Long-Term Safety Assessment of Niraparib in Patients With Recurrent Ovarian Cancer: Results From the ENGOT-OV16/NOVA Trial

Mansoor R. Mirza,[1] Anne Dørum,[2] Benedict Benigno,[3] Sven Mahner,[4] Paul Bessette,[5] Isabel M. Bover Barcelo,[6] Dominique Berton,[7] Jonathan Ledermann,[8] Bobbie J. Rimel,[9] Jørn Herrstedt,[10] Susie Lau,[11] Ulrich Canzler,[12] Isabel Palacio Vázquez,[13] Elsa Kalbacher,[14] Joseph Buscema,[15] Domenica Lorusso,[16] Philip Debruyne,[17] Ilan Bruchim,[18] Wei Guo,[19] Izabela Malinowska,[19] Floris de Jong,[19] Ursula A. Matulonis[20]

[1]Nordic Society of Gynaecological Oncology (NSGO), Rigshospitalet–Copenhagen University Hospital, Copenhagen, Denmark; [2]Nordic Society of Gynaecological Oncology (NSGO), Radiumhospitalet, Oslo, Norway; [3]Northside Hospital, Atlanta, GA, USA; [4]Arbeitsgemeinschaft Gynäkologische Onkologie (AGO), University Hospital, Ludwig-Maximilians University of Munich, Munich, Germany; [5]University of Sherbrooke, Sherbrooke, Quebec, Canada; [6]Hospital Son Llàtzer, Palma, Spain; [7]Groupe d'Investigateurs Nationaux pour l'Étude des Cancers Ovariens (GINECO), Institut de Cancérologie de l'Ouest (ICO) Centre René Gauducheau, Saint-Herblain, France; [8]National Cancer Research Institute (NCRI), University College London, London, UK; [9]Cedars-Sinai Medical Center, West Hollywood, CA, USA; [10]University of Copenhagen, Copenhagen, Denmark; [11]McGill University, Montreal, Quebec, Canada; [12]Department of Gynecology and Obstetrics, TU Dresden, Dresden, Germany; [13]Hospital Universitario Central de Asturias, Asturias, Spain; [14]CHRU Besançon, Hôpital Jean Minjoz, Besançon, France; [15]Arizona Oncology Associates, Tucson, AZ, USA; [16]Multicentre Italian Trials in Ovarian Cancer/Mario Negri Gynecologic Oncology (MITO/MaNGO), Fondazione IRCCS National Cancer Institute, Milan, Italy; [17]Belgian Gynaecological Oncology Group (BGOG), Kortrijk Cancer Centre, AZ Groeninge, Kortrijk, Belgium; [18]Israeli Society of Gynecologic Oncology (ISGO), Hillel Yaffe Medical Center, Hadera, affiliated with the Technion–Israel Institute of Technology, Haifa, Israel; [19]TESARO: A GSK Company, Waltham, MA, USA; [20]Dana-Farber Cancer Institute, Boston, MA, USA

