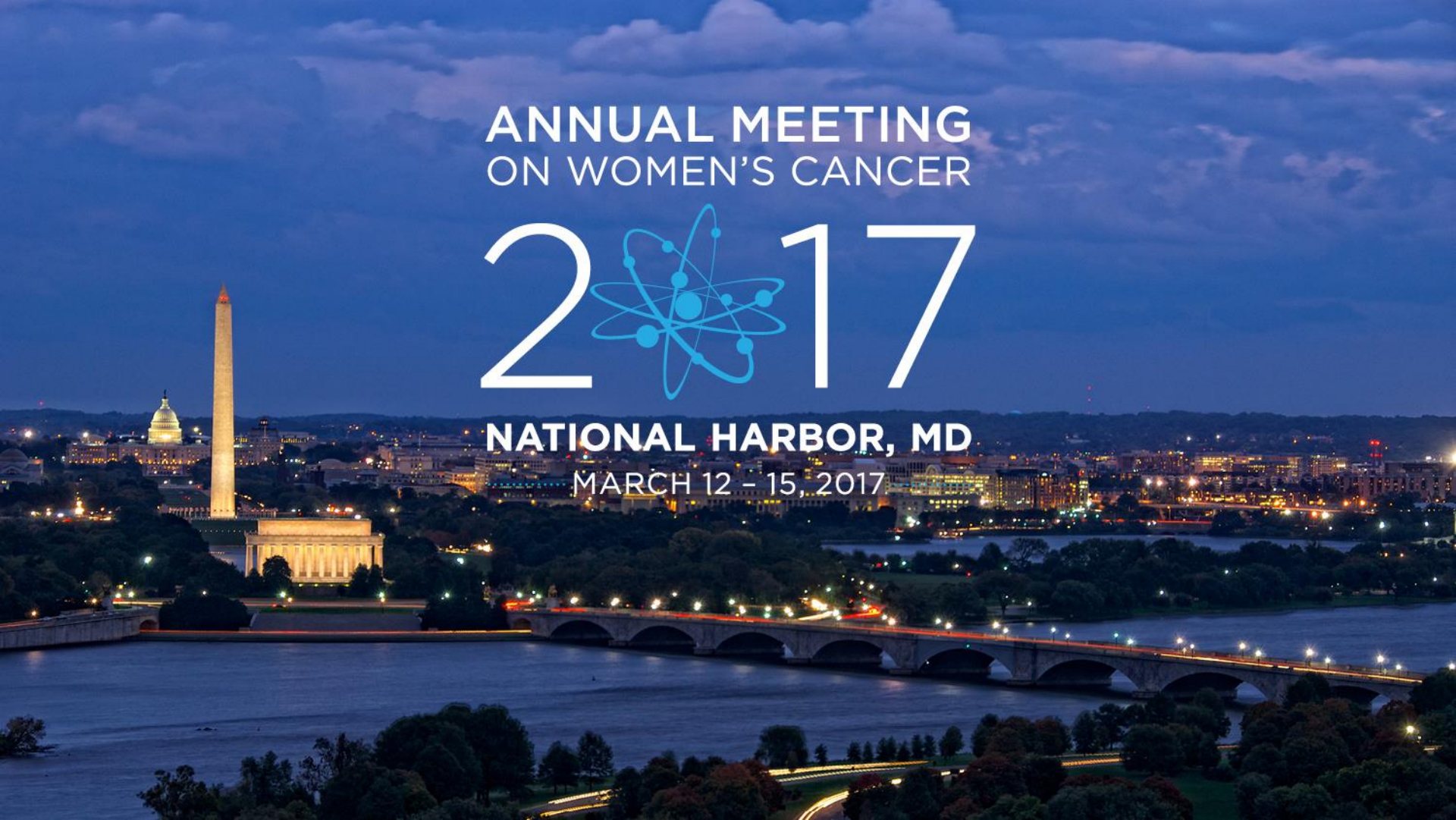
ANNUAL MEETING
ON WOMEN'S CANCER
2017
NATIONAL HARBOR, MD
MARCH 12 – 15, 2017

Treatment with olaparib monotherapy in the maintenance setting significantly improves progression-free survival in patients with platinum-sensitive relapsed ovarian cancer: Results from the Phase III SOLO2 study

