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Health-related quality of life in patients with newly diagnosed advanced ovarian cancer treated with niraparib vs placebo: Results from the phase 3 randomized PRIMA/ENGOT-OV26/GOG-3012 trial

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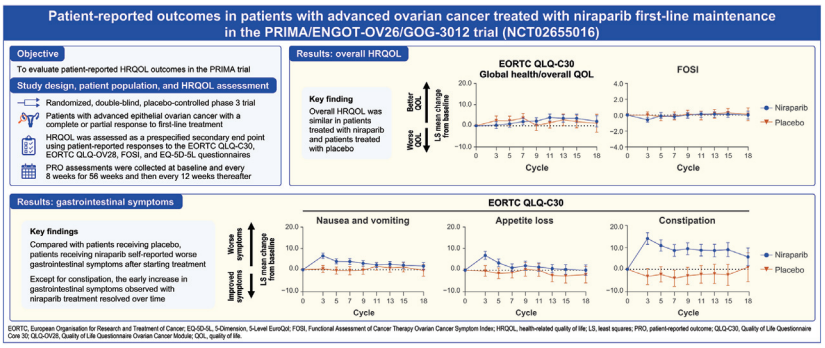
HIGHLIGHTS

- Detailed analysis of patient-reported outcomes from the PRIMA trial of niraparib as a first-line maintenance therapy.
- Compared with placebo, niraparib-treated patients self-reported worse symptoms of constipation, nausea/vomiting, and appetite loss.
- Except for constipation, the increase in gastrointestinal symptoms compared with placebo resolved over time.
- No worsening of fatigue, headache, insomnia, or abdominal pain over time were noted on self-reported questionnaires.
- Overall quality of life was generally maintained with niraparib treatment despite patient-reported gastrointestinal symptoms.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective. To assess patient-reported health-related quality of life (HRQoL) in patients with ovarian cancer (OC) who received niraparib as first-line maintenance therapy.

Methods. PRIMA/ENGOT-OV26/GOG-3012 (NCT02655016) enrolled patients with newly diagnosed advanced OC who responded to first-line platinum-based chemotherapy. Patients were randomized (2:1) to niraparib or placebo once daily in 28-day cycles until disease progression, intolerable toxicity, or death. HRQoL was assessed as a prespecified secondary end point using patient-reported responses to the European Organisation for Research and Treatment of Cancer QOL Questionnaire (EORTC QLQ-C30), the EORTC QLQ Ovarian Cancer Module (EORTC QLQ-OV28), the Functional Assessment of Cancer Therapy–Ovarian Symptom Index (FOSI), and EQ-5D-5L questionnaires. Assessments were collected at baseline and every 8 weeks (±7 days) for 56 weeks, beginning on cycle 1/day 1, then every 12 weeks (±7 days) thereafter while the patient received study treatment.

Results. Among trial participants (niraparib, $n = 487$; placebo, $n = 246$), PRO adherence exceeded 80% for all instruments across all cycles. Patients reported no decline over time in HRQoL measured via EORTC QLQ-C30 Global Health Status/QoL and FOSI overall scores. Scores for abdominal/gastrointestinal symptoms (EORTC QLQ-OV28) and nausea and vomiting, appetite loss, and constipation (EORTC QLQ-C30) were higher (worse symptoms) in niraparib-treated patients than placebo-treated patients; except for constipation, these differences resolved over time. Patients did not self-report any worsening from baseline of fatigue, headache, insomnia, or abdominal pain on questionnaires.

Conclusions. Despite some early, largely transient increases in gastrointestinal symptoms, patients with OC treated with niraparib first-line maintenance therapy reported no worsening in overall HRQoL.

1. Introduction

Most (approximately 70%) patients with advanced ovarian cancer (OC) who respond to platinum-taxane combination chemotherapy will eventually experience disease recurrence [1,2]. Maintenance treatment with poly(ADP-ribose) polymerase (PARP) inhibitors with or without antiangiogenic therapy has emerged as an important option to help delay and/or reduce the risk of disease recurrence [3–6].

Niraparib, an oral, highly selective PARP inhibitor, has been shown to significantly extend progression-free survival (PFS) when given as first-line maintenance therapy in patients with newly diagnosed OC after complete or partial disease response to platinum-based chemotherapy [7,8]. In the primary analysis of the phase 3, PRIMA/ENGOT-OV26/GOG-3012 trial, patients treated with niraparib experienced significantly longer PFS than those treated with placebo, regardless of biomarker status [7]. In the niraparib arm, the most common grade ≥ 3 adverse events were hematological (anemia, thrombocytopenia, and neutropenia); the most common any-grade nonhematological adverse events were nausea, constipation, fatigue, headache, insomnia, vomiting and abdominal pain [7].

In a subsequent ad hoc analysis conducted after additional follow-up time, the PFS benefit of niraparib treatment was maintained and no additional safety signals were identified [9].

Patient-reported outcome (PRO) measures are critical tools for examining health-related quality of life (HRQoL) in patients with OC [10]. Evaluation of the patient treatment experience is particularly relevant for maintenance therapy, where the treatment goal is generally not curative but rather to delay progression and patients can stay on treatment for months, if not years. For niraparib, topline assessment of PRO data from PRIMA found no difference in HRQoL between patients who received niraparib and those who received placebo [7]. However, the analysis did not evaluate PROs for symptoms potentially associated with known adverse events. In particular, there is significant interest in better understanding niraparib-treated patients' experience of

fatigue, a common symptom of anemia, and gastrointestinal symptoms, which have been reported with niraparib maintenance therapy [11]. To address this knowledge gap, the current analysis from the PRIMA study provides a detailed assessment of PRO findings across patient populations with a specific focus on patient-reported experiences for symptoms and domains most closely associated with the safety profile of niraparib.

