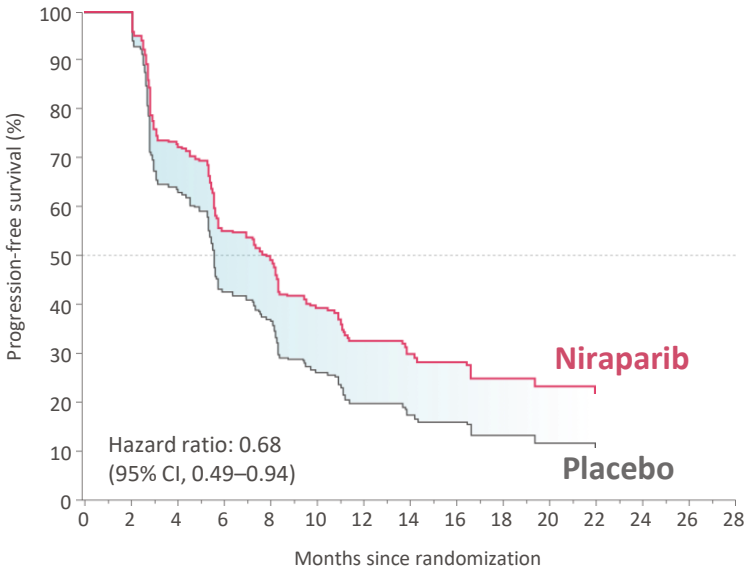
HRd/*BRCA*m



HRd/*BRCA*wt



HRp



- Niraparib provided similar clinical benefit in HRd subgroups (*BRCA*mut and *BRCA*wt)

Niraparib provided clinically significant benefit in the *BRCA*mut subgroup

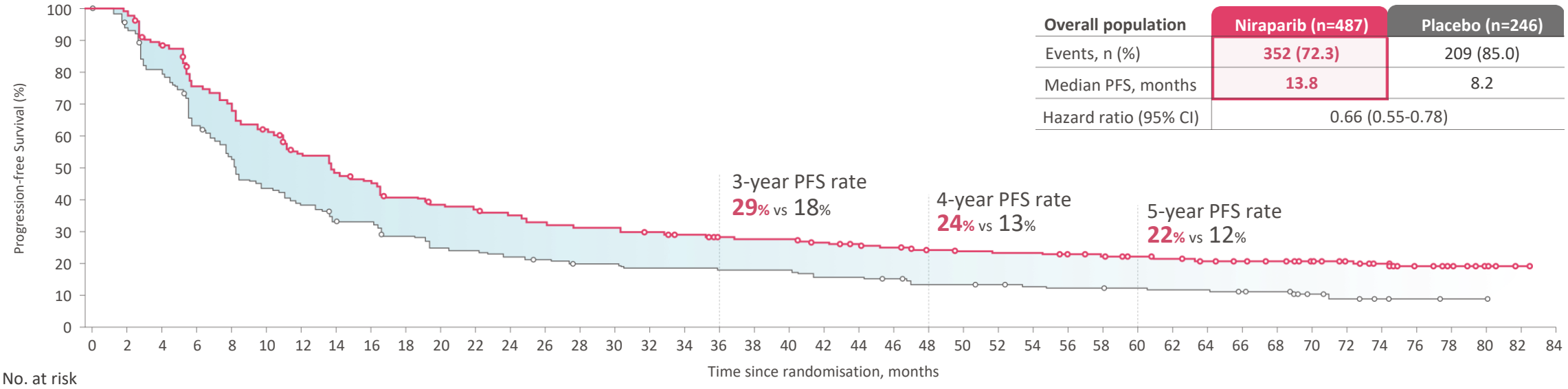
PRIMA 6.2 year updated long-term analysis

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

Data cutoff date, 8 April 2024; median follow-up, 6.2 years

↳ **Niraparib PFS benefit sustained with additional follow-up in the Overall populations**

Investigator-assessed PFS in overall



Overall population	Niraparib (n=487)	Placebo (n=246)
Events, n (%)	352 (72.3)	209 (85.0)
Median PFS, months	13.8	8.2
Hazard ratio (95% CI)	0.66 (0.55-0.78)	

No. at risk

Niraparib	487	461	406	342	316	278	243	216	204	181	168	162	153	141	135	134	128	122	118	116	114	108	103	99	89	86	85	85	82	79	74	70	66	63	60	41	35	28	16	11	8	1	0
Placebo	246	226	191	150	125	103	92	78	77	66	57	55	51	48	43	43	40	40	39	39	39	34	34	32	27	27	26	24	23	23	22	21	21	19	18	8	6	4	3	1	1	0	

[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. Monk BJ, et al. 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. Ann Oncol. 2024 Nov;35(11):981-992.

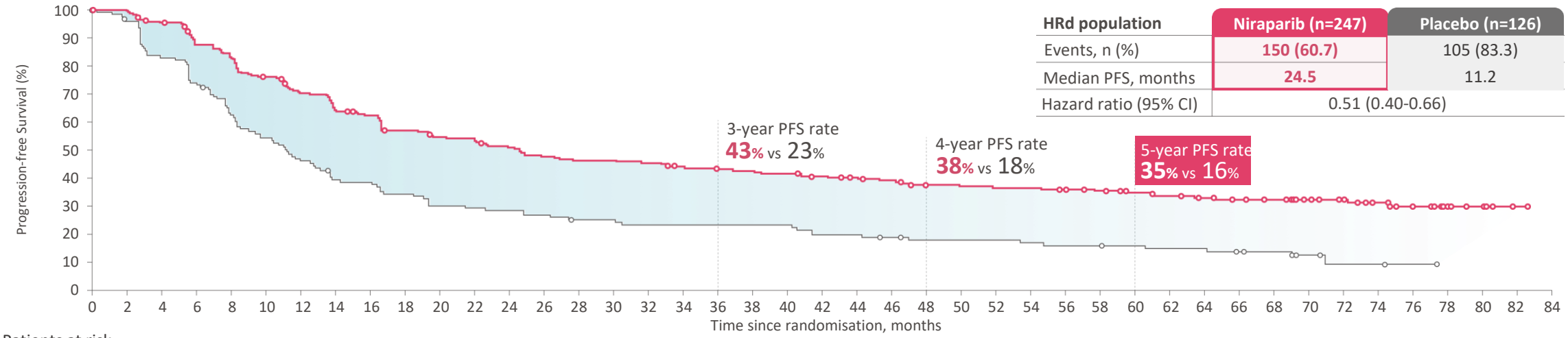
PRIMA 6.2 year updated long-term analysis

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

Data cutoff date, 8 April 2024; median follow-up, 6.2 years

↳ **Niraparib PFS benefit sustained with additional follow-up in the HRd populations**

Investigator-assessed PFS in HRd



HRd population	Niraparib (n=247)	Placebo (n=126)
Events, n (%)	150 (60.7)	105 (83.3)
Median PFS, months	24.5	11.2
Hazard ratio (95% CI)	0.51 (0.40-0.66)	

Patients at risk

Niraparib	247	235	221	200	189	173	158	143	138	125	119	116	110	103	100	100	98	93	91	89	87	83	79	77	69	68	67	67	64	62	58	55	52	49	46	33	29	24	15	10	8	1	0
Placebo	126	118	102	91	76	66	57	47	46	41	36	35	34	32	28	28	26	26	26	26	26	22	22	20	18	18	18	17	16	16	15	14	14	12	11	5	3	3	2	0			

- **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]**

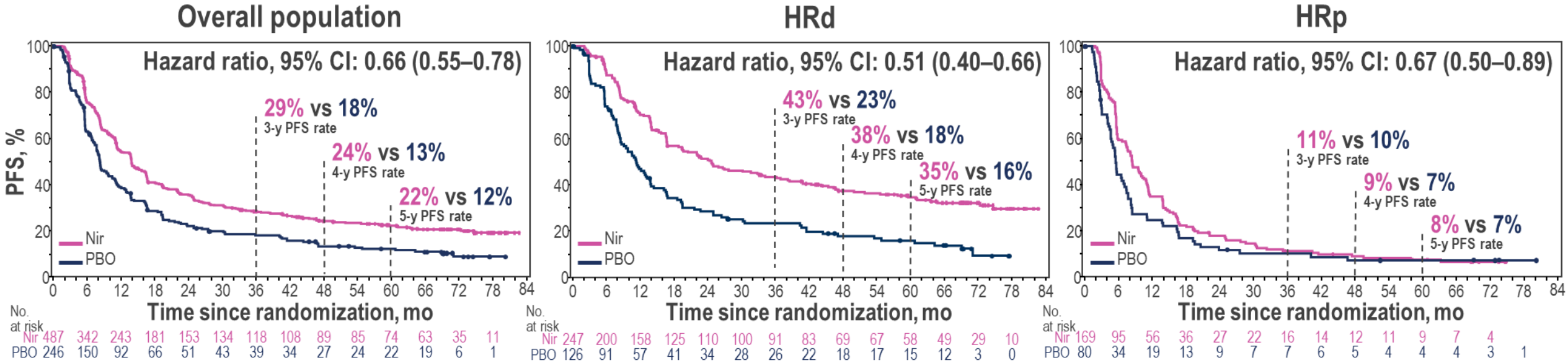
[a] At study start, patients were monitored for disease progression (CT/MRI) every 12 weeks (3 cycles); in August 2019, the protocol was amended to monitor patients who stayed on study treatment for more than 2 years for disease progression every 24 weeks (6 cycles).
[b] PFS hazard ratios and associated 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. Monk BJ, et al. 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. Ann Oncol. 2024 Nov;35(11):981-992.

PRIMA 6.2 year updated long-term analysis

Niraparib PFS benefic 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.

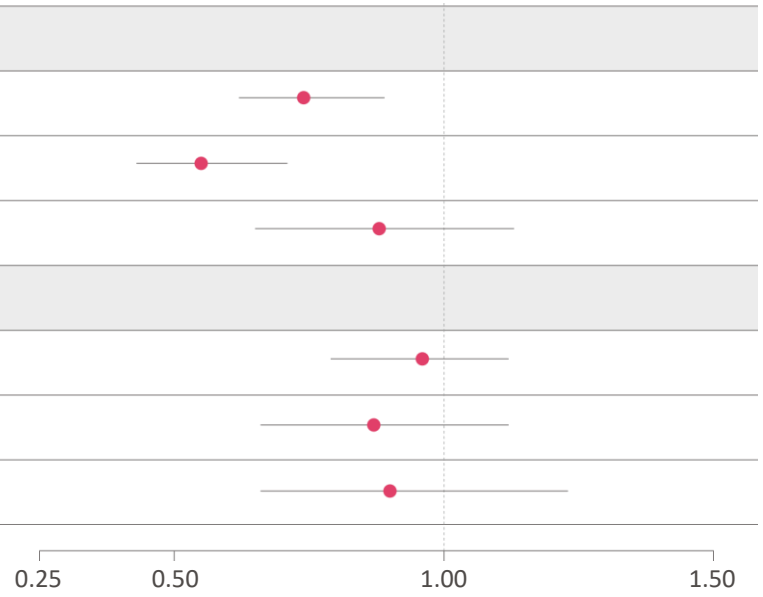
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PRIMA 6.2 year updated long-term analysis

- ## Secondary clinical endpoints

↳ **TFST results consistent with PFS analysis; PFS2 showed no difference between treatment arms**

	Niraparib		Placebo		Hazard ratio (95% CI)
	n/Na	Median, mo	n/Na	Median, mo	
TFST[b]					
Overall	355/487	17.0	192/246	12.0	0.74 (0.62–0.89)
HRd	156/247	26.9	96/126	13.9	0.55 (0.43–0.71)
HRp	143/169	11.6	64/80	7.9	0.88 (0.65–1.18)
PFS2[b]					
Overall	321/487	30.1	154/246	27.6	0.96 (0.79–1.17)
HRd	138/247	43.4	71/126	39.3	0.87 (0.66–1.17)
HRp	130/169	21.4	56/80	18.1	0.90 (0.66–1.23)



The size of each dot is proportional to the subgroup sample size.

[a] Number of patients with event/total number of patients in the population.

[b] Hazard ratios and 95% CIs for overall and HRd populations calculated using stratified Cox proportional hazards models with randomization stratification factors. Hazard ratios and 95% CIs for HRp population calculated using unstratified Cox proportional hazards models.

HRd homologous recombination deficient HRp homologous recombination proficient PFS progression-free survival PFS2 progression-free survival 2 TFST time to first subsequent therapy.

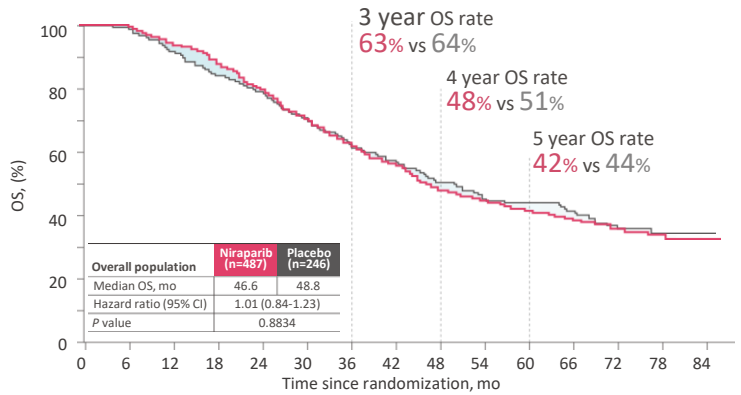
1. Monk BJ, et al. Niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer: final overall survival results from the PRIMA/ENGOT-OV26/GOG-3012 trial. Ann Oncol. 2024 Nov;35(11):981-992. & supplementary.

PRIMA 6.2 year updated long-term analysis

- **Final OS** (62.5% maturity in overall population)

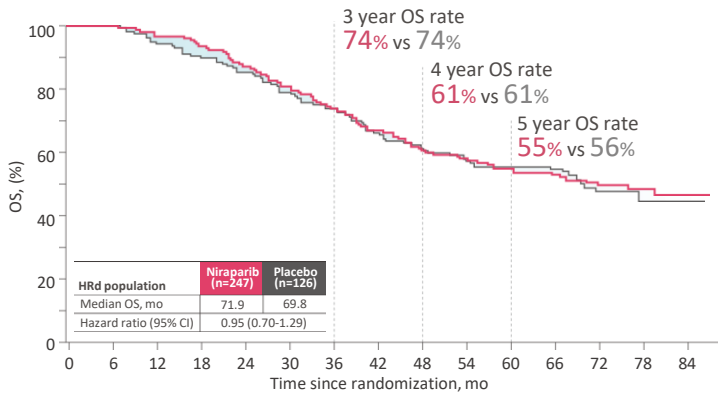
↳ **No difference in OS between niraparib and placebo arms in the overall, HRd, and HRp populations**

Overall[a]



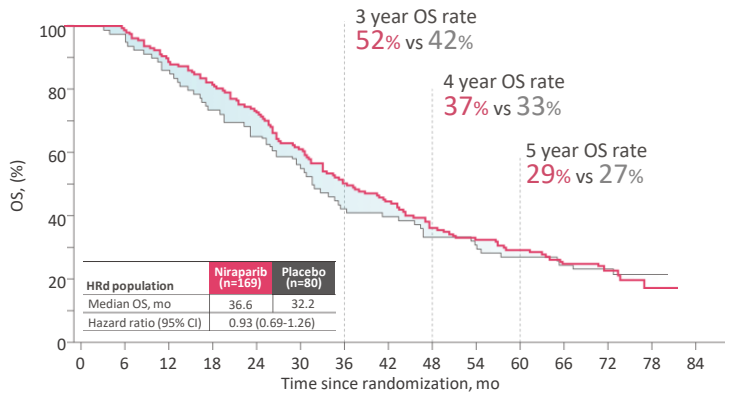
Niraparib	487	480	451	418	378	334	294	261	227	208	192	177	115	39	5
Placebo	246	242	223	204	191	171	153	138	121	111	105	100	62	17	3

HRd[a]



Niraparib	247	245	238	224	207	191	173	156	143	134	126	121	75	31	5
Placebo	126	126	118	112	107	98	91	82	75	70	68	67	40	14	3

HRp[b]



Niraparib	169	164	148	134	120	101	84	73	60	53	47	40	29	5	
Placebo	80	76	67	57	51	44	33	31	26	25	21	19	14	2	

↳ OS results for all prespecified biomarker-defined subgroups consistent with overall population[c]

↳ **Assessment of long-term efficacy outcomes in high-risk aOC may be complicated by multiple factors**

- **Patient population**
- **Extended Post-progression survival**
- **Subsequent therapy**

[a] Hazard ratios and 95% CIs for overall and HRd populations calculated using stratified Cox proportional hazards model with randomization stratification factors. [b] Hazard ratio and 95% CI for HRp population calculated using unstratified Cox proportional hazards model. [c] OS results for the HRnd population (unstratified): hazard ratio (95% CI), 1.39 (0.88–2.19).

aOC advanced ovarian cancer HRd homologous recombination deficient HRnd homologous recombination status not determined HRp homologous recombination proficient OS overall survival Nir niraparib PBO placebo