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Bringing Together the Best in Women's Cancer Care

Verbal disclosure

- Eric Pujade-Lauraine reports advisory board membership and honoraria from AstraZeneca, and advisory board membership, honoraria, and speaker's bureau membership from Roche
- Jonathan A Ledermann reports honoraria from AstraZeneca, honoraria from Pfizer, and advisory roles from AstraZeneca, Clovis Oncology, Pfizer, and Roche
- Richard T Penson reports honoraria, a consulting and advisory role, and receipt of research funding from AstraZeneca
- Amit M Oza reports a non-compensated advisory role and investigator role for AstraZeneca, Clovis Oncology, Tesaro, and Pfizer
- Jacob Korach reports no disclosures
- Tomasz Huzarski reports no disclosures
- Andrés Poveda reports consulting and advisory roles from Advaxis, AstraZeneca, PharmaMar, and Roche
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- Michael Friedlander reports honoraria and advisory roles from AstraZeneca, and Pfizer
- Nicoletta Colombo reports honoraria and advisory roles from AstraZeneca, Pfizer, Clovis Oncology, Roche, PharmaMar, and Immunogen

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The 295 patients and their families, and…

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A Floquet
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Study Sponsor:
AstraZeneca

Background

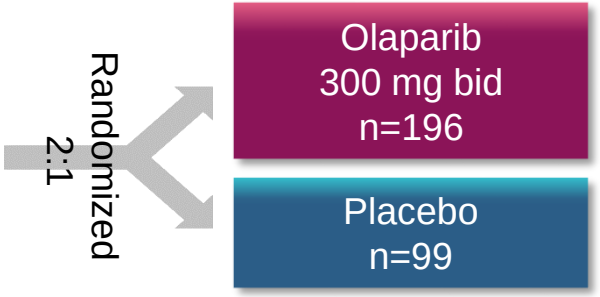
- Olaparib is the first-in-class PARP inhibitor
- In a Phase II trial (Study 19), olaparib maintenance therapy (capsules) provided a significant progression-free survival (PFS) improvement over placebo in all-comer patients with platinum-sensitive, relapsed, high-grade serous ovarian cancer[1]
  - The PFS benefit was greatest for patients with a *BRCA1/2* mutation[2]
- SOLO2/ENGOT-Ov21 (NCT01874353) was a Phase III trial to confirm findings from Study 19 in the *BRCA1/2* mutation subgroup using the olaparib tablet formulation

