Quality of life in patients with advanced high-grade ovarian cancer receiving maintenance therapies after first-line chemotherapy in the randomized Phase III PAOLA-1/ENGOT-ov25 trial (NCT02477644)

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INTRODUCTION/BACKGROUND

- Maintenance therapy in advanced ovarian cancer has been a major breakthrough in gynecologic oncology. PAOLA-1/ENGOT-ov25 was a Phase III trial exploring the efficacy and safety of a 2-year first-line (1L) maintenance therapy with olaparib plus bevacizumab (bev) versus placebo plus bev in patients with advanced ovarian cancer regardless of *BRCA1* and/or *BRCA2* mutation (BRCAm). The study met its primary objective, with a statistically significant improvement in progression-free survival (PFS) in the intent-to-treat (ITT) population.
- Identification of homologous recombination repair defect (HRD phenotype) besides BRCAm led to the successful introduction of 1L maintenance schedules with poly(ADP-ribosyl) polymerase (PARP) inhibitors, such as olaparib.
- Assessing health-related quality of life (HRQoL) is critical in maintenance trials where patients have few or no disease-related symptoms. Besides preventing progression, it is mandatory that maintenance therapy has no detrimental effect on HRQoL. Delaying relapse and time until deterioration might have a positive influence on HRQoL.
- Preliminary analyses reported that olaparib did not alter global health-related quality of life (G-HRQoL).[1]
- Here, we analyzed HRQoL by domains and molecular subgroups, and explored the impact of disease progression on HRQoL.

METHODOLOGY

- HRQoL was a secondary endpoint of the PAOLA-1 study, and was assessed using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 cancer-specific questionnaire and the QLQ-OV28 ovarian module at randomization and every 12 weeks thereafter until 2 years of follow-up regardless of whether disease progressed or not.
- The minimal important difference for clinically relevant change was fixed at 10 points.
- Longitudinal data were analyzed by mixed model for repeated measures (MMRM) and time until definitive deterioration (TUDD). TUDD was defined as the time interval between inclusion in the study and the occurrence of the first clinically significant deterioration of at least 10 points (maintained over time) or death, within the 2-year follow-up period.
- Analyses were undertaken in the ITT population and in the HRD-positive subgroup.
- HRQoL analyses at disease progression (± 60 days) were explored. Mean change in HRQoL between post-progression and pre-progression was reported for each HRQoL domain with its 95% confidence interval (CI).

Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

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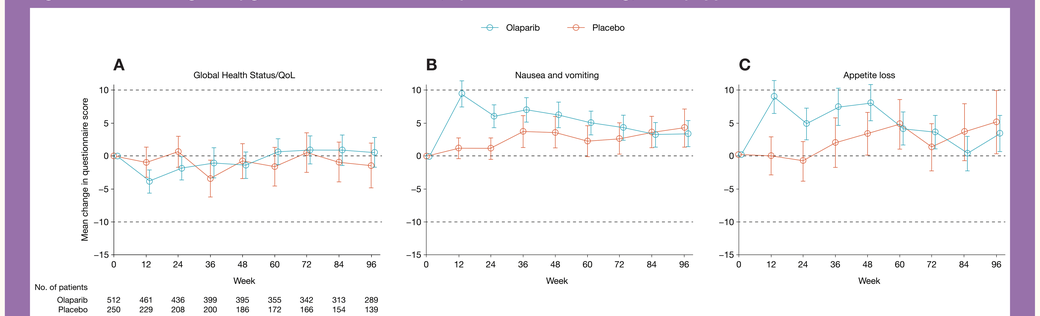
MAIN RESULTS

Figure 1. Mean change in A) global health status/QoL, B) nausea and vomiting, and C) appetite loss



QoL, quality of life.

Figure 2. TUDD Global QoL in A) ITT and B) HRD positive

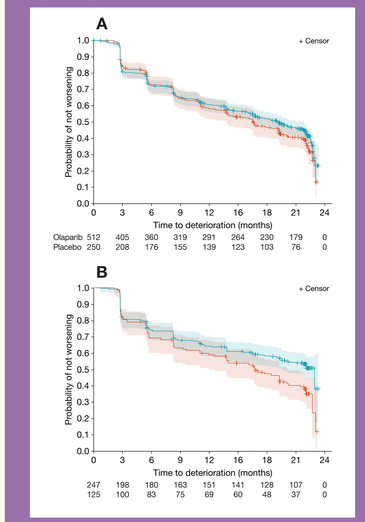
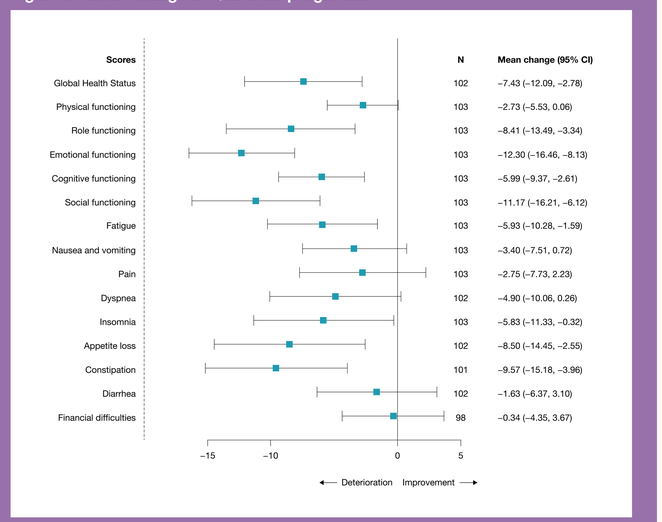


Figure 3. Mean change in QoL after progression



RESULTS

- 806 patients were randomly assigned to olaparib plus bev (n=537) or placebo plus bev (n=269). 465 patients had disease progression over 2 years of follow-up.
- Compliance to HRQoL questionnaires was high at baseline (95%) and over time (>70%).
- MMRM models by HRQoL domain did not reveal a clinically relevant difference between treatment arms over time. TUDD of G-HRQoL did not differ between arms (hazard ratio [HR] 0.88, 95% CI 0.72–1.07) (Figure 1A; Figure 2A). However, nausea and vomiting, together with appetite loss, were more frequently reported in the experimental arm, at least until Week 24, although the difference between arms was not clinically relevant (Figure 1B; Figure 1C).
- In the HRD-positive subgroup (n=372), no difference by domain between treatment arms was observed. Interestingly, G-HRQOL was statistically significant in favour of the olaparib plus bev arm versus the placebo plus bev arm (HR 0.70, 95% CI 0.52–0.93) (Figure 2B).
- In contrast, HRQoL questionnaires available at disease progression showed a clinically significant deterioration in emotional (mean change −12.30 points; 95% CI −16.46 to −8.13) and social (−11.17 points; 95% CI −16.21 to −6.12) functioning in both treatment arms at disease progression, among 103 patients with HRQoL questionnaires available at disease progression (Figure 3).

CONCLUSIONS

- HRQoL investigation was feasible on a long-term basis in PAOLA-1. These data support the relevance of long-term HRQoL measures in gynecologic oncology maintenance trials. Long-term HRQoL measure is an unmet need in general and our data support its feasibility.
- Olaparib plus bev maintenance therapy had no detrimental effect on the G-HRQoL scores, a finding of importance considering that nearly 50% of patients who had response to platinum-based chemotherapy in PAOLA-1 had no evidence of disease at study entry.
- Use of an effective maintenance therapy in patients with high-grade ovarian cancer, in the 1L setting, is likely to delay the clinically significant deterioration in emotional and social functioning we identified in patients at disease progression across the PAOLA-1 treatment arms.

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