Platinum-sensitive recurrent ovarian cancer Diversity and Heath Equity in Gynecologic Cancer Clinical Trials

Bhavana Pothuri, MD, MS
Professor, NYU Grossman School of Medicine, Depts of Ob/Gyn and Medicine
Medical Director, Clinical Trials Office (CTO)
Director, Gynecologic Oncology Clinical Trials
Laura & Isaac Perlmutter Cancer Center, *NCI Designated Comprehensive Cancer Center*
Associate Clinical Trial Advisor, GOG Partners
Director of Diversity and Health Equity for Clinical Trials, GOG Foundation

November 11, 2022

GOG FOUNDATION®
Transforming the standard of care™

GOG Highlight Reel

Disclosures

Research support: AstraZeneca, Clovis Oncology, Tesaro/GSK, Clovis Roche/Genentech, Merck, Eisai, Mersana, Celsion, Sutro, Karyopharm, Imab, SeaGen, Toray

Advisory boards: Tesaro/GSK Inc, AstraZeneca, Merck, Eisai, Lily, Mersana, Sutro, Toray, SeaGen, Celsion, Imab, Onconova, Toray, GOG Foundation

Outline

- Ariel 3
- Solo 3
- Atalante
- Diversity in Gynecologic Cancer Trial Enrollment
- Upcoming Phase 3 Trials in PSOC

Overall Survival Results From ARIEL3: A Phase 3 Randomised, Double-blind Study of Rucaparib vs Placebo Following Response to Platinum-Based Chemotherapy for Recurrent Ovarian Carcinoma

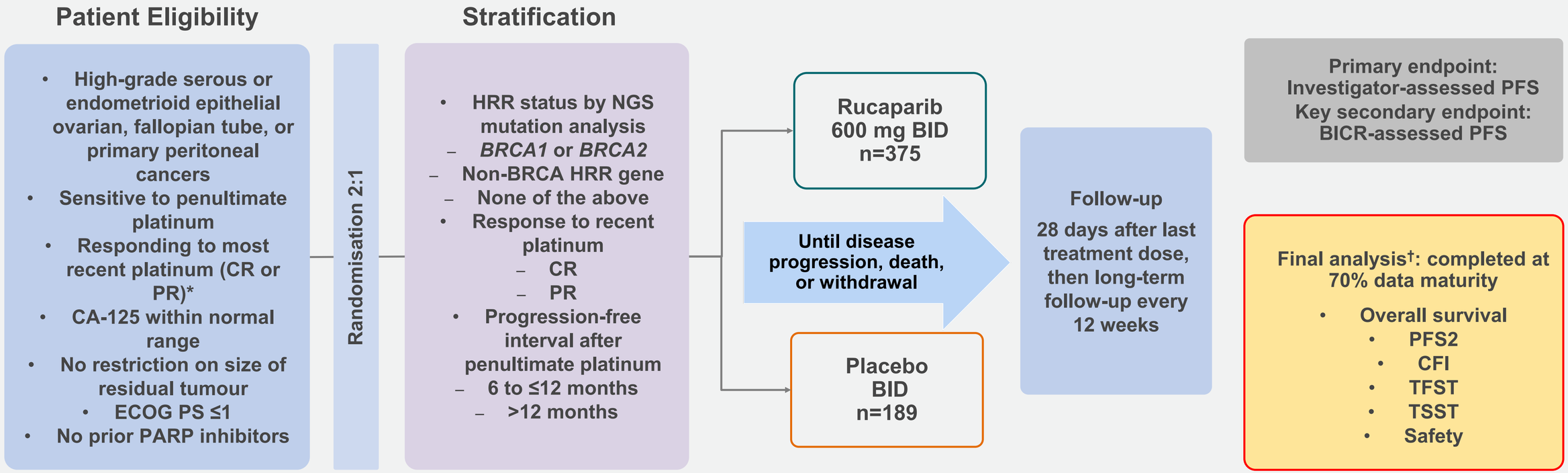
Robert L. Coleman,[1*] Amit M. Oza,[2] Domenica Lorusso,[3] Carol Aghajanian,[4] Ana Oaknin,[5] Andrew Dean,[6] Nicoletta Colombo,[7] Johanne I. Weberpals,[8] Andrew R. Clamp,[9] Giovanni Scambia,[10] Alexandra Leary,[11] Robert W. Holloway,[12] Margarita Amenedo Gancedo,[13] Peter C. Fong,[14] Jeffrey C. Goh,[15] David M. O'Malley,[16] Sandra Goble,[17] Lara Maloney,[17] Jonathan A. Ledermann[18]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [3]MITO and Gynecologic Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [4]Memorial Sloan Kettering Cancer Center, New York, NY; [5]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [6]St John of God Subiaco Hospital, Subiaco, WA, Australia; [7]European Institute of Oncology and University of Milan-Bicocca, Milan, Italy; [8]Ottawa Hospital Research Institute, Ottawa, ON, Canada; [9]The Christie NHS Foundation Trust and University of Manchester, Manchester, UK; [10]Fondazione Policlinico Universitario A. Gemelli IRCCS and Scientific Directorate, Rome, Italy; [11]Gustave Roussy Cancer Center, INSERM U981, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Villejuif, France; [12]Florida Hospital Cancer Institute, Orlando, FL, USA; [13]Oncology Center of Galicia, La Coruña, Spain; [14]Auckland City Hospital, Grafton, Auckland, New Zealand; [15]Cancer Care Services, Royal Brisbane and Women's Hospital, Herston, QLD, Australia, and University of Queensland, St Lucia, QLD, Australia; [16]The Ohio State University, James Cancer Center, Columbus, OH, USA; [17]Clovis Oncology, Inc., Boulder, CO; [18]UCL Cancer Institute, University College London and UCL Hospitals, London, UK

*Affiliation where the work was conducted; current affiliation: US Oncology Research, The Woodlands, TX

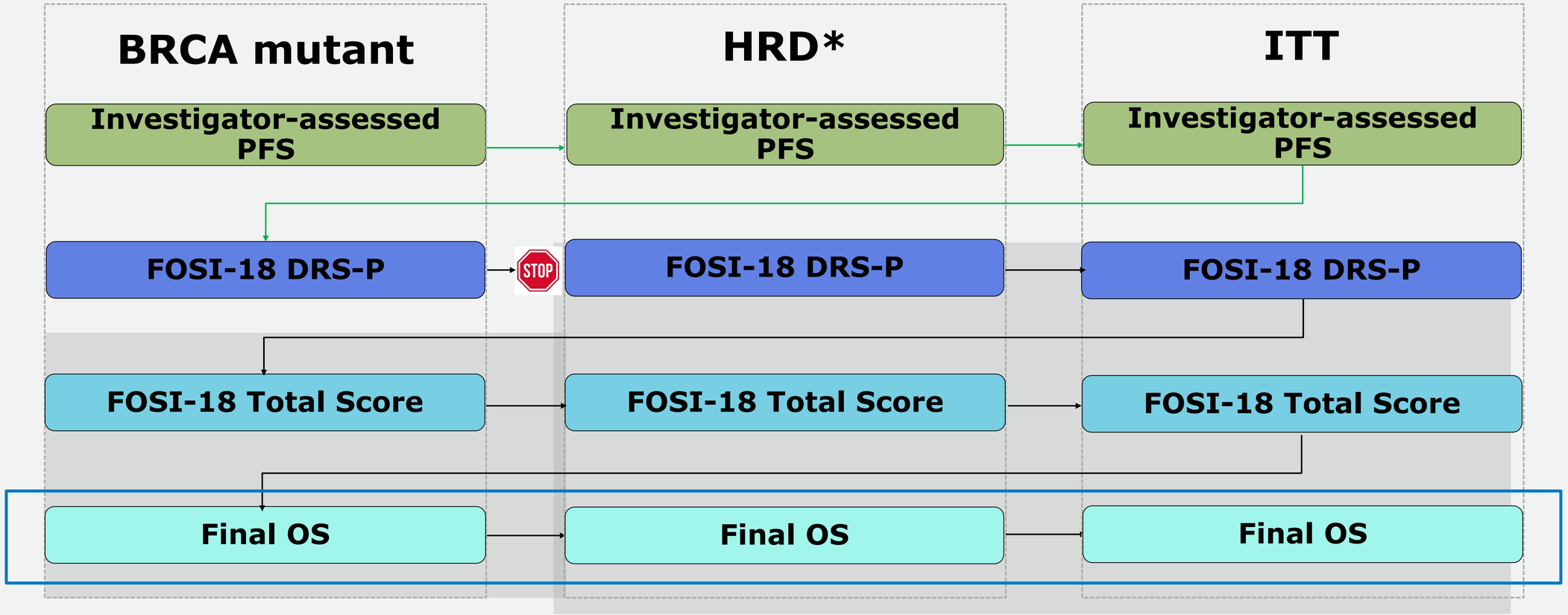
Originally presented at IGCS Annual Global Meeting, 29 Sep to 1 Oct 2022, New York, NY, USA.

ARIEL3 Study Design



A hypothesis of superiority in overall survival was not prespecified in the protocol/study design.
*CR (defined by RECIST) or PR (defined by RECIST and/or a GCIG CA-125 response [CA-125 within normal range]) maintained until entry to ARIEL3 (≤8 weeks from last dose of chemotherapy). †Analyses were done for the molecularly defined nested cohorts (BRCA mutant, HRD, and ITT), and exploratory analyses were done in the non-nested subgroups of patients with BRCA wild-type carcinoma.
BICR, blinded independent central review; BID, twice daily; BRCA, *BRCA1* and *BRCA2;* CA-125, cancer antigen 125; CFI, chemotherapy-free interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; GCIG, Gynecological Cancer InterGroup; HRD, homologous recombination deficiency; HRR, homologous recombination repair; NGS, next-generation sequencing; PARP, poly(ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PFS2, PFS on the subsequent line of therapy; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumours version 1.1; TFST, time to start of first subsequent therapy; TSST, time to start of second subsequent therapy.

ARIEL3 Step-down Analysis



- No statistical significance was observed in the first secondary endpoint of time to worsening in the FOSI-18 DRS-P subscale in the BRCA mutant cohort[1]; therefore, no further statistical significance of subsequent endpoints can be claimed

*Includes BRCA-mutant and BRCA–wild-type/LOH-high groups.
BRCA, *BRCA1* and *BRCA2*; DRS-P, disease related symptom-physical subscale; FOSI-18, FACT-Ovarian Symptom Index-18; HRD, homologous recombination deficiency; ITT, intent-to-treat; OS, overall survival; PFS, progression-free survival.

1. Coleman et al. *Lancet.* 2017;390:1949-61.

Patient Disposition

	Rucaparib	Placebo
Randomized, % (n)	**100 (375)**	**100 (189)**
Treated, % (n)	**99.2 (372)**	**100 (189)**
Ongoing, % (n)*	**4.0 (15)**	**0**
Discontinued, % (n)†	**96.0 (360)**	**100 (189)**
Disease progression	**69.4 (250)**	**92.1 (174)**
Clinical progression	**3.1 (11)**	**3.2 (6)**
Adverse event	18.1 (65)	0.5 (1)
Withdrew consent‡	5.0 (18)	3.2 (6)
Investigator decision	1.1 (4)	0 (0)
Other§	3.3 (12)	1.1 (2)

- Median duration of follow-up was 6.4 years for rucaparib and 6.4 years for placebo

Data cutoff date: 4 April 2022.

***All patients remaining on treatment after the data cutoff date transitioned to receiving rucaparib via other access mechanisms. †Percentages in subcategories are based on the number of patients who discontinued study drug. ‡Includes categories of patient withdrew consent and withdrew consent for treatment only.** §Includes categories of pregnancy, study terminated by sponsor, unknown, noncompliance, and other.