1. Ledermann JA *et al* 2012; 2. Ledermann JA *et al* 2014

SOLO2/ENGOT-Ov21: study design

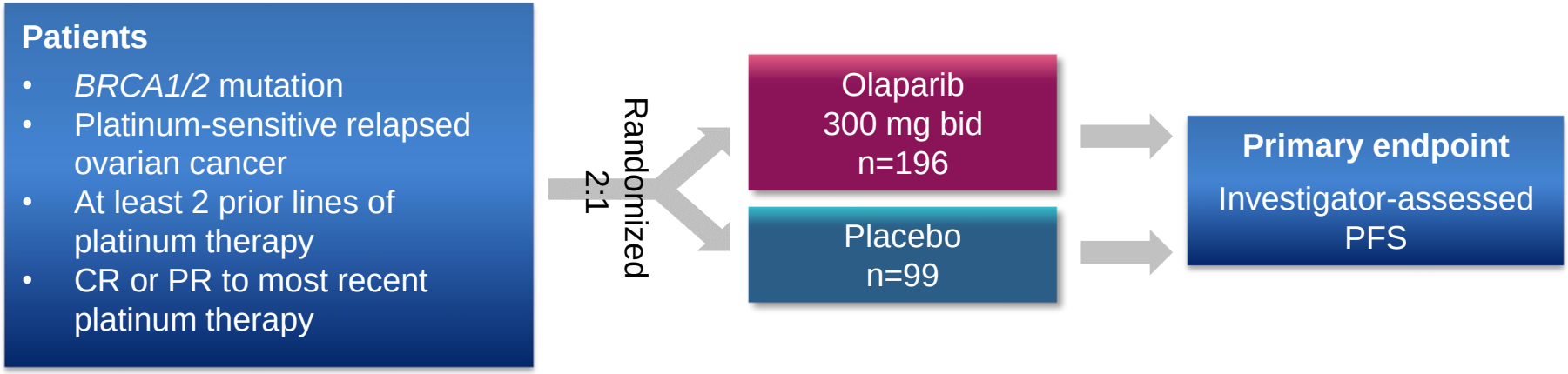
Patients

- *BRCA1/2* mutation
- Platinum-sensitive relapsed ovarian cancer
- At least 2 prior lines of platinum therapy
- CR or PR to most recent platinum therapy



CR, complete response; PR, partial response

SOLO2/ENGOT-Ov21: study design



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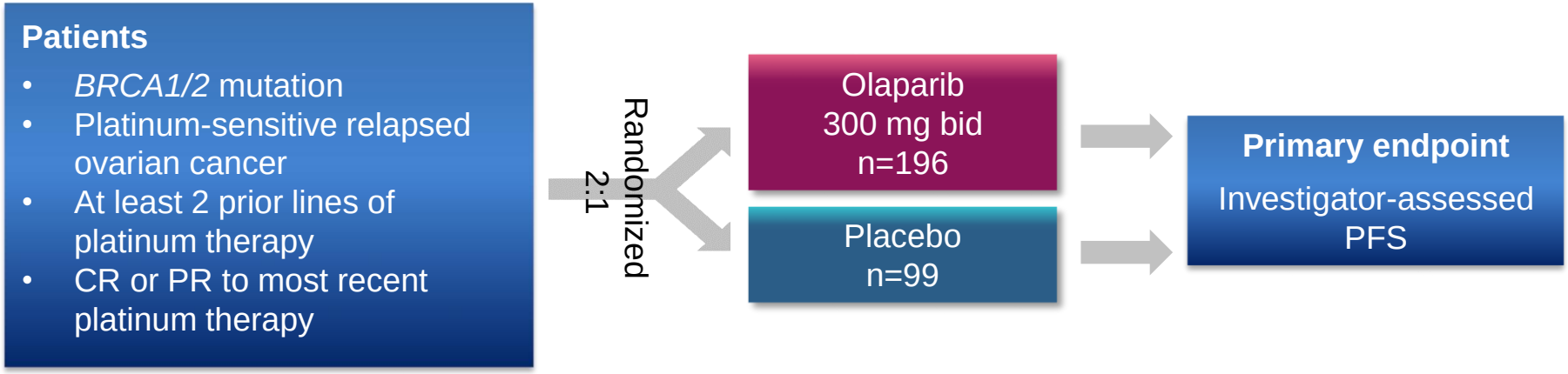
SOLO2/ENGOT-Ov21: study design



Sensitivity analysis: PFS by blinded independent central review (BICR)

- Key secondary endpoints:
  - Time to first subsequent therapy or death (TFST), time to second progression (PFS2), time to second subsequent therapy or death (TSST), overall survival (OS)
  - Safety, health-related quality of life (HRQoL*)

