Aktuelles vom ESMO und ASCO 2022

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ESGO Centre of Excellence in Endometrial Cancer Surgery

Europäisches Zentrum für Eierstockkrebs

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Ovarian Cancer has the highest mortality rate amongst gynecological cancer

7th

-most common gyn. Cancer wordlwide[1]

4th

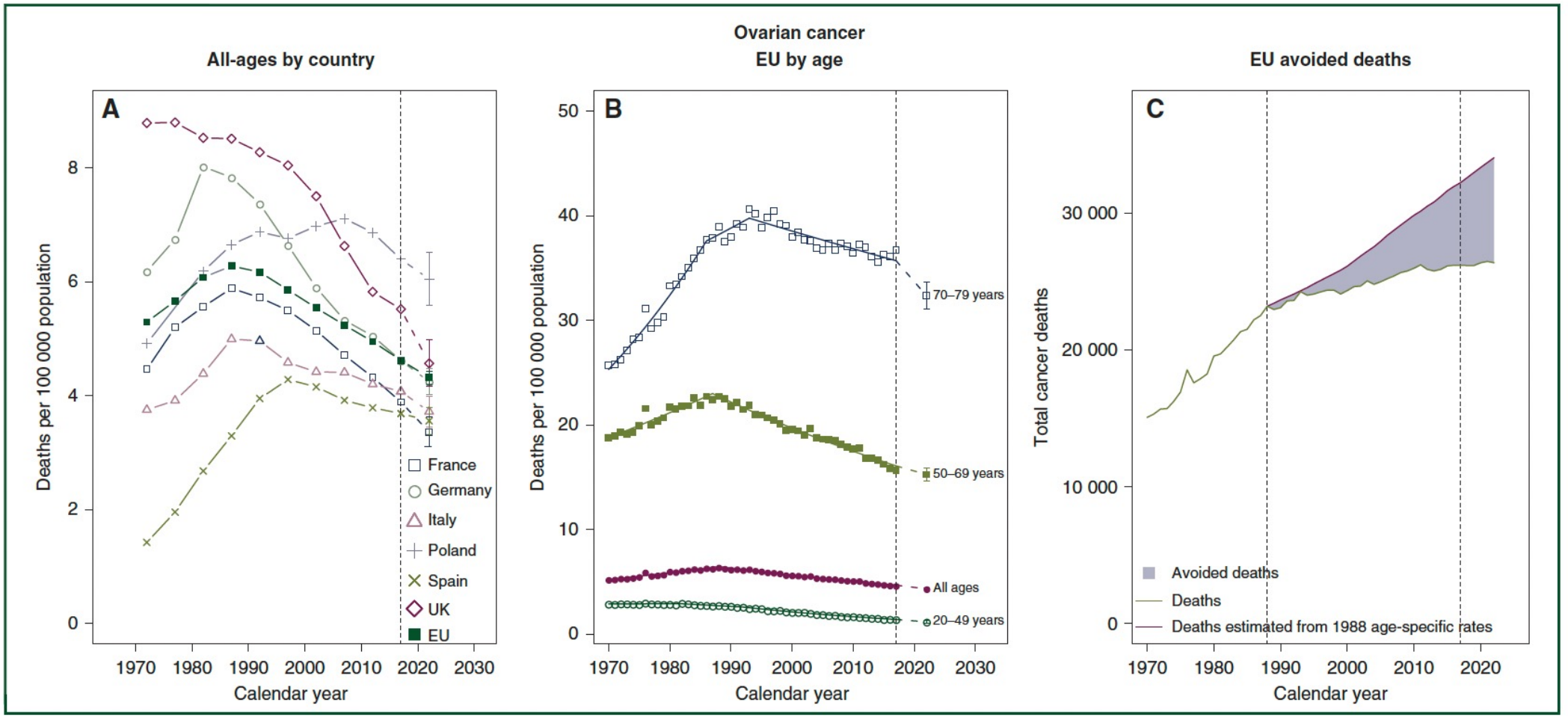
-most common cancer in women after breast and cervical cancer

5–11 /100.000

Incidencerate[1]

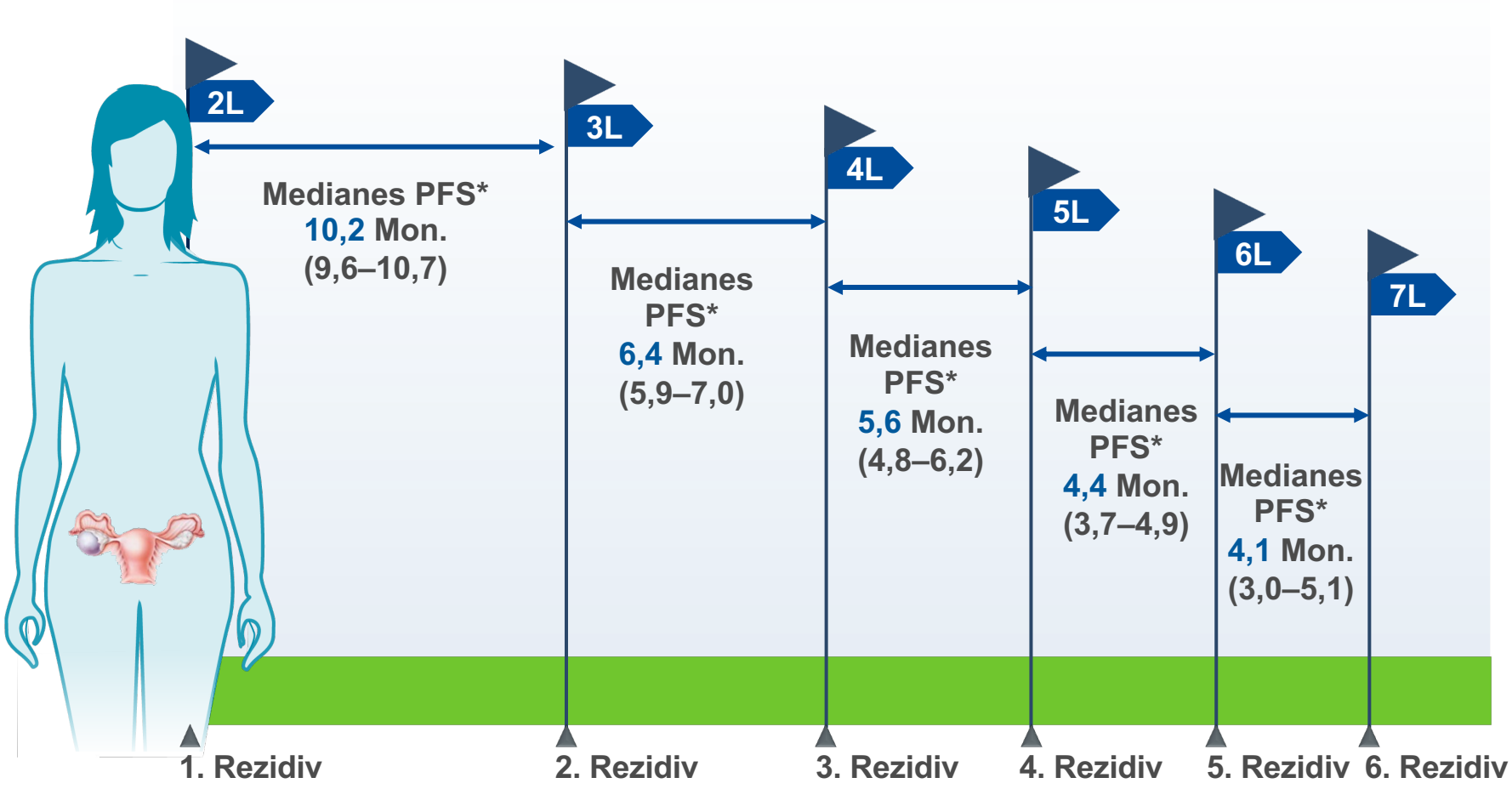
	New diagnosed 2013	Deaths 2013	
Breast	71.640	17.853	~ 25%
Endometrial	10.870	2.579	~ 24%
Ovar	**7.320**	**5.466**	**~ 75%**
Cervical	4.640	1.550	~ 33%
Sum	94.470	27.448	~ 29%
All Cancers	229.900	101.775	~ 44%

1. WCRF: Worldwide data. https://www.wcrf.org/dietandcancer/ovarian-cancer . Accessed 5 October 2018.
2. World Health Organization. Cancer Today. http://gco.iarc.fr/today/online-analysis table?v=2018&mode=cancer&mode_population=continents&population=900&populations=900&key=asr&sex=2&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=5&group_ Accessed 5 October 2018



- Slight decrease in the incidence of ovarian cancer
- Also a general tendency observed in the EU and UK (interestingly more men and less woman with cancer in the UK)
- Possible reasons: treatment improvements (surgery, chemotherapy, Bevacizumab, PARP), HRT (widespread in Germany)

Bei ca. 80% der Patientinnen mit fortgeschrittenem Ovarialkarzinom tritt nach Erstlinien-Therapie ein Rezidiv auf



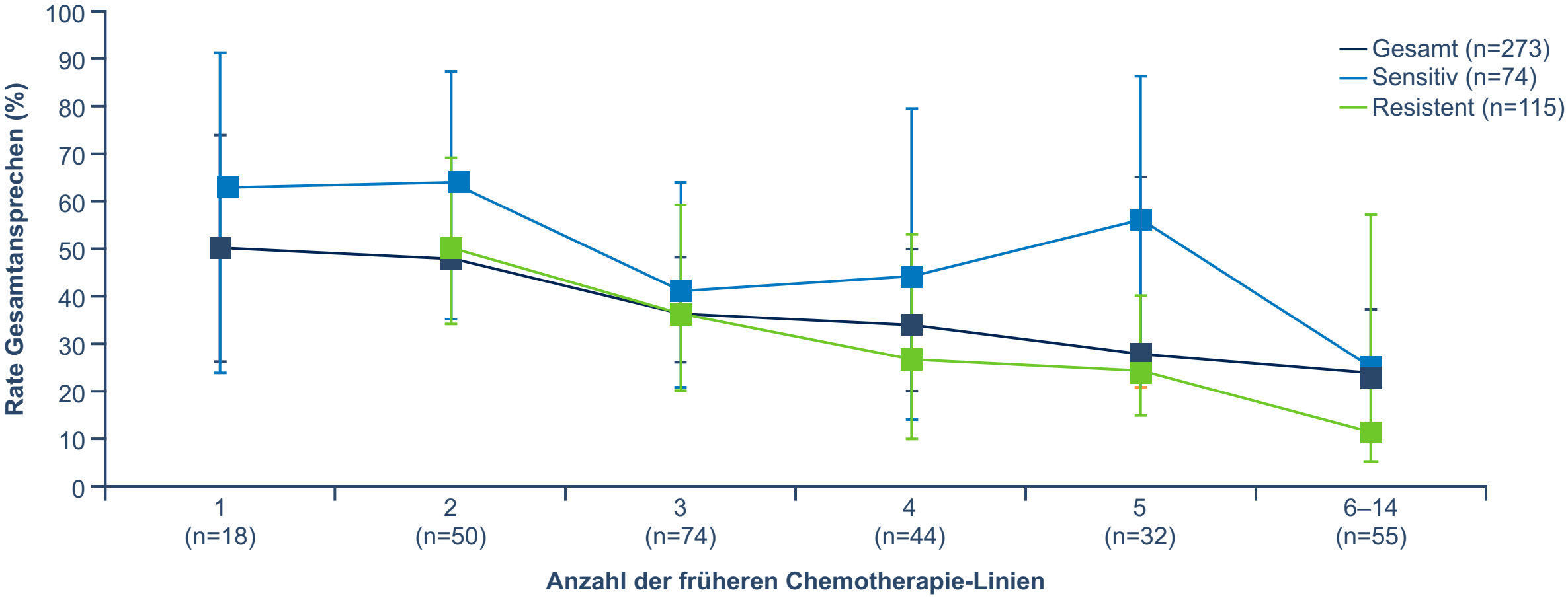
Das progressionsfreie Überleben (PFS) verkürzt sich mit jeder nachfolgenden Therapie-Linie

*** PFS wurde berechnet vom Start der Chemotherapie bis zur Krankheitsprogression.**

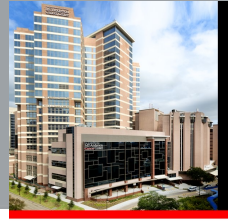
PFS=progressionsfreies Überleben; L= Therapielinie.

Hanker LC et al. *Ann Onc.* 2012;23(10):2605-2612.

Bei jedem weiteren Rezidiv veringert sich das Therapieansprechen



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



Normal Risk Ovarian Screening Study (NROSS): 21-Year Update

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Making Cancer History®

Abstract No. 5522

Abstract

PURPOSE The Normal Risk Ovarian Screening Study (NROSS) tested a two-stage screening strategy in post-menopausal women at conventional hereditary risk where significantly rising CA125 prompted transvaginal sonography (TVS) and abnormal TVS prompted surgery to detect ovarian cancer.

METHODS A total of 7,856 healthy postmenopausal women were screened annually for a total of 50,596 women-years in a single arm study (NCT00539162). Serum CA125 was analyzed with the Risk of Ovarian Cancer Algorithm (ROCA) each year. If risk was normal (<1:2000), women returned in a year. If risk was elevated (>1:500), TVS was undertaken immediately and if risk was intermediate, CA125 was repeated in 3 months, risk recalculated, and the participant re-triaged. An average of 2% of participants were referred to TVS annually.

RESULTS Thirty-four patients were referred for operations detecting 15 ovarian cancers and 2 borderline tumors with 12 in early stage (I-II). In addition, 7 endometrial cancers were detected with 6 in early stage. Thus, the positive predictive value (PPV) of the NROSS trial was 50% (17/34) for detecting ovarian cancer and 74% (25/34) for any cancer, far exceeding the minimum acceptable study endpoint of 10% PPV. As 4 ovarian cancers and 2 borderline tumors were diagnosed within a year of each participant's last normal risk, the sensitivity for detecting ovarian and borderline cancer was 74% (17/23) and 70% of ROCA-detected cases (12/17) were in stage I-II. NROSS screening reduced incidence of late stage (III-IV) disease by 34% compared to the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) control arm and by 30% compared to US SEER values. Results of our NROSS trial contrast dramatically with those of the recently reported UKCTOCS that showed only a modest 14% early-stage shift, underlying a lack of reduction in mortality. Across multiple randomized trials of mammography, those trials that demonstrated at least a 20% late-stage incidence reduction had a significant mortality reduction, whereas those with less of a stage shift did not.

CONCLUSION An elevated ROCA, characterized by a significantly rising CA125, prompted referral of 2% of participants to TVS each year and required only 2 operations to detect each case of ovarian cancer, indicating that CA125 used in this way is adequately specific for effective screening. While the NROSS trial was not powered to detect reduced mortality, the high specificity, PPV and marked stage shift support further development of this strategy.

Rationale of Ovarian Cancer Screening

- Ovarian cancer limited to the ovaries (Stage I) can be cured up to **90%** of cases, and when disease has spread to the pelvis (Stage II), 5-year survival can exceed **70%**, but most **(70-75%)** ovarian cancer are diagnosed in late stage (III-IV).
- Computer simulation indicates that mortality could be reduced by **10-30%** if ovarian cancer were diagnosed at an earlier stage (I/II) and stage shift affected mortality.

Requirement of Ovarian Cancer Screening

- In postmenopausal women in the United States, the prevalence of ovarian cancer is only **1 in 2,500** and to achieve PPV of 10%, minimum requirements are
- Sensitivity ≥ 75% for asymptomatic disease
- Specificity: 99.6%

Two Stage Screening

Fig 1. CA125 rises in ovarian cancer, but not benign disease (3 women with ovarian cancer & 3 women with benign disease)

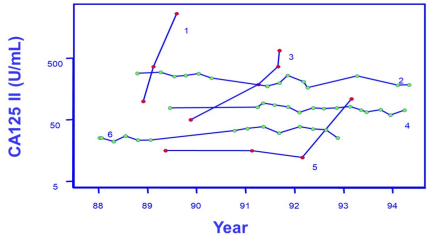
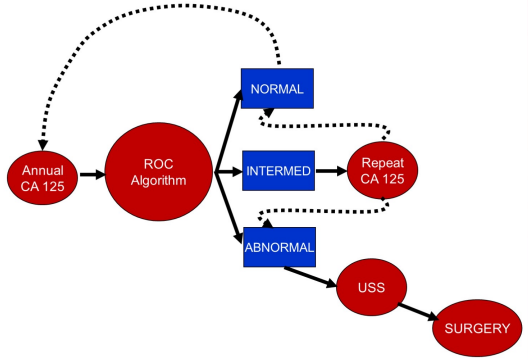


Fig 2. Two stage screening strategy using the Bayesian Risk of Ovarian Cancer Algorithm (ROCA)



ROCA calculates risk of ovarian cancer based on rising CA125
- Participants were triaged into:

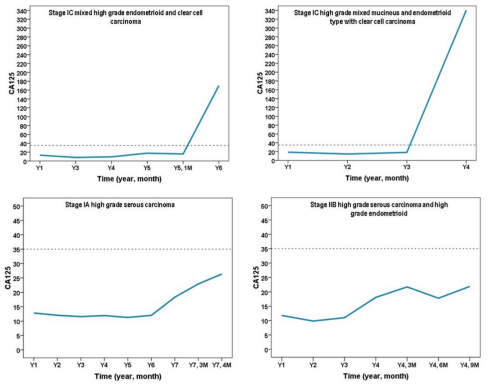
-normal risk **(< 1/2,000)** – to return in one year for a CA125
-intermediate (**1/2,000 ≤ risk ≤1/500)** - to repeat CA125 in three months
-high-risk (**> 1/500)** – to perform TVS and be referred to a gynecologic oncologist for possible surgery based on an abnormal TVS

Results

- Over the last **21** years, **7,856** postmenopausal women at conventional risk were screened annually to provide **50,596** woman years of screening.
- Only **2%** of participants were referred to TVS each year.
- Only **2** operations were performed to detect each case of ovarian cancer.
- **34** Operations were prompted by the algorithm to detect **17** cases of ovarian cancer – 2 borderline and 15 invasive high grade - with **12 (70%)** in Stage I or II.
- **Six** ovarian cancers were not detected, so the sensitivity for detecting ovarian and borderline cancer was **74% (17/23).**
- **7** endometrial cancers were also detected with **6** in early stage.
- PPV was **50%** for detecting ovarian cancer **(17/34)** and **74%** for any cancer **(25/34)**, far exceeding the minimum acceptable study endpoint of **10%** PPV.
- NROSS screening reduced late stage (III-IV) disease by **34%** compared to UKCTOCS controls **(76%)** and by **30%** compared to US SEER values **(60%)**.

