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Predictors of long-term progression-free survival in patients with ovarian cancer treated with niraparib in the PRIMA/ENGOT-OV26/GOG-3012 study

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ABSTRACT

Objective To identify characteristics associated with long-term progression-free survival (≥2 years) in patients with advanced ovarian cancer treated with niraparib first-line maintenance therapy in the phase III PRIMA/ENGOT-OV26/GOG-3012 study.

Methods In this post hoc analysis of PRIMA, patients randomized to niraparib were grouped based on investigator-assessed progression-free survival (progressive disease/censoring <2 years or ≥2 years after randomization). Variables assessed for predictive value were Eastern Cooperative Oncology Group performance status, International Federation of Gynecology and Obstetrics (FIGO) stage at diagnosis, clinical response to platinum-based chemotherapy, number of prior chemotherapy cycles, primary tumor location, body mass index, categorical age, debulking surgery type, number of baseline target lesions, number of baseline non-target lesions, *BRCA*/homologous recombination-deficiency status, residual disease status, and duration from end of chemotherapy to randomization. Logistic regression modeling using backward elimination (significance level=0.15) identified covariates associated with long-term progression-free survival (clinical cut-off date November 17, 2021).

Results Of 487 patients randomized to niraparib, 152 (31%) had progressive disease/censoring ≥2 years after randomization. Multivariable logistic regression modeling using backward elimination identified *BRCA1/2* mutation/homologous recombination deficiency status (p<0.0001), FIGO stage (p=0.041), primary tumor location (p=0.095), and number of baseline non-target lesions (p=0.0001) to be associated with long-term progression-free survival. Patients significantly more likely to achieve progression-free survival of ≥2 years in the final model were those with *BRCA1*- and *BRCA2*-mutated/homologous recombination-deficient tumors or *BRCA* wild-type/not determined/homologous recombination-deficient tumors (vs *BRCA* wild-type/homologous recombination-proficient/not determined tumors), FIGO stage III (vs IV), and 0 or 1 baseline non-target lesions (vs ≥2 baseline non-target lesions).

Conclusions The hypothesis-generating results of this analysis suggest that *BRCA1/2* mutation/homologous recombination-deficiency status, FIGO stage, and number of baseline non-target lesions may predict progression-free survival of ≥2 years in patients with advanced ovarian cancer receiving niraparib first-line maintenance therapy.

Trial registration number NCT02655016.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Based on the results of the primary analysis of the PRIMA/ENGOT-OV26/GOG-3012 (NCT02655016) study, niraparib was approved for the maintenance treatment of patients with newly diagnosed advanced-stage ovarian cancer that responded to first-line platinum-based chemotherapy, irrespective of biomarker status.

WHAT THIS STUDY ADDS

⇒ Although multiple prognostic factors have been identified for progression-free survival in patients with advanced ovarian cancer, factors associated with long-term progression-free survival in patients treated with niraparib first-line maintenance have not been characterized to date. *BRCA1*- and *BRCA2*-mutated/homologous recombination-deficient tumors or *BRCA* wild-type/not determined/homologous recombination-deficient tumors (vs *BRCA* wild-type/homologous recombination-proficient/not determined tumors), FIGO stage III (vs stage IV) disease, and 0 or 1 baseline non-target lesions (vs ≥2 lesions) were associated with a higher likelihood of progression-free survival of ≥2 years in patients treated with niraparib with advanced ovarian cancer.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results of the present study are hypothesis generating. These results may help inform treatment decisions and clinical outcome expectations for patients with advanced ovarian cancer.

INTRODUCTION

Most patients with ovarian cancer present with advanced disease at diagnosis, which is associated with a 5-year survival rate of approximately 30%.[1] While surgery combined with platinum-based chemotherapy remains the standard of care, maintenance therapy with poly(ADP-ribose) polymerase (PARP) inhibitors and antiangiogenic agents (alone or in combination) has been shown to improve progression-free survival and may also lead to clinically meaningful improvements in overall survival in specific biomarker populations.[2–5]