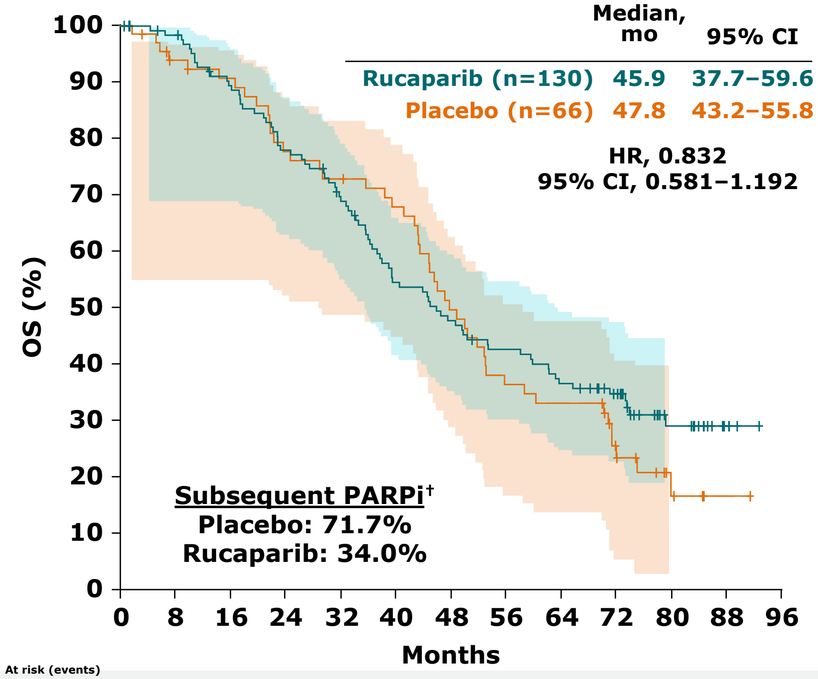
Summary of Subsequent Therapy

	BRCA mutant		HRD*		ITT	
	Rucaparib (n=130)	Placebo (n=66)	Rucaparib (n=236)	Placebo (n=118)	Rucaparib (n=375)	Placebo (n=189)
Patients without subsequent anticancer therapy, % (n)	**27.7 (36)**	**9.1 (6)**	**23.7 (56)**	**11.0 (13)**	**21.9 (82)**	**11.1 (21)**
Disposition of patients, % (n)†						
Ongoing	19.4 (7)	0	25.0 (14)	0	18.3 (15)	0
Died	30.6 (11)	33.3 (2)	26.8 (15)	38.5 (5)	31.7 (26)	38.1(8)
Other‡	50.0 (18)	66.7 (4)	48.2 (27)	61.5 (8)	50.0 (41)	61.9 (13)
Patients with ≥1 subsequent anticancer therapy, % (n)	**72.3 (94)**	**90.9 (60)**	**76.3 (180)**	**89.0 (105)**	**78.1 (293)**	**88.9 (168)**
No. subsequent regimens, % (n)§						
1	22.3 (21)	23.3 (14)	20.0 (36)	19.0 (20)	19.1 (56)	20.2 (34)
2	30.9 (29)	16.7 (10)	26.1 (47)	19.0 (20)	25.9 (76)	22.0 (37)
3	18.1 (17)	13.3 (8)	18.9 (34)	17.1 (18)	20.5 (60)	17.3 (29)
≥4	28.7 (27)	46.7 (28)	35.0 (63)	44.8 (47)	34.5 (101)	40.5 (68)
Median, No. (range)	2 (1–8)	3 (1–8)	3 (1–8)	3 (1–8)	3 (1–10)	3 (1–8)
Patients with subsequent PARP inhibitor containing regimen, % (n)§	**34.0 (32)**	**71.7 (43)**	**27.2 (49)**	**59.0 (62)**	**20.8 (61)**	**45.8 (77)**

Data cutoff date: 4 April 2022.
*Includes BRCA-mutant and BRCA wild-type/LOH-high groups. †Percentages are based on the number of patients without subsequent treatment reported. ‡Includes categories of withdrew consent, missing subsequent treatment data, discontinued on study but rolled over to receive treatment through rucaparib access programs or other mechanisms. §Percentages are based on the number of patients with subsequent treatment reported.
BRCA, *BRCA1* and *BRCA2*; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; PARP, poly(ADP-ribose) polymerase.

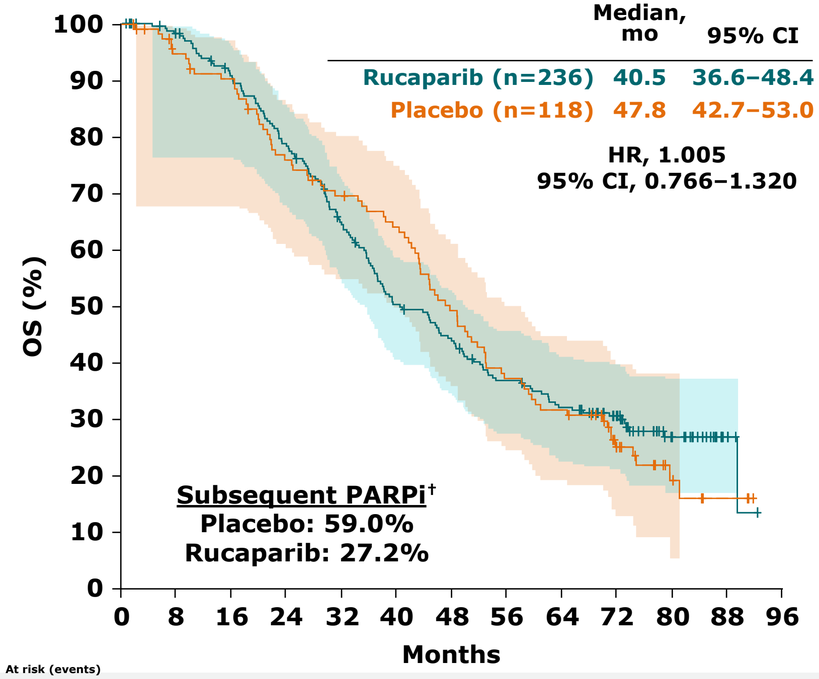
Final OS: Nested Cohorts

BRCA-Mutant Cohort



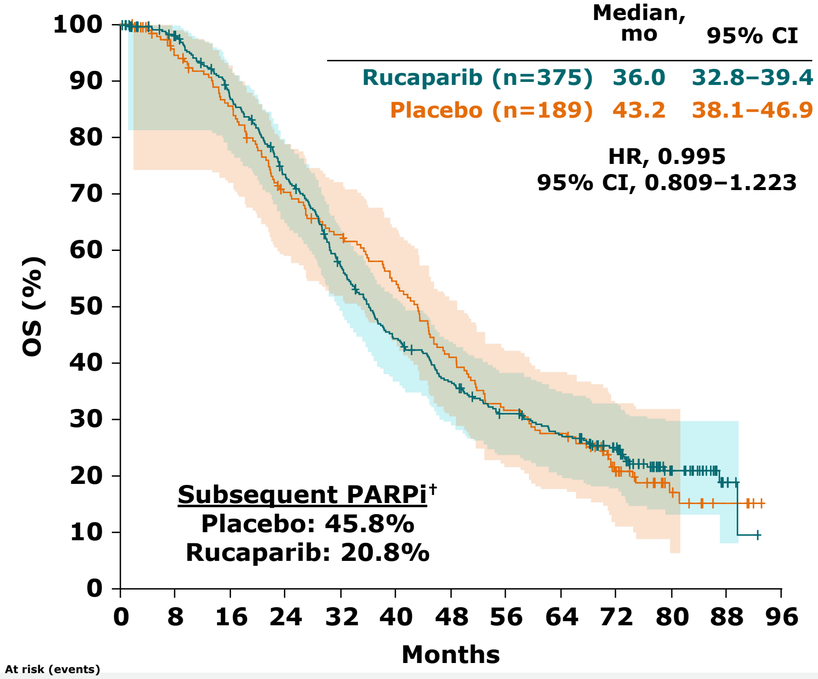
At risk (events)														
Rucaparib	130 (0)	123 (2)	110 (13)	96 (27)	84 (37)	65 (55)	57 (63)	50 (69)	43 (76)	35 (78)	15 (82)	4 (82)	0 (82)	
Placebo	66 (0)	59 (4)	56 (6)	48 (14)	45 (17)	41 (20)	30 (31)	22 (39)	20 (41)	11 (46)	4 (48)	1 (48)	0 (48)	

HRD Cohort*



At risk (events)														
Rucaparib	236 (0)	224 (4)	204 (21)	177 (48)	143 (79)	110 (111)	96 (124)	78 (140)	67 (150)	53 (153)	25 (158)	5 (158)	0 (159)	
Placebo	118 (0)	107 (6)	101 (11)	84 (27)	76 (34)	69 (40)	53 (56)	40 (69)	34 (75)	20 (81)	7 (84)	3 (85)	0 (85)	

ITT Population



At risk (events)														
Rucaparib	375 (0)	350 (8)	307 (47)	255 (96)	197 (151)	152 (195)	124 (221)	101 (240)	87 (252)	68 (259)	29 (268)	5 (269)	0 (270)	
Placebo	189 (0)	170 (10)	152 (26)	122 (53)	108 (66)	93 (80)	70 (103)	54 (119)	47 (126)	27 (136)	10 (139)	4 (140)	0 (140)	

- Nearly half (45.8%) of patients randomised to the placebo group received subsequent PARP inhibitor therapy

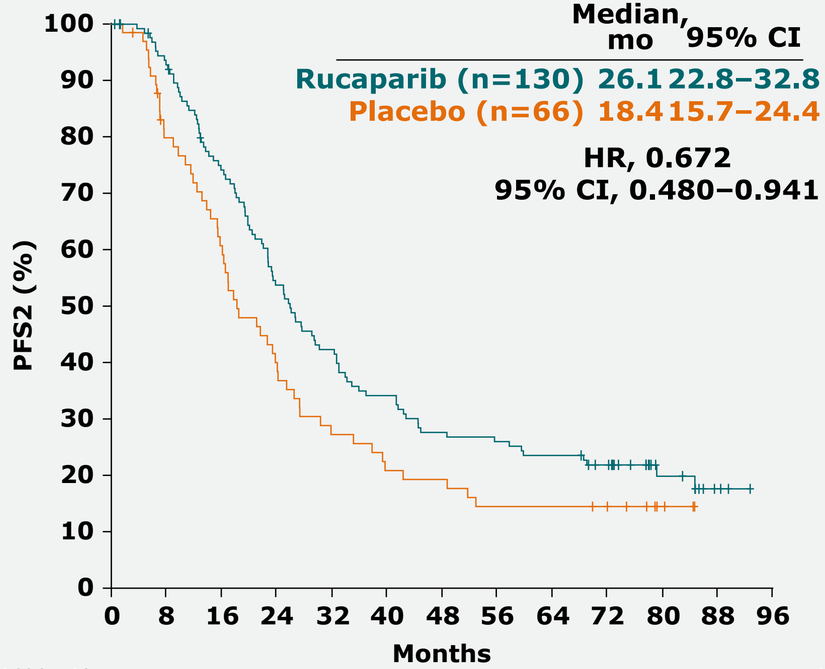
Data cutoff date: 4 April 2022.

***Includes BRCA-mutant and BRCA–wild-type/LOH-high groups. †Patients receiving a PARP inhibitor during any subsequent treatment.**

BRCA, *BRCA1* and *BRCA2*; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mo, months; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor.

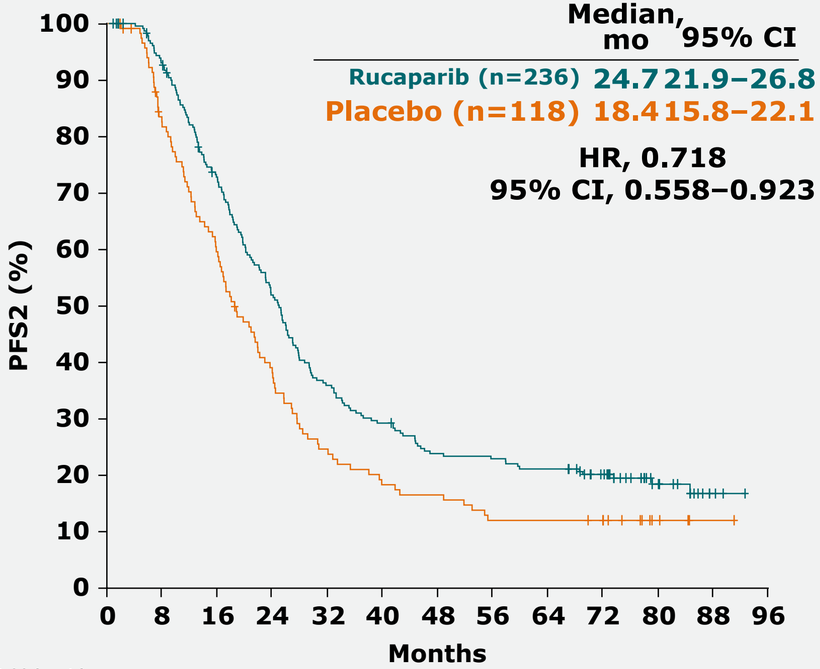
Post-progression Outcomes: PFS2 (Nested Cohorts)

BRCA-Mutant Cohort



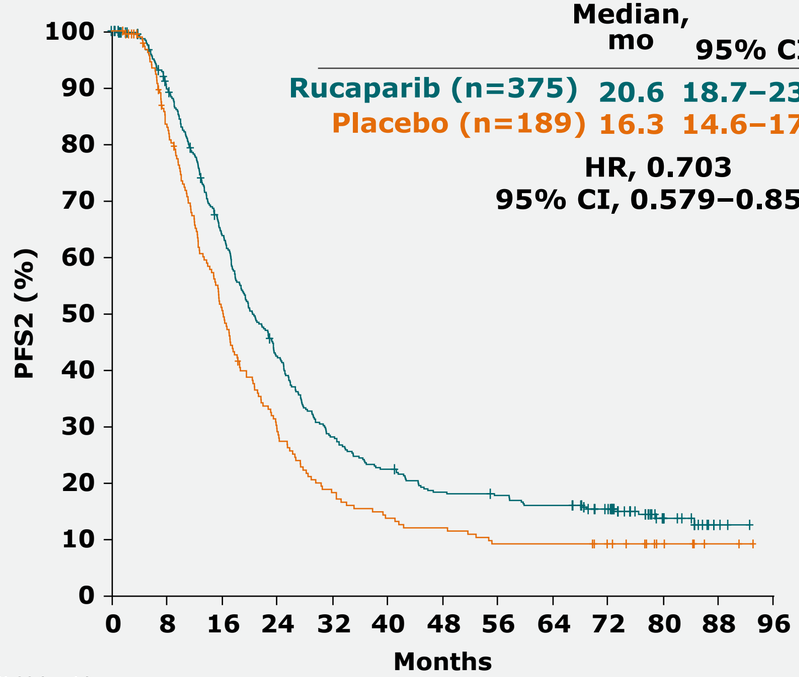
At risk (events)													
Rucaparib	130 (0)	117 (8)	92 (31)	66 (57)	52 (71)	42 (81)	34 (89)	32 (91)	29 (94)	24 (96)	10 (97)	3 (98)	0 (98)
Placebo	66 (0)	50 (13)	39 (25)	25 (38)	18 (45)	13 (50)	12 (51)	9 (54)	9 (54)	8 (54)	3 (54)	0 (54)	

HRD Cohort*



At risk (events)													
Rucaparib	236 (0)	211 (17)	161 (65)	115 (110)	80 (145)	65 (160)	52 (172)	50 (174)	46 (178)	36 (180)	16 (182)	3 (183)	0 (183)
Placebo	118 (0)	92 (21)	67 (47)	41 (71)	27 (85)	20 (92)	18 (94)	13 (99)	13 (99)	12 (99)	4 (99)	1 (99)	0 (99)

ITT Population



At risk (events)													
Rucaparib	375 (0)	324 (34)	228 (127)	149 (204)	99 (254)	79 (274)	64 (288)	61 (290)	55 (296)	44 (298)	19 (301)	3 (302)	0 (302)
Placebo	189 (0)	150 (30)	92 (88)	53 (125)	33 (145)	24 (154)	21 (157)	16 (162)	16 (162)	14 (162)	6 (162)	2 (162)	0 (162)

- Post-progression outcomes (PFS2, CFI, TFST, TSST) were similar to those previously reported at a data cutoff of December 31, 2017[1]

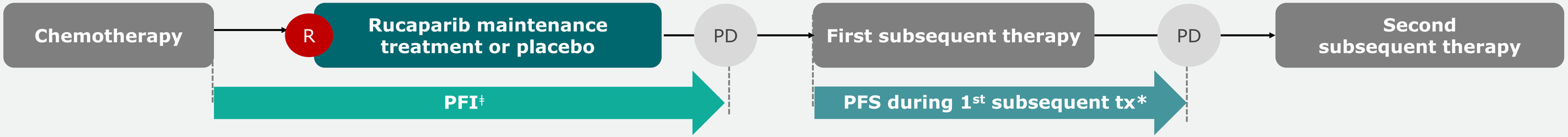
Data cutoff date: 4 April 2022.

