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Time to First Subsequent Therapy (TFST) and Progression-Free Survival 2 (PFS2) From the Phase 3 Randomized, Double-Blind PRIMA/ENGOT-V26/GOG-3012 Study in Patients With Newly Diagnosed Ovarian Cancer

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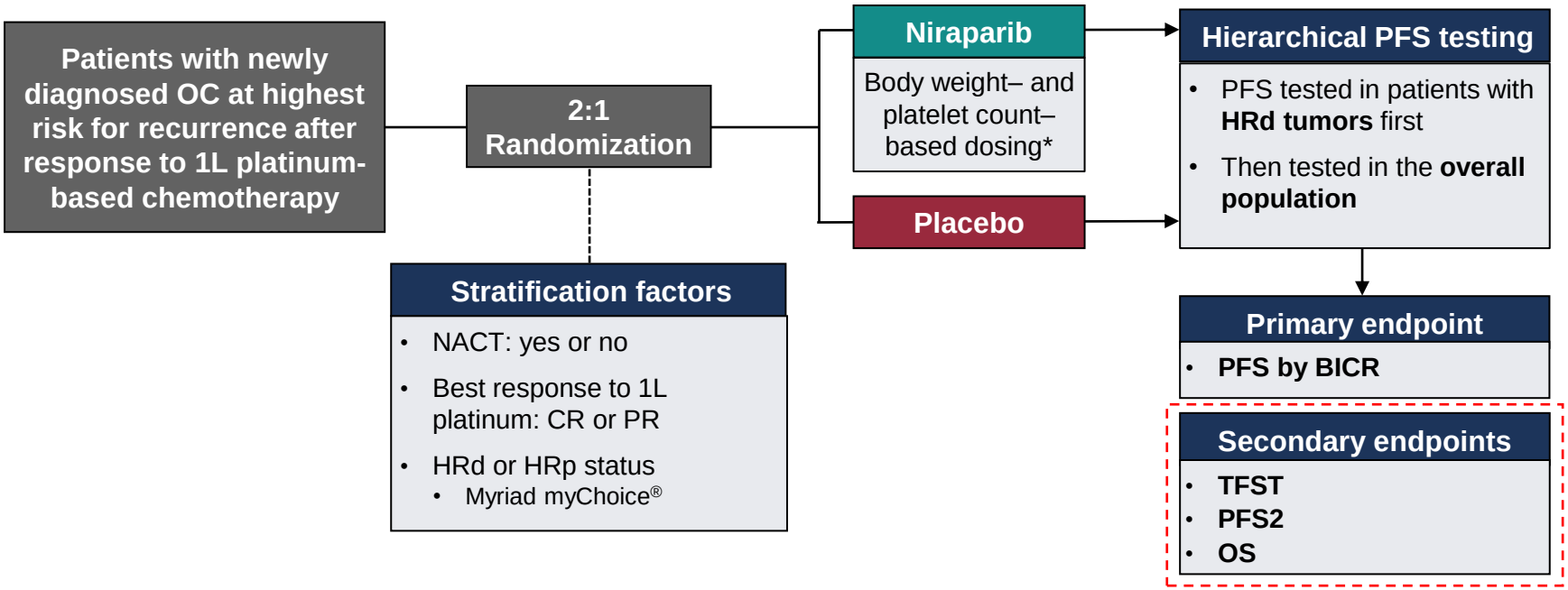
Disclosures

