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# Final Overall Survival and Long-Term Safety in the ENGOT-OV16/NOVA Phase 3 Trial of Niraparib in Patients with Recurrent Ovarian Cancer

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- **Dr. Matulonis** reports consulting fees from Agenus, AstraZeneca, Blueprint Medicines, Boehringer Ingelheim, GSK, Merck, NextCure, Novartis, and Trillium; and data and safety monitoring board participation for Advaxis, Alkermes, and Symphogen.

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# Unlabeled/Investigational Uses

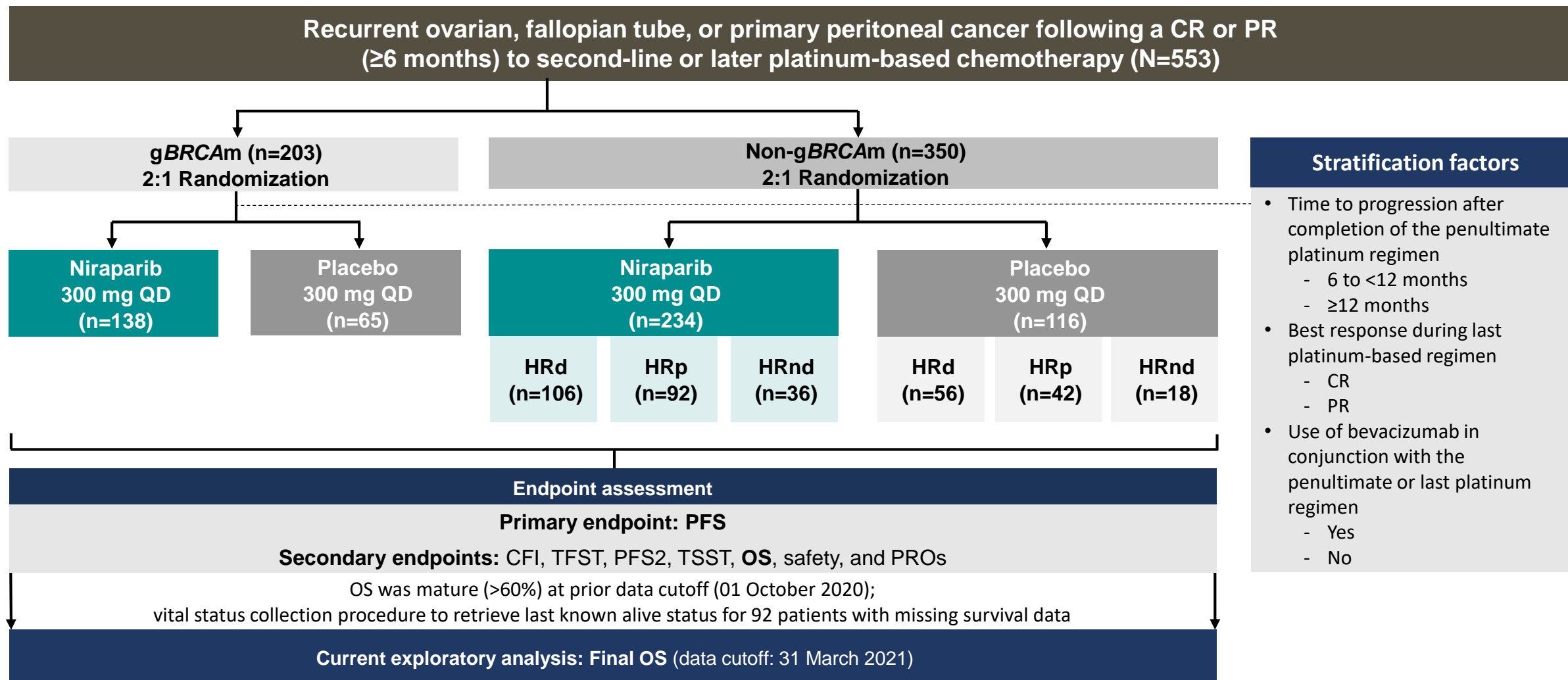
I will be discussing the unlabeled use (United States) of niraparib for the treatment of adult patients with non-germline *BRCA*-mutated recurrent ovarian, fallopian tube, or primary peritoneal cancer following a complete response or partial response ( $\geq 6$  months) to second-line or later platinum-based chemotherapy.