***Includes BRCA-mutant and BRCA–wild-type/LOH-high groups.**

BRCA, *BRCA1* and *BRCA2*; CFI, chemotherapy-free interval; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mo, months; PFS2, progression-free survival on the subsequent line of therapy; TFST, time to start of first subsequent therapy; TSST, time to start of second subsequent therapy.

1. Ledermann et al. *Lancet Oncol*. 2020;21:710-22.

Exploratory Analysis of PFS During First Subsequent Platinum-Based Chemotherapy



	ITT Population			PFI ≤6 months			PFI 6–12 months			PFI >12 months		
	Event rate	Median, mo (95% CI)	Log-rank *P* value	Event rate	Median, mo (95% CI)	Log-rank *P* value	Event rate	Median, mo (95% CI)	Log-rank *P* value	Event rate	Median, mo (95% CI)	Log-rank *P* value
Rucaparib	163/174	7.0 (6.2–7.8)	<0.0001	30/30	5.4 (2.8–7.7)	0.2139	58/61	7.4 (6.1–8.6)	0.0056	75/83	7.1 (6.2–9.7)	0.0017
Placebo	61/76	11.3 (9.9–14.1)		14/16	8.3 (3.3–10.9)		38/46	11.3 (9.4–14.4)		9/14	18.5 (10.3–NA)	

- In the ITT population, 9.2% of patients in the rucaparib group and 25.0% in the placebo group received a PARP inhibitor maintenance therapy following their first subsequent platinum-based chemotherapy

Data cutoff date: 4 April 2022.
*Progression free survival from the start of first subsequent therapy to disease progression. ‡From date of last chemotherapy prior to randomisation to date of PD on ARIEL3 treatment. CI, confidence interval; ITT, intent-to-treat; mo, months; NA, not applicable; PD, disease progression; PFI, progression-free interval; PFS, progression-free survival; R, randomisation.

Overall survival by number of prior lines of chemotherapy in patients with BRCA-mutated platinum-sensitive relapsed ovarian cancer receiving olaparib treatment or non-platinum chemotherapy in SOLO3

Charles A. Leath III,[1] Giovanni Scambia,[2] Ricardo Villalobos Valencia,[3] Nicoletta Colombo,[4] David Cibula,[5] Mariusz Bidziński,[6] Jae-Weon Kim,[7] Joo Hyun Nam,[8] Radoslaw Madry,[9] Carlos Hernandez,[10] Paulo Mora,[11] Sang Young Ryu,[12] Mei-Lin Ah-See,[13] Elizabeth S. Lowe,[14] Natalia Lukashchuk,[15] Dave Carter,[16] Richard T. Penson[17]

[1]Division of Gynecologic Oncology, O'Neal Comprehensive Cancer Center, University of Alabama, Birmingham, AL, USA; [2]Division of Gynecologic Oncology, Università Cattolica del Sacro Cuore-Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy; [3]Department of Medical Oncology, Centro Medico Dalinde, Mexico City, Mexico; [4]Division of Gynecologic Oncology, University of Milan-Bicocca and IEO European Institute of Oncology IRCCS, Milan, Italy; [5]Gynecologic Oncology Center, Department of Obstetrics and Gynecology, First Faculty of Medicine, Charles University and General University, Prague, Czech Republic; [6]Department of Gynecologic Oncology, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [7]Department of Obstetrics and Gynecology, Seoul National University Hospital, Seoul, South Korea; [8]Department of Obstetrics and Gynecology, Asan Medical Center, Seoul, South Korea; [9]Department of Gynecological Oncology, Medical University K. Marcinkowski and the Clinical Hospital of the Transfiguration, Poznań, Poland; [10]Oaxaca Site Management Organization, Oaxaca de Juarez, Mexico; [11]Instituto COI de Educação e Pesquisa, Rio de Janeiro, Brazil; [12]Department of Obstetrics and Gynecology, Korea Institute of Radiological and Medical Sciences, Seoul, South Korea; [13]Oncology R&D, Late-stage Development, AstraZeneca, Cambridge, UK; [14]Global Medicines Development, Oncology, AstraZeneca, Gaithersburg, MD, USA; [15]Translational Medicine, Oncology R&D, AstraZeneca, Cambridge, UK; [16]Biostatistics, Oncology Biometrics, Oncology R&D, AstraZeneca, Cambridge, UK; [17]Division of Hematology and Oncology, Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA

Scan for:

- **Slides**

GOG FOUNDATION®

GOG Highlight Reel

Study Design

N=266

- Relapsed, high-grade serous or endometrioid ovarian, primary peritoneal and/or fallopian tube cancer
  - gBRCAm
- ECOG performance status 0–2
  - ≥2 previous lines of PBC
- No prior PARP inhibitor therapy
  - Platinum sensitive

Olaparib tablets 300 mg bid (N=178)

Non-platinum chemotherapy† (N=88)
- PLD (n=47)
- Paclitaxel (n=20)
- Gemcitabine (n=13)
- Topotecan (n=8)

2:1 randomization, open-label

Stratification factors:
- Selected chemotherapy* (PLD vs paclitaxel vs gemcitabine vs topotecan)
- Number of prior lines of chemotherapy (2 or 3 vs ≥ 4)
- Time to progression after previous PBC (6–12 months vs >12 months)

Study treatment until disease progression

Primary endpoint
- ORR by BICR (RECIST v1.1)

Secondary endpoints

Included:
- OS
- PFS by BICR
- PFS2
- TFST
- TSST
- TDT
- HRQoL
- Safety

Primary ORR analysis DCO: October 10, 2018

Final OS analysis DCO: April 16, 2021

- First patient enrolled: February 24, 2015
- Last patient enrolled and randomized to receive study treatment: April 10, 2018

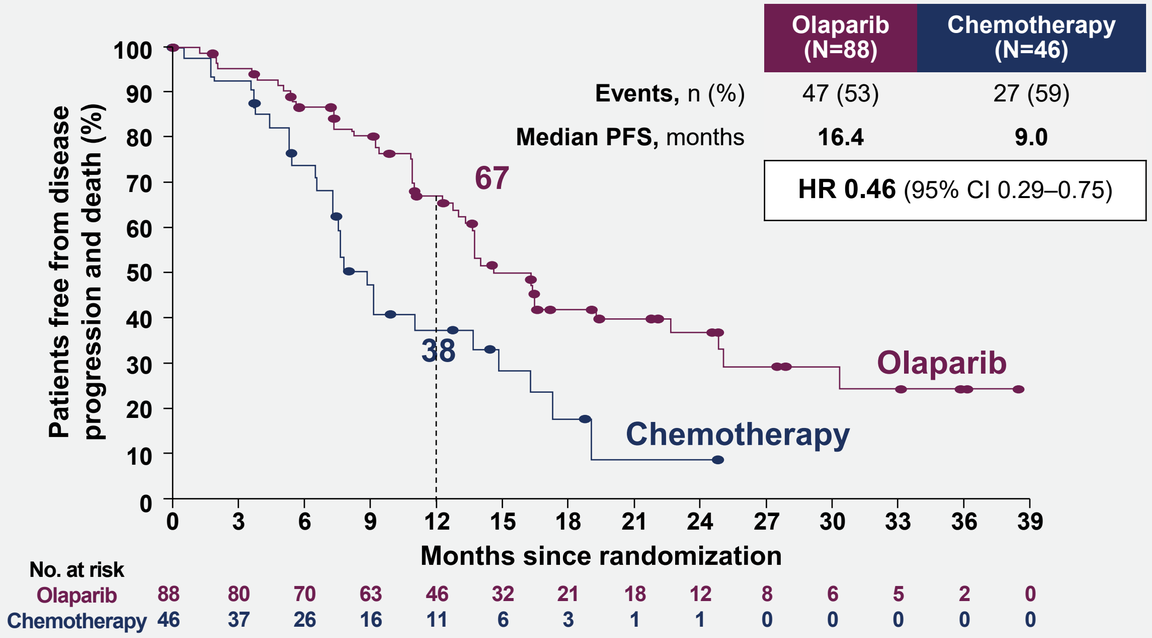
*For each patient, the investigator declared their choice of non-platinum chemotherapy before randomization;
†PLD, 50 mg/m^2 on Day 1 q4w; paclitaxel, 80 mg/m^2 on Days 1, 8, 15, and 22 q4w; gemcitabine, 1000 mg/m^2 on Days 1, 8, and 15 q4w; topotecan, 4 mg/m^2 on Days 1, 8, and 15 q4w.

BICR, blinded independent central review; bid, twice daily; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; PARP, poly(ADP-ribose) polymerase; PFS2, second progression-free survival; PLD, pegylated liposomal doxorubicin; q4w, every 4 weeks; RECIST, Response Evaluation Criteria In Solid Tumors; TDT, time to treatment discontinuation or death; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death.

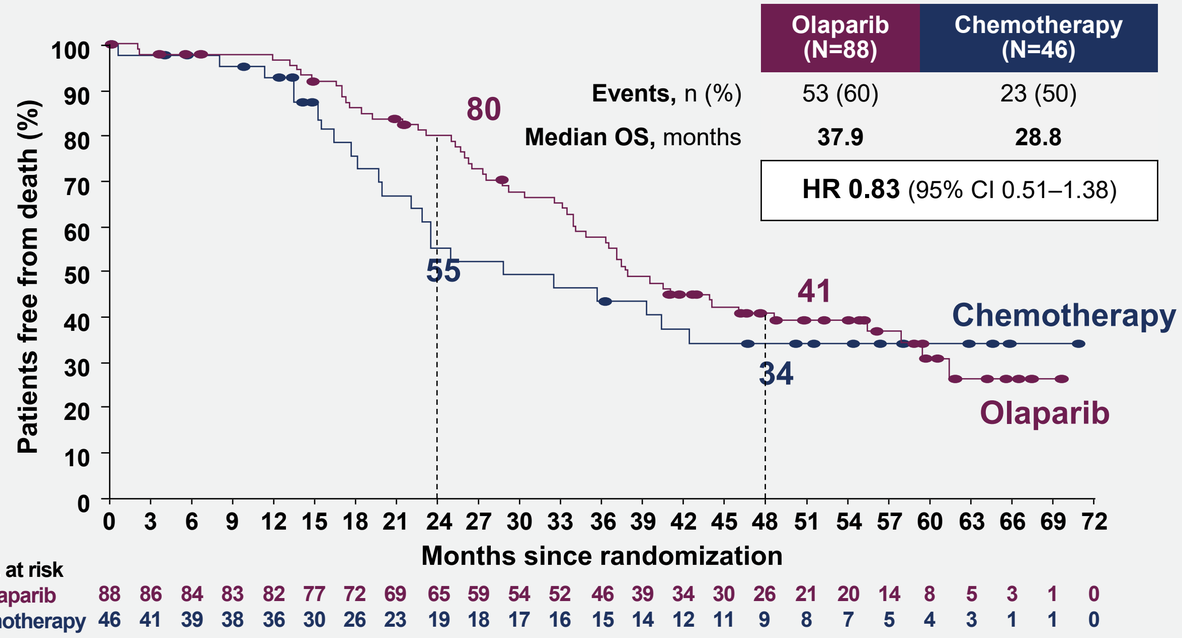
Post hoc subgroup: 2 prior lines of chemotherapy

PFS and OS favored olaparib over chemotherapy

PFS



OS

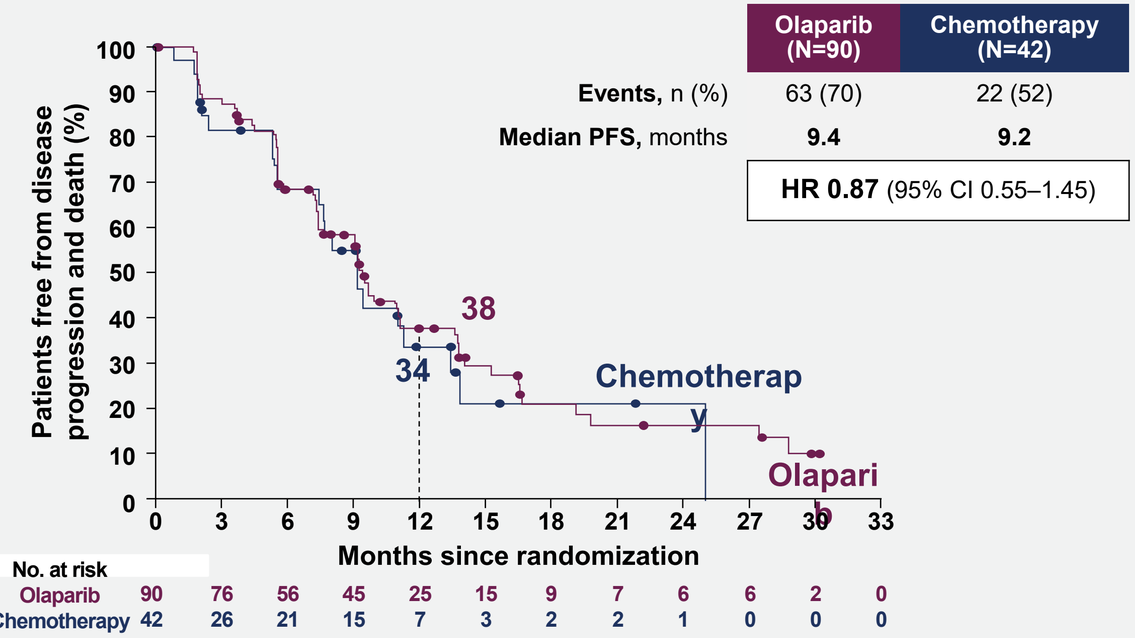


PFS DCO: October 10, 2018; **OS DCO**: April 16, 2021.

