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Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: 5-year follow-up from SOLO1

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The SOLO1 trial[1]

5-year survival for newly diagnosed advanced ovarian cancer is 30-50% and patients are at high risk of relapse;[2,3] treatment goals in this setting include delay of recurrence and, for some patients, increased chance of cure

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer
- BRCAm
- ECOG performance status 0–1
- Cytoreductive surgery*
- In clinical complete response or partial response after platinum-based chemotherapy

Olaparib 300 mg bid (N=260)

For up to **2 years** or until disease progression

Placebo (N=131)

Primary endpoint[1]

- PFS (investigator-assessed)

Secondary endpoints included:

- PFS2
- TSST
- Safety

*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease.
BRCAm, deleterious or suspected deleterious germline or somatic mutation on *BRCA1* and/or *BRCA2*; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; PFS, progression-free survival; PFS2, time to second progression or death; TSST, time to second subsequent therapy or death

1. Moore *et al. N Engl J Med* 2018;379:2495–505; 2. Tewari *et al. J Clin Oncol* 2019;37:2317–28; 3. Ledermann *et al. Ann Oncol* 2013;24:vi24–vi32

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Primary analysis DCO: 17 May 2018	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	102 (39)	96 (73)
Median PFS, months	**NR**	**13.8**
HR 0.30 (95% CI 0.23–0.41)		
P<0.001		

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BRCAm, deleterious or suspected deleterious germline or somatic mutation on *BRCA1* and/or *BRCA2*; DCO, data cut-off; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; NR, not reached; PFS, progression-free survival; PFS2, time to second progression or death; TSST, time to second subsequent therapy or death

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We assessed efficacy and safety with long-term follow-up, 5 years after the last patient was randomized (DCO: 5 March 2020)

Median follow-up for PFS:

Olaparib	Placebo
4.8 years	5.0 years

*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease.

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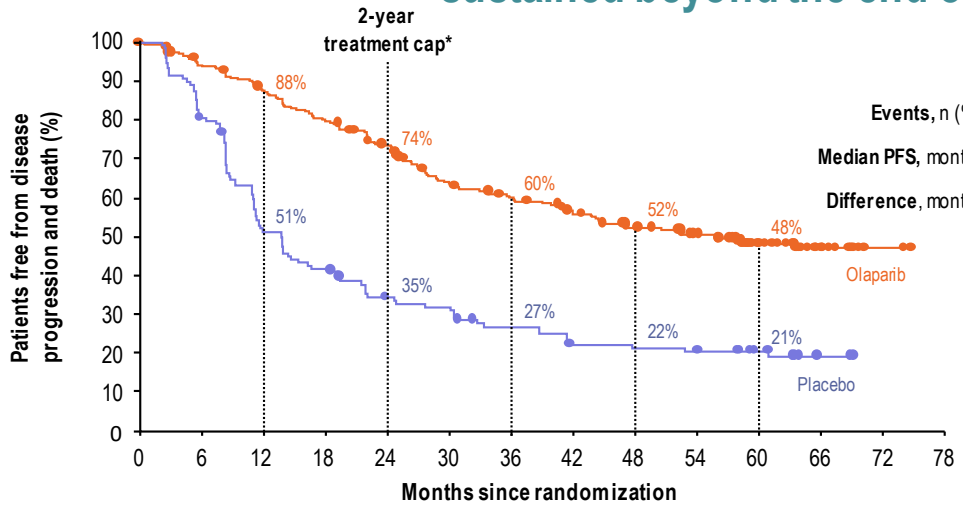
PFS benefit of maintenance olaparib was sustained beyond the end of treatment



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	
	HR 0.33 (95% CI 0.25–0.43)	

Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

No. at risk

Olaparib	260	229	212	194	173	140	129	115	101	91	58	30	2	0
Placebo	131	103	65	53	41	38	30	24	23	22	16	3	0	

*13 patients, all in the olaparib arm, continued study treatment past 2 years; †n=130 (safety analysis set)
Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