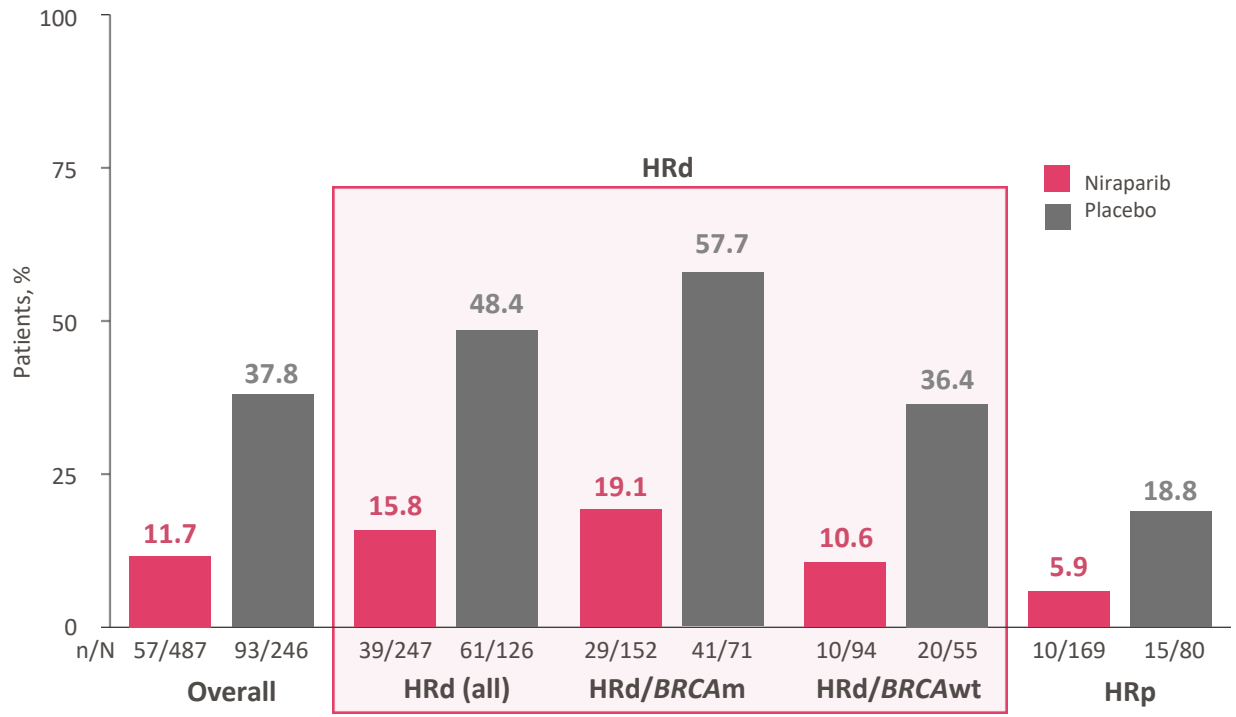
1. González-Martín A, et al. Final Overall survival in patients with newly diagnosed advanced ovarian cancer treated with niraparib first-line maintenance: results from PRIMA/ENGOT-OV26/GOG-3012. presented at ESMO 2024, Barcelona, Spain, Sep 13-17, 2024.

PRIMA 6.2 year updated long-term analysis

- **Subsequent PARP inhibitor therapy**

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

Subsequent PARP inhibitor therapy[a]



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	
	Niraparib (n=487)	Placebo (n=246)	Niraparib (n=247)	Placebo (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 BRCAm BRCA-mutated BRCAwt BRCAwild-type HRd homologous recombination deficient HRp homologous recombination proficient Nir niraparib PARP poly(ADP-ribose) polymerase PBO placebo.

1. Monk BJ, et al. 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. Ann Oncol. 2024 Nov;35(11):981-992. & supplementary.

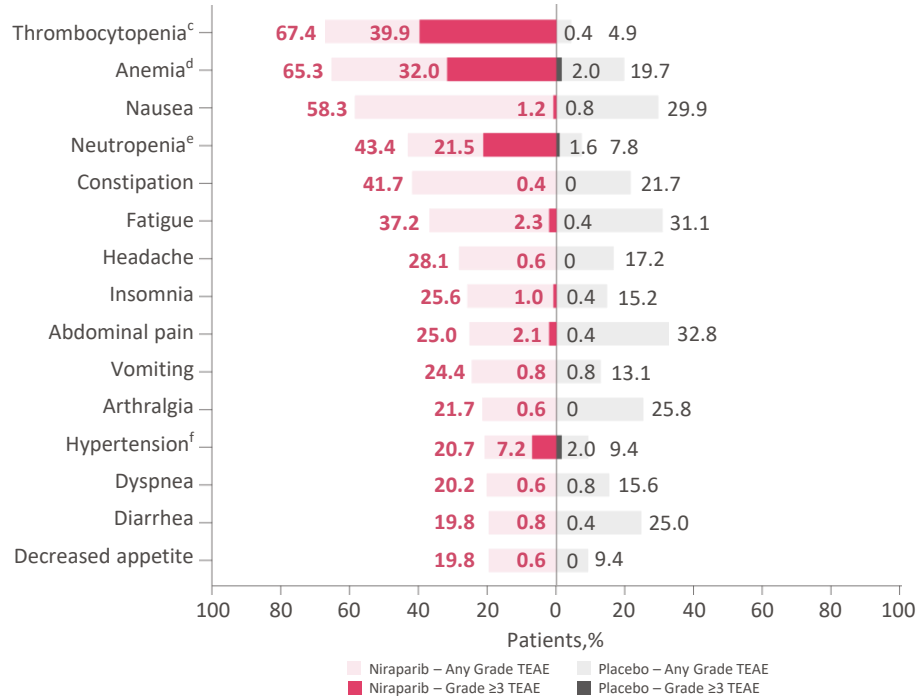
PRIMA 6.2 year updated long-term analysis

- **Updated long-term safety**

With up to 7 years of follow-up, no new safety signals observed

- Median treatment exposure was 11.3 and 8.3 months in the niraparib and placebo arms, respectively
- Most common grade ≥3 TEAEs in the niraparib arm were thrombocytopenia, anemia, and neutropenia
- Lower frequency of hematologic toxicities with the ISD than with the FSD[a]
- MDS/AML rate: Niraparib: 2.3% vs Placebo: 1.6%
- No notable difference in contribution of treatment-related AEs to cause of death between arms, including across subgroups
  - Primary cause of death in both arms was disease progression

TEAEs reported in ≥20% of patients[b]



[a] The ISD is the globally approved starting dose for niraparib 1L maintenance therapy; dosing is individually adjusted according to body weight and platelet count. [b] The most common TEAEs reported in ≥20% of patients treated with niraparib (all niraparib, niraparib FSD, niraparib ISD) in randomized patients who received ≥1 dose of study drug (N=728).
[c] Includes thrombocytopenia and platelet count decreased. d Includes anemia, hemoglobin decreased, red blood cell decreased, hematocrit decreased, and anemia macrocytic. e Includes neutropenia, neutrophil count decreased, febrile neutropenia, and neutropenic sepsis. f Includes hypertension, blood pressure increased, and blood pressure fluctuation.

AE adverse event AML acute myeloid leukemia FSD fixed starting dose ISD individualized starting dose MDS myelodysplastic syndromes TEAE treatment-emergent adverse event.

1. Monk BJ, et al. 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. Ann Oncol. 2024 Nov;35(11):981-992. & supplementary.

PRIMA 6.2 year updated long-term analysis

• Conclusions for PRIMA final analysis

Median follow-up, 6.2 years

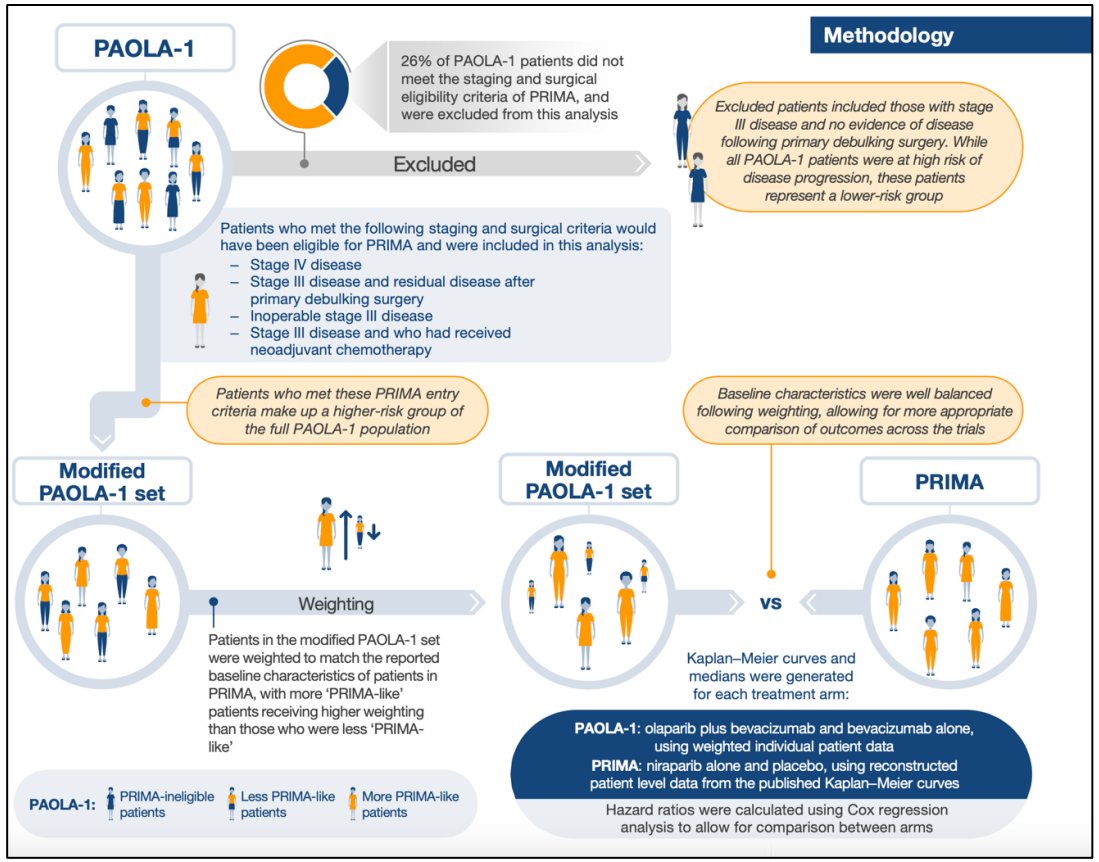
- **PRIMA enrolled patients with advanced high-grade serous/endometrioid OC at high risk for recurrence**
- **Sustained PFS benefit observed with niraparib with additional follow-up in the overall and HRd populations**
  - **Among patients who were alive at 5 years in the HRd population, those who received niraparib were twice as likely to be progression free as patients who received placebo (35% vs 16%)**
  - **Remaining progression free is critical to maintain health-related quality of life**
    No difference in OS between niraparib and placebo arms in overall population
- **No difference in OS between niraparib and placebo arms in overall population and by HRd status**
  - **3-fold higher subsequent PARP inhibitor use in placebo arm than niraparib arm across populations (HRd: 48.4% vs 15.8%)**
- **Long-term safety remained consistent with the identified safety profile of niraparib**
- **Long-term data support the benefit of niraparib as 1L maintenance therapy regardless of HRd status**

1L first-line HRD homologous recombination deficiency HRd homologous recombination deficient OC ovarian cancer OS overall survival PARP poly(ADP-ribose) polymerase PFS progression-free survival.

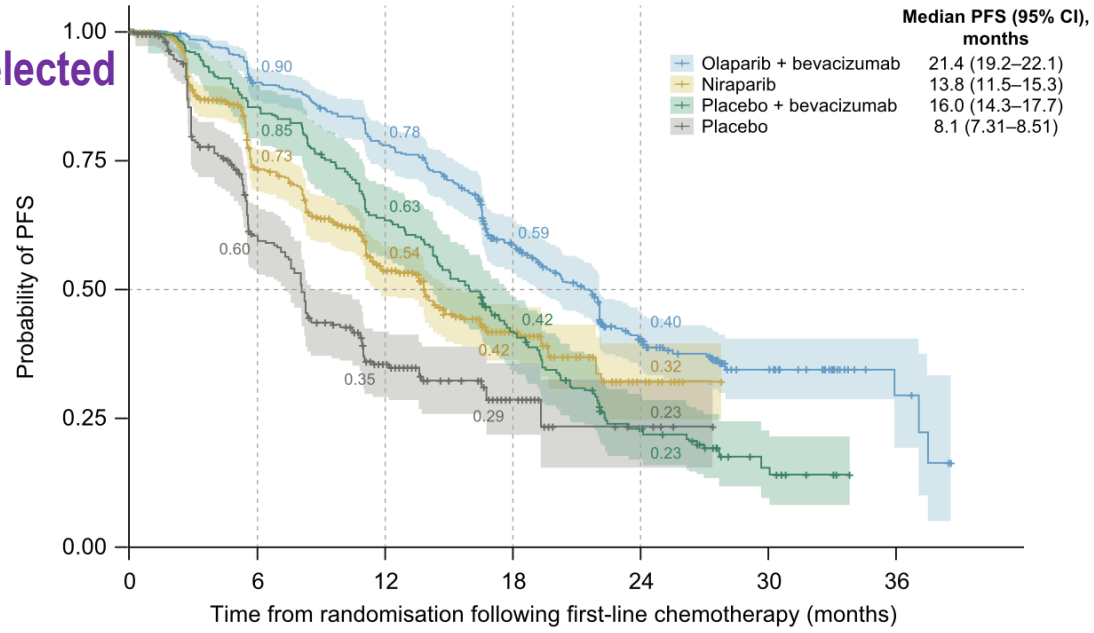
1. Monk BJ, et al. Niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer: final overall survival results from the PRIMA/ENGOT-OV26/GOG-3012 trial. Ann Oncol. 2024 Nov;35(11):981-992. & supplementary Appendix.

Population-adjusted indirect comparisons

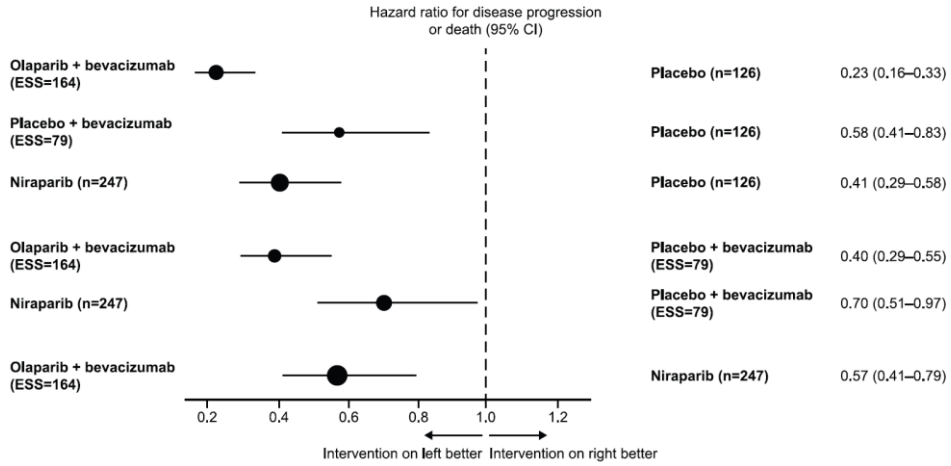
PAOLA-1 vs. PRIMA



After matching Biomarker-unselected



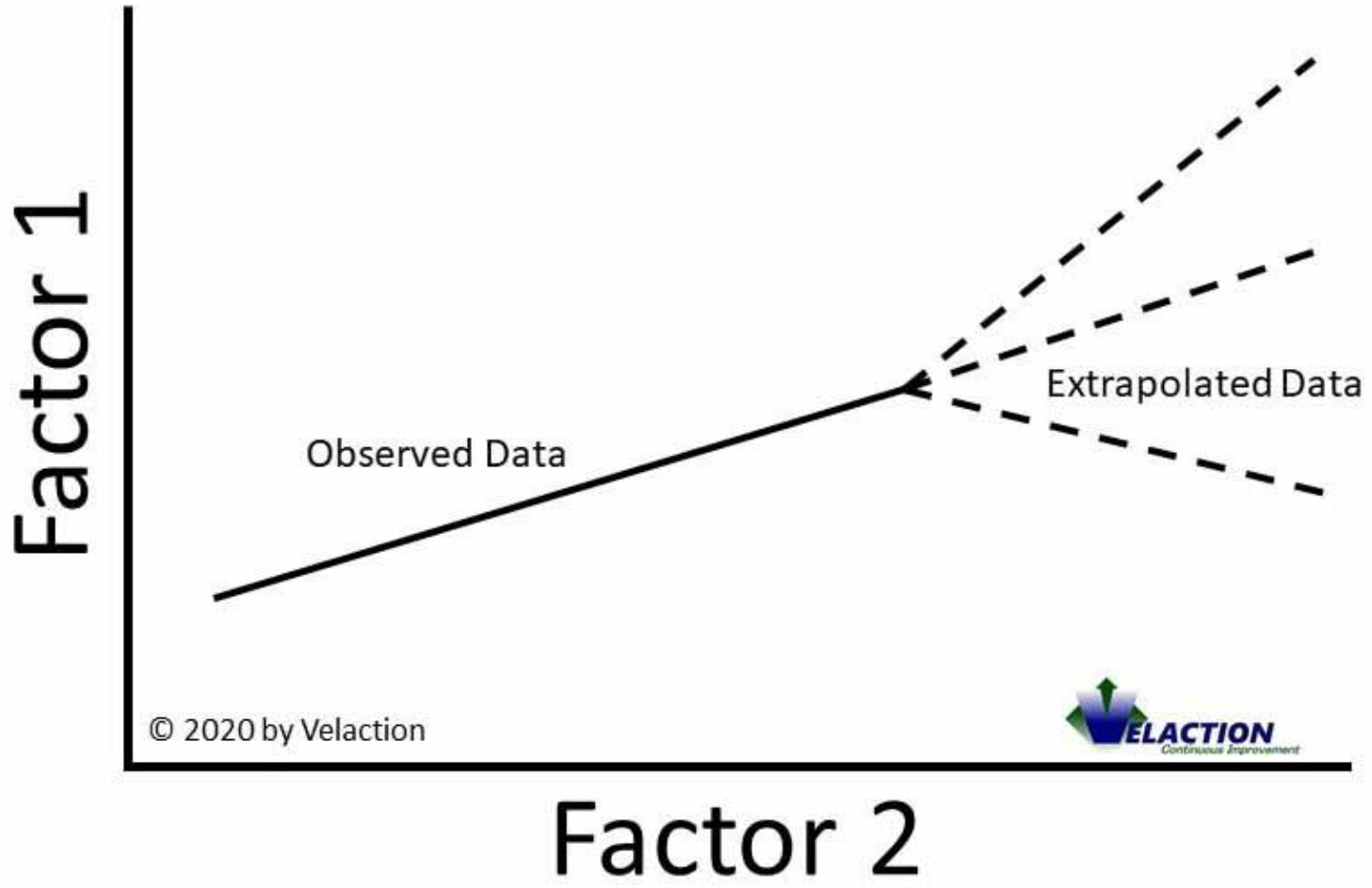
HRD-positive



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

For broader population…

Extrapolation is the key of scientific advancement





Real-world evidence (1) 1NSPIRE

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study



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ABSTRACT ONLY · Volume 36, Supplement 2, S794-S795, September 2025

