News

ADDING OLAPARIB TO BEVACIZUMAB MAINTENANCE IMPROVES PROGRESSION-FREE SURVIVAL IN JAPANESE PATIENTS WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER

The Japan subset showed similar progression-free survival to the overall PAOLA-1 population

Findings from a subgroup analysis of the phase III PAOLA-1/ENGOT-ov25 study presented at the ESMO Asia Virtual Congress 2020, held from 20 to 22 November 2020, show that the addition of olaparib to bevacizumab maintenance following standard platinum-based therapy plus bevacizumab provided a progression-free survival (PFS) benefit over bevacizumab alone in the Japan subset of patients with advanced ovarian cancer.

Professor Keiichi Fujiwara of the Gynaecologic Oncology Department at the Saitama Medical University International Medical Centre in Saitama, Japan presented data from the Japanese subset of patients participating in the international phase III PAOLA-1/ENGOT-ov25 study (NCT02477644).

Previously reported findings (***Ray-Coquard I, et al. N Engl J Med 2019;381:2416-2428. DOI: 10.1056/NEJMoa1911361.)*** demonstrated that patients with newly diagnosed advanced ovarian cancer receiving maintenance olaparib in addition to standard first-line platinum-based chemotherapy plus bevacizumab had a statistically significant PFS benefit (hazard ratio [HR] 0.59; 95% confidence interval [CI] 0.49–0.72).

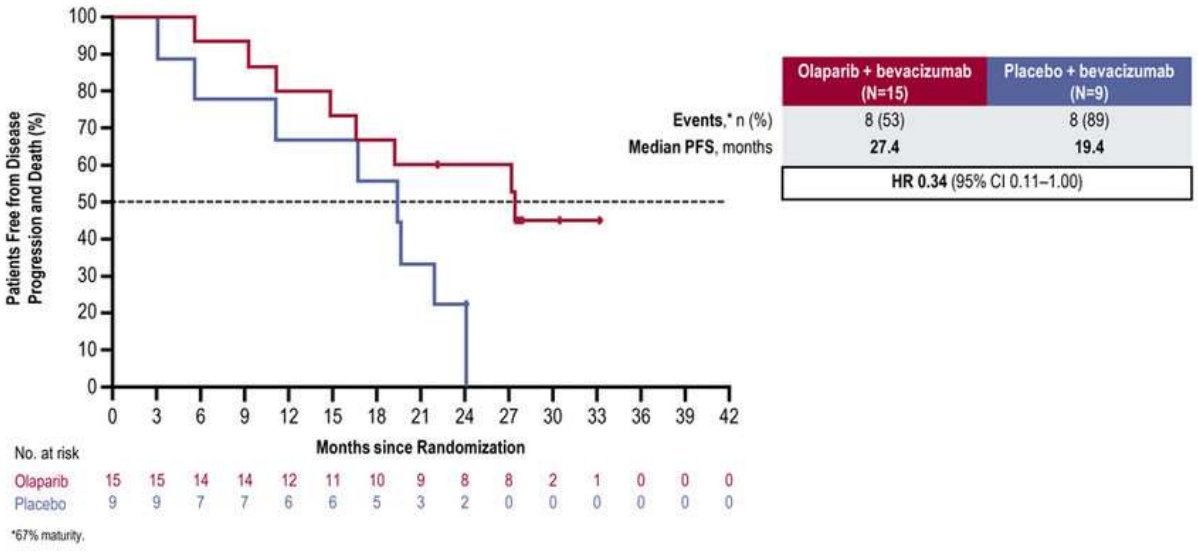
The PAOLA-1/ENGOT-ov25 study enrolled patients with newly diagnosed, FIGO (International Federation of Gynecology and Obstetrics) stage III–IV, high-grade serous or endometrioid ovarian cancer, fallopian tube, or primary peritoneal cancer who had no evidence of disease or were in clinical complete or partial response following first-line treatment with platinum-based chemotherapy plus bevacizumab.

Folllowing 2:1 randomisation, where patients were stratified by first-line treatment outcome and tumour *BRCA* mutation status, in the Japan subset 15 patients received oral olaparib tablets at 300 mg twice daily for up to 24 months plus bevacizumab at 15 mg/kg on day one every 3 weeks for up to 15 months and nine patients received bevacizumab alone.