In patients with newly diagnosed ovarian cancer that responded to first-line platinum-based chemotherapy, maintenance treatment with the PARP inhibitor niraparib was evaluated in the PRIMA/ENGOT-OV26/GOG-3012 (PRIMA) trial.[6] PRIMA enrolled patients with primary advanced ovarian cancer at high risk for disease progression. Niraparib maintenance therapy significantly extended blinded independent central review-assessed progression-free survival versus placebo in patients with homologous recombination-deficient tumors and those in the overall (intent-to-treat) population.[6] The most common grade ≥3 treatment-emergent adverse events were hematologic, consistent with the established niraparib safety profile.[6] In the long-term analysis, investigator-assessed progression-free survival results were consistent with the primary analysis findings, and no new safety signals were detected.[7] Patients treated with niraparib were more likely to be alive and progression-free at 4 years than patients treated with placebo.[7]

In the PRIMA trial, conditional progression-free survival analyses in the intent-to-treat population showed that 67% of patients treated with niraparib who were alive and progression-free at the 2-year landmark were expected to remain so at the 4-year landmark, demonstrating the robust long-term efficacy of niraparib first-line maintenance.[8] Multiple prognostic factors for disease progression in patients with advanced ovarian cancer, including *BRCA*/homologous recombination-deficiency status and disease stage, have been identified.[9–16] In real-world observational studies of patients with advanced ovarian cancer who received PARP inhibitor first-line maintenance, complete response to platinum-based chemotherapy, *BRCA2* mutations, platinum-free interval ≥12 months, and a lower cumulative number of risk factors were associated with longer progression-free survival, whereas elevated CA125 levels, non–high-grade serous carcinoma, receipt of neoadjuvant chemotherapy, and lack of *BRCA* mutation were associated with shorter progression-free survival.[17–19] In this post hoc analysis of PRIMA, we sought to identify baseline characteristics associated with long-term progression-free survival in patients randomized to niraparib.

METHODS

PRIMA Trial

The study design and primary analysis results have been previously published for PRIMA/ENGOT-OV26/GOG-3012 (NCT02655016).[6] Briefly, PRIMA was a phase III trial that enrolled patients with newly diagnosed advanced (International Federation of Gynecology and Obstetrics [FIGO] stage III or IV) high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer (collectively referred to as ovarian cancer) with complete or partial response to first-line platinum-based chemotherapy at high risk for disease progression. After first-line chemotherapy, patients were randomized 2:1 to receive oral niraparib or placebo once daily.

At study initiation, all patients received a fixed starting dose of 300 mg once daily; however, the protocol was amended to incorporate an individualized starting dose based on baseline body weight and platelet count. Randomization stratification factors were clinical response to first-line chemotherapy (complete/partial response), receipt of neoadjuvant chemotherapy (yes/no), and tumor homologous recombination-deficiency status (homologous recombination-deficient vs homologous recombination-proficient or not determined per the MyChoice CDx [Myriad Genetics, Salt Lake City, Utah, USA]). PRIMA was conducted according to the principles of the Declaration of Helsinki, good clinical practice, and all local laws under the auspices of an independent data safety and monitoring committee (Institutional Review Board list; see Online Supplemental Table 1).

All patients provided written informed consent.[6] The primary endpoint, progression-free survival (defined as the time from randomization after completion of platinum-based chemotherapy to the earliest date of objective disease progression on imaging [according to the Response Evaluation Criteria in Solid Tumors, version 1.1][20] or death from any cause) was assessed by blinded independent central review in the homologous recombination-deficient and overall (intent-to-treat) populations per prespecified hierarchical testing.[6] Beyond the primary analysis, the protocol specified investigator assessment of progression-free survival, which was shown to be concordant with blinded independent central review progression-free survival in the primary analysis.[6 7]

Post Hoc Analysis of Long-Term Predictors of Progression-Free Survival

This post hoc analysis analyzed factors associated with long-term progression-free survival (defined as ≥2 years) in patients randomized to niraparib in the intent-to-treat population. The 2-year cut-off was selected based on conditional progression-free survival analyses in the intent-to-treat population which showed that about two-thirds of patients treated with niraparib who were alive and progression-free at the 2-year landmark were expected to remain so at the 4-year landmark.[8] Patients treated with niraparib were grouped based on their investigator-assessed progression-free survival status (progressive disease/censoring <2 years, hereafter referred to as progression-free survival <2 years, vs progressive disease/censoring ≥2 years after randomization, hereafter referred to as progression-free survival ≥2 years).

Patients without evaluable baseline/post-baseline radiological assessments were censored at the date of randomization (unless death, disease progression, or subsequent anticancer therapy initiation occurred within 2 visits of randomization). Patients who had not died, experienced disease progression, or initiated subsequent anticancer therapy and those who had died, experienced disease progression, or initiated subsequent anticancer therapy after ≥2 missed radiological assessments were censored at the date of the latest evaluable radiological assessment.