1227eP Real-world (rw) outcomes in patients (pts) with epithelial ovarian cancer (EOC) who received first-line maintenance (1LM) niraparib: Final results from the 1NSPIRE chart review study

F.B. Musa [1] · B.J. Rimel [2] · J. Lim [3] · ... · A. Golembesky [8] · P.H. Thaker [9] · L.M. Landrum [10] ... Show more

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

Background

- In PRIMA/ENGOT-OV26/GOG-3012, a phase 3 trial of patients with newly diagnosed advanced EOC that responded (ie, CR or PR) to PBCT and with a high risk of recurrence, **1LM niraparib monotherapy improved PFS vs placebo, regardless of HRD status**[1–3]
  - After 6.2 years of follow-up:
    - In the overall population, median PFS was 13.8 months vs 8.2 months for placebo (hazard ratio, 0.66; 95% CI, 0.55–0.78)[3]
    - In the HRd subgroup, median PFS was 24.5 months vs 11.2 months for placebo (hazard ratio, 0.51; 95% CI, 0.40–0.66)
    - In the HRp subgroup, median PFS was 8.4 months vs 5.4 months for placebo (hazard ratio, 0.67; 95% CI, 0.50–0.89)

- Real-world clinical outcomes of patients receiving 1LM niraparib monotherapy have been previously reported.[4–6] However, more studies are needed to better characterize outcomes for patients with advanced EOC by **HRD status** who receive 1LM niraparib monotherapy in routine clinical practice

1LM, first-line maintenance; BRCAm, BRCA-mutated; BRCAwt, BRCA wild-type; EOC, epithelial ovarian cancer; CR, complete response; PR, partial response; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PFS, progression-free survival; PR, partial response

References 1. González-Martín A, et al. N Engl J Med. 2019;381(25):2391–2402. 2. González-Martín A, et al. Eur J Cancer. 2023;189:112908. 3. Monk BJ, et al. Ann Oncol. 2024;35(11):981–992. 4. Rimel B, et al. Oncol Ther. 2024;12(3):465–475. 5. Chase DM, et al. Oncol Ther. 2024;12(3):599–607. 6. Salani R, et al. Future Oncol. 2025;21(2):213–219. 7. F. B. Musa, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

Study design

- In this US-based, retrospective, multicenter, medical chart review study, eligible patients were aged ≥18 years, diagnosed with EOC, and initiated 1LM niraparib monotherapy between 1 April 2020 and 1 April 2023 (inclusive)

- Patients were followed from 1LM niraparib monotherapy initiation (index date) to death, loss to follow-up, or start of data collection(site-specific initiation visit date), whichever occurred first

- rwTTNT and rwPFS were estimated using Kaplan–Meier methods and examined among:
  – Biomarker subgroups of the overall population: HRd, HRp, BRCAwt/HRD status unknown
  – Patients with a CR/PR to 1L PBCT)

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

• Results: Patients

	☑ All patients	☑ Patients with CR/PR to 1L PBCT
Age	Median age, 67 y (IQR, 60-73 y) Age group at index: <75 y, 80.7% ≥75 y, 19.3%	Median age, 68 y (IQR, 60–73 y) Age group at index: <75 y, 79.8% ≥75 y, 20.2%
Race	12.4% black/ African American/ other minority race 5.0% Hispanic or Latino	12.4% Black/ African American/ other minority race 5.6% Hispanic or Latino
Region	46.8% Midwest 27.5% South 25.7% Northeast 0% West	49.4% Midwest 26.4% South 24.2% Northeast 0% West
Practice type	57.3% Community based 38.1% University based 3.7% Both	57.3% Community based 37.6% University based 4.5% Both
Insurance type	25.2% Employer based 51.8% Medicare 22.9% Other/ unknown/uninsured	21.9% Employer based 56.2% Medicare 21.9% Other/ unknown/uninsured

Characteristic	All patients (N=218)	Patients with CR/PR to 1L PBCT (n=178)
ECOG PS at index		
0–1	192 (88.1)	156 (87.6)
2	7 (3.2)	5 (2.8)
Missing	19 (8.7)	17 (9.6)
Stage at initial diagnosis		
I-II	11 (5.0)	7 (3.9)
III	132 (60.6)	107 (60.1)
IV	39 (17.9)	33 (18.5)
Unknown	36 (16.5)	31 (17.4)
Histology		
Serous	194 (89.0)	158 (88.8)
Other[a]	24 (11.0)	20 (11.2)
Biomarker status		
HRd	82 (37.6)	62 (34.8)
*BRCA*m	24 (11.0)	21 (11.8)
*BRCA*wt	49 (22.5)	35 (19.7)
BRCA unknown	9 (4.1)	6 (3.4)
HRp	57 (26.1)	47 (26.4)
*BRCA*wt/HRD status unknown	66 (30.3)	57 (32.0)
Both *BRCA* and HRD status unknown	13 (6.0)	12 (6.7)
Type of surgery		
PCS	85 (39.0)	66 (37.1)
ICS	110 (50.5)	96 (53.9)
No surgery	18 (8.3)	13 (7.3)
Unknown/missing	5 (2.3)	3 (1.7)
Residual disease status[b]		
Visible residual disease	45 (23.1)	35 (21.6)
No visible residual disease	114 (58.5)	96 (59.3)
Unknown/missing	39 (20.0)	33 (20.4)
Received 1L platinum-containing regimen	217 (99.5)	178 (100.0)
Received 1L bev-containing regimen	19 (8.7)	18 (10.1)
Follow-up time, median (IQR), mo	22.6 (16.1-33.5)	23.6 (16.4-33.8)

Values in table are n (%) unless noted otherwise.
[a]Other includes clear cell, mucinous, endometrioid, epithelial not otherwise specified, or unknown.
[b]Among patients who received cytoreductive surgery.

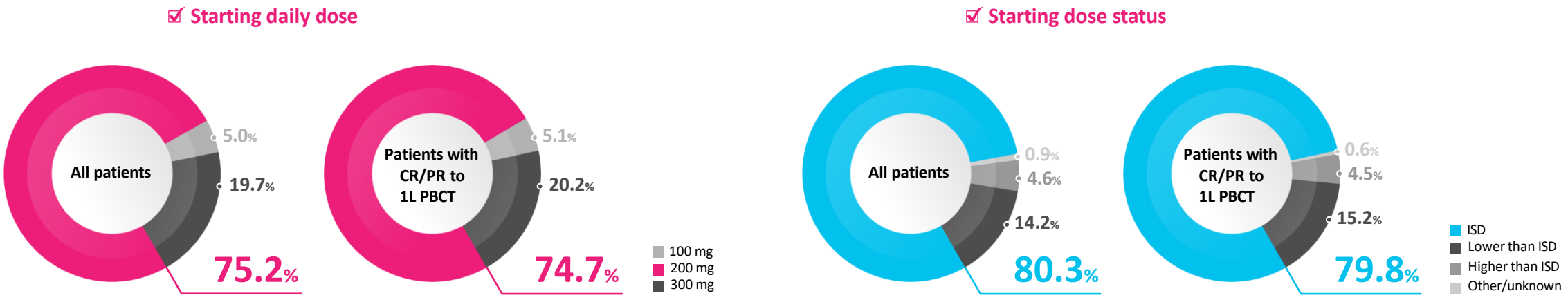
- This final analysis included data from 218 patients across 18 US sites
  – Median (IQR) follow-up time was 22.6 months (16.1–33.5 months)
- Overall, 178 patients (81.7%) had a CR/PR to 1L PBCT, and 31 (14.2%) had stable disease
- Demographic and clinical characteristics were similar between the overall patient population and the subgroup of patients with a CR/PR
- Overall, **37.6% of patients had HRd, 26.1% had HRp, and 30.3% had BRCAwt/HRD status unknown**
  – Both BRCA and HRD status were unknown for 6.0% of patients overall

1L, first-line; bev, bevacizumab; BRCAm, BRCA-mutated; BRCAwt, BRCA wild-type; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; ICS, interval cytoreductive surgery; PBCT, platinum-based chemotherapy; PCS, primary cytoreductive surgery; PR, partial response.
Reference 1. F. B. Musa, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

- ## Results: Niraparib dosing characteristics
  - Median (IQR) time to niraparib initiation from end of 1L treatment was 48 days (35–66 days) in the overall population
    - 0–30 days from end of 1L (n=49; 22.5%)
    - 31–60 days from end of 1L (n=100; 45.9%)
    - 61–90 days from end of 1L (n=49; 22.5%)
    - >90 days from end of 1L (n=20; 9.2%)
  - Most patients (n=164; 75.2%) started niraparib at a 200-mg starting daily dose; 175 (80.3%) initiated niraparib at their weight- and platelet-based individualized starting dose

Niraparib dosing characteristics



CR, complete response; ISD, individualized starting dose; PBCT, platinum-based chemotherapy; PR, partial response.

Reference 1. F. B. Musa, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

Results: Niraparib discontinuation

- Of 218 patients, **156 (71.6%) discontinued niraparib** during the study period. Discontinuation occurred most frequently because of*:
  - **Disease progression (n=92; 59.0%)**
  - Prespecified event of special interest† (n=23; 14.7%)
  - Toxicity (n=23; 14.7%)
  - Completed treatment (n=14; 9.0%)
  - Patient request (n=12; 7.7%)

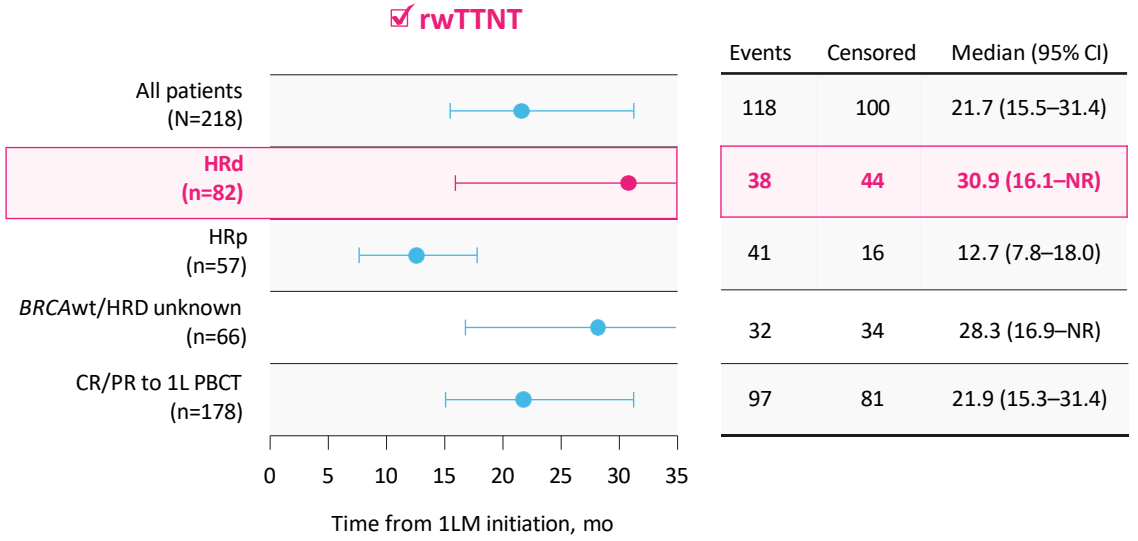
- Niraparib dosing characteristics in the subgroup of patients with a CR/PR to 1L PBCT were similar to those of the overall population

*There could be ≥1 reason for discontinuation, so percentages may exceed 100%.
†Data were collected from patient medical charts on the following prespecified events of special interest: thrombocytopenia, anemia, neutropenia, MDS, AML, and SPMs.
CR, complete response; ISD, individualized starting dose; PBCT, platinum-based chemotherapy; PR, partial response.
Reference 1. F. B. Musa, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

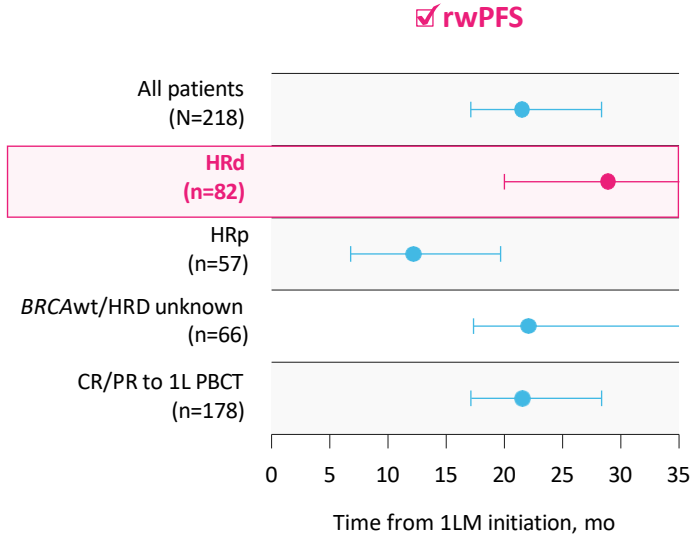
Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

- **Results**
  - Overall, the observed median rwTTNT and rwPFS were both 21.7 months for all patients
  - When examining real-world outcomes by biomarker subgroup, the longest observed median rwTTNT and rwPFS were among patients with HRd status
  - Observed median rwTTNT and rwPFS among patients in the subgroup of patients with CR/PR to 1L PBCT were similar to those in the overall population

Real-world outcomes among all patients, stratified by biomarker status, and among patients with CR/PR to 1L PBCT



	Events	Censored	Median (95% CI)
All patients (N=218)	118	100	21.7 (15.5–31.4)
HRd (n=82)	**38**	**44**	**30.9 (16.1–NR)**
HRp (n=57)	41	16	12.7 (7.8–18.0)
*BRCA*wt/HRD unknown (n=66)	32	34	28.3 (16.9–NR)
CR/PR to 1L PBCT (n=178)	97	81	21.9 (15.3–31.4)



	Events	Censored	Median (95% CI)
All patients (N=218)	120	98	21.7 (17.3–28.6)
HRd (n=82)	**37**	**45**	**29.1 (20.1–NR)**
HRp (n=57)	43	14	12.3 (6.9–19.9)
*BRCA*wt/HRD unknown (n=66)	34	32	22.2 (17.5–NR)
CR/PR to 1L PBCT (n=178)	99	79	21.7 (17.3–28.6)

PRIMA median PFS
-Overall population: 13.8 months
-HRd: 24.5 months
-HRp: 8.4 months

1LM, first-line maintenance; BRCAwt, BRCA wild-type; CR, complete response; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; NR, not reached; PBCT, platinum-based chemotherapy; PR, partial response; rwPFS, real-world progression-free survival; rwTTNT, real-world time to next treatment.