Patient characteristics were generally well balanced; 20% of patients in the olaparib/bevacizumab arm and 22% of patients in the bevacizumab-alonearm had a tumour *BRCA* mutation and 67% of patients in each arm had homologous recombination deficiency (HRD)-positive status.

The primary endpoint was investigator-assessed PFS per modified RECIST v1.1. PFS was prolonged with the addition of olaparib according to both investigator and BICR assessment With a median follow-up time of 27.7 months in the olaparib/bevacizumab arm and 24.0 months in the bevacizumab alone arm, median PFS per investigator assessment was 27.4 months (95% CI 11.1–not reached) versus 19.4 months (95% CI 3.1–24.0) in the respective treatment arms (HR, 0.34; 95% CI, 0.11–1.00). Median PFS according to blinded independent central review (BICR) was 27.2 months versus 18.3 months, respectively (HR 0.40; 95% CI 0.13–1.23).

Olaparib in combination with bevacizumab maintenance therapy reduced the risk of disease progression or death by 66% compared with bevacizumab alone in the Japan subset of the PAOLA-1 study.



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By investigator assessment PFS events occurred in 53% of patients receiving olaparib/bevacizumab versus 89% of patients receiving bevacizumab alone and according to BICR, PFS events occurred in 47% versus 78% of patients, respectively.

Adverse events (AEs) of Common Terminology Criteria for Adverse Events (CTCAE) Grade ≥3 (version 4.03) were reported by 73% of patients receiving olaparib/bevacizumab compared with 33% of patients receiving bevacizumab alone. The most commonly reported of these were anaemia in five and leukopenia in four patients treated with olaparib/bevacizumab. No cases of myelodysplastic syndrome, acute myeloid leukaemia or new primary malignancies were observed.

Dose interruptions due to an AE occurred in 73% of patients receiving olaparib/bevacizumab versus 44% of patients receiving bevacizumab alone, and discontinuations were reported for 27% versus 11% of patients in the respective groups. Sixty percent of patients treated with olaparib/bevacizumab had dose reductions.

Conclusions

The authors found that patients in the Japan subset of PAOLA-1, demonstrated efficacy results that were generally consistent with those in the overall population, but that the proportion of patients experiencing a Grade ≥3 AEwas generally higher in the subset than in the overall population.They noted that the subgroup analysis was limited by the small number of patients.

Reference

236O – Fujiwara K, Fujiwara H, Yoshida H, *et al.* Olaparib (ola) plus bevacizumab (bev) as maintenance (mx) therapy in patients (pts) with newly diagnosed advanced ovarian carcinoma (OC): Japan subset of the PAOLA-1 trial. ESMO Asia Virtual Congress 2020 (20-22 November).

OLAPARIB MAINTENANCE REDUCES THE RISK OF RECURRENCE IN NEWLY DIAGNOSED PATIENTS WITH ADVANCED OVARIAN CANCER HARBOURING A BRCA MUTATION

The benefits in patients with advanced ovarian cancer and a BRCA mutation lasted well-beyond the two-year olaparib maintenance treatment

Maintenance therapy with olaparib following platinum-based chemotherapy provided a substantial benefit with regard to progression-free survival (PFS) among women with newly diagnosed advanced ovarian cancer and a *BRCA1* and/or *BRCA2* mutation (*BRCAm*), according to long-term SOLO1 findings presented at the ESMO Asia Virtual Congress 2020, held from 20 to 22 November 2020**.**