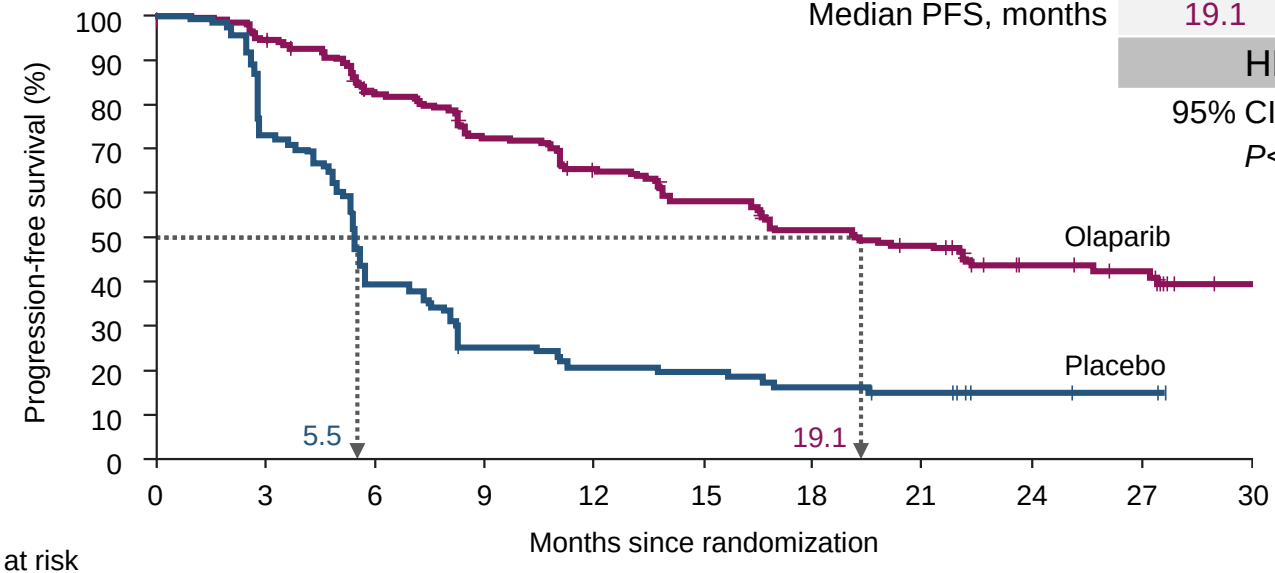
*Primary endpoint for HRQoL was trial outcome index (TOI) of the FACT-O (Functional Assessment of Cancer Therapy – Ovarian)

Demographic and baseline characteristics

Characteristic		Olaparib (n=196)	Placebo (n=99)
Age, median (range)		56 (28–83)	56 (39–78)
Primary tumor type, n (%)	Ovarian	162 (82.7)	86 (86.9)
	Fallopian tube or primary peritoneal	31 (15.8)	13 (13.1)
	Other/missing	3 (1.5)	0
Prior platinum regimens, n (%)	2 lines	110 (56.1)	62 (62.6)
	3 lines	60 (30.6)	20 (20.2)
	≥4 lines	25 (12.8)	17 (17.2)
Platinum-free interval, n (%)	6–12 months	79 (40.3)	40 (40.4)
	>12 months	117 (59.7)	59 (59.6)
Response to platinum therapy, n (%)	Complete response	91 (46.4)	47 (47.5)
	Partial response	105 (53.6)	52 (52.5)

PFS by investigator assessment

	Olaparib (n=196)	Placebo (n=99)
Events (%)	107 (54.6)	80 (80.8)
Median PFS, months	19.1	5.5
HR 0.30		
95% CI 0.22 to 0.41		
P<0.0001		