# Background: ENGOT-OV16/NOVA Study Design



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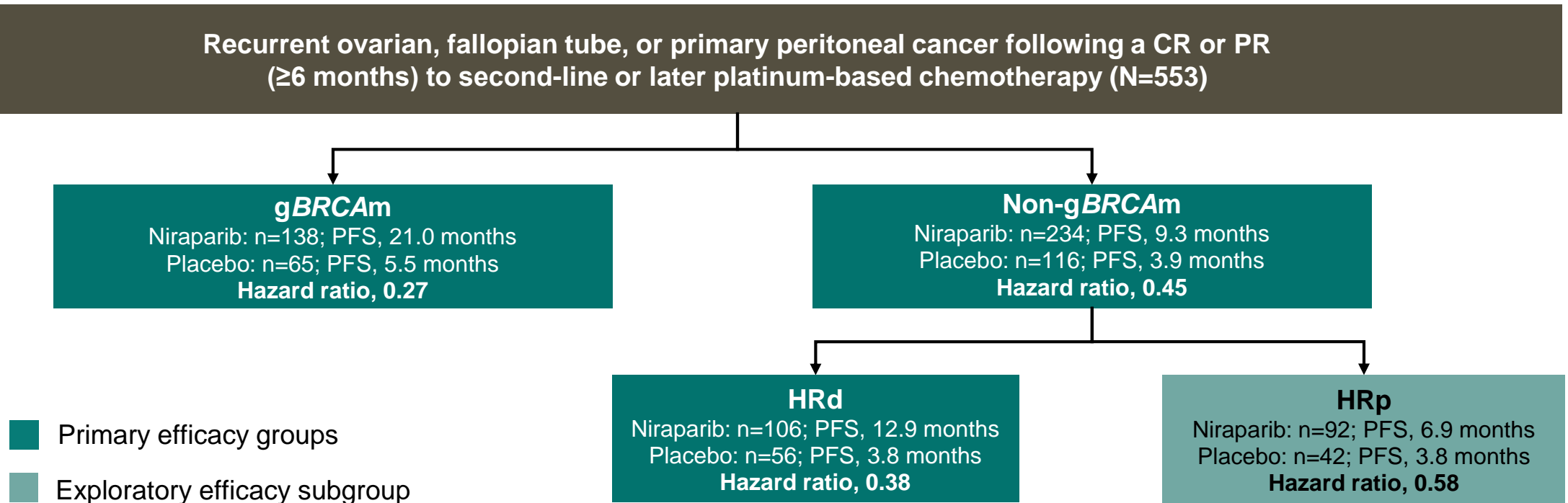


# Background: ENGOT-OV16/NOVA Study Endpoints Summary



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- In the primary analysis, niraparib maintenance therapy significantly prolonged PFS regardless of *gBRCAm* or HRD biomarker status (median follow up, 16.9 months)



Data cutoff: 20 June 2016.

CR, complete response; *gBRCAm*, germline *BRCA* mutant; HRd, homologous recombination deficient; HRD, homologous recombination deficiency; HRp, homologous recombination proficient; PFS, progression-free survival; PR, partial response.

Mirza MR, et al. *N Engl J Med*. 2016;375:2154–2164.