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Disclosures

Company Name	Honoria/ Expenses	Consultancy/ Advisory Board	Research Funding	Royalties/ Patents	Ownership/ Equity Position	Employee	Other
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AstraZeneca		X	X				
Biocad		X					
Boehringer Ingelheim		X	X				
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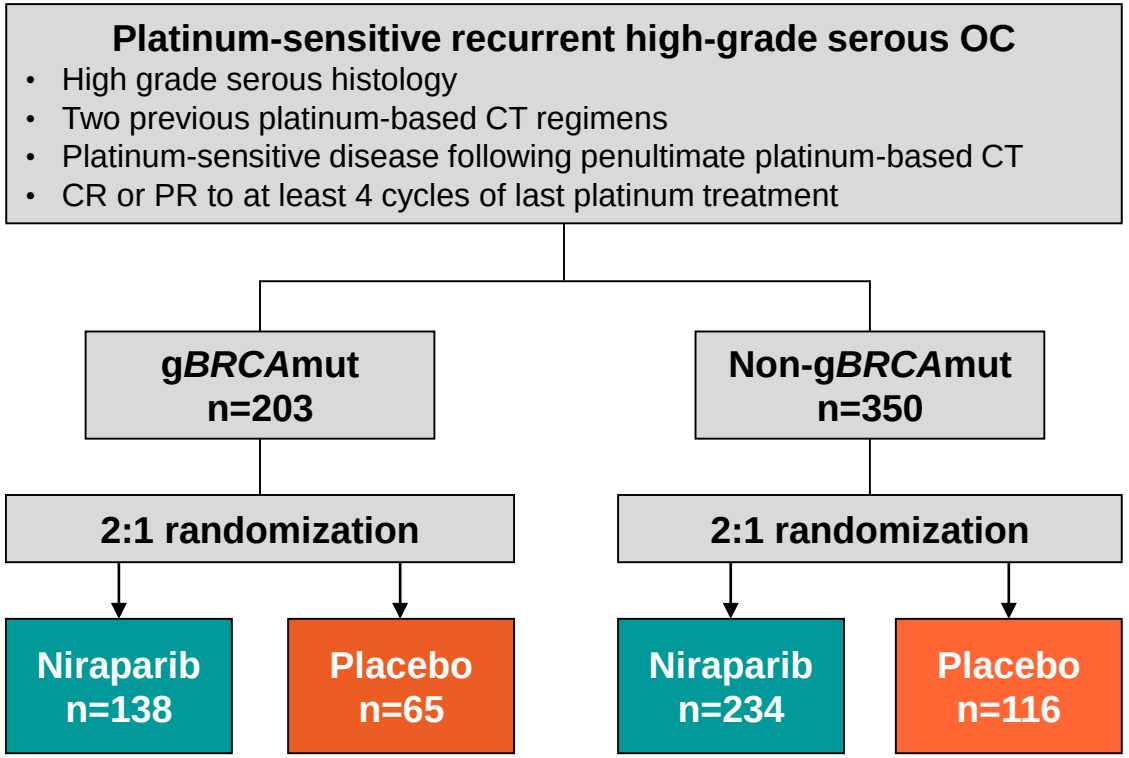
Pfizer		X	X				
Roche		X	X				
SeattleGenetics		X					
Sera Prognostics Inc.							X
Sotio		X					
TESARO: A GSK Company		X	X				

Niraparib and the ENGOT-OV16/NOVA Trial

- Niraparib is a PARP inhibitor approved in US and Europe for maintenance therapy in patients with recurrent OC who had a CR or PR to platinum-based chemotherapy and in US for the treatment of patients with advanced OC who have been treated with 3+ prior CT regimens and whose cancer is associated with HRD positive status[1,2]

- The ENGOT-OV16/NOVA trial enrolled two cohorts based on patient *BRCA* status

- Here we assess the long-term safety of niraparib, which is crucial for long-term maintenance treatment



Safety data assessed by following intervals:
- By month for months 1 to 12
- Pooled for months 13 to 24 and 25 to 48

NOVA First Patient In: August 2013
Efficacy Data Cutoff: June 20, 2016
Safety Data Cutoff: September 2017

Mirza M.R. et al., *NEJM* 2016

1. ZEJULA® [prescribing information]. Accessed 29 October 2019; 2. ZEJULA® [EPAR summary for the public]. Accessed 29 October 2019
CR, complete response; CT, chemotherapy; HRD, homologous recombination deficiency; mut, mutant; OC, ovarian cancer; PR, partial response; TEAE, treatment-emergent adverse event.