Fig 3. CA125 values over time prior to operations prompted by the ROCA. a) Early-Stage Cases (*Gray dashed line indicates conventional CA125 cut off, 35U/mL)

a) Early Stage Cases



Discussion

Stage shift & Mortality
- In NROSS, stage I-II increased from **24% to 70%** relative to UKCTOCS control, an absolute difference of **46%.**
- In UKCTOCS, stage I-II disease increased from **24%** to **38%**, an absolute difference of only **14%.**
- The magnitude of the stage shift in the UKCTOCS may not have been sufficient to reduce mortality.
- In early trials of mammography for breast cancer, not all trials were positive and those showed mortality reduction had a stage shift of **>20%.**

Stage Shift in NROSS >> UKCTOCS
- The NROSS was a much smaller trial and outcomes could reflect statistical variation.
- Difficulties were encountered with TVS imaging in the UKCTOCS where in a retrospective review of **1,000** archived cases, ovaries and fallopian tubes could be identified in only **50%** of cases compared to **77%** in a report from Kentucky.
- In the NROSS, blood for CA125 was drawn in glass tubes without gel and serum was separated and frozen (-80° C) on the same day, whereas in the UKCTOCS blood was drawn in gel separation tubes, shipped at ambient temperature and separated and frozen after up to **56** hours.
- A modest systematic reduction in CA125 levels in the UKCTOCS could have decreased the ability to detect early-stage disease.

Conclusion

- Two stage screening with the ROCA and TVS is adequately specific for early detection of ovarian cancer with CA125.
- Sensitivity for early-stage disease is encouraging and could be further improved with multiple biomarkers.

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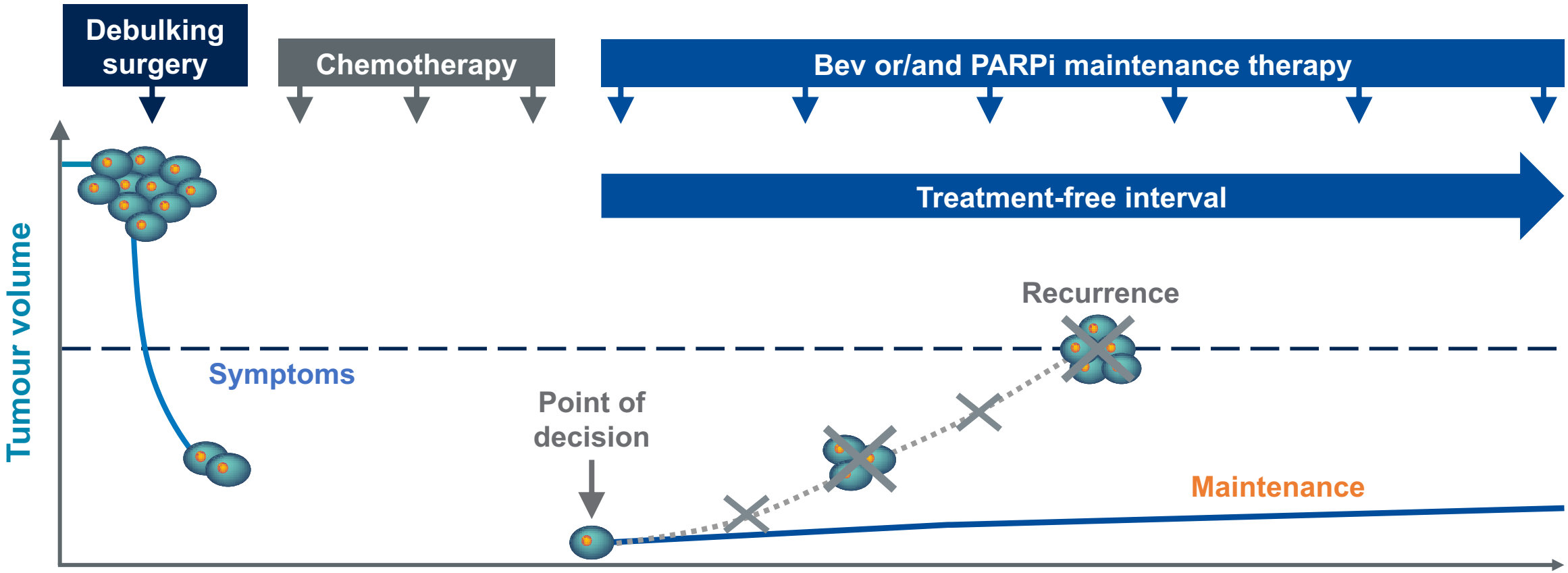
CHAR

A new era since the approval of PARPi in the first line setting



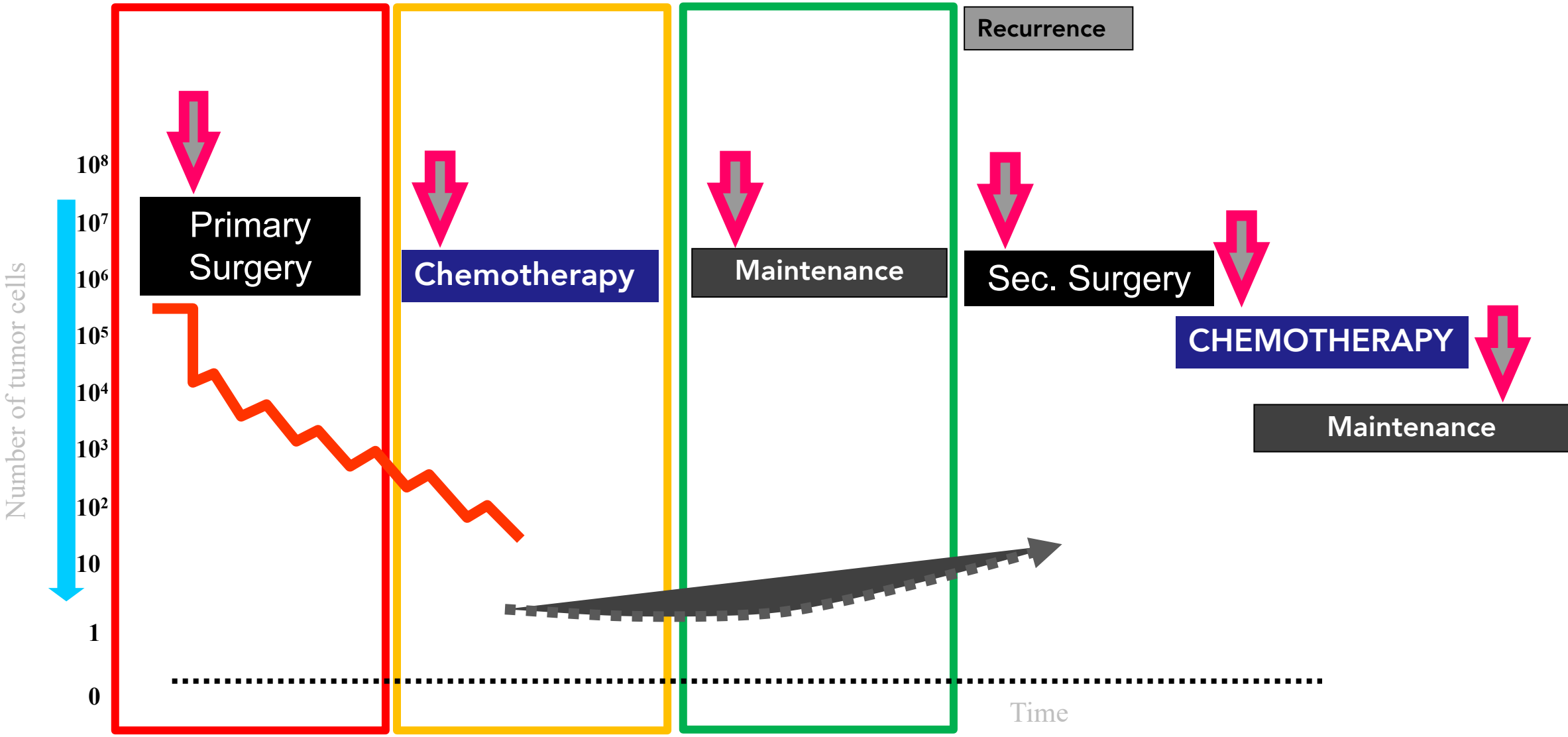
PARP, poly ADP ribose polymerase

Trials of PARP inhibitors in front line treatment of ovarian cancer

	SOLO1	PAOLA-1	PRIMA	PRIME	ATHENA	VELIA
Entry	BRCA mutation	All comers	All comers ('high risk')	All comers	All comers	All comers
Drug/Placebo	Olaparib	Bevacizumab + Olaparib	Niraparib	Niraparib	Rucaparib	Veliparib + Chemo followed by maintenance
Duration	24 months	15 months bevacizumab 24 months olaparib	36 months or to progression	36 months or to progression	24 months	24 months maintenance

Moore et al NEJM 2018; Ray-Coquard et al NEJM 2019; Gonzalez-Martin et al NEJM 2019; Li et al SGO 2022; Monk et al J Clin Oncol 2022; Coleman et al NEJM 2019

Treatment of Ovarian Cancer- “Three Pillar Model“ (Sehouli 2019)



STUDY DESIGN: SOLO1/GOG-3004

Primary and updated PFS analysis

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer
- *BRCA*m
- ECOG performance status 0-1
- Cytoreductive surgery*
- In clinical complete† response or partial response after platinum-based chemotherapy

Olaparib 300 mg bid (N=260)

2:1 randomization

Stratified by response to platinum-based chemotherapy

Placebo (N=131)

For up to **2 years** or until disease progression‡

Primary endpoint[1]

- Investigator-assessed PFS (modified RECIST 1.1)

Secondary endpoints

- OS
- TFST
- TSST
- Safety

Primary analysis[1] DCO: 17 May 2018	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	102 (39.2)	96 (73.3)
Median PFS, months	NR	13.8
3-year PFS rate, %	60.4	26.9
	HR 0.30 (95% CI 0.23-0.41)	
	P<0.001	

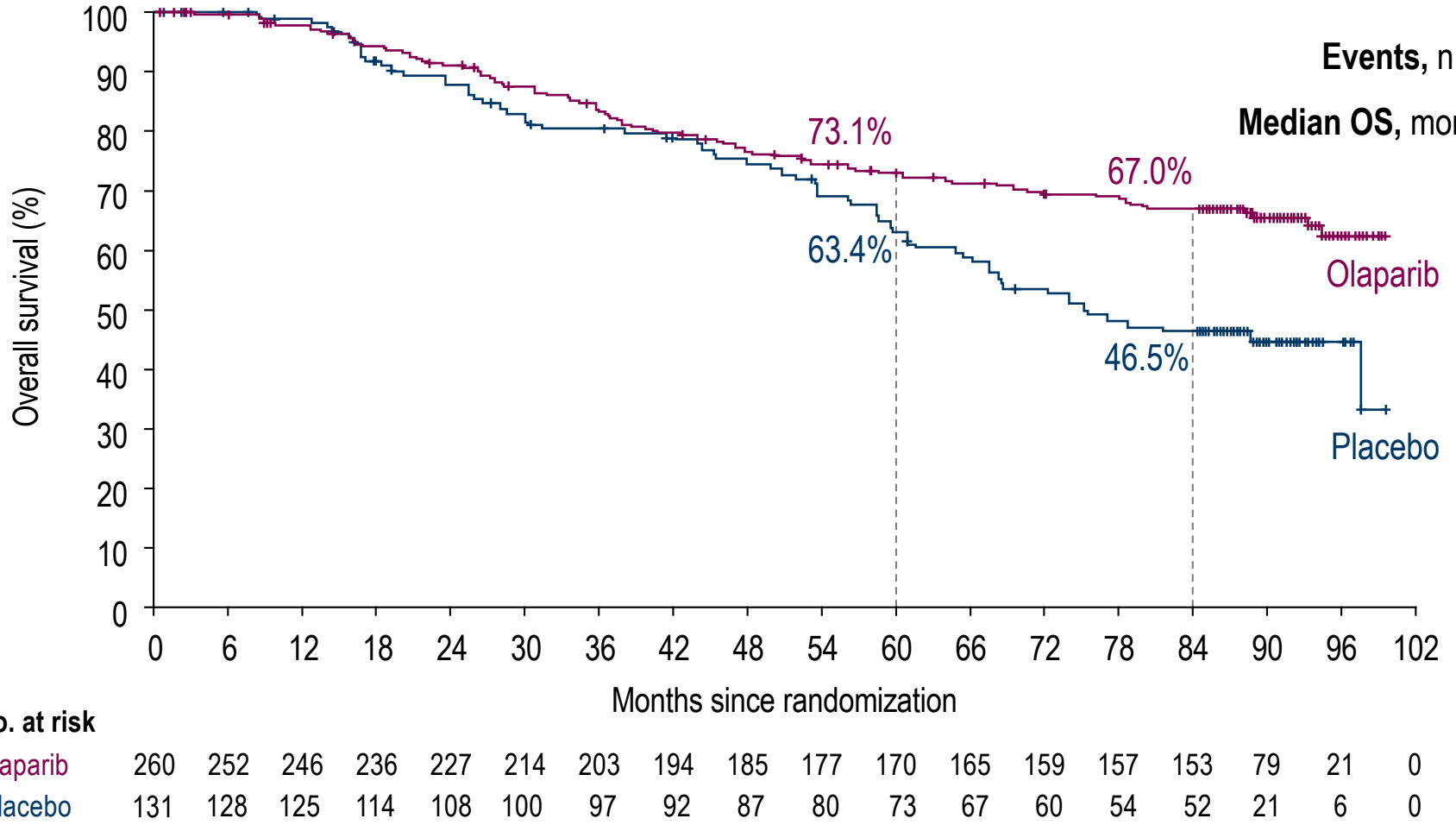
Updated analysis[2] DCO: 5 Mar 2020	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45.4)	100 (76.3)
Median PFS, months	56.0	13.8
5-year PFS rate, %	48.3	20.5
	HR 0.33 (95% CI 0.25-0.43)	

*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease; †Including patients with no evidence of disease; ‡Patients with evidence of disease at 2 years could continue to receive study treatment if, in the investigator's opinion, this was in the patient's best interest. [1]Moore K et al. N Engl J Med 2018;379:2495–505; [2]Banerjee S et al. Lancet Oncol 2021;22:1721–31.

bid, twice daily; ***BRCA*m**, *breast cancer antigen* mutation; **CI**, confidence interval; **DCO**, data cut-off; **ECOG**, Eastern Cooperative Oncology Group; **FIGO**, International Federation of Gynecology and Obstetrics; **HR**, hazard ratio; **NR**, not reached; **OS**, overall survival; **PFS**, progression-free survival; **RECIST v1.1,** Response Evaluation Criteria in Solid Tumors version 1.1; **TFST**, time to first subsequent therapy or death; **TSST**, time to second subsequent therapy or death.

Overall survival (OS) at 7-year (y) follow-up (f/u) in patients (pts) with newly diagnosed advanced ovarian cancer (OC) and a *BRCA* mutation (*BRCA*m) who received maintenance olaparib in the SOLO1/GOG-3004 trial
Paul DiSilvestro et al. ESMO 2022, Abstract 517O

Maintenance olaparib provided a clinically meaningful OS benefit in BRCAm pt. – SOLO1 Trial



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

*$P<0.0001$ required to declare statistical significance

PARIS 2022 ESMO congress

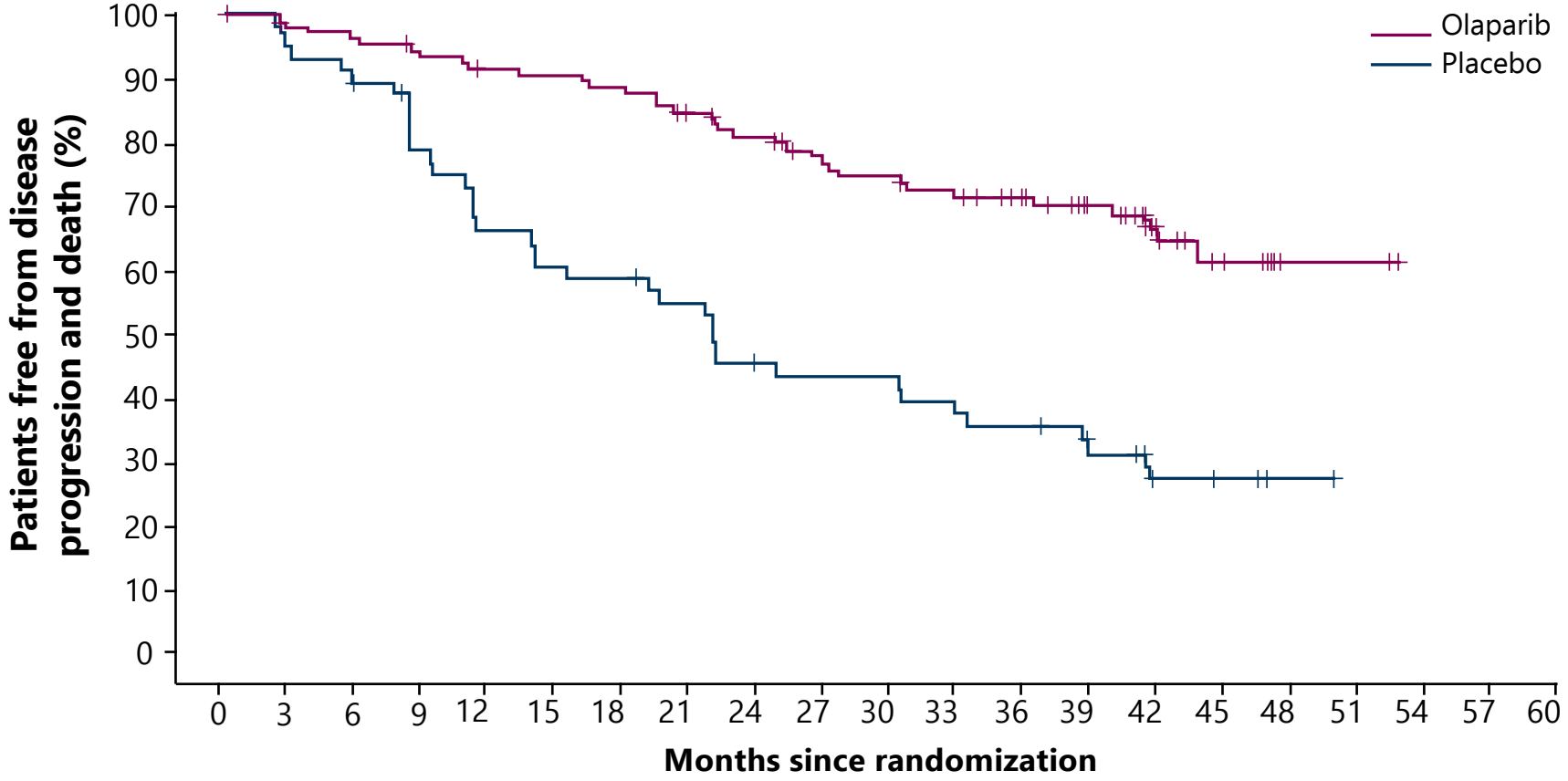
Final Results of the SOLO1 Trial presented by I. Ray-Couquard at ESMO 2022