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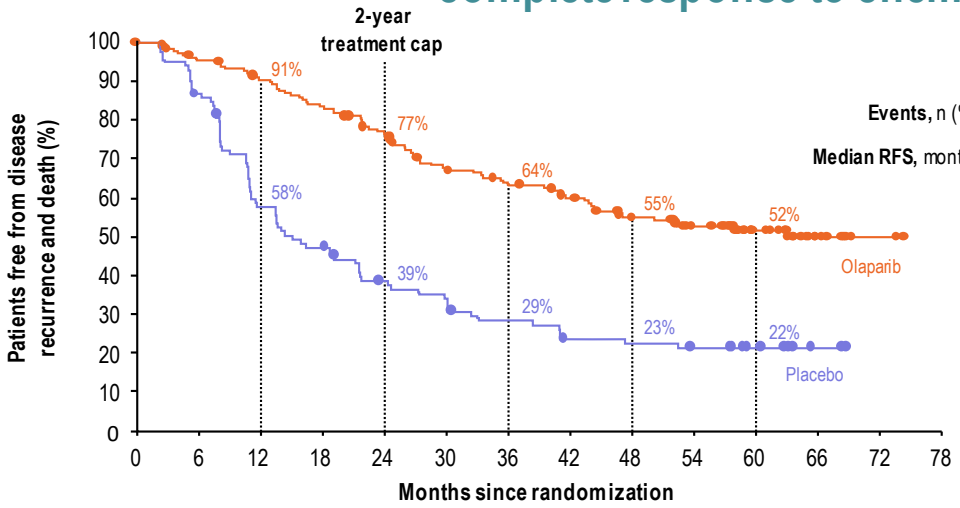
Recurrence-free survival in patients who achieved complete response to chemotherapy



	Olaparib (N=189)	Placebo (N=101)
Events, n (%)	79 (42)	74 (73)
Median RFS, months	**NR**	**15.3**
HR 0.37 (95% CI 0.27–0.52)		

Recurrence-free survival

defined *post hoc* as time from randomization to disease recurrence* or death for patients in complete response† to platinum-based chemotherapy at baseline

No. at risk

Olaparib	189	169	159	147	132	107	99	89	75	66	42	19	2	0
Placebo	101	85	56	46	35	32	25	20	19	18	12	2	0	

*New lesions by imaging; †Based on electronic case report form data
RFS, recurrence-free survival
73% and 77% of olaparib- and placebo-arm patients, respectively, were in CR at baseline. Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

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Secondary efficacy outcomes* support the observed PFS benefit

	Overall		Patients in CR at baseline	
PFS2	Olaparib (n=260)	Placebo (n=131)	Olaparib (n=189)	Placebo (n=101)
Events, n (%)	80 (31)	61 (47)	49 (26)	45 (45)
Event free at 5 years, %	64	41	68	44
Median, months	NR	42.1	NR	52.9
	HR 0.46 (95% CI 0.33–0.65)		**HR 0.48** (95% CI 0.32–0.71)	
TSST				
Events, n (%)	95 (37)	77 (59)	64 (34)	56 (55)
Event free at 5 years, %	62	36	65	39
Median, months	NR	40.7	NR	47.7
	HR 0.46 (95% CI 0.34–0.63)		**HR 0.50** (95% CI 0.35–0.72)	

*Measured from randomization. CR, complete response. DCO: 5 March 2020

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	HR 0.46 (95% CI 0.34–0.63)		**HR 0.50** (95% CI 0.35–0.72)	

Safety profile remained consistent with the primary DCO

n (%)	Olaparib (n=260)	Placebo (n=130)
Any AE	256 (98)	120 (92)
Grade ≥3 AE	103 (40)	25 (19)
Serious AE	55 (21)	17 (13)
AE leading to dose interruption	136 (52)	22 (17)
AE leading to dose reduction	75 (29)	4 (3)
AE leading to treatment discontinuation	30 (12)	4 (3)
MDS/AML	3 (1)	0 (0)
New primary malignancy	7 (3)	5 (4)

No additional cases of MDS/AML reported; incidence remained <1.5%

Follow-up for MDS/AML continued until death due to any cause

*Measured from randomization. AE, adverse event; AML, acute myeloid leukaemia; CR, complete response; MDS, myelodysplastic syndrome. DCO: 5 March 2020

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Conclusions

- We present data from the SOLO1 trial after the longest duration of follow-up for any PARP inhibitor in the newly diagnosed advanced ovarian cancer setting
- The benefit derived from maintenance olaparib was sustained substantially beyond the end of treatment
  - Median PFS was 56 months, whereas median treatment duration was only 25 months
- More than half of women in complete response at baseline who received maintenance olaparib for 2 years remained free from relapse 5 years later
- No new safety signals were observed with long-term follow-up
  - No new cases of MDS/AML were reported and incidence of new primary malignancies remained balanced between arms
- These results provide further evidence to support the use of maintenance olaparib as a standard of care for women with newly diagnosed advanced ovarian cancer and a BRCA mutation, and suggest the possibility of long-term remission or even cure for some patients

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