Multivariable logistic regression modeling using backward elimination (significance level=0.15) was used to identify baseline characteristics associated with long-term progression-free survival (Figure 1). As previously described, the least significant variable that did not meet the significance level for remaining in the model was removed. This

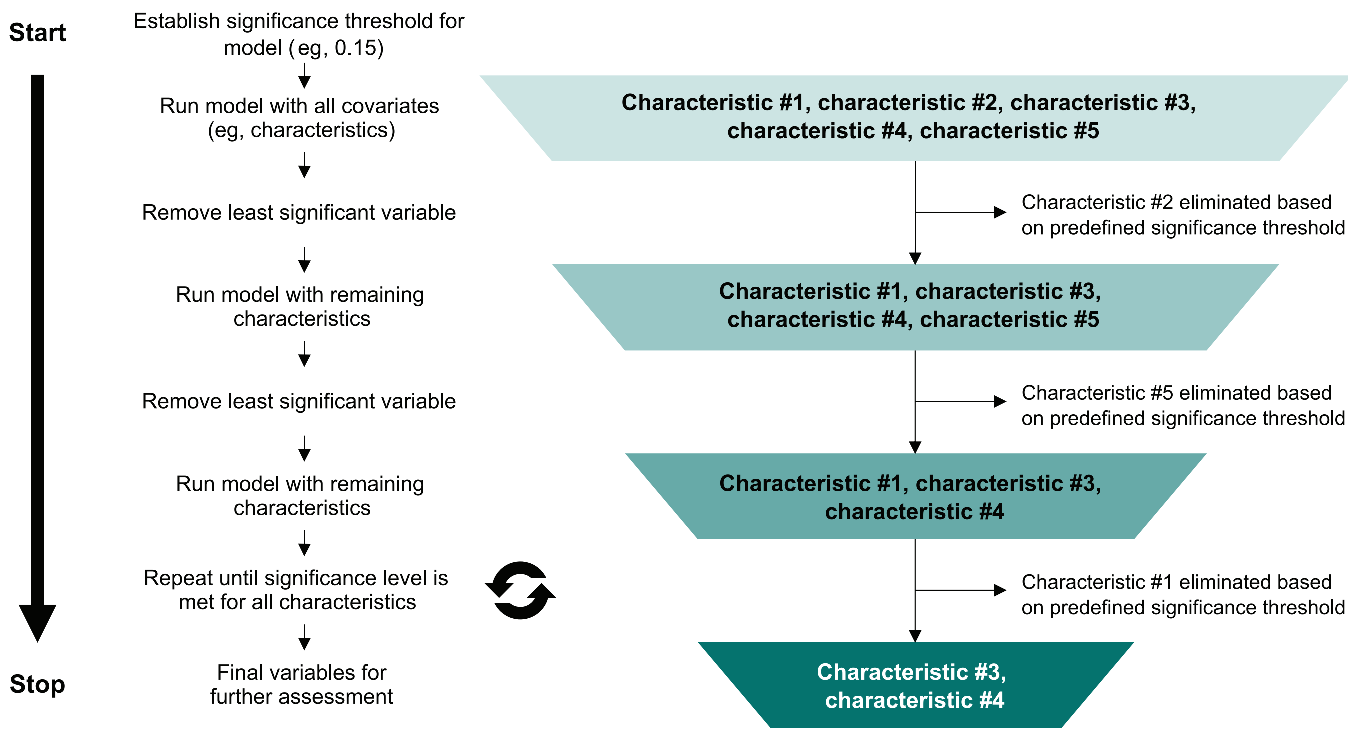

Figure 1 Multivariable logistic regression modeling method using backward elimination to identify characteristics for further assessment.

process was repeated until all variables in the model that did not meet the specified significance level had been removed.[21]