Patient characteristics – SOLO1

	Olaparib (N=260)	Placebo (N=131)
FIGO stage, n (%)		
III	220 (84.6)	105 (80.2)
IV	40 (15.4)	26 (19.8)
BRCAm, n (%)		
BRCA1	191 (73.5)	91 (69.5)
BRCA2	66 (25.4)	40 (30.5)
Both *BRCA1* and *BRCA2*	3 (1.2)	0
History of cytoreductive surgery, n (%)		
Upfront surgery	**161 (61.9)**	**85 (64.9)**
Residual macroscopic disease	37 (23.0)	22 (25.9)
No residual macroscopic disease	123 (76.4)	62 (72.9)
Unknown	1 (0.6)	1 (1.2)
Interval cytoreductive surgery	**94 (36.2)**	**43 (32.8)**
Residual macroscopic disease	18 (19.1)	7 (16.3)
No residual macroscopic disease	76 (80.9)	36 (83.7)
No surgery	**4 (1.5)**	**3 (2.3)**
Response after surgery/platinum-based chemotherapy, n (%)		
Clinical complete response*	213 (81.9)	107 (81.7)
Clinical partial response	47 (18.1)	24 (18.3)

*Includes patients with no evidence of disease

Figure 3. Kaplan-Meier estimate of investigator-assessed PFS in stage III patients who underwent upfront surgery and had no residual disease



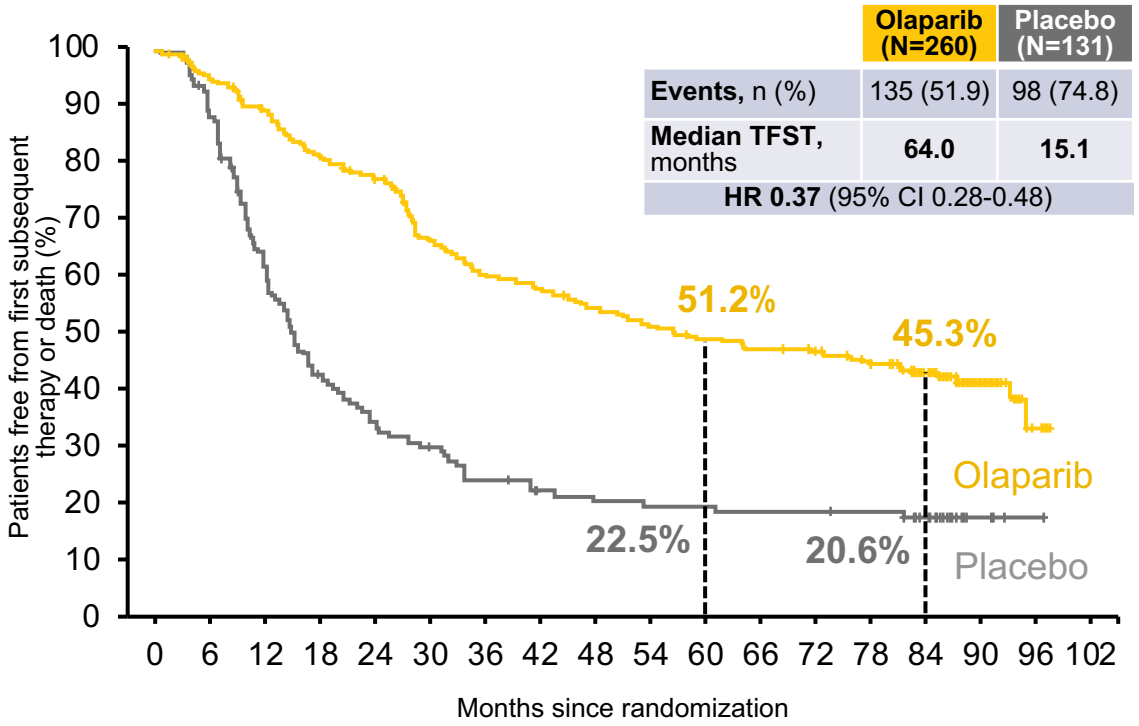
Num. patients at risk:

Olaparib	114	105	102	99	96	95	93	87	82	72	70	66	57	48	25	18	3	3	0	0	0
Placebo	58	53	50	43	36	33	32	29	23	22	22	19	18	13	4	3	1	0	0	0	0

FROM: Mathews C, SOLO 1 trial, ASCO 2019

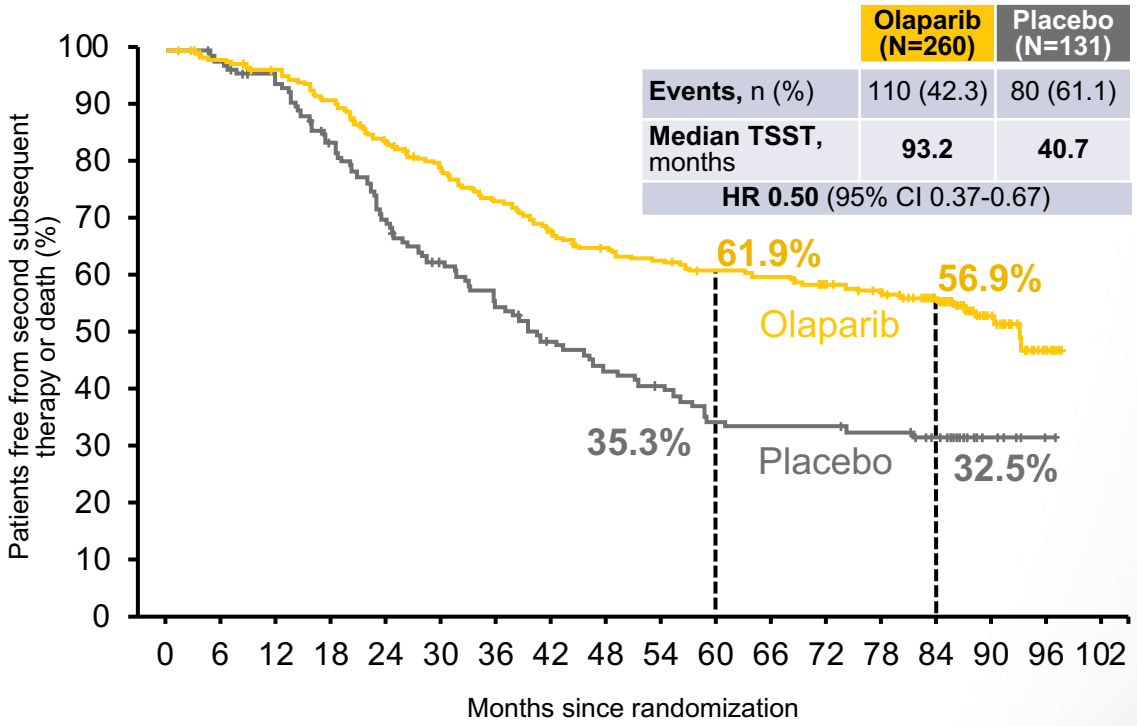
TFST AND TSST BENEFIT

TFST was substantially delayed by olaparib treatment



No. at risk																		
Olaparib	260	240	223	203	190	160	147	141	132	125	119	115	111	102	75	31	5	0
Placebo	131	114	79	55	45	39	32	28	26	25	25	24	24	23	18	4	1	0

TSST benefit extended beyond 1st subsequent therapy



No. at risk																		
Olaparib	260	248	240	227	206	188	175	162	153	148	142	140	132	125	95	41	8	0
Placebo	131	126	118	102	85	74	65	56	50	46	39	38	38	36	30	9	1	0

CI, confidence interval; **HR**, hazard ratio; **TFST**, time to first subsequent therapy or death; **TSST**, time to second subsequent therapy or death.

Overall survival (OS) at 7-year (y) follow-up (f/u) in patients (pts) with newly diagnosed advanced ovarian cancer (OC) and a BRCA mutation (BRCAm) who received maintenance olaparib in the SOLO1/GOG-3004 trial
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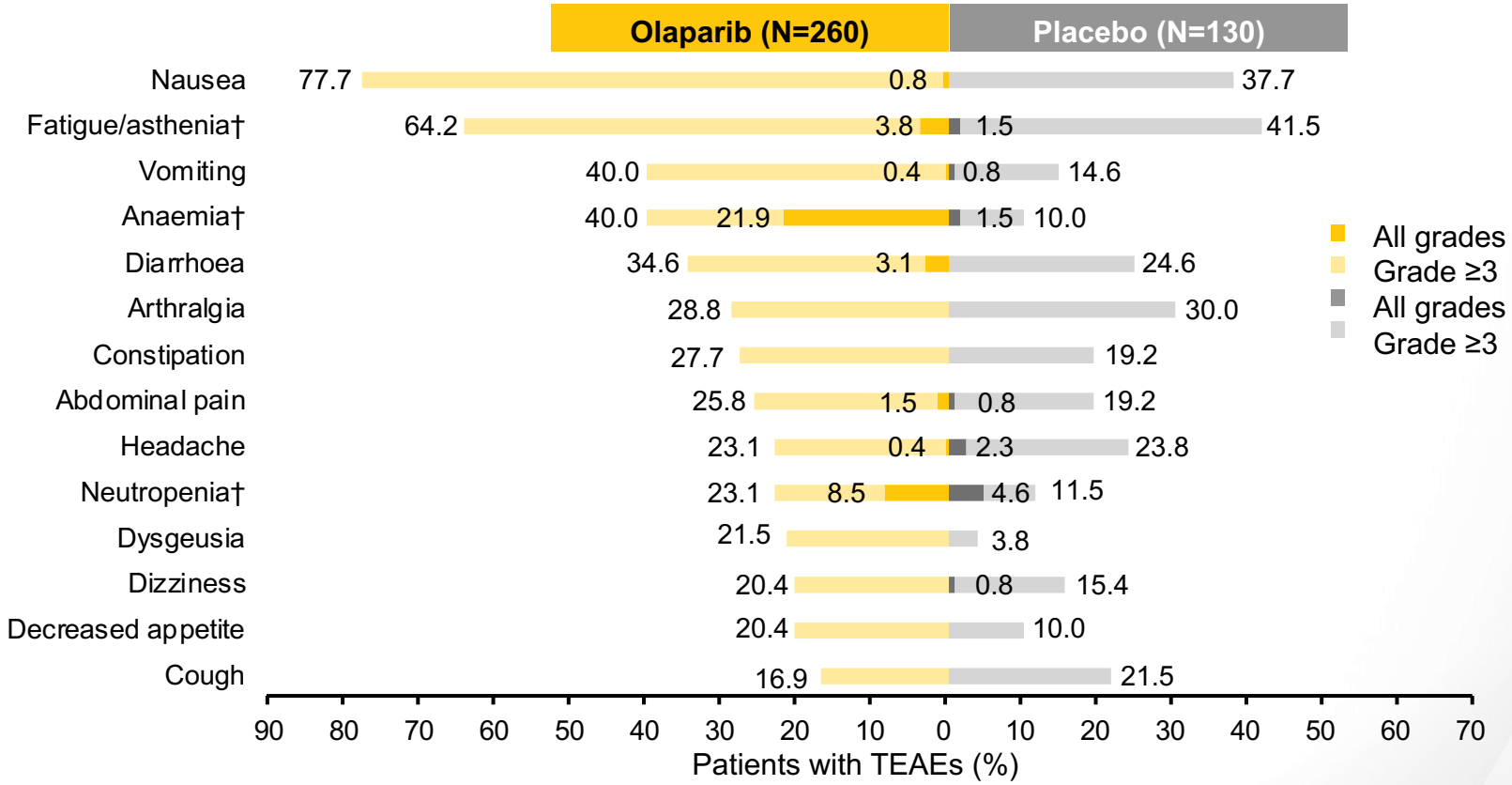
SAFETY

AEs of special interest

	7-year descriptive OS analysis (DCO 7 March 2022)	
	Olaparib (N=260)	Placebo (N=130)
AEs of special interest, n (%)		
MDS/AML[#]	4 (1.5)	1 (0.8)
New primary malignancies[#]	14 (5.4)[‡]	8 (6.2)[¶]
Pneumonitis/ILD	5 (1.9)	0

Most frequent treatment-emergent AEs*



[#]Proactively followed up until death due to any cause; [‡]Breast cancer (n=10), lip and/or oral cavity cancer (n=1), thyroid cancer (n=1), pancreatic adenocarcinoma (n=1) and gall bladder adenocarcinoma (n=1); [¶]Breast cancer (n=5), lung adenocarcinoma (n=1), squamous cell carcinoma of the tongue (n=1) and chronic myeloid leukemia (n=1); *All grades, frequency ≥20% in either treatment arm; †Grouped-term TEAEs. All-grade thrombocytopenia (grouped term) occurred in 11.2% of patients in the olaparib group and 3.8% of patients in the placebo group and grade ≥3 thrombocytopenia (grouped term) occurred in 0.8% and 1.5%, respectively.

AE, adverse event; **AML**, acute myeloid leukaemia; **DCO**, data cutoff; **ILD**, interstitial lung disease; **MDS**, myelodysplastic syndrome; **OS**, overall survival; **TEAE**, treatment-emergent adverse event.

Overall survival (OS) at 7-year (y) follow-up (f/u) in patients (pts) with newly diagnosed advanced ovarian cancer (OC) and a BRCA mutation (BRCAm) who received maintenance olaparib in the SOLO1/GOG-3004 trial **Paul DiSilvestro et al.** ESMO 2022, Abstract 517O

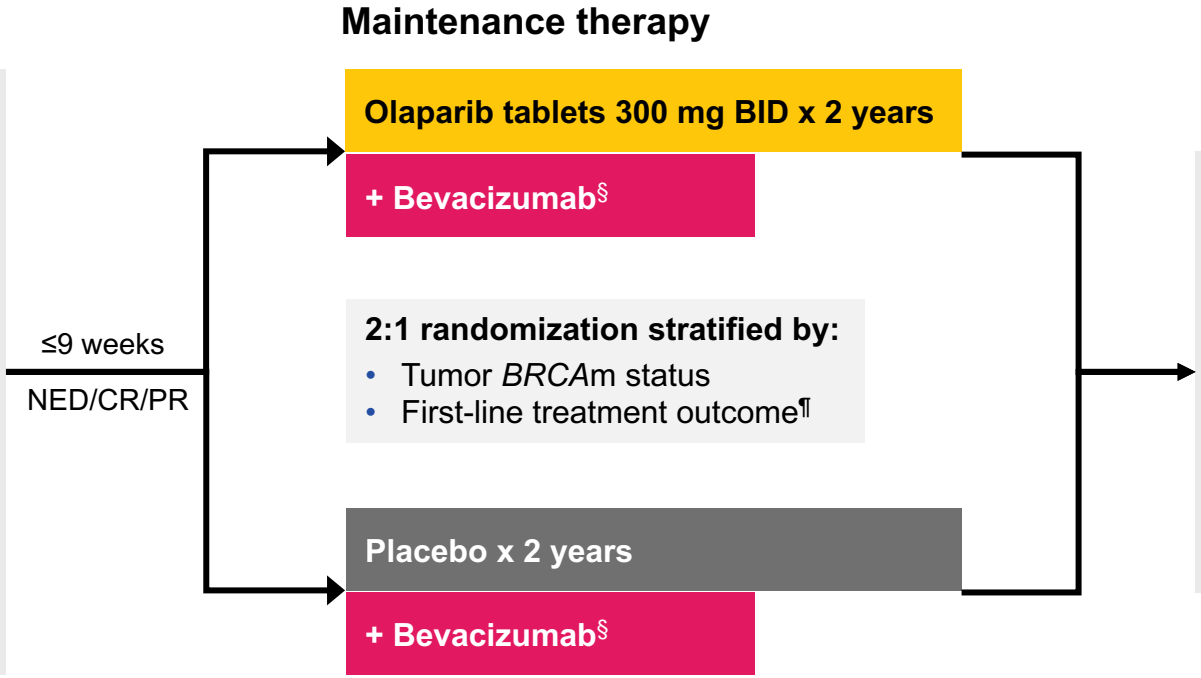
STUDY DESIGN: PAOLA-1/ENGOT-OV25

Patients:

- Newly diagnosed, FIGO stage III–IV high-grade serous or endometrioid ovarian, fallopian tube and/or primary peritoneal cancer*

First-line treatment:

- Upfront or interval surgery
- Platinum-taxane based chemotherapy plus ≥2 cycles of bevacizumab†‡



Primary endpoint:

- Investigator-assessed PFS (RECIST v1.1)

Key secondary endpoint:

- PFS2
- OS (planned for 3 years after the primary PFS analysis or 60% data maturity)

*Patients with other epithelial non-mucinous ovarian cancer were eligible if they had a gBRCAm; †Patients must have received ≥4 and ≤9 cycles of platinum-based chemotherapy; ‡Patients must have received ≥3 cycles of bevacizumab with the last 3 cycles of chemotherapy, apart from patients undergoing interval surgery who were permitted to receive only 2 cycles of bevacizumab with the last 3 cycles of chemotherapy; §Bevacizumab 15 mg/kg every 3 weeks for a total of 15 months, including when administered with chemotherapy; ¶According to timing of surgery and NED/CR/PR.