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NOVA Baseline Characteristics

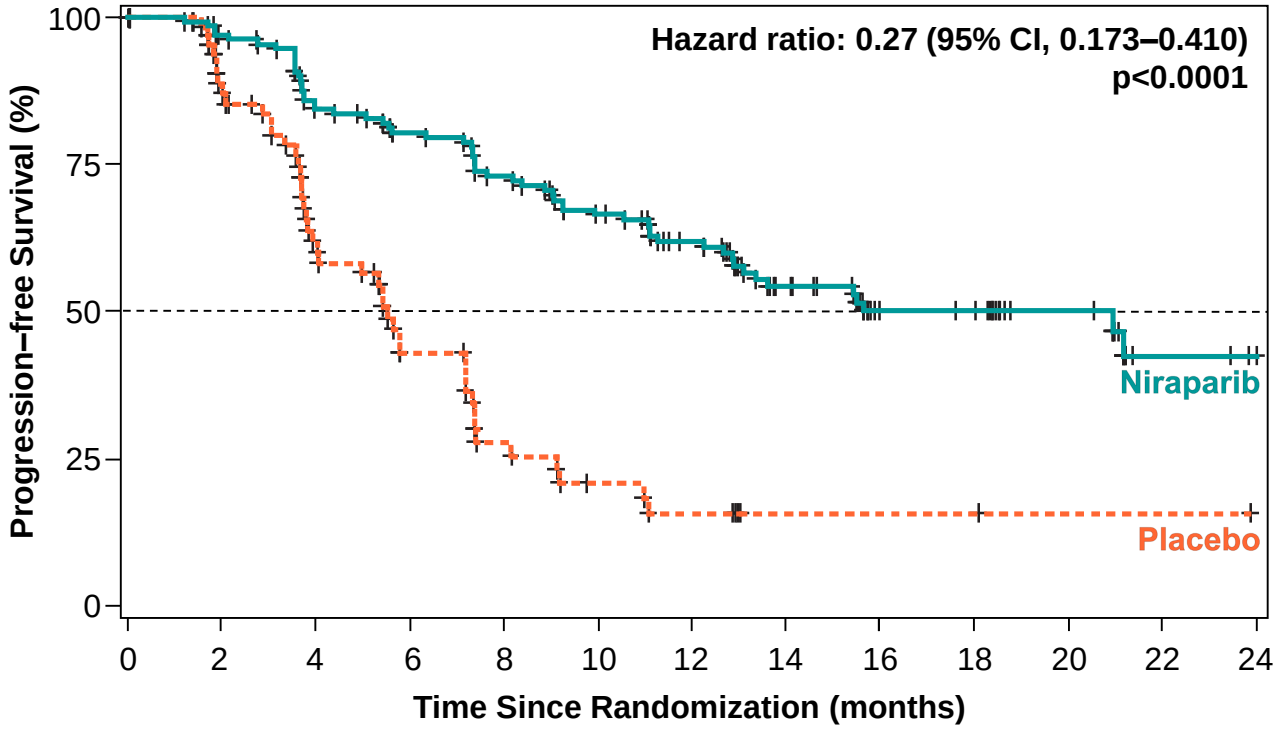
Characteristic	g*BRCA*mut		Non-g*BRCA*mut	
	Niraparib n=138	Placebo n=65	Niraparib n=234	Placebo n=116
Age, years				
Median	57.0	58.0	63.0	60.5
(min, max)	(36, 83)	(38, 73)	(33, 84)	(34, 82)
ECOG performance status, n (%)				
0	91 (65.9)	48 (73.8)	160 (68.4)	78 (67.2)
1	47 (34.1)	17 (26.2)	74 (31.6)	38 (32.8)
Primary tumor site, n (%)				
Ovarian	122 (88.4)	53 (81.5)	192 (82.1)	96 (82.8)
Primary peritoneal	7 (5.1)	6 (9.2)	24 (10.3)	8 (6.9)
Fallopian tube	9 (6.5)	6 (9.2)	18 (7.7)	11 (9.5)
Lines of previous chemotherapy, n (%)				
2	70 (50.7)	30 (46.2)	155 (66.2)	77 (66.4)
≥3	67 (48.6)	35 (53.8)	79 (33.8)	38 (32.8)
Time to progression after penultimate platinum therapy, n (%)				
6 to <12 months	54 (39.1)	26 (40.0)	90 (38.5)	44 (37.9)
≥12 months	84 (60.9)	39 (60.0)	144 (61.5)	72 (62.1)
Best response to most recent platinum therapy, n (%)				
Complete response	71 (51.4)	33 (50.8)	117 (50.0)	60 (51.7)
Partial response	67 (48.6)	32 (49.2)	117 (50.0)	56 (48.3)

Mirza, et al. *NEJM* 2016

CR, complete response; CT, chemotherapy; mut, mutant; PR, partial response.