Based on prior association with ovarian cancer prognosis, the authors selected the following baseline variables for inclusion in the logistic regression model: Eastern Cooperative Oncology Group (ECOG) performance status scores (0 vs 1), FIGO stage at diagnosis (III vs IV), clinical response to platinum-based chemotherapy (complete vs partial response), number of prior chemotherapy cycles (6, 7–9, or missing), primary tumor location (ovarian, primary peritoneal, or fallopian tube), body mass index (<18 kg/m^2, 18–<25 kg/m^2, 25–<30 kg/m^2, or ≥30 kg/m^2), categorical age (<65 years vs ≥65 years), type of debulking surgery (primary debulking surgery, interval debulking surgery, or no surgery), number of baseline target lesions (0 vs ≥1), number of baseline non-target lesions (0, 1, or ≥2), *BRCA*/homologous recombination-deficiency status (*BRCA1*/homologous recombination-deficient, *BRCA2*/homologous recombination-deficient, *BRCA* wild-type/not determined/homologous recombination-deficient, or *BRCA* wild-type/not determined/homologous recombination-proficient/not determined), residual disease status (no visible residual disease after neoadjuvant chemotherapy/interval debulking surgery, visible residual disease after primary debulking surgery, or missing/no surgery), and duration from end of chemotherapy to date of randomization in weeks. Categories for target (0 and ≥1) and non-target (0, 1, and ≥2) lesions at baseline were determined based on sample size. Potential characteristics of interest including race, ethnicity, and location of baseline target/non-target lesions, although important, were excluded from the multivariate logistic regression model because of low sample sizes (see Online Supplemental Table 2).

Correlations between the variables were evaluated to check for multicollinearity (linear dependence between multiple independent variables),[22] and all correlation coefficients were confirmed to be <0.70, indicating that the variables were not linearly dependent. As a sensitivity analysis, an alternative definition of categorical progression-free survival was used in which patients who were censored <2 years were excluded because their exact progression date was unavailable; this definition was less conservative because it did not assume that patients who were censored <2 years experienced disease progression <2 years after randomization. Using the less conservative definition, 45 patients were excluded from the progression-free survival <2 years category. All analyses were conducted using data from the updated ad hoc analysis (clinical cut-off date November 17, 2021) and performed using SAS version 9.4. Associations with p values <0.05 were considered significant.

RESULTS

Baseline Characteristics by Progression-Free Survival Status

In the PRIMA trial, 487 patients were randomized to receive niraparib. Overall, 335 (68.8%) patients had progression-free survival of <2 years and 152 (31.2%) patients had progression-free survival of ≥2 years. Baseline demographic characteristics were similar across sub-groups (Table 1). Compared with patients with progression-free survival of <2 years, more patients with progression-free survival of ≥2 years had no visible residual disease, ovarian primary tumor site, ECOG performance status scores of 0, FIGO stage III disease at diagnosis, fewer target and non-target lesions

Table 1 Baseline characteristics associated with long-term progression-free survival status in patients treated with niraparib		
	Long-term progression-free survival status	
	<2 years (n=335)	**≥2 years (n=152)**
Event counts for investigator-assessed progression-free survival, n (%)		
Censored	45 (13.4)	110 (72.4)
Event	290 (86.6)	42 (27.6)
Demographic characteristics		
Age, n (%)		
<65 years	201 (60.0)	96 (63.2)
≥65 years	134 (40.0)	56 (36.8)
Body mass index, n (%)		
<18.5 kg/m^2 (underweight)	5 (1.5)	3 (2.0)
18.5–<25 kg/m^2 (normal range)	146 (43.6)	68 (44.7)
25–30 kg/m^2 (overweight)	113 (33.7)	48 (31.6)
≥30 kg/m^2 (obese)	71 (21.2)	33 (21.7)
Clinical characteristics		
ECOG performance status, n (%)		
0	222 (66.3)	115 (75.7)
1	113 (33.7)	37 (24.3)
FIGO stage, n (%)		
III	207 (61.8)	111 (73.0)
IV	128 (38.2)	41 (27.0)
Primary tumor location, n (%)		
Ovarian	259 (77.3)	129 (84.9)
Primary peritoneal	26 (7.8)	8 (5.3)
Fallopian tube	50 (14.9)	15 (9.9)
Baseline target lesions, n (%)		
0	284 (84.8)	143 (94.1)
≥1	51 (15.2)	9 (5.9)
Baseline non-target lesions, n (%)*		
0	206 (61.5)	125 (82.2)
1	71 (21.2)	19 (12.5)
≥2	58 (17.3)	8 (5.3)
BRCA/homologous recombination-deficiency status, n (%)		
BRCA1 mutated/homologous recombination-deficient	59 (17.6)	46 (30.3)
BRCA2 mutated/homologous recombination-deficient	15 (4.5)	32 (21.1)
BRCA wild-type/not determined/homologous recombination-deficient	63 (18.8)	32 (21.1)
BRCA wild-type/homologous recombination-proficient/not determined	198 (59.1)	42 (27.6)
Type of debulking surgery, n (%)		
Primary debulking surgery	111 (33.1)	47 (30.9)
Interval debulking surgery	213 (63.6)	103 (67.8)
No surgery	11 (3.3)	2 (1.3)
Residual disease status, n (%)		
No visible residual disease	145 (43.3)	79 (52.0)
Visible residual disease	162 (48.4)	58 (38.2)
Missing/no surgery	28 (8.4)	15 (9.9)