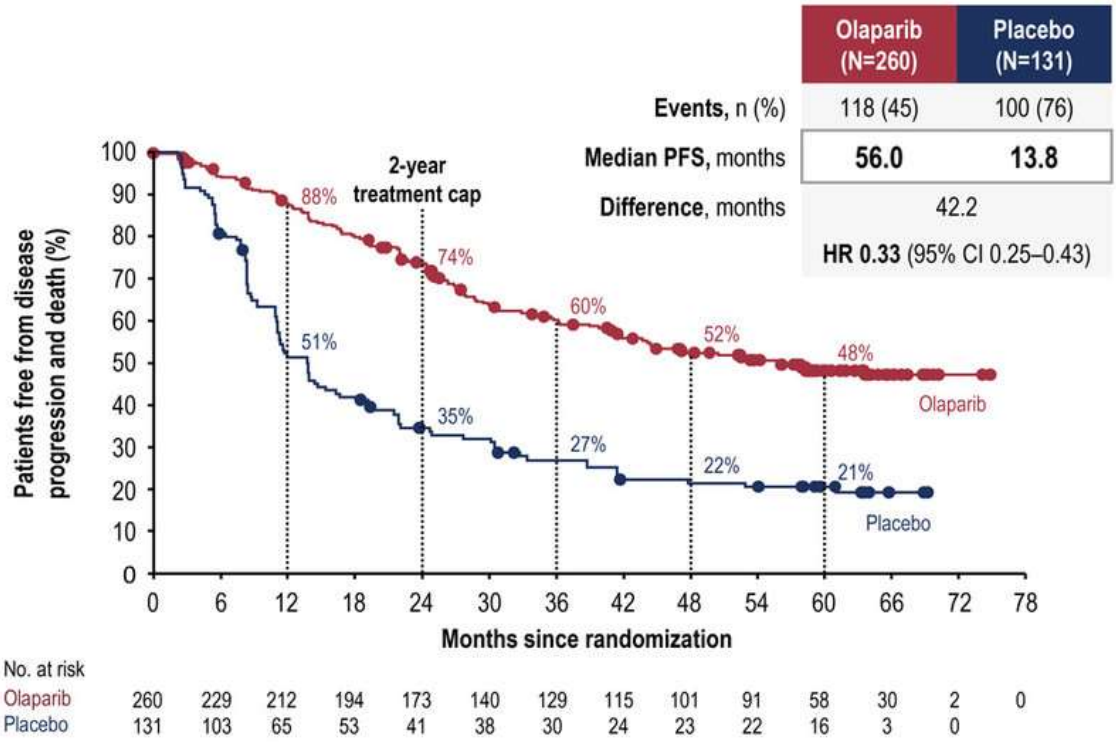
Michael Friedlander of the Medical Oncology Department, University of New South Wales Clinical School, Prince of Wales Hospital in Randwick, Australia presented updated findings on behalf of colleagues with 5 years of follow-up from the SOLO1 (NCT01844986; GOG-3004) study. He noted that, because of the high risk of relapse in patients with newly diagnosed advanced ovarian cancer, the 5-year survival rates are just 30–50%, which makes delaying recurrence, prolonging survival, and increasing the chance of cure the primary treatment goals.

The SOLO1 study (**Moore K, *et al. N Engl J Med* 2018;379:2495-2505. DOI: 10.1056/NEJMoa181085.** enrolled patients with ovarian cancer and a *BRCAm* who were in clinical response after first-line platinum-based chemotherapy. Following 2:1 randomisation, 260 patients received maintenance oral olaparib in 300 mg tablets twice daily and 131 patients received placebo for up to 2 yea) rs or until progression. Previously reported results from SOLO1 demonstrated a significant PFS benefit from maintenance olaparib; with median follow-up of 41 months, the median PFS was not reached (NR) with olaparib, compared with 13.8 months with placebo (hazard ratio [HR] 0.30; $p < 0.001$).

The primary endpoint was investigator-assessed PFS per modified RECIST v1.1. For patients in complete response (CR) at baseline, recurrence-free survival (RFS) was defined *post hoc* as time from randomisation to disease recurrence characterised by new lesions by imaging, or death.

The median treatment duration was 24.6 months with olaparib and 13.9 months with placebo; median follow-up was 4.8 and 5.0 years, respectively.

During follow-up, PFS events were observed in 45% of patients on olaparib versus 76% of patients on placebo. With olaparib maintenance, median PFS was 56.0 months, compared with 13.8 months with placebo (HR 0.33; 95% confidence interval [CI] 0.25–0.43). At 1, 2, 3, 4, and 5 years, 87.7%, 73.6%, 60.1%, 52.3%, and 48.3% of patients receiving olaparib maintence were progression-free, compared with 51.4%, 34.6%, 26.9%, 21.5%, and 20.5% of patients receiving placebo, respectively.