NOVA PFS Results

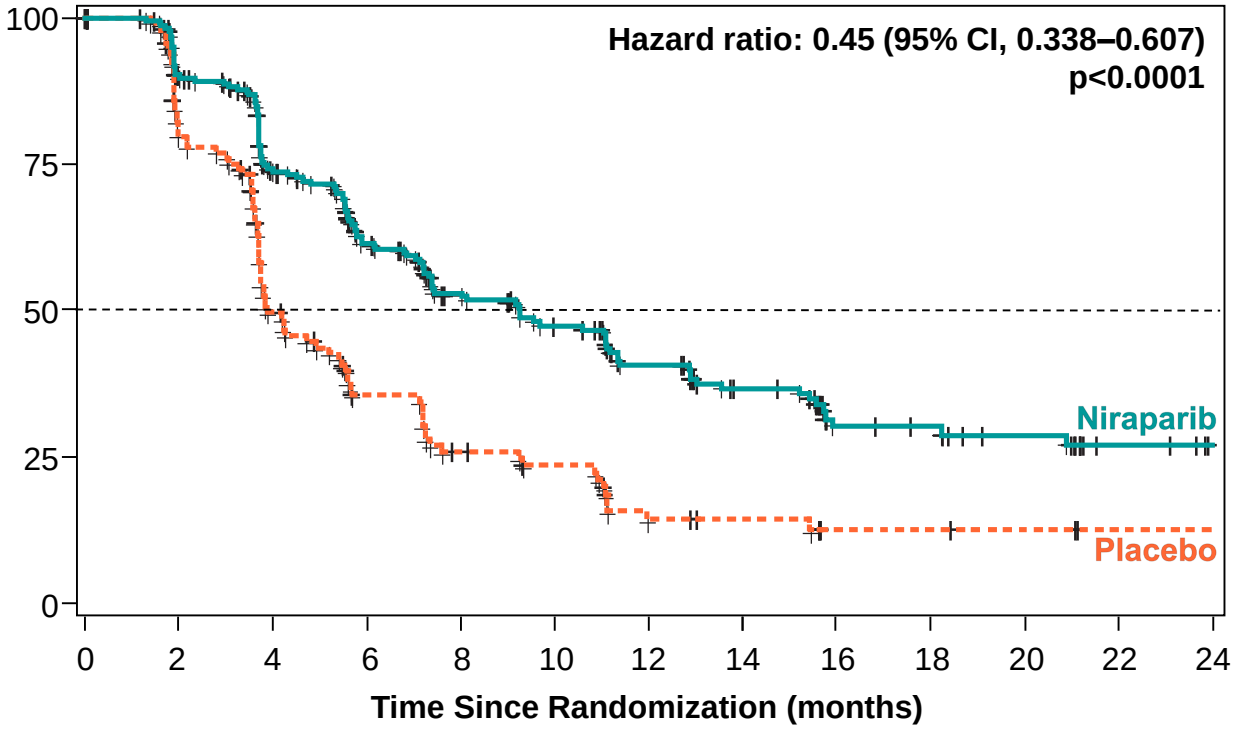
g*BRCA*mut



Treatment	mPFS (95% CI), months	Patients without PD or death, %		
		12 months	18 months	24 months
Niraparib (n=138)	21.0 (12.9–NR)	62%	50%	42%
Placebo (n=65)	5.5 (3.8–7.2)	16%	16%	16%