Continued

Table 1 Continued

	Long-term progression-free survival status	
	<2 years (n=335)	≥2 years (n=152)
Clinical response after platinum-based chemotherapy, n (%)		
Complete response	214 (63.9)	123 (80.9)
Partial response	121 (36.1)	29 (19.1)
Prior chemotherapy cycles, n (%)		
6	226 (67.5)	107 (70.4)
7–9	92 (27.5)	32 (21.1)
Missing	17 (5.1)	13 (8.6)
Duration from end of chemotherapy to randomization, median (IQR), weeks	8.14 (4.6)	8.00 (4.3)

Receipt of neoadjuvant chemotherapy was not selected for evaluation because of high correlation with type of debulking surgery.
*Per the RECIST guidelines (version 1.1), when >1 measurable lesion is present at baseline, all lesions (≤5 total lesions and ≤2 lesions/organ) should be identified as target lesions. Excess lesions (>5) and non-measurable disease are designated as non-target lesions.[20]
ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; RECIST, Response Evaluation Criteria in Solid Tumors.

at baseline, *BRCA1*/2-mutated/homologous recombination-deficient tumors, and complete response to prior platinum-based chemotherapy (Table 1).

Factors Associated with Long-Term Progression-Free Survival

In the logistic regression model, FIGO stage at diagnosis, primary tumor site, number of baseline non-target lesions, and *BRCA*/homologous recombination-deficiency status were associated with long-term progression-free survival (Table 2 and Figure 2). The final adjusted ORs from the multivariable logistic regression are shown in Figure 3. Patients who had *BRCA1*-mutated/homologous recombination-deficient, *BRCA2*-mutated/homologous recombination-deficient, or *BRCA* wild-type/*BRCA* not determined/homologous recombination-deficient tumors were more likely to achieve progression-free survival of ≥2 years than those with *BRCA* wild-type/homologous recombination-proficient/homologous recombination not determined tumors (*BRCA1*-mutated/homologous recombination-deficient: OR 3.73 [95% CI 2.19 to 6.34]; *BRCA2*-mutated/homologous recombination-deficient: OR 10.75 [95% CI 5.16 to 22.41]; *BRCA* wild-type/

Table 2 Factors associated with long-term progression-free survival in patients treated with niraparib using the alternative definition of categorical progression-free survival

Baseline characteristic	OR (95% CI)	Overall p value
ECOG performance status vs 1		
0	1.54 (0.94 to 2.52)	0.086
FIGO stage at diagnosis vs stage IV		
III	1.79 (1.11 to 2.88)	0.018
Primary tumor location vs ovarian		
Primary peritoneal	0.49 (0.18 to 1.30)	0.090
Fallopian	0.53 (0.26 to 1.07)	
BRCA/homologous recombination-deficiency status vs *BRCA* wild-type/homologous recombination-proficient/homologous recombination not determined		
BRCA1 mutated/homologous recombination-deficient	3.81 (2.20 to 6.62)	
BRCA2 mutated/homologous recombination-deficient	12.55 (5.62 to 28.06)	<0.0001
BRCA wild-type/*BRCA* not determined/homologous recombination-deficient	2.95 (1.63 to 5.35)	
Baseline non-target lesion number vs ≥2 lesions		
0	5.52 (2.42 to 12.56)	<0.0001
1	2.43 (0.93 to 6.37)	

p value estimated using the type III test for analysis of effects.
This analysis was conducted as a sensitivity analysis for the definition of categorical long-term progression-free survival.
ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics.