Post hoc subgroup: ≥3 prior lines of chemotherapy

PFS numerically favored olaparib over chemotherapy; however, OS favored chemotherapy over olaparib

PFS

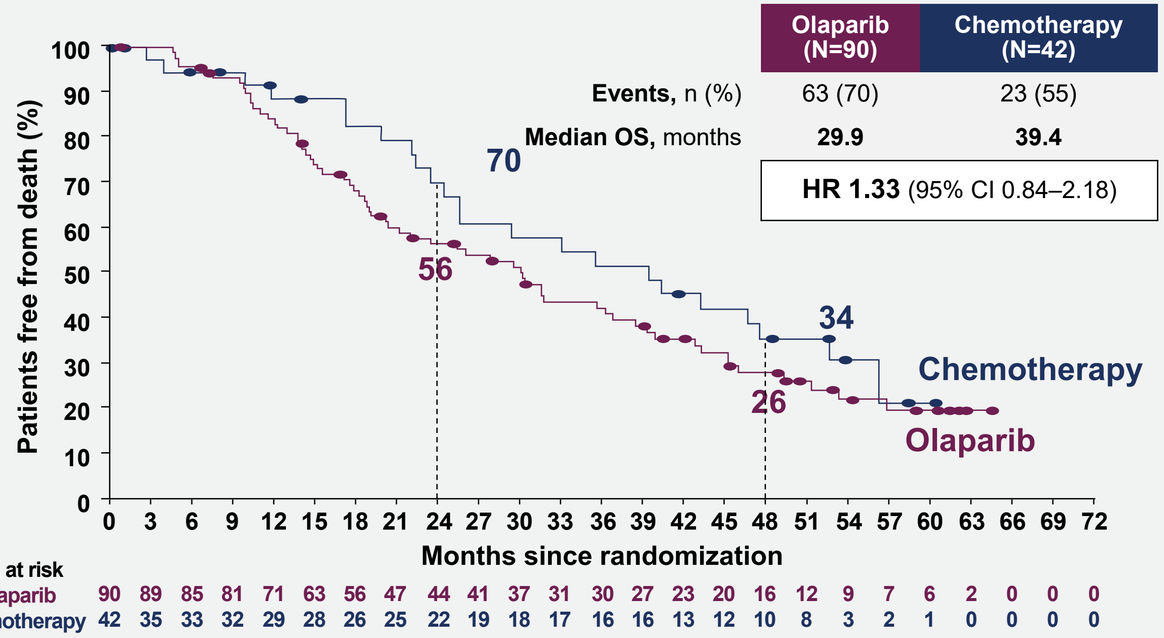


	Olaparib (N=90)	Chemotherapy (N=42)
Events, n (%)	63 (70)	22 (52)
Median PFS, months	**9.4**	**9.2**

HR 0.87 (95% CI 0.55–1.45)

No. at risk												
Olaparib	90	76	56	45	25	15	9	7	6	6	2	0
Chemotherapy	42	26	21	15	7	3	2	2	1	0	0	0

OS



	Olaparib (N=90)	Chemotherapy (N=42)
Events, n (%)	63 (70)	23 (55)
Median OS, months	**29.9**	**39.4**

HR 1.33 (95% CI 0.84–2.18)

No. at risk																									
Olaparib	90	89	85	81	71	63	56	47	44	41	37	31	30	27	23	20	16	12	9	7	6	2	0	0	0
Chemotherapy	42	35	33	32	29	28	26	25	22	19	18	17	16	16	13	12	10	8	3	2	1	0	0	0	0

PFS DCO: October 10, 2018; **OS DCO**: April 16, 2021.

Summary of efficacy results

2 prior lines of chemotherapy	Favorable OS and PFS with olaparib vs chemotherapy supported by ORR
≥3 prior lines of chemotherapy	PFS and ORR numerically favored olaparib vs chemotherapy; however, OS favored chemotherapy vs olaparib

	OS				PFS			ORR	
		Median OS, months			Median PFS, months			ORR,† %	
Subgroup	HR (95% CI)*	Olaparib	Chemo-therapy	HR (95% CI)	Olaparib	Chemo-therapy	HR (95% CI)	Olaparib	Chemo-therapy
All patients		34.9	32.9	**1.07** (0.76–1.49)	13.4	9.2	**0.62** (0.43–0.91)	72.2	51.4
2 prior lines of chemotherapy		37.9	28.8	**0.83** (0.51–1.38)	16.4	9.0	**0.46** (0.29–0.75)	85.5	60.5
3 prior lines of chemotherapy		25.2	32.9	**1.20** (0.66–2.29)	11.1	7.4	**0.43** (0.24–0.80)	67.6	31.8
≥3 prior lines of chemotherapy		29.9	39.4	**1.33** (0.84–2.18)	9.4	9.2	**0.87** (0.55–1.45)	58.7	41.2
≥4 prior lines of chemotherapy		30.2	43.2	**1.58** (0.77–3.69)	7.4	NC	**2.92** (1.17–9.78)	50.0	58.3

OS DCO: April 16, 2021. PFS and ORR DCO: October 10, 2018.

*The analysis in all patients was performed using a stratified log-rank test with factors as recorded in Interactive Voice Response System for time to disease progression after the end of last PBC (6–12 months vs > 12 months) in the full analysis set. The analysis in the prior line of chemotherapy subgroups was performed using a single Cox proportional hazards model containing the treatment term, the subgroup covariate of interest and the treatment by subgroup interaction for each subgroup. Size of circle is proportional to the number of events. Blue band represents the 95% CI for the overall (all patients) HR;

†Unconfirmed ORR is based on BICR in the measurable disease population.

NC, not calculable.

PARIS 2022 ESMO congress

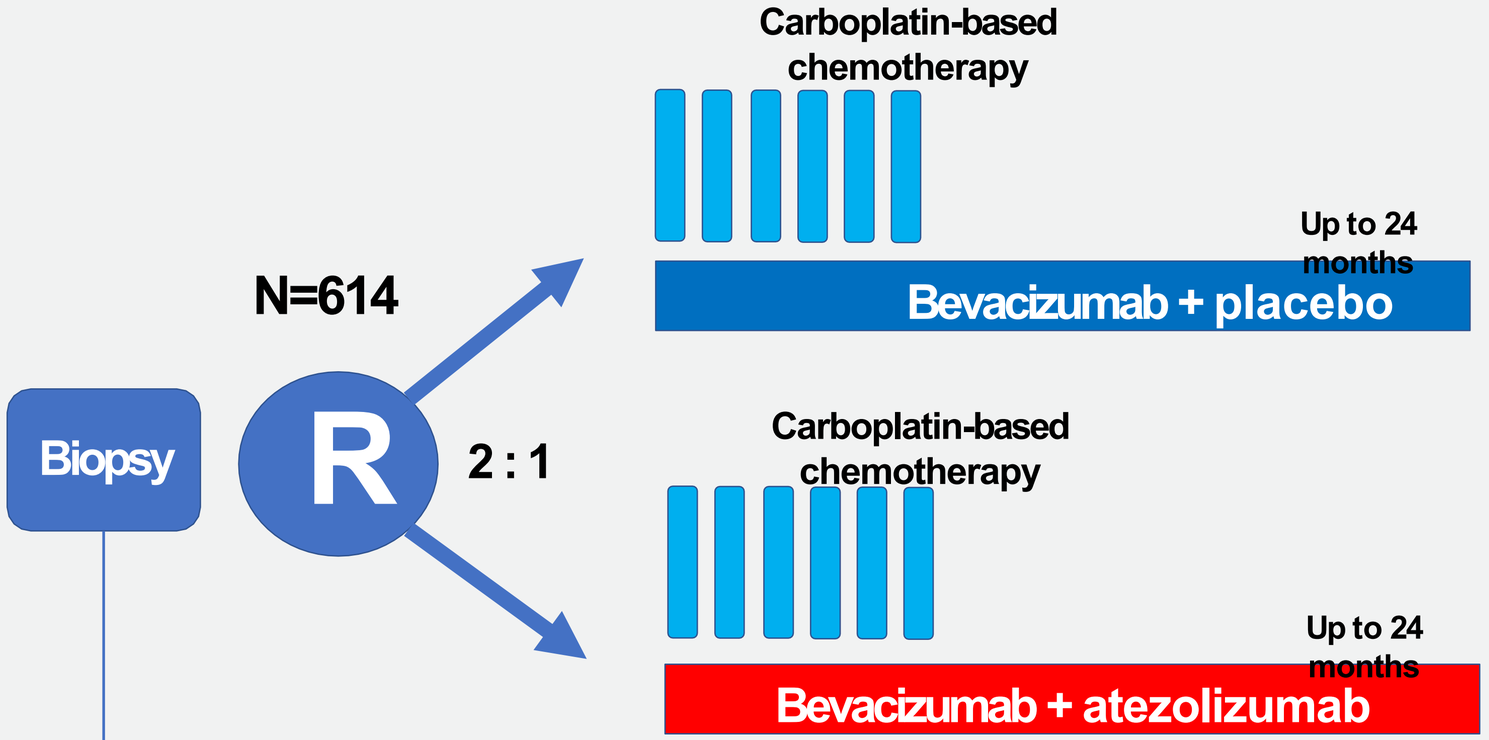
ATALANTE
Atezolizumab and Avastin
in late recurrent disease

A randomized, double-blinded, phase III study of atezolizumab versus placebo in patients with late relapse of epithelial ovarian, fallopian tube, or peritoneal cancer treated by platinum-based chemotherapy and bevacizumab. GINECO-OV236b/ENGOT-ov29

J.E. Kurtz, E. Pujade-Lauraine, A. Oaknin, L. Belin, I. Tsibulak, D. Cibula, I. Vergote, O. Rosengarten, M. Rodrigues, N. de Gregorio, J. Martinez-Garcia, P. Pautier, M.A. Mouret Reynier, F. Selle, V. D'Hondt, F. Joly Lobbedez, E. Bultot Boissier, A. Floquet, P.-E. Heudel, F. Heitz

ATALANTE

- Relapsed non-mucinous epithelial OC
- Platinum-free interval >6 mos
- 1 or 2 prior chemotherapy lines
- ECOG PS ≤1