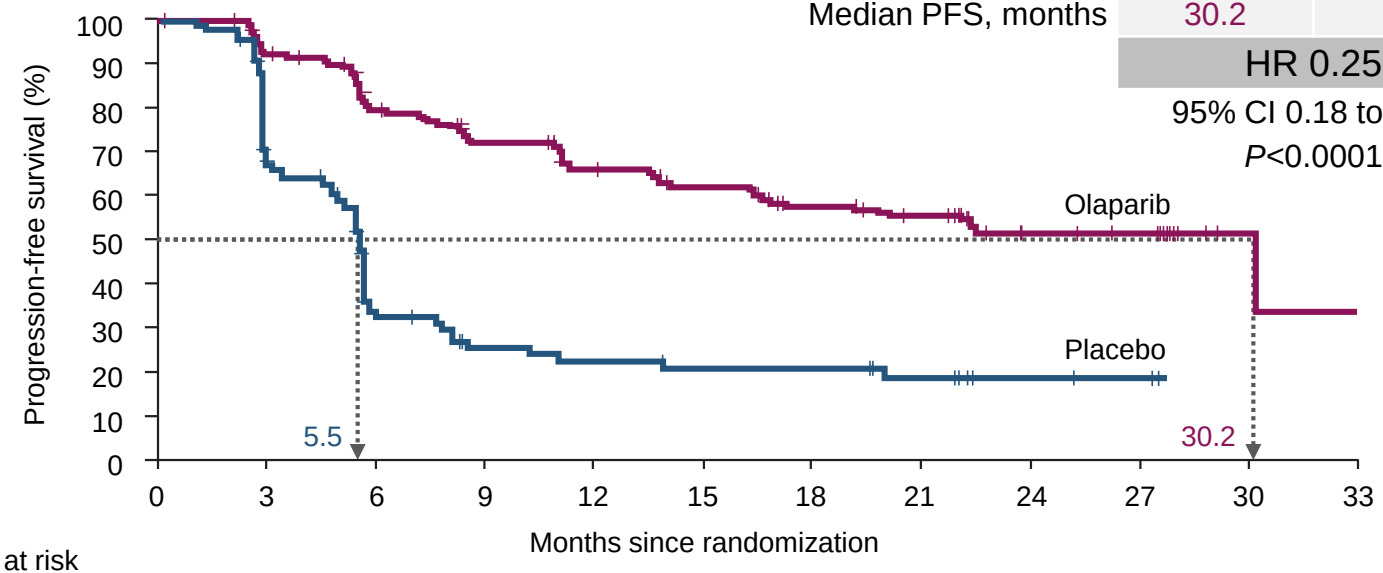
No. at risk

Olaparib	196	182	156	134	118	104	89	82	32	29	3
Placebo	99	70	37	22	18	17	14	12	7	6	0

Median follow-up was 22.1 months in the olaparib group and 22.2 months for placebo