In SOLO1, the risk of disease progression or death was reduced by 67% for women with advanced ovarian cancer and a *BRCA* mutation who received maintenance olaparib, compared with placebo, with the benefit sustained substantially beyond the end of treatment.

Among patients in CR at baseline, median RFS was NR in 189 patients receiving olaparib, compared with 15.3 months in 101 patients receiving placebo (HR 0.37; 95% CI 0.27–0.52), which tranlates to a 63% reduction in the risk of disease recurrence or death. In these patients, at 1, 2, 3, 4, and 5 years, 91.0%, 77.2%, 64.0%, 55.2%, and 51.9% of olaparib-treated patients were recurrence-free, compared with 58.0%, 39.0%, 28.9%, 23.0%, and 21.8% of patients receiving placebo, respectively. Maintenance olaparib demonstrated a safety profile that was consistent with previous observations.

No new cases of myelodysplastic syndrome or acute myeloid leukaemia were reported, and the incidence of new primary malignancies remained balanced between arms at 3% with olaparib and 4% with placebo.

Conclusions

According to the investigators, patients with a *BRCAm* and newly diagnosed advanced ovarian cancer sustained the benefit provided by 2 years of maintenance olaparib beyond the end of treatment; after 5 years, almost half of the patients were progression-free, compared with 20%

of patients receiving placebo. In addition, over 50% of patients in CR after first-line platinum-based chemotherapy remained free from relapse 5 years later.

They noted that the 5-year follow-up in this study is the longest for any PARP inhibitor in this setting, and no new safety signals were observed.

Reference

234O – Friedlander ML, Moore K, Colombo N *et al.* Maintenance olaparib for patients (pts) with newly diagnosed, advanced ovarian cancer (OC) and a BRCA mutation (BRCAm): 5-year (y) follow-up (f/u) from SOLO1. ESMO Asia Virtual Congress 2020 (20–22 November).

EFFICACY IS MANTAINED WHEN NIRAPARIB DOSE IS TAILORED TO PATIENT CHARACTERISTICS IN PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER

Chinese patients receiving niraparib, a potent inhibitor of PARP 1/2, benefited from an individualised starting dose

Chinese patients with platinum-sensitive recurrent ovarian cancer (PSROC) receiving a starting dose of niraparib that was individualised according to each patient's baseline body weight and platelet count demonstrated prolonged median progression-free survival (mPFS) compared to patients receiving placebo. These findings were from a subgroup analysis of the phase III NORA study presented at the ESMO Asia Virtual Congress 2020, held from 20 to 22 November 2020**.**

According to Jianqing Zhu of the Department of Gynaecologic Oncology, Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital) in Hangzhou, China, niraparib maintenance therapy with individualised dosing significantly improved the outcome of Chinese patients with PSROC.It is consistent with the intent-to-treat (ITT) population in NORA.