# Objectives and Methodology



- **Objectives**

- To report the final updated OS and long-term safety results from the phase 3 ENGOT-OV16/NOVA study of niraparib maintenance therapy in patients with platinum-sensitive recurrent ovarian cancer

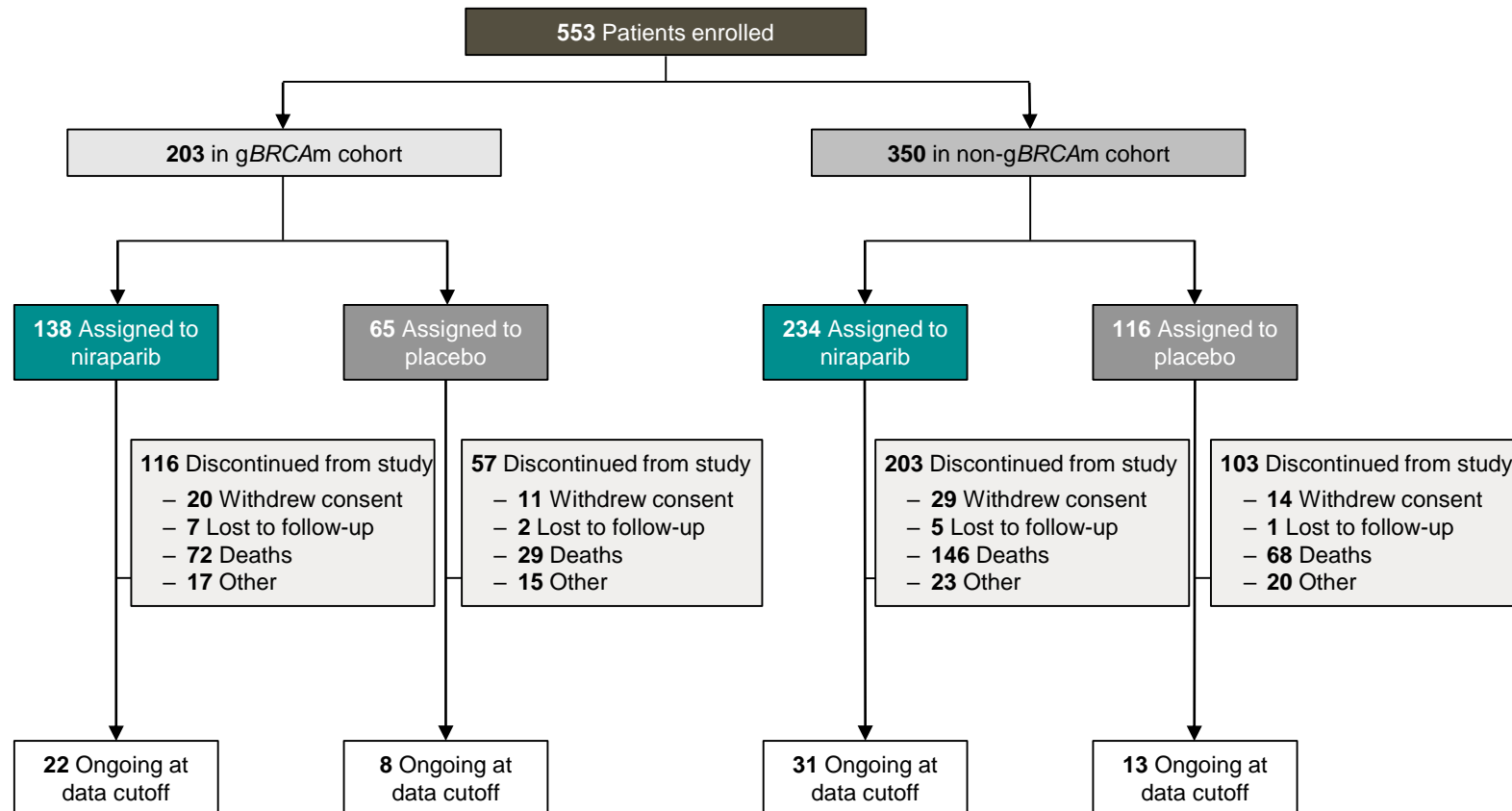
- **Methods**

- The pre-planned OS analysis for ENGOT-OV16/NOVA was presented previously (SGO 2021) but was associated with missing data on survival status and post-progression therapies
- After the mature (>60%) OS analysis was presented to the FDA (data cutoff: 01 October 2020), the agency recommended further data retrieval
- Data retrieval efforts reduced missing survival status from 17% to  $\approx$  2%, and the data cutoff was extended by 6 months, up to the date of study unblinding
- Final OS was evaluated in both cohorts and was also evaluated in the non-gBRCAm cohort by HRD status as exploratory analyses