- Dr. Sileny Han has nothing to disclose

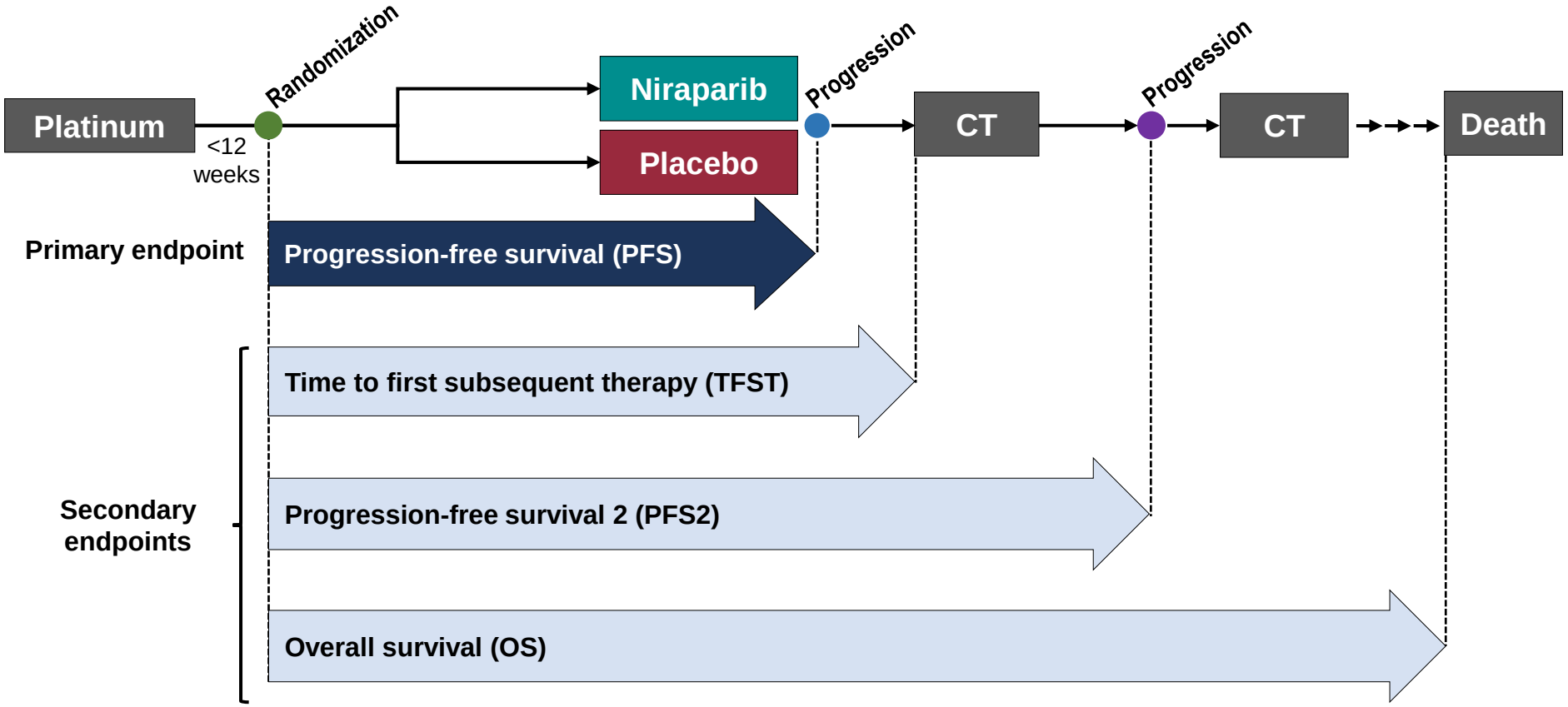
PRIMA Trial Design

- PRIMA is a randomized, double-blind, placebo-controlled phase 3 trial of niraparib as 1L maintenance treatment after response to platinum-based chemotherapy
- OS was a key efficacy secondary endpoint
- PFS2 and TFST were additional efficacy secondary endpoints



Patients received treatment until disease progress or a maximum of 36 months.
*After November 27, 2017, patients with body weight <77 kg and/or platelet count <150,000/μL started at 200 mg QD; all other patients started at 300 mg QD.
1L, first-line; BICR, blinded independent central review; CR, complete response; HRd, homologous recombination deficient; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; QD, once daily; TFST, time to first subsequent therapy.

Endpoint Definitions



Data cutoff May 17, 2019.
CT, chemotherapy.

Baseline Patient Demographics and Characteristics

Parameter	HRd		Overall	
	Niraparib (n=247)	Placebo (n=126)	Niraparib (n=487)	Placebo (n=246)
Age, median (range), years	58 (32–83)	58 (33–82)	62 (32–85)	62 (33–88)
Weight, median, kg	65	65	66	66
Stage at initial diagnosis, n (%)				
III	161 (65)	78 (62)	318 (65)	158 (64)
IV	86 (35)	48 (38)	169 (35)	88 (36)
Prior NACT, n (%)				
Yes	156 (63)	80 (63)	322 (66)	167 (68)
No	91 (37)	46 (37)	165 (34)	79 (32)
Best response to 1L platinum-based CT, n (%)				
CR	185 (75)	93 (74)	337 (69)	172 (70)
PR	62 (25)	33 (26)	150 (31)	74 (30)
Homologous recombination test status, n (%)				
HRd	247 (100)	126 (100)	247 (51)	126 (51)
HRp	–	–	169 (35)	80 (33)
HRnd	–	–	71 (15)	40 (16)