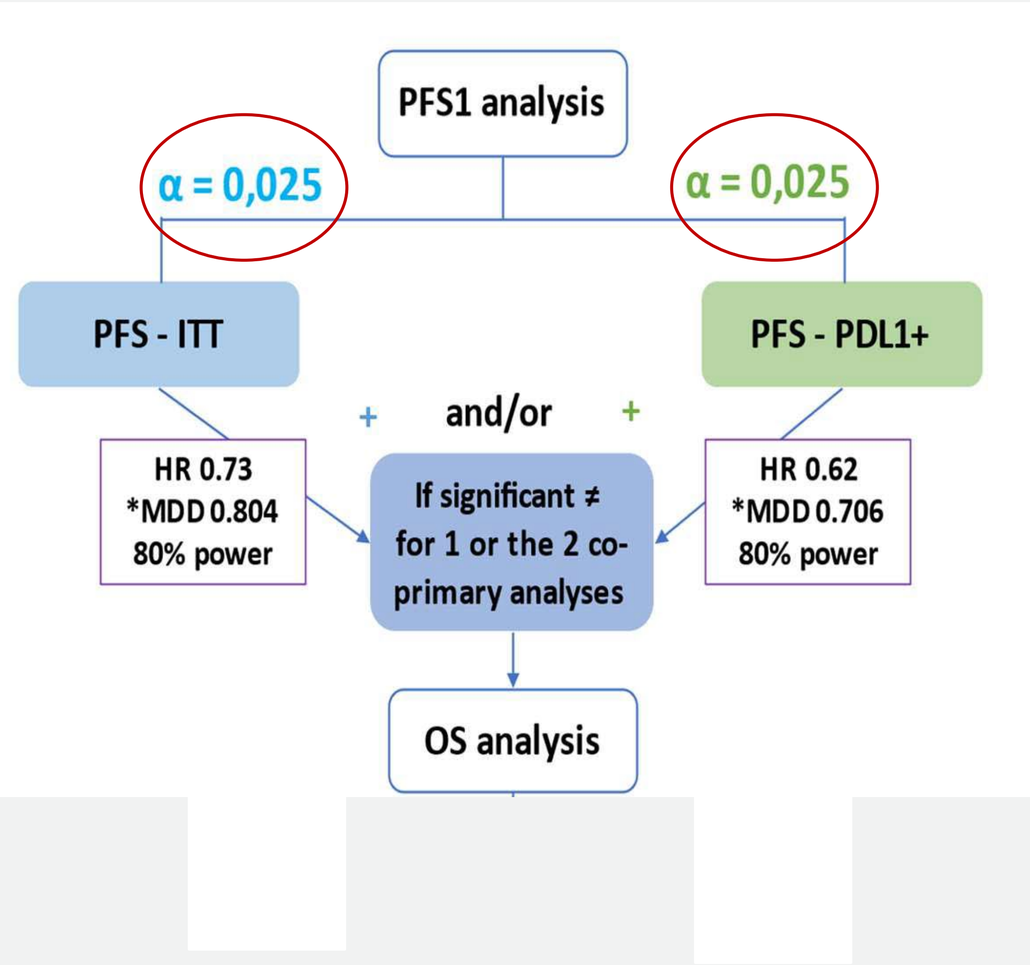
Stratification factors

- PD-L1 ≥ 1% on immune cells vs <1% vs unknown (Ventana clone SP142)
- Chemotherapy: Cb-PLD or gemcitabine or paclitaxel
- Platinum-free interval: 6-12 vs >12 months

- Co-primary endpoints are progression-free survival (PFS1) according to investigator in the ITT and PD-L1-positive populations
- Secondary endpoints: TSST, TFST, OS, safety (NCI CTCAE V 4.03) and HrQoL (EORTC QLQ-C30, QOLQ OV-28, EQ5D-5L)

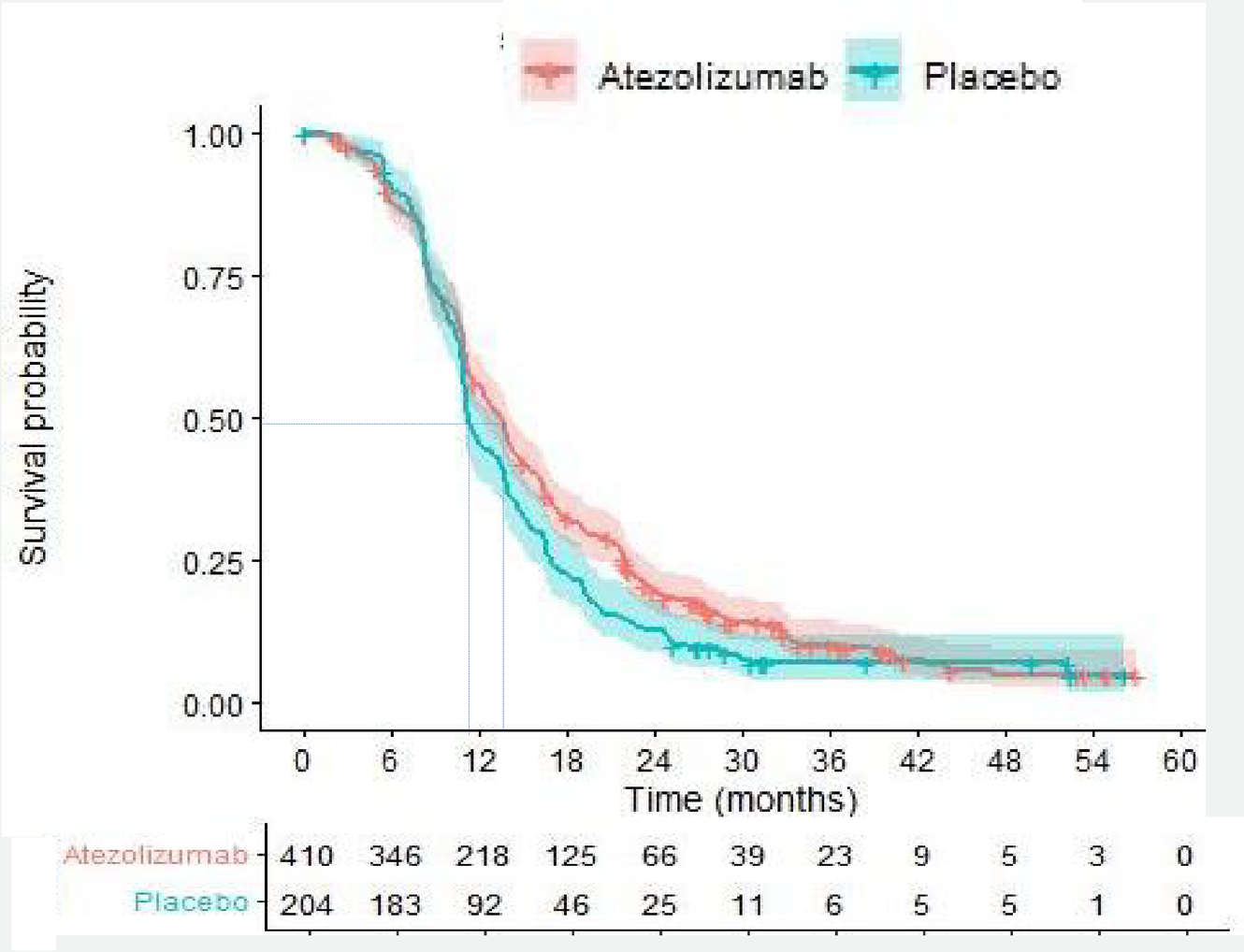
Statistical Considerations

- PFS1 was analyzed using a Cox model adjusted by stratification factors with a two-sided α level at 0.025 and 80% power for each PFS co-primary in the ITT and PD-L1-positive populations
- 491 events in the ITT and 186 in the PD-L1-positive populations were expected to show a reduction in the risk of progression of 27% (difference of median PFS1 of 4.8 months) and of 38% (difference of median PFS1 of 9.0 months), respectively
- Following a hierarchical approach, if either of the co-primary PFS1 comparisons was significant, overall survival could then be analyzed in both the ITT and PD-L1-positive populations



*MDD=Minimal Detectable Difference

Progression-free survival (ITT)

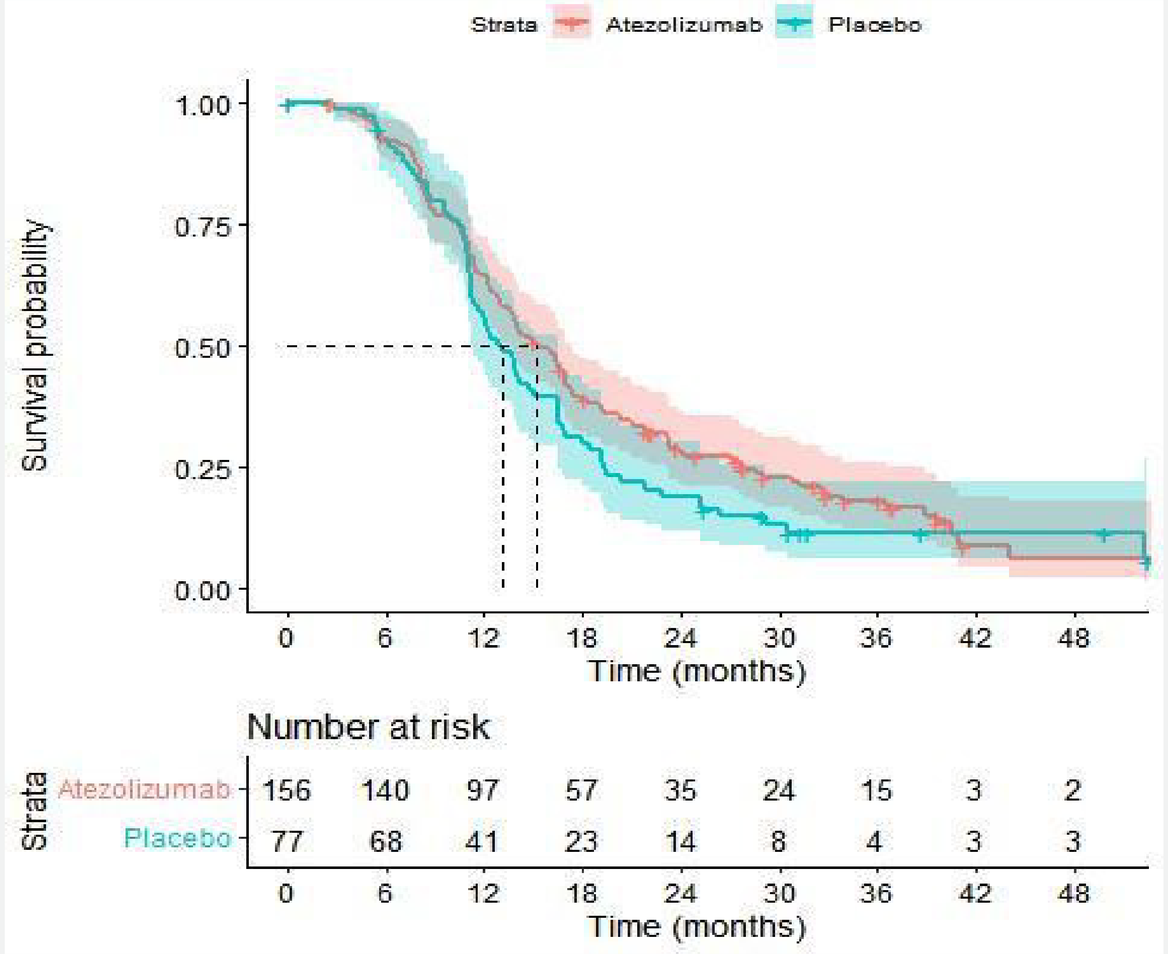


Treatment Arm	N	Event N (%)	PFS at 6m % (95% CI)	PFS at 12m % (95% CI)	PFS at 18m % (95% CI)	Median PFS (95% CI)
Atezo	410	348 (85)	88 (85-91)	56 (51- 61)	32 (28-37)	**13.5 mos** (12.2-14.2)
Placebo	204	187 (92)	91 (87- 95)	46 (39- 53)	23 (18-30)	**11.3 mos** (11.0-13.5)
		Hazard ratio= 0.83 [0.69-0.99]				**P=.041**

median follow-up : 36.6 months

The ATALANTE trial did not meet its primary objective: PFS1 in the ITT population

PFS in the PD-L1 positive population

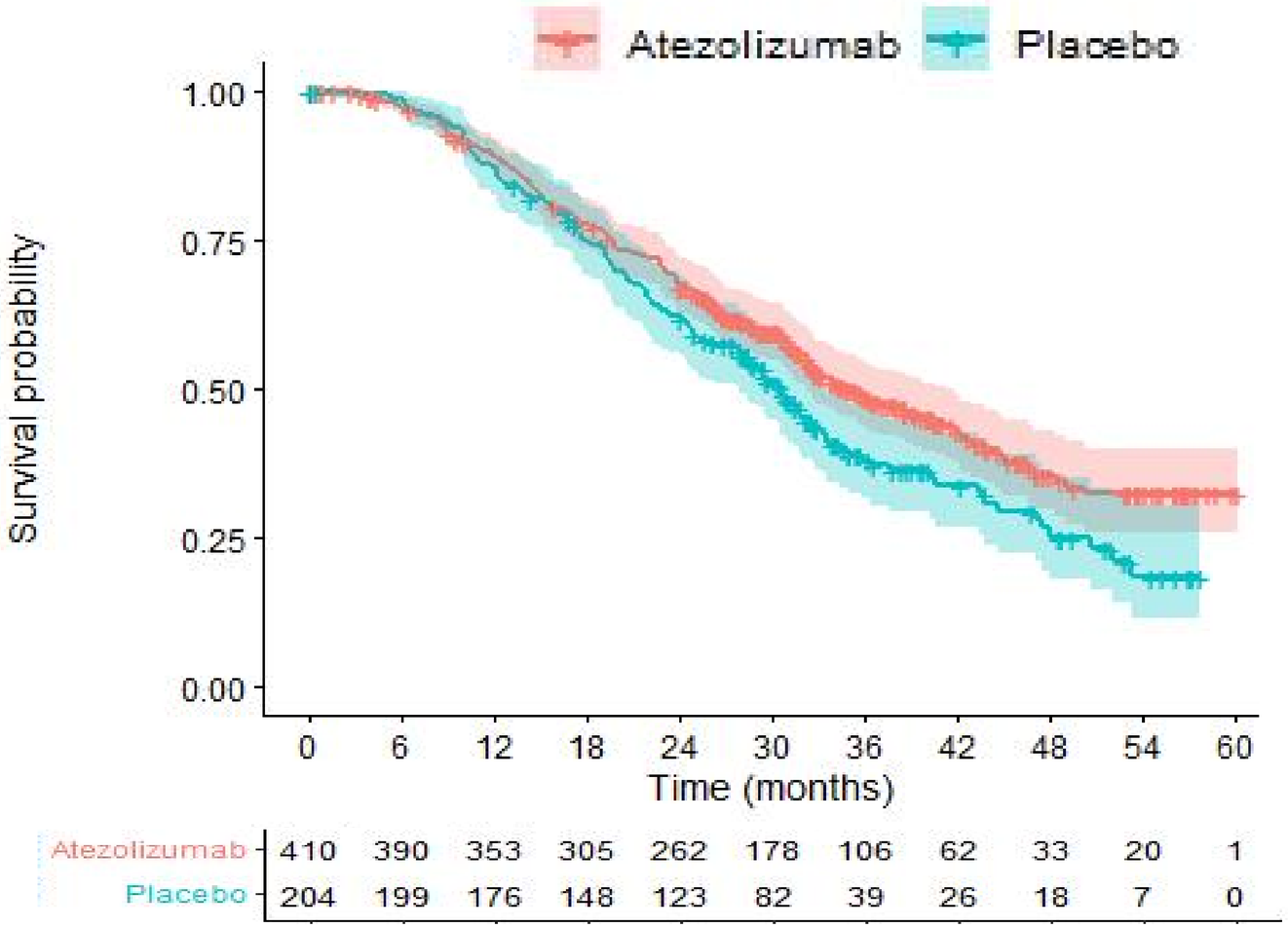


Treatment Arm	N	Events N (%)	PFS at 6m % (95% CI)	PFS at 12m % (95% CI)	PFS at 18m % (95% CI)	Median PFS (95% CI)
Atezo	156	124 (79)	93 (89-97)	64 (57- 72)	39 (32-47)	**15.2 mos** (13.6-17.3)
Placebo	77	66 (86)	92 (86- 98)	55 (45- 68)	31 (22-44)	**13.1 mos** (11.3-16.5)
		Hazard ratio= 0.86 [0.63-1.16]				***P*=.30**