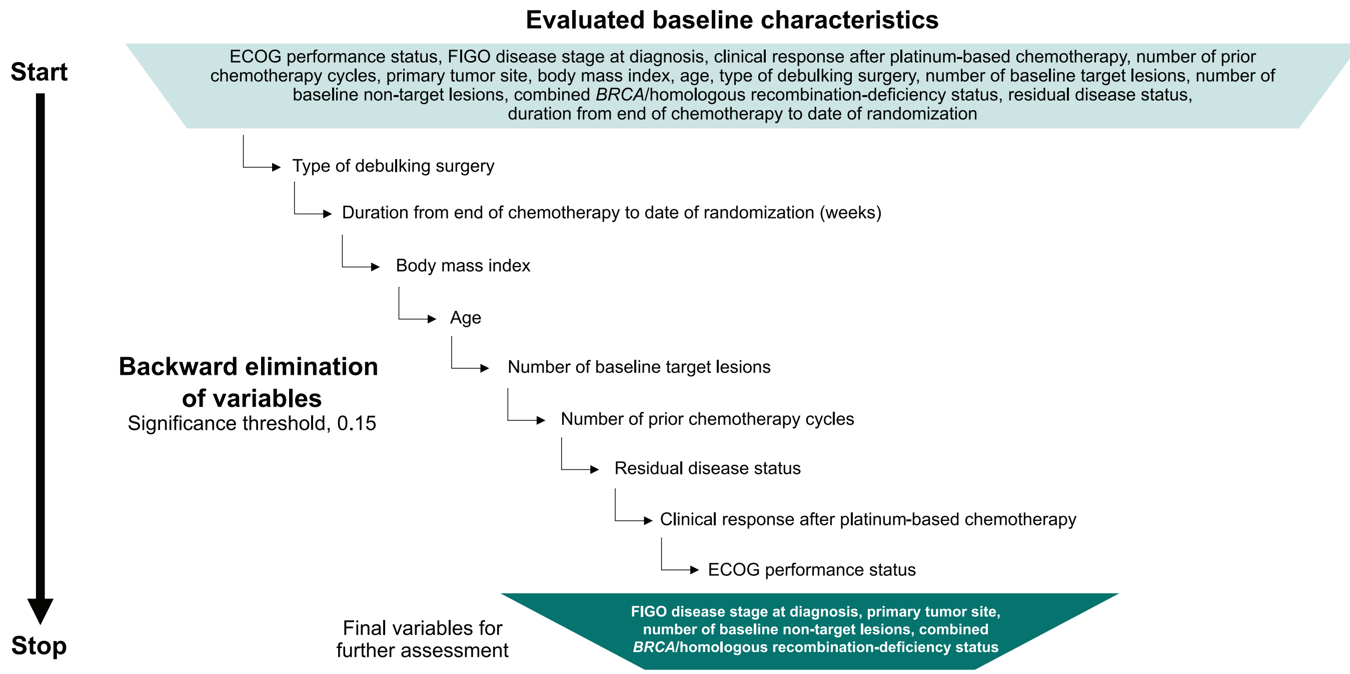

Figure 2 Backward elimination of baseline characteristics associated with investigator-assessed progression-free survival of <2 years versus ≥2 years in patients treated with niraparib in the intent-to-treat population. Variables for the multivariate logistic regression model were selected using backward elimination with a 15% significance level. ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics.

not determined/homologous recombination-deficient: OR 2.49 [95% CI 1.42 to 4.37]; overall p<0.0001).

Patients with FIGO stage III disease at baseline were more than 1.5 times as likely to achieve progression-free survival of ≥2 years than those with stage IV disease (OR 1.62 [95% CI 1.02 to 2.57]; overall p=0.041). Patients with 0 and 1 non-target lesions were more than twice as likely to achieve progression-free survival of ≥2 years than patients with ≥2 non-target lesions (0 lesions: OR 4.67 [95% CI 2.08 to 10.49]; 1 lesion: OR 2.20 [95% CI 0.86 to 5.65]; overall p=0.0001). Compared with patients with ovarian tumors, patients with primary tumor location of fallopian tube and primary peritoneal had decreased odds of progression-free survival of ≥2 years, although the association was not significant (fallopian tube: OR 0.54 [95% CI 0.28 to 1.05]; primary peritoneal: OR 0.53 [95% CI 0.21 to 1.33]; Figure 3; overall p=0.095). The sensitivity analysis using the less conservative definition of long-term progression-free survival yielded results similar to those from the analysis using the more conservative definition, except for the addition of ECOG performance status in the final logistic regression model (Table 2). ECOG performance status of 0 (vs 1) was associated with an increased odds of