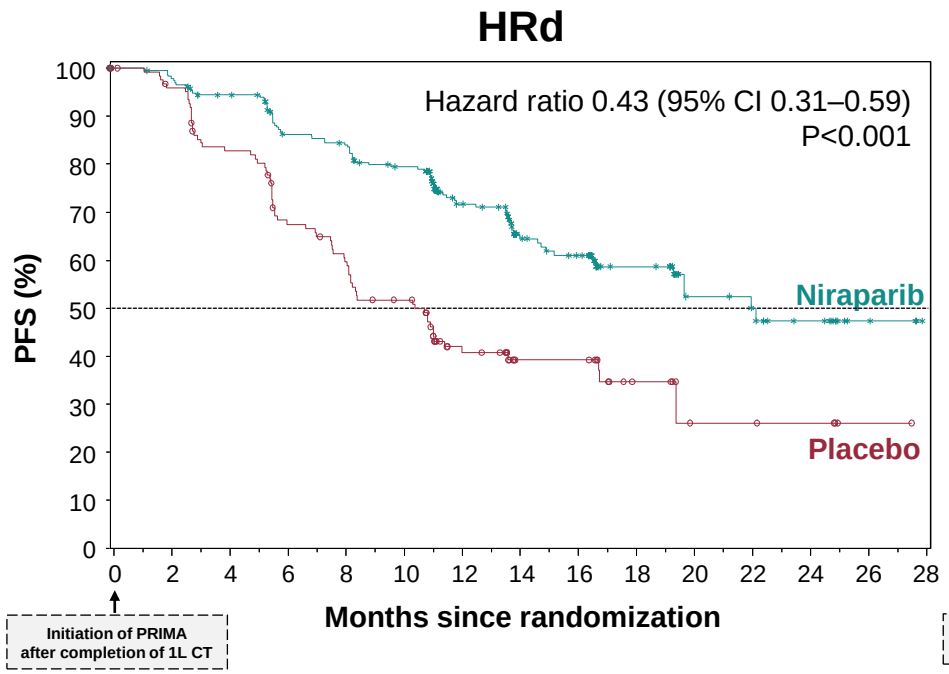
Of the overall population (N=733):

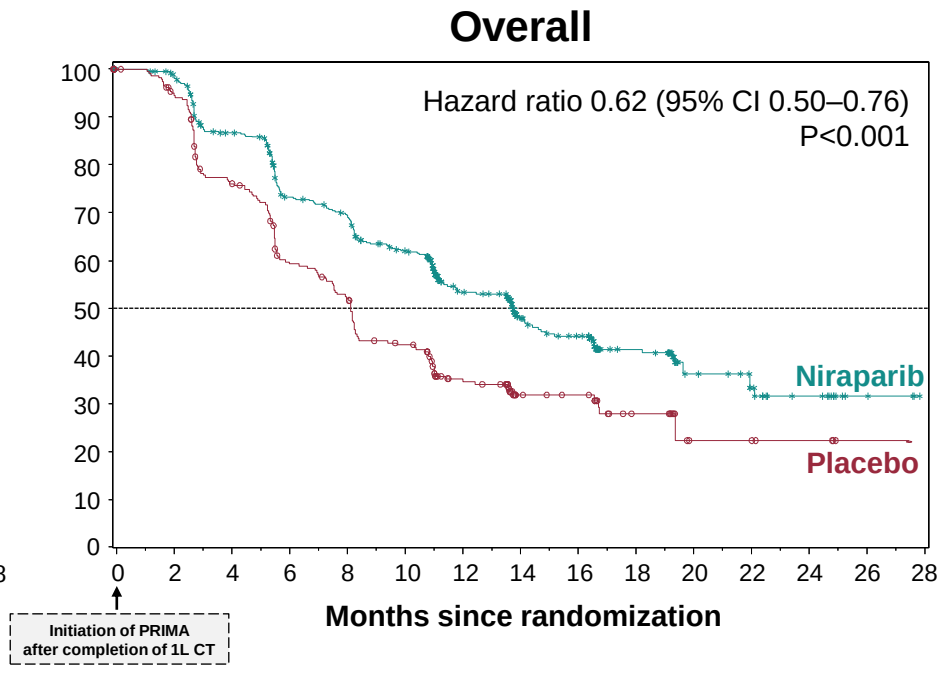
- 35% had stage IV cancer
- 67% received NACT
- 31% had a PR to 1L platinum-based CT
- 51% had HRd tumors
- 30% had *BRCA*mut tumors
- 34% had HRp tumors

1L, first-line; CR, complete response; CT, chemotherapy; HRd, homologous recombination deficient; HRnd, homologous recombination not determined; HRp, homologous recombination proficient; mut, mutation; NACT, neoadjuvant chemotherapy; PR, partial response.