BID, twice daily; **CR,** complete response; **FIGO,** International Federation of Gynecology and Obstetrics; **g*BRCA*m,** germline *BRCA* mutation; **NED,** no evidence of disease; **OS,** overall survival; **PBC,** platinum-based chemotherapy; **PFS,** progression-free survival; **PFS2,** time from randomization to second progression or death; **PR,** partial response; **RECIST,** Response Evaluation Criteria in Solid Tumours.

Final overall survival (OS) results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)
Isabelle L. Ray-Coquard et al. ESMO 2022, Abstract LBA29

PATIENT CHARACTERISTICS

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

CR, complete response; **FIGO,** International Federation of Gynecology and Obstetrics; **HRD,** homologous recombination deficiency; **NED,** no evidence of disease; **PR,** partial response; **t*BRCA*m,** tumour *BRCA* mutation.

**BRCA*m status by central labs and HRD status by Myriad myChoice HRD Plus; patients in t*BRCA*m and HRD positive excluding t*BRCA*m subgroups do not equal the total number of patients in the HRD-positive subgroup because of different testing methods.

Final overall survival (OS) results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)
Isabelle L. Ray-Coquard et al. ESMO 2022, Abstract LBA29

PATIENT DISPOSITION AT FINAL DCO

	Olaparib + bevacizumab (N=537)	Placebo + bevacizumab (N=269)
Randomized, n	537	269
Treated, n (%)	535	267
Patients who withdrew from study, n (%)		
Total	537 (100)	269 (100)
Patient lost to follow-up	6 (1)	0 (0)
Death	286 (53)	158 (59)
Consent withdraw	15 (3)	6 (2)
Study completed	230 (43)	105 (39)
Median duration of treatment,* months		
Olaparib/placebo	17.3	15.6
Bevacizumab	11.0	10.6
Median duration of follow-up for OS, months (IQR)	61.7 (57.5-67.0)	61.9 (58.1-66.8)

*Median duration of treatment with bevacizumab since randomization.

DCO, data cut-off; **IQR**, interquartile range; **OS,** overall survival.

Final overall survival (OS) results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)
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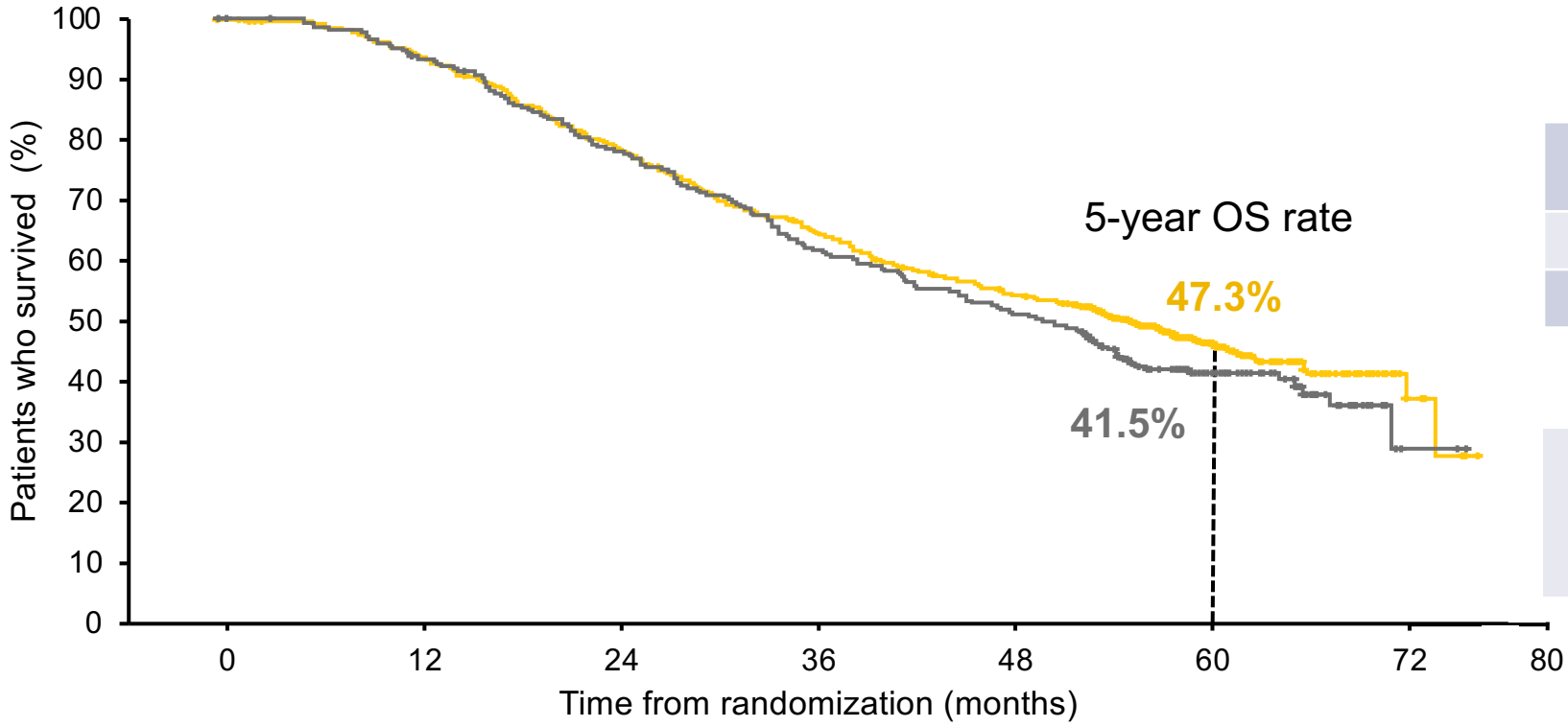
OS ANALYSIS

ITT population



	Olaparib + bevacizumab (N=537)	Placebo + bevacizumab (N=269)
Events, n (%) [55% maturity]	288 (53.6)	158 (58.7)
Median OS, months	**56.5**	**51.6**
5-year OS rate, %	**47.3**	**41.5**
	HR 0.92 (95% CI 0.76–1.12); **P=0.4118**	

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

No. at risk																										
Olaparib + bev	537	530	528	517	503	480	463	440	420	398	376	357	347	329	308	295	286	276	262	217	169	113	82	40	19	4	0
Placebo + bev	269	267	264	261	250	242	229	220	208	199	188	179	166	160	154	146	139	132	121	96	76	51	37	20	5	2	0

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

CI, confidence interval; **HR,** hazard ratio; **ITT,** intent-to-treat; **OS,** overall survival; **PARP,** poly(ADP-ribose) polymerase.

Final overall survival (OS) results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)
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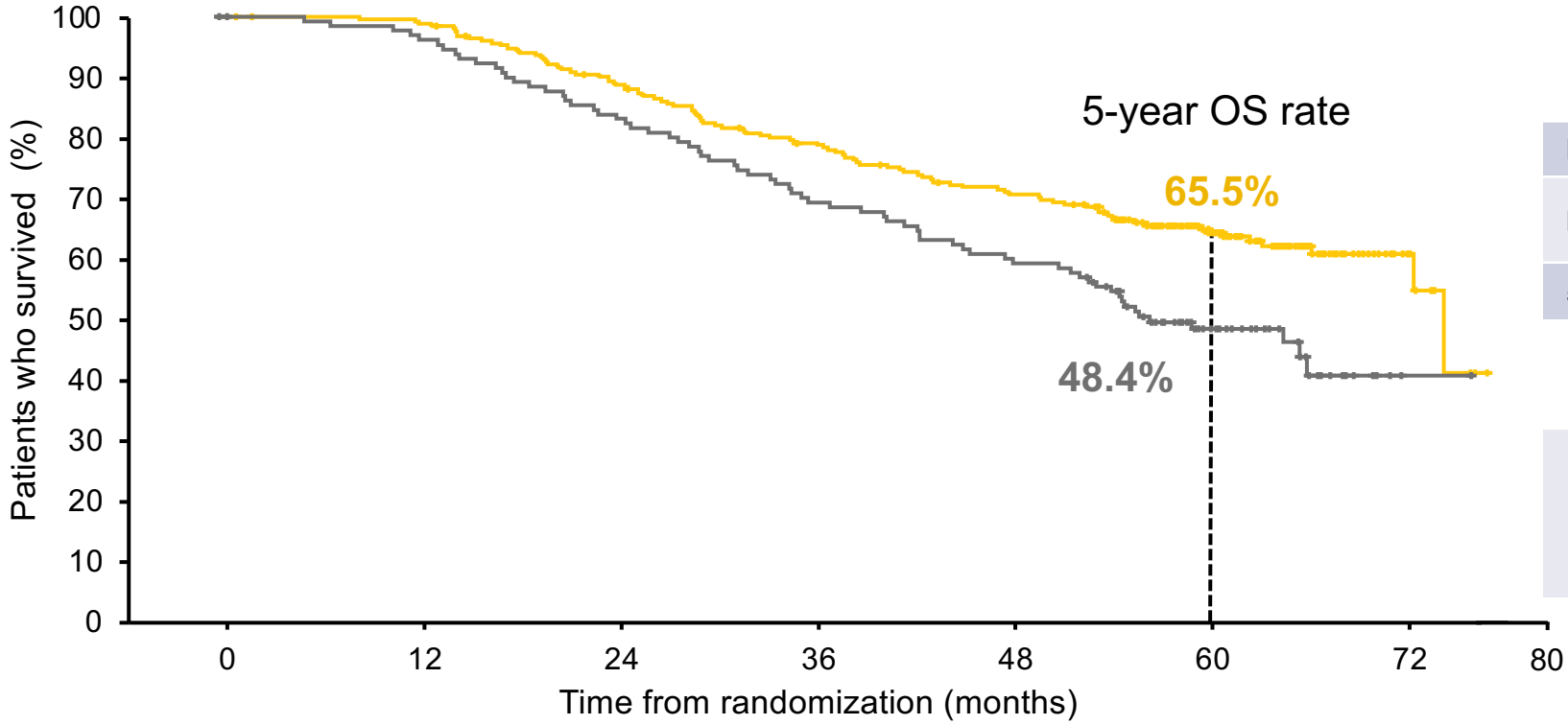
OS ANALYSIS

OS was prolonged in the HRD-positive subgroup



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	93 (36.5)	69 (52.3)
Median OS, months	**75.2** (unstable)*	**57.3**
5-year OS rate, %	**65.5**	**48.4**
	HR 0.62 (95% CI 0.45–0.85)	

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

No. at risk																										
Olaparib + bev	255	253	253	252	252	244	238	231	225	215	205	200	195	189	183	176	174	170	164	142	116	83	62	32	17	4	0
Placebo + bev	132	130	129	128	126	121	117	114	109	105	100	96	91	89	86	82	79	77	70	59	44	29	21	9	2	1	0

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

*Median unstable; <50% data maturity. HRD positive defined as a t*BRCA*m and/or genomic instability score of ≥42 on the Myriad myChoice HRD Plus assay.
CI, confidence interval; **HR,** hazard ratio; **HRD,** homologous recombination deficient; **OS,** overall survival; **PARP,** poly(ADP-ribose) polymerase; **t*BRCA*m,** tumour *BRCA* mutation.

Final overall survival (OS) results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)
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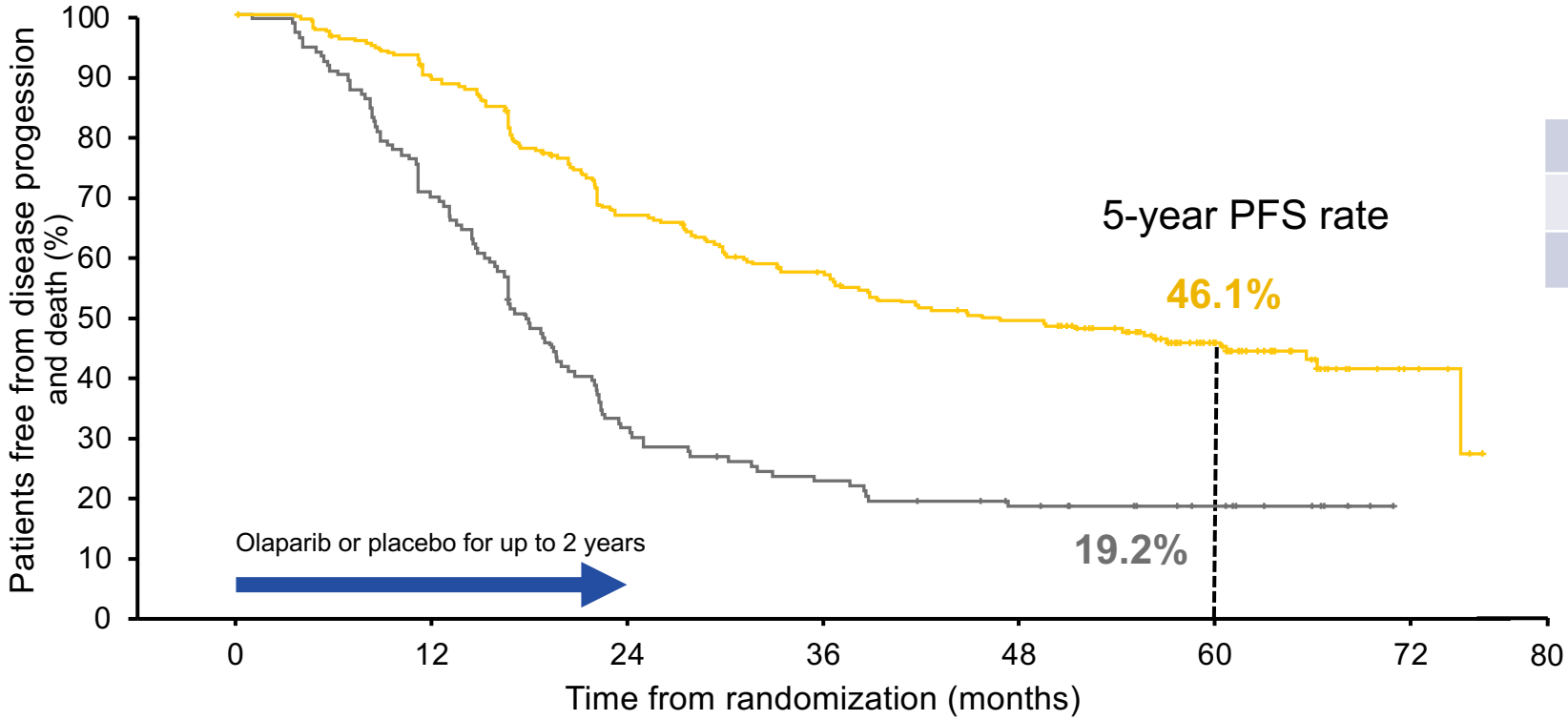
UPDATED PFS

HRD-positive population*



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	136 (53.3)	104 (78.8)
Median OS, months	**46.8**	**17.6**
5-year OS rate, %	**46.1**	**19.2**
	HR 0.41 (95% CI 0.32–0.54)	

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

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

*Descriptive analysis; PFS by investigator-assessment (modified RECIST v1.1).
CI, confidence interval; **HR,** hazard ratio; **HRD,** homologous recombination deficient; **OS,** overall survival, **PFS,** progression-free survival; **RECIST**, Response Evaluation Criteria in Solid Tumours.

Final overall survival (OS) results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)
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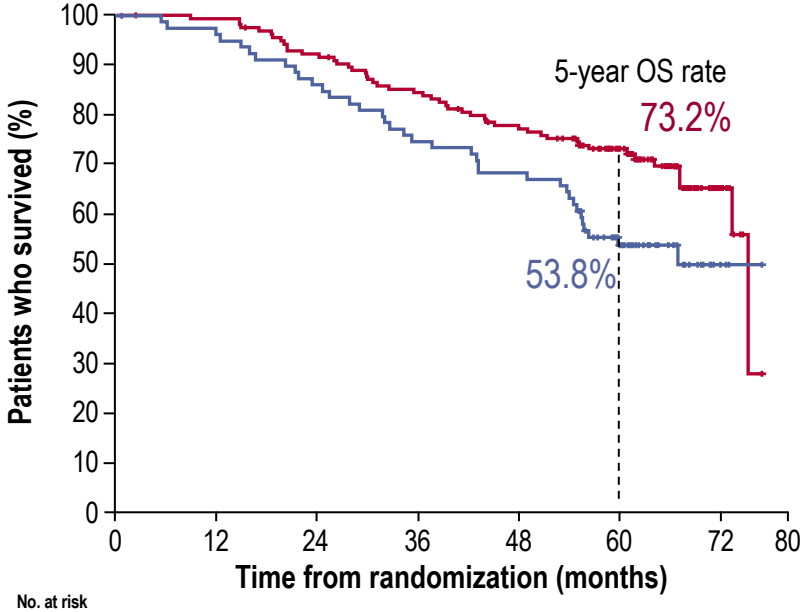
OS by BRCAm and HRD status in the PAOLA Trial

BRCAm*

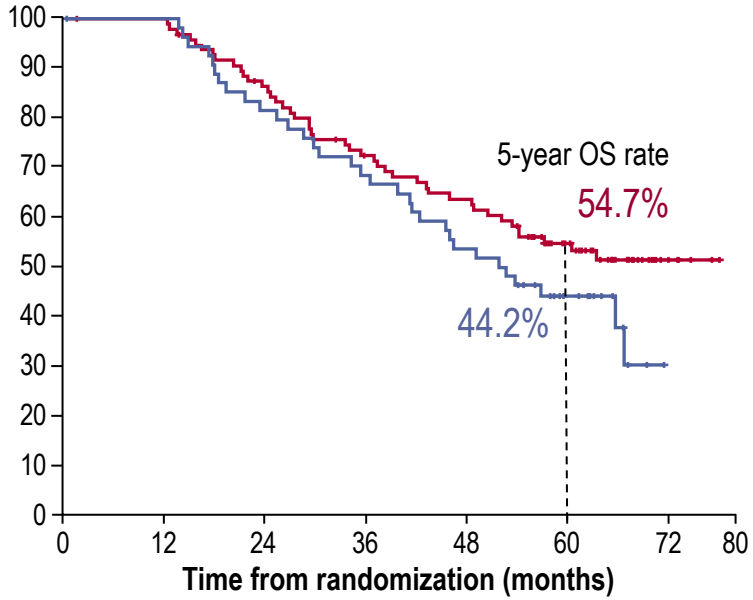


No. at risk

Olaparib + bevacizumab	157	156	156	155	155	152	150	144	143	139	134	131	130	127	123	118	117	115	112	99	80	55	42	21	11	2	0
Placebo + bevacizumab	80	79	78	77	76	74	72	71	68	66	64	61	59	58	58	54	54	53	50	40	33	22	17	10	3	1	0

