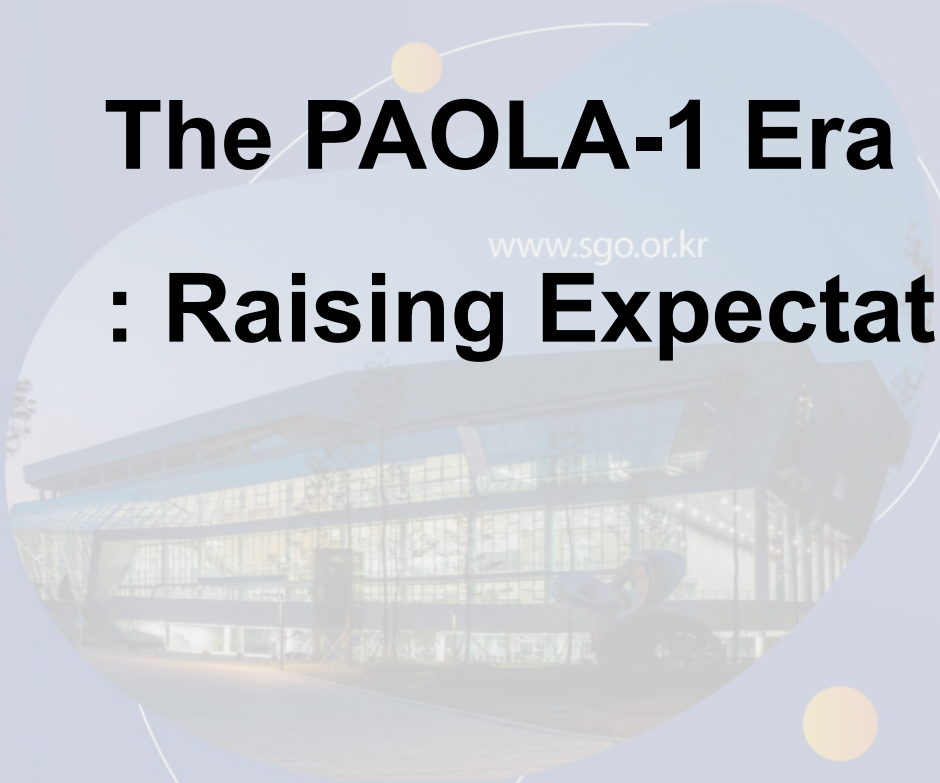
The PAOLA-1 Era

www.sgo.or.kr

: Raising Expectations for Long-Term Survival

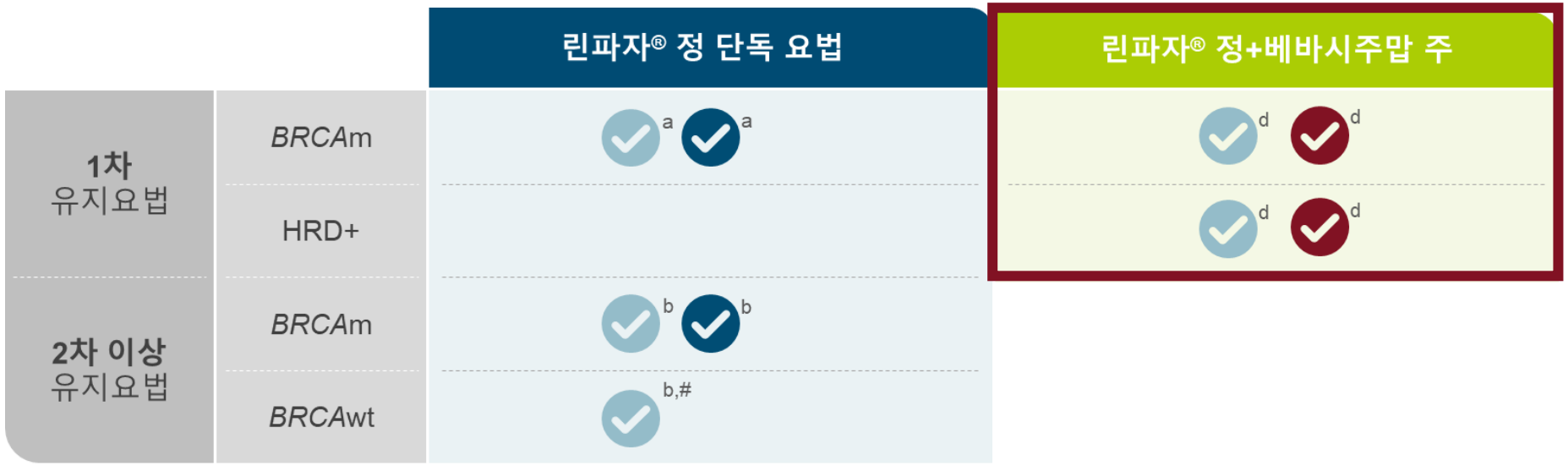


이유영, 삼성서울병원

DECLARATION OF INTERESTS

Nothing to declare

린파자® 정의 보험급여 사항



허가 적응증

보험 급여 (백금계 항암제 완료 후 8주 이내 투여*)

* 유지요법 시행 직전 투여된 백금기반요법(bevacizumab 포함 요법 제외)은 최소 4주기 이상 투여해야 하며, 이전에 PARP 억제제를 투여받은 적이 없어야 하며, 1차 유지요법의 경우 최초 투여 후 2년까지 급여 인정, 2차 이상 유지요법은 기간 제한 없음[c]

병용 화학요법 부분 급여 (Bevacizumab 7.5mg/kg 병용 급여) (린파자는 100/100적용입니다.)

FIGO stage IIIb, IIIc 환자 중 suboptimally debulked
(잔존 종양 크기 > 1cm)이거나 stage IV 상피성 난소암, 난관암 또는 원발성 복막암

1) Bevacizumab은 7.5mg/kg로 투여하며, 화학요법 제2주기에서 제6주기까지 Bevacizumab을 병용 투여하고, 이후 단독 투여하며 최대 18주기까지 급여 인정함. (단, 질병 진행 시 투여중단)

2) 허가사항 범위 내에서 상기에 해당 하지 않는 front-line 요법의 경우 'Bevacizumab'은 약값 전액을 본인이 부담토록 함(1차, 고식적요법)

[a] 1차 백금기반 항암화학요법에 반응 (부분 또는 완전반응)한 진행성 BRCA 변이 고도 상피성 난소암, 난관암 또는 일차 복막암 성인 환자
[b] 2차 이상의 백금기반요법에 반응 (부분 또는 완전반응)한 백금민감성 재발성 고도 상피성 난소암 (난관암 또는 일차 복막암 포함) 성인 환자
[c] 단, 2년간 또는 질병이 진행되거나 수용할 수 없는 독성이 나타나기 전까지 치료를 지속할 수 있으며, 2년차에 완전반응(방사선적 질병 증거가 없음)을 나타내는 환자들은 투여를 중단함. 2년차에 질병의 증거가 있으나, 주치의가 볼 때 치료를 지속함으로써 추가적 이익을 나타낼 수 있다고 판단하는 환자는 2년 이후에도 치료를 받을 수 있음
[d] 1차 백금기반 항암화학요법과 베바시주맙 병용 투여요법에 반응 (부분 또는 완전반응)한 상동재조합결핍 (HRD) 양성 (BRCA 변이 또는 유전체 불안정성으로 정의)인 고도 상피성 난소암, 난관암 또는 일차 복막암 성인 환자
2차 이상 유지요법 중 BRCAwt환자군 에서 린파자는 100/100 적용입니다.
※ 보험 급여에 대한 세부사항은 반드시 건강보험심사평가원 공고 전문을 확인해 주십시오.

BRCAm=breast cancer gene mutation; **BRCAwt**=breast cancer gene wild type; **HRD**=homologous-recombination deficiency; **PARP**=poly ADP-ribose polymerase inhibitor

1. 린파자®정 허가사항, 식품의약품안전처. Available at: https://nedrug.mfds.go.kr pbp/CCBBB01/getItemDetailCache?cacheSeq=2019075 37aupdateTs2025-03-24%20 15:29:33.032249b (Accessed on June 2025). **2.** 제2025-73호 「요양급여의 적용기준 및 방법에 관한 세부사항」 일부개정(5월 1일 시행)
3. 건강보험심사평가원 공고 제2025-152호 「암환자에게 처방·투여하는 약제에 대한 요양급여의 적용기준 및 방법에 관한 세부사항」 일부개정(7월 1일 시행).

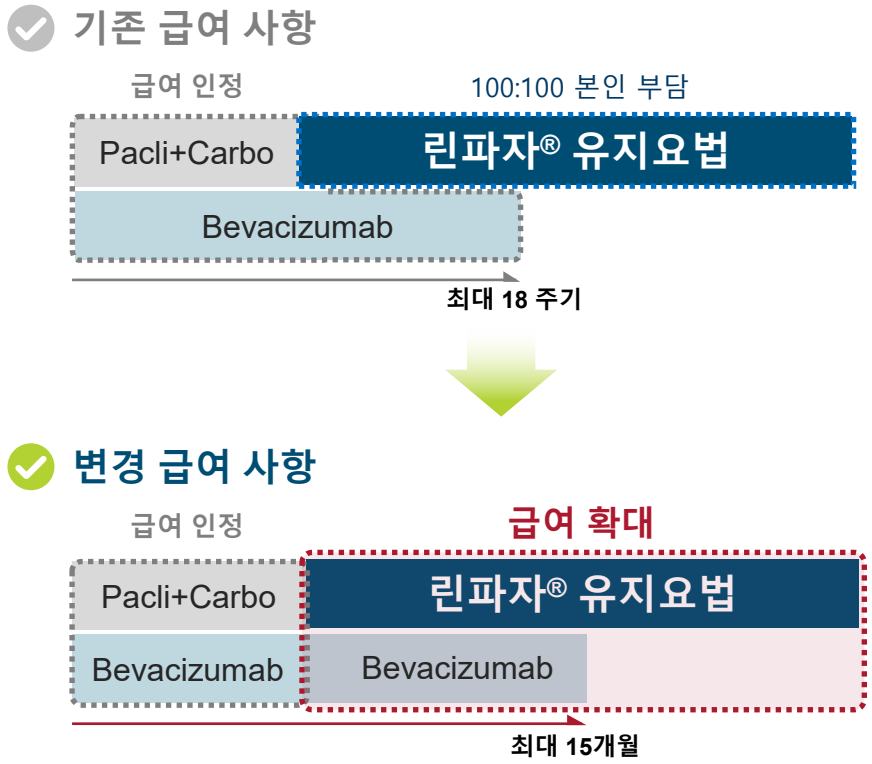
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PAOLA-1(린파자®정+베바시주맙 주) 급여확대 공고예고

- **시행예정일 : 2026.11.1.**

<table>
<tr><th>구 분</th><th>공고 의견조회(안)</th></tr>
<tr><td></td><td></td></tr>
<tr><td>10. 난소암/
난관암/
일차복막암
(Ovarian
Cancer/
Fallopian
Tube
Cancer/
Primary
Peritoneal
Cancer)</td><td>4. 유지요법(maintenance)
<table>
<tr><th>연번</th><th>항암요법</th><th>투여대상</th><th>투여단계</th></tr>
<tr><td>3</td><td>olaparib(tablet) +
bevacizumab주3</td><td>1차 백금 기반 항암화학요법과 베바시주맙 병용투여 요법에 반응(CR 또는 PR)한 상동재조합결핍 양성(BRCA 변이 또는 유전체 불안정성)인 고도 상피성 난소암, 난관암, 일차 복막암

※ Bevacizumab은 7.5mg/kg로 투여함
※ Olaparib은 최대 2년, Bevacizumab은 1차 백금기반 항암화학요법을 포함하여 최대 15개월까지 급여 인정함</td><td>-</td></tr>
</table>
주3. 'Bevacizumab + Paclitaxel + Carboplatin' 병용요법 종료 후 7주기부터 해당 유지요법을 투여하며, 이전에 PARP 억제제를 투여 받은 적이 없어야 함</td></tr>
</table>



건강보험심사평가원. 「암환자에게 처방·투여하는 약제에 대한 공고 개정(안)에 대한 의견조회」, 2026.10.22. (Accessed 2026.10.22.)

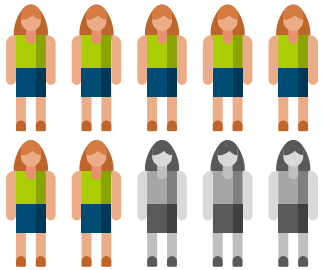
완치를 목적으로 한 치료에도 불구하고, 진행성 난소암 환자의 약 70%는 1차 치료 이후 재발을 경험합니다.

표준치료

- Platinum-based chemotherapy
- Bevacizumab

10-18 개월

무진행 생존기간 중앙값[2,3,4]



~70%

1차 치료 후 3년 이내 재발[1]

Despite optimal upfront surgery and the administration of front-line paclitaxel–carboplatin chemotherapy, ~70% of patients will relapse in the first 3 years[1]



38%

5년 생존율[5]

(For ovarian cancer, European mean age- standardized 5-year survival was low [37.6%, 95% CI 37.1–38.0])[5]

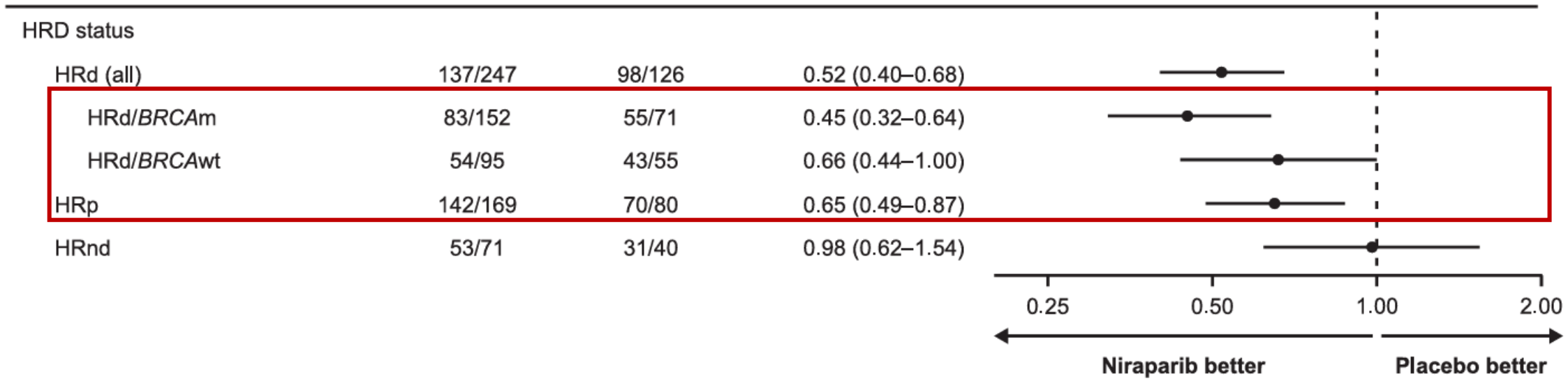
진행성 난소암 환자의 생존율 개선을 위한 새로운 1차 치료제의 개발이 필요했습니다.[6]

1. Ledermann JA, *et al.* Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann. Oncol.2013;24 Suppl 6:vi24-32. **2.** Bookman MA, *et al.* Evaluation of new platinum-based treatment regimens in advanced-stage ovarian cancer: a Phase III Trial of the Gynecologic Cancer Intergroup. *J Clin Oncol.* 2009;27(9):1419-1425. **3.** Burger RA, *et al.* Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Engl J Med.* 2011;365(26):2473-2483. **4.** Perren TJ, *et al.* A phase 3 trial of bevacizumab in ovarian cancer. *N Engl J Med.* 2011;365(26):2484-2496. **5.** de Angelis R, *et al.* Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a population-based Study. *Lancet Oncol.* 2014;15(1):23-34. **6.** Moore K, et al. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. 2018;379:2495–2505.