PFS: Primary Endpoint

- Niraparib significantly improved PFS in patients with HRd tumors and in the overall population

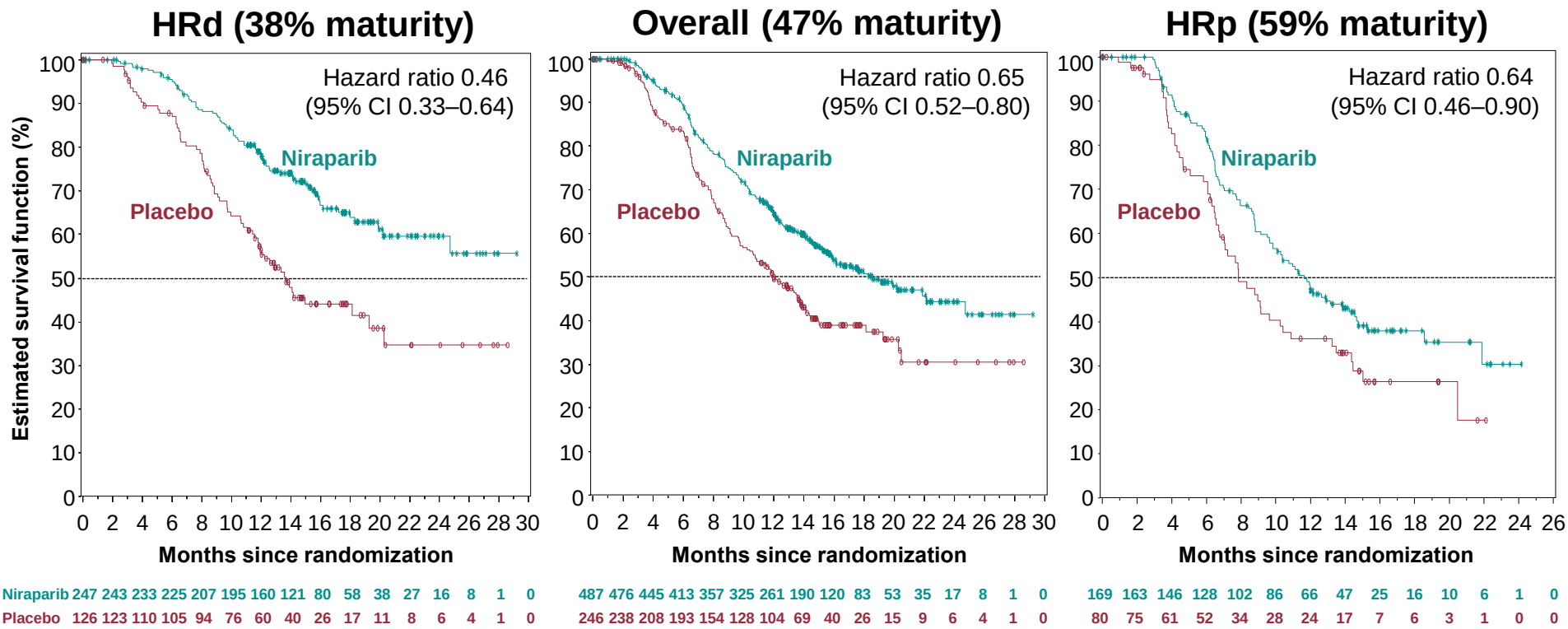




1L, first-line; CI, confidence interval; CT, chemotherapy; HRd, homologous recombination deficient; PFS, progression-free survival.

TFST: Prespecified Interim Analysis of Secondary Endpoint

- Consistent with PFS, niraparib improved TFST in all patients



CI, confidence interval; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PFS, progression-free survival; TFST, time to first subsequent therapy.