2. Methods

2.1. Study design

The study design and primary analysis results for the phase 3 double-blind, placebo-controlled PRIMA/ENGOT-OV26/GOG-3012 study (NCT02655016) have been described previously [7]. In brief, the study enrolled patients 18 years or older with newly diagnosed, histologically confirmed, advanced (International Federation of Gynecology and Obstetrics [FIGO] stage III/IV), high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer (collectively referred to as OC) who had a complete or partial response following 6–-9 cycles of first-line platinum-based chemotherapy. Patients were eligible for enrollment regardless of homologous recombination deficiency (HRD) status. Tumor samples underwent central tumor HR testing (myChoice® HRD test; Myriad Genetics, Inc., Salt Lake City, UT, USA). Tumors that had a deleterious *BRCA* mutation, a genomic instability score ≥ 42, or both were considered homologous recombination deficient (HRd); tumors that were *BRCA* wild-type and had a genomic instability score < 42 were considered HR proficient (HRp). Patients in whom tumor HR status was not determined (HRnd) were eligible and included in the overall population [7].

Patients were randomized 2:1 to receive niraparib or placebo orally once daily in 28-day cycles until progressive disease or intolerable toxicity. Stratification factors were clinical response after first-line platinum-based chemotherapy (complete or partial response), receipt of neoadjuvant chemotherapy (yes or no), and tumor HRD status (HRd vs HRp/HRnd). At study start, all patients received a fixed starting dose of 300 mg; subsequently, the protocol was amended to incorporate an individualized starting dose of 200 or 300 mg based on baseline body weight and platelet count. The study was performed in accordance with the tenets of the Declaration of Helsinki, Good Clinical Practices, and all local laws under the auspices of an independent data and safety monitoring committee; all patients gave informed written consent [7].

2.2. End points and PRO instruments

The primary end point of the trial was PFS assessed by blinded independent central review. Patient HRQoL was a secondary end point and was assessed using the European Organisation for Research and Treatment of Cancer [EORTC] Quality of Life Questionnaire [EORTC QLQ-C30] [12], the EORTC Quality of Life Questionnaire Ovarian Cancer module [EORTC QLQ-OV28]) [13], the Functional Assessment of Cancer Therapy–Ovarian Symptom Index [FOSI] [14], and the EQ-5D-5L [15] (Table 1). See Supplemental Methods for additional information on the PRO measures.

Table 1
PRO instruments, end points, and analyses.

Instrument	Response options	Domains assessed	Score range	Higher scores indicate	End points and analyses
EORTC QLQ-C30 [16,17] European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire	4-point Likert scale	**Functional scales**: physical, role, emotional, cognitive, social function	0–100	Better functioning	For all scores at each time point: • Data completeness • Baseline scores • LSM change from baseline • Select item-level responses for QLQ-C30[a] and QLQ-OV28[b]
	4-point Likert scale	**Symptoms**: fatigue, nausea & vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties	0–100	Worse symptoms	
	7-point numeric rating scale	**Global health status/QoL**	0–100	Better QoL	
EORTC QLQ-OV28 [17,18] European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module	4-point Likert scale	**Functional scales**: body image, sexuality, attitude toward disease/treatment	0–100	Better functioning	
	4-point Likert scale	**Symptoms**: abdominal/gastrointestinal symptoms, peripheral neuropathy, hormonal/menopausal symptoms, other chemotherapy side effects, hair loss	0–100	Worse symptoms	
FOSI [19–21] Functional Assessment of Cancer Therapy Ovarian Cancer Symptom Index	5-point Likert scale	**Symptoms**: fatigue, nausea, bloating, worry, pain, vomiting, cramping, QoL	0–32	Better (fewer) symptoms/Better health	For all scores at each time point: • Data completeness • Baseline scores • LSM change from baseline • Select item-level responses[c]
EQ-5D-5L [22]	5-point Likert scale	**Health state for 5 domains**: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. The application of country-specific weights for each item yields a **health utility index (HUI)**[d]	HUI < 0–1	Better QoL	For the instrument: • Data completeness For the HUI: • Baseline scores • LSM change from baseline
	Visual analog scale	**Visual analog scale (VAS)**	0–100	Better QoL	For VAS: • Baseline scores • LSM change from baseline

HUI, health utility index; LSM, least squares mean; PRO, patient-reported outcome; QoL, quality of life.
[a] Item-level responses for the overall population for constipation, pain interference with daily activity, diarrhea, lacked appetite, trouble sleeping, needed rest, felt weak, tired, felt nauseated, vomited, and pain.
[b] Item-level responses for the overall population for abdominal pain, change in bowel habit, and dissatisfied with body.
[c] Item-level responses for the overall population for quality of life, nausea, and vomiting.
[d] The United States value set was used for the analysis.

Patients completed PRO assessments at baseline (defined as the most recent measurement prior to the first administration of the study drug including day 1 of cycle 1) and every 8 weeks (±7 days) for 56 weeks and every 12 weeks (±7 days) thereafter while receiving study treatment. PRO assessments were also collected at the time of treatment discontinuation and at specified intervals after the last dose of study treatment. Patients completed paper versions of PRO instruments in their native language either during a site visit or remotely (returned by mail). Language-specific questionnaires were available for all participating countries. For study visits, patients filled out PRO instruments before undergoing any other procedures. This analysis reports PRO data for on-treatment intervals only.

2.3. Statistical analysis

All data presented are from the primary analysis data cut (clinical cutoff date: May 17, 2019), and results are reported by treatment arm. The study was not powered to determine a treatment difference in the PRO end points. Summary statistics for observed baseline values included means and standard deviations for the overall population. PRO questionnaire adherence, calculated as the number of completed questionnaires divided by the number of questionnaires that were expected to be completed at each visit, was assessed over time in the overall population by treatment arm.