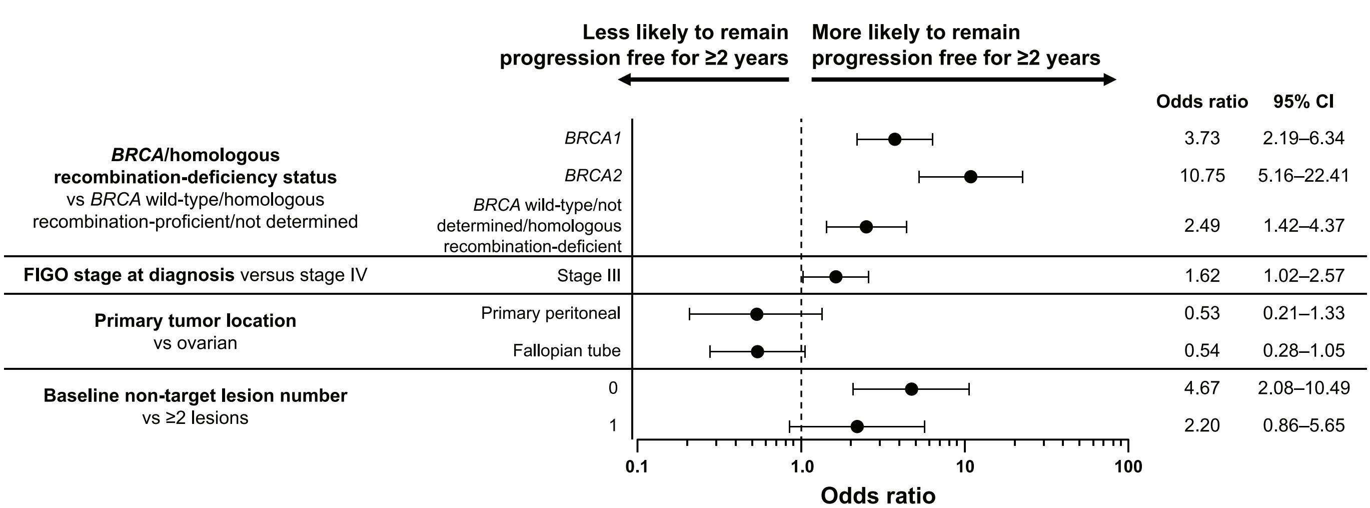

Figure 3 Factors associated with long-term progression-free survival in patients treated with niraparib. FIGO, International Federation of Gynecology and Obstetrics.

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progression-free survival of ≥2 years, although the association was not significant (OR 1.54 [95% CI 0.94 to 2.52]; p=0.086).

DISCUSSION

Summary of Main Results

In this post hoc analysis of PRIMA, disease stage at diagnosis, primary tumor site, number of baseline non-target lesions, and *BRCA*/homologous recombination-deficiency status were associated with long-term progression-free survival by multivariable logistic regression modeling using backward elimination with a 15% significance level.

Results in the Context of Published Literature

Several prognostic factors have been associated with prolonged long-term survival in patients with advanced ovarian cancer including residual disease, *BRCA*-mutated/homologous recombination-deficient tumors, lower disease stage, and cytoreductive surgery.[9–16 23 24] Although complete cytoreduction is associated with improved outcomes regardless of whether patients undergo primary or interval debulking surgery,[23 24] residual disease status and surgery modality were not identified as predictors of long-term progression-free survival in this study. In part, this may be because patients with stage III ovarian cancer who had no visible residual disease after primary debulking surgery were ineligible to participate in PRIMA, and the results were not stratified based on surgical outcomes after primary versus interval debulking surgery.[6]