Reference 1. F. B. Musa, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with epithelial ovarian cancer who received first-line maintenance niraparib: final results from the 1NSPIRE chart review study

Conclusions

- **Real-world outcomes aligned with expectations for key biomarker subgroups, with numerically longer rwTTNT and rwPFS observed in the HRd subgroup** versus the overall population

- For patients with advanced EOC receiving 1LM niraparib monotherapy in routine clinical practice, real-world outcomes exceeded expectations based on the PRIMA trial results. This was true in all biomarker subgroups, including patients with HRp status
  - This finding may be due to:
    · The inclusion of patients with stage III EOC and no visible residual disease in the 1NSPIRE study
    · Clinicians' ability to identify those most likely to benefit from niraparib in routine clinical practice

- Compared with all patients, **baseline demographic and clinical outcomes were similar in the subgroup of patients with a CR or PR to 1L PBCT**

Reference 1. F. B. Musa, et al. presented at 2025 EMSO Annual Meeting, Sep 2025



Real-world evidence (2) EUROPA

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

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ABSTRACT ONLY · Volume 36, Supplement 2, S736-S737, September 2025

1104P Real-world (rw) outcomes in patients (pts) with advanced ovarian cancer (aOC) receiving niraparib (nir) as first-line maintenance (1LM) in the EUROPA study

A. Fagotti [1] · J-S. Frenel [2] · M. Saint-Ghislain [3] · ... · K. Vitanova [7] · Y. Nam [7] · I. Braicu [8] ... Show more

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

Background

- Niraparib monotherapy was approved as **1LM treatment for patients with aOC** based on results from the phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial, which demonstrated improved PFS versus placebo, regardless of HRD status[1–3]
  – The PRIMA trial enrolled patients who were at a high risk for disease progression, excluding patients with stage III aOC who had no visible residual disease after PCS

- There are limited real-world data from the EU describing 1LM niraparib monotherapy use and outcomes for patients **not represented in the PRIMA trial who had stage III aOC with no visible residual disease after PCS**

1LM, first-line maintenance; BRCAm, BRCA-mutated; BRCAwt, BRCA wild-type; EOC, epithelial ovarian cancer; CR, complete response; PR, partial response; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PFS, progression-free survival; PR, partial response

References 1. González-Martín A, et al. N Engl J Med. 2019;381(25):2391–2402. 2. González-Martín A, et al. Eur J Cancer. 2023;189:112908. 3. Monk BJ, et al. Ann Oncol. 2024;35(11):981–992. 4. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

Study design

- EUROPA is a noninterventional, multicenter, retrospective cohort study of patients with aOC across 4 sites in France, Germany, and Italy
- EUROPA included patients with **epithelial aOC who initiated 1LM niraparib monotherapy** (index date) between 1 October 2018 and 31 March 2023
- Patients were followed from the index date to the earliest of death, loss to follow-up, or end of the study period (30 September 2023)
- rwTTD, rwTTNTD, and rwPFS were assessed using Kaplan–Meier methods

TTD, time to treatment discontinuation
TTNTD, time to next treatment or death

- All results were described for the overall 1LM niraparib cohort and for a subgroup with stage III aOC and no visible residual disease after PCS
- Results were also analyzed separately for Italy

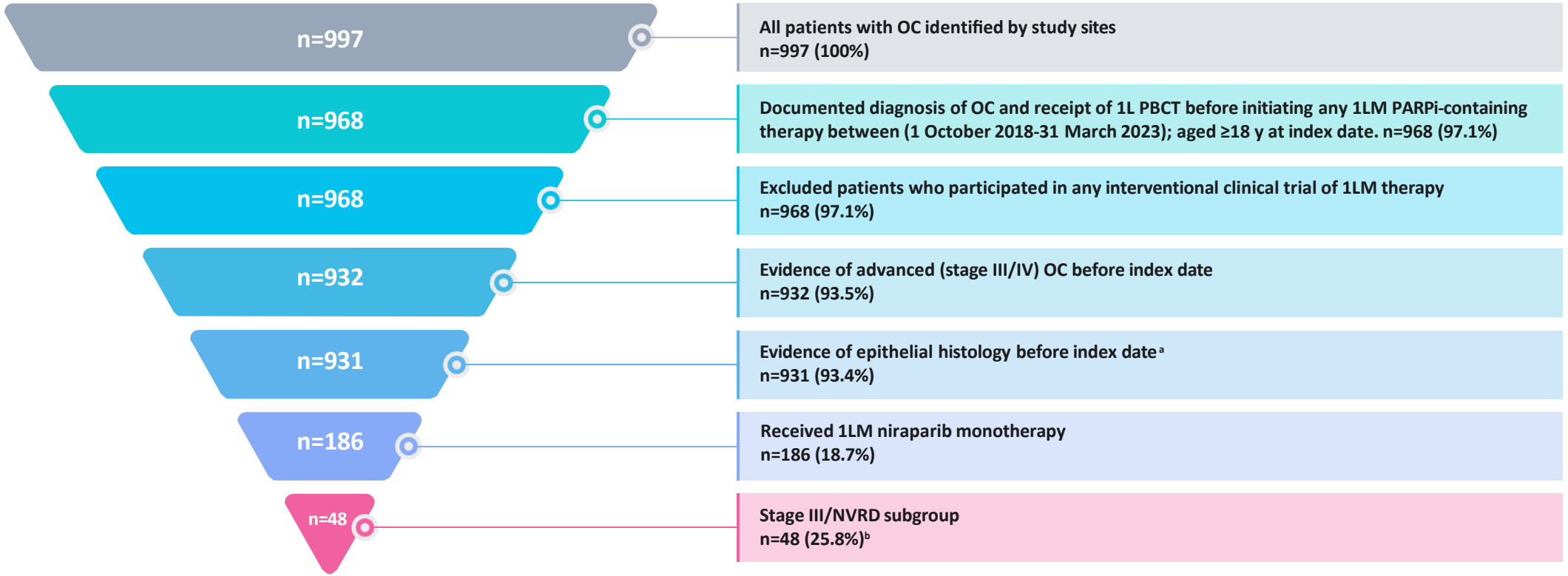
1L, first-line; 1LM, first-line maintenance; NVRD, no visible residual disease; OC, ovarian cancer; PARPi, poly(ADP-ribose) polymerase inhibitor; PBCT, platinum-based chemotherapy

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

- **Study design**

Eligibility criteria and study population attrition



[a]Includes serous, endometrioid, clear cell, mucinous, transitional cell, mixed, epithelial not otherwise specified, or unknown/not documented epithelial histological subtype.
[b]Percentage calculated out of the total number of patients who received 1LM niraparib monotherapy (N=186).

1L, first-line; 1LM, first-line maintenance; NVRD, no visible residual disease; OC, ovarian cancer; PARPi, poly(ADP-ribose) polymerase inhibitor; PBCT, platinum-based chemotherapy

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

• Results: Patients

Patient demographics and clinical characteristics for the overall cohort and for the subgroup with stage III aOC and no visible residual disease after PCS

☑ Overall cohort

- **186** patients
- **147** patients from Italy
- **22** patients from France
- **17** patients from Germany
- Median age, **64.0 y** (IQR, **54.0-74.0 y**)
- ECOG PS at index:
  0-1: **170 (91.4)**
  2: **5 (2.7)**
  Missing: **11 (5.9)**
- Median follow-up, **19.1 mo** (IQR, **11.3-28.7 mo**)

☑ Stage III NVRD subgroup

- **48** patients
- **39** patients from Italy
- **2** patients from France
- **7** patients from Germany
- Median age, **60.5 y** (IQR, **52.0-65.0 y**)
- ECOG PS at index:
  0-1: **45 (93.8)**
  2: **1 (2.1)**
  Missing: **2 (4.2)**
- Median follow-up, **29.8 mo** (IQR, **24.2-33.6 mo**)

Characteristic		Overall cohort (n=186)	Stage III NVRD subgroup (n=48)
Stage at initial diagnosis	III	124 (66.7)	48 (100.0)
	IV	62 (33.3)	0
Histology	High-grade serous	177 (95.2)	45 (93.8)
	Other[a]	9 (4.8)	3 (6.3)
Type of surgery received	PCS only	81 (43.5)	48 (100.0)
	ICS only	86 (46.2)	0
	Multiple cytoreductive surgeries	2 (1.1)	0
	No surgery	17 (9.1)	0
Residual disease status[b]	No visible residual disease	142 (84.0)	48 (100.0)
	Visible residual disease	17 (10.1)	0
	Missing	10 (5.9)	0
***BRCA* mutation status**	*BRCA*m	3 (1.6)	1 (2.1)
	*BRCA*wt	180 (96.8)	46 (95.8)
	Missing/untested	3 (1.6)	1 (2.1)
HRD status[c]	HRd	17 (9.1)	3 (6.3)
	HRp	19 (10.2)	2 (4.2)
	Missing/untested	146 (78.5)	42 (87.5)
	Indeterminate[d]	4 (2.2)	1 (2.1)
Combined HRD/ *BRCA* status	HRd	19 (10.2)	4 (8.3)
	*BRCA*m	3 (1.6)	1 (2.1)
	*BRCA*wt	16 (8.6)	3 (6.3)
	HRp or *BRCA*wt/HRD status unknown[c]	164 (88.2)	43 (89.6)
	Missing/untested or indeterminate[d]	3 (1.6)	1 (2.1)
Niraparib starting daily dose	100 mg	12 (6.5)	1 (2.1)
	200 mg	159 (85.5)	41 (85.4)
	300 mg	7 (3.8)	4 (8.3)
	Missing/other	8 (4.3)	2 (4.2)
Niraparib starting dose status	ISD	156 (83.9)	42 (87.5)
	Lower than ISD	18 (9.7)	2 (4.2)
	Higher than ISD	4 (2.2)	1 (2.1)
	Missing	8 (4.3)	3 (6.3)

Unless otherwise stated, values shown in table are n (%). Because of rounding, the percentages for some categories may not total 100%.
[a]Other includes clear cell, mixed, and epithelial not otherwise specified.
[b]Among patients who received cytoreductive surgery.
[c]Patients with unknown HRD status due to absence of HRD test or indeterminate test result. dIndicates an indeterminate test result.

1LM, first-line maintenance; aOC, advanced ovarian cancer; BRCAm, BRCA-mutated; BRCAwt, BRCA wild-type; ECOG PS, Eastern Cooperative Oncology Group performance status; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; ICS, interval cytoreductive surgery; ISD, individualized starting dose; NVRD, no visible residual disease; PCS, primary cytoreductive surgery.

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

Results: Patients

- There were 186 patients in the overall 1LM niraparib cohort. Of those, **48 (25.8%) had stage III aOC and no visible residual disease after PCS**
- Demographic and clinical characteristics were similar for all patients in the 1LM niraparib cohort and the subgroup with stage III aOC and no visible residual disease after PCS
- Although BRCA status was known for most patients, HRD status was unknown for ~80% of patients in the overall 1LM niraparib cohort due to low HRD testing rates

1LM, first-line maintenance; aOC, advanced ovarian cancer; BRCAm, BRCA-mutated; BRCAwt, BRCA wild-type; ECOG PS, Eastern Cooperative Oncology Group performance status; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; ICS, interval cytoreductive surgery; ISD, individualized starting dose; NVRD, no visible residual disease; PCS, primary cytoreductive surgery

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Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

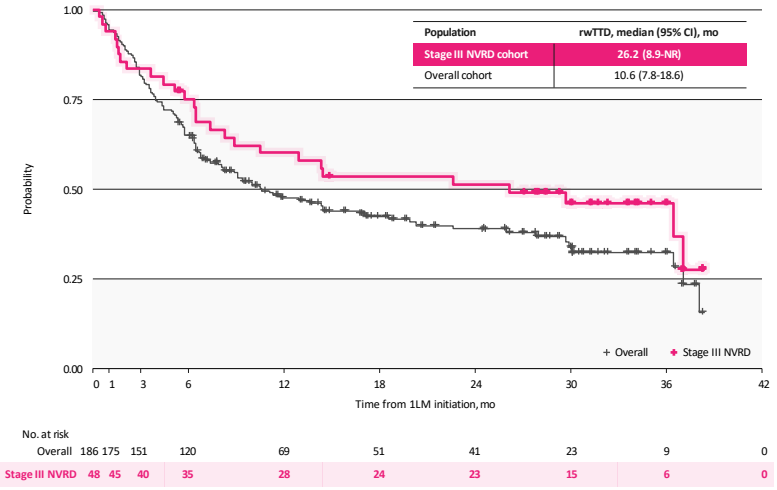
TTD, time to treatment discontinuation
TTNTD, time to next treatment or death

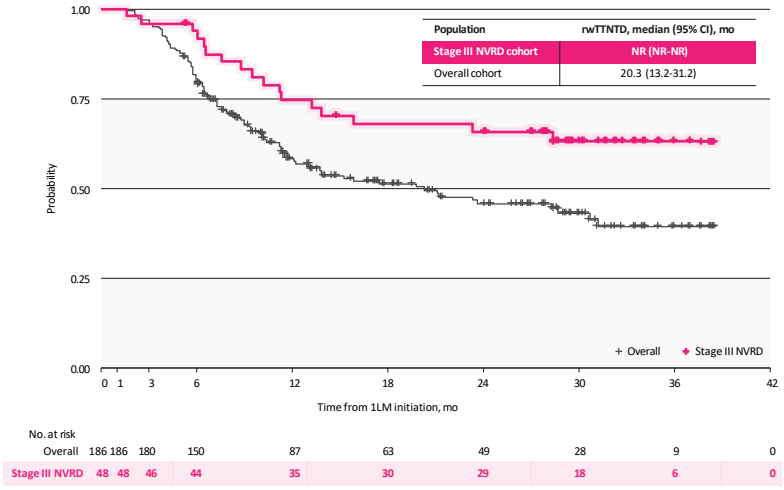
PRIMA median PFS
-Overall population: 13.8 months
-HRd: 24.5 months
-HRp: 8.4 months

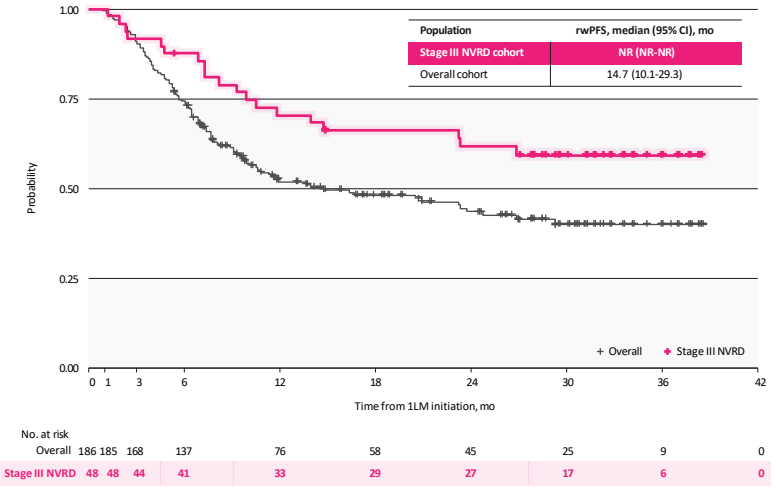
• Results

- Median (IQR) time from diagnosis to 1LM therapy initiation was 8.3 months (7.6–9.4 months) for the overall cohort and 7.6 months (6.9–8.3 months) for the stage III NVRD cohort
- **Median (95% CI) rwTTD was longer in the subgroup of patients with stage III aOC and no visible residual disease after PCS** (26.2 months [8.9 months–not reached]) than in the overall 1LM niraparib cohort (10.6 months [7.8–18.6 months])
- **Median rwTTNTD and rwPFS were 20.3 months (13.2–31.2 months) and 14.7 months (10.1–29.3 months),** respectively, in the overall niraparib cohort but not reached in the subgroup of patients with stage III aOC and no visible residual disease after PCS

Observed rwTTD, rwTTNTD , and rwPFS from the start of 1LM niraparib in the overall cohort and in the subgroup of patients with stage III aOC and no visible residual disease after PCS







1LM, first-line maintenance; aOC, advanced ovarian cancer; NR, not reached; NVRD, no visible residual disease; PCS, primary cytoreductive surgery; rwPFS, real-world progression-free survival; rwTTD, real-world time to treatment discontinuation; rwTTNTD, real-world time to next treatment or death

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

- **Results**
  - **rwTTD, rwTTNTD, and rwPFS probabilities were consistently higher for the subgroup of patients with stage III aOC and no visible residual disease after PCS** at 12, 24, and 36 months after the index date

rwTTD, rwTTNTD, and rwPFS probabilities at 12, 24, and 36 months after the index date

Probability (95% CI)	Overall cohort (n=186)	Stage III NVRD subgroup (n=48)
rwTTD		
12 mo	0.47 (0.41-0.55)	0.60 (0.47-0.76)
24 mo	0.39 (0.32-0.47)	0.51 (0.39-0.68)
36 mo	0.32 (0.25-0.42)	0.46 (0.33-0.63)
rwTTNTD		
12 mo	0.58 (0.51-0.66)	0.75 (0.63-0.88)
24 mo	0.46 (0.38-0.54)	0.66 (0.53-0.81)
36 mo	0.39 (0.31-0.50)	0.63 (0.50-0.79)
rwPFS		
12 mo	0.52 (0.45-0.60)	0.70 (0.59-0.85)
24 mo	0.43 (0.36-0.52)	0.62 (0.49-0.77)
36 mo	0.40 (0.33-0.49)	0.59 (0.47-0.75)

NVRD, no visible residual disease; rwPFS, real-world progression-free survival; rwTTD, real-world time to treatment discontinuation; rwTTNTD, real-world time to next treatment or death.