Least squares (LS) mean change from baseline was estimated using a mixed-effects model for repeated measures (MMRM) to adjust for data variability. The MMRM included treatment, visit, and treatment-by-visit interaction as explanatory variables, with the baseline value as a covariate along with the baseline-by-visit interaction. Treatment, visit, and treatment-by-visit interactions were fixed effects in the model; the patient was treated as a random effect. An unstructured covariance matrix was used to model the within-patient variance, and the Kenward-Roger approximation was used to estimate the degrees of freedom. Restricted maximum likelihood estimation was used. An overall adjusted mean

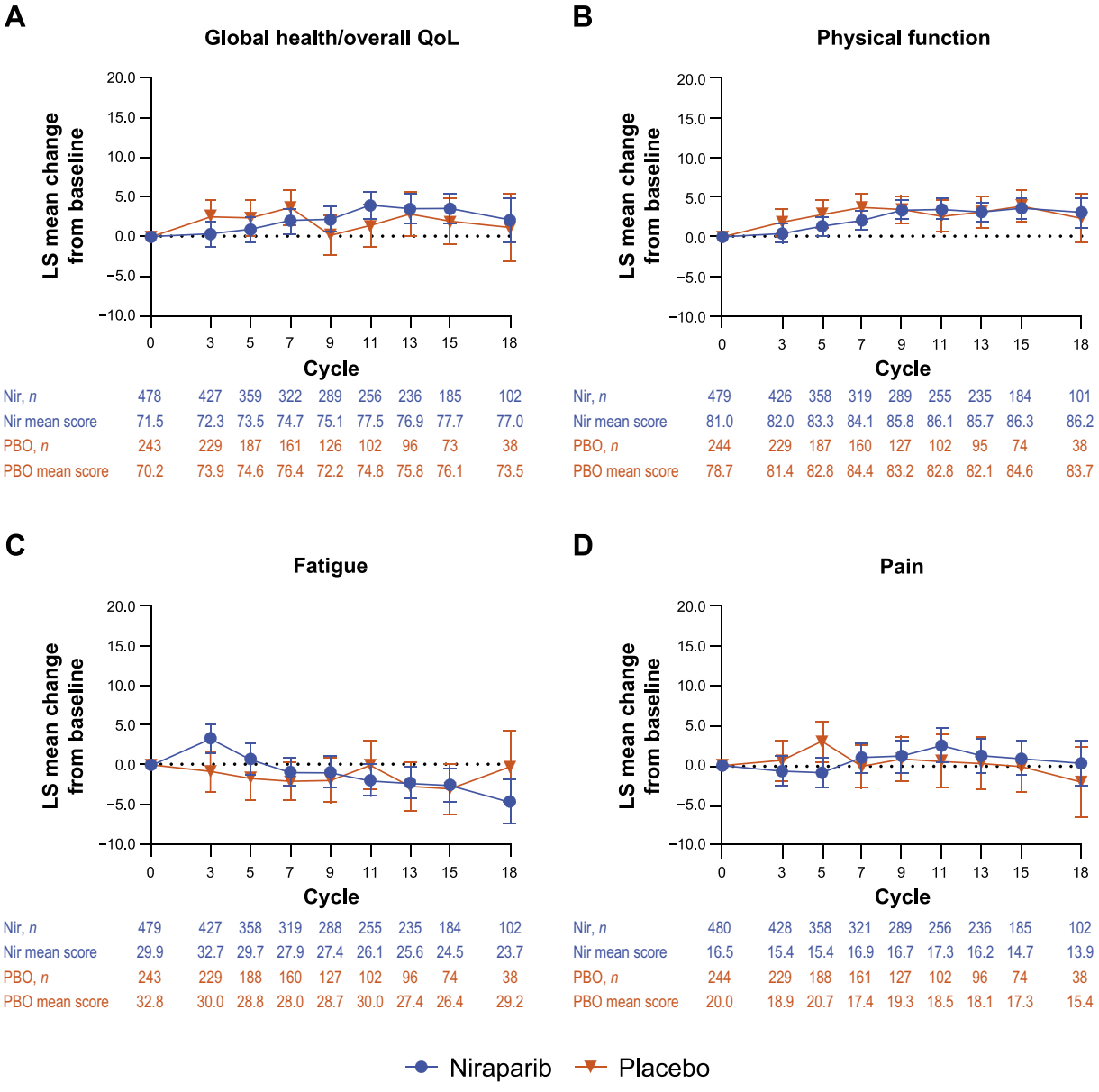

Fig. 1. EORTC QLQ-C30 LS mean change from baseline over time in the overall population through cycle 18. The LS mean change from baseline scores with 95% confidence intervals (represented by error bars) over time are reported for (A) the global health/overall QoL score, (B) physical function score, and symptom-specific scores for (C) fatigue and (D) pain. The numbers underneath each graph detail the number of patients with data at each cycle and the mean score at each cycle for each treatment arm. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; LS, least squares; Nir, niraparib; PBO, placebo; QoL, quality of life.

estimate of the treatment difference was derived, representing the average treatment effect over visits, giving each visit equal weight. If the fit of the unstructured covariance structure failed to converge, alternative covariance structures were explored to reach convergence. For each PRO instrument, the MMRM analysis population included patients in the overall (intent to treat) population who had a baseline assessment and at least one postbaseline PRO assessment. The analysis included baseline and postbaseline visits unless a visit had excessive missing data (defined as >75% missing data). Methods for handling incomplete PRO instruments were performed according to their scoring manuals.