Consistent with previously identified prognostic factors for advanced ovarian cancer,[9 11 15 16] *BRCA*-mutated/homologous recombination-deficient tumors and lower disease stage at diagnosis were associated with increased odds of long-term progression-free survival. Of note, patients with *BRCA* wild-type/not determined/homologous recombination-deficient tumors treated with niraparib were more likely to achieve progression-free survival of ≥2 years than those with *BRCA* wild-type/homologous recombination-proficient/homologous recombination not determined tumors. Despite significant interest in identifying characteristics associated with response to PARP inhibitor maintenance beyond *BRCA* mutation status,[25 26] a recent meta-analysis of PARP inhibitor clinical trials in patients with ovarian cancer only identified *BRCA* mutation, homologous recombination-deficient status, and sensitivity to platinum-based therapy as effective prognostic factors for progression-free survival.[26] While there are similarities between PRIMA and other phase III PARP inhibitor maintenance trials, key differences exist. Patients with *BRCA* wild-type/not determined tumors were excluded from SOLO1 (olaparib monotherapy maintenance), whereas the majority of patients in the PRIMA, PAOLA-1/ENGOT-OV25 (combined olaparib and bevacizumab maintenance therapy), ATHENA-MONO/GOG-3020/ENGOT-OV45 (rucaparib monotherapy maintenance), and PRIME (niraparib monotherapy maintenance) trials had *BRCA* wild-type/not determined tumors.[6 27–30]

In addition, while PRIMA excluded patients with stage III ovarian cancer with no visible residual disease after primary debulking surgery (which has been associated with more favorable survival outcomes),[6 31] the majority of patients in SOLO1, PAOLA-1, ATHENA-MONO, and PRIME had no visible residual disease after primary or interval debulking surgery.[27–30 32] In PRIMA, approximately half of all patients had post-operative residual disease or did not undergo surgery,[33] while a smaller fraction of patients in SOLO1 (~1/4) and PRIME (~1/5) did.[27 29] In PRIMA, nearly 66% of patients received neoadjuvant chemotherapy/interval debulking surgery or did not undergo surgery[33]; this percentage was smaller in SOLO1 (~33%) and in PAOLA-1, ATHENA-MONO, and PRIME (~50% for each).[27–30] Moreover, while PRIMA, SOLO1, ATHENA-MONO, and PRIME included PARP inhibitor monotherapy arms,[6 27–29] PAOLA-1 did not include an olaparib monotherapy arm, making it difficult to determine the specific contribution of each individual agent.[30] Given these differences in trial design, patient population, and clinical risk factors for disease progression, the predictors that were identified in this study may not be generalizable across other PARP inhibitor trials.

Strengths and Weaknesses

As a retrospective post hoc analysis, these results should be interpreted as hypothesis generating. While progression-free survival was a pre-specified endpoint, comparative analyses between patients who achieved progression-free survival of ≥2 years versus those with progression-free survival of <2 years were not. Potential characteristics of interest including race, ethnicity, and location of baseline target/non-target lesions were not included in the multivariate logistic regression model because of low sample sizes. Also, baseline characteristics with a predictive value for long-term progression-free survival may have been excluded from the analysis via backward elimination because of sample size effects.

Because the PRIMA trial enrolled patients at high risk for disease progression or death, enrolment eligibility criteria may also have influenced the results of this analysis. In addition to excluding patients with stage III disease who underwent primary debulking surgery and had no visible residual disease, PRIMA excluded patients with CA125 levels outside the normal range and those who did not achieve a decrease in CA125 levels of >90% during front-line therapy that was stable for ≥7 days. Because lower CA125 levels after chemotherapy have been associated with improved survival,[34] this exclusion could have impacted long-term progression-free survival results. While the risks of progression based on surgery timing and post-operative residual disease status in PRIMA were previously reported,[33] the volume of residual disease was not quantified in PRIMA, and its potential impact on progression-free survival remains uncharacterized. Additionally, PRIMA was limited to patients with high-grade serous or endometrioid tumors; thus, the applicability of our findings to patients with other ovarian cancer sub-types remains uncharacterized.

According to the revised RECIST guidelines (version 1.1),[20] patients with non-target lesions at baseline may have also had target lesions at baseline. Descriptive data regarding the combination of target and non-target lesions at baseline were not collected in this study. Consistent with the PRIMA eligibility criteria that required patients to have a complete or partial response to first-line platinum-based chemotherapy,[6] few patients in this analysis (especially those with progression-free survival of ≥2 years) had target lesions at baseline, and the majority of disease detected consisted of non-target lesions. The limited sample size may explain, at least in part, why a correlation between progression-free survival and number of baseline target lesions was not observed.

In this analysis, patients censored after <2 years were assumed to have disease progression at the time of censoring. The sensitivity analysis excluded these patients and the results were similar to those including these patients, indicating the robustness of our results to the censoring assumption. Validation of our findings is required because the results were based on a single trial. Given the sensitivity of the backward selection method on the choice of alpha