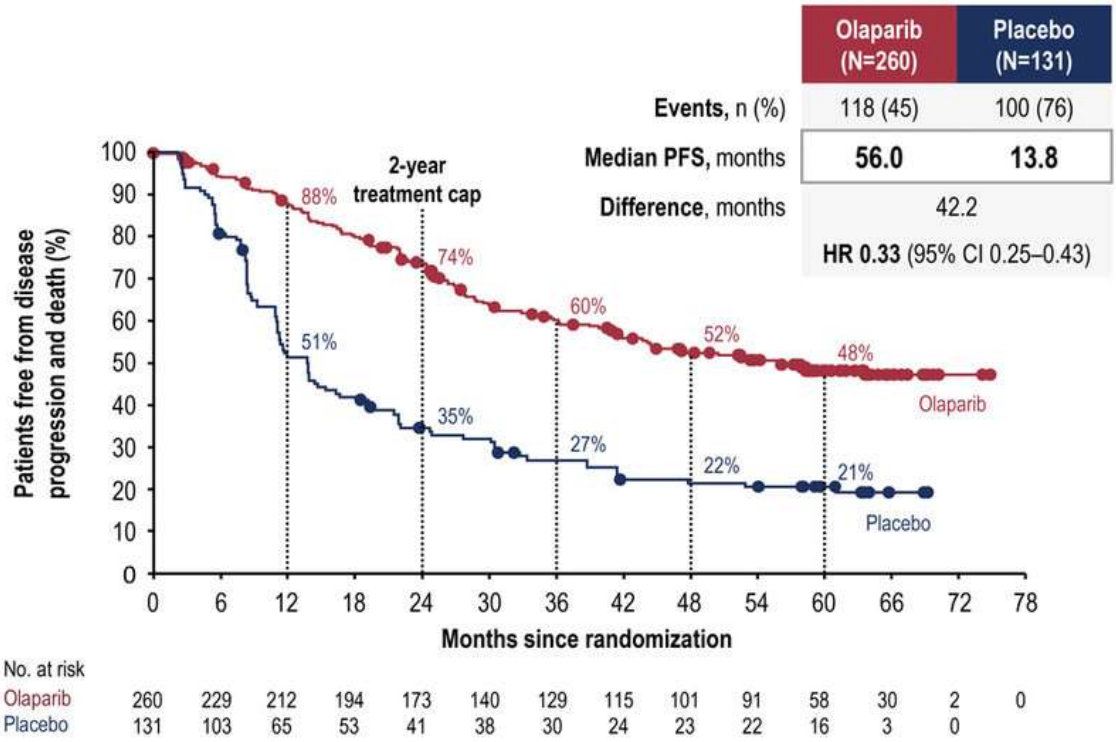
Professor Zhu presented findings from NORA, which was conducted in 32 hospitals throughout China. The study enrolled women aged ≥18 years with PSROC and either high-grade serous histologic or germline *BRCA* mutation features, who achieved a complete or partial response after completion of the last round of platinum therapy.

In the double-blinded, randomised, placebo-controlled phase III NORA (NCT03705156) study, following 2:1 randomisation patients were treated with oral niraparib at 300 mg once daily or placebo. After first 16 patients were treated with the fixed starting dose of 300 mg once daily, the protocol was amended to adopt an individualised starting dosing regimen according to the baseline body weight and platelet count; that is 300 mg once daily for patients with baseline body weight ≥77kg and platelet count ≥150×10^3/μL and for all other patients 200 mg once daily as the starting dose.

The primary endpoint was PFS assessed by blinded independent central review.

Among the 265 randomised patients in the ITT population, the majority of patients (94% [249/265], ITT population) received individualised starting dose. The individualised starting dose subgroup patients had median body weight of 61 kg, and most patients (n=235) received niraparib 200 mg or matched placebo, the minority of patient (n=14) met criteria of receiving 300mg once daily as starting dose.

With individualised dosing, patients treated with niraparib had significantly longer mPFS of 18.3 months than that of 5.4 months observed in the placebo group (hazard ratio [HR] 0.30; 95% confidence interval [CI] 0.21–0.43).



Median progression-free survival in the NORA study.

Regarding the safety anlysis, with niraparib versus placebo the incidence of grade ≥3 treatment emergent adverse events (Aes) was 48.8% versus 20.5%, and the incidences of ≥3 grade haematological AEs of decreased neutrophil count were 20.5% versus 8.4%, decreased platelet count 9.6% versus 1.2%, and anaemia 13.9% versus 2.4%, respectively.

Conclusions

According to the authors this is the first randomised, placebo-controlled phase III study to demonstrate the efficacy and safety of niraparib in Chinese patients with platinum-sensitive recurrent ovarian cancer. They noted that an individualised starting dose of niraparib is effective and well tolerated. Furthermore, they advised that it should be considered standard clinical practice in this patient population.

Reference

235O – Wu X, Zhu J, Yin R, *et al.* Efficacy and safety of Niraparib in Chinese Patients with Platinum-Sensitive Recurrent Ovarian Cancer (NORA) with Individualized Starting Dose: A Subgroup Analysis of A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial. ESMO Asia Virtual Congress 2020 (20-22 November).