PFS sensitivity analysis using BICR

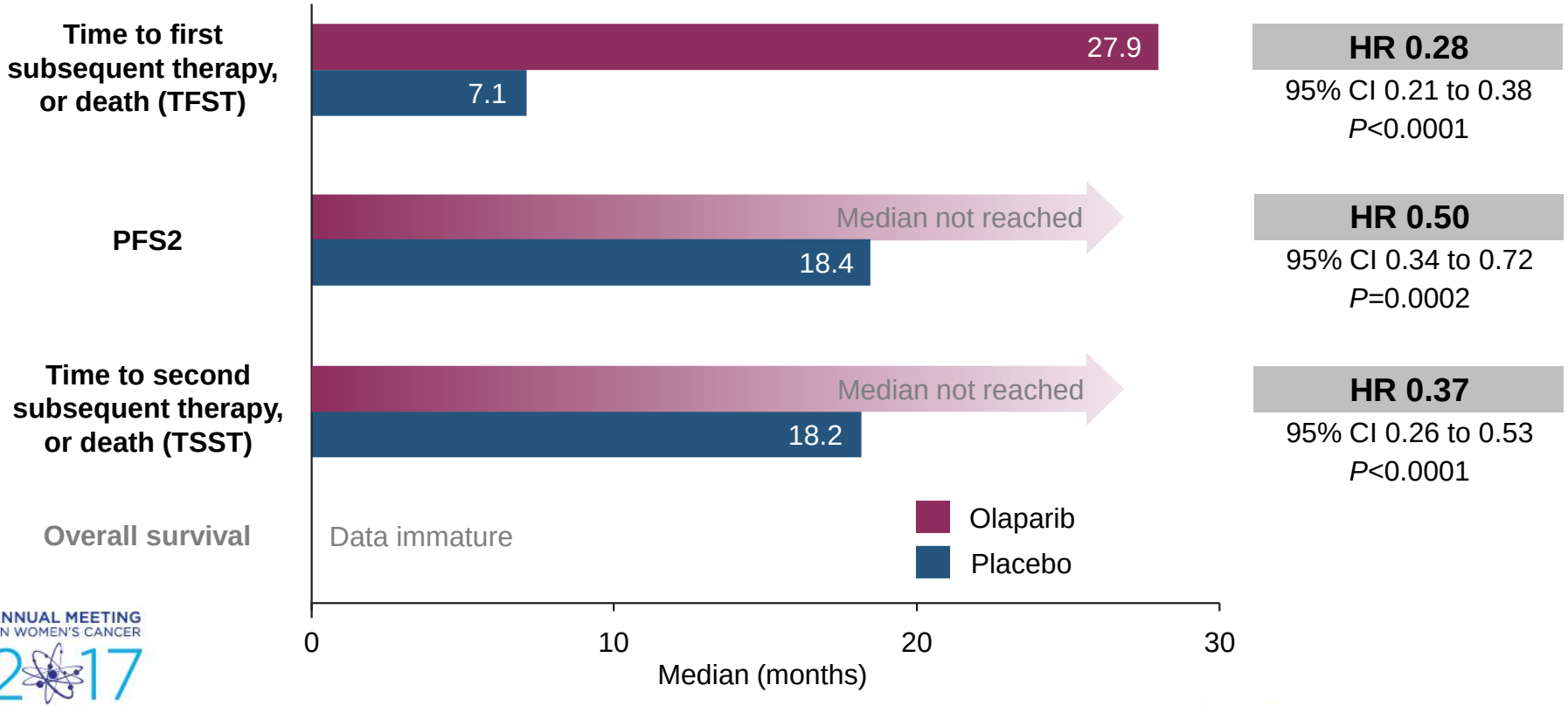
	Olaparib (n=196)	Placebo (n=99)
Events (%)	81 (41.3)	70 (70.7)
Median PFS, months	30.2	5.5
HR 0.25		
95% CI 0.18 to 0.35		
P<0.0001		