LS mean change from baseline (95% CI) data over time for the overall, HRd, and HRp populations are reported for EORTC-QLQ-C30 (global health and overall quality of life [QoL], physical function, fatigue, pain, nausea and vomiting, appetite loss, constipation, and diarrhea), EORTC-QLQ-OV28 (abdominal/gastrointestinal symptoms, attitude toward disease/treatment, other chemotherapy side effects), FOSI, and EQ-5D-5L (HUI and VAS). For the EQ-5D-5L weighted health state utility value calculations, the United States value set was used. In the overall population, individual item responses related to rest, weakness, pain, problems sleeping, fatigue, loss of appetite, nausea, constipation, vomiting, and diarrhea were reported for EORTC QLQ-C30; abdominal pain, change in bowel habits, and body dissatisfaction for EORTC QLQ-OV28; and content with QoL, nausea, fatigue, pain, and vomiting for FOSI. All analyses were conducted using SAS software, version 9.4 (copyright 2013 SAS Institute Inc., Cary, NC, USA).

3. Results

The PRIMA study enrolled and randomized a total of 733 patients (niraparib, 487; placebo, 246). Primary analysis results, including detailed baseline demographic and clinical characteristics, have been published previously [7].

3.1. PRO adherence and baseline scores

Patient PRO adherence rates remained consistently high (>80%) across all instruments and all time points throughout the trial in both

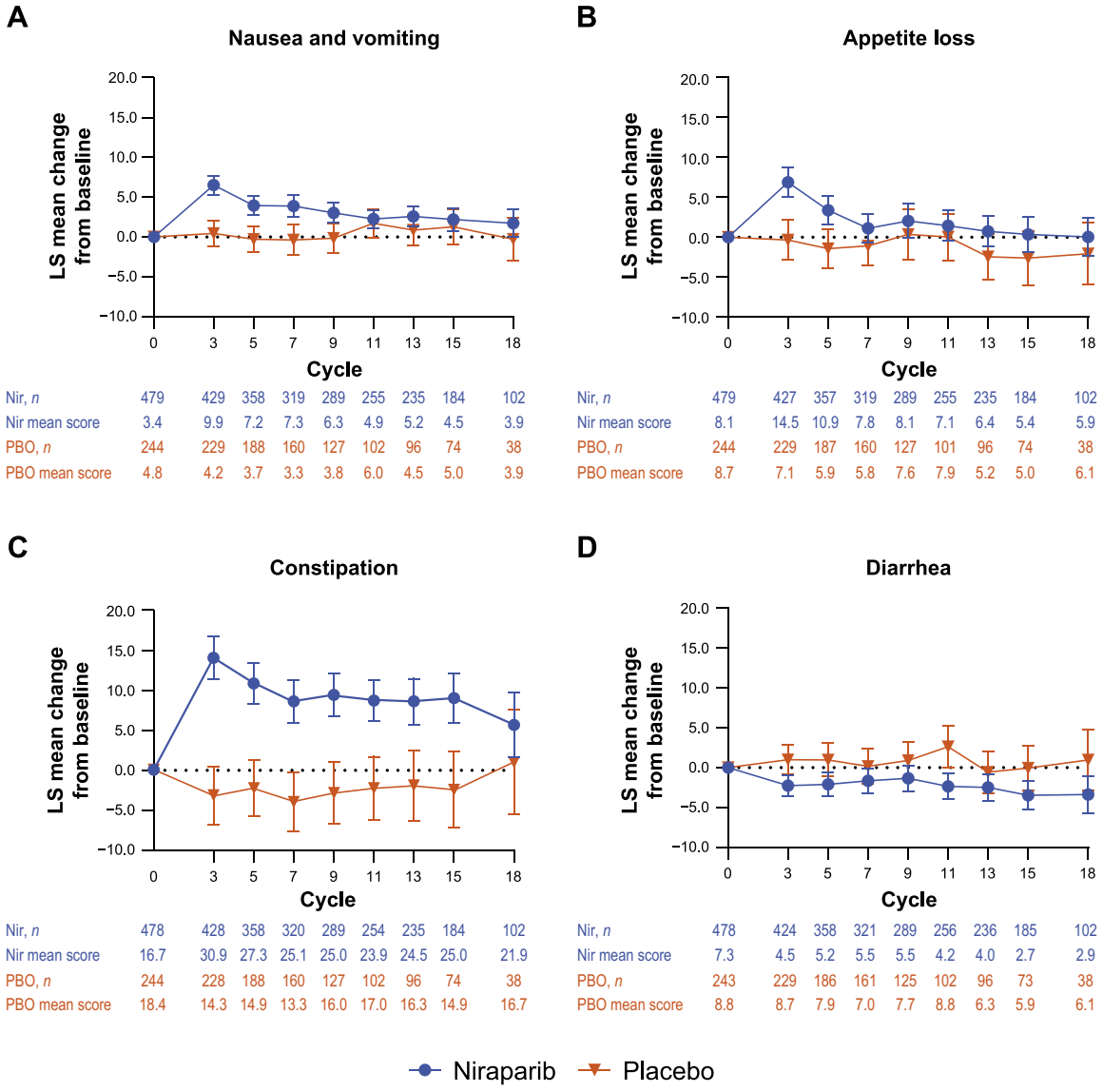

Fig. 2. EORTC QLQ-C30 LS mean change from baseline over time for gastrointestinal symptoms in the overall population through cycle 18. The LS mean change from baseline scores with 95% confidence intervals (represented by error bars) over time are reported for (A) nausea and vomiting, (B) appetite loss, (C) constipation, and (D) diarrhea. The numbers underneath each graph detail the number of patients with data at each cycle and the mean score at each cycle for each treatment arm. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; LS, least squares; Nir, niraparib; PBO, placebo; QoL, quality of life.

treatment arms (Supplementary Fig. S1). All PRO scores at baseline were similar between the niraparib and placebo arms in the overall, HRd, and HRp populations (Supplemental Table S1).