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Unmet Need for PFS Improvement in HRD/BRCAwt Patients

Forest Plot of Hazard Ratios of PFS in PRIMA

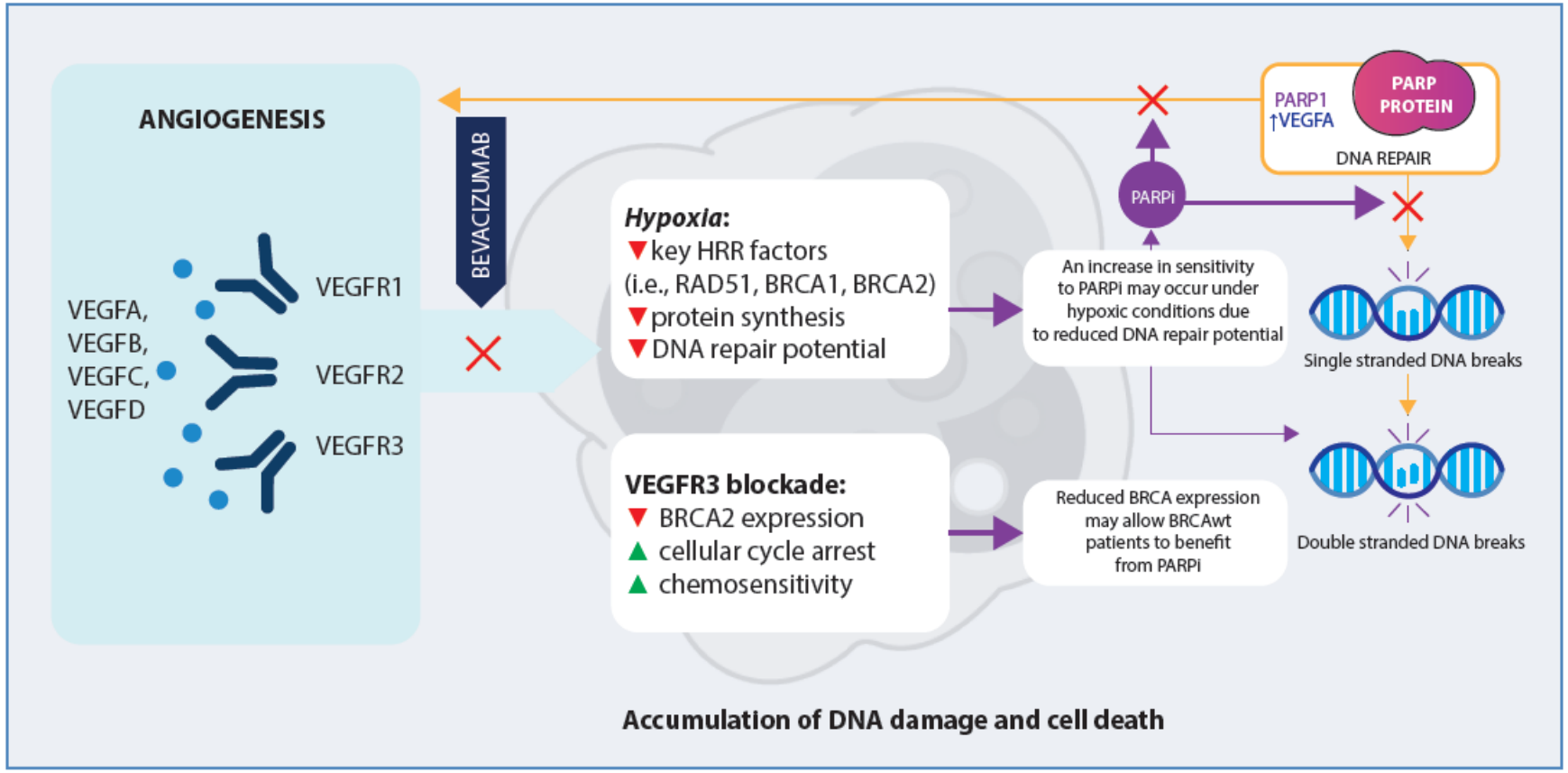


PFS benefit with niraparib monotherapy varied across HRD subgroups, especially in HRd/BRCAwt group

Gonzalez-Martin A et al., European Journal of Cancer 189 (2023) 112908

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Bevacizumab Enhance Sensitivity to PARPi



Schematic Presentation of the Synergistic Effect of Olaparib in Combination with Bevacizumab

Inhibit Angiogenesis

→ Induce hypoxia
→ Reduce DNA repair potential

➔ Increased HRD
➔ Enhance sensitivity to PARPi

VEGFR Blockade

→ Lower BRCA2 expression

➔ Allow BRCAwt patients to benefit from PARPi

Bodnar L et al., Oncol Clin Pract 2026; 22: e00526075
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PAOLA-1: Olaparib maintenance in newly diagnosed advanced ovarian cancer patients treated with chemotherapy and bevacizumab1,2

Sponsored by ARCAGY research[1,2]

- FIGO stage III–IV high-grade ovarian cancer (serous or endometrioid)* or non mucinous BRCAm
- Surgery (upfront or interval)
- Platinum taxane-based chemotherapy
- ≥3 cycles of bevacizumab†

NED/CR/PR

Olaparib (300 mg BID) x 2 years
+ bevacizumab†

2:1 randomisation; **N=806**

Stratification by tBRCA status‡ and 1L treatment outcome

Placebo x 2 years
+ bevacizumab†

2 years' maintenance treatment

Primary endpoint

- Investigator-assessed PFS (modified RECIST 1.1) Sensitivity analysis by BICR

Secondary endpoints

- TFST
- PFS2
- TSST
- OS
- Safety
- PRO/HRQoL

Pre-specified exploratory endpoints

- PFS in pre-defined subgroups including tBRCAm and Myriad myChoice® CDx

N=762 patients were planned to be randomised in the study so that maturity of the PFS data is ~60%. 458 events will give >80% power, at 5% alpha, to show HR 0.75, mPFS from 15.8 months (control) to 21.1 months (olaparib)

*Also includes fallopian tube and primary peritoneal cancer.
†Bevacizumab: 15 mg/kg intravenous, every 3 weeks for a total of 15 months, including when administered with chemotherapy.
‡By central labs

1. Ray-Coquard I, et al. N Engl J Med. 2019;381:Clinical Study Protocol; 2. Lorusso D, et al. Int J Gynecol Cancer. 2024;34:550–558.

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PAOLA-1 Inclusion Criteria

	Inclusion Criteria
선행 항암치료	**Platinum-Taxane 기반 항암치료 6–9주기** 단, platinum 요법과 관련된 비혈액학적 독성(신경독성, 과민반응 등)으로 platinum 치료를 조기에 종료해야 하는 경우에는 **최소 4주기 허용**
Bevacizumab 병용	마지막 항암치료 3주기와 병용하여 **최소 3주기 투여** **IDS를 받은 경우**에는 마지막 항암치료 3주기 중 **최소 2주기 병용 허용**
치료 반응·수술	선행치료 후 NED(질병의 증거 없음), 완전반응 또는 부분반응인 환자를 포함하였으며, **일차 또는 중간 종양감축수술을 받은 환자 모두 등록 가능**
전환 시점·안전성	**마지막 항암치료 투여 후 3–9주 사이 무작위배정** 주요 독성은 탈모 및 말초신경병증을 제외하고 CTCAE 1등급 이하로 회복되어야 함

ClinicalTrials.gov. PAOLA-1: Olaparib Plus Bevacizumab as Maintenance Treatment in Patients With Advanced Ovarian Cancer (NCT02477644). Available at: https://clinicaltrials.gov/study/NCT02477644. Accessed October 2026.

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Baseline patient characteristics were well balanced between arms

		Olaparib + bevacizumab (n=537)	Placebo + bevacizumab (n=269)
Age, median years (range)		61 (32–87)	60 (26–85)
FIGO stage, n (%)	III IV	378 (70) 159 (30)	186 (69) 83 (31)
HRD status*, n (%)	HRD positive tBRCAm HRD positive excluding tBRCAm HRD negative/HRD unknown HRD negative	255 (47) 157 (29) 97 (18) 282 (53) 192 (36)	132 (49) 80 (30) 55 (20) 137 (51) 85 (32)
History of cytoreductive surgery, n (%)	**Upfront surgery** Residual macroscopic disease No residual macroscopic disease	271 (50) 111 (41) 160 (59)	138 (51) 53 (38) 85 (62)
	Interval cytoreductive surgery† Residual macroscopic disease No residual macroscopic disease	228 (42) 65 (29) 163 (71)	110 (41) 35 (32) 75 (68)
	No surgery	38 (7)	21 (8)
Response after surgery/platinum-based chemotherapy, n (%)	NED CR PR	290 (54) 106 (20) 141 (26)	141 (52) 53 (20) 75 (28)

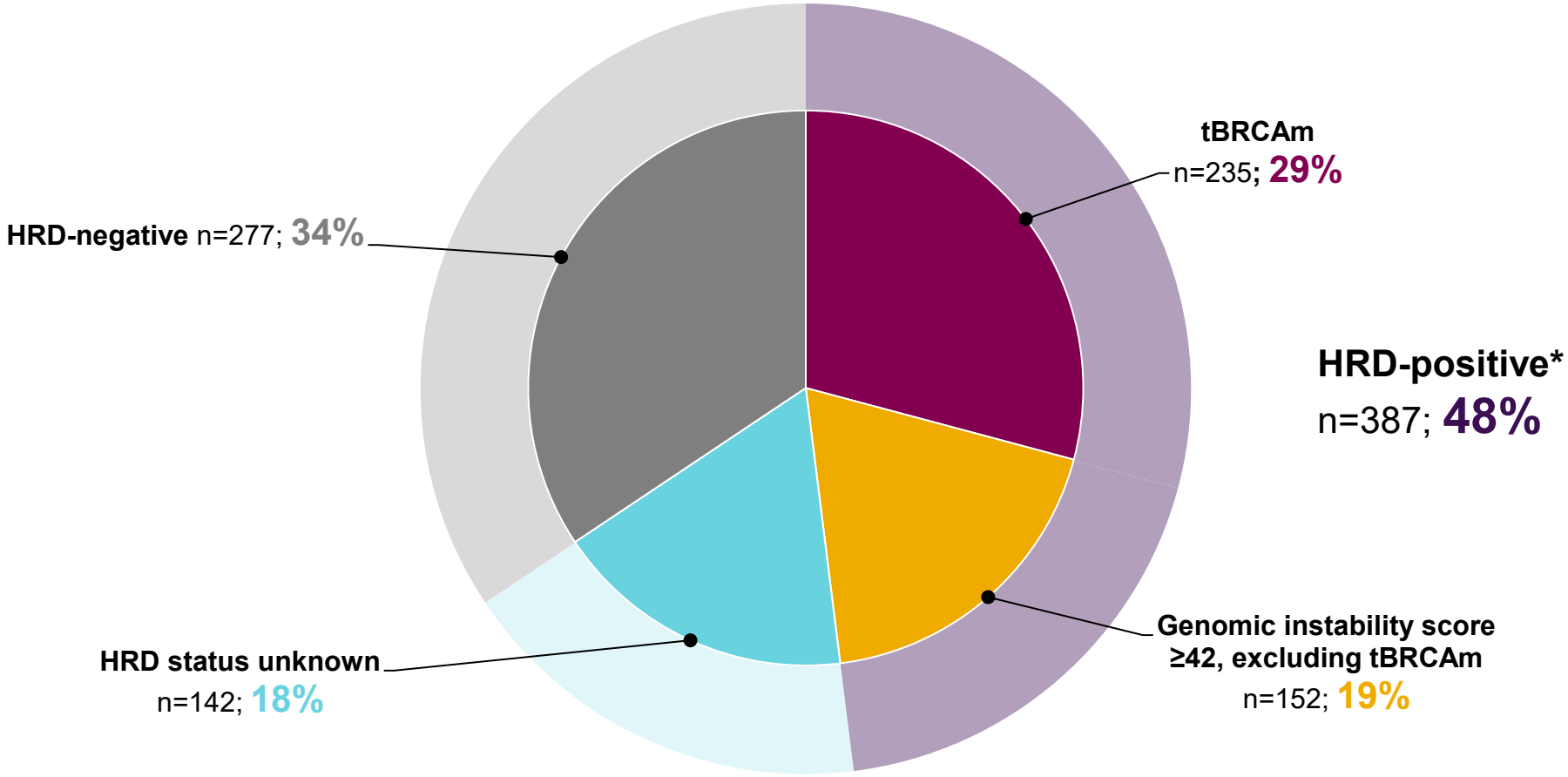
*BRCAm status by central labs; HRD status by Myriad myChoice HRD Plus; patients in tBRCAm and HRD positive excluding tBRCAm subgroups do not equal the total number of patients in the HRD-positive subgroup because of different testing methods.
Final OS DCO: 22 March 2022. Final OS analysis planned for 3 years after the primary PFS analysis or 60% data maturity

Ray-Coquard I, et al. Presented at ESMO Congress 2022. 9–13 September. Paris, France

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Approximately 50% of patients in PAOLA-1 were HRD-positive*

Around half of HRD-positive patients were tBRCAm*



*HRD-positive determined by tBRCAm and/or Myriad myChoice® CDx genomic instability score ≥42

Reasons for HRD status unknown: 4.2% missing; 2.1% fail; 11.3% inconclusive

Ray-Coquard I, et al. Presentation LBA2_PR presented at ESMO Annual Conference 2019, 27 September - 1 October, Barcelona, Spain.

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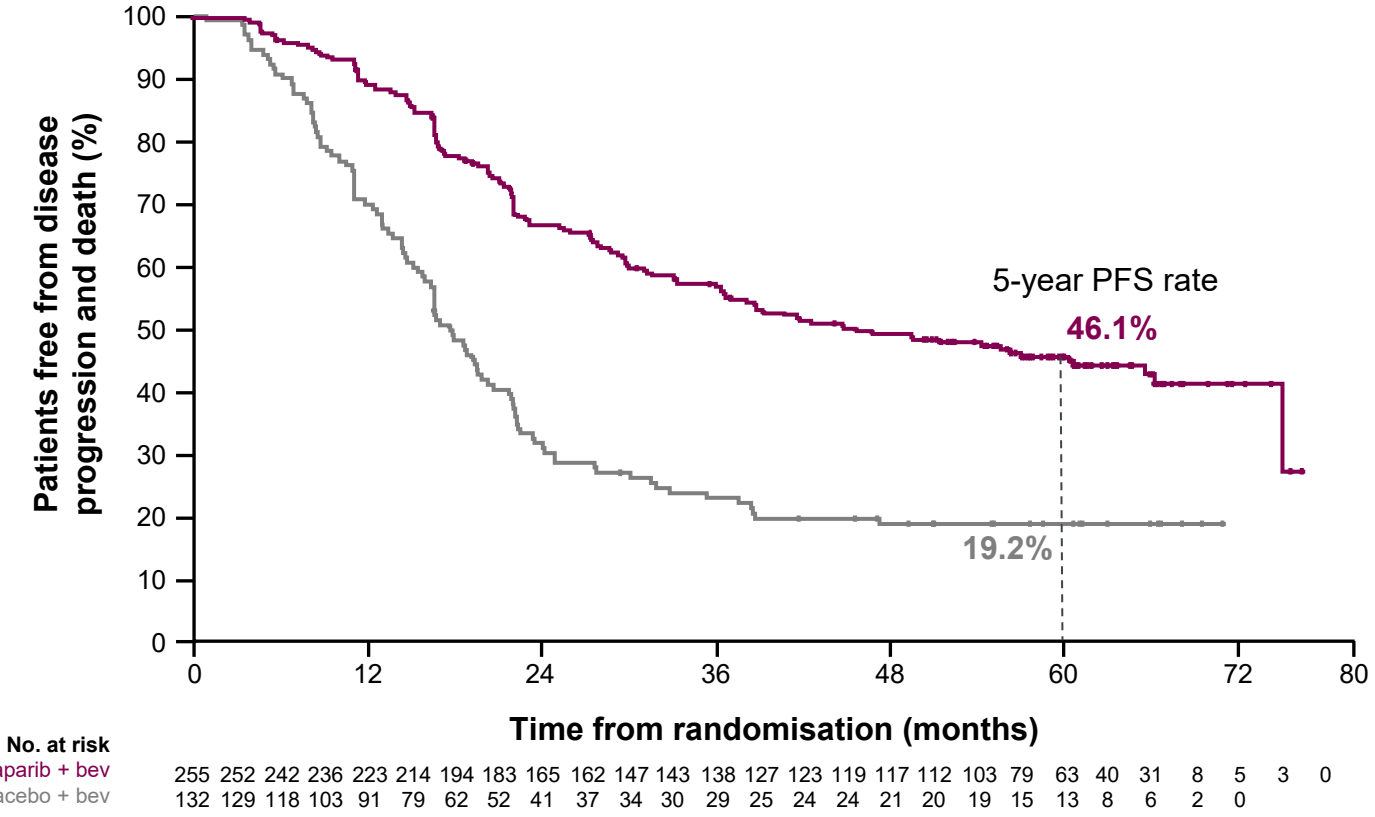
Final PFS analysis

Data cut-off March 2022

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Median PFS for HRD-positive* patients at the final OS DCO was almost 4 years in the olaparib + bevacizumab arm1,2

46.1% of patients in olaparib + bev arm were progression free at 5 years vs 19.2% in bev arm



	Olaparib + bevacizumab (n=255)	Placebo + bevacizumab (n=132)
Events, n (%)	136 (53.3)	104 (78.8)
Median PFS, months	46.8	17.6
5-year PFS rate, %	46.1	19.2

HR 0.41
95% CI, 0.32–0.54

59% reduction in risk of disease progression or death for olaparib + bevacizumab vs bevacizumab alone†

Final OS DCO: 22 March 2022.

