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

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Objectives: Newly diagnosed advanced ovarian cancer patients (pts) are at high risk of relapse and 5-year survival is 30–50%. Delay of recurrence, prolonged survival and, for some pts, increased chance of cure are goals of treatment in this setting. In SOLO1 (NCT01844986; GOG-3004) pts with advanced ovarian cancer and a BRCA1 and/or BRCA2 mutation (BRCAm) who were in response after first-line platinum-based chemotherapy derived significant progression-free survival (PFS) benefit from maintenance olaparib vs placebo (median 41 months follow-up; median not reached vs 13.8 months; hazard ratio 0.30; P < 0.001; Moore et al. NEJM 2018). We report analyses after 5-years of follow-up (data cut-off [DCO]: March 5, 2020), performed to assess the long-term efficacy and tolerability of maintenance olaparib for newly diagnosed advanced ovarian cancer.

Methods: Pts received maintenance olaparib (tablets; 300 mg bid) or placebo for up to 2 years or until progression. PFS and recurrence-free survival (RFS) were investigator-assessed by modified RECIST v1.1. An exploratory subgroup analysis of PFS in higher-risk (stage IV disease, stage III disease with residual disease following primary debulking surgery, inoperable stage III disease, or stage III disease and had undergone interval surgery) and lower-risk (stage III disease without residual disease following primary debulking surgery) pts was carried out. For pts in complete response at baseline, RFS was defined post hoc as time from randomization to disease recurrence (new lesions by imaging) or death.

Results: A total of 260 pts were randomized to olaparib; 131 to placebo (median treatment duration 24.6 vs 13.9 months, respectively). After a median of 4.8 and 5.0 years of follow-up, median PFS was 56 vs 14 months in the olaparib and placebo arms, respectively (Table). In the higher-risk subgroup 42% of olaparib-arm vs 17% of placebo-arm pts were free from progression at 5 years; in the lower-risk subgroup 56% vs 25% of pts, respectively, were progression free at this time point. Among pts in complete response at baseline, risk of disease recurrence or death was reduced by 63%. The safety profile of olaparib was consistent with previous observations. No new cases of myelodysplastic syndrome or acute myeloid leukaemia were reported (previous DCO: olaparib, 3/260 [1%]; placebo, 0/130), and incidence of new primary malignancies remained balanced between arms (olaparib, 7/260 [3%]; placebo, 5/130 [4%]).

Conclusions: For pts with a BRCAm and newly diagnosed advanced ovarian cancer, the benefit derived from 2 years of maintenance olaparib was sustained beyond the end of treatment, and after 5 years, almost half of pts were progression free vs 20% with placebo. This benefit was consistent across higher- and lower-risk pts. Over 50% of pts in complete response after first-line platinum-based chemotherapy remained free from relapse 5 years after randomization. A total of 5 years of follow-up is the longest for any PARP inhibitor in this setting and no new safety signals were observed.