3.2. LS mean change from baseline

PROs were evaluated over time using LS mean change from baseline, with results reported through cycle 18, which corresponds to the median follow-up time for the overall population (13.8 months). Thereafter, the decreasing number of patients with data for each cycle makes interpretation difficult; for transparency, available data for all instruments through cycle 30 are included in the supplemental materials. LS mean change from baseline data over time for EORTC-QLQ-C30 domains of interest are reported in Figs. 1 and 2 and Supplementary Fig. S2. Through cycle 18, the LS mean change from baseline scores for global health/overall QoL and physical function were similar across treatment arms and remained generally stable over time (Fig. 1 A–B). There was a slight downward trend in niraparib-treated patients for fatigue LS mean change from baseline scores from cycle 3 to cycle 18, indicating symptom improvement; placebo LS mean change from baseline scores remained consistent through cycle 18 and showed no difference compared with niraparib (Fig. 1C). Symptom LS mean change from baseline scores for pain were generally similar across treatment arms through cycle 18 (Fig. 1D).

EORTC QLQ-C30 LS mean change from baseline scores for gastrointestinal symptoms (nausea and vomiting, appetite loss, and constipation) were higher (worse symptoms) in niraparib-treated patients than in placebo-treated patients, primarily during early treatment (Fig. 2). Differences between treatment arms resolved after cycle 9 for nausea and vomiting and after cycle 5 for appetite loss (Fig. 2 A–B). In the niraparib arm, constipation LS mean change from baseline scores trended downward from cycle 3 to cycle 7 but remained consistently higher than in the placebo arm through cycle 18 (Fig. 2C). Diarrhea LS mean change from baseline scores trended higher (worse symptoms) in placebo-treated patients than in niraparib-treated patients over time, although there was no separation between treatment arms except for cycle 11 (Fig. 2D).

For the EORTC-QLQ-OV28 abdominal/gastrointestinal symptoms domain, niraparib-treated patients tended to have slightly higher LS mean change from baseline scores (worse symptoms) than placebo-treated patients over time, but there was no separation between arms except for cycle 3 (Fig. 3A; Supplementary Fig. S3). Attitude toward disease/treatment generally improved over time in both arms, indicating better functioning (Fig. 3B). After an initial decrease at cycle 3, little to

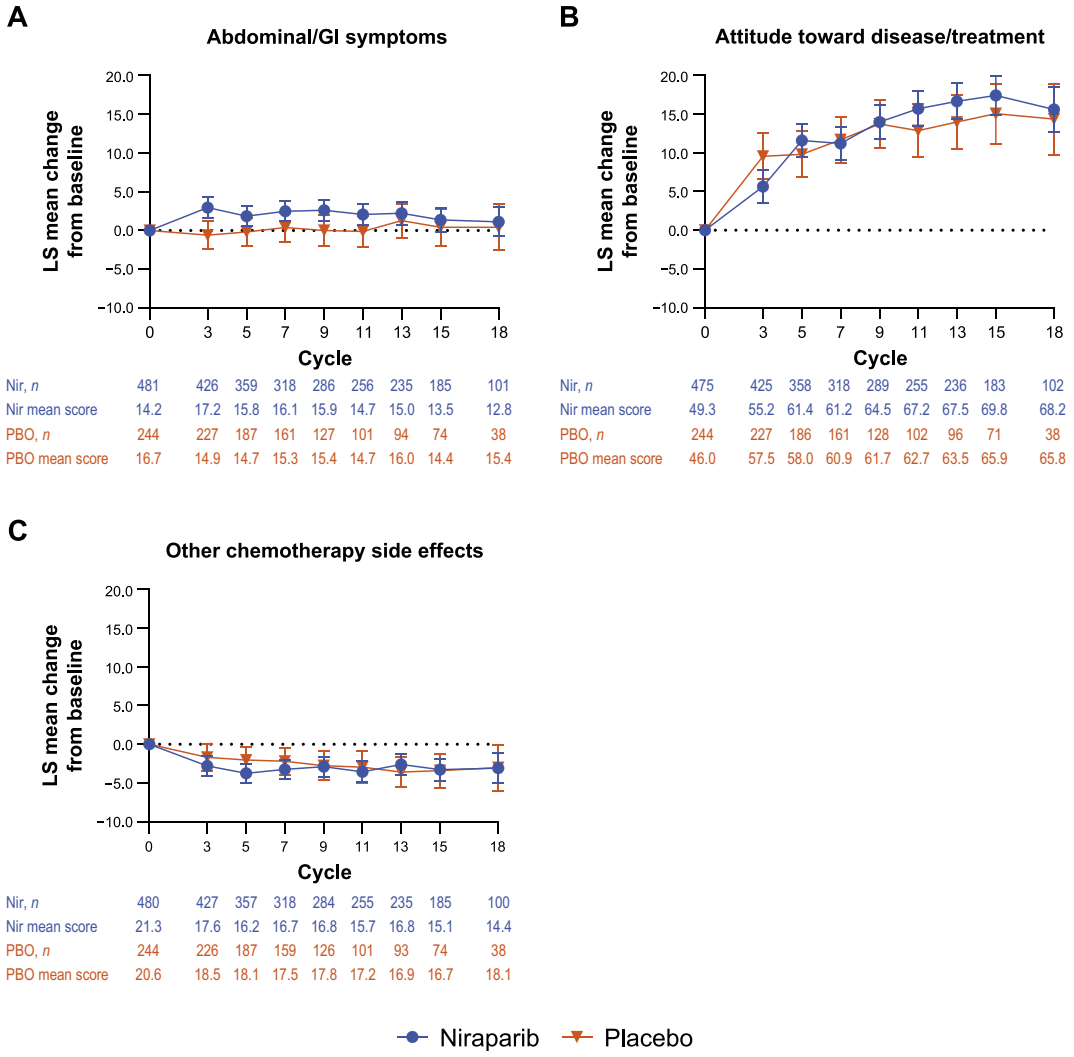

Fig. 3. EORTC QLQ-OV28 LS mean change from baseline over time in the overall population through cycle 18. The LS mean change from baseline scores with 95% confidence intervals (represented by error bars) over time are reported for (A) abdominal/GI symptoms, (B) attitude toward disease/treatment, and (C) other chemotherapy side effects. The numbers underneath each graph detail the number of patients with data at each cycle and the mean score at each cycle for each treatment arm. EORTC QLQ-OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module; GI, gastrointestinal; LS, least squares; Nir, niraparib; PBO, placebo.

no change over time was observed for LS mean change from baseline scores for other chemotherapy side effects (Fig. 3C).