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

- ## Results: Subgroup

Patient demographics and clinical characteristics for the overall cohort from Italy and for the subgroup of patients from Italy with stage III aOC and no visible residual disease after PCS

☑ Overall Italy cohort	☑ Stage III NVRD subgroup from Italy
147 patients	39 patients
Median age, 64.0 y (IQR, 54.0-73.0 y)	Median age, 60.0 y (IQR, 51.0-65.0 y)
ECOG PS at index: 0-1: 140 (95.2) 2: 3 (2.0) Missing: 4 (2.7)	ECOG PS at index: 0-1: 38 (97.4) 2: 1 (2.6) Missing: 0
Median follow-up, 21.1 mo (IQR, 11.6-30.1 mo)	Median follow-up, 30.4 mo (IQR, 27.8-34.1 mo)

Characteristic		Overall Italy cohort (n=147)	Stage III NVRD subgroup from Italy (n=39)
Stage at initial diagnosis	III	99 (67.4)	39 (100.0)
	IV	48 (32.7)	0
Histology	High-grade serous	143 (97.3)	37 (94.9)
	Other[a]	4 (2.7)	2 (5.1)
Type of surgery received	PCS only	64 (43.5)	39 (100.0)
	ICS only	75 (51.0)	0
	Multiple cytoreductive surgeries	0	0
	No surgery	8 (5.4)	0
Residual disease status[b]	No visible residual disease	128 (92.1)	39 (100)
	Visible residual disease	11 (7.9)	0
	Missing	0	0
BRCA mutation status	*BRCA*m	1 (0.7)	0
	*BRCA*wt	146 (99.3)	39 (100)
	Missing/untested	0	0
HRD status[c]	HRd	6 (4.1)	1 (2.6)
	HRp	8 (5.4)	0
	Missing/untested	132 (89.8)	38 (97.4)
	Indeterminate[d]	1 (0.7)	0
Combined HRD/ *BRCA* status	HRd	7 (4.8)	1 (2.6)
	*BRCA*m	1 (0.7)	0
	*BRCA*wt	6 (4.1)	1 (2.6)
	HRp or *BRCA*wt/HRD status unknown[c]	140 (95.2)	38 (97.4)
	Missing/untested or indeterminate[d]	0	0
Niraparib starting daily dose	100 mg	8 (5.4)	1 (2.6)
	200 mg	135 (91.8)	36 (92.3)
	300 mg	4 (2.7)	2 (5.1)
	Missing/other	0	0
Niraparib starting dose status	ISD	135 (91.8)	37 (94.9)
	Lower than ISD	11 (7.5)	2 (5.1)
	Higher than ISD	1 (0.7)	0
	Missing	0	0

Unless otherwise stated, values shown in table are n (%). Because of rounding, the percentages for some categories may not total 100%.
[a]Other includes clear cell, mixed, and epithelial not otherwise specified.
[b]Among patients who received cytoreductive surgery.
[c]Patients with unknown HRD status due to absence of HRD test or indeterminate test result.
[d]Indicates an indeterminate test result.

1LM, first-line maintenance; aOC, advanced ovarian cancer; BRCAm, BRCA-mutated; BRCAwt, BRCA wild-type; ECOG PS, Eastern Cooperative Oncology Group performance status; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; ICS, interval cytoreductive surgery; ISD, individualized starting dose; NVRD, no visible residual disease; PCS, primary cytoreductive surgery.

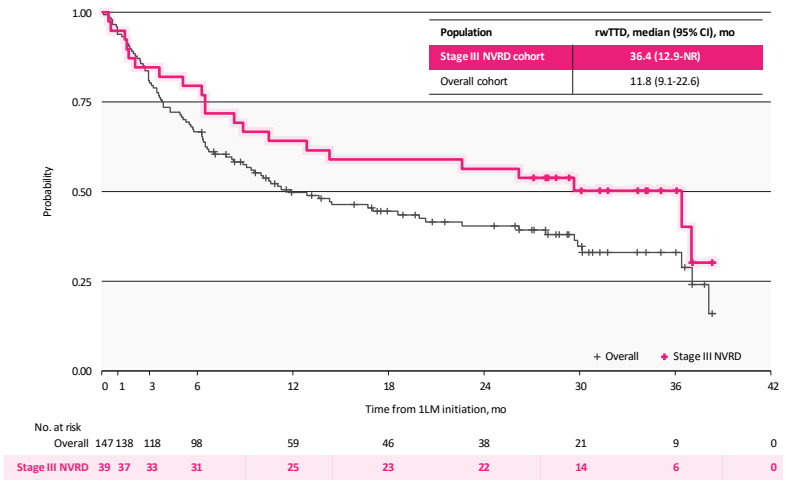
Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

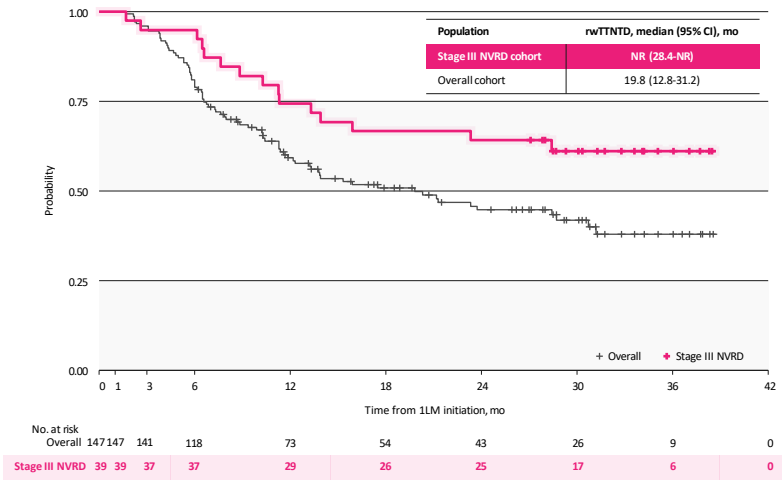
Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

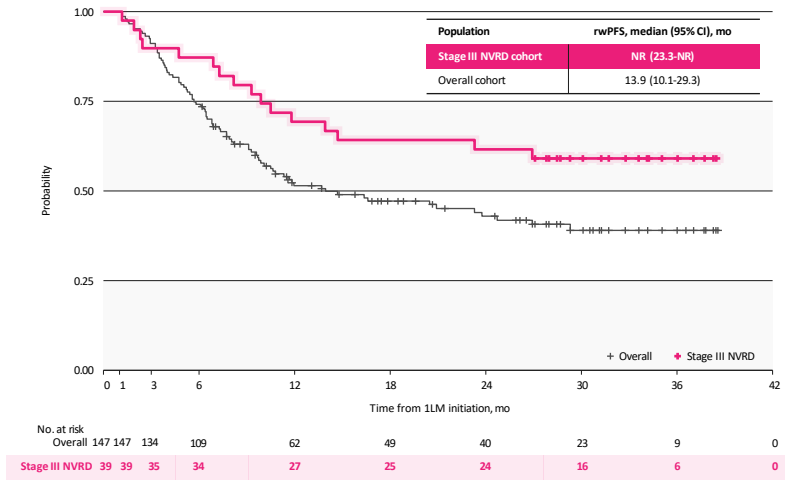
PRIMA median PFS
-Overall population: 13.8 months
-HRd: 24.5 months
-HRp: 8.4 months

- **Results_ subgroup**

Observed rwTTD, rwTTNTD, and rwPFS from the start of 1LM niraparib in the overall cohort from Italy and in the subgroup of patients from Italy with stage III aOC and no visible residual disease after PCS







1LM, first-line maintenance; aOC, advanced ovarian cancer; NR, not reached; NVRD, no visible residual disease; PCS, primary cytoreductive surgery; rwPFS, real-world progression-free survival; rwTTD, real-world time to treatment discontinuation; rwTTNTD, real-world time to next treatment or death.

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

- **Results_subgroup**

rwTTD, rwTTNTD, and rwPFS probabilities at 12, 24, and 36 months after the index date

Probability (95% CI)	Overall Italy cohort (n=147)	Stage III NVRD subgroup from Italy (n=39)
rwTTD		
12 mo	0.50 (0.42-0.59)	0.64 (0.51-0.81)
24 mo	0.40 (0.33-0.50)	0.56 (0.43-0.74)
36 mo	0.33 (0.25-0.44)	0.50 (0.36-0.69)
rwTTNTD		
12 mo	0.59 (0.52-0.68)	0.74 (0.62-0.89)
24 mo	0.45 (0.37-0.54)	0.64 (0.51-0.81)
36 mo	0.38 (0.29-0.49)	0.61 (0.47-0.79)
rwPFS		
12 mo	0.51 (0.44-0.60)	0.69 (0.56-0.85)
24 mo	0.43 (0.35-0.52)	0.62 (0.48-0.79)
36 mo	0.39 (0.31-0.49)	0.59 (0.45-0.77)

NVRD, no visible residual disease; rwPFS, real-world progression-free survival; rwTTD, real-world time to treatment discontinuation; rwTTNTD, real-world time to next treatment or death.

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

Real-world outcomes in patients with advanced ovarian cancer receiving niraparib as first-line maintenance in the EUROPA study

Conclusions

- **Patients with stage III disease and no visible residual disease after PCS receiving 1LM niraparib monotherapy had better clinical outcomes** than those in the overall 1LM niraparib cohort
  - This was consistent across rwTTD, rwTTNTD, and rwPFS

- The clinical benefit of 1LM niraparib monotherapy in the PRIMA trial may have been underestimated because of the exclusion of patients with stage III aOC with no visible residual disease after PCS

Reference 1. A. Fagotti, et al. presented at 2025 EMSO Annual Meeting, Sep 2025



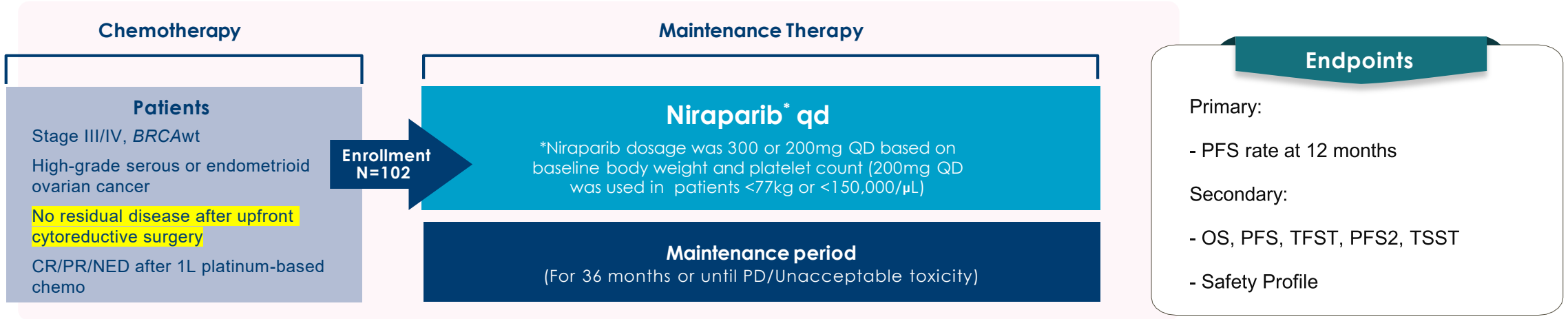
POLO

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

POLO

PI : Jae Weon Kim, Seoul National University Hospital

(A Phase IV open-label, multicenter study of niraparib as maintenance therapy in ***BRCA* wild-type**, **newly diagnosed** advanced ovarian cancer patients in Korea)



Key Inclusion Criteria

- FIGO stage **III-IV, High grade serous or endometroid pathology**
- Participant has confirmed as **both germline and somatic *BRCA1/2* wild-type** by institution's test.
- **No visible residual tumor after primary cytoreductive surgery** (or optimally debulked)
- CR or PR following platinum first-line treatment
- Participant who is able to provide tumor slides obtained during cytoreductive surgery for a prospective examination of the homologous recombination deficiency (HRD).

1. Prof.Kim, Personal data

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Objectives

- Ovarian cancer, a leading cause of deaths from gynecologic cancer, is a global burden, with an estimated 314,000 new cases and 207,000 deaths annually.

- The recent introduction of poly(ADP ribose) polymerase (PARP) inhibitor maintenance therapy has led to unprecedented improvements in the survival of patients with epithelial ovarian cancer

- The phase 3 PRIMA trial demonstrated that **first line niraparib maintenance therapy significantly prolonged progression free survival (PFS) in patients with newly diagnosed advanced ovarian cancer, but only those at high risk for relapse were enrolled.**

- Thus , we aimed to **evaluate the efficacy and safety profile of niraparib maintenance therapy** in BRCA wild type, low risk advanced ovarian cancer

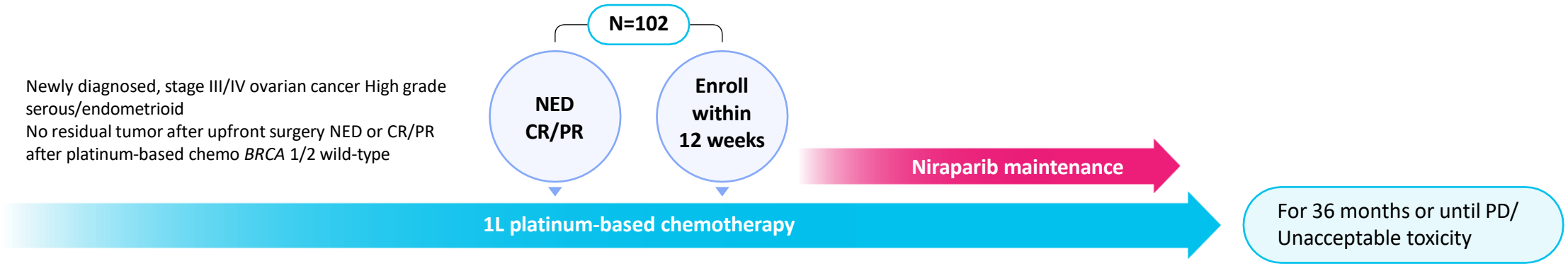
1. S.I. Kim, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Methods

- The POLO, a multi center, single arm, phase 4 trial, included patients with **BRCA wild type, FIGO stage III IV high-grade serous or endometrioid ovarian cancer** who achieved no visible residual tumor after primary cytoreductive surgery, followed by postoperative platinum-based chemotherapy.
- Patients who received neoadjuvant chemotherapy were excluded.
- The ACTHRD™ test from ACT Genomics was used to detect homologous recombination deficiency (HRD) in a tumor.
- All patients received niraparib maintenance therapy with an individualized starting dose for three years or until disease progression, unacceptable toxicity, or withdrawal of patient consent
- The primary endpoint was **12 month PFS rate.** The secondary endpoints included **overall survival (OS), which is not sufficiently mature, PFS by HRD status, and safety profile.**

Study design



1. S.I. Kim, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Results

Patients' characteristics

		N=101, %
Age (yr)	Mean ± SD	56.7 ± 9.3
ECOG	0	77 (76.2)
	1	24 (23.8)
Menopause	Yes	30 (29.7)
	No	71 (70.3)
FIGO stage	IIIA	12 (11.9)
	IIIB	19 (18.8)
	IIIC	53 (52.5)
	IVA	4 (4.0)
	IVB	13 (12.9)
Histologic type	High-grade serous	96 (95.0)
	High-grade endometrioid	3 (3.0)
	Other	2 (2.0)
gBRCA1/2 mutation	**No**	**101 (100.0)**
tBRCA1/2 mutation	No	101 (100.0)
HRD	**Positive**	**68 (67.3)**
	Negative	27 (26.7)
	Not determined	6 (5.9)



- In total, 102 patients were enrolled in this study
- One patient identified with a somatic *BRCA1* gene mutation was excluded from survival analysis but included in safety profile analysis.
- By data cutoff (February 10, 2025), median follow up was 20.3 months (IQR, 15.6 27.5), during which 35 patients relapsed and 6 patients died of the disease.

BRCA, Breast Cancer Susceptibility Gene; HRD, Homologous Recombination Deficiency; IQR, InterQuartile Range

1. S.I. Kim, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

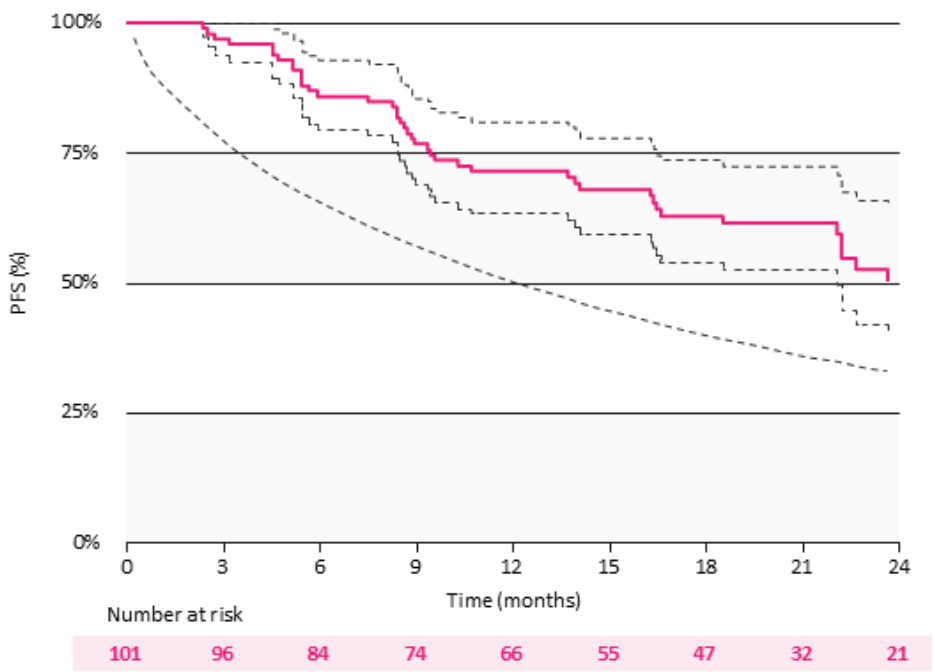
◆Results

- **The 12-month PFS rate was 71.5%** (95% CI, 54.6%–83.0%), which was significantly higher than the null hypothesis of the study (45.0%; one-sided test P <0.0001).
- **In both HRD positive (n=68) and negative (n=27) subgroups, a significantly improved 12 month PFS rate** was observed: 66.0% (95% CI, 45.0% 80.6%) and 80.3% (95% CI, 44.2% 94.3%), respectively

- Data cutoff: February 10, 2025
- Median follow-up: 20.3 months (IQR, 15.6–27.5)
- 35 patients relapsed and 6 patients died of the disease.