	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**
PARPi as subsequent treatment, n (%)	38 (24.2)	44 (55.0)
	HR 0.60 (95% CI 0.39–0.93)	

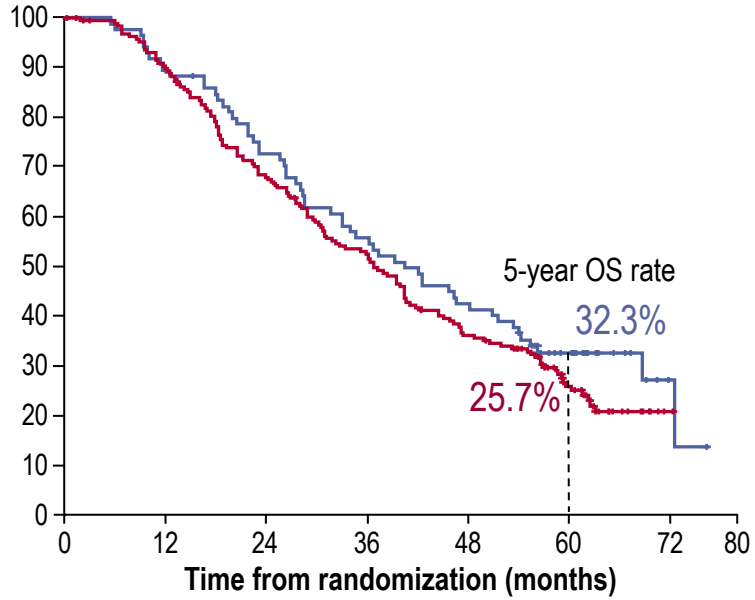
HRD positive‡ excluding BRCAm



	97	96	96	96	96	91	87	86	81	76	71	70	66	63	61	59	58	55	52	45	37	29	22	12	5	2	0
	55	54	54	54	54	51	48	46	44	42	40	39	37	36	33	32	29	28	24	21	15	9	6	2	0		

	Olaparib + bevacizumab (N=97)	Placebo + bevacizumab (N=55)
	44 (45.4)	32 (58.2)
	NR	52.0
	54.7	**44.2**
	9 (9.3)	23 (41.8)
	HR 0.71 (95% CI 0.45–1.13)	

HRD negative†



	192	187	186	179	169	157	146	135	126	119	109	100	97	89	77	72	66	62	57	43	30	16	11	5	1	0	
	85	85	84	83	76	74	71	65	60	56	51	48	46	43	41	38	35	33	31	21	17	11	8	5	2	1	0

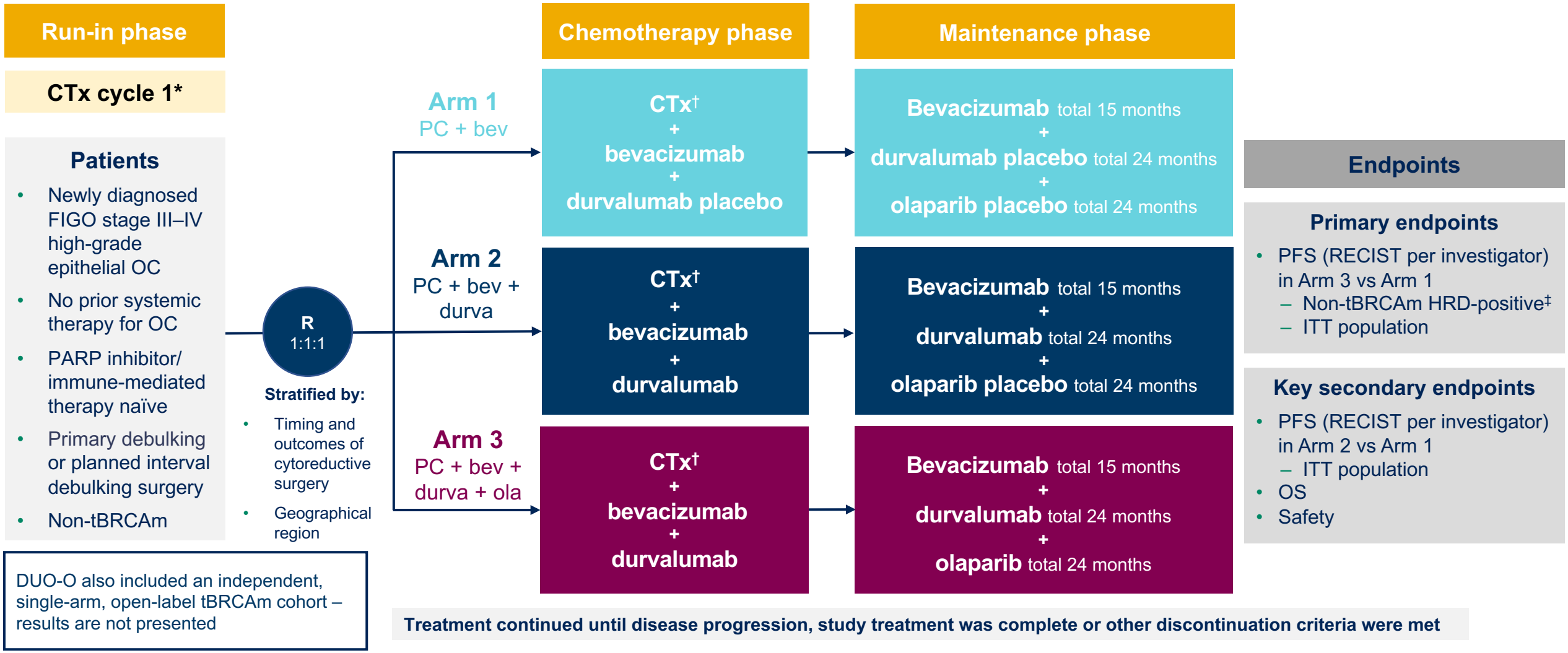
	Olaparib + bevacizumab (N=192)	Placebo + bevacizumab (N=85)
	140 (72.9)	58 (68.2)
	36.8	40.4
	25.7	**32.3**
	46 (24.0)	34 (40.0)
	HR 1.19 (95% CI 0.88–1.63)	

*By central labs; †Unstable median; <50% data maturity; ‡By Myriad myChoice HRD Plus. NR, not reported.

Implications of First-line PARP inhibitor studies

- Recommended that all patients with high grade ovarian cancers are tested for gBRCA mutations
- In some countries/centres, patients are first tested for tBRCA mutations
- PARP inhibitors (alone or olaparib/bevacizumab) should be offered to all patients with BRCA mutated ovarian tumours in response to platinum-based therapy
- It seems plausible that a proportion of patients are cured with PARP inhibitors, but recurrence remains a problem for many, and requires a deeper understanding of the mechanisms of PARPi resistance

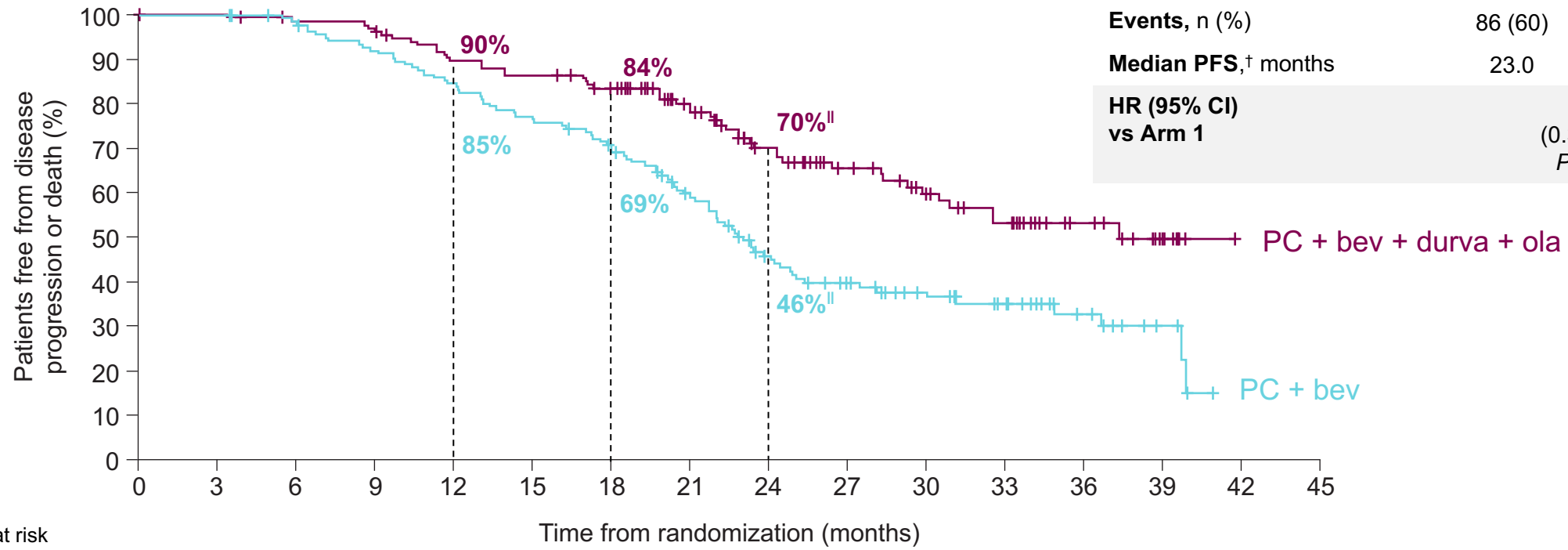
DUO-O study design



Dosing and schedule: bevacizumab (15 mg/kg IV q3w); durvalumab (1120 mg IV q3w); olaparib (300 mg po bid); chemotherapy: paclitaxel 175 mg/m^2 IV q3w and carboplatin at AUC5 or AUC6 IV q3w. PFS interim analysis DCO: December 5, 2022.
*With or without bevacizumab according to local practice; †Cycles 2–6; ‡Genomic instability score ≥42 assessed prospectively by Myriad MyChoice CDx assay.
AUC, area under the curve; bev, bevacizumab; bid, twice daily; CTx, chemotherapy; DCO, data cutoff; durva, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; ITT, intent-to-treat; IV, intravenous; ola, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; po, by mouth; q3w, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumors.

PFS: HRD-positive subgroup
Arm 3 vs Arm 1

	Arm 1 PC + bev N=143	Arm 3 PC + bev + durva + ola N=140
Median follow-up,* months	28.8	25.6
Events, n (%)	86 (60)	49 (35)
Median PFS,† months	23.0	37.3‡
HR (95% CI) vs Arm 1	**0.49** (0.34–0.69)§ *P*<0.0001	



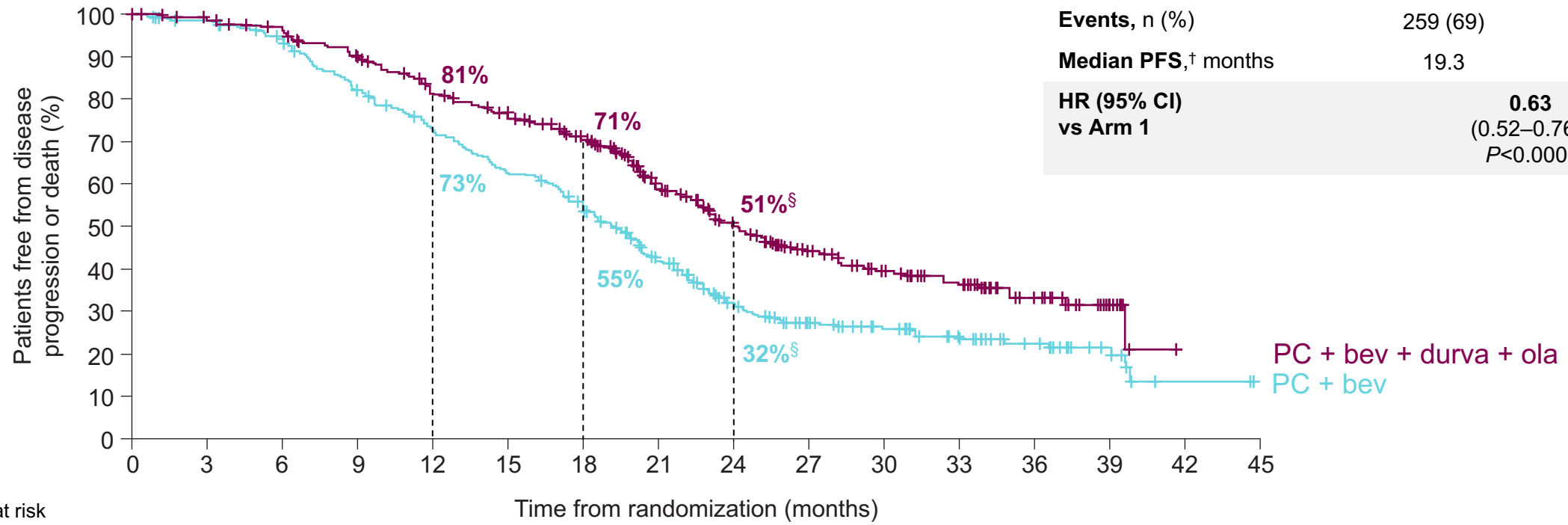
Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

*In censored patients; †Medians and rates were estimated by KM method; ‡Median PFS in Arm 3 unstable; §HR and CI were estimated from a stratified Cox proportional hazards model. *P* value from a stratified log rank text. Model stratified by timing and outcome of cytoreductive surgery; ‖24-month PFS rates unstable.
CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier.

PFS: ITT population
Arm 3 vs Arm 1

	Arm 1 PC + bev N=378	Arm 3 PC + bev + durva + ola N=378
Median follow-up,* months	25.5	23.3
Events, n (%)	259 (69)	193 (51)
Median PFS,† months	19.3	24.2
HR (95% CI) vs Arm 1	**0.63** (0.52–0.76)‡ *P*<0.0001	



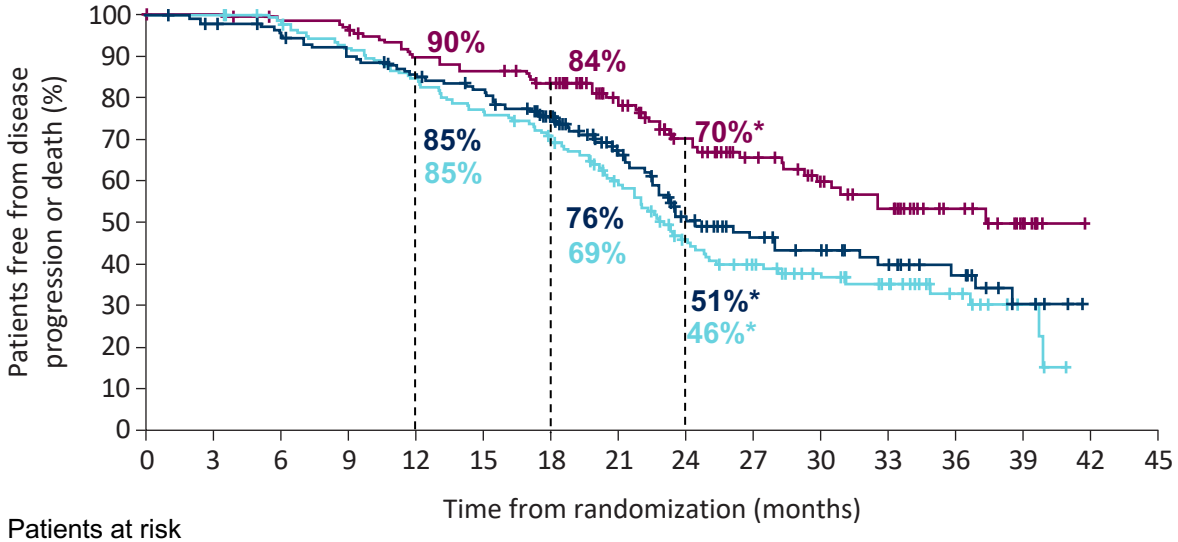
Patients at risk

Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	

*In censored patients; †Medians and rates were estimated by KM method; ‡HR and CI were estimated from a stratified Cox proportional hazards model. Model stratified by timing and outcome of cytoreductive surgery and geographical region. *P* value from a stratified log rank text; §24-month PFS rates unstable.