*HRD positive defined as tBRCAm and/or genomic instability score ≥42 in the Myriad myChoice® CDx; †Descriptive analysis

1.Ray-Coquard I, et al. Presented at ESMO Congress 2022. 9–13 September. Paris, France. 2. Ray-Coquard I, et al. Ann Oncol 2023;34:681–92

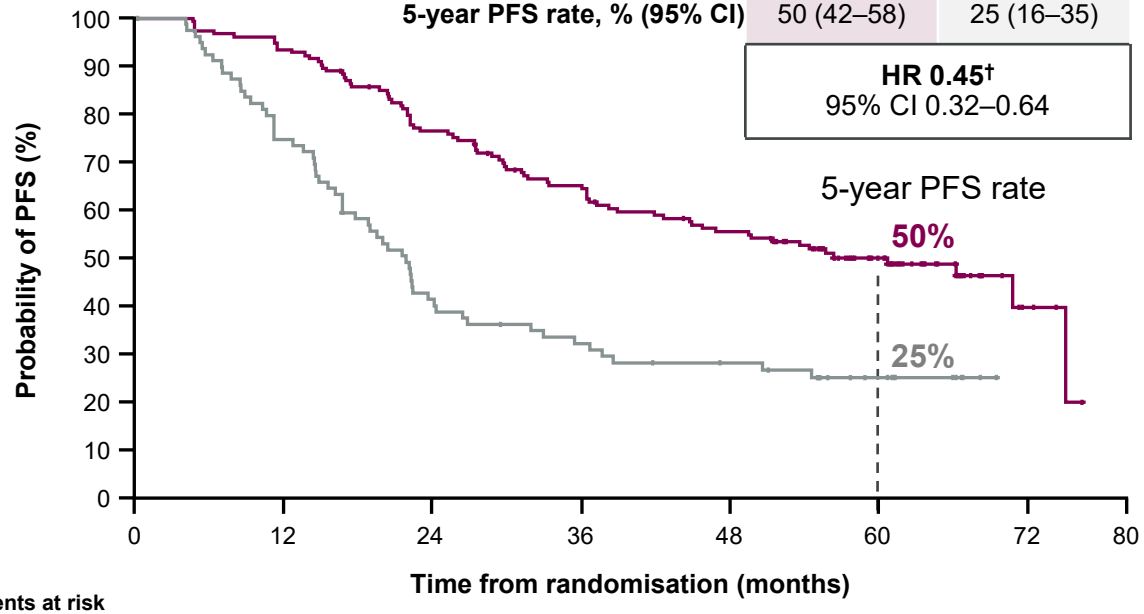
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A substantial 5-year PFS benefit was seen in HRD-positive* patients regardless of tBRCAm status

tBRCAm

	Olaparib + bevacizumab (n=157)	Placebo + bevacizumab (n=80)
Events, n (%)	78 (50)	58 (73)
Median PFS, months	60.7	21.7
5-year PFS rate, % (95% CI)	50 (42–58)	25 (16–35)

HR 0.45†
95% CI 0.32–0.64



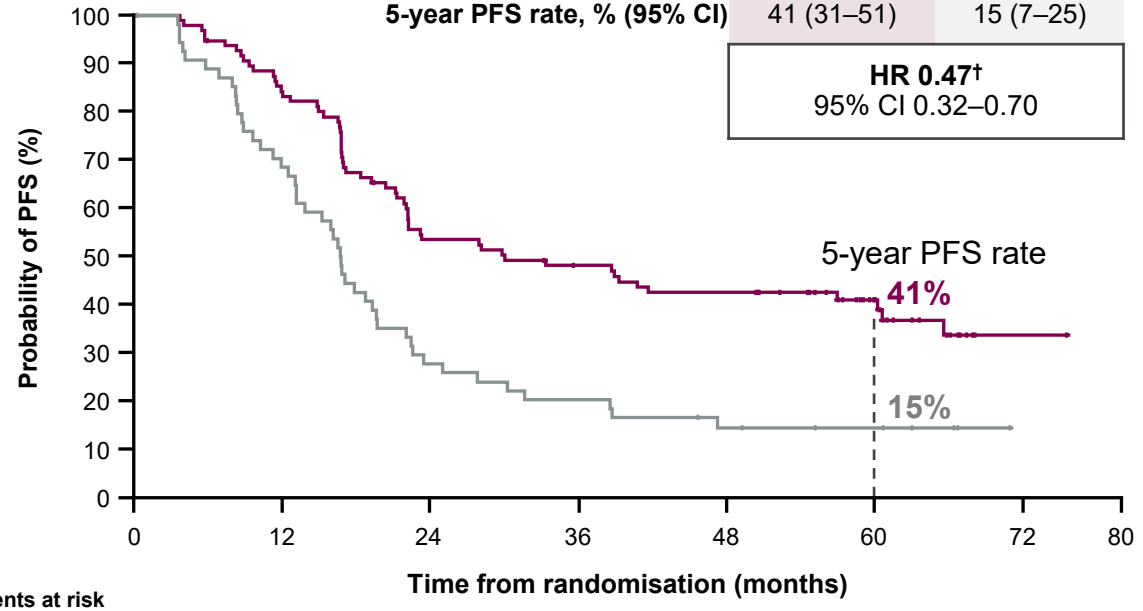
Patients at risk

Olaparib + bev	157	154	150	148	144	138	131	125	116	113	102	98	96	87	86	82	80	78	70	50	40	27	22	8	4	2	0
Placebo + bev	80	79	73	66	59	52	45	40	32	28	27	25	24	21	20	20	19	18	17	12	10	6	5	1	0		

HRD-positive patients excluding tBRCAm

	Olaparib + bevacizumab (n=97)	Placebo + bevacizumab (n=55)
Events, n (%)	58 (60)	46 (84)
Median PFS, months	30.0	16.6
5-year PFS rate, % (95% CI)	41 (31–51)	15 (7–25)

HR 0.47†
95% CI 0.32–0.70



Patients at risk

Olaparib + bev	97	96	90	86	79	76	64	60	50	50	46	46	43	41	38	38	38	36	35	29	22	14	10	1	1	1	0
Placebo + bev	55	54	48	41	37	32	23	19	15	14	13	11	11	9	9	9	7	6	6	5	5	4	3	1	0		

Final OS DCO: 22 March 2022.

*HRD positive defined as tBRCAm and/or genomic instability score ≥42 in the Myriad myChoice® CDx assay. †Descriptive analysis

Gonzalez-Martin A, et al. Eur. J. Cancer. 174 (2022) 221-231

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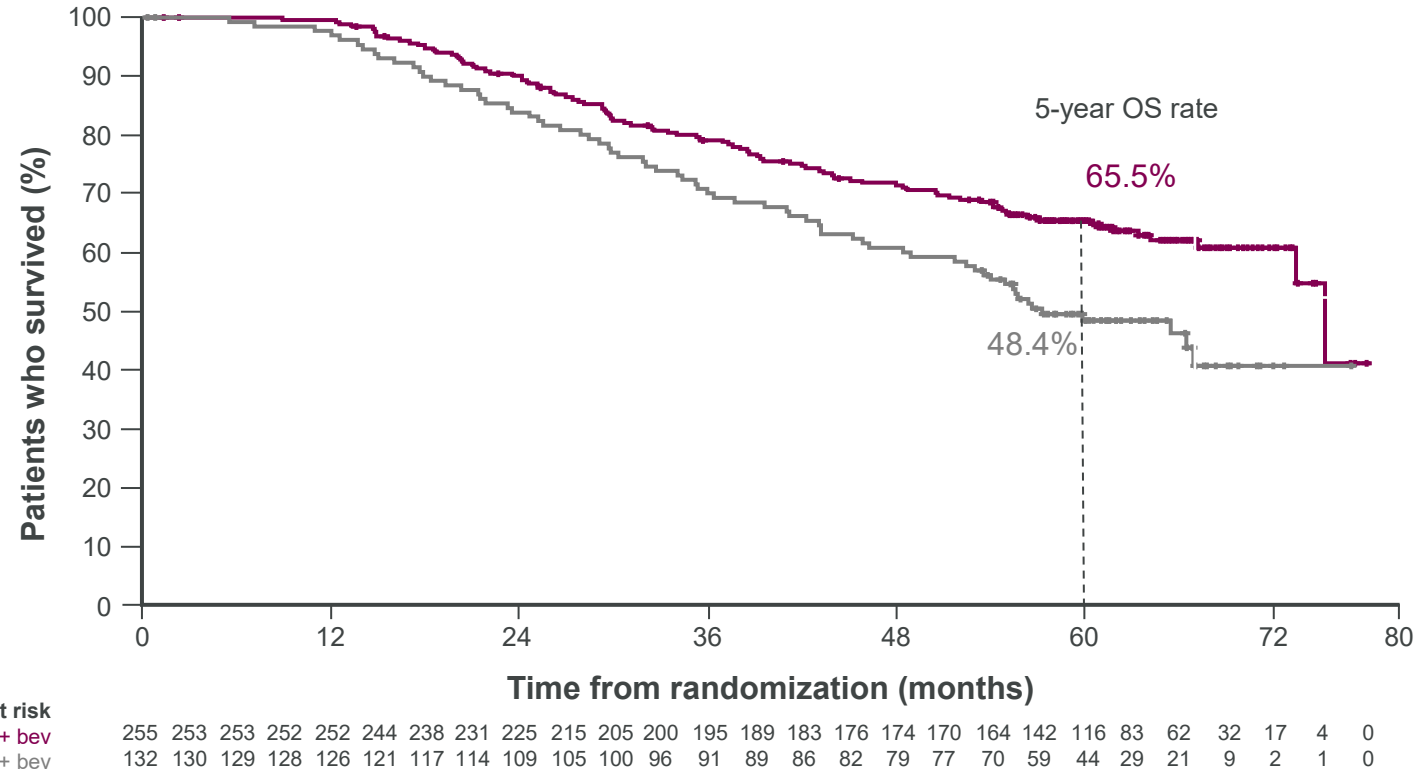
Final OS analysis

Data cut-off March 2022

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Olaparib + bev provided a clinically meaningful improvement in OS in HRD-positive patients

At 5 years, 65.5% of patients receiving olaparib + bevacizumab were still alive vs 48.4% who received bevacizumab alone



	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 + bev: **17.3%** (44/255)
Placebo + bev: **50.8%** (67/132)

*Median unstable; <50% data maturity
Final OS DCO: 22 March 2022. Final OS analysis planned for 3 years after the primary PFS analysis or 60% data maturity.
Median time from first cycle of chemotherapy to randomization = 6 months
*Descriptive analysis
Ray-Coquard I, et al. Presented at ESMO Congress 2022. 9–13 September. Paris, France

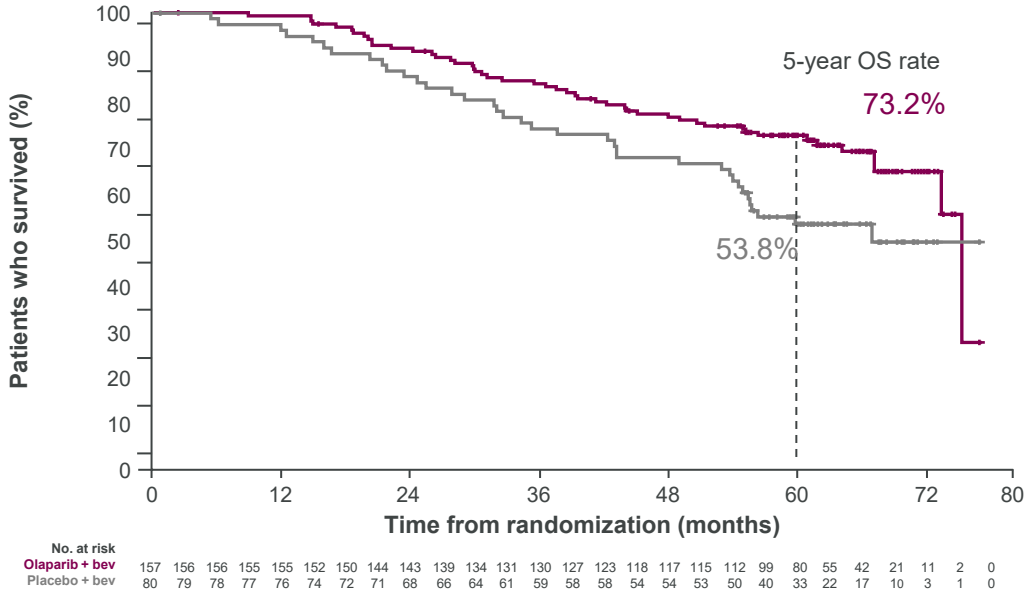
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OS subgroup analysis by BRCAm and HRD status

The addition of olaparib to bevacizumab prolonged OS in HRD+ patients regardless of BRCA status.

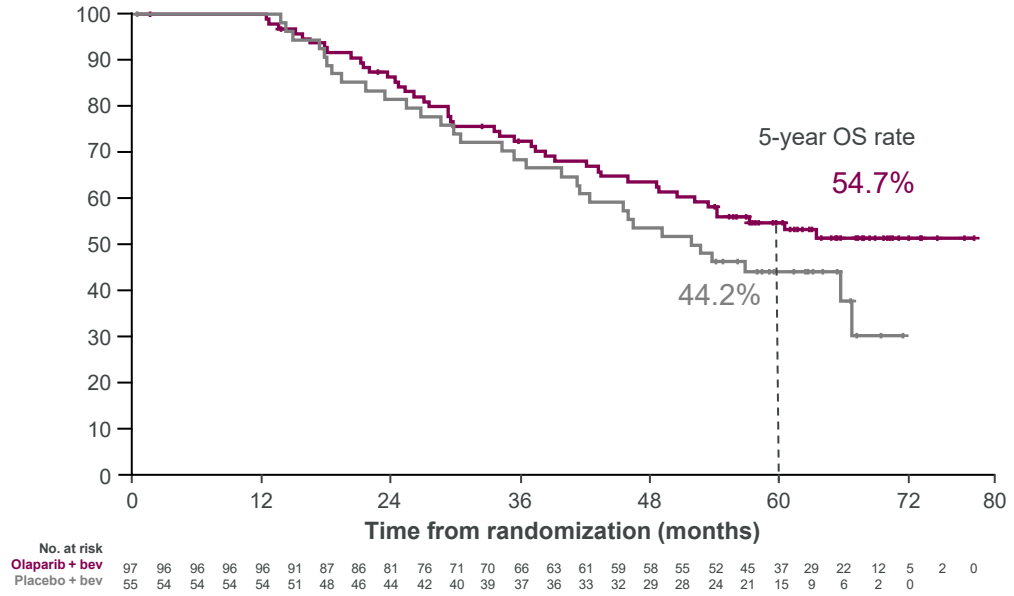
BRCAm*

	Olaparib + bevacizumab (n=157)	Placebo + bevacizumab (n=80)
Events, n (%)	48 (30.6)	37 (46.3)
Median OS, months	**75.2** (unstable)‡	**66.9**
5-year OS rate, %	**73.2**	**53.8**
	HR 0.60 (95% CI, 0.39–0.93)	



HRD-positive,† excluding tBRCAm

	Olaparib + bevacizumab (n=97)	Placebo + bevacizumab (n=55)
Events, n (%)	44 (45.4)	32 (58.2)
Median OS, months	**NR**	**52.0**
5-year OS rate, %	**54.7**	**44.2**
	HR 0.71 (95% CI, 0.45–1.13)	



*By central labs; †By Myriad myChoice® HRD Plus; ‡Unstable median; <50% data maturity

Final OS DCO: 22 March 2022. Final OS analysis planned for 3 years after the primary PFS analysis or 60% data maturity.