# Patient Disposition and Survival Status



- Median follow-up at the data cutoff (date of study unblinding) was >75 months across both cohorts and treatment arms
- Survival status was available for 97.6% of patients (540 of 553)





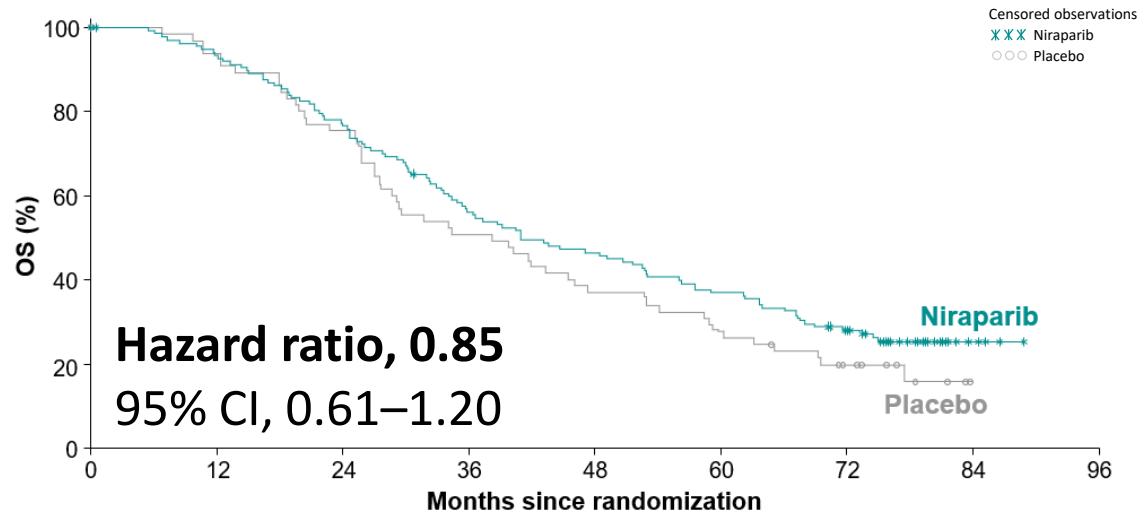
# Final OS for the gBRCAm and Non-gBRCAm Cohorts



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- Overall OS maturity was 77.9%