The ATALANTE trial did not meet its co-primary objective:

PFS1 in the PD-L1 positive population

Overall Survival (ITT)



Treatment Arm	N	Events N (%)	Median OS (95% CI)
Atezo	410	207 (51)	**35.5 mos** (32.4-41.3)
Placebo	204	126 (62)	**30.6 mos** (27.9-33.6)
	Hazard ratio= 0.81 [0.65-1.01]		

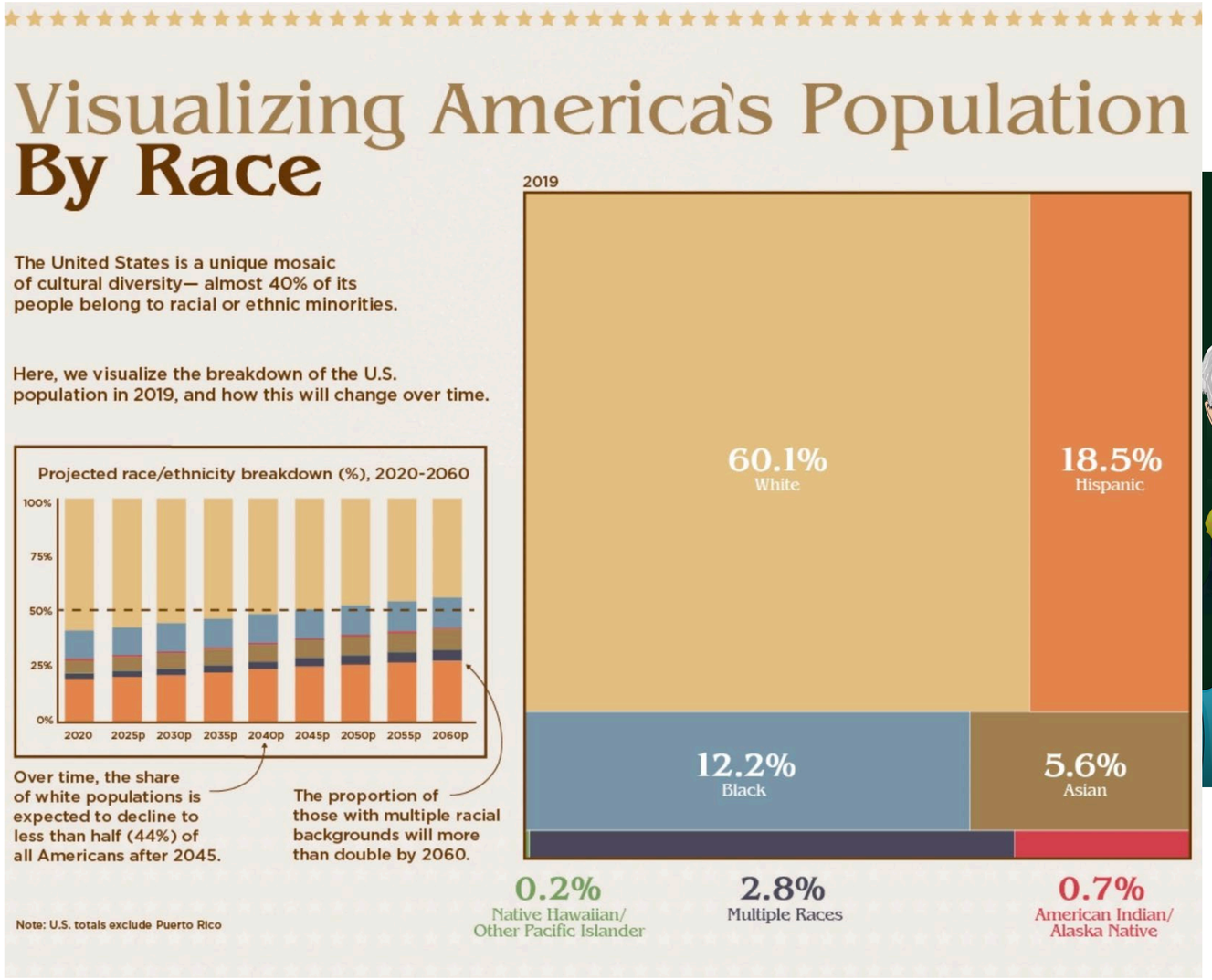
- **Overall survival data not mature (333 events out of 491 expected): longer follow-up needed**
- **Trend in favor of the atezolizumab arm in the ITT population**

GOG FOUNDATION

GOG Highlight Reel

Discussion

2020 United States Census Data



Source: Visualizing the US Population by Race, visualcapitalist.com

Disparity in Phase 1 gynecologic oncology clinical trials

Race of participants in gynecologic oncology phase 1 clinical trials according to cancer.

Cancer site	White	Black	Other	Total
Ovary	1559 (88)	73 (4)	147 (8)	1779 (100)
Cervix	263 (48)	54 (10)	227 (42)	544 (100)
Endometrium	37 (63)	9 (15)	13 (22)	59 (100)
Multiple	91 (90)	4 (4)	6 (6)	101 (100)
Total	1950 (79)	140 (6)	393 (16)	2483 (100)[a]

Relation between race of participants and disease incidence in gynecologic oncology phase 1 clinical trials.

	CDC white incidence per 1000	CDC black incidence per 1000[a]	Expected W:B ratio	Observed white (n)	Observed black (n)	Observed W:B ratio	Difference in ratios
Ovary	13.1	9.7	1 to 0.74	1559	73	1 to 0.04	18.5-fold
Endometrial	24.5	21.2	1 to 0.87	37	9	1 to 0.24	3.6-fold
Cervix	7.9	10.7	1 to 1.35	263	54	1 to 0.2	6.8-fold

[a] Comparison between white vs black participants; other races excluded.

Awad E, Paladugu R, Jones N, et. Al Gynecol Oncol. 2020 Jun;157(3):729-732. doi: 10.1016/j.ygyno.2020.03.002. Epub 2020 Mar 13. PMID: 32173047.

New FDA Guidance on “Diversity Plans to Improve Enrolment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials; Guidance for Industry”

1 Diverse groups need to be a part of the study to evaluate whether a study drug is effective and safe for everyone who will be administered study drug, or what side effects might emerge in one ethnic group or another

2 Sponsors must present effectiveness and safety data by gender, age, and ethnic group (eg, race, ethnicity, ancestry) and must identify any modifications of dose or dose interval needed for a specific subgroup, as applicable

3 Sponsors should discuss their strategy to enrol a diverse study population at any time throughout the medical product’s development

4 A Diversity Plan is required for clinical studies intended to support a marketing submission for a standalone BLA

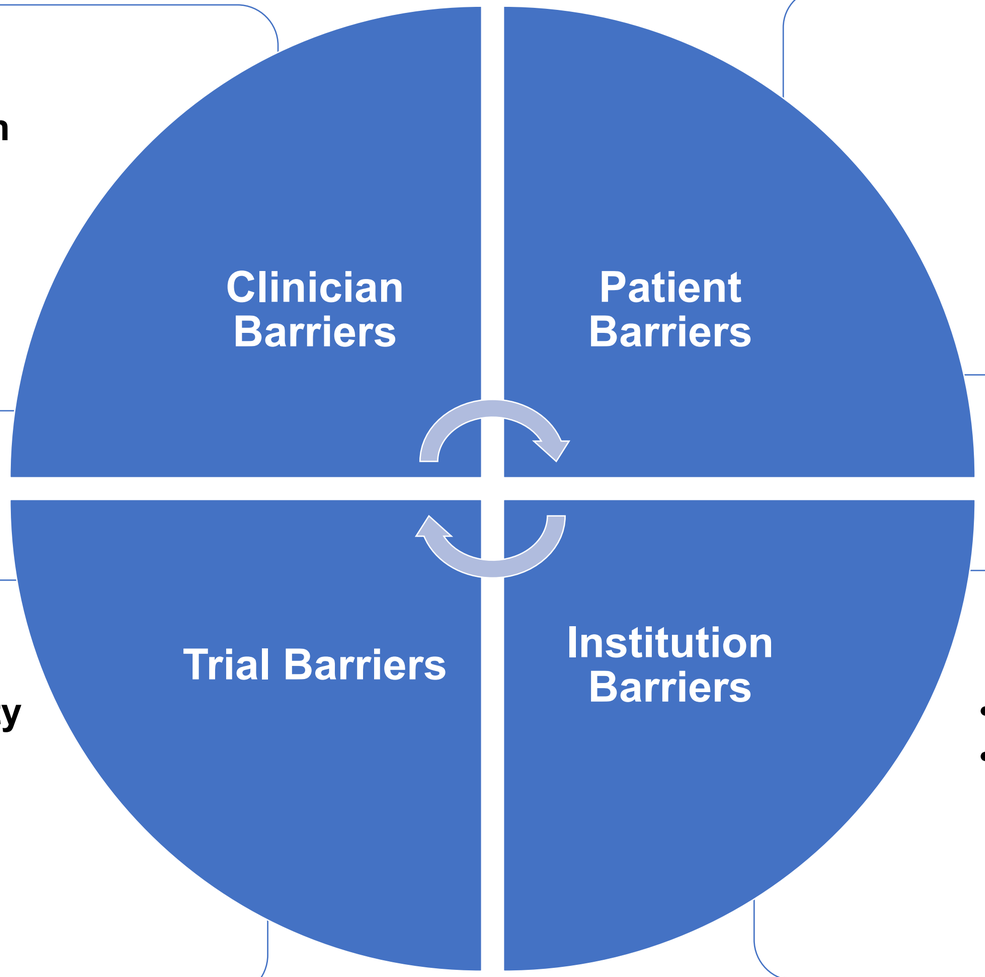
Federal Legislation passed incentives to review barriers and develop new policies for advancing equity in FDA’s Actions in June 2022*

https://www.fda.gov/media/157635/download

* Hwang and Brawley. 2022, NEJM, New Federal Incentives for Diversity in Clinical Trials

Barriers to Achieving DEI in Clinical Trials

- Bias
- Limited time, personnel to search for trials



- Limited info
- Financial barriers
- Distrust
- Language

- Restrictive eligibility criteria
- Numerous visits

- Access to trials
- Diversity of research staff

Trends in Clinical Trial Accrual of Underrepresented Patients with Gynecologic Malignancy

Hannah Charli Karpel, MS[1], Olivia Lara, MD[2], Michelle Lightfoot, MD, MPH[2,3], Bhavana Pothuri, MD, MS[2,3]

