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# Time without symptoms or toxicity in patients with recurrent ovarian cancer receiving niraparib maintenance treatment versus placebo: A TWiST analysis of the ENGOT-OV16/NOVA trial

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# Disclosures

- Ursula A. Matulonis:
  - Chief, Division of Gynecologic Oncology
  - Received personal fees to provide advice and consult for Merck, Clovis Oncology, Geneos, Mersana, and Immunogen outside of the submitted work.

# Identify the delay in disease progression not offset by toxic effects due to nausea, vomiting or fatigue

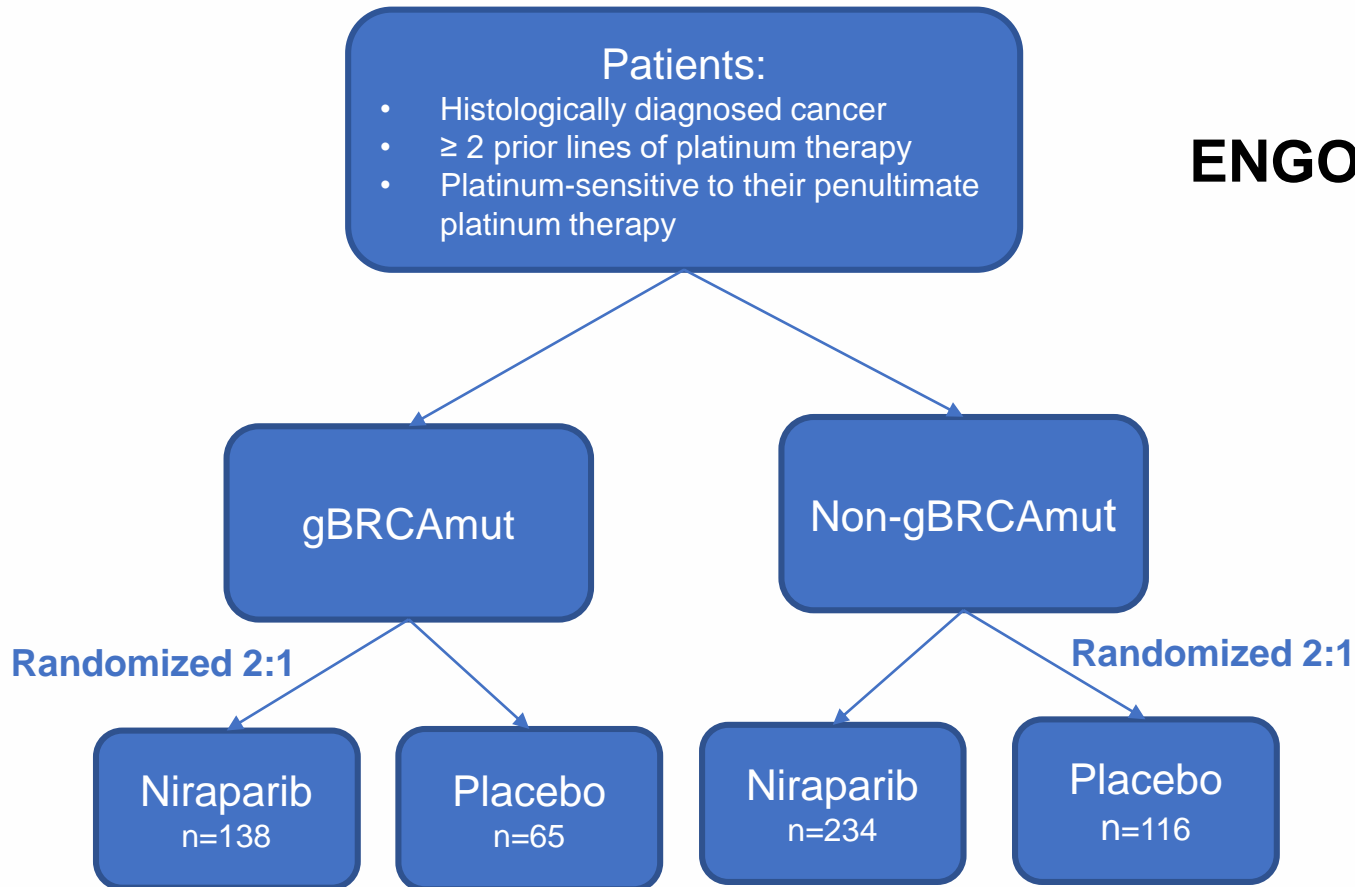
- Objective:

- Estimate the difference in time without symptoms or toxicity (TWiST) between treatment with maintenance niraparib or placebo in the ENGOT-OV16/NOVA trial

[1] Mirza et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. *N Engl J Med* 2016. 375: 2154–2164.

[2] Oza et al. Quality of life in patients with recurrent ovarian cancer treated with niraparib versus placebo (ENGOT-OV16/NOVA): results from a double-blind, phase 3, randomised controlled trial. *The Lancet Oncology* 2018.0

# Data were sourced from the ENGOT-OV16/NOVA trial



## ENGOT-OV16/NOVA trial (NCT01847274)

- Randomized controlled phase III trial
- Recurrent ovarian cancer patients
- Niraparib was assessed for safety and efficacy compared to the placebo in both the gBRCAmut and non-gBRCAmut cohorts
- Primary endpoint – progression-free survival (PFS)

# Identify the delay in disease progression not offset by toxic effects due to nausea, vomiting or fatigue

- **Topline Results:**

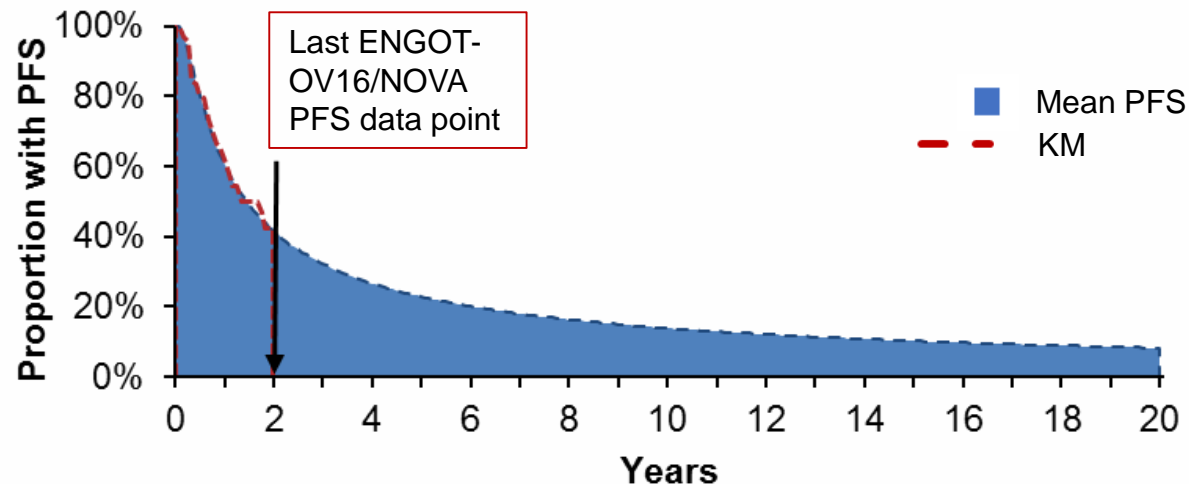
- Treatment with maintenance niraparib significantly delayed disease progression compared to placebo - Mirza *et al.* 2016<sup>1</sup>
  - gBRCAmut; 21.0 vs. 5.5 months, non-gBRCAmut; 9.3 vs. 3.9 months
- Quality of life (remained stable through niraparib treatment and pre-progression period - Oza *et al.* 2018<sup>2</sup>
  - QOL parameters tested: EQ-5D-5L, EQ-5D-5L-VAS, and FOSI

[1] Mirza et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. *N Engl J Med* 2016. 375: 2154–2164.