No. at risk

Olaparib	196	176	148	128	112	103	88	82	30	28	3	1
Placebo	99	62	26	18	16	14	14	11	6	5	0	0

Secondary efficacy endpoints



Total adverse events

Characteristic, n (%)	Olaparib (n=195)	Placebo (n=99)
Any AE	192 (98.5)	94 (94.9)
Any AE grade ≥3	72 (36.9)	18 (18.2)
Any SAE	35 (17.9)	8 (8.1)
Any AE leading to dose reduction	49 (25.1)	3 (3.0)
Any AE leading to discontinuation of study treatment	21 (10.8)	2 (2.0)
Any AE with an outcome of death	1 (0.5)	0

AE, adverse event; SAE, serious adverse event

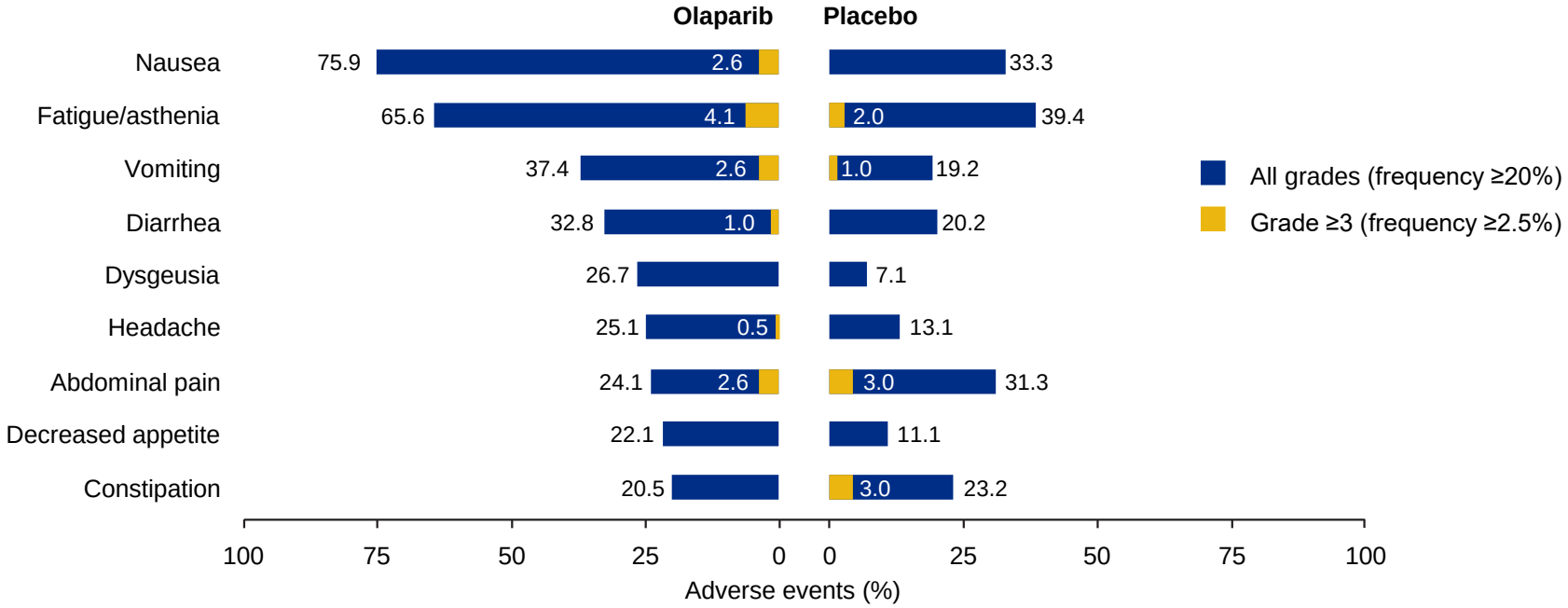
Most common hematologic adverse events

Event, n (%)	Olaparib (n=195)		Placebo (n=99)	
	All grades	Grade ≥3	All grades	Grade ≥3
Anemia*	85 (43.6)	38 (19.5)	8 (8.1)	2 (2.0)
Neutropenia*	38 (19.5)	10 (5.1)	6 (6.1)	4 (4.0)
Thrombocytopenia*	27 (13.8)	2 (1.0)	3 (3.0)	1 (1.0)

MDS/AML: 4 cases in olaparib group (2.1%), including one case of CMML
4 cases in placebo group (4.0%)

*Grouped terms

Most common non-hematologic adverse events



Other AEs of interest
Elevated ALT: 10 patients in olaparib group (5.1%) vs 4 patients in placebo group (4.0%)
Elevated AST: 4 patients in olaparib group (2.1%) vs 4 patients in placebo group (4.0%)

Health-related quality of life: TOI of the FACT-O

TOI over first 12 months	Olaparib (n=185)	Placebo (n=94)
Change from baseline, adjusted mean	−2.90	−2.87

Estimated difference in adjusted means = −0.03 (95% CI −2.19 to 2.13, *P*=0.98)