Ray-Coquard I, et al. Presented at ESMO Congress 2022. 9–13 September. Paris, France

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PFS & OS by Clinical Risk

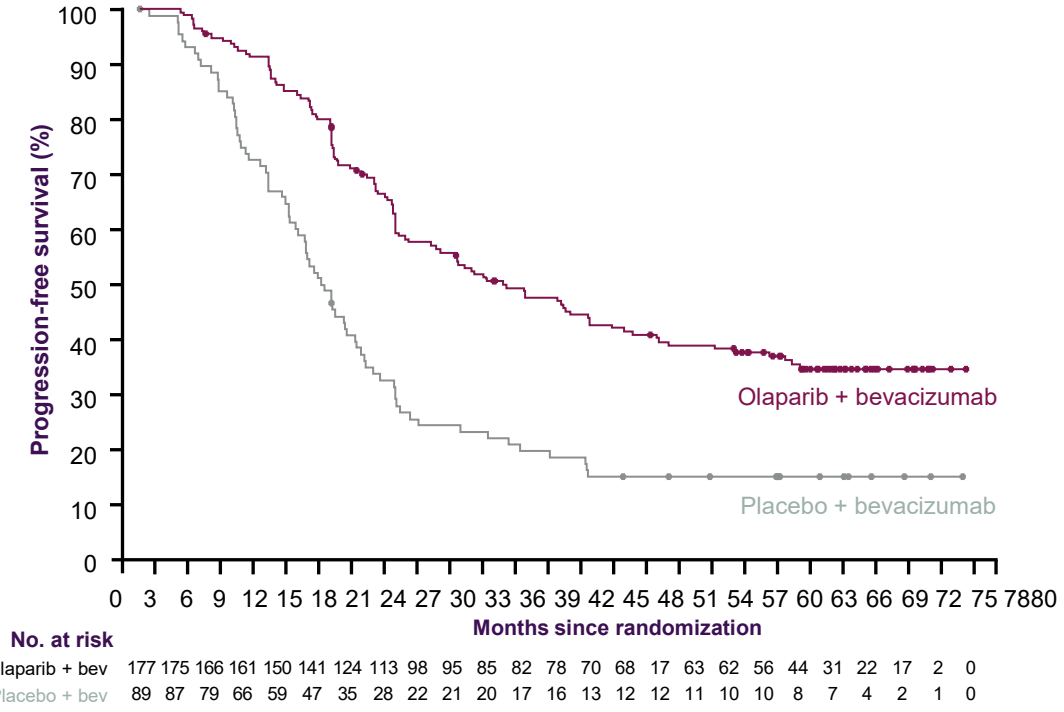
© AstraZeneca 2026

PFS & OS in Higher Risk HRD Positive Patients

Stage III patents with PDS and no residual disease

PFS

	Olaparib + bevacizumab (n=177)	Placebo + bevacizumab (n=89)
Events, n (%)	110 (62)	74 (83)
Median PFS, months	31.3	15.9
5-year PFS rate, % (95% CI)	35†	15†
	HR 0.46 (95% CI 0.34–0.61)	

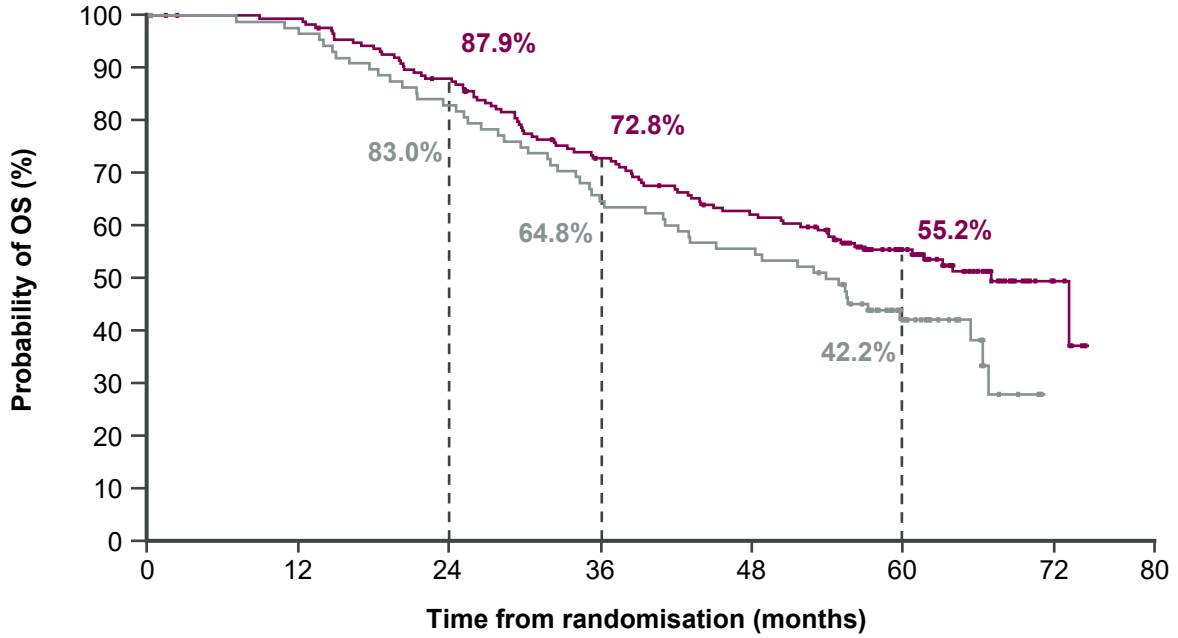


No. at risk

Olaparib + bev	177	175	166	161	150	141	124	113	98	95	85	82	78	70	68	17	63	62	56	44	31	22	17	2	0
Placebo + bev	89	87	79	66	59	47	35	28	22	21	20	17	16	13	12	12	11	10	10	8	7	4	2	1	0

OS

	Olaparib + bevacizumab (n=177)	Placebo + bevacizumab (n=89)
Events, n (%)	82 (46.3)	53 (59.6)
Median OS, months	67.0†	54.0
5-year OS rate, %	55.2	42.2
	HR 0.70 (95% CI 0.50–1.00)	
PARP inhibitor as subsequent treatment, %	18.6	56.2



Patients at risk

Olaparib + bev	177	175	175	174	174	166	163	156	152	143	133	128	123	117	112	105	103	100	96	82	69	49	36	15	8	0
Placebo + bev	89	88	88	87	85	81	79	76	73	69	66	62	57	56	53	50	49	47	43	36	24	14	10	4	0	

Higher risk patients defined as those with FIGO stage III disease who had undergone upfront surgery and had residual disease or who had received neoadjuvant chemotherapy or FIGO stage IV patients. Lower-risk patients were those with FIGO stage III disease who had undergone upfront surgery and had complete resection[2]

†Kaplan-Meier estimates. ‡ Unstable median due to lack of events. 1. Lorusso D, et al. *Int J Gynecol Cancer.* 2024;34:550–558. 2. Harter P et al. Gynecol Oncol. 2022;164:254–64.

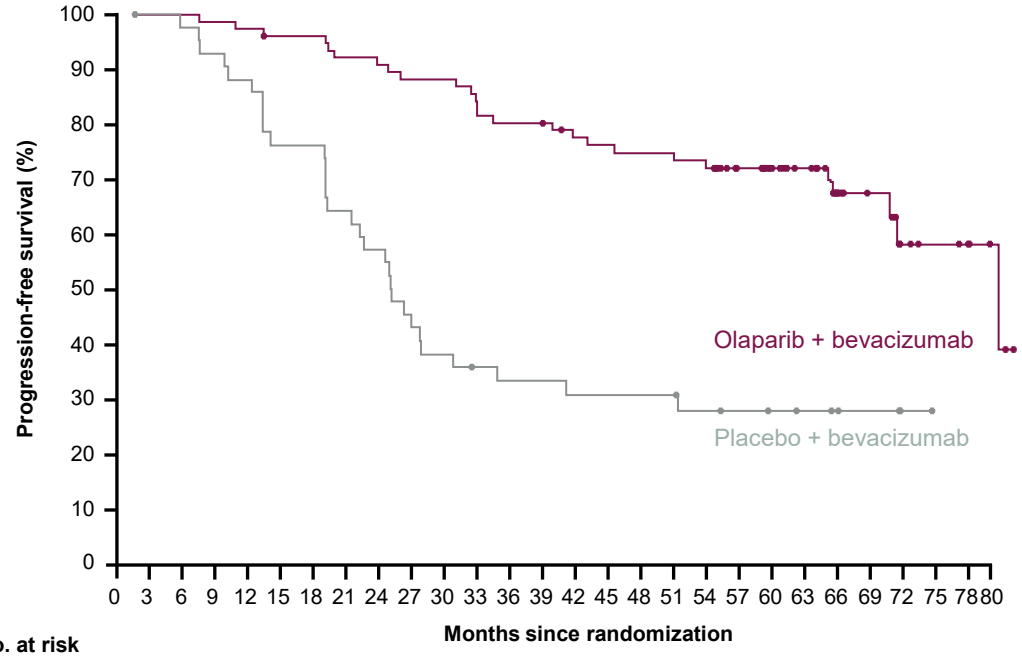
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PFS & OS in Lower Risk HRD Positive Patients

Stage III patients with PDS and residual disease, patients who received NACT, Stage IV patients

PFS

	Olaparib + bevacizumab (n=78)	Placebo + bevacizumab (n=43)
Events, n (%)	26 (33)	30 (70)
Median PFS, months	75.2‡	22.3
5-year PFS rate, % (95% CI)	72†	28†
	HR 0.26 (95% CI 0.15–0.45)	

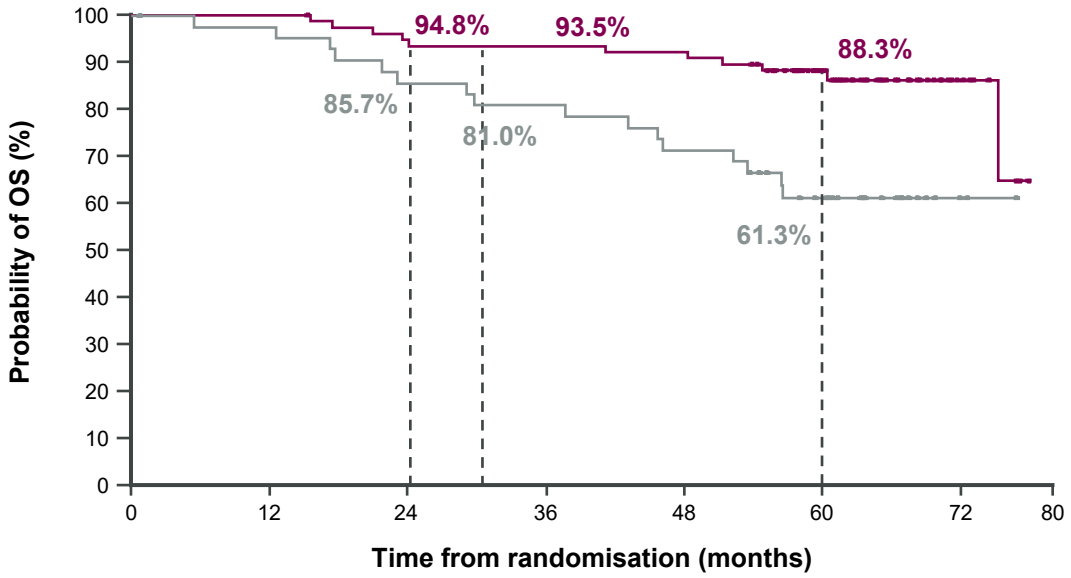


No. at risk

Olaparib + bev	78	77	76	75	73	73	70	70	67	67	62	61	60	57	55	55	54	50	47	35	32	18	14	6	5	3	0
Placebo + bev	43	42	39	37	32	32	27	24	19	16	14	13	13	12	12	12	10	10	9	7	6	4	4	1	0		

OS

	Olaparib + bevacizumab (n=78)	Placebo + bevacizumab (n=43)
Events, n (%)	11 (14.1)	16 (37.2)
Median OS, months	NE	NE
5-year OS rate, %	88.3	61.3
	HR 0.31 (95% CI 0.14–0.66)	
PARP inhibitor as subsequent treatment, %	14.1	39.5



Patients at risk

Olaparib + bev	78	78	78	78	78	78	75	75	73	72	72	72	72	72	71	71	71	70	68	60	47	34	26	17	9	4	0
Placebo + bev	43	42	41	41	41	40	38	38	36	36	34	34	34	33	33	32	30	30	27	23	20	15	11	5	2	1	0

Higher risk patients defined as those with FIGO stage III disease who had undergone upfront surgery and had residual disease or who had received neoadjuvant chemotherapy or FIGO stage IV patients. Lower-risk patients were those with FIGO stage III disease who had undergone upfront surgery and had complete resection[2]

†Kaplan-Meier estimates. ‡ Unstable median due to lack of events. 1. Lorusso D, et al. *Int J Gynecol Cancer.* 2024;34:550–558. 2. Harter P et al. Gynecol Oncol. 2022;164:254–64.