Median duration of follow-up: 16.4 months

Non-g*BRCA*mut



Treatment	mPFS (95% CI), months	Patients without PD or death, %		
		12 months	18 months	24 months
Niraparib (n=234)	9.3 (7.2–11.2)	41%	30%	27%
Placebo (n=116)	3.9 (3.7–5.5)	14%	12%	12%

Median duration of follow-up: 17.5 months

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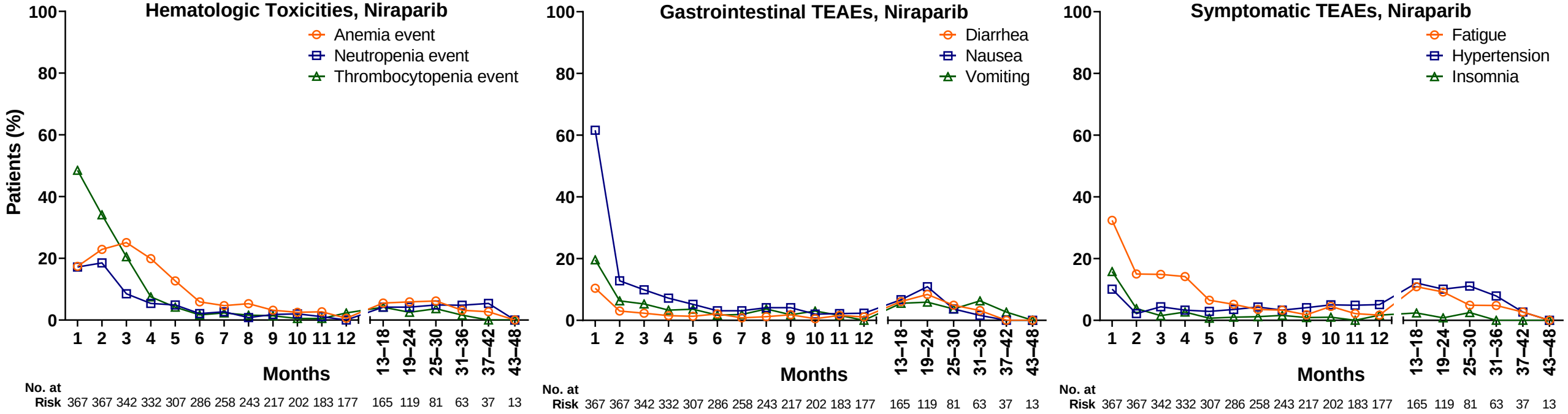
Mirza, et al. *NEJM* 2016

CI, confidence interval; mPFS, median progression-free survival; mut, mutant; PD, progressive disease.