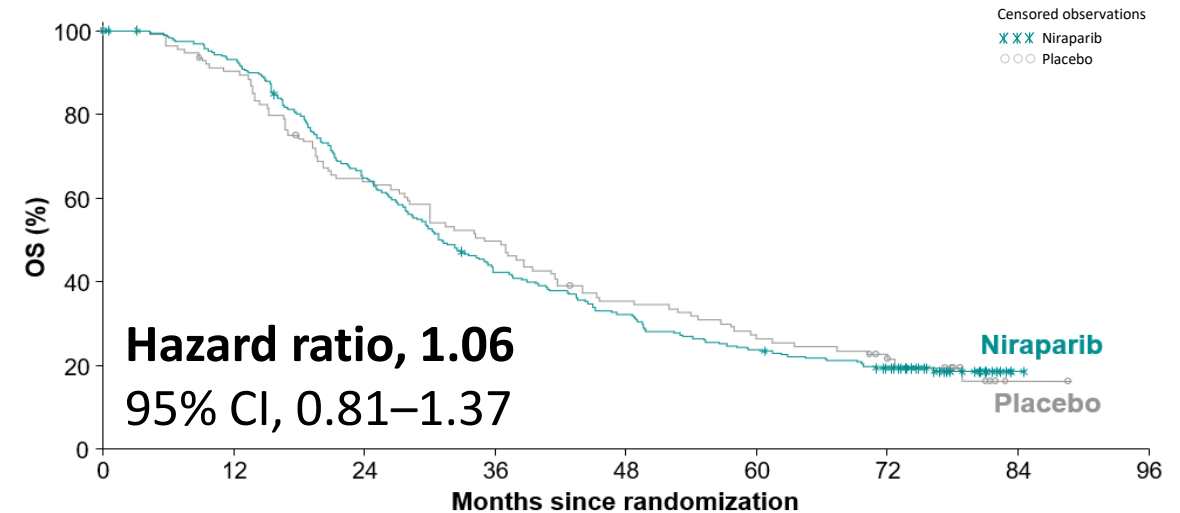
**gBRCAm (75.9% maturity)**



Patients at risk

Niraparib	138	128	105	76	63	50	33	4	0
Placebo	65	61	49	33	24	18	10	0	

**Non-gBRCAm (79.1% maturity)**



Patients at risk

Niraparib	234	215	149	96	73	54	36	1	0
Placebo	116	103	72	56	39	29	21	1	0

# Final OS for the gBRCAm and Non-gBRCAm Cohorts and by HRD Subgroup in the Non-gBRCAm Cohort



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Recurrent ovarian, fallopian tube, or primary peritoneal cancer following a CR or PR  
(≥6 months) to second-line or later platinum-based chemotherapy (N=553)

## gBRCAm

Niraparib: n=138; mOS, 40.9 (34.9–52.9)

Placebo: n=65; mOS, 38.1 (27.6–47.3)

**Hazard ratio, 0.85 (0.61–1.20)**

## Non-gBRCAm

Niraparib: n=234; mOS, 31.0 (27.8–35.6)

Placebo: n=116; mOS, 34.8 (27.9–41.4)

**Hazard ratio, 1.06 (0.81–1.37)**

## HRd

Niraparib: n=106; mOS, 35.6 (28.3–43.4)

Placebo: n=56; mOS, 41.4 (33.9–57.6)

**Hazard ratio, 1.29 (0.85–1.95)**

## HRp

Niraparib: n=92; mOS, 27.9 (22.6–32.8)

Placebo: n=42; mOS, 27.9 (19.2–44.0)

**Hazard ratio, 0.93 (0.61–1.41)**

## HRnd

Niraparib: n=36; mOS, 29.8 (23.6–35.7)

Placebo: n=18; mOS, 20.2 (13.9–37.8)

**Hazard ratio, 0.62 (0.29–1.35)**

# CFI, TFST, PFS2, and TSST



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Secondary efficacy endpoint	<i>gBRCAm</i>	Non- <i>gBRCAm</i>
<b>CFI</b>		
Median in niraparib vs placebo, months	20.0 vs 9.4	13.4 vs 8.7
Hazard ratio (95% CI)	<b>0.39</b> (0.268–0.561)	<b>0.56</b> (0.428–0.727)
<b>TFST</b>		
Median in niraparib vs placebo, months	19.1 vs 8.6	12.4 vs 7.4
Hazard ratio (95% CI)	<b>0.57</b> (0.412–0.783)	<b>0.58</b> (0.454–0.740)
<b>PFS2</b>		
Median in niraparib vs placebo, months	29.9 vs 22.7	19.5 vs 16.1
Hazard ratio (95% CI)	<b>0.70</b> (0.500–0.968)	<b>0.80</b> (0.627–1.022)
<b>TSST</b>		
Median in niraparib vs placebo, months	29.7 vs 19.6	20.3 vs 16.7
Hazard ratio (95% CI)	<b>0.63</b> (0.451–0.878)	<b>0.84</b> (0.654–1.077)