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Population-adjusted indirect treatment comparison of PFS: PAOLA-1 vs. PRIMA



Check for updates

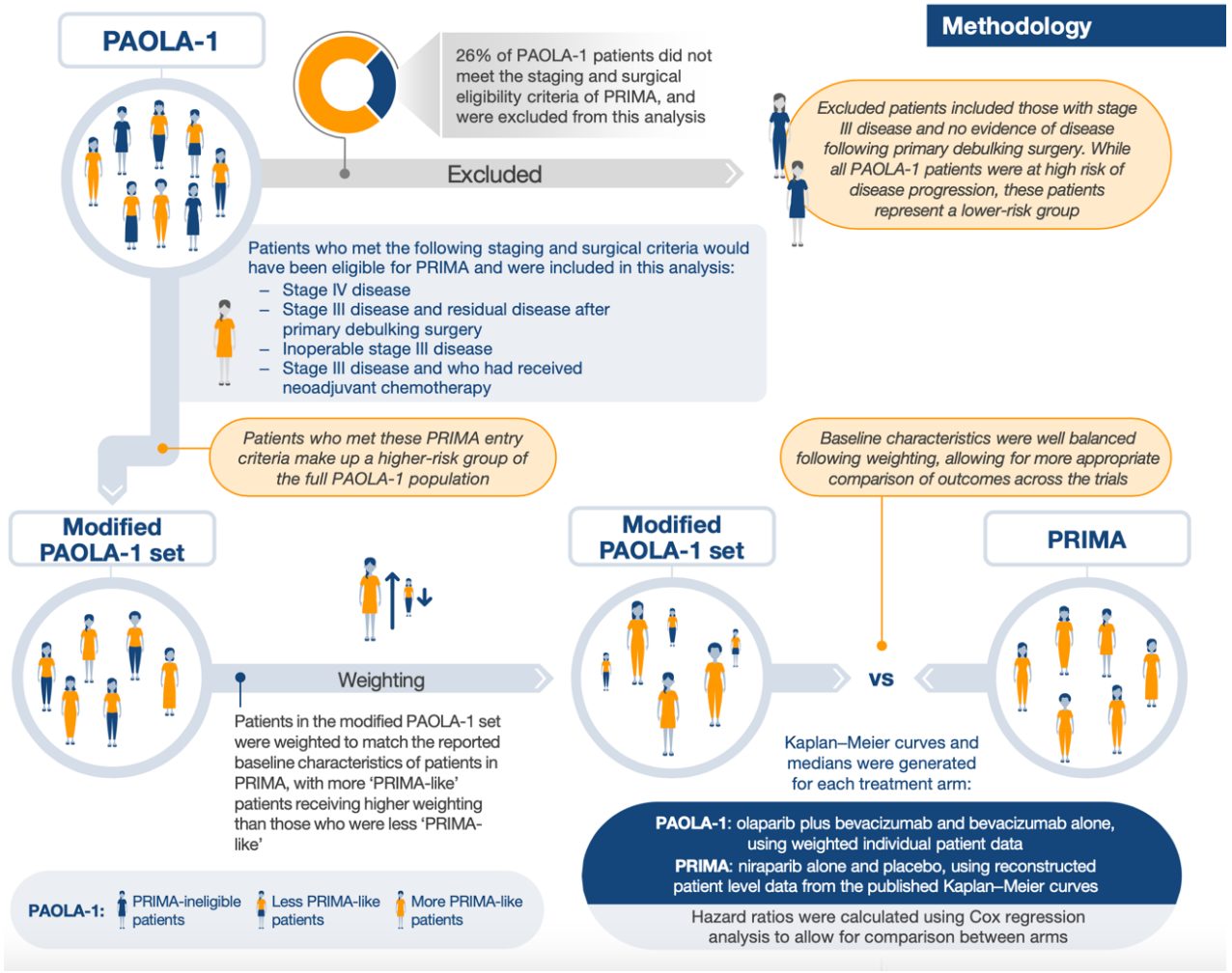
Therapeutic Advances in Medical Oncology — *Original Research*

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

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

Ther Adv Med Oncol
2021, Vol. 13: 1–14
DOI: 10.1177/17588359211049639

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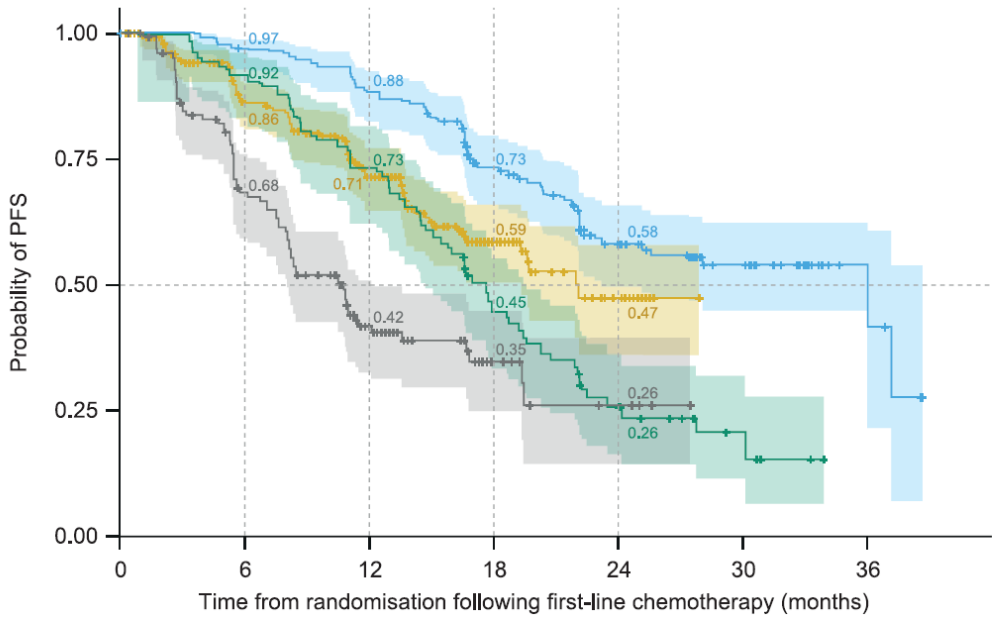


Hettle R et al., Ther Adv Med Oncol 2021;13:1-14

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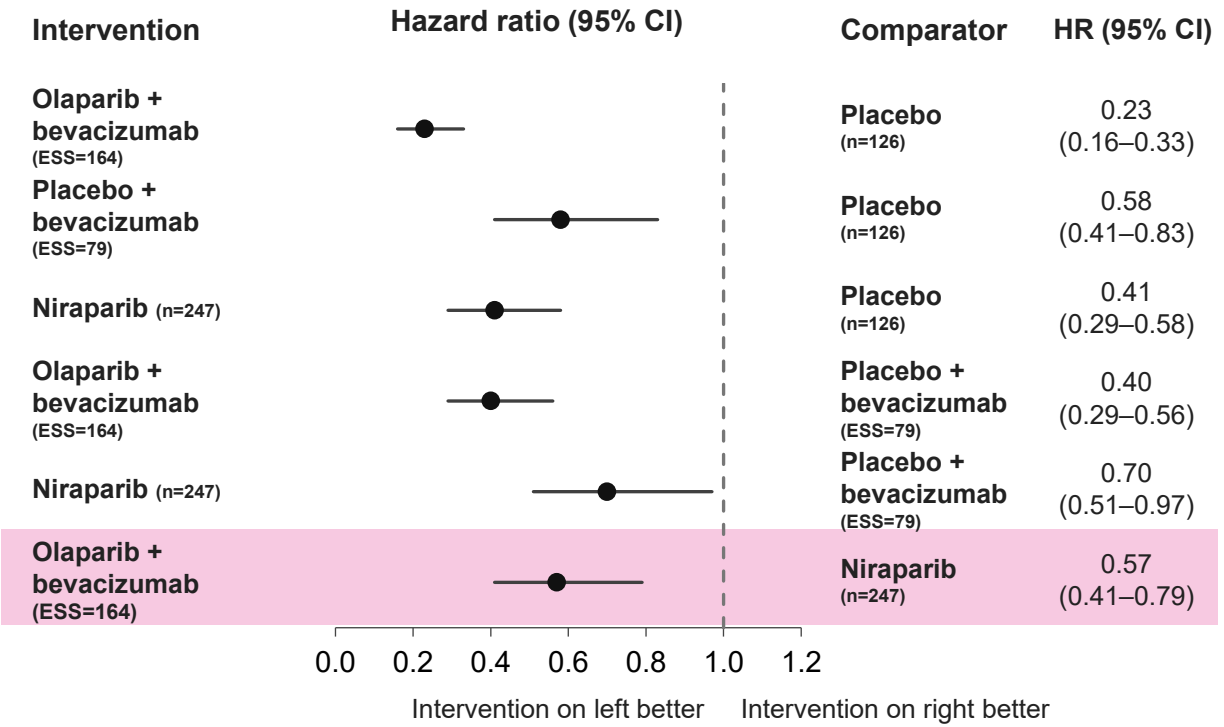
Population-adjusted indirect treatment comparison of PFS: PAOLA-1 vs. PRIMA

Kaplan-Meier Curves



	Median PFS (95% CI), months
Olaparib + bevacizumab	36.0 (23.2–NA)
Niraparib	22.0 (19.3–NA)
Placebo + bevacizumab	17.6 (14.7–19.6)
Placebo	10.5 (8.05–12.1)

Forest Plot in HRD Positive Patients



Hettle R et al., Ther Adv Med Oncol 2021;13:1-14

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Safety, tolerability and HRQoL

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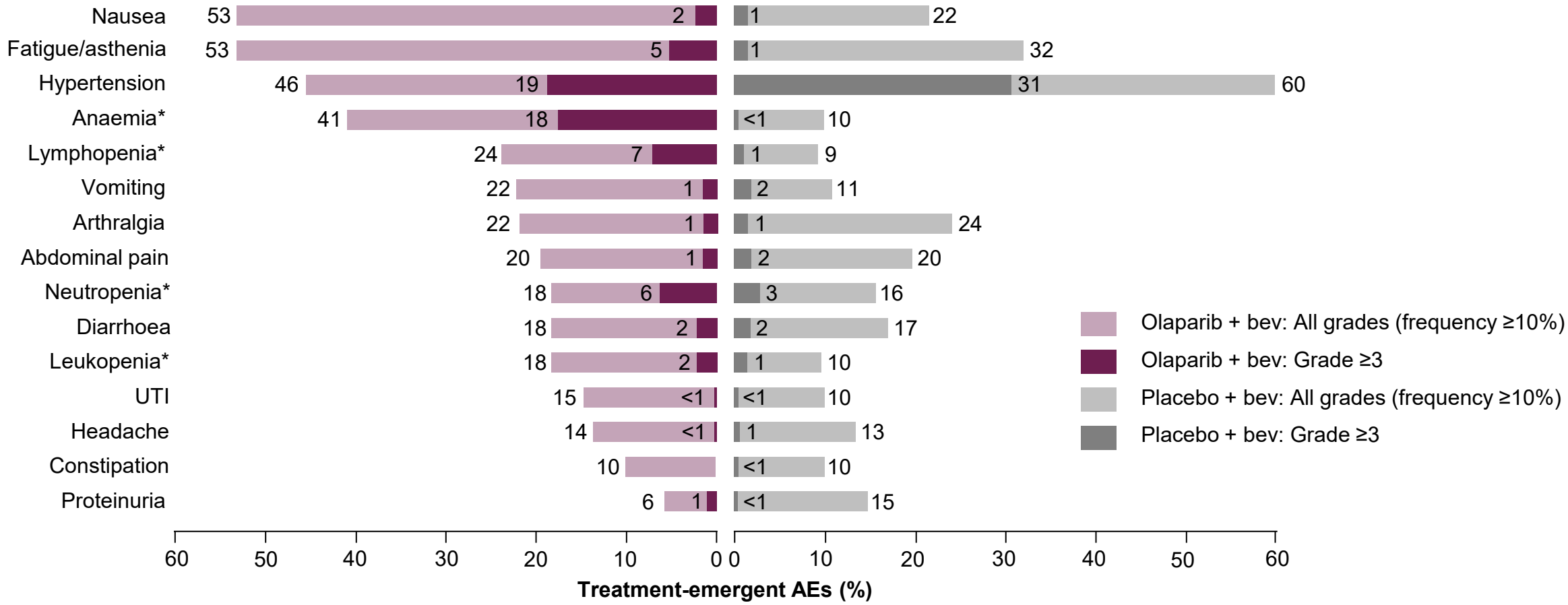
The safety profile of olaparib in the PAOLA-1 trial was consistent with previous trials of olaparib

	Olaparib + bevacizumab (n=535)	Placebo + bevacizumab (n=267)
Median duration of treatment with olaparib/placebo,* months (range) **Median duration of treatment with bevacizumab since randomisation*,** months (range)	17.3 (0.0–33.0) 11.0 (0.7–21.4)	15.6 (0.1–26.2) 10.6 (0.7–17.1)
All grade AEs, n (%)	531 (99)	256 (96)
Grade ≥3 AEs, n (%)	303 (57)	136 (51)
Serious AEs, n (%)	167 (31)	83 (31)
AEs leading to death, n (%)	1 (<1)	4 (2)
AEs leading to dose interruption of olaparib or placebo, n (%)	291 (54)	65 (24)
AEs leading to dose reduction of olaparib or placebo, n (%)	220 (41)	20 (7)
AEs leading to treatment discontinuation of olaparib or placebo,* n (%)	109 (20)	15 (6)

*HRD positive defined as tBRCAm and/or Myriad myChoice® CDx genomic instability score ≥42
†Neoadjuvant treatment may have included bevacizumab
Ray-Coquard I, et al. N Engl J Med. 2019;381:Supplementary appendix

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The AE profile of olaparib in PAOLA-1 was consistent with previous trials of olaparib



Secondary data cut-off: March 2020. Median duration of follow-up: olaparib, 35.5 months; placebo, 36.5 months

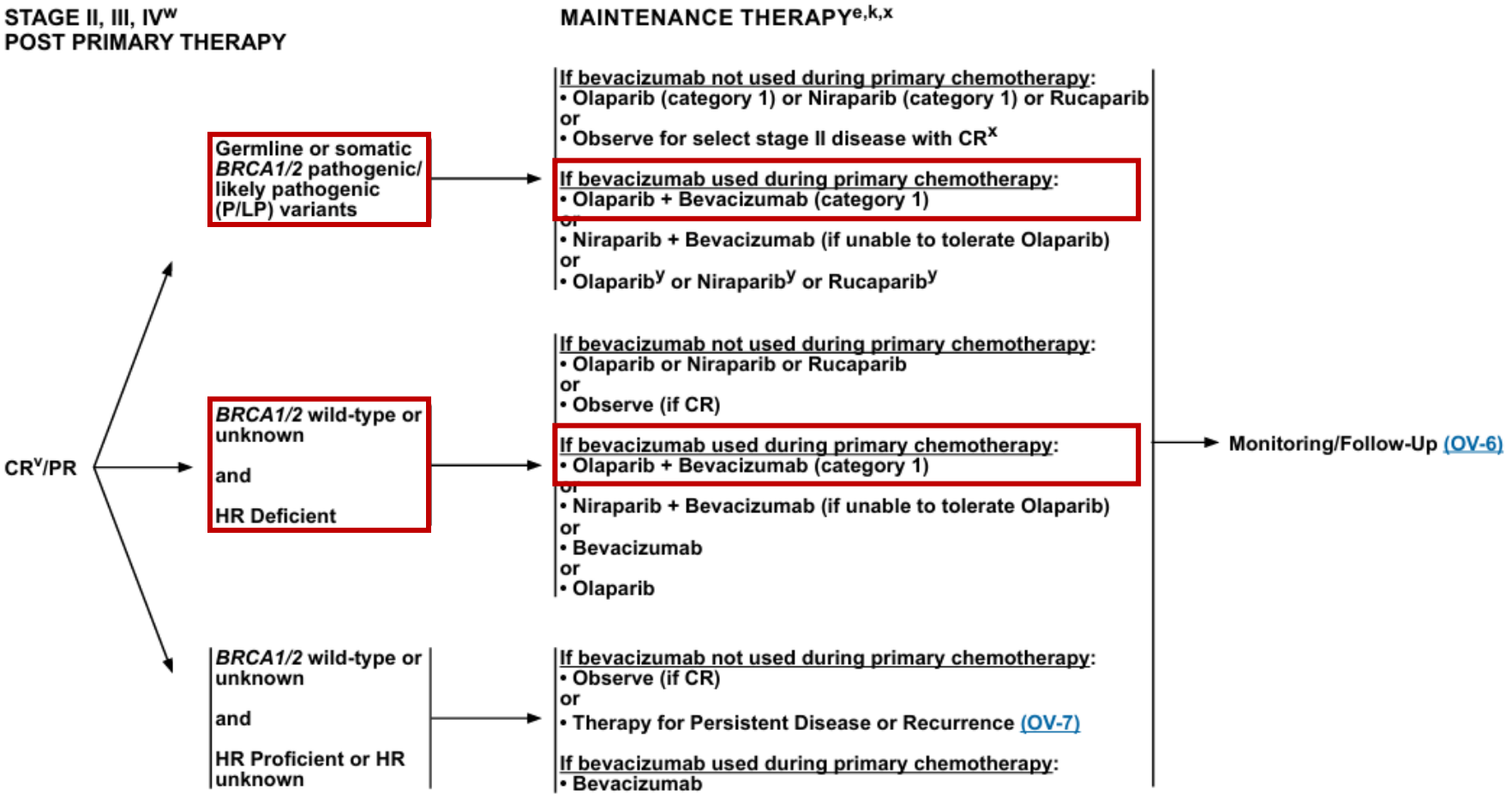
All-grade grouped-term thrombocytopenia occurred in 8% of olaparib plus bevacizumab patients and 3% of placebo plus bevacizumab patients; grade ≥3 grouped-term thrombocytopenia occurred in 2% of olaparib plus bevacizumab patients and <1% of placebo plus bevacizumab patients

*Grouped terms.