[2] Oza et al. Quality of life in patients with recurrent ovarian cancer treated with niraparib versus placebo (ENGOT-OV16/NOVA): results from a double-blind, phase 3, randomised controlled trial. *The Lancet Oncology* 2018.0

# PFS was extrapolated over 20-years to estimate the expected benefits beyond the length of the ENGOT-OV16/NOVA trial

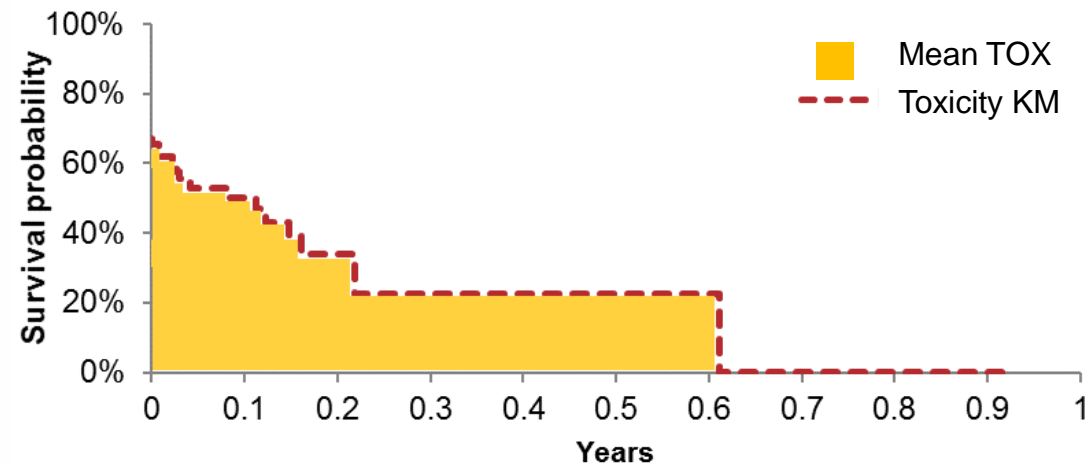
- Survival curves were used to extrapolate PFS ENGOT-OV16/NOVA data for niraparib and placebo over 20-years for both the gBRCAmut and non-gBRCAmut cohorts
- The 20-year period was based on ovarian cancer clinical expert opinion, and this approach has been accepted in 2 previous health technology appraisal submissions<sup>3,4</sup>



**Step 1: Mean PFS was calculated as the area under the curve and is represented in years**

# Time with toxicity was estimated from the number of days patients experienced toxic effects due to grade $\geq 2$ nausea, vomiting or fatigue in the ENGOT-OV16/NOVA trial

- Time with toxicity (TOX) was estimated from the number of days patients experienced grade  $\geq 2$  symptomatic adverse events (AEs):
  - Nausea, vomiting and fatigue
  - AEs were included post randomization and prior to disease progression
- Using this data toxicity Kaplan-Meier curves were estimated for both the *gBRCA*mut and non-*gBRCA*mut cohorts



**Step 2: Mean TOX was calculated as the area under the curve and is represented in years**



TWiST was calculated as PFS without toxicity due to grade  $\geq 2$  symptomatic adverse events: nausea, vomiting and fatigue

TWiST is an established methodology that partitions PFS into two health states:

1. Time with toxicity (TOX)

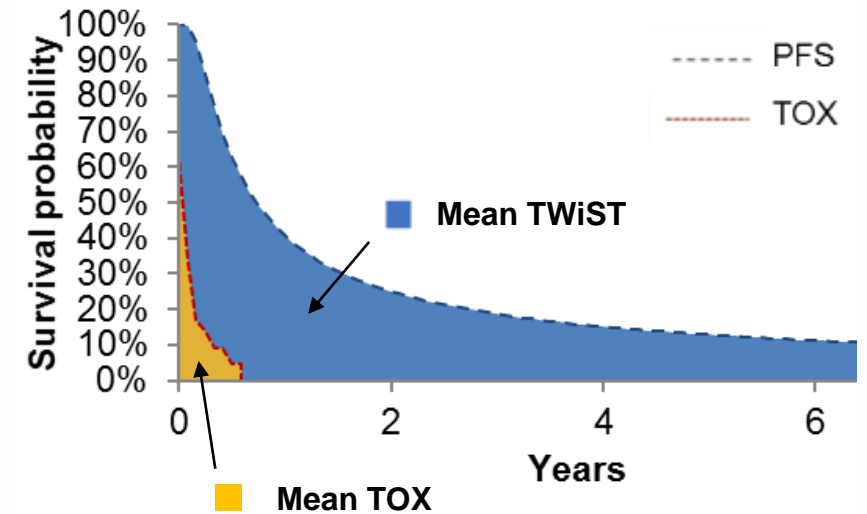
2. Time without symptoms (i.e. progression) or toxicity (TWiST)

TWiST was calculated as PFS without toxicity due to grade  $\geq 2$  symptomatic adverse events: nausea, vomiting and fatigue

TWiST is an established methodology that partitions PFS into two health states:

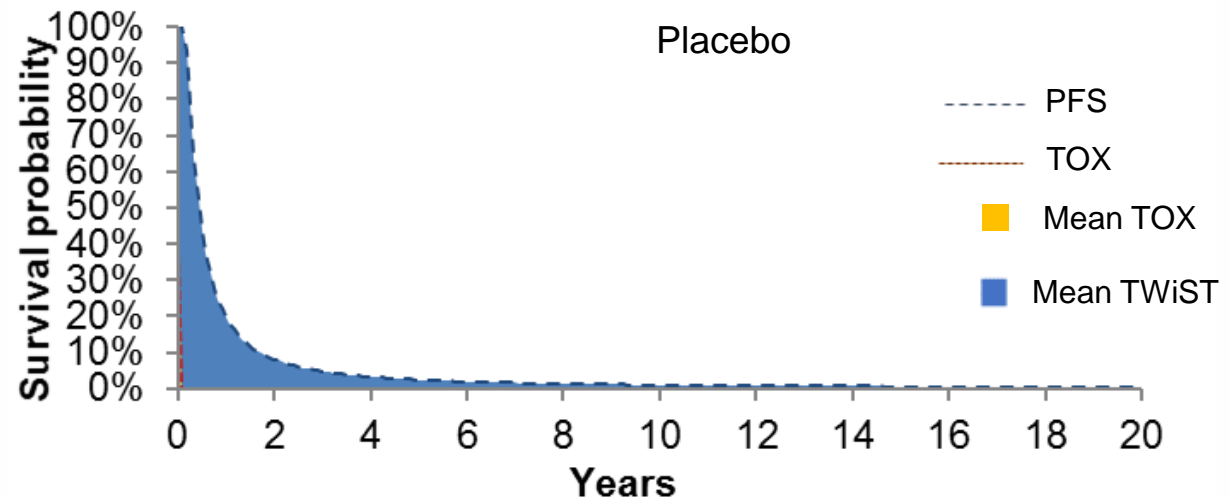
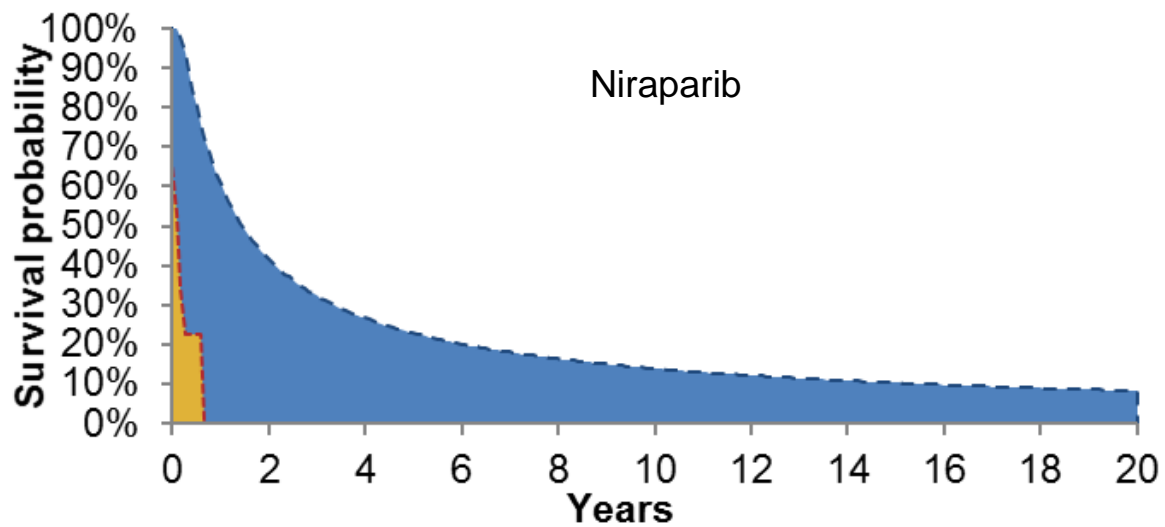
1. Time with toxicity (TOX)