Survival outcomes in ITT population

☑ **Progression-free survival**



	Event	Rate	95% CI Lower	95% CI Upper
3 mon	3	97.00%	83.34%	99.49%
6 mon	14	85.86%	70.52%	93.57%
9 mon	23	76.65%	60.13%	87.02%
12 mon	28	71.47%	54.59%	83.00%
15 mon	31	67.93%	50.70%	80.24%
18 mon	35	62.82%	45.17%	76.19%
24 mon	41	50.06%	29.91%	67.26%

HRD, Homologous Recombination Deficiency; PFS, Progression-free survival; CI, confidence interval; ITT, intention to treat

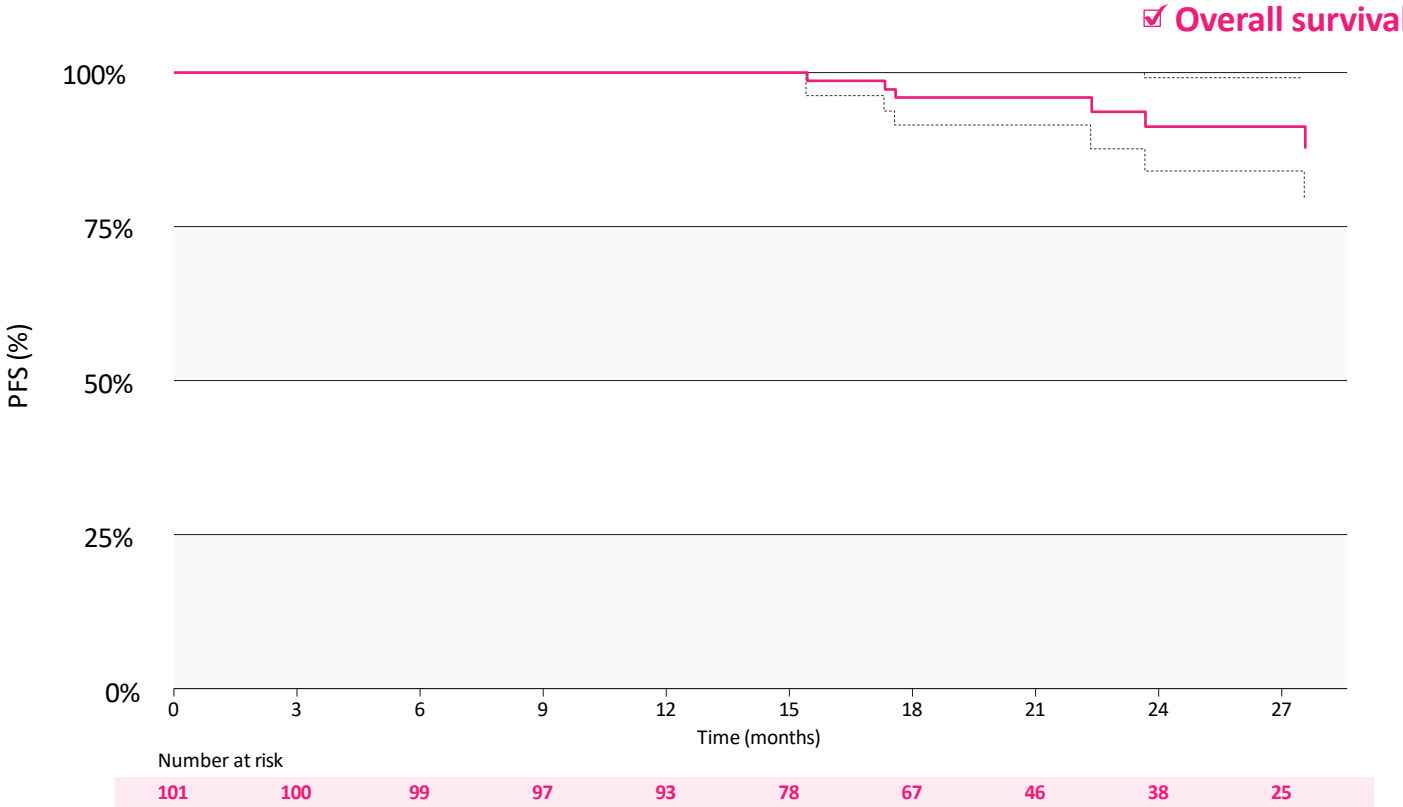
1. S.I. Kim, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Results

» The median OS was not reached.

Survival outcomes in ITT population



	Event	Rate	95% CI Lower	95% CI Upper
3 mon	0	100.00%	-	-
6 mon	0	100.00%	-	-
9 mon	0	100.00%	-	-
12 mon	0	100.00%	-	-
15 mon	0	100.00%	-	-
18 mon	3	95.88%	79.48%	99.23%
24 mon	5	91.25%	69.88%	97.69%

- Data cutoff: February 10, 2025
- Median follow-up: 20.3 months (IQR, 15.6–27.5)
- 35 patients relapsed and 6 patients died of the disease.

HRD, Homologous Recombination Deficiency; PFS, Progression-free survival; CI, confidence interval; ITT, intention to treat

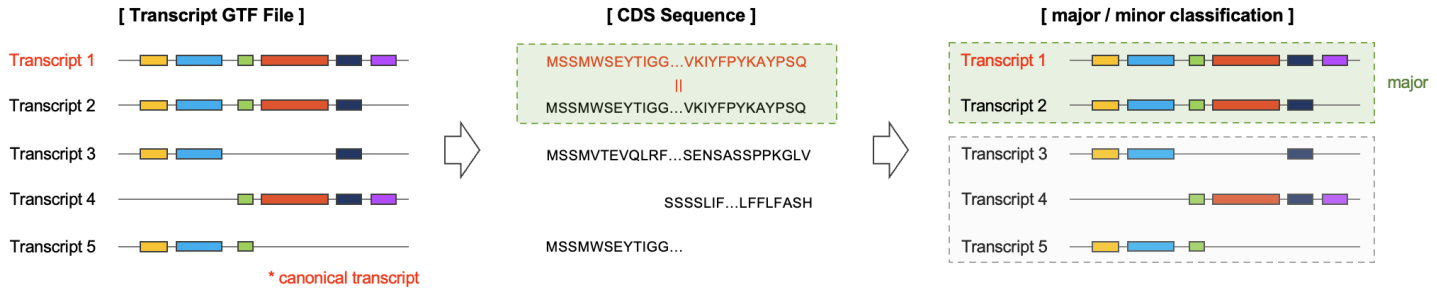
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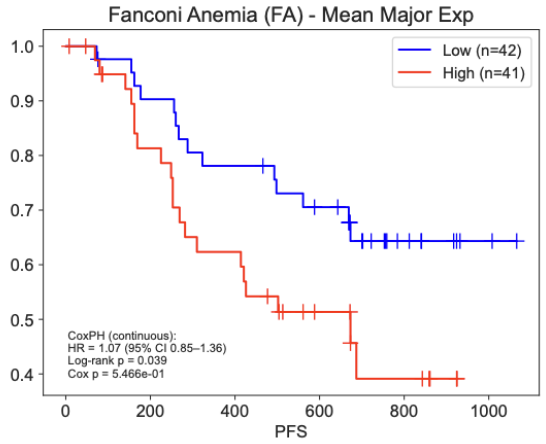
POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

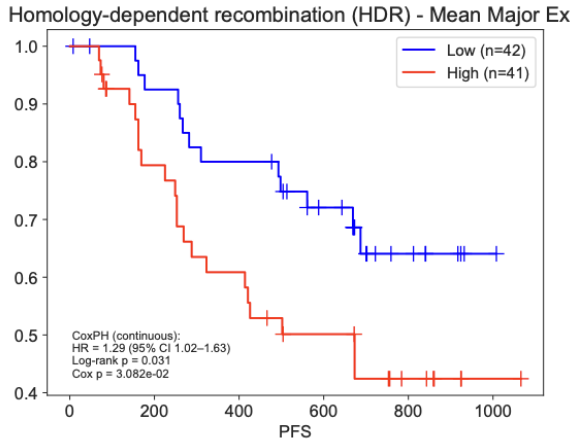
◆Results

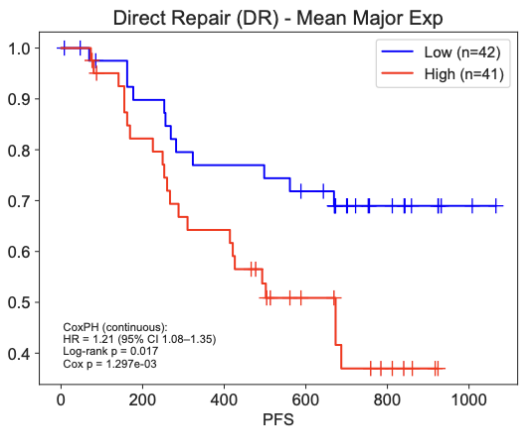
✓ Gene functionality ~ DNA repair pathway

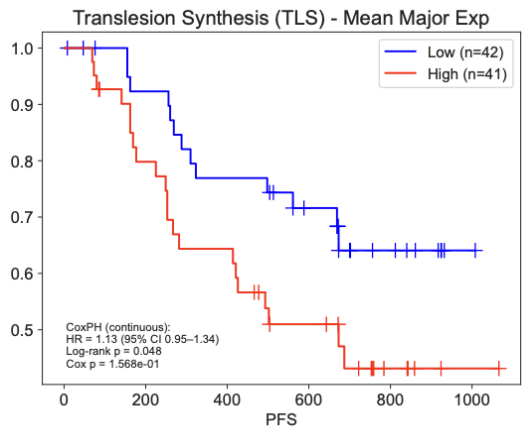
- DNA repair 관련 유전자 set을 사용하여 유전자 발현량과 PFS로 survival 분석 진행 → FA, HDR, DR, TLS gene set에서 PARPi 반응성과 유의한 negative correlation 확인











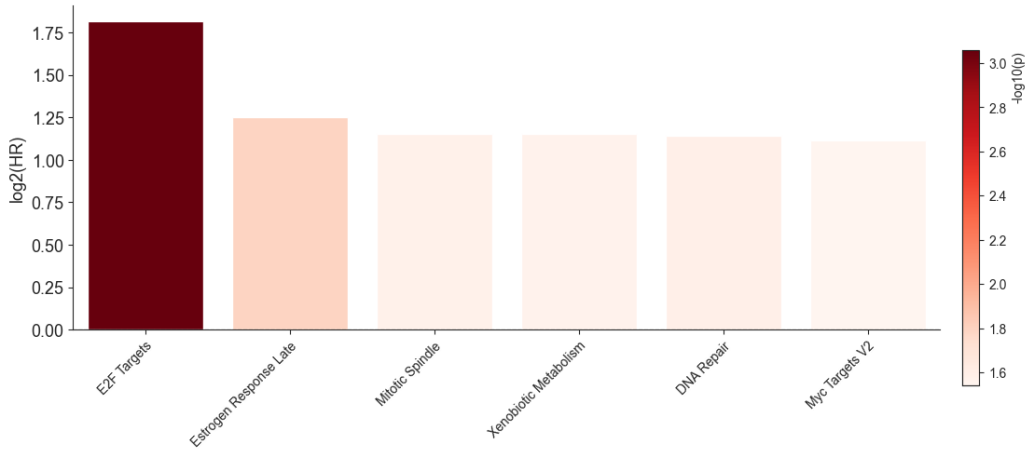
1. Prof.Kim, Personal data

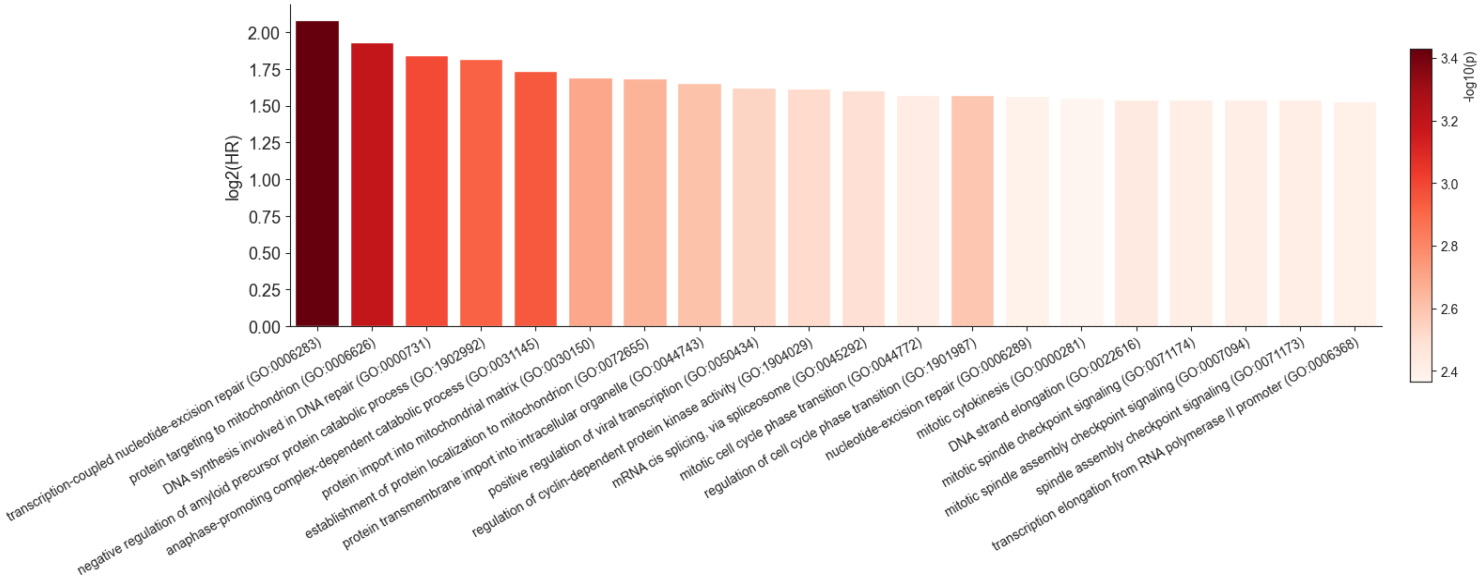
POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Results

✓ ssGSEA: MsigDB Hallmark gene set & GO Biological Process

- 샘플별 gene functionality metric → ssGSEA score → survival analysis
- Myc target V2, DNA repair, xenobiotic metabolism, mitotic spindle, estrogen response late, E2F targets → 많이 발현할수록 PARPi 반응성 떨어짐
- TC-NER, DNA repair, mitotic cell cycle phase transition .. → 많이 발현할수록 PARPi 반응성 떨어짐





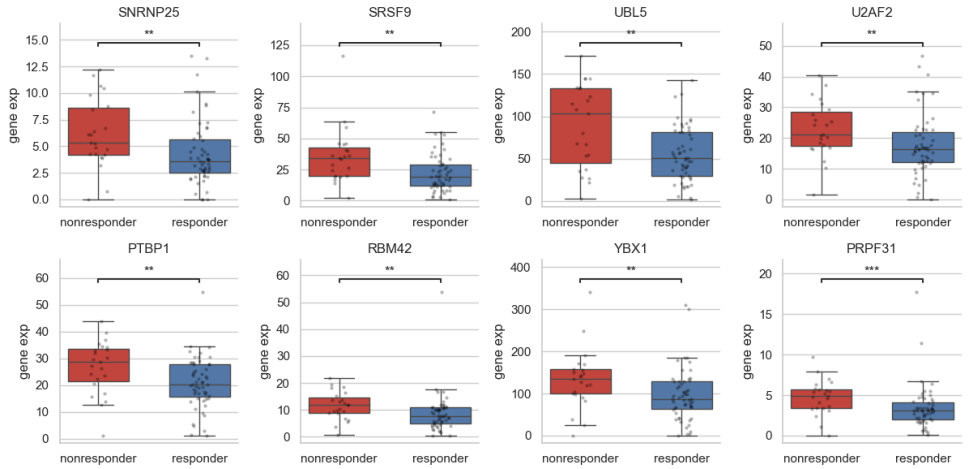
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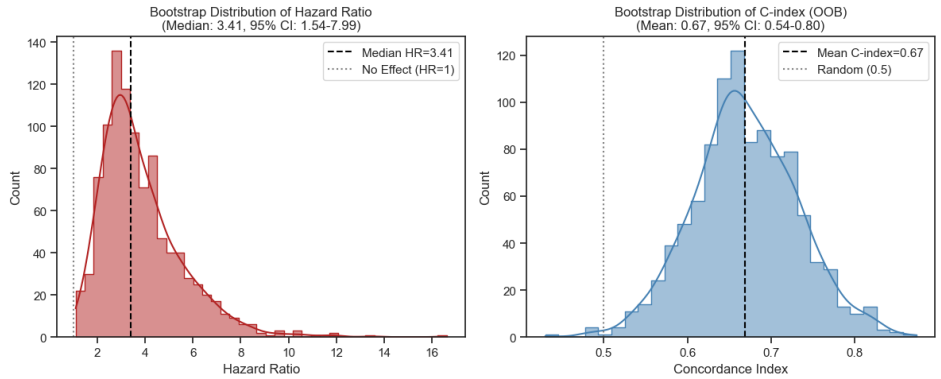
POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Results

✓ Splice factor analysis

- Splice factor gene expression: p<0.01 만족하는 유의한 SF genes → 많이 발현할수록 PARPi 반응성 떨어짐
- 8개 SF의 mean exp = Splicing Score
- Bootstrap 1000회: median cox HR 3.41, mean c-index 0.67