DUO-O/trial: extending benefit

HRD-positive



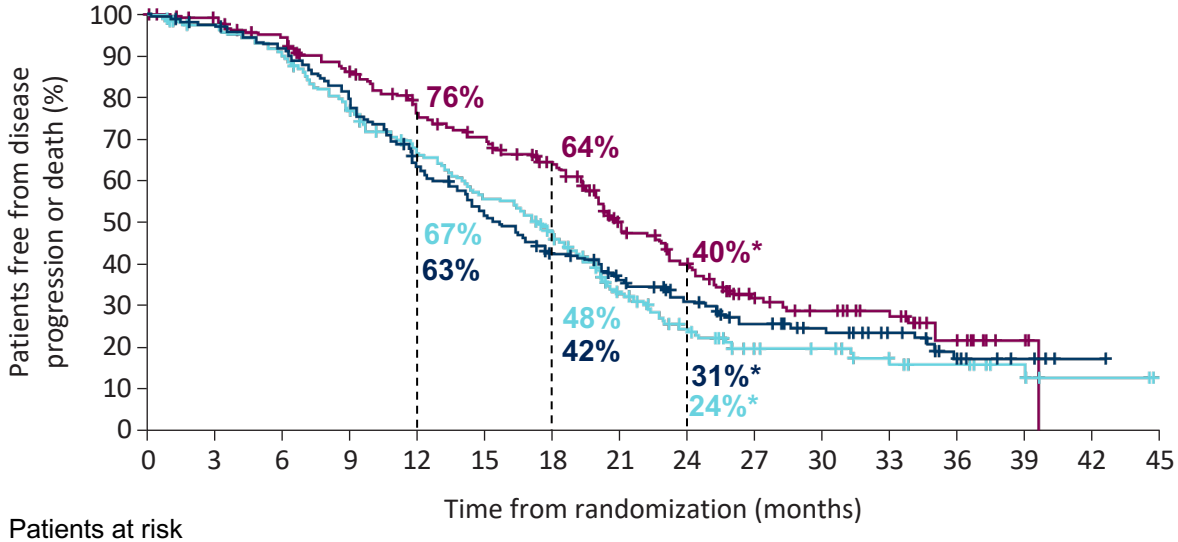
Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 2	148	142	137	128	118	112	94	66	45	34	28	21	15	7	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

	Arm 1 PC + bev N=143	Arm 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	**Olaparib + bevacizumab (N=97)**	**Placebo + bevacizumab (N=55)**	49 (35)
Median PFS, months†			37.3‡
HR (95% CI) vs Arm 1	43 (44)	40 (73)	**0.51** (0.36–0.72)§
	28.1*	**16.6**	

PAOLA: HR 0.43 (95% CI 0.28–0.66)

HRD-negative



Patients at risk

Arm 1	216	203	188	159	135	112	92	55	34	21	19	12	9	5	2	0
Arm 2	199	189	177	153	120	97	76	59	45	33	25	17	8	4	1	0
Arm 3	211	202	190	169	145	132	111	75	57	33	26	20	10	3	0	

	Arm 1 PC + bev N=216	Arm 2 PC + bev + durva N=199	Arm 3 PC + bev + durva + ola N=211
Events, n (%)	157 (73)	142 (71)	127 (60)
Median PFS, months†	17.4	15.4	20.9
HR (95% CI) vs Arm 1		**0.94** (0.75–1.18)§	**0.68** (0.54–0.86)§

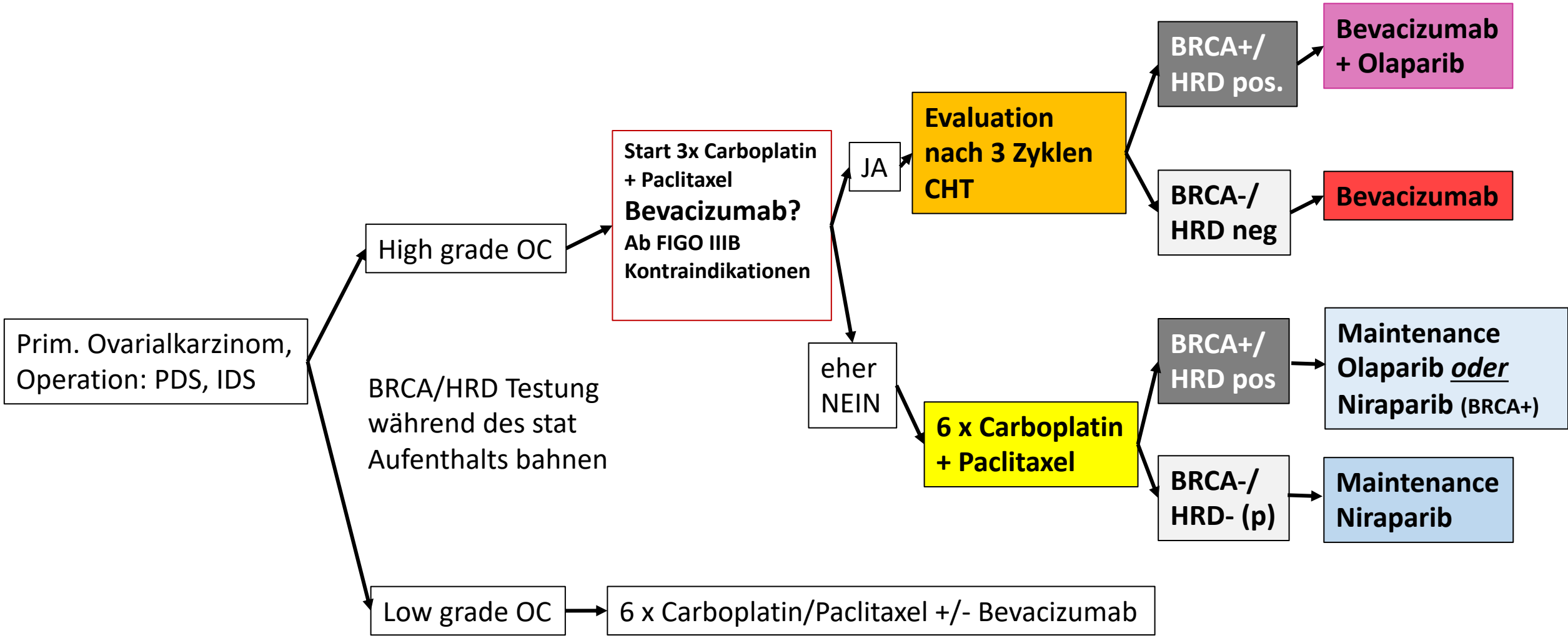
*24-month PFS rates unstable; †Medians and rates were estimated by KM method; ‡Median PFS in HRD-positive subgroup Arm 3 and Arm 2 unstable; §HR and CI were estimated from an unstratified Cox proportional hazards model.

Dr Philipp Harter

90s? 00s? Or now?

Only surgery? Neoadjuvant CHT? Only CHT? Maintenance: PARP only, Bev only, PARP+Bev, IO?

Therapie Algorithmus Charité



THE DARK SIDE OF the MOON

44% of all gynegological cancers are OC!

- **80% of OC patients have a relapse in the first 2-3 years**
- **OC is a chronic disease**
- **Despite current novel treatment algorithms the prognosis remains poor**
- **Surgical and systematic treatment have significant impact on QoL**
- **Many patients are constantly under treatment**
- **We still „only“ have BRCA/HRD as „biomarker“**
- **Many unadressed questions regarding the role of secondary and tertiary surgical and/or systemic treatment**

CHIPOR trial (NCT01376752): Multicenter randomized phase III trial

- First relapse of epithelial ovarian cancer
- PFI ≥6 months
- Response to 6 cycles of platinum-based chemotherapy
- Complete surgery achievable

N=415

Median laparotomy
Complete resection

SURGERY

CC0/1

Randomization during surgery

R 1:1

HIPEC
(cisplatin 75 mg/m^2 41°C for 60 min)
n=207

No HIPEC
n=208

SOC maintenance therapy

Stratification:
- **Center**
- **Residual disease (none vs <0.25 cm)**
- **PFI (6–12 vs >12–18 vs >18 months)**
- **Planned PARP inhibitor (yes vs no)[a]**

[a]Added Oct 8, 2020

CC0 = no macroscopic residual; CC1 = residual <0.25 cm; PFI = platinum-free interval; SOC = standard of care

CHIPOR trial: Baseline (pre-randomization) characteristics

Characteristics	No HIPEC (n=208)	HIPEC (n=207)
Median age (IQR), years	**59** (53–67)	**62** (55–68)
FIGO stage III/IV at primary treatment, %	84%	88%
Bevacizumab (first-line setting), n (%)	73 (35%)	64 (31%)
Median PFI (IQR), months	**17.8** (11.8–25.3)	**17.4** (10.6–26.6)
High-grade serous or grade 3 endometrioid, n (%)[a]	**165 (82%)**	**159 (79%)**
Completed 6 cycles of chemotherapy, n (%)	189 (91%)	188 (91%)
Surgery to CC0, n (%)	**180 (87%)**	**180 (87%)**

[a]Missing in 7 patients in the No HIPEC arm and 6 in the HIPEC arm

IQR = interquartile range

CHIPOR trial: Severe morbidity and mortality (within 30 days after surgery)*

No. of patients (%)	No HIPEC (n=208)	HIPEC (n=207)
Median duration of surgery (IQR), min	218 (160–282)	337 (272–407)
Digestive tract resection	78 (38%)	85 (41%)
Stoma diversion	10 (4.8%)	20 (9.7%)
Grade ≥3 morbidity	41 (20%)	82 (40%)
Blood disorders	16 (8%)	28 (14%)
Digestive tract disorders	14 (7%)	18 (9%)
Mortality	3 (1.4%)	0

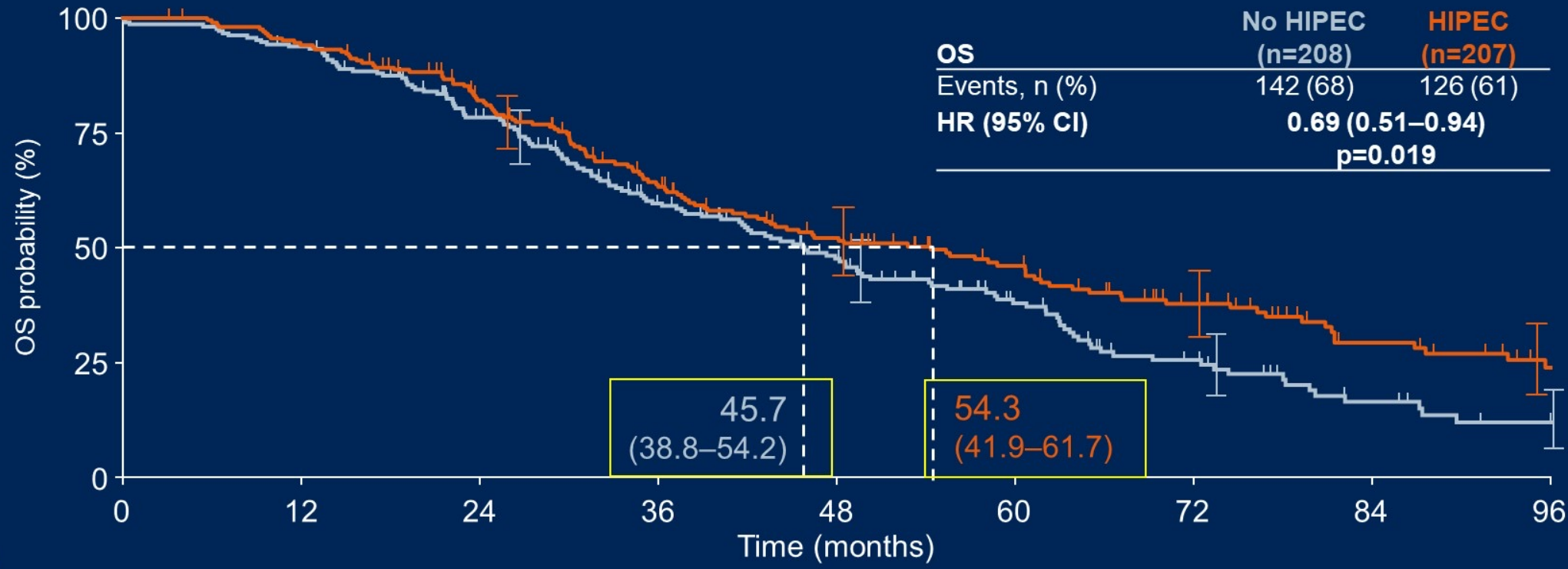
*CTCAE V04

CHIPOR trial: Kidney failure

No. of patients (%)	No HIPEC (n=208)	HIPEC (n=207)
Severe kidney failure	3 (1.4%)	21 (10%)
Before thiosulfate amendment[a]	1/154 (0.7%)	19/156 (12%)
After thiosulfate amendment[a]	2/54 (3.7%)	2/51 (3.9%)

[a]Thiosulfate amendment, June 2018

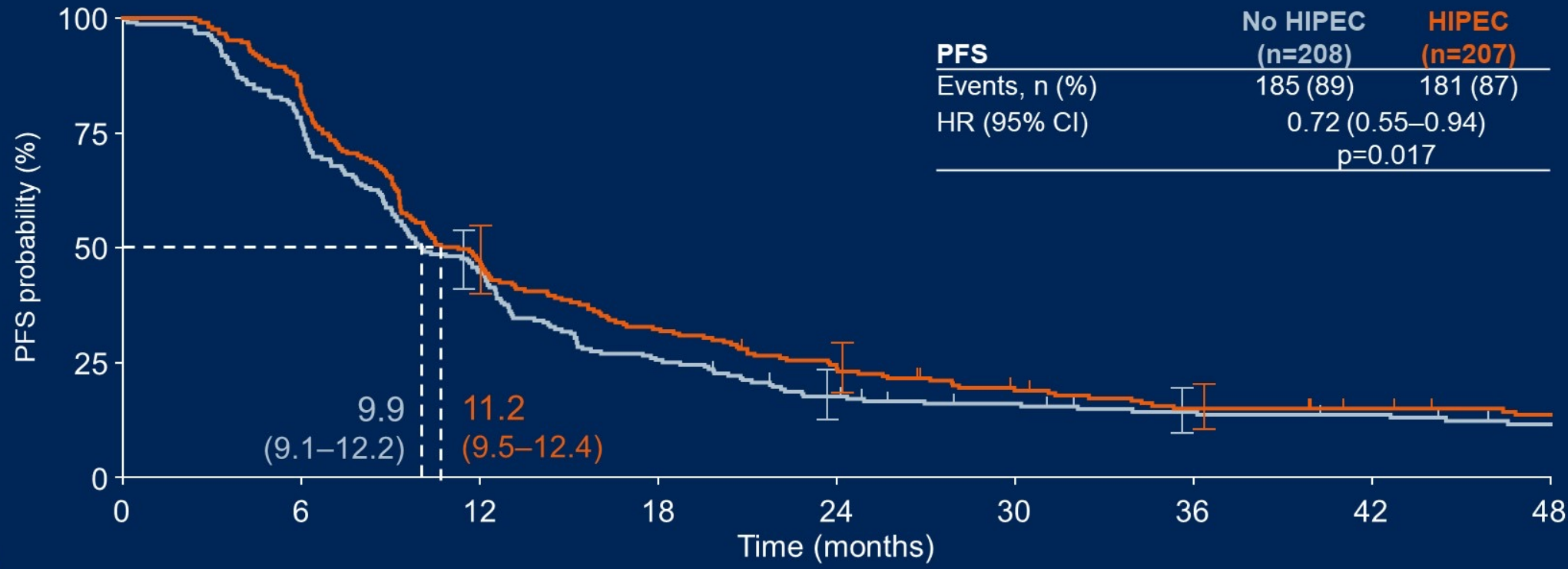
CHIPOR trial: Primary endpoint (OS, ITT population)



OS	No HIPEC (n=208)	HIPEC (n=207)
Events, n (%)	142 (68)	126 (61)
HR (95% CI)	**0.69 (0.51–0.94)**	
	p=0.019	

No. at risk									
HIPEC	207	193	158	113	87	65	44	25	15
No HIPEC	208	194	150	106	75	48	27	13	7

CHIPOR trial: PFS (secondary endpoint)



PFS	No HIPEC (n=208)	HIPEC (n=207)
Events, n (%)	185 (89)	181 (87)
HR (95% CI)	0.72 (0.55–0.94) p=0.017	

2023 ASCO ANNUAL MEETING

Phase III MIRASOL (GOG 3045/ENGOT-ov55) Study: Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers with High Folate Receptor-Alpha (FRα) Expression

Kathleen N. Moore[1], Antoine Angelergues[2], Gottfried E. Konecny[3], Susana Banerjee[4], Sandro Pignata[5], Nicoletta Colombo[6], John Moroney[7], Casey Cosgrove[8], Jung-Yun Lee[9], Andrzej Roszak[10], Shani Breuer[11], Jacqueline Tromp[12], Diana Bello Roufai[13], Lucy Gilbert[14], Rowan Miller[15], Tashanna Myers[16], Yuemei Wang[17], Anna Berkenblit[17], Domenica Lorusso[18], Toon Van Gorp[19]

[1]Stephenson Cancer Center University of Oklahoma College of Medicine, Oklahoma City, OK, USA; [2]Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France; [3]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [4]The Royal Marsden NHS Foundation Trust - Royal Marsden Hospital, London, UK; [5]Istituto Nazionale Tumori- G. Pascale, Naples, Italy; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]The University of Chicago, Chicago, IL, USA; [8]The Ohio State University, Columbus, OH, USA; [9]Severance Hospital, Seoul, South Korea; [10]Wielkopolskie Centrum Onkologii, Poznan, Poland; [11]Hadassah Ein Kerem – Sharett, Jerusalem, Israel; [12]Amsterdam UMC, Amsterdam, The Netherlands; [13]Hopital Rene Huguenin, Institut Curie, Saint-Cloud, France; [14]McGill University Health Centre, Montreal, Canada; [15]University College London Hospital, London, UK; [16]Baystate Medical Center, Springfield, MA, USA; [17] ImmunoGen, Inc., Waltham, MA, USA; [18]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [19]University Hospital Leuven Leuven Cancer Institute, Leuven, Belgium