2. Time without symptoms (i.e. progression) or toxicity (TWiST)



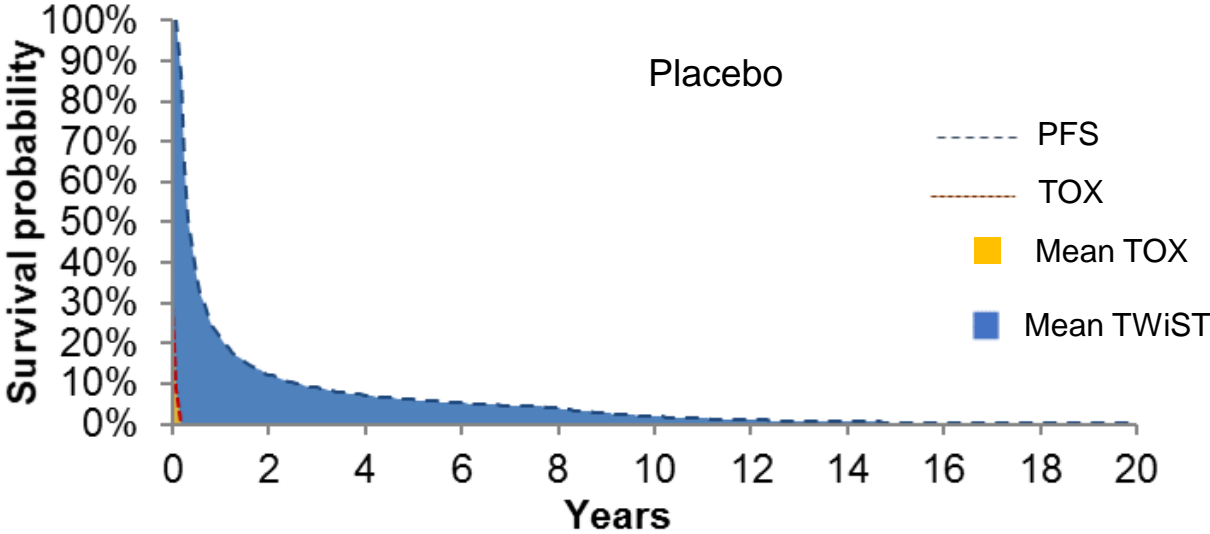
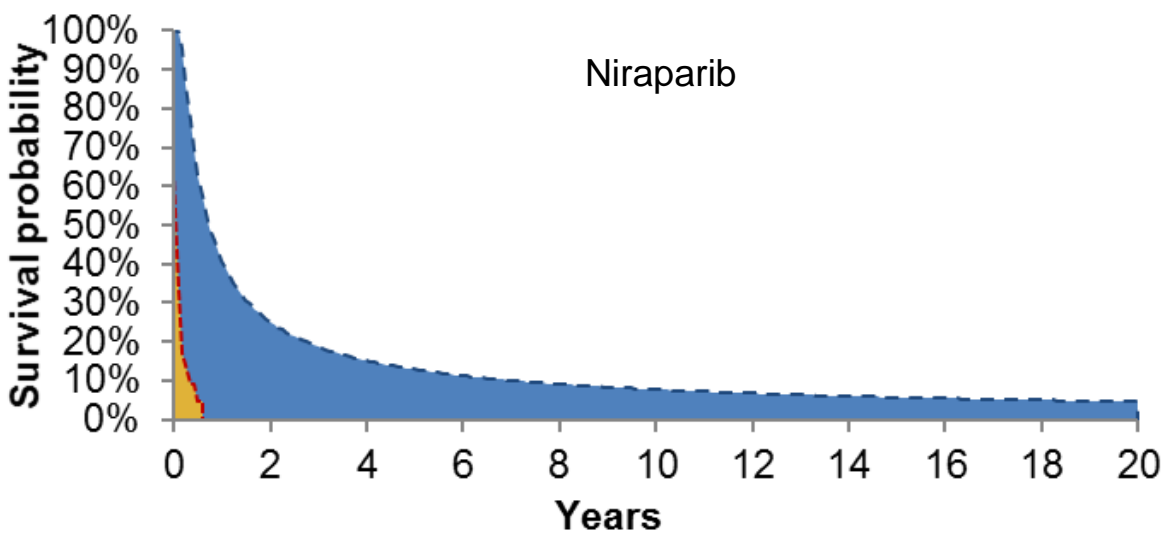
Mean TWiST = mean PFS – mean TOX