1. Prof.Kim, Personal data

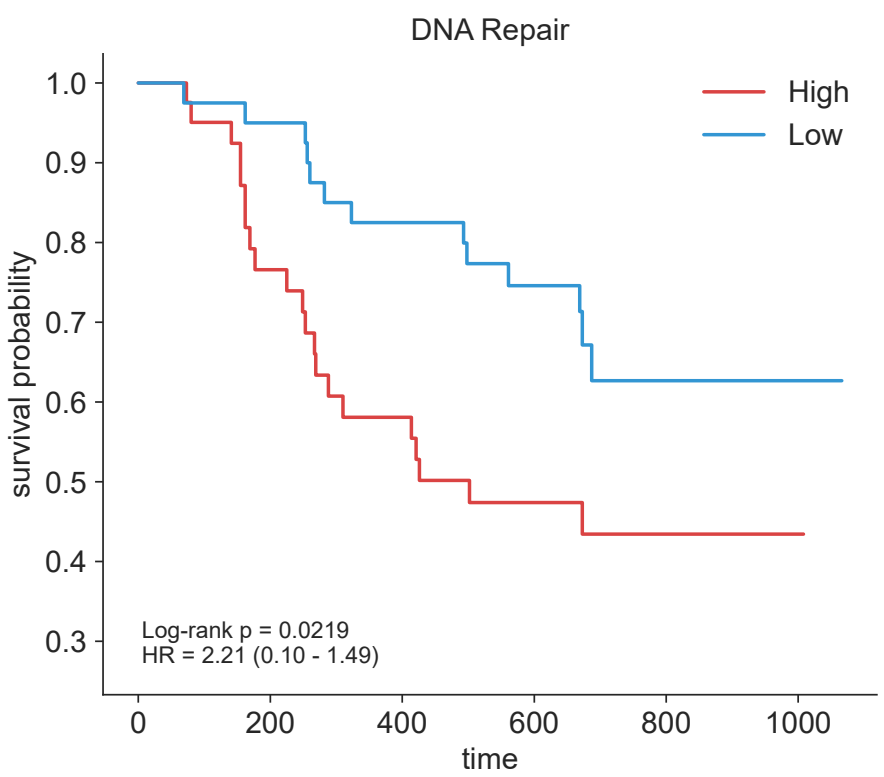
POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

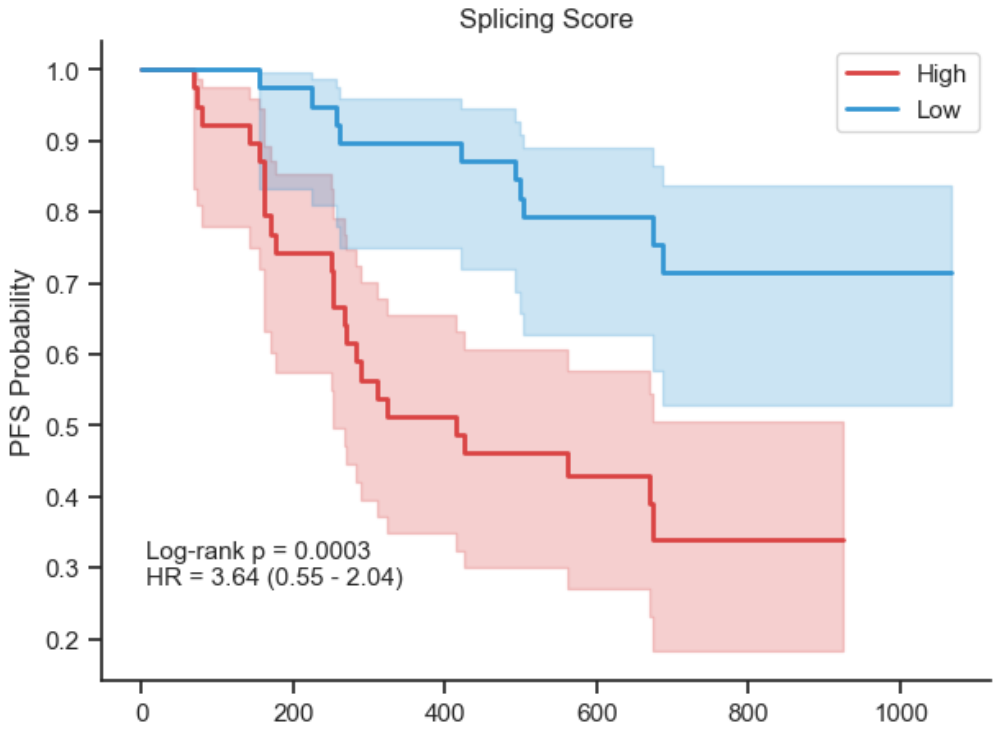
◆Results

» Transcriptomic HRD predicted PFS and response to niraparib more precisely.

Survival outcomes in ITT population

Progression-free survival





1. Prof.Kim, Personal data

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Safety profile analysis (n=102)

- In safety profile analysis (n=102), **7 (6.9%) discontinued niraparib due to treatment emergent adverse events.**
- The most common adverse events of grade 3 or higher were **neutropenia (n=26, 25.5%) and anemia (n=18, 17.6%).**
- None developed acute myeloid leukemia or myelodysplastic syndrome.
- **No treatment related deaths occurred.**

1. S.I. Kim, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

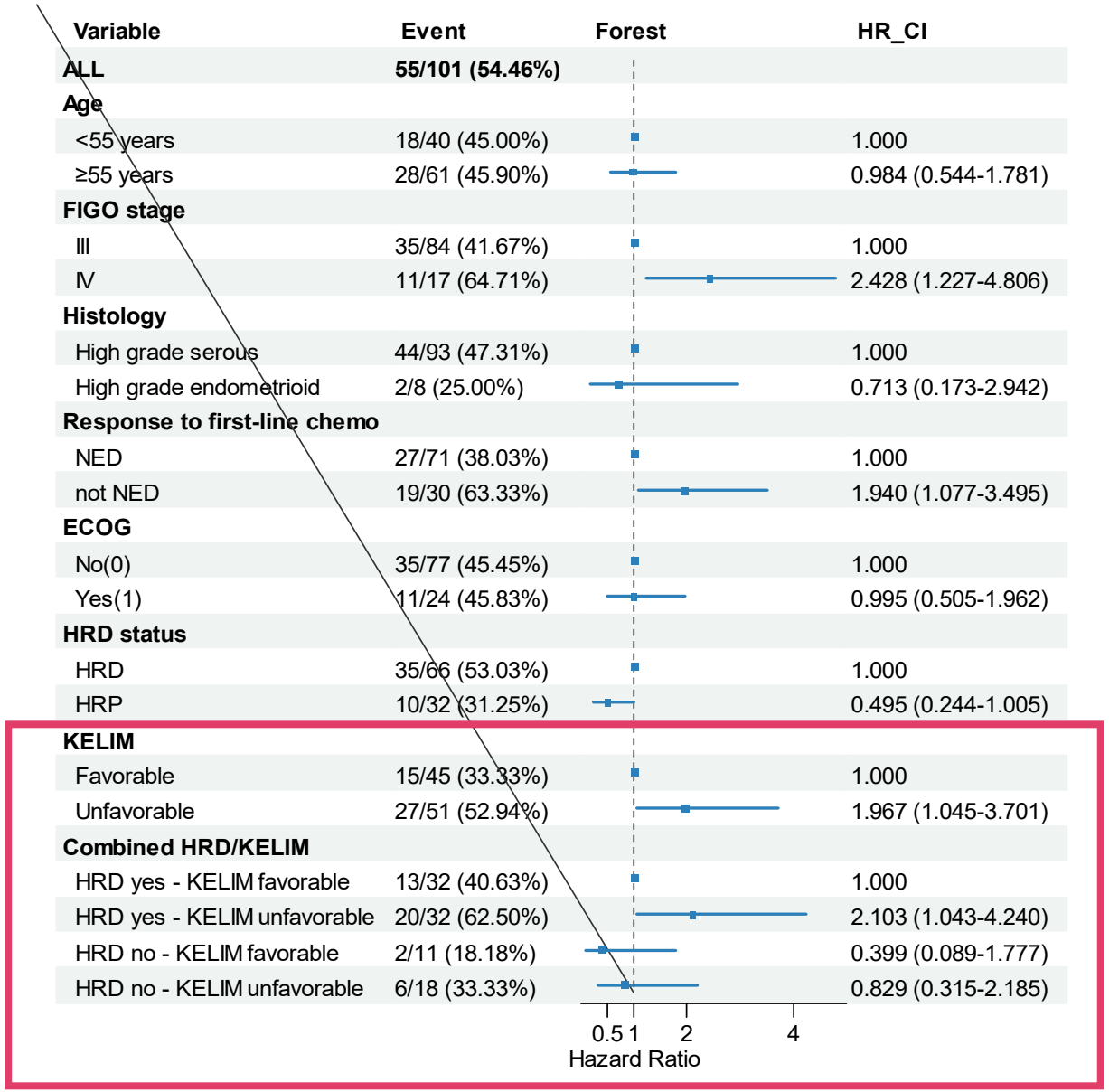
POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer

◆Conclusions

- **First line niraparib maintenance was effective** in patients with BRCA wild type, low risk advanced ovarian cancer.
- The POLO trial met the primary endpoint and further long term survival analyses and biomarker studies are scheduled.

1. S.I. Kim, et al. presented at 2025 EMSO Annual Meeting, Sep 2025

POLO trial :
First line niraparib maintenance therapy in BRCA wild type, low risk advanced ovarian cancer



KELIM

In ovarian cancer, KELIM (Cancer Antigen 125 ELIMination rate constant K) is a modeled kinetic mathematical score used to calculate how quickly CA-125 tumor marker levels decrease during the first 100 days of chemotherapy. It serves as a highly reliable marker of a tumor's **primary chemosensitivity** (how sensitive the cancer is to platinum-based chemotherapy treatments). BK Biomarker Kinetics +1

Core Thresholds & Categorization

The score is calculated using online tools, such as the Biomarker-Kinetics CA-125 KELIM Calculator, and requires at least three separate CA-125 measurements taken within the first 100 days after starting chemotherapy. BK Biomarker Kinetics

- **Favorable KELIM (Score ≥ 1.0):** Indicates that the tumor is highly sensitive to chemotherapy.
- **Unfavorable KELIM (Score < 1.0):** Indicates lower chemosensitivity and a higher risk of treatment resistance. ScienceDirect.com +1

KELIM

Modeled CA-125 KELIM™ in patients with stage III-IV high grade serous ovarian carcinomas treated with first-line adjuvant post-operative chemotherapy after primary cytoreductive surgery

For patients with stage III or IV high grade serous ovarian carcinomas treated with adjuvant post-operative carboplatin – paclitaxel regimen (every 3 weeks or weekly) in first-line setting, after primary cytoreductive surgery.

This model does not apply in patients treated in recurrent setting.

CA-125 KELIM™ is calculated with at least 3 CA-125 values measured within the first 100 days **(or less)** after chemotherapy start.

For scientific studies ≥ 2 patients, the website team should be contacted at biomarkers.kinetics@univ-lyon1.fr



Biomarker-Kinetics™ CA-125 neo-adjuvant CA-125 adjuvant PSA hCG News Publications Team Contact Terms of use

Modeled CA-125 KELIM™ in patients with stage III-IV high grade serous ovarian carcinomas treated in first-line setting with neo-adjuvant chemotherapy

For patients with stage III or IV high grade serous ovarian carcinomas treated with neoadjuvant chemotherapy with carboplatin – paclitaxel in first line setting (every 3 weeks or weekly), with the intent of a potential interval cytoreductive surgery (disease in place when the chemotherapy is started). **This model does not apply to patients treated in recurrent setting.**

CA-125 KELIM™ is calculated with **at least 3** CA-125 values measured **within the first 100 days (or less)** after chemotherapy start.

For scientific studies involving more than 2 patients, the website team should be contacted at biomarkers.kinetics@univ-lyon1.fr

Platinum sensitivity

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Original Article

Open Access

Development of Web-Based Nomograms to Predict Treatment Response and Prognosis of Epithelial Ovarian Cancer

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Ju-Hyun Kim, MD[7]
Maria Lee, MD, PhD[1]
Hee Seung Kim, MD, PhD[1]
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Dae-Shik Suh, MD, PhD[7]
Taesung Park, PhD[3]
Yong-Sang Song, MD, PhD[1]

Purpose

Discovery of models predicting the exact prognosis of epithelial ovarian cancer (EOC) is necessary as the first step of implementation of individualized treatment. This study aimed to develop nomograms predicting treatment response and prognosis in EOC.

Materials and Methods

We comprehensively reviewed medical records of 866 patients diagnosed with and treated for EOC at two tertiary institutional hospitals between 2007 and 2016. Patients' clinicopathologic characteristics, details of primary treatment, intra-operative surgical findings, and survival outcomes were collected. To construct predictive nomograms for platinum sensitivity, 3-year progression-free survival (PFS), and 5-year overall survival (OS), we performed stepwise variable selection by measuring the area under the receiver operating characteristic curve (AUC) with leave-one-out cross-validation. For model validation, 10-fold cross-validation was applied.

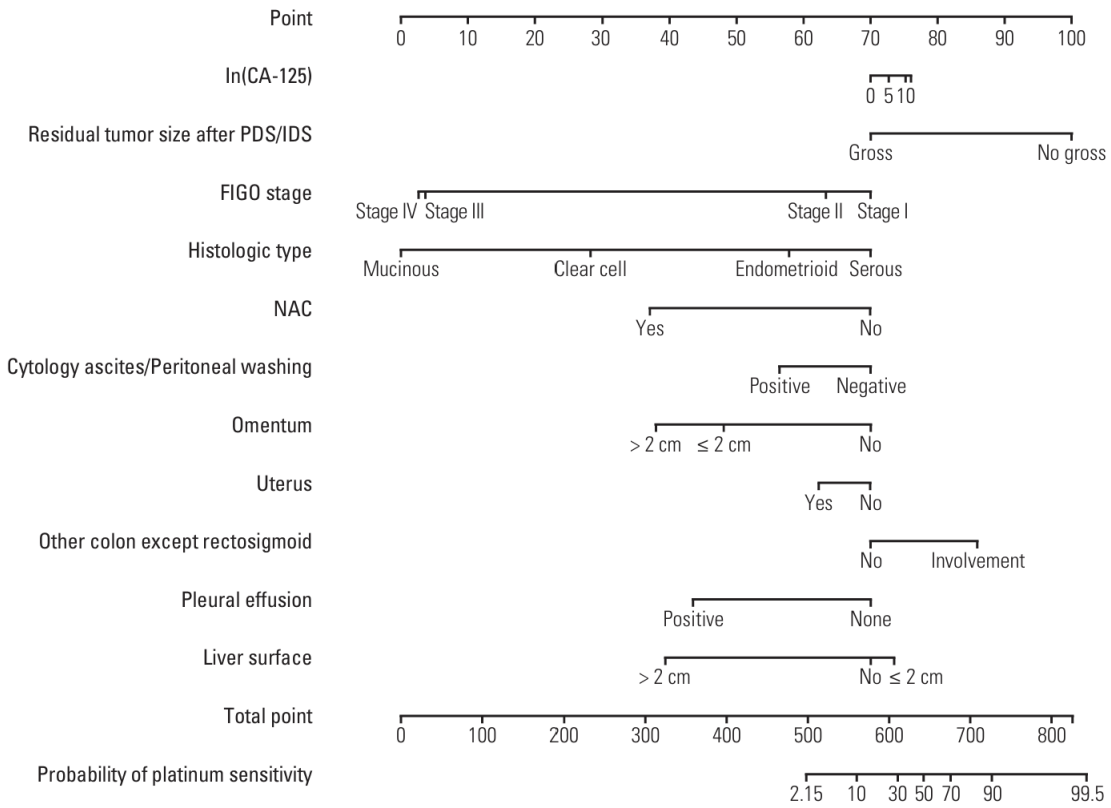


Fig. 4. The developed nomogram predicting platinum sensitivity. CA-125, cancer antigen 125; FIGO, International Federation of Gynecology and Obstetrics; NAC, neoadjuvant chemotherapy.

Platinum sensitivity

cancers

MDPI

Article

Development of Machine Learning Models to Predict Platinum Sensitivity of High-Grade Serous Ovarian Carcinoma

Suhyun Hwangbo [1,†], Se Ik Kim [2,†], Ju-Hyun Kim [3], Kyung Jin Eoh [4], Chanhee Lee [1], Young Tae Kim [5], Dae-Shik Suh [6], Taesung Park [1,7,*] and Yong Sang Song [2,8,*]

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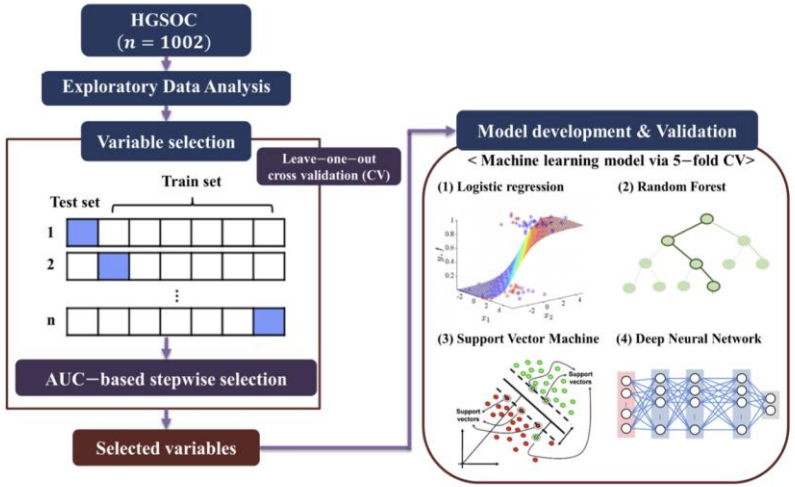


Figure 1. Overall workflow of statistical analysis.