Conclusions

- SOLO2 demonstrated a statistically significant PFS improvement in patients receiving olaparib, by investigator assessment and BICR
- The PFS benefit was supported by a significant delay in TFST, PFS2 and TSST in the olaparib group
- With the exception of anemia, toxicity was mostly low grade
- SOLO2 is the first Phase III trial of olaparib tablets as maintenance treatment and showed a significant benefit in patients with platinum-sensitive, relapsed ovarian cancer and a *BRCA1/2* mutation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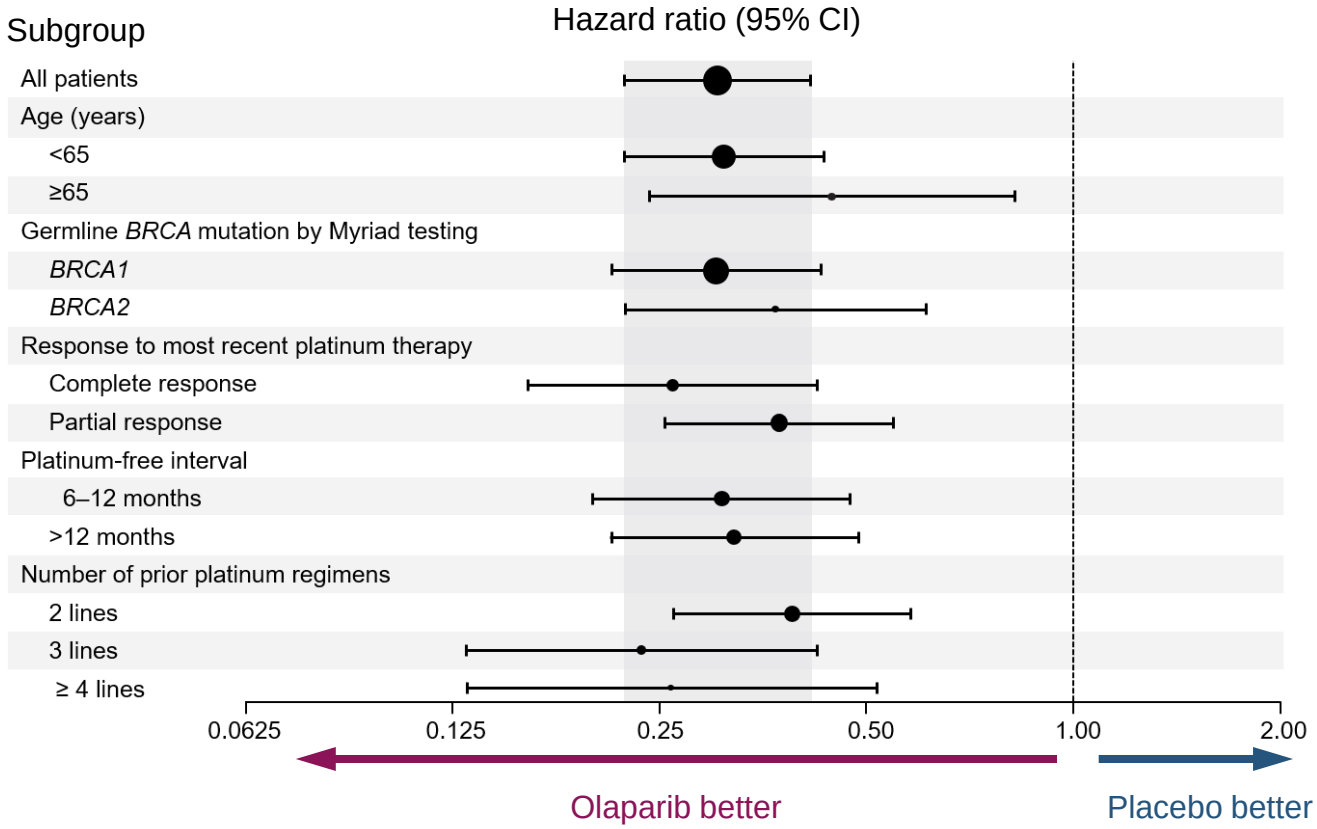
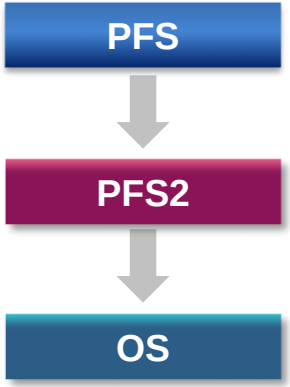
Subgroup analysis of PFS



Hierarchy of statistical testing

Multiple testing procedure



- PFS is tested first using the full alpha. Subsequently, PFS2 is tested only if PFS is statistically significant
- If PFS2 is significant at either the interim or final analyses, the full alpha will be carried forward to OS
- Statistical significance will be declared at the interim analysis for PFS2 if the one-sided $P<0.0125$
- Statistical significance will be declared at the interim analysis for OS if the null hypothesis for PFS2 is rejected at the PFS analysis and the observed P value for OS is $P<0.0001$

Supportive secondary endpoints: TDT, TFST, TSST

TDT, time to treatment discontinuation or death;
TFST, time to first subsequent therapy or death;
TSST, time to second subsequent therapy or death

Proportion of patients event free after 18 months and after 24 months on treatment

Study endpoint	Patient status	Olaparib (n=196), %	Placebo (n=99), %
PFS (investigator assessed)	Progression free, 18 months	51.1	16.2
	Progression free, 24 months	43.0	15.1
PFS (BICR)	Progression free, 18 months	58.7	21.7
	Progression free, 24 months	52.7	19.9
TDT	Discontinuation free, 18 months	51.8	17.2
	Discontinuation free, 24 months	44.8	13.1
PFS2	Second progression free, 18 months	71.8	52.4
	Second progression free, 24 months	59.2	37.3
TFST	First subsequent therapy free, 18 months	65.0	21.8
	First subsequent therapy free, 24 months	54.1	17.3
TSST	Second subsequent therapy free, 18 months	75.8	50.7
	Second subsequent therapy free, 24 months	65.7	33.0

Key study dates

Study event	Date
First subject in (FSI)	3 September 2013
Last subject in (LSI)	21 November 2014
Database lock (DBL)	19 October 2016