FOSI LS mean change from baseline scores also showed little variation over time in both the niraparib and placebo arms (Fig. 4; Supplementary Fig. S4). EQ-5D-5L HUI and VAS scores were similar between treatment arms, with VAS scores trending upward (better HRQoL) over time (Supplementary Fig. S5, S6). Results for patients with HRd or HRp tumors were similar to the overall population for the EORTC QLQ-C30 (Supplementary Fig. S7), EORTC QLQ-OV28 (Supplementary Fig. S8), FOSI (Supplementary Fig. S9), and EQ-5D-5L (Supplementary Fig. S10).

3.3. Item-level responses

Individual item responses were reported for selected items asking about symptoms commonly reported with niraparib: nausea, constipation, fatigue, vomiting, abdominal pain, and insomnia. Overall, item-level responses were generally similar between the niraparib and placebo arms for the overall patient population across instruments (Fig. 5, Supplementary Fig. S11). As noted above, niraparib-treated patients consistently reported higher scores (worse symptoms) for constipation than placebo-treated patients for the EORTC QLQ-C30. For the individual question of "Have you been constipated?", roughly half of niraparib-treated patients responded with "not at all" through cycle 18; ≈40% for cycles 3–5, ≈50% for cycles 7–15, and 57.8% for cycle 18 (Fig. 5A). For patients who responded in the affirmative, "a little" was the most common response through cycle 18 (25.5%–38.5%), followed by "quite a bit" (9.8%–14.7%; Fig. 5A). Less than 10% of patients responded "very much" at any cycle through cycle 18 (Fig. 5A, Supplementary Fig. S11 A). For the other gastrointestinal symptoms (i.e., appetite loss, nausea, and vomiting) where niraparib-treated patients scored higher than placebo-treated patients early during treatment (cycles 3–9) on the EORTC QLQ-C30 symptom domains, "not at all" and "a little" were the most common responses in niraparib-treated patients who self-reported experiencing symptoms through cycle 18 (Supplementary Fig. S11 D, I, J).

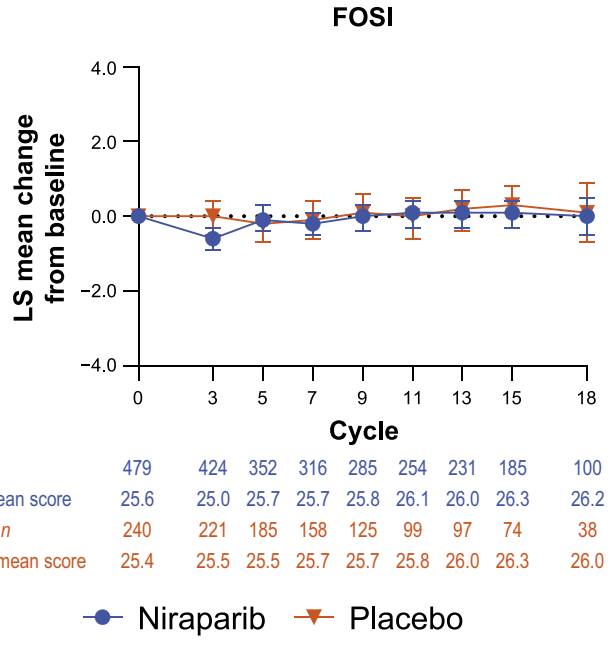

Fig. 4. FOSI LS mean change from baseline over time in the overall population through cycle 18. The LS mean change from baseline scores with 95% confidence intervals (represented by error bars) over time are reported. The numbers underneath each graph detail the number of patients with data at each cycle and the mean score at each cycle for each treatment arm. FOSI, Functional Assessment of Cancer Therapy–Ovarian Symptom Index; LS, least squares; Nir, niraparib; PBO, placebo.

For the EORTC QLQ-OV28 gastrointestinal questions, the percentage of niraparib-treated patients who self-reported no change in bowel habits generally increased over time (cycles 3–18, 42.2%–66.3%); for patients who did report a change in bowel habits, "a little" was the most common response (22.8%–36.3%; Fig. 5B). Similar patterns were observed in placebo-treated patients (Fig. 5B, Supplementary Fig. S11 M). For the individual question of "Did you have abdominal pain?", patients self-reported little pain regardless of treatment arm, with <3.0% of patients responding "very much" and <8% responding "quite a bit" at any cycle through cycle 18 (Supplementary Fig. S11 L).

For the FOSI question on fatigue (I have a lack of energy), the percentage of patients in the niraparib arm who responded with "not at all" or "a little" generally increased through cycle 15, whereas the percentage of patients who responded with "somewhat" generally decreased through cycle 15. Less than 5% of niraparib-treated patients responded with "very much" at any cycle for the fatigue question; similar results were observed in placebo-treated patients (Supplementary Fig. 11S). Item-level responses to questions on QoL and body dissatisfaction were also generally similar across treatment arms.