1. Gonzalez-Martin A, et al. Eur. J. Cancer. 174 (2022) 221-231; 2. Moore K, et al. N Engl J Med 2018;379:2495-505;
3. Pujade-Lauraine E, et al. Lancet Oncol. 2017;18:1274-84; 4. Ledermann J, et al. Lancet Oncol. 2014;15:852-61

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2026 NCCN Clinical Guidelines for Ovarian cancer



[e] In the absence of a *BRCA1/2* mutation, HRD status has been correlated with magnitude of benefit from PARPi maintenance in clinical trials. For PARPi therapy in advanced stage disease, include measure of HR (OV-C).
[k] See Principles of Systemic Therapy (OV-D) and Management of Drug Reactions (OV-E).
[v] No definitive evidence of disease.
[w] Post primary treatment recommendations for stage II–IV high-grade serous or grade 2 or 3 endometrioid carcinoma; consider for clear cell carcinoma or carcinosarcoma with a *BRCA1/2* mutation.
[x] Data are limited for maintenance therapy with a PARPi for patients with stage II disease.
[y] After first-line therapy with bevacizumab, data are limited on maintenance therapy with a single-agent PARPi (olaparib, niraparib, or rucaparib) for patients with a germline or somatic *BRCA1/2* P/LP variants. However, based on the magnitude of benefit of PARPi maintenance therapy for other subgroups, single-agent PARPi can be considered.

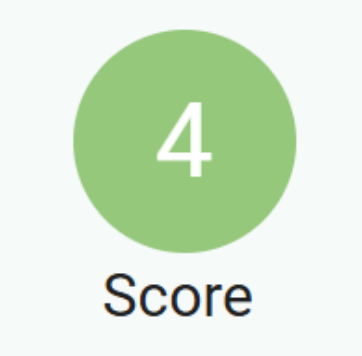
Note: All recommendations are category 2A unless otherwise indicated.

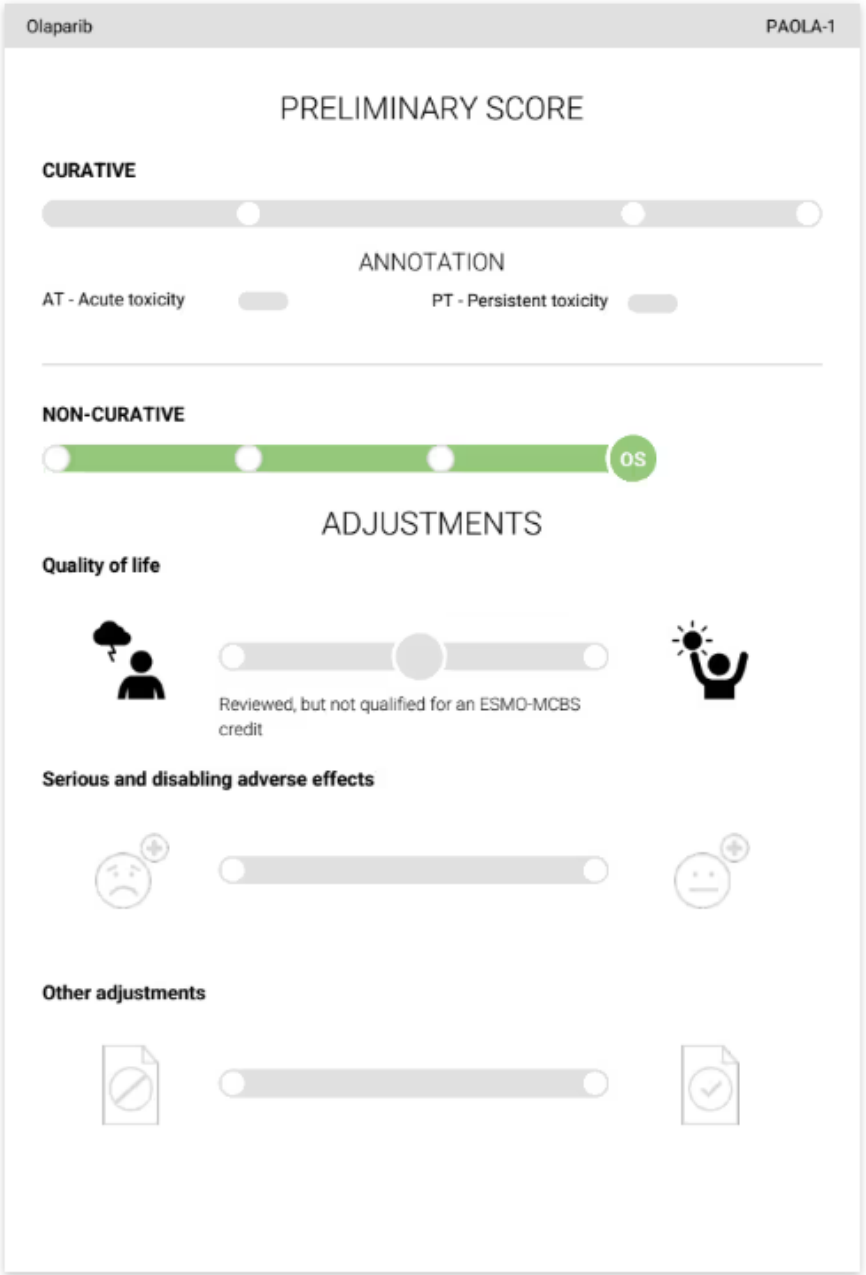
Version 1.2026, 02/25/26 © 2026 National Comprehensive Cancer Network® (NCCN®), All rights reserved. NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN.

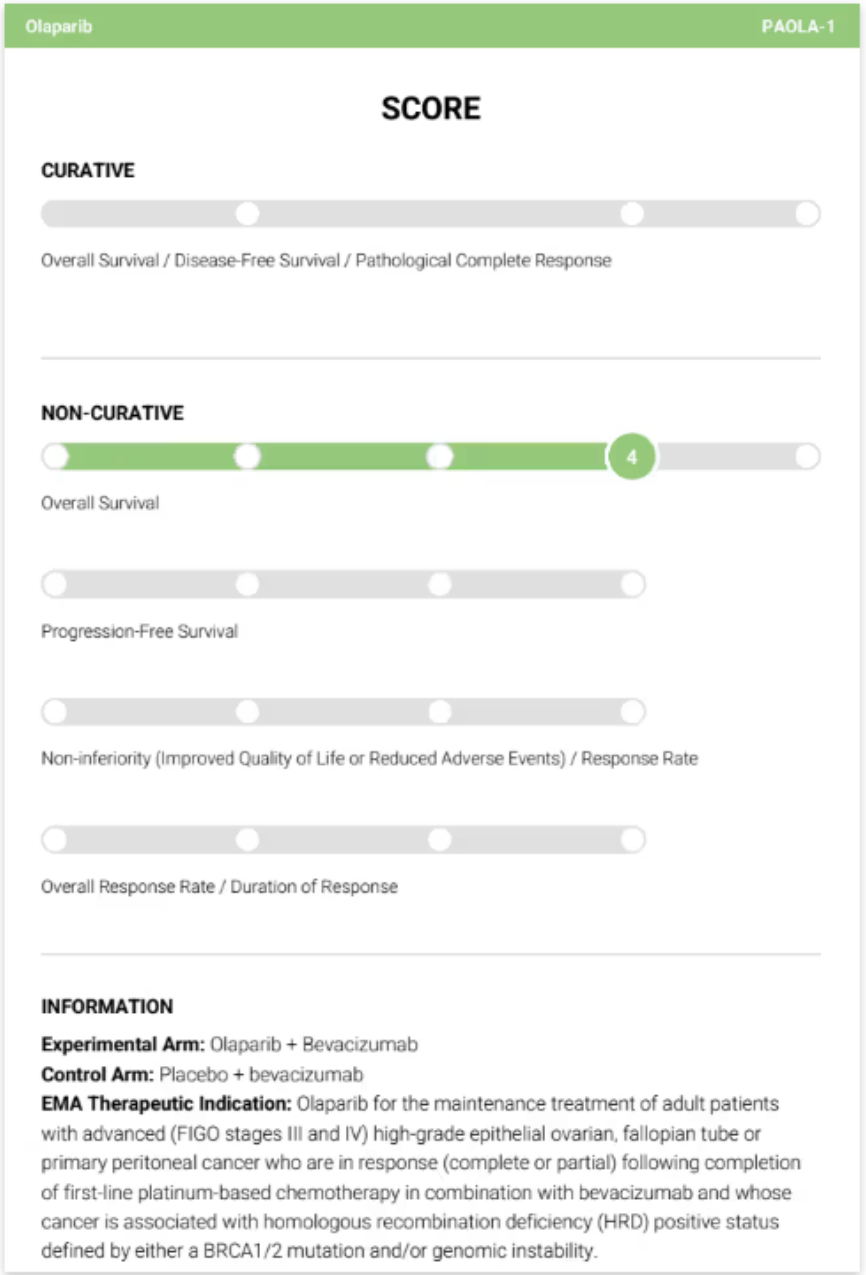
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ESMO-MCBS Scorecard

- **Olaparib**
- **PAOLA-1**
- **Tumor type: HRD+**





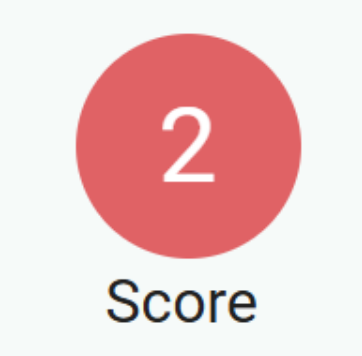


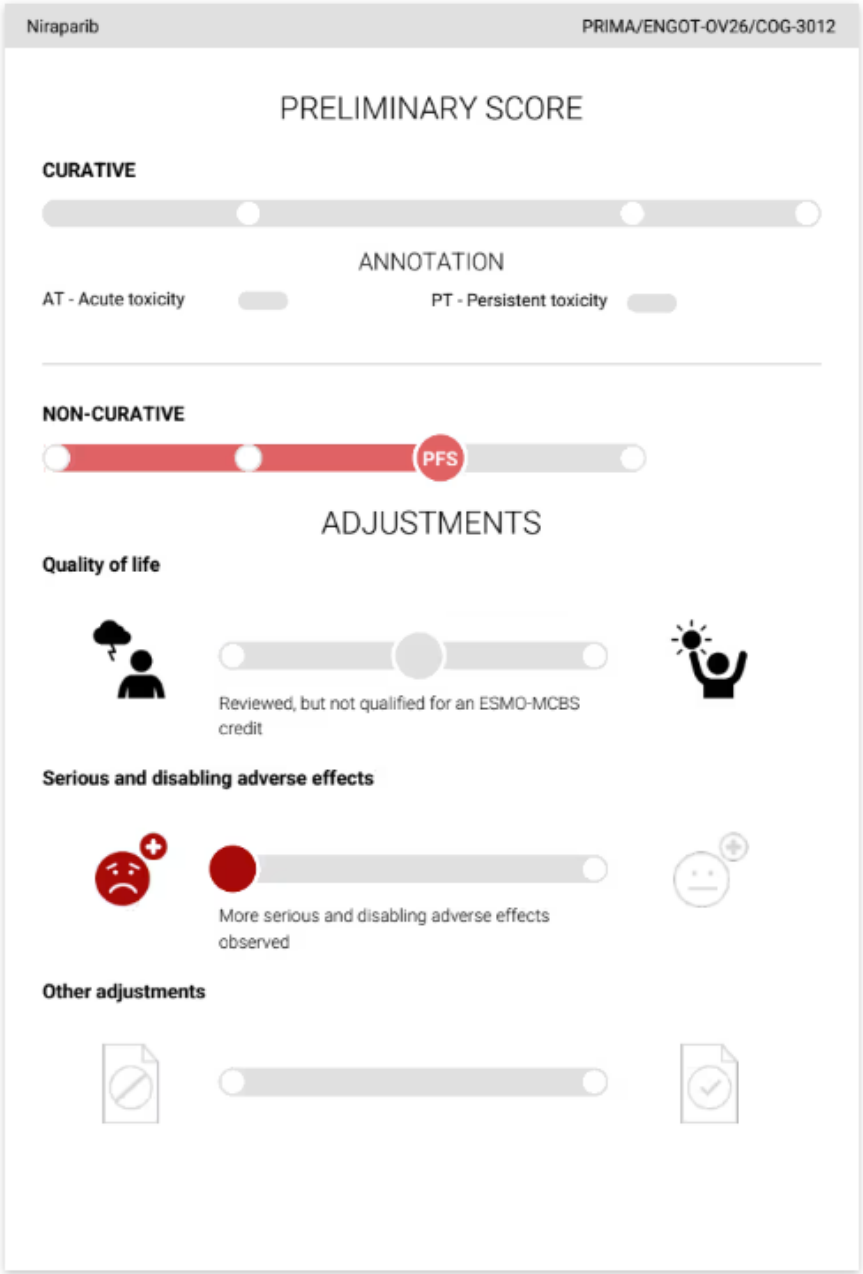
ESMO-MCBS v2.0, https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards?scorecard=217 Accessed on 2026 Apr

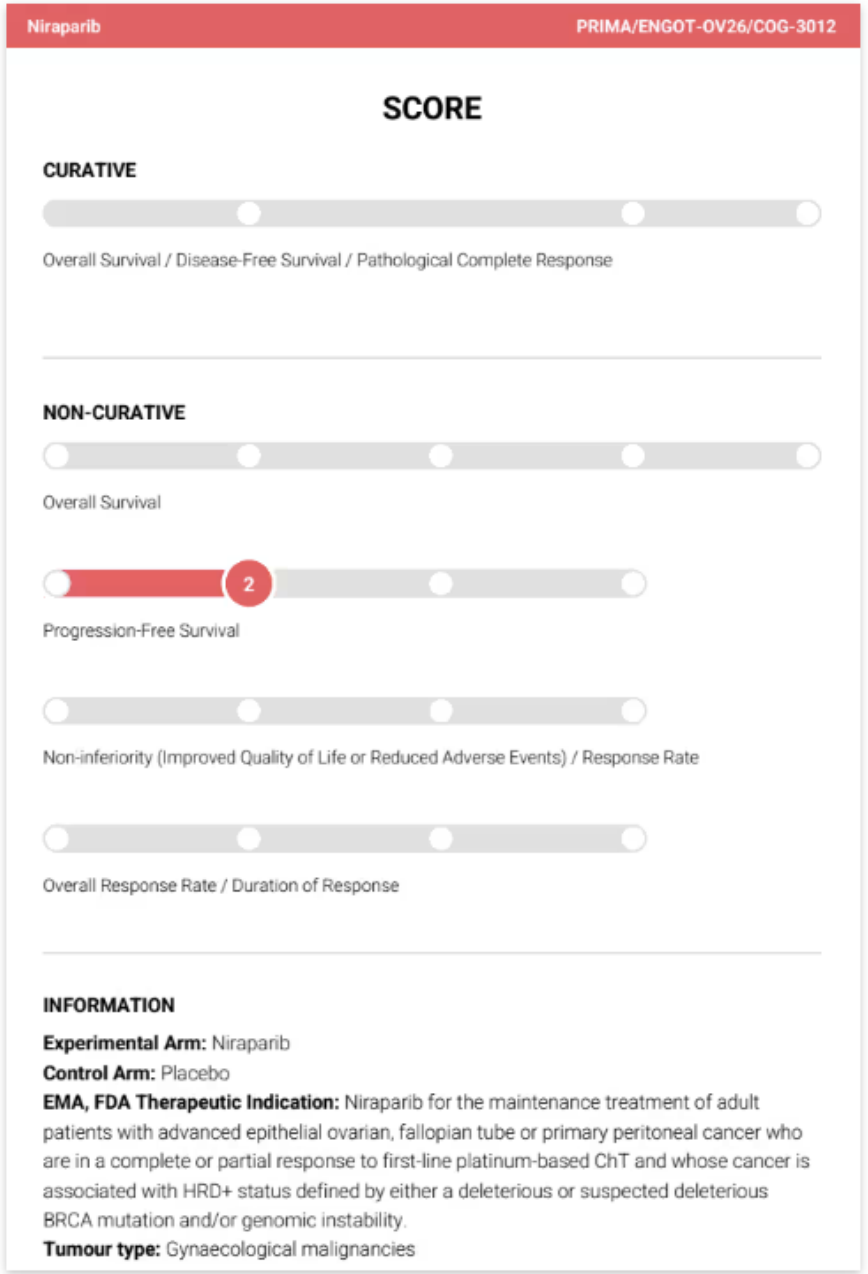
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ESMO-MCBS Scorecard

- **Niraparib**
- **PRIMA**
- **Tumor type: HRD+**







ESMO-MCBS v2.0, https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards?scorecard=245 Accessed on 2026 Apr

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Case Presentation

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환자내원사유 초음파, CT상 난소암의심 진료후 양성일경우 의사변경설

상기 환자는 우측난소 4.45*3.5*2.44cm 고형종양이 발견되어 2023년 8월 8일 복부 골반ct촬영하였습니다. ROMA 폐경 후 고위험 (CA125 98.3, HE4 162)입니다. 난소의 악성종양 의심되어 귀원으로 전원하오니 고진선처 바랍니다.