ENGOT European Network of Gynaecological Oncological Trial groups

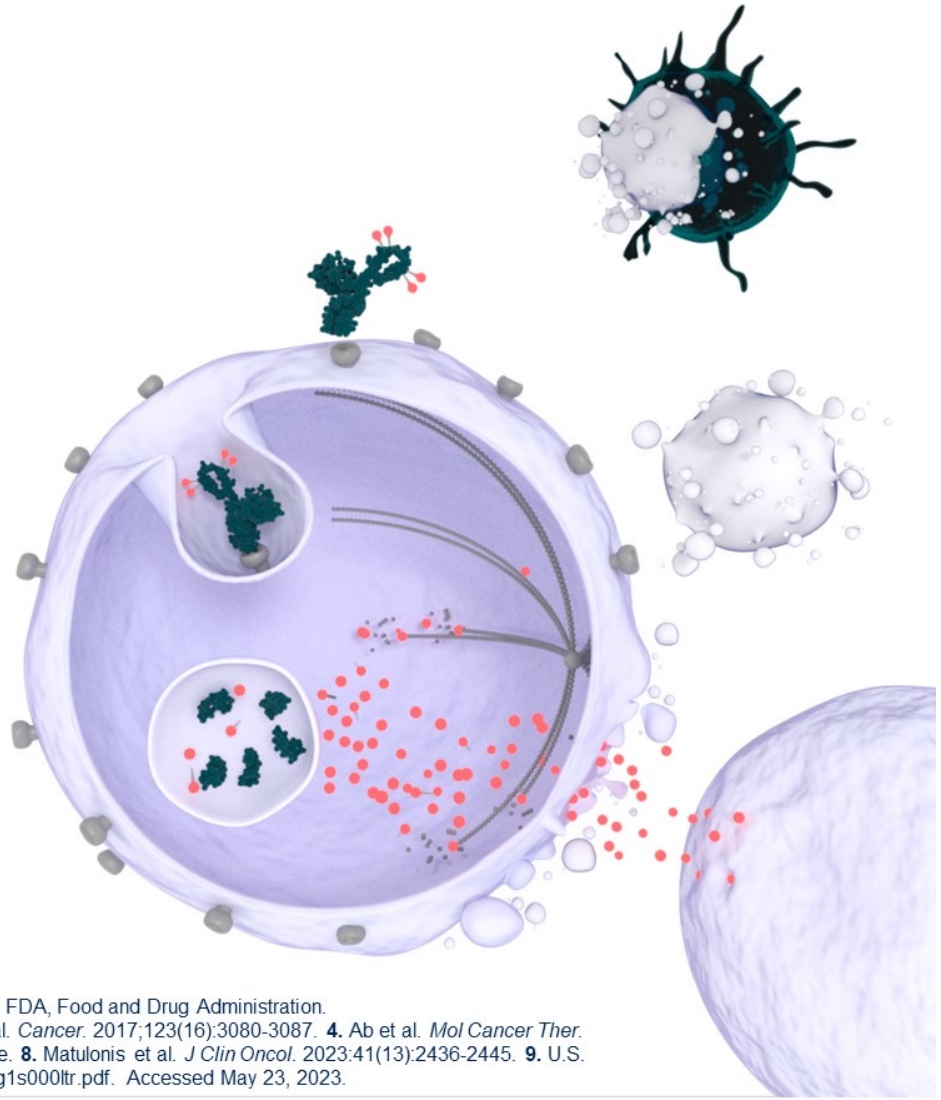
GOG FOUNDATION® Transforming the standard of care™

PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

ASCO® AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Background

- No trial has shown an overall survival (OS) benefit in platinum-resistant ovarian cancer (PROC)[1, 2]
- Mirvetuximab soravtansine (MIRV) is an ADC comprising a FRα-binding antibody, cleavable linker, and maytansinoid DM4, a potent tubulin-targeting agent[3,4]
- FRα is expressed in ~90% of ovarian carcinomas,[5,6] with 35-40%[7] of PROC tumors exhibiting high FRα expression (≥75% of tumor cells positive with ≥2+ intensity)[8]
- MIRV demonstrated an ORR of 32% and mDOR 6.9 months in the single-arm study, SORAYA[8], of BEV pre-treated PROC to support accelerated approval by the FDA[9]
- MIRASOL is the confirmatory, randomized, global phase 3 trial designed to support full approval in the US and EU



PFS, progression-free survival; OS, overall survival; FRα, folate receptor alpha; ORR, objective response rate; mDOR, median duration of response; FDA, Food and Drug Administration.

1. Pujade-Lauraine et al. *J Clin Oncol*. 2014;32(13):1302-1308. **2.** Richardson et al. *JAMA Oncol*. 2023;10.1001/jamaoncol.2023.0197. **3.** Moore et al. *Cancer*. 2017;123(16):3080-3087. **4.** Ab et al. *Mol Cancer Ther*. 2015;14(7):1605-1613. **5.** Markert et al. *Anticancer Res*. 2008;28(6A):3567-3572. **6.** Martin et al. *Gynecol Oncol*. 2017;147(2):402-407. 7. Data on file. **8.** Matulonis et al. *J Clin Oncol*. 2023:41(13):2436-2445. **9.** U.S. FOOD & DRUG ADMINISTRATION. BLA ACCELERATED APPROVAL. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/761310Orig1s000ltr.pdf. Accessed May 23, 2023.

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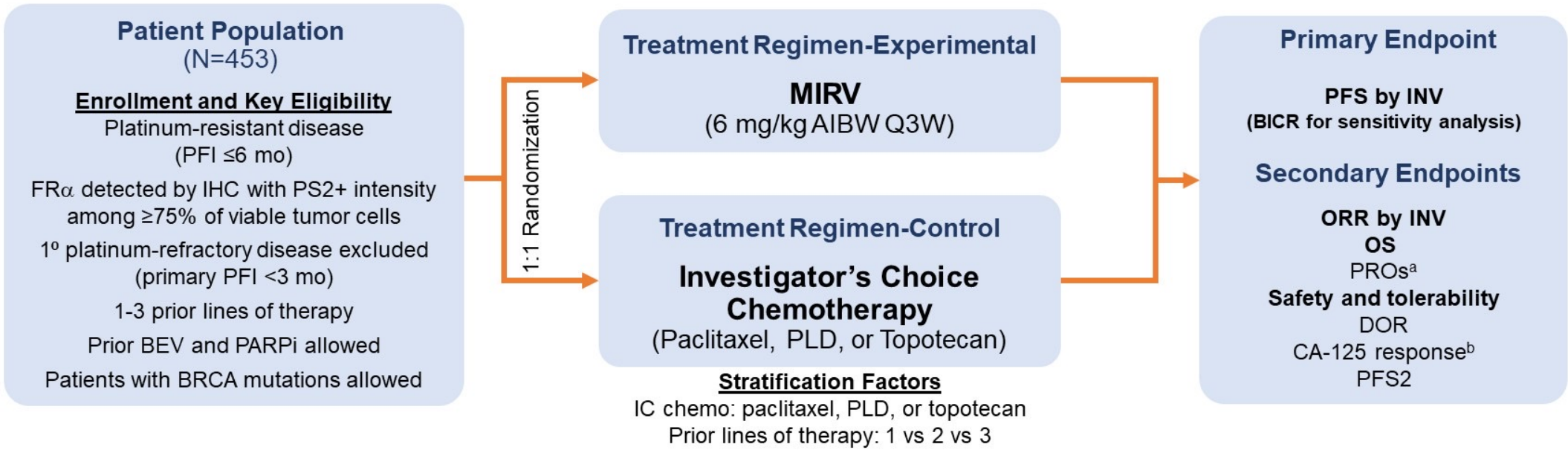
MIRASOL (NCT04209855) – Study Design[1,2]

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



AIBW, adjusted ideal body weight; BEV; bevacizumab; BICR, blinded independent central review; BRCA, BReast CAncer gene; CA-125, cancer antigen 125; chemo, chemotherapy; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PFI, platinum-free interval; PFS, progression-free survival; PFS2, time from randomization until second disease progression; PLD, pegylated liposomal doxorubicin; PROs, patient-reported outcomes; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.
[a]PROs will be measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, 28-item Ovarian Cancer Module (OV28) study instrument.
[b]Gynecological Cancer InterGroup (GCIG) criteria.

1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855
2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting; May 29-31, 2020; Virtual. Abstract TPS6103.

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Baseline Demographics (N=453)

Characteristics		MIRV (n=227)	IC Chemo (n=226)
Age, median (range)	Age in years	63 (32-88)	62 (29-87)
Stage at initial diagnosis, n (%)[a]	I-II III IV	9 (4) 137 (60) 76 (33)	9 (4) 147 (65) 65 (29)
BRCA mutation, n (%)	Yes No/Unknown	29 (13) 198 (87)	36 (16) 190 (84)
No. of prior systemic therapies, n (%)	1 2 3	29 (13) 90 (40) 108 (48)	34 (15) 88 (39) 104 (46)
Prior exposure, n (%)	Bevacizumab PARPi Taxanes	138 (61) 124 (55) 227 (100)	143 (63) 127 (56) 224 (99)
Primary platinum-free interval, n (%)[b]	≤ 12 months > 12 months	146 (64) 80 (35)	142 (63) 84 (37)
Platinum-free interval, n (%)[c]	≤ 3 months > 3 - ≤6 months	88 (39) 138 (61)	99 (44) 124 (55)

Data cutoff: March 6, 2023
BRCA, BReast cancer gene; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor.
[a]Five patients (2%) in the MIRV arm and five patients in the IC chemo arm (2%) were missing information for stage at initial diagnosis. [b]One patient (<1%) in the MIRV arm was missing information on primary platinum-free interval.
[c]One patient (<1%) in the MIRV arm and 3 patients (1%) in the IC chemo arm enrolled with platinum-free interval of >6 months

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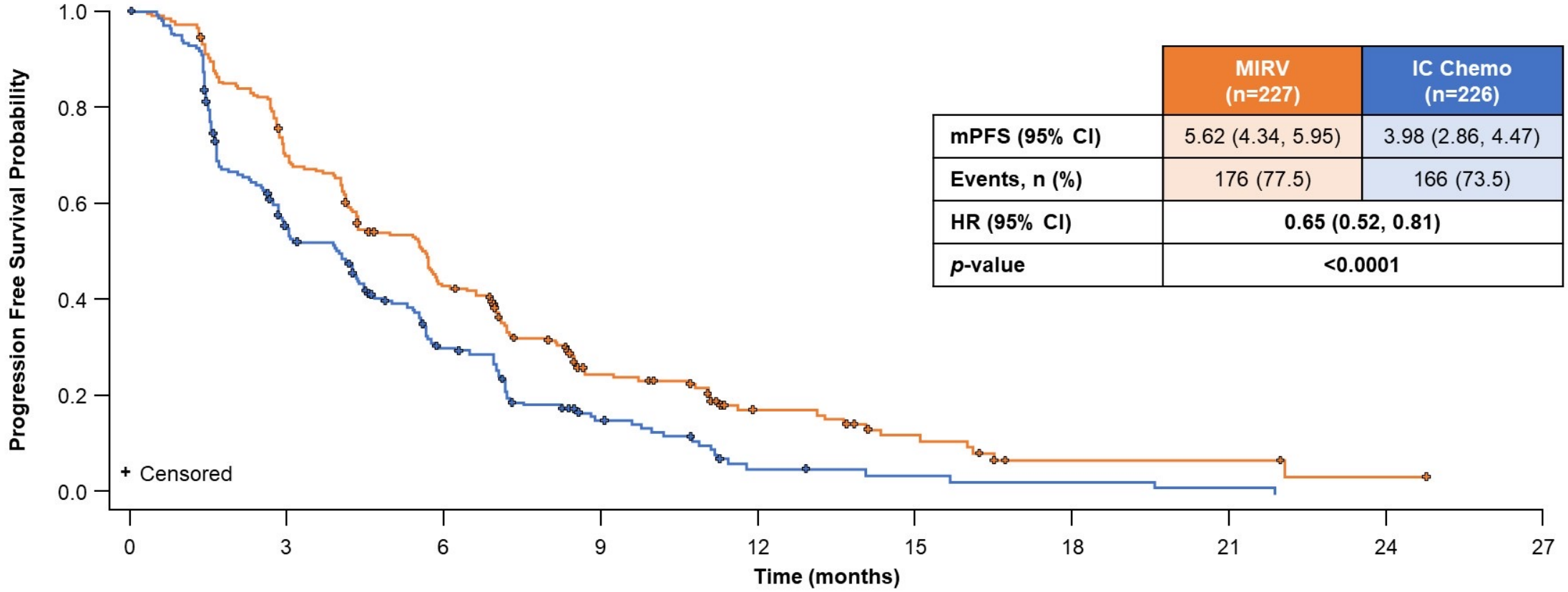
Primary Endpoint: Progression-Free Survival by Investigator



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

No. Participants at Risk

MIRV — IC Chemo

MIRV	227	151	89	38	18	10	3	3	1	0
IC Chemo	226	98	48	19	5	3	2	1	0	

Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mPFS, median progression-free survival; CI, confidence interval; HR, hazard ratio.

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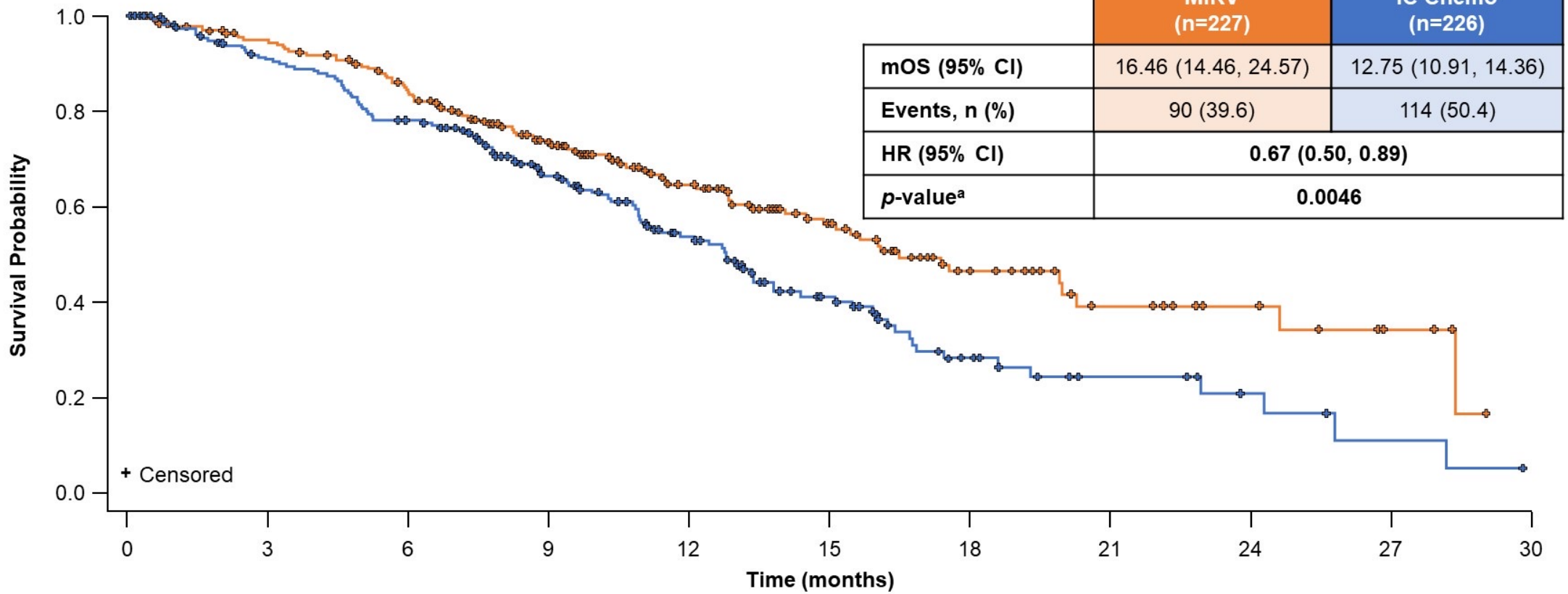
Overall Survival

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



No. Participants at Risk

MIRV	227	204	175	128	82	53	28	15	9	4	0
IC Chemo	226	185	157	107	68	39	18	9	5	2	0

Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.

[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

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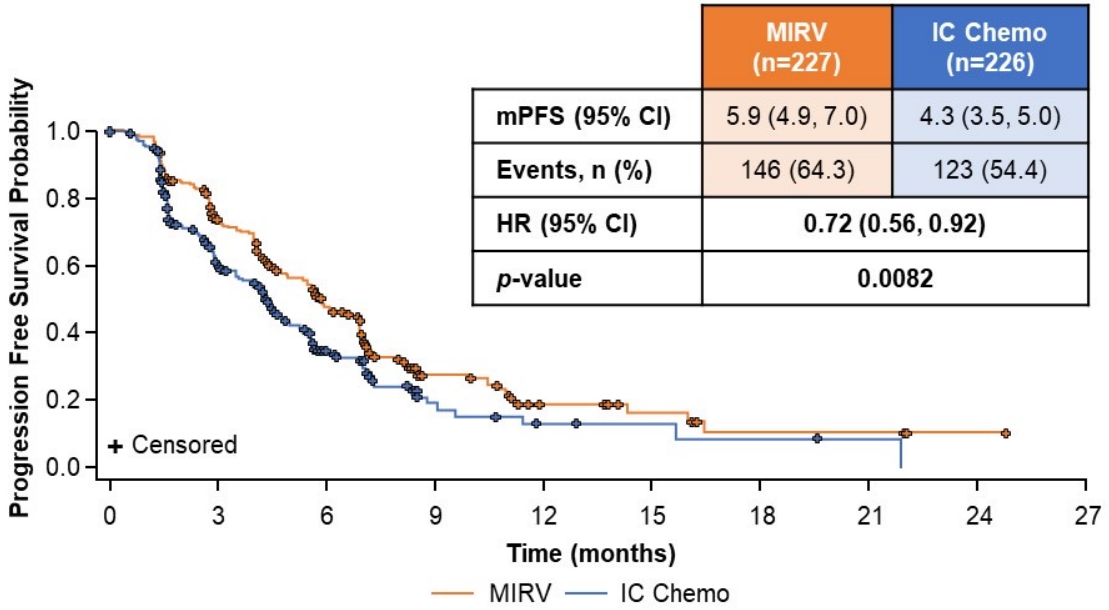
Progression-Free Survival and Objective Response Rate by Blinded Independent Central Review

Progression-Free Survival



	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.9 (4.9, 7.0)	4.3 (3.5, 5.0)
Events, n (%)	146 (64.3)	123 (54.4)
HR (95% CI)	0.72 (0.56, 0.92)	
p-value	0.0082	

No. Participants at Risk

MIRV	227	146	83	28	12	7	3	3	1	0
IC Chemo	226	95	36	10	4	3	2	1	0	

Best Overall Response

	MIRV (n=227)	IC Chemo (n=226)
ORR, n (%) 95% CI	82 (36) (29.9, 42.7)	33 (15) (10.3, 19.9)
CR, n (%)	16 (7)	4 (2)
PR, n (%)	66 (29)	29 (13)
SD, n (%)	97 (43)	107 (47)
PD, n (%)	32 (14)	45 (20)
Not Evaluable, n (%)	16 (7)	41 (18)

Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mPFS, median progression-free survival; HR, hazard ratio; ORR, objective response rate; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