# gBRCAmut cohort treated with niraparib experienced greater PFS without toxicity due to nausea, vomiting or fatigue



	Mean PFS (95% CI, SE)	Mean TOX (95% CI, SE)	Mean TWiST	Incremental TWiST
Niraparib	4.14 years (2.20, 7.04; 1.25)	0.31 years (0.19, 0.44; 0.06)	<b>3.83 years</b>	<b>2.95 years</b>
Placebo	0.91 years (0.51, 1.90; 0.35)	0.03 years (0.01, 0.06; 0.01)	<b>0.88 years</b>	

# Non-gBRCAmut cohort treated with niraparib experienced greater PFS without toxicity due to nausea, vomiting or fatigue
















	Mean PFS (95% CI, SE)	Mean TOX (95% CI, SE)	Mean TWiST	Incremental TWiST
Niraparib	2.59 years (1.60, 3.82; 0.56)	0.13 years (0.08, 0.17; 0.02)	<b>2.46 years</b>	<b>1.34 years</b>
Placebo	1.14 years (0.65, 1.98; 0.33)	0.02 years (0.01, 0.04; 0.01)	<b>1.12 years</b>	

# Patients treated with niraparib in the ENGOT-OV16/NOVA trial experienced a mean TWiST benefit compared to placebo

- This TWiST benefit means that patients treated with niraparib experienced more progression-free time without symptoms or toxicities due to nausea, vomiting or fatigue compared to placebo

# Acknowledgments

We thank the 553 patients and their families for participating in this trial

 NSGO	 AGO	 GEICO	 GINECO	 NCRI	 MITO MaNGO	 BGOG	 ISGO	 CEEGOG	 AGO	 Hungary	 Canada	 USA	
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