[1]NYU Grossman School of Medicine, [2]NYU Langone Health,

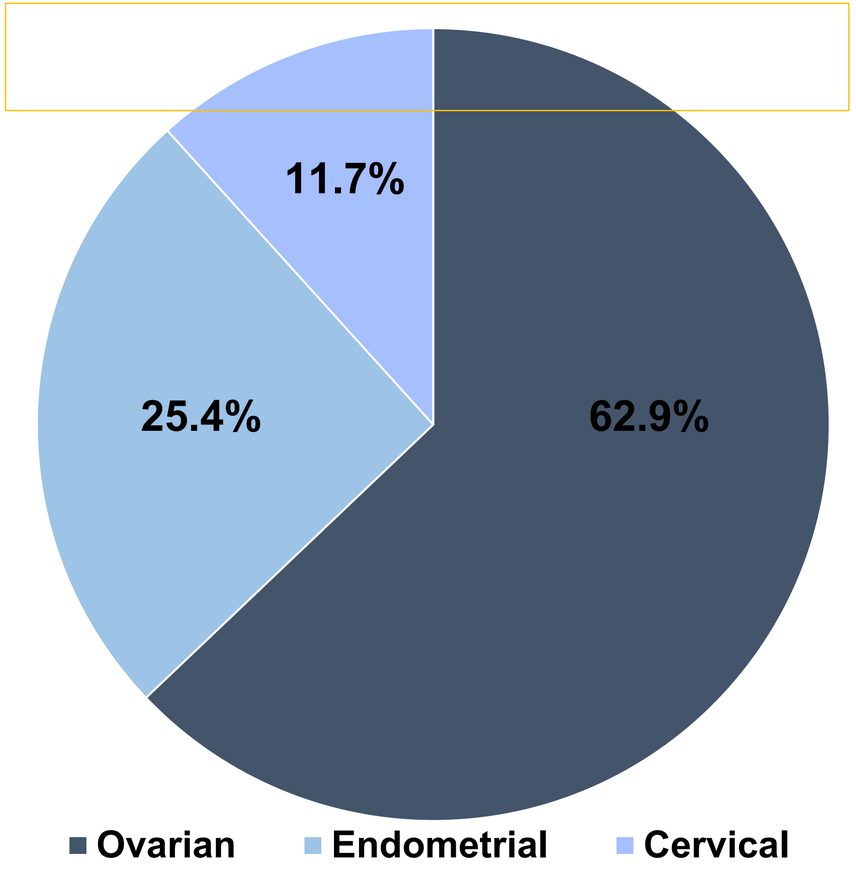
[3]Perlmutter Cancer Center

GOG FOUNDATION

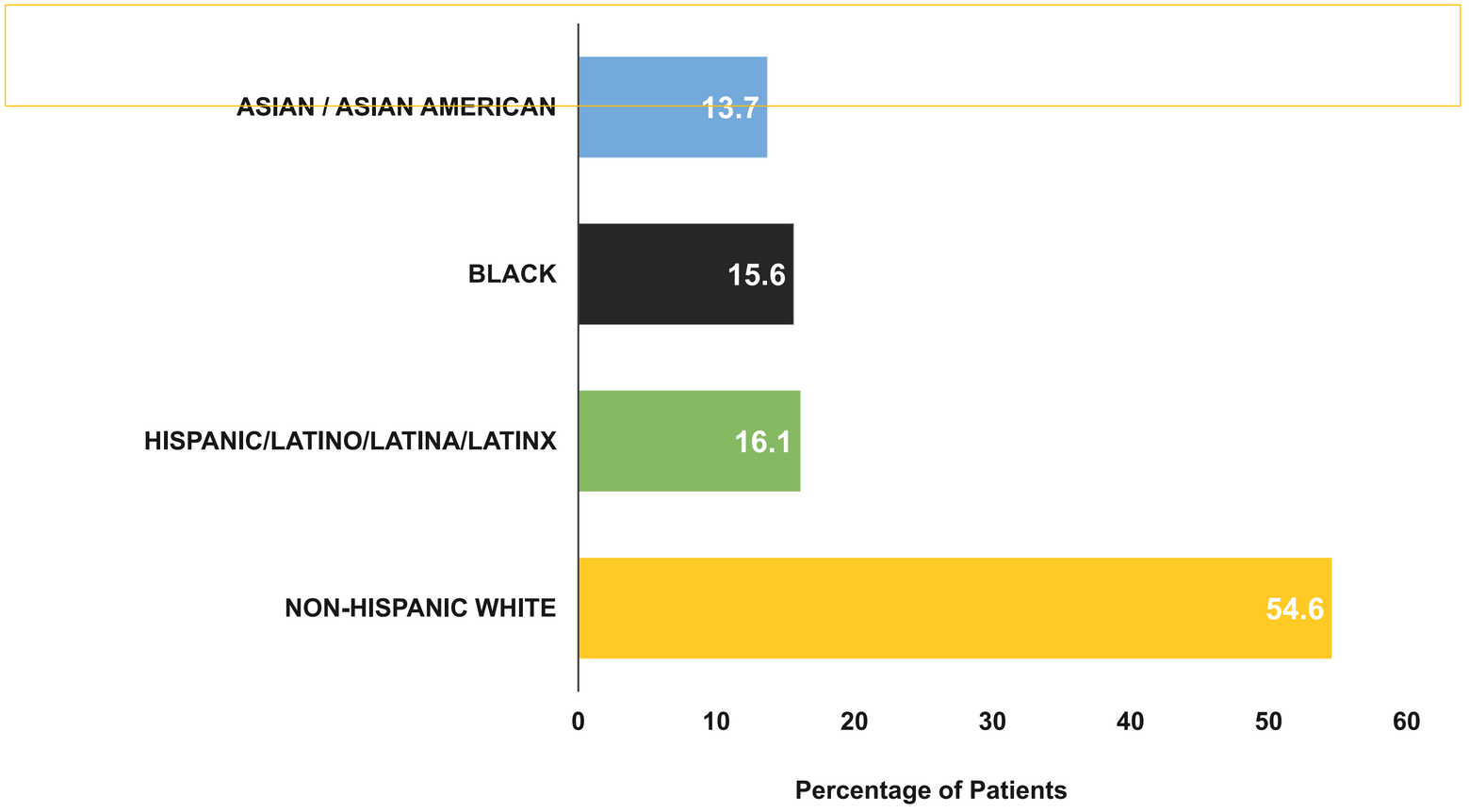
GOG Highlight Reel

Clinical Trial Characteristics

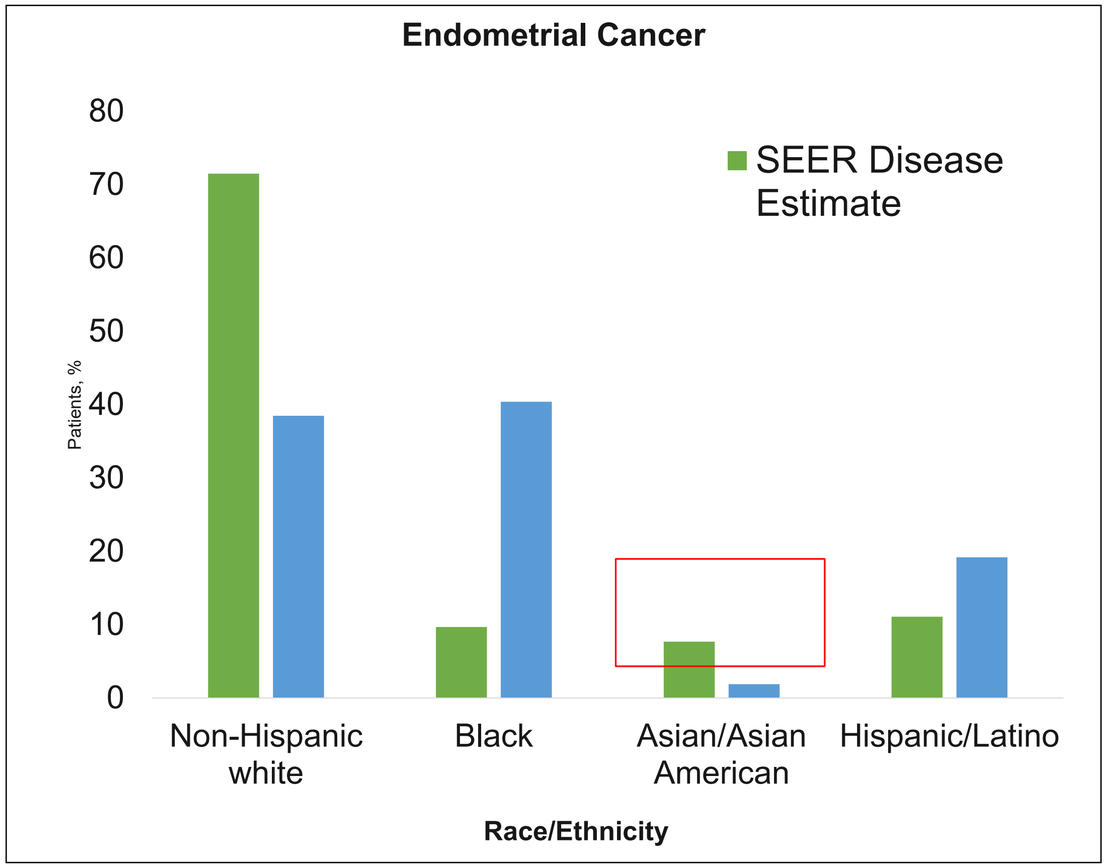
Disease Sites

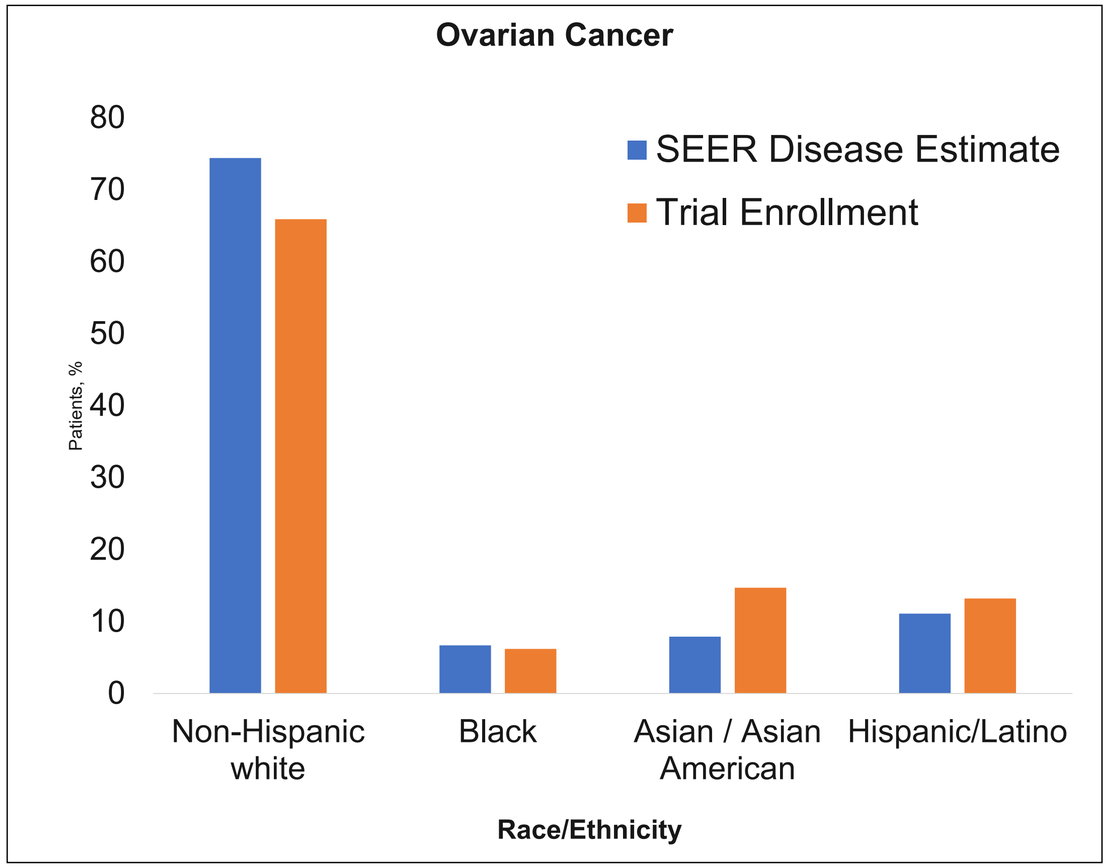


Race and Ethnicity



Trial Enrollment and Disease Estimate by Race and Ethnicity





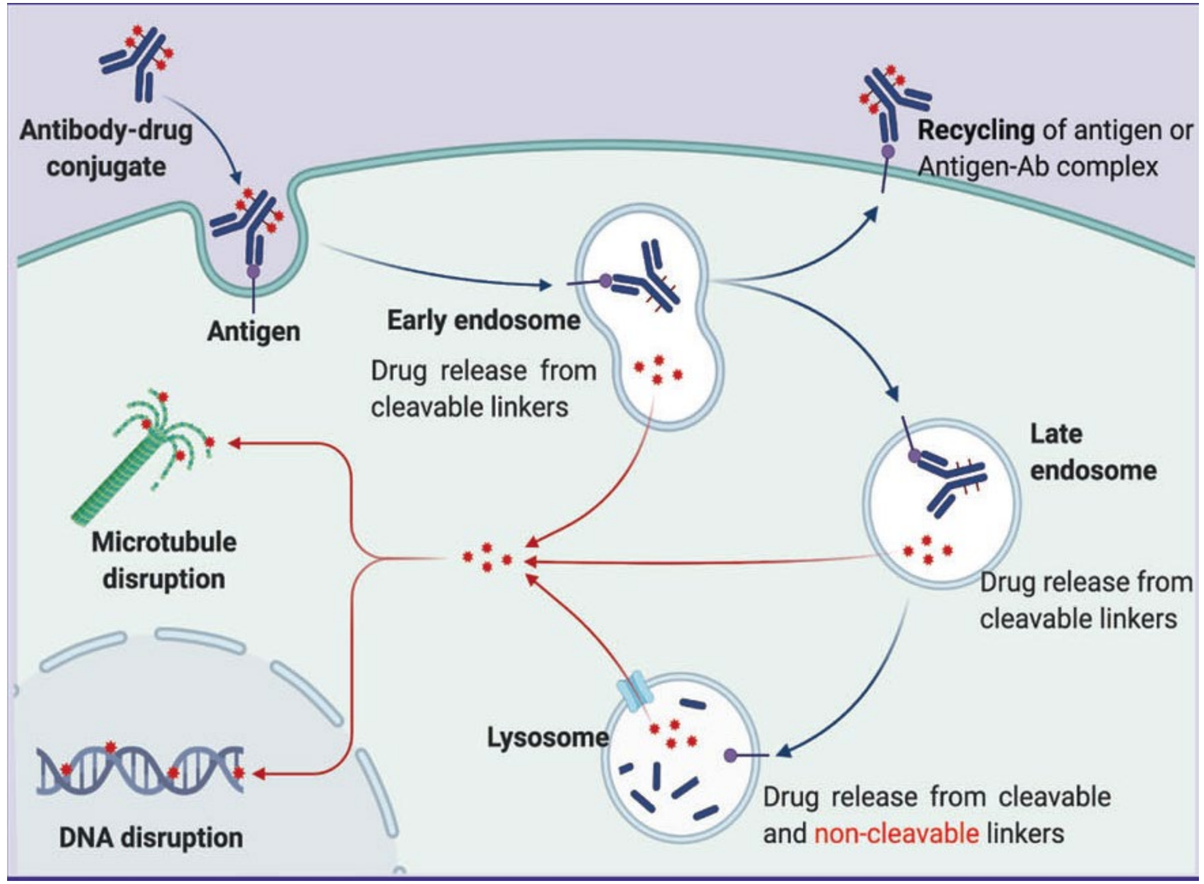
Clinical Trial Accrual by Race/Ethnicity Pre and Post NCI Call-to-Action in 2020