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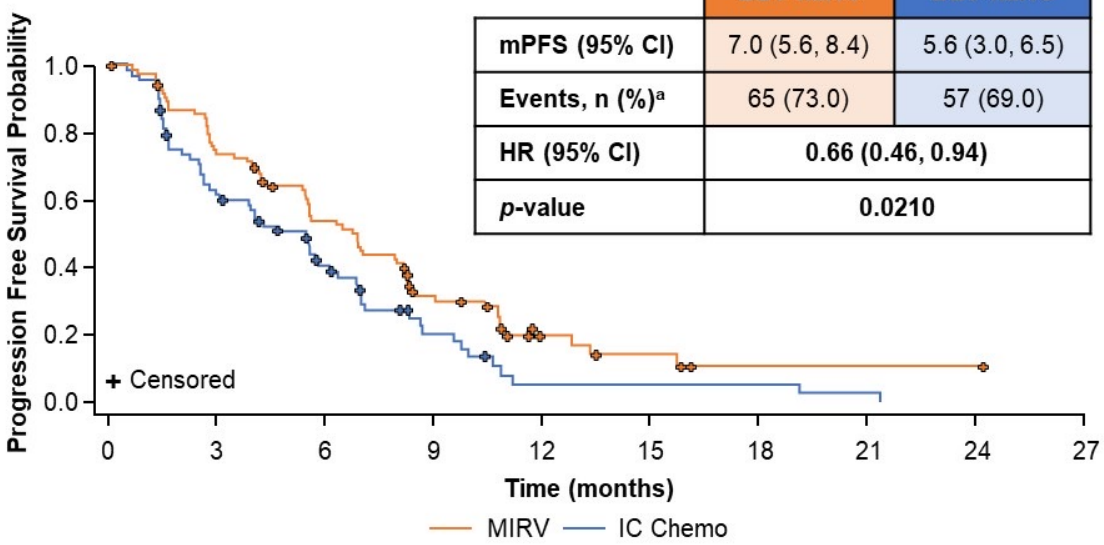
Progression-Free Survival in Bevacizumab Naïve and Prior Bevacizumab Subsets by Investigator

BEV-naïve

	MIRV BEV-naïve	IC Chemo BEV-naïve
mPFS (95% CI)	7.0 (5.6, 8.4)	5.6 (3.0, 6.5)
Events, n (%)[a]	65 (73.0)	57 (69.0)
HR (95% CI)	0.66 (0.46, 0.94)	
p-value	0.0210	

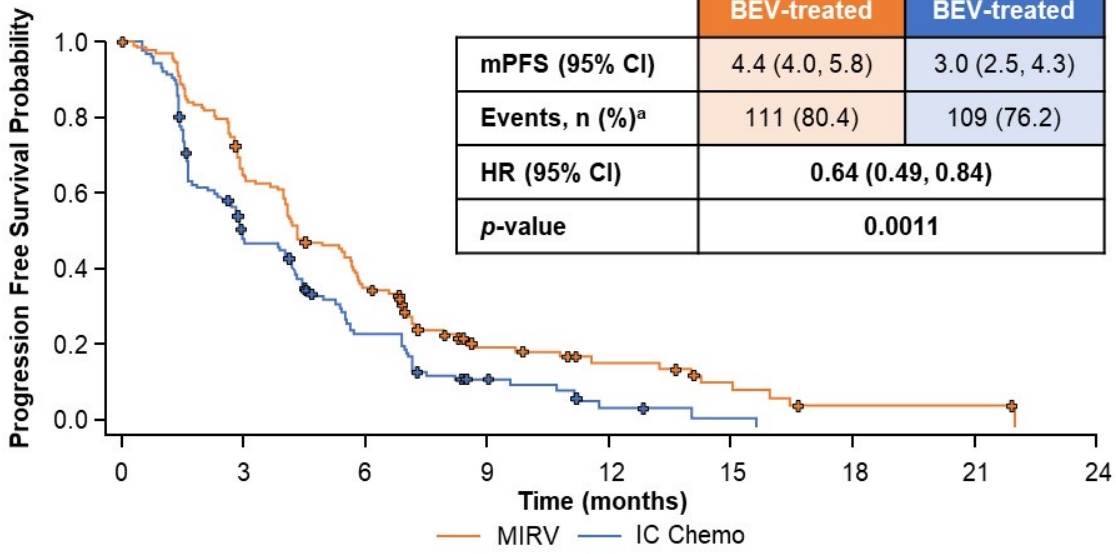


No. Participants at Risk

MIRV	89	63	42	21	7	4	1	1	1	0
IC Chemo	83	42	23	9	2	2	2	1	0	

BEV-treated

	MIRV BEV-treated	IC Chemo BEV-treated
mPFS (95% CI)	4.4 (4.0, 5.8)	3.0 (2.5, 4.3)
Events, n (%)[a]	111 (80.4)	109 (76.2)
HR (95% CI)	0.64 (0.49, 0.84)	
p-value	0.0011	



No. Participants at Risk

MIRV	138	88	47	17	11	6	2	2	0	
IC Chemo	143	56	25	10	3	1	0			

Data cutoff: March 6, 2023
BEV, bevacizumab; HR, hazard ratio; CI, confidence interval; mPFS, median progression-free survival; MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice of chemotherapy.
Patients were not stratified for prior BEV.
[a]Percentage of PFS events was calculated out of the total number of patients in each treatment arm: n=227 for MIRV and n=226 for IC Chemo.

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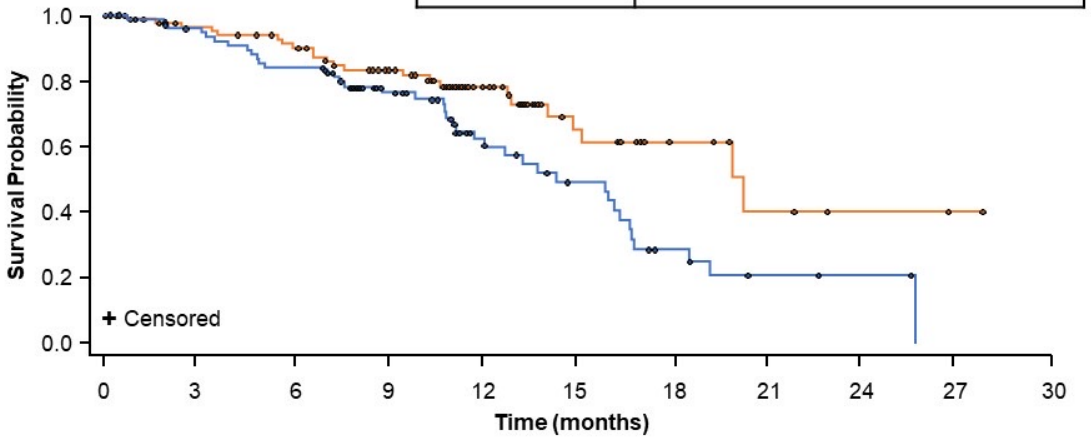
Overall Survival in Bevacizumab Naïve and Prior Bevacizumab Subsets by Investigator

BEV-naïve

	MIRV BEV-naïve	IC Chemo BEV-naïve
mOS (95% CI)	20.2 (14.8, NE)	14.4 (11.8, 16.7)
Events, n (%)[a]	23 (25.8)	39 (47.0)
HR (95% CI)	0.51 (0.31, 0.86)	
p-value	0.0099	

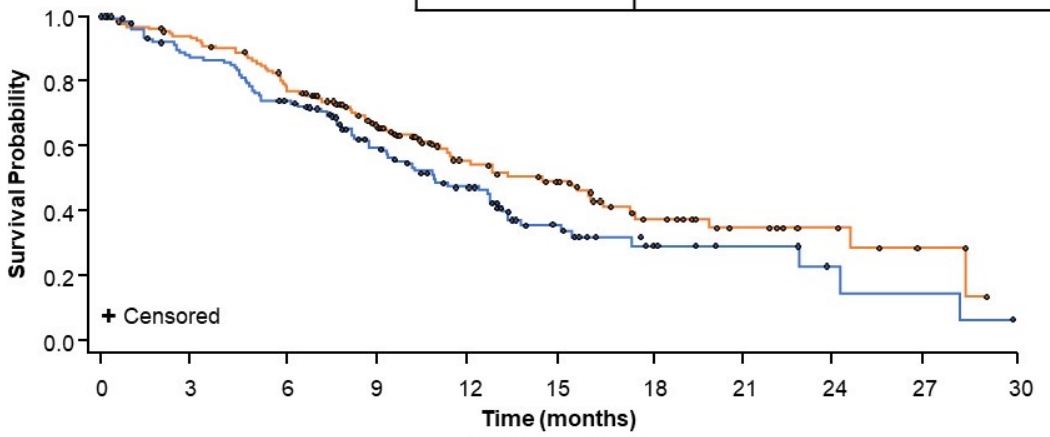


No. Participants at Risk											
MIRV	89	79	71	57	35	17	8	4	2	1	0
IC Chemo	83	72	63	44	26	17	8	3	2	0	

MIRV — IC Chemo

BEV-treated

	MIRV BEV-treated	IC Chemo BEV-treated
mOS (95% CI)	15.4 (11.3, 17.5)	10.9 (9.4, 13.3)
Events, n (%)[a]	67 (48.6)	75 (52.4)
HR (95% CI)	0.74 (0.54, 1.04)	
p-value	0.0789	



No. Participants at Risk											
MIRV	138	125	104	71	47	36	20	11	7	3	0
IC Chemo	143	113	94	63	42	22	10	6	3	2	0

MIRV — IC Chemo

Data cutoff: March 6, 2023

BEV, bevacizumab; HR, hazard ratio; CI, confidence interval; NE, not estimable; mOS, median overall survival; MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice of chemotherapy.

[a]Percentage of OS events was calculated out of the total number of patients in each treatment arm: n=227 for MIRV and n=226 for IC Chemo.

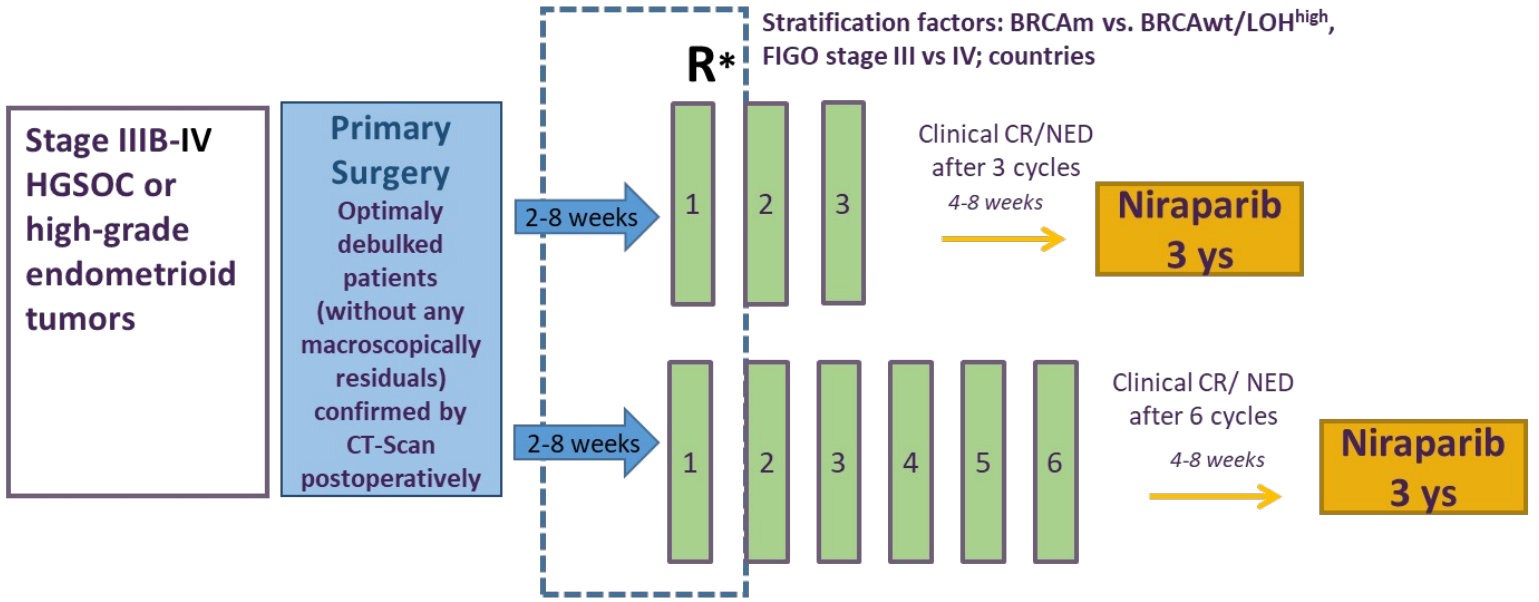
PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

ENGOT-ov62 / NOGGO ov53 /N-PLUS

A Phase II randomized, open label non-inferiority study of NiraParib maintenance after 3 vs. 6 cycles of platinum-based chemotherapy in completely debUlked advanced HRDpositive high-grade ovarian cancer patientS in first line therapy

- ENGOT model: a
- Sponsor: NOGGO e.V.
- Cooperating groups: BGOG, AGO-A, MaNGO, GEICO
- No. of already recruited patients: 0
- Planned No. of patients: 640
- Status: not yet recruiting
- Other important information: CTIS part I submission done, content review ongoing

ENGOT-ov62 / Study design



Key Inclusion Criteria:

- Female patient, age ≥ 18 years
- FIGO Stage III--IV high-grade ovarian cancer (all histological types, except mucinous histology)
- Complete primary debulked patients (without any macroscopically residuals), confirmed by CT-Scan postoperatively

Primary Endpoint:

Recurrence free survival

Secondary Endpoints:

- OS
- TFST, TWIST
- PFS2, PROs, safety, cost effectiveness

* DEcrEaSing ChemotherApy in optimaLly debulked OvArian Cancer IniTiativE

Thank you!

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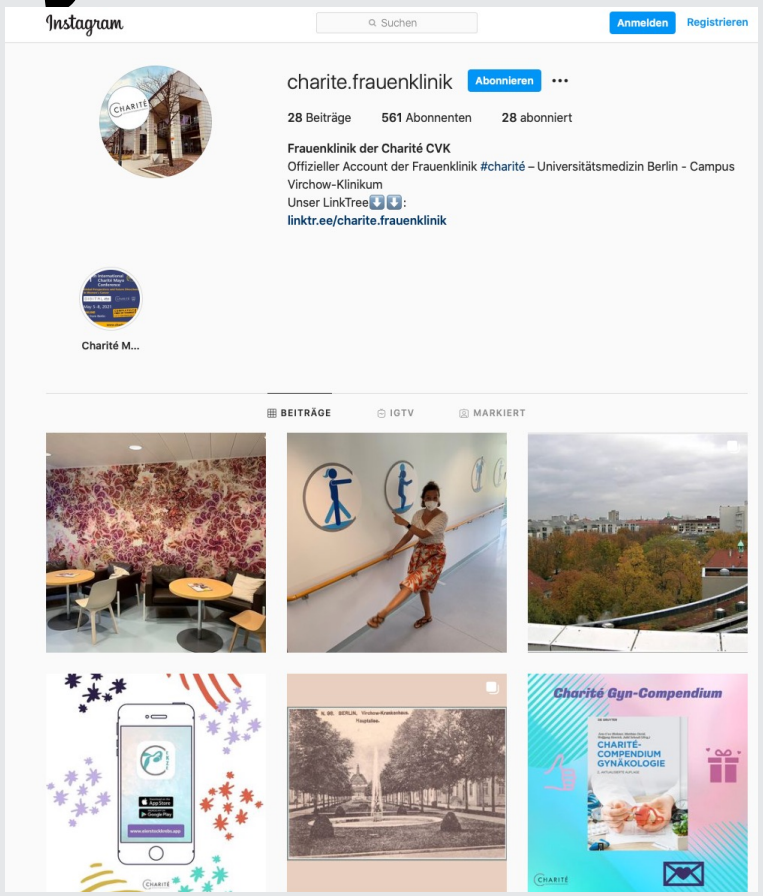

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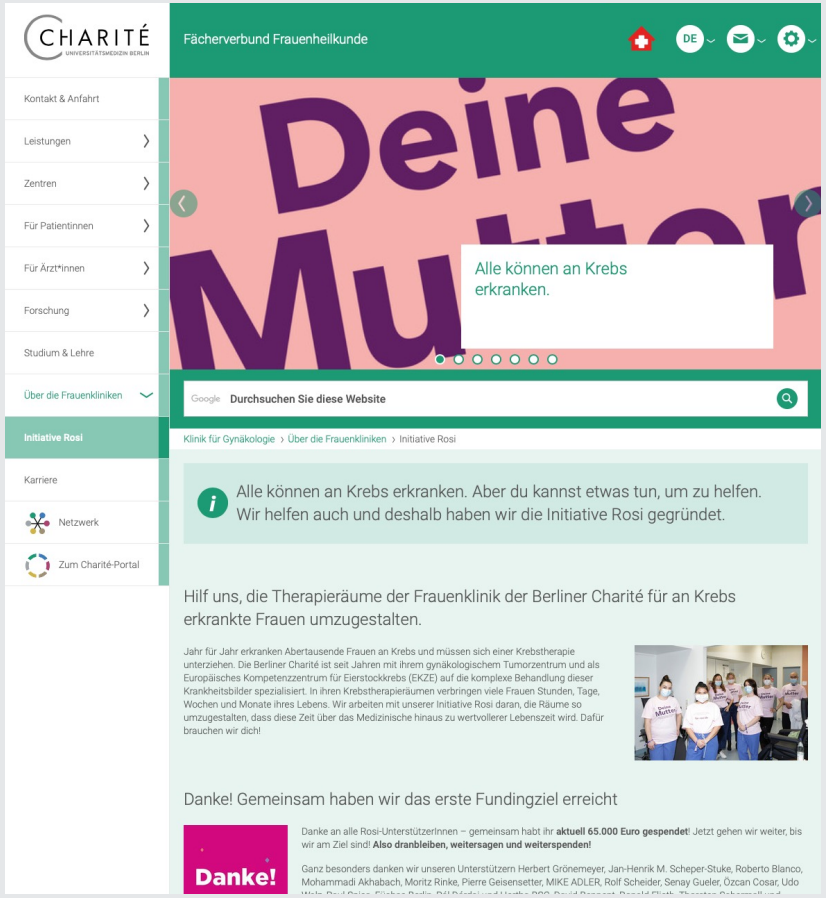

Klinik für Gynäkologie mit Zentrum für Onkologische Chirurgie Charité-Campus Virchow Klinikum

Direktor: Prof. Dr. med. Dr. h.c. Jalid Sehouli

Europäisches Kompetenzzentrum für Eierstockkrebs (EKZE)

Charité/ Campus Virchow-Universitätsmedizin Berlin