4. Discussion

In this detailed assessment of PRO data from the PRIMA primary analysis, results indicate that first-line niraparib maintenance therapy did not have a significant, deleterious impact on HRQoL in patients with OC. LS mean change from baseline scores were generally similar between treatment arms over time for all instruments examined in the overall, HRd, and HRp populations. Consistent with the known safety profile of niraparib [7,11,23], niraparib-treated patients self-reported worse gastrointestinal symptoms than placebo-treated patients on the EORTC QLQ-C30 (nausea and vomiting, appetite loss, and constipation). Except for constipation, the worsening did not meet the threshold for minimal clinically important difference (±10-point change) [24] and was temporary, with the differences between treatment arms resolving after cycle 9. Niraparib-treated patients also reported worse symptoms than placebo-treated patients over time on the EORTC QLQ-OV28 abdominal/gastrointestinal symptoms domain; however, the amount of change was not clinically meaningful (<10-point change), and there was no clear separation between treatment arms. Niraparib-treated patients self-reported no worsening of fatigue over time across questionnaires, and LS mean change from baseline scores for fatigue were generally similar across treatment arms.

The EORTC QLQ-C30 and EORTC QLQ-OV28 instruments assess gastrointestinal symptoms differently, with the broader QLQ-C30 focused on chemotherapy-related symptoms (e.g., vomiting, nausea, diarrhea, and constipation) and the OC-specific QLQ-OV28 focused on OC-related symptoms (e.g., abdominal pain, bloated feeling, problems with clothing feeling too tight) [13,16,18,25]. In this analysis, niraparib-treated patients self-reported worse gastrointestinal symptoms than placebo-treated patients across both the EORTC QLQ-C30 and EORTC QLQ-OV28 symptom domains, but the separation between treatment arms was most notable in the EORTC QLQ-C30 symptom domains. At the individual question level, the most common response in patients who self-reported gastrointestinal symptoms in either the EORTC QLQ-C30 or EORTC QLQ-OV28 was "a little," and <10% of patients in either treatment arm responded "very much" at any cycle for any question through cycle 18.

Although the importance of reporting PRO and HRQoL data from clinical trials involving patients with OC is widely recognized [10,24], there is little standardization in what instruments are used and reported for trials of first-line maintenance therapies in patients with advanced OC, hindering data interpretation and generalization of findings. Consistent with our findings, available PRO data from SOLO-1, PAOLA-1, VELIA/GOG-3005, ATHENA–MONO/GOG-3020/ENGOT-ov45 indicate that PARP inhibitor first-line maintenance therapy did not negatively impact overall HRQoL of patients, with no significant differences