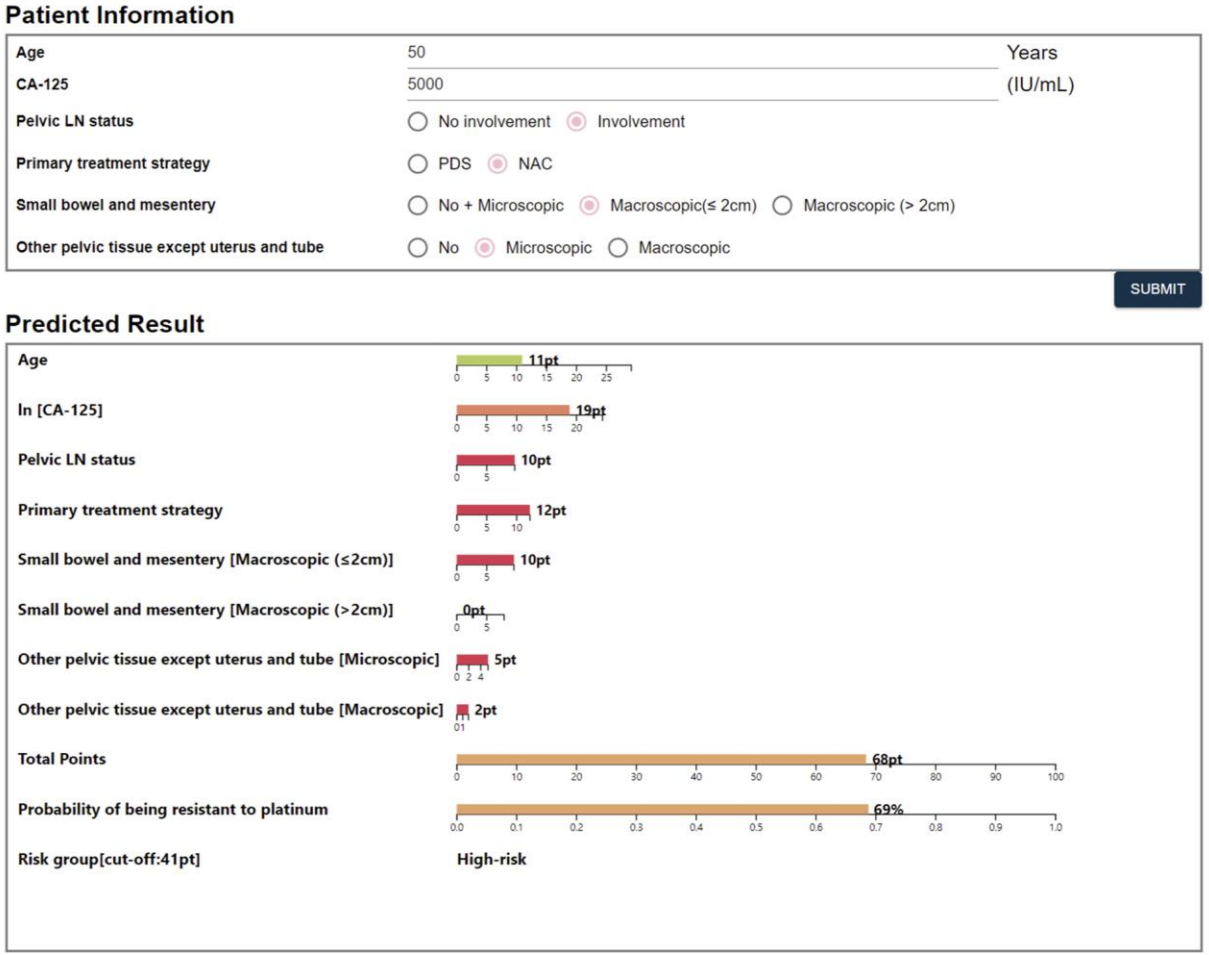


Figure 4. Web-based nomogram predicting platinum sensitivity.

PARPi sensitivity



LETTER ▸ Clin Transl Med. 2024 May 8;14(5):e1693. doi: 10.1002/ctm2.1693

Proteomic landscaping of high‐grade serous ovarian carcinoma identifies stearoyl‐CoA desaturase 5 as a potential predictive biomarker for poly(ADP‐ribose) polymerase inhibitor response

Se Ik Kim [1,2], Hyeyoon Kim [3,4], Kisoon Dan [3], Hong‐Beom Park [5,6], Cheol Lee [7,8], Hee Seung Kim [1,2], Hyun Hoon Chung [1,2], Jae‐Weon Kim [1,2], Noh Hyun Park [1,2], Dohyun Han [6,9,✉], Maria Lee [1,2,✉]

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My question:

Platinum sensutivity

$=$

$\approx$

$\neq$

PARPi sensitivity



Desitny is predetermined…?



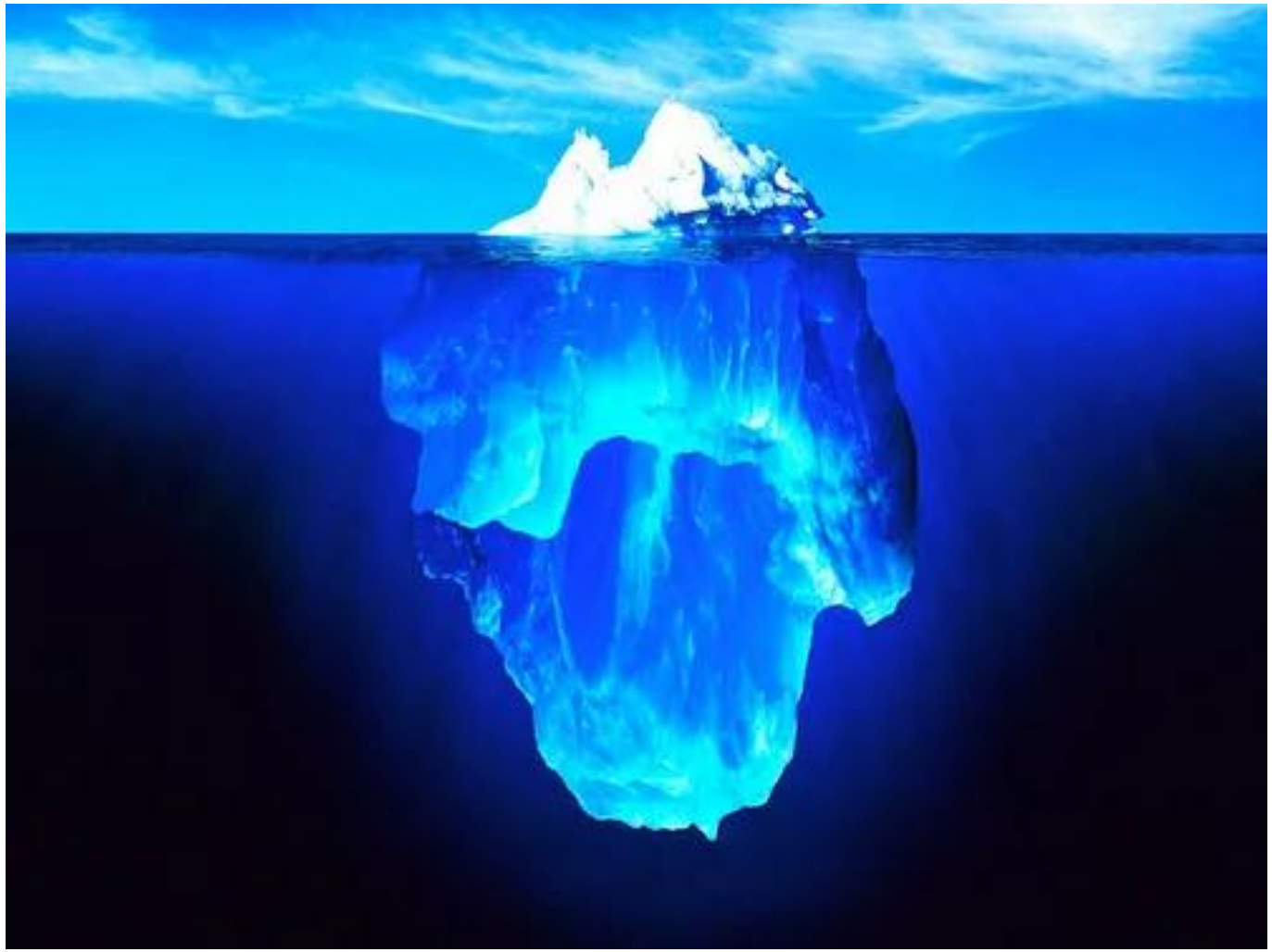
Clinical scenarios

Prediction (1)	Prediction (2)	Action
PI-resistant	Do you think PARPi can change patients' destiny?	Yes → PARPi + Bev PAPRi + Bev + alpha? No → Bev only Enroll to clinical trials
PI-sensitive	PARPi very sensitive	→ PARPi only
	PAPRi less sensitive	→ PAPRi + Bev
	PARPi resistant	→ Bev only PARPi + Bev PARPi + Bev+ alpha? Enroll to clinical trials



Conclusions

Conclusions

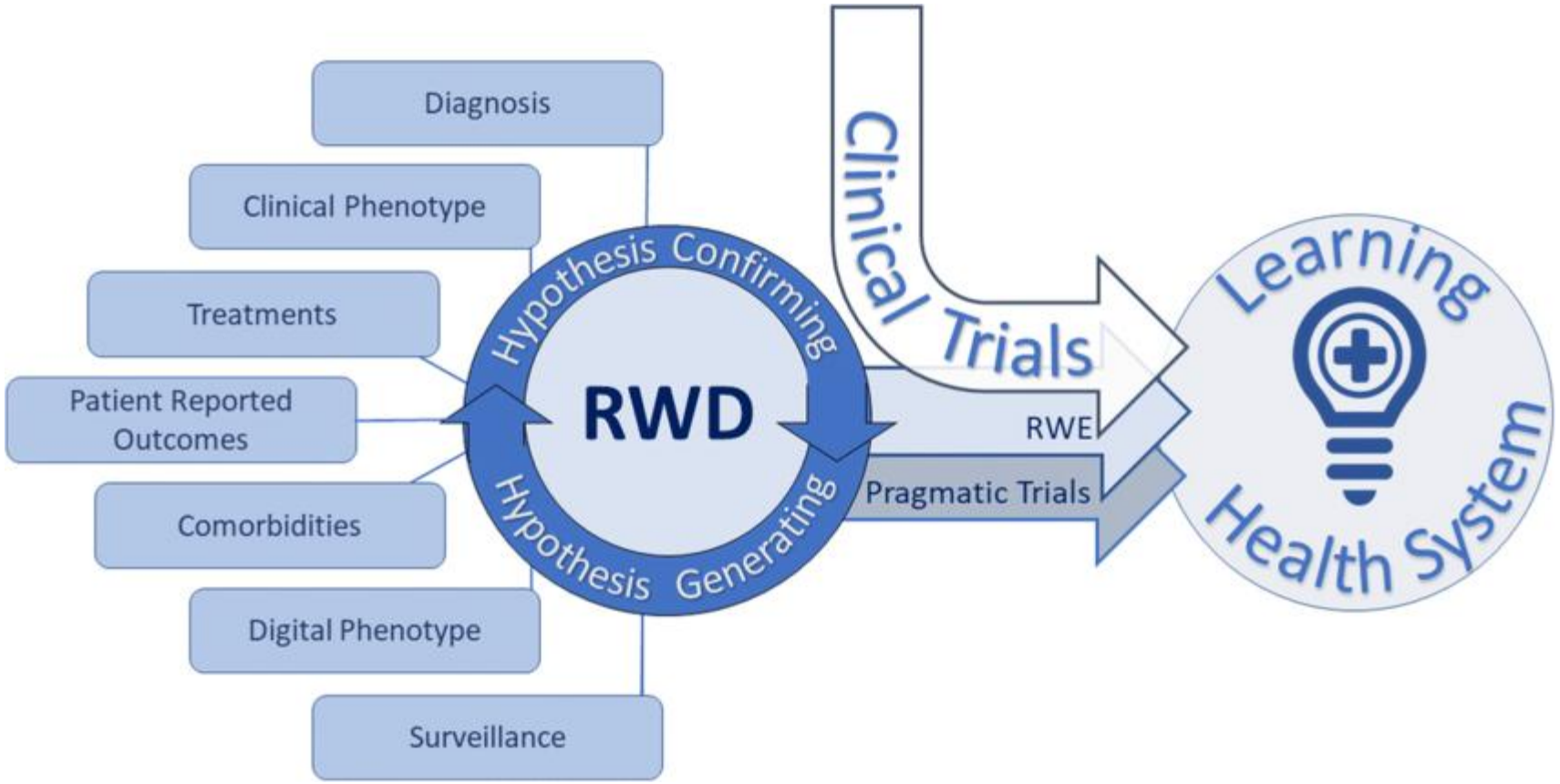


Conclusions

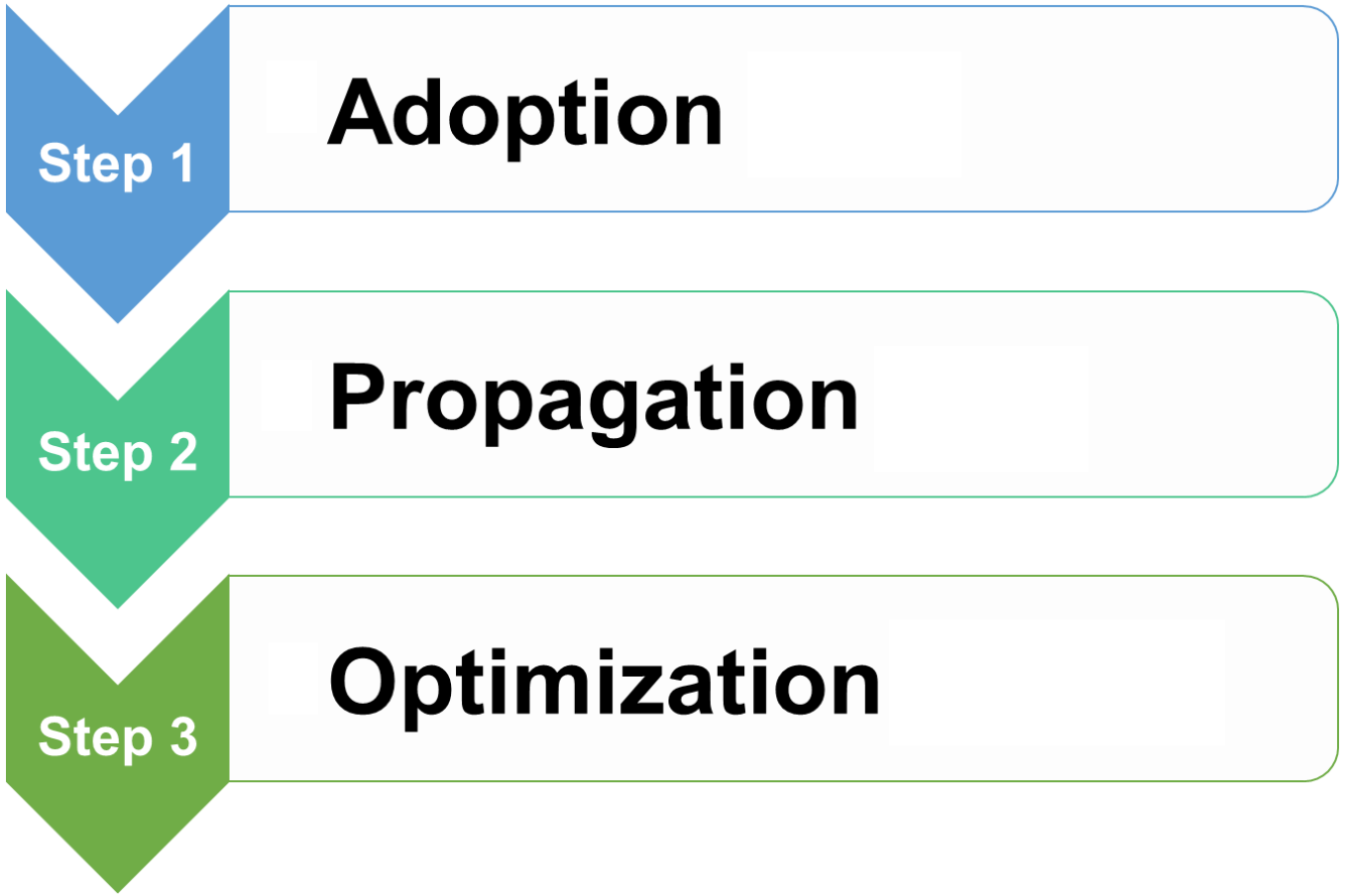
- PARP inhibitors are changing the current landscape of treatment in ovarian cancer.
- Unmet needs
  - Optimal patient & drug selection
  - What is the best biomarkers for PARP inhibitors?
  - Treatment after PARP inhibitors?
  - Ongoing clinical trials: e.g., ADCs
  - Toxicities in combination strategies



Conclusions



Conclusions




Thank you!
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