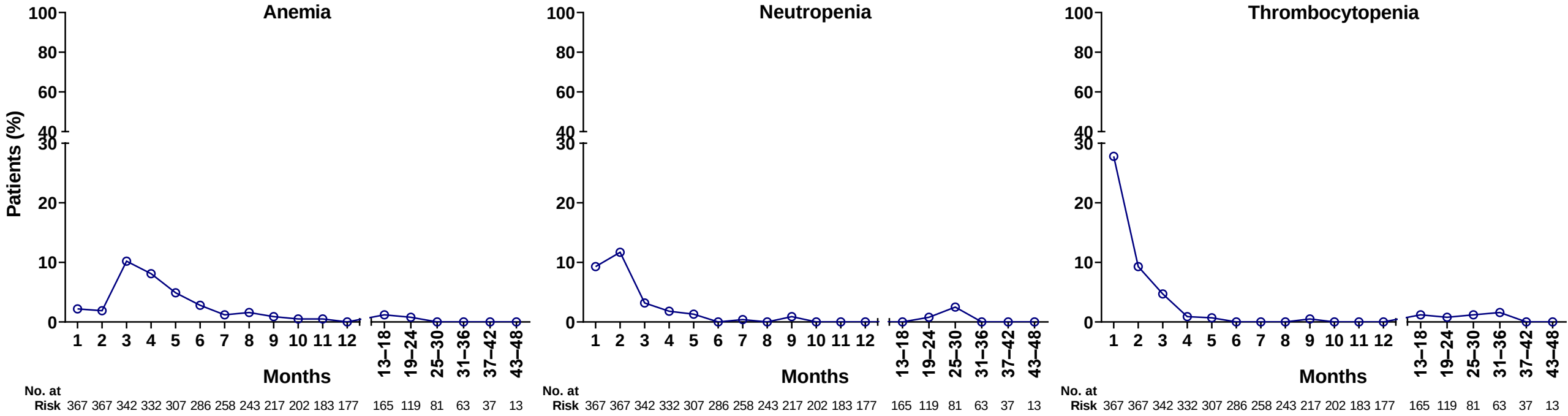
NOVA Long Term Safety – Any Grade TEAEs



- Nausea, fatigue, and thrombocytopenia saw the greatest decline after month 1
  - TEAE incidence stabilized during the initial treatment period and remained low thereafter
- Note that months 13–48 are cumulative TEAE incidences for 6-month periods

TEAE, treatment-emergent adverse event..