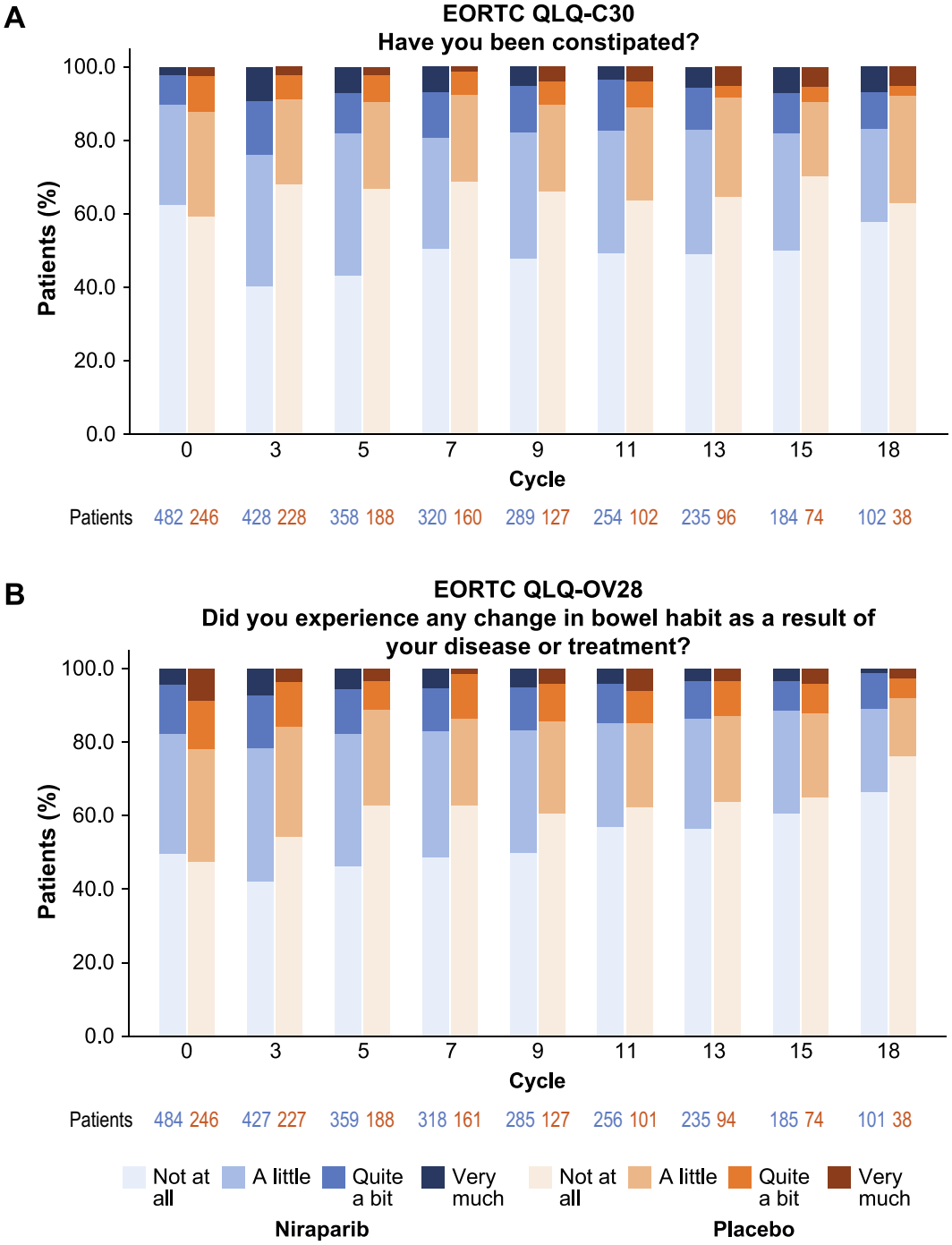

Fig. 5. Individual item responses for the overall population for the (A) EORTC QLQ-C30 "Have you been constipated?" and (B) EORTC QLQ-OV28 "Did you experience any change in bowel habit as a result of your disease or treatment?" BL, baseline; C, cycle; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; EORTC QLQ-OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module.

detected across treatment arms [26–29]. Our results are also concordant with a quality-adjusted time without symptoms of disease or toxicity (Q-TwiST) analysis in PRIMA that found that niraparib maintenance therapy significantly extended both the quality-adjusted PFS and quality-adjusted time without symptomatic OC or toxicities in patients compared with placebo [30]. PROs have also been reported for the ENGOT-OV16/NOVA trial that evaluated niraparib maintenance therapy in the recurrent setting. Similar to PRIMA, niraparib treatment in NOVA did not adversely affect PRO-assessed HRQoL compared with placebo [31]. A TwiST analysis of NOVA also showed the benefit of niraparib in extending the time without symptomatic OC or toxicities compared with placebo [32].

PRO assessments conducted during the PRIMA study were limited by the timing of each PRO assessment. Importantly, the first postbaseline PRO measurement was completed at 8 weeks, which may have missed early differences between treatment arms. Most adverse events (AEs), especially hematologic AEs such as thrombocytopenia, usually occur within ≈4 weeks from the start of niraparib treatment. Patients who experienced early gastrointestinal adverse events may also have either adjusted to the events or altered how they took niraparib (e.g., with or without food, changed time of day)

or used supportive medications, such as antiemetics or laxatives, to alleviate symptoms. Furthermore, the spaced-out nature of the PRO assessments may have missed symptoms such as fatigue that are associated with hematological AEs, which are detected through acute changes in laboratory values. Other common symptoms and difficulties associated with hematologic AEs, such as bruising or the need for transfusions, would not have been captured within the scope of the PRO questionnaires themselves. Additionally, although the collection of PRO data and assessment of HRQoL was prespecified, the study was not powered to detect differences in PRO end points between treatment arms, and no a priori hypotheses were included in the prespecified analysis plan. Lastly, it is important to note that the PRIMA patient population was highly selective, and results from PRIMA may not be generalizable to the greater population of patients with OC.

5. Conclusions

Overall, PRO data collected during the PRIMA trial shows that while there was a transient increase in self-reported gastrointestinal symptoms early during treatment, niraparib maintenance therapy did not adversely affect overall HRQoL of patients with OC that had a complete or partial response to platinum-based chemotherapy. These data support that niraparib is a well-tolerated option for first-line maintenance therapy in patients with OC.

Previous presentation

The data presented in this manuscript were previously presented as an oral presentation at ESMO 2020 and presented as either an oral or poster encore presentation at ESGO-SOA 2020, CSCO 2020, JSOG 2021, and DGGG 2021.

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Data-sharing statement

Please refer to GSK weblink to access GSK's data sharing policies and as applicable seek anonymised subject level data via the link https://www.gsk-studyregister.com/en/.

CRediT authorship contribution statement

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Declaration of competing interest

Dr. Pothuri reports institutional grant support from AstraZeneca, Celsion, Clovis Oncology, Eisai, Genentech/Roche, GSK, I-Mab, Immunogen, Incyte, Karyopharm, Merck, Mersana, Onconova, Seagen, Sutro Biopharma, and Toray; consulting fees from AstraZeneca, GSK, GOG Foundation, Merck, and Seagen; support for attending meetings from GOG Partners; advisory board fees from Arquer Diagnostics, Atossa, Clovis Oncology, Deciphera, Eisai, Elevar Therapeutics, GOG Foundation, I-Mab, Immunogen, Lily, Merck, Mersana, Natera, Onconova, Regeneron, Sutro Biopharma, Tesaro/GSK, Toray, and VBL Therapeutic.

Dr. Han has nothing to disclose.

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Dr. Burger reports receiving travel support from Genentech and Mersana Therapeutics, stock from Genentech and Mersana Therapeutics, and is an employee of Genentech and Mersana Therapeutics.

Dr. Gaba reports consulting fees, advisory board, and honoraria fees from AstraZeneca, Clovis Oncology, GSK, MSD, and PharmaMar, and support for attending meetings from AstraZeneca, Clovis Oncology, GSK, and MSD.

Dr. Van Le has nothing to disclose.

Dr. Guerra reports AstraZeneca, Clovis Oncology, GSK, Merck, Pharmamar, Roche, and Tesaro; honoraria from AstraZeneca, Clovis Oncology, GSK/Tesaro, and Merck; payment for expert testimony from AstraZeneca, Clovis Oncology, GSK, Merck, Tesaro; travel support from GSK, Roche, and Tesaro; advisory board participation for AstraZeneca, GSK, Merck, and Tesaro.

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Dr. Jardon has nothing to disclose (deceased).

Dr. Pisano has nothing to disclose.

Dr. Peen has nothing to disclose.

Dr. Mäenpää reports honoraria from AstraZeneca, Eisai, and GSK.

Dr. Gupta was an employee of GSK at the time the analysis was conducted; currently an employee of Mersana Therapeutics.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2024.01.021.

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