Race/Ethnicity	Pre NCI (N=108), N (%)	Post NCI (N=97), N (%)	p-value
Non-Hispanic white	63 (58.3)	49 (50.5)	0.3
Black	8 (7.4)	24 (24.7)	0.001
Hispanic / Latino / Latina/Latinx	16 (14.8)	17 (17.5)	0.6
Asian / Asian American	21 (19.4)	7 (7.2)	0.01

Discussion

Platinum Sensitive Ovarian Cancer Recurrence: Upcoming Phase 3 Studies with ADC's

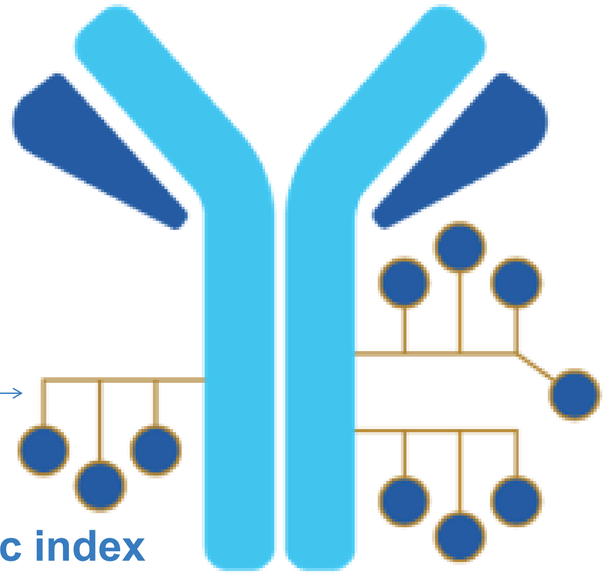
- **GOG-3049/UP-NEXT – UpRi versus placebo**
- **GOG-3078/GLORIOSA – Mirvetuximab/Bevacizumb versus Bevacizumab**



- ADC, antibody-drug conjugate.
- 1. Fu Z et al. *Signal Transduct Target Ther*. 2022;7(1):93. 2. Shim H. *Biomolecules*. 2020;10(3):360.

Upifitimab Rilsodotin (UpRi)

XMT-1536 (upifitamab rilsodotin; UpRi): : A potent NaPi2b Dolaflexin ADC with a high drug-to-antibody ratio and a controlled bystander effect



Dolaflexin
Improved therapeutic index vs other platforms

- **Polymer scaffold**
- **High Drug to Antibody Ratio (DAR) ~10-12**
- **Excellent drug like properties**

DolaLock Payload
Efficacy without severe neutropenia, neuropathy, or ocular toxicity

- **Novel auristatin**
- **Controlled bystander effect**
- **Selectively toxic to rapidly dividing cells**
- **Not a PgP substrate**
- **Induces immunogenic cell death**

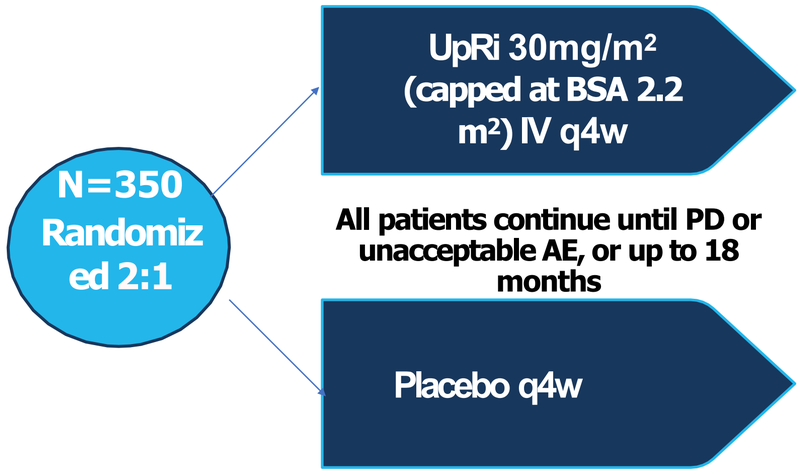
GOG-3049 / ENGOT-ov71-NSGO-CTU

UP-NEXT

Phase 3 Study of UpRi Monotherapy Maintenance vs Placebo in Platinum-Sensitive Recurrent Ovarian Cancer

Key Enrollment Criteria

- Patients with platinum-sensitive recurrent HGSOC[a]
- Best response to last line of treatment: NED, CR, PR, or SD[b]
- 2–4 prior platinum-containing chemotherapy regimens[c]
- NaPi2b-positive (TPS ≥75%) tumor (archival or fresh biopsy)
- Prior PARPi required for patients with known deleterious *BRCA* mutations



Primary Endpoint

- PFS by BICR

Secondary Endpoints

- PFS by Investigator
- ORR by Investigator
- OS
- Safety

Download trial card PDF

NCT05329545: Trial Currently Enrolling Patients

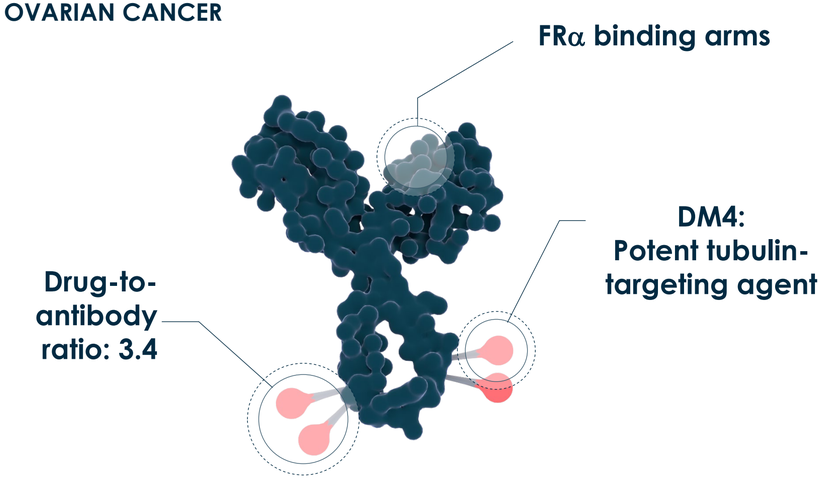
[a] HGSOC, including fallopian tube and primary peritoneal cancer. [b] Carboplatin or cisplatin ±paclitaxel, docetaxel, pegylated liposomal doxorubicin, or gemcitabine. [c] For SD, no increase in disease confirmed by central review of imaging and absence of CA-125 rise >15% in 7 days prior to first dose.

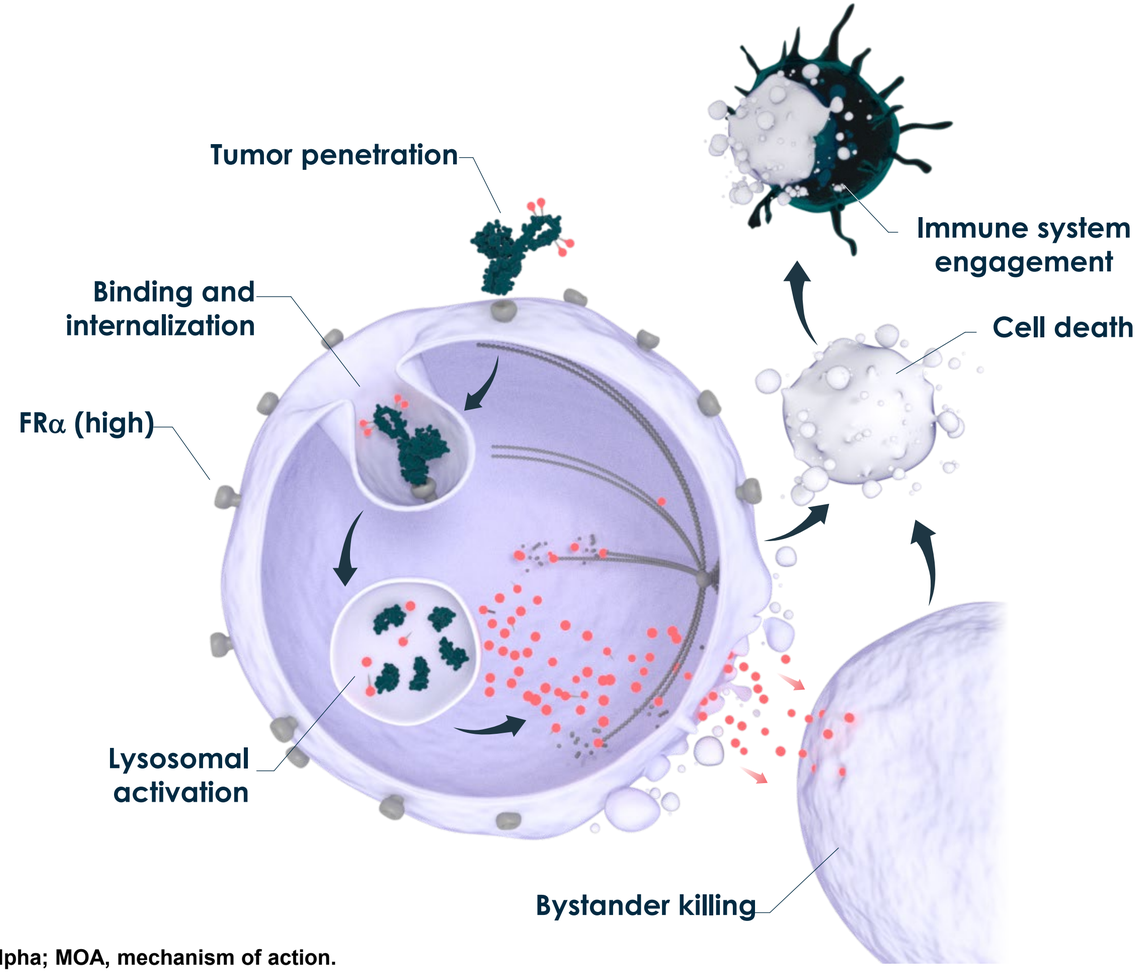
AE, adverse event; BICR, blinded independent central review; *BRCA*mut, breast cancer susceptibility gene mutated; CR, complete response; HGSOC, high-grade serous ovarian cancer; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; NED, no evidence of disease; ORR, overall response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PD, progressive disease; PFS, progression-free survival; PR, partial response; q4w, every 4 weeks; SD, stable disease; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

Mechanism of Action of Mirvetuximab Soravtansine

Name[1,2]: IMGN853
Antibody target: High FRα[3]
Payload: DM4[3]
Conjugation: Via lysine (random)[4]
DAR[5]: ~ 3.4
MOA: Microtubule disruption[3]
Bystander targeting: Yes[3]

OVARIAN CANCER





DAR, drug-to-antibody ratio; FRα, folate receptor alpha; MOA, mechanism of action.

1. Mirvetuximab soravtansine. ImmunoGen website. https://www.immunogen.com/category/mirvetuximab-soravtansine/. Accessed December 14, 2021. 2. Skaletskaya A, et al. SITC. 2016 (abstract 316). 3. Moore K, et al. Presented at: 2022 American Society of Clinical Oncology Annual Meeting; May 30-June 3, 2014; Chicago, Illinois. Abstract TPS6103. 4. Ab O, et al. *Mol Cancer Ther*. 2015;14(7):1605-1613. 5. Manzano A, Ocaña A. *Cancers (Basel)*. 2020;12(8):2223.

GLORIOSA

RANDOMIZED PHASE 3 TRIAL FOR MIRVETUXIMAB + BEVACIZUMAB MAINTENANCE IN FRα-HIGH PLATINUM-SENSITIVE OVARIAN CANCER

INITIATING IN Q4 2022

STRATIFIED BY:
Prior PARPI
Prior Bevacizumab
Response to prior therapy

PRIMARY ENDPOINT
PFS

SECONDARY ENDPOINTS
OS, DOR

ENROLLMENT AND KEY ELIGIBILITY
438 patients
Platinum-sensitive HGS ovarian cancer
1 prior platinum treatment
Prior PARPi required if BRCA+
CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

1:1 Randomization
Mirvetuximab 6 mg/kg+ Bevacizumab
vs
Bevacizumab

GOG FOUNDATION

FRα: folate receptor alpha; PFS: progression free survival; ; OS: overall survival; DOR: duration of response; PARPi: poly ADP-ribose polymerase inhibitor; BRCA: BReast CAncer gene; CR: complete response; PR: partial response; SD: stable disease

GOG Highlight Reel