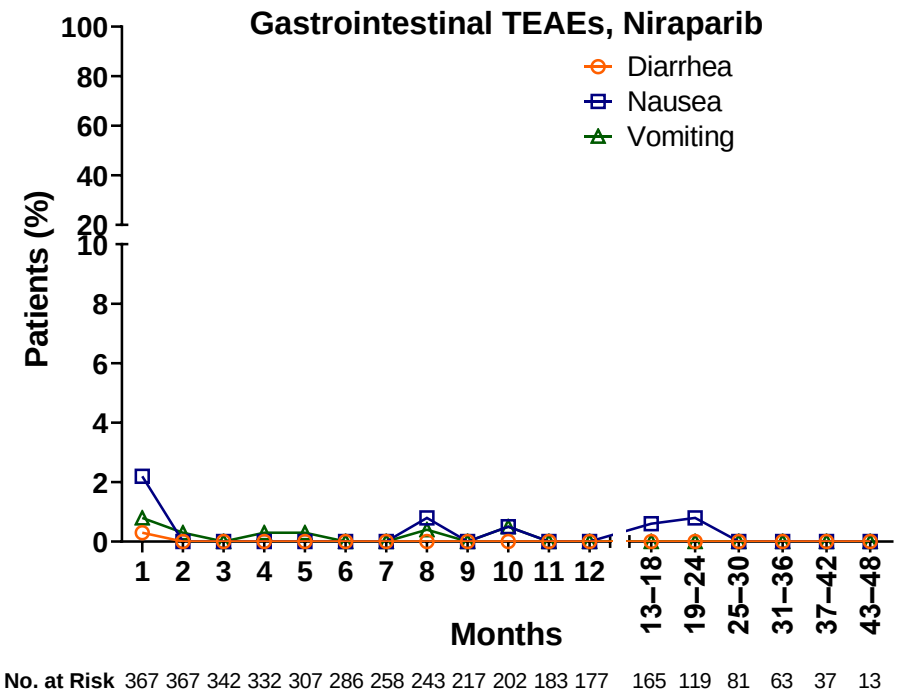
Grade ≥3 Hematologic TEAEs, Niraparib

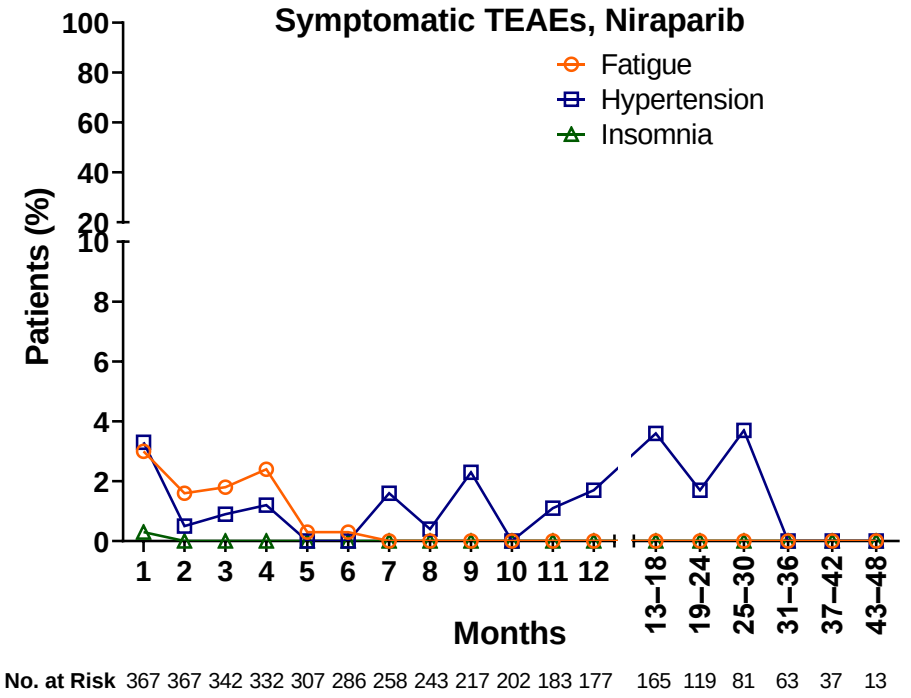


- Anemia increased until month 3 and declined thereafter
- Neutropenia increased from month 1 to 2 and decreased sharply after
- Thrombocytopenia events declined sharply after month 1

TEAE, treatment-emergent adverse event..

Grade ≥3 TEAEs





- Grade ≥3 GI and symptomatic TEAEs were low (<5% at each time point) for patients receiving niraparib
- Note that months 13–48 are cumulative TEAE incidences for 6-month periods

GI, gastrointestinal; TEAE, treatment-emergent adverse event..

Conclusions

- In the NOVA study, niraparib significantly improved PFS in patients with recurrent ovarian cancer regardless of *BRCA* or HRD status
- Long-term tolerability is crucial for patient compliance in long-term maintenance treatment
- In the NOVA trial, patients receiving niraparib experienced:
  - Dose reductions occurring mostly in month 1
  - A sharp decline in any grade and grade ≥3 thrombocytopenia after month 1
  - Low GI and symptomatic TEAEs after month 1
- Patients receiving niraparib benefit from once daily dosing and simple dose modification to regulate TEAEs
  - Morning/evening dosing can help control insomnia and nausea
  - Dose modifications can control hematologic toxicity
- These data support the safe long-term use of niraparib as maintenance therapy in recurrent ovarian cancer

CI, confidence interval; HR, hazard ratio: mut, mutant; ROC, recurrent ovarian cancer; TEAE, treatment-emergent adverse event.

Acknowledgments

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Median Duration of TEAEs

Median duration of TEAEs (Q1–Q3), days			
Preferred term	**Niraparib (n=367)**	**Placebo (n=179)**	**Overall (N=546)**
Anemia	63.0 (24.0–126.0)	47.0 (8.5–178.5)	62.0 (24.0–126.0)
Diarrhea	13.0 (2.0–96.0)	27.5 (3.0–137.0)	15.5 (2.0–115.0)
Fatigue	330.0 (58.5–998.0)	766.5 (146.0–1018)	391.5 (74.0–1002)
Hypertension	732.0 (54.0–977.0)	30.0 (7.0–950.0)	666.5 (335.0–964.0)
Insomnia	328.0 (36.0–1020)	675.0 (57.0–963.0)	347.5 (37.0–1005)
Nausea	68.5 (17.0–322.5)	52.5 (7.5–320.5)	64.5 (16.0–320.5)
Neutropenia	26.0 (14.0–54.0)	86.0 (29.0–221.0)	29.0 (15.0–71.0)
Thrombocytopenia	22.0 (15.0–44.0)	28.0 (8.0–29.0)	23.0 (15.0–44.0)
Vomiting	5.0 (2.0–31.0)	3.0 (1.0–11.0)	4.0 (2.0–23.0)