# Follow-up Treatment by Cohort



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Type of treatment, n (%)	gBRCAm			Non-gBRCAm		
	Niraparib (n=138)	Placebo (n=65)	Overall (n=203)	Niraparib (n=234)	Placebo (n=116)	Overall (n=350)
Any follow-up anticancer therapy	102 (73.9)	50 (76.9)	152 (74.9)	175 (74.8)	97 (83.6)	272 (77.7)
Any PARP inhibitor	37 (26.8)	32 (49.2)	69 (34.0)	16 (6.8)	17 (14.7)	33 (9.4)
Any platinum therapies	81 (58.7)	40 (61.5)	121 (59.6)	134 (57.3)	69 (59.5)	203 (58.0)
Any bevacizumab therapy	26 (18.8)	10 (15.4)	36 (17.7)	55 (23.5)	29 (25.0)	84 (24.0)
Any taxane therapy	48 (34.8)	24 (36.9)	72 (35.5)	96 (41.0)	47 (40.5)	143 (40.9)
Any doxorubicin therapy	46 (33.3)	25 (38.5)	71 (35.0)	95 (40.6)	51 (44.0)	146 (41.7)
Any gemcitabine therapy	34 (24.6)	22 (33.8)	56 (27.6)	80 (34.2)	46 (39.7)	126 (36.0)
Any other therapy	53 (38.4)	24 (36.9)	77 (37.9)	100 (42.7)	58 (50.0)	158 (45.1)

# Overall Safety Profile



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- The safety profile of niraparib in the ENGOT-OV16/NOVA study was consistent with that observed in previous data readouts.<sup>1,2</sup> No new safety signals were detected
- The incidence of grade  $\geq 3$  adverse events (including thrombocytopenia, anemia, neutropenia, hypertension, fatigue, and GI disorders) was consistent with that observed in previous data readouts<sup>1,2</sup>

Overall population, n (%)	Niraparib (n=367)	Placebo (n=179)
Any TEAE	367 (100.0)	172 (96.1)
Any TRAE	359 (97.8)	126 (70.4)
Any TEAE with CTCAE toxicity grade $\geq 3$	281 (76.6)	43 (24.0)
Any TRAE with CTCAE toxicity grade $\geq 3$	244 (66.5)	10 (5.6)
Any serious TEAE	127 (34.6)	29 (16.2)
Any serious TRAE	74 (20.2)	4 (2.2)
Any TEAE leading to dose interruption	255 (69.5)	27 (15.1)
Any TEAE leading to dose reduction	254 (69.2)	9 (5.0)
Any TEAE leading to treatment discontinuation	67 (18.3)	4 (2.2)
Any TEAE leading to death	5 (1.4)	2 (1.1)

Safety population. Data cutoff: 31 March 2021.

CTCAE, Common Terminology Criteria for Adverse Events; GI, gastrointestinal; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

1. Mirza MR, et al. *N Engl J Med*, 2016;375:2154–2164; 2. Matulonis U, et al. *Gynecol Oncol*. 2021;162(suppl. 1):S24–S25.



# Incidence of Myelodysplastic Syndrome/Acute Myeloid Leukemia



- As of the 31 Mar 2021 data cutoff, 3.8% of patients (14/367) who received niraparib and 1.7% of patients (3/179) who received placebo developed MDS/AML
- One additional case was reported in the *gBRCAm* cohort since the 01 October 2020 data cutoff

## Incidence of MDS/AML based on final DCO of 31 Mar 2021

Niraparib	Placebo
<b>Overall</b>	
(n=367)	(n=179)
14 (3.8)	3 (1.7)
<b><i>gBRCAm</i></b>	
(n=136)	(n=65)
10 (7.4)	2 (3.1)
<b>non-<i>gBRCAm</i></b>	
(n=231)	(n=114)
4 (1.7)	1 (0.9)














# Conclusions



- We provide an updated exploratory analysis of ENGOT-OV16/NOVA long-term follow-up data
- Analyses were confounded by imbalances in post-progression therapy (including subsequent PARP inhibitors) by treatment arm in both the *gBRCAm* and non-*gBRCAm* cohorts, including the HRD subgroups
  - Lack of biological plausibility in numerical OS outcomes in HRD subgroups
- The OS hazard ratio for the *gBRCAm* cohort was 0.85 and the OS hazard ratio for the non-*gBRCAm* cohort was 1.06, with expected wide CIs given that ENGOT-OV16/NOVA was not powered for formal OS analyses
- Secondary endpoints, including CFI, TFST, PFS2, and TSST, demonstrated a persistent treatment effect in favor of niraparib in both the *gBRCAm* and non-*gBRCAm* cohorts
- No new safety signals were observed with long-term follow-up

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