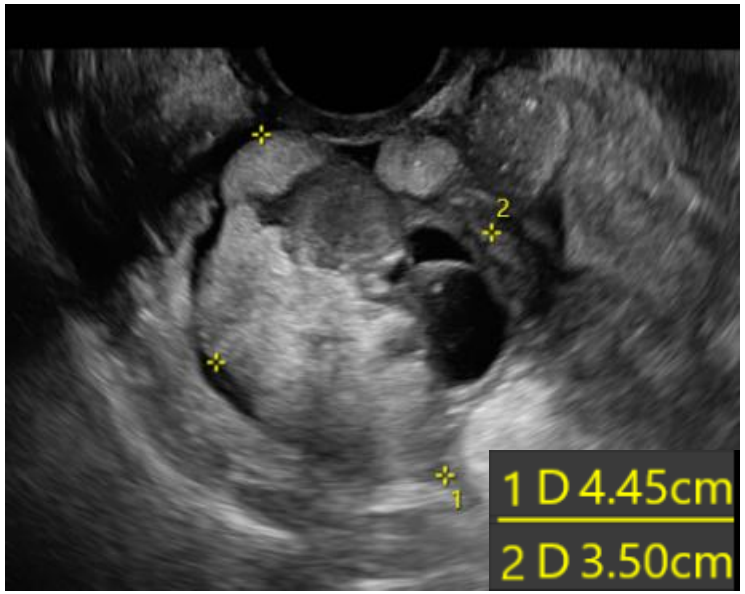
Tumor marker : 2023-08-02
AFP: 3.1
CEA: < 0.5
CA125: 98.3
CA19-9: 2.79
HE4: 162.00

Para : (3) - (0) - (4)(2,2) - (2)(1,1)
분만형태 : 자연분만

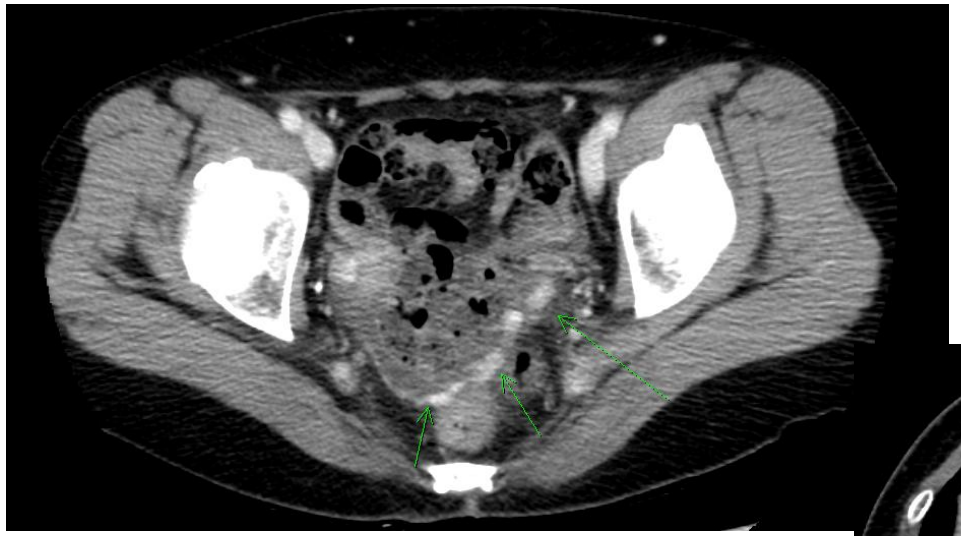
<ROMA (Risk of Ovarian Malignancy Algorithm)>

검사항목		결과	단위
BL371411	HE4	161.0	pmol/L
BL3714	CA125	114.0	U/mL

검사항목	결과	High risk of finding epithelial ovarian cancer	Low risk of finding epithelial ovarian cancer
ROMA score			
Pre-menopausal	59.6 %	≥ 11.4%	<11.4%
Post-menopausal	66.0 %	≥ 29.9%	<29.9%

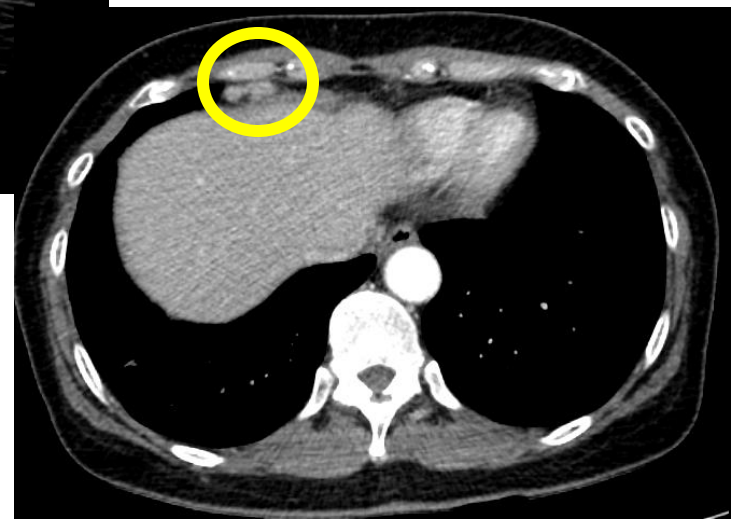


Ultrasound



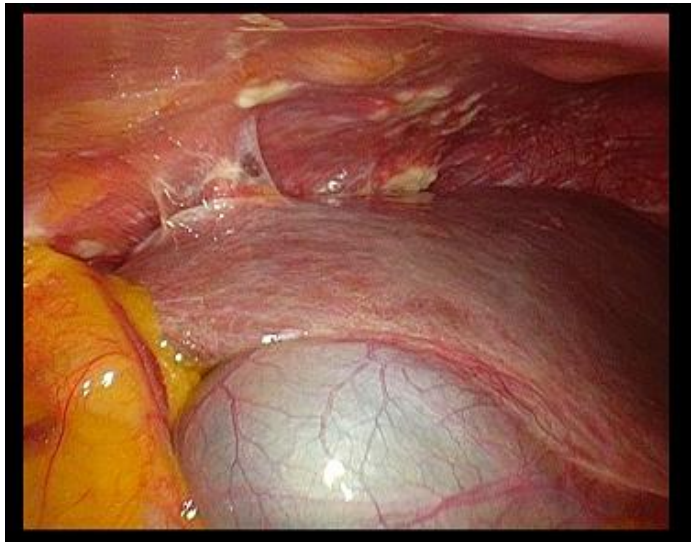
AP CT

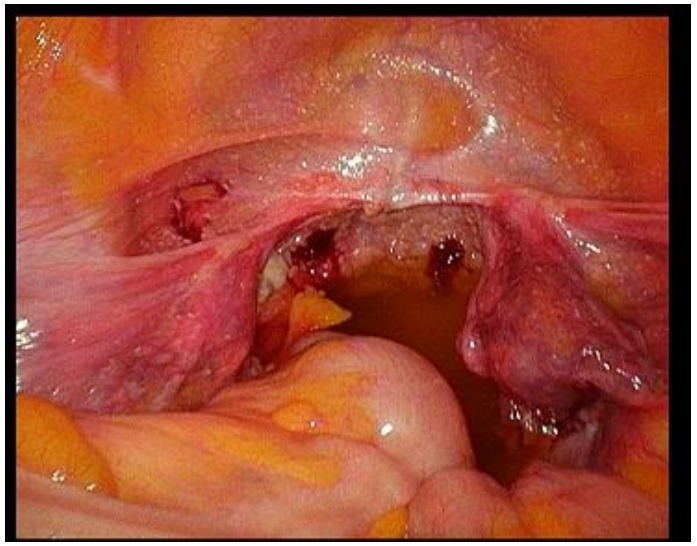
Chest CT



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2023-08-23 [RO] Open BSO TOMT c Pelvic peritonectomy c PCDS removal c Rectal serosa removal c Rectal serosa reinforcement c Paracolic gutter removal c Colon serosa reinforcement c Mesentary nodule removal c Rt.Diaphragm stripping c Splenectomy





Diagnosis (2020 WHO):
. HIGH-GRADE SEROUS CARCINOMA, grade 3, bilateral ovaries

+ Greatest dimension: 3.5 cm (right ovary) and 1.2 cm (left ovary)
+ Lymphovascular invasion: Absent
+ Ovarian surface extension: PRESENT (bilateral)
+ Salpingeal extension: PRESENT (right)

+ Pelvic peritoneal extension: PRESENT
+ Extrapelvic peritoneal extension: PRESENT
- Omentum: PRESENT
- Spleen: PRESENT (capsule)
- Right diaphragm: PRESENT
- Ligamentum teres: Absent
- Mesentery: PRESENT
- Right paracolic gutter: PRESENT
- Left paracolic gutter: PRESENT

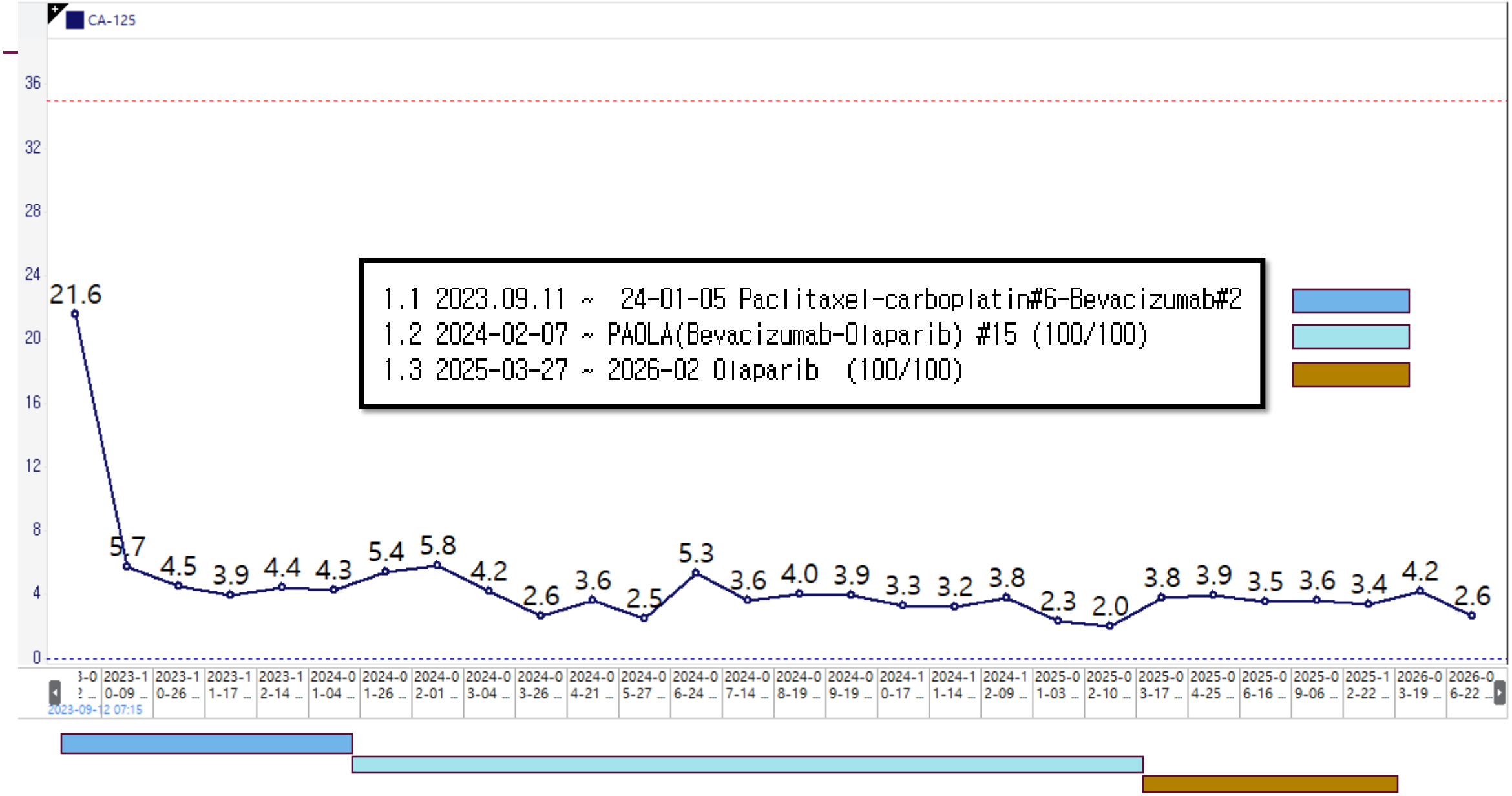
FIGO stage IVB
PDS
R0
→ High vs Low risk
BRCAwt/HRD (64)

상동 재조합 결핍(HRD)	유전체 불안정성	BRCA	유전체 불안정성 점수
양성	양성	음성	(64)

◇ QC 정보

DNA (SNV)	DNA (CNV)
Pass	Pass

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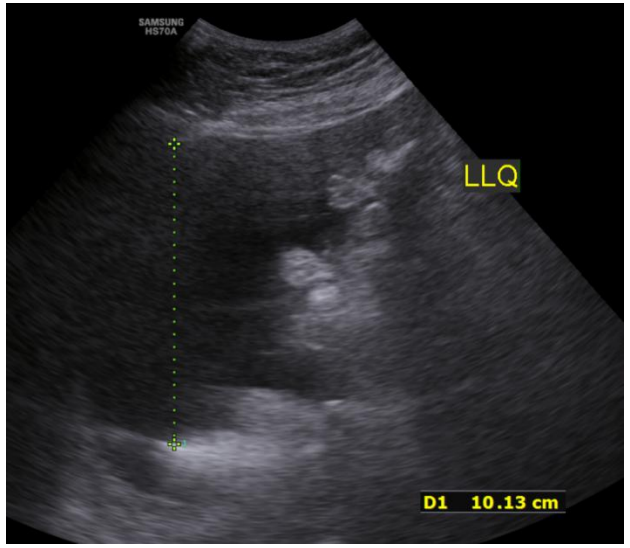
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* 환자내원사유 ct상 난소암 /교수님지정

교수님 안녕하십니까?
복부팽만감으로 내원하였고 초음파에서 RT.adenexa에 large lobulateed solid mass가 관찰되고 ascites가 있었습니다.
ovarian cancer with a sictes로 추정되어 의뢰드리오니 고진 선처 부탁드립니다.