PFS2: Prespecified Interim Analysis of Secondary Endpoint

- Preliminary data numerically favors niraparib maintenance in all biomarker subgroup, including HRp

- PFS2 event rates are low; therefore, definitive conclusions cannot be drawn (updated data will be presented at a future meeting)

	HRd		Overall		HRp	
Patients	**Niraparib (n=247)**	**Placebo (n=126)**	**Niraparib (N=487)**	**Placebo (N=246)**	**Niraparib (n=169)**	**Placebo (n=80)**
Hazard ratio (95% CI)	0.84 (0.49–1.45)		0.81 (0.58–1.14)		0.56 (0.34–0.91)	
Maturity rate	15%		20%		27%	

CI, confidence interval; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PFS2, progression-free survival 2.

Summary of Post-Progression Therapy

- In the overall population, 37% of patients were still receiving niraparib as compared with 28% in the placebo group at the time of the primary analysis[1]
- Among the patients who had progressed, a higher proportion in the placebo group had received subsequent treatments compared with the niraparib group
- After progression, the majority of patients received a platinum-based regimen

	HRd		Overall		HRp	
Patients, n (%)	**Niraparib (n=245)**	**Placebo (n=125)**	**Niraparib (N=484)**	**Placebo (N=244)**	**Niraparib (n=165)**	**Placebo (n=79)**
Received post-progression therapy*	74 (30)	**62 (50)**	198 (41)	**125 (51)**	87 (52)	**45 (57)**

	HRd		Overall		HRp	
Post-progression regimen,† n (%)	**Niraparib (n=74)**	**Placebo (n=62)**	**Niraparib (N=198)**	**Placebo (N=125)**	**Niraparib (n=87)**	**Placebo (n=45)**
Platinum (carboplatin, cisplatin, oxaliplatin)	62 (84)	46 (74)	152 (77)	96 (77)	61 (70)	35 (78)
Doxorubicin (adriamycin, liposomal doxorubicin)	41 (55)	26 (42)	99 (50)	66 (53)	43 (49)	28 (62)
Gemcitabine	32 (43)	18 (29)	76 (38)	44 (35)	29 (33)	23 (51)
Taxane (paclitaxel, docetaxel, nab-paclitaxel)	17 (23)	13 (21)	62 (31)	30 (24)	32 (37)	11 (24)
Bevacizumab	12 (16)	9 (15)	39 (20)	31 (25)	14 (16)	17 (38)
PARP inhibitors	7 (10)	7 (11)	7 (4)	11 (9)	0	3 (7)
Other	10 (14)	5 (8)	28 (14)	9 (7)	15 (17)	3 (7)

*Reported for the safety population; data cutoff May 17, 2019.
†Reported for the efficacy population. Patients could receive ≥1 therapy.
1. González-Martín A, *N Engl J Med* 2019;381:2391–2402.

OS: Prespecified Interim Analysis of Key Secondary Endpoint

- Interim analysis of OS numerically favors niraparib over placebo
  - Overall population: 84% vs 77% at 2 years
  - HRd: 91% vs 85% alive at 2 years
  - HRp: 81% vs 59% alive at 2 years

- OS event rates are low; therefore, definitive conclusions cannot be drawn. Updated data will be presented at a future meeting

	HRd		Overall		HRp	
Patients	**Niraparib (n=247)**	**Placebo (n=126)**	**Niraparib (N=487)**	**Placebo (N=246)**	**Niraparib (n=169)**	**Placebo (n=80)**
24-month Survival	91%	85%	84%	77%	81%	59%
Hazard ratio (95% CI)	0.61 (0.27–1.39)		0.70 (0.44–1.11)		0.51 (0.27–0.97)	
Maturity rate	7%		11%		16%	

CI, confidence interval; HRd, homologous recombination deficient; HRp, homologous recombination proficient; OS, overall survival.

Conclusions

- Niraparib provided a long-term benefit across a broad population of patients with OC, and treatment benefit continued beyond the first progression

- For TFST, there were significant advantages in favor of niraparib in the overall population and in patients with both HRd and HRp tumors

- Although PFS2 and OS analyses are immature, data numerically favor niraparib maintenance vs placebo with benefit in all biomarker subgroups

HRd, homologous recombination deficient; HRp, homologous recombination proficient; OC, ovarian cancer; OS, overall survival; PFS2, progression-free survival 2; TFST, time to first subsequent therapy.

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AGO Study Group

BGOG Belgian Gynaecological Oncology Group

NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit

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