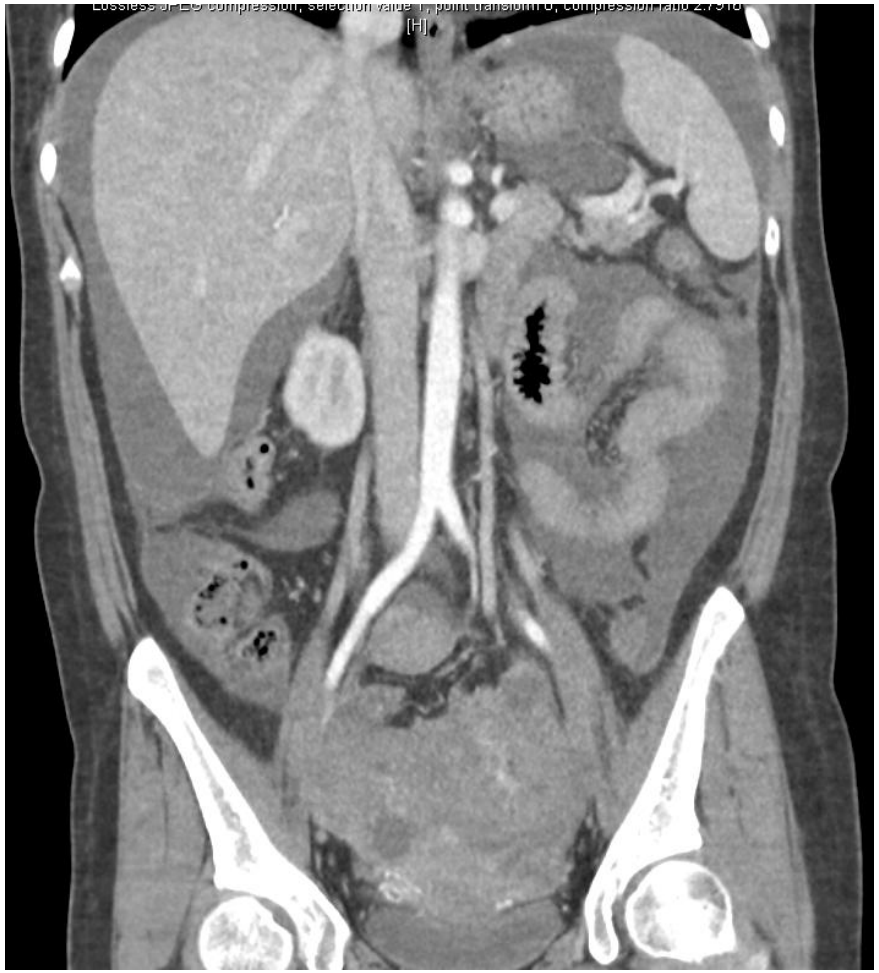
CA-125 (U/mL):▲3128.0



Ultrasound



Pelvis MRI



AP CT

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[R1] TAH c BSO c PLND c both IP ligament remove
c pelvic peritonectomy c bladder peritonectomy
c PCDS mass remove c falciform ligament remove c TOMT
c appendectomy c Lt paracolic gutter mass remove
c mesenteric nodule remove
c LAR

```
Diagnosis (2020 WHO):
. HIGH-GRADE SEROUS CARCINOMA, grade 3, bilateral ovaries

+ Greatest dimension: 5 cm (right ovary) and 5 cm (left ovary)
+ Lymphovascular invasion: PRESENT (substantial)
+ Ovarian surface extension: PRESENT (bilateral)
+ Salpingeal extension: PRESENT (bilateral)
+ Uterine extension: PRESENT (serosa, myometrium, and endometrium)

+ Lymph node metastasis: PRESENT (5/21)
- Left pelvic (0/8)
- Right pelvic (2/7) (0.4 cm)
- "Left IP ligament" (1/1)
- Rectum (2/5)

+ Pelvic peritoneal extension: PRESENT
+ Extrapelvic peritoneal extension: PRESENT
- Pelvic peritoneum: PRESENT
- Bladder peritoneum: PRESENT
- Left pelvic peritoneum: PRESENT
- Right pelvic peritoneum: PRESENT
- Falciform ligament: PRESENT
- Mesenteric nodule: PRESENT
- Right IP ligament: PRESENT
- Left IP ligament: PRESENT (metastasis to lymph node)
- Left round ligament: PRESENT
- Left paracolic gutter: PRESENT
- Parametrium: PRESENT
- Cul de sac mass: PRESENT
- Rectum: PRESENT (subserosa)
- Omentum: PRESENT
- Appendix: PRESENT (subserosa)
```

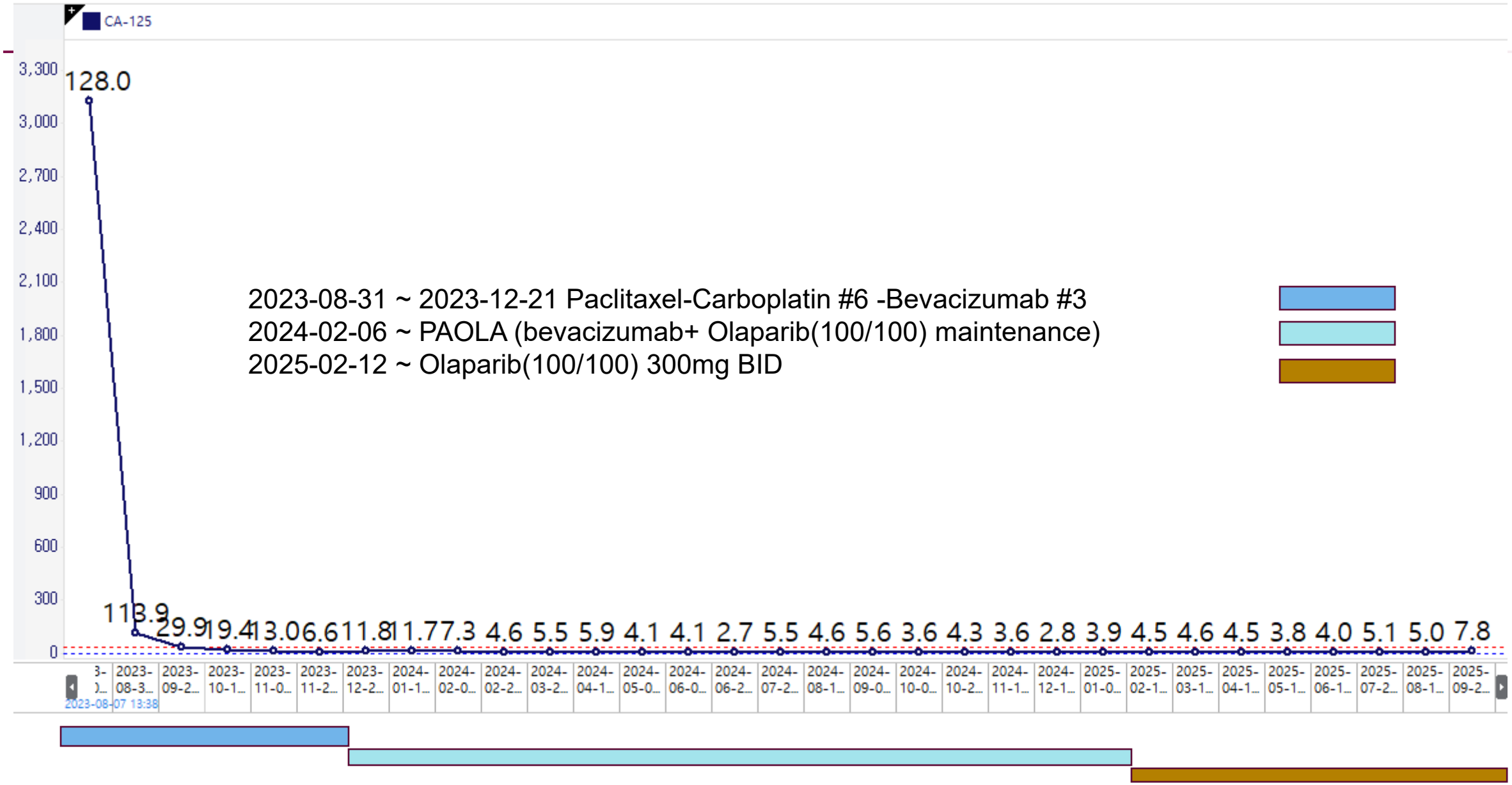
FIGO stage IIIC
PDS, R1
BRCAwt/HRD (58)

상동 재조합 결핍(HRD)	유전체 불안정성	BRCA	유전체 불안정성 점수
양성	양성	음성	(58)

◇ QC 정보

DNA (SNV)	DNA (CNV)
Pass	Pass

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57/F

* 환자내원사유	신환/과확인/난소암 4기 진단 받음 (난소암 림프전이)/원내 0200 r/o 다발성 복부 림프종양 상기 환자는 상기 병명하에 정밀검사 및 치료를 위해서 전원 합니다.

Tumor marker : 2025-04-06
CA125 1405.3
CA15-3 209.7
CA19-9 17.3
CEA 1.3

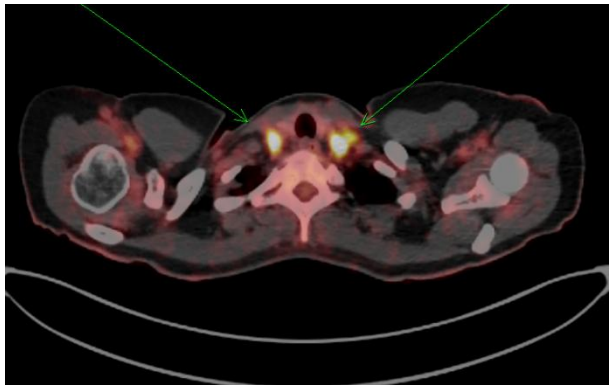
【검사명】 【단위】 2025-05-08 10:32:15

CA-125 (U/mL):▲681.6
CA-19-9 (U/mL):▲39.8

(207876)
Lymph node, left supraclavicular, US guided core needle aspiration :

. METASTATIC CARCINOMA, consistent with HIGH GRADE SEROUS CARCINOMA

<< Result of immunohistochemistry (according to outside report) >>
. p53: 3+ (≥2/3) (abnormal)
. PAX-8: Positive
. WT-1: Positive





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1.1 25-04-09 Lymph node, left supraclavicular, US guided core needle aspiration
ROS)) METASTATIC CARCINOMA, consistent with HIGH GRADE SEROUS CARCINOMA
1.2 s/p Paclitaxel - Carboplatin #1 ~ #3 (NAC) (25-05-11 ~ 25-07-01)

mRAH BSO ureterolysis (both) PCDS mass removal
total omentectomy morrison's pouch removal
splenectomy right diaphragm mass removal
right paracolic gutter mass removal
mesenteric LN removal (#1)
RO

```
< BRCA1 Gene Mutation Analysis Report >

= RESULT ============================================================
  Pathogenic Variant: Detected
  Identified Variant: NM_007294.4(BRCA1):c.1840A>T, p.(Lys614*), heterozygous

  (see INTERPRETATION, RECOMMENDATION and COMMENTS)
=====================================================================
```

```
Diagnosis (2020 WHO):
. HIGH-GRADE SEROUS CARCINOMA, grade 3, bilateral ovaries
. Status post neoadjuvant chemotherapy (NAC)

+ Greatest dimension: 4 cm (right ovary) and 3.5 cm (left ovary)
+ Lymphovascular space invasion: PRESENT (substantial)
+ Ovarian surface extension: Absent
+ Salpingeal extension: PRESENT (bilateral)
+ Uterine extension: PRESENT (serosa)

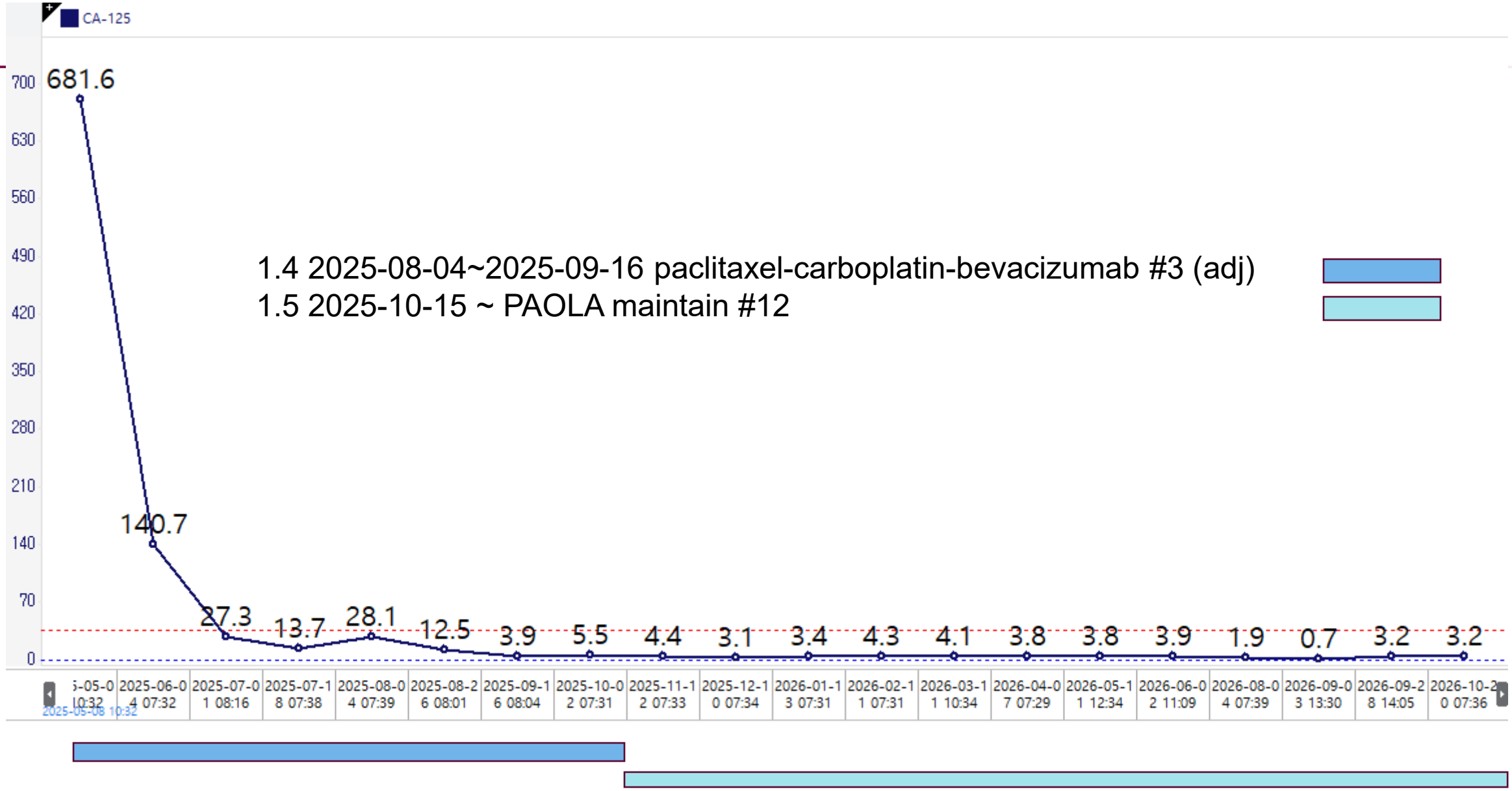
+ Lymph node metastasis: Absent (0/1)
- Mesenteric (0/1)

+ Pelvic peritoneal extension: PRESENT
+ Extrapelvic peritoneal extension: PRESENT
- Ligamentum teres: Absent
- Right paracolic gutter: Absent
- Morison pouch: Absent
- Right diaphragm mass: Absent
- PCDS mass: PRESENT
- Spleen: Absent
- Omentum: PRESENT

+ Chemotherapy regression score (CRS) after NAC:
- Omentum: CRS 3
- Right adnexa: CRS 2
- Left adnexa: CRS 2
```

FIGO stage IVB
NAC, R0
gBRCA1m

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1.4 2025-08-04~2025-09-16 paclitaxel-carboplatin-bevacizumab #3 (adj)

1.5 2025-10-15 ~ PAOLA maintain #12

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Summary

Maintenance treatment with olaparib + bevacizumab provided a **clinically meaningful PFS and OS** benefit **irrespective of clinical risk status**:

- Median PFS in HRD-positive patients was almost 4 years (46.8 months) in the olaparib plus bevacizumab arm vs 17.6 months in the control arm
- 38% reduction in the risk of death was observed with olaparib + bevacizumab vs bevacizumab alone (HR 0.62; 95% CI 0.45–0.85) in HRD positive patients.

No new safety signals were observed with longer-term follow-up.

- Incidence of MDS/AML and new primary malignancies remained low and balanced between arms.

In HRD positive patients, **PAOLA-1 based regimen** is **the only NCCN Category 1 recommendation**.

Anticipated reimbursement expansion could improve access to olaparib plus bevacizumab maintenance therapy for eligible patients.

1. Lorusso D, et al. Presented at ESMO Gynaecological Cancers Congress 2023. 23–24 February. Barcelona, Spain. 2. Lorusso D, et al. *Int J Gynecol Cancer.* 2024;34:550–558
3.Ray-Coquard I, et al. Presented at ESMO Congress 2022. 9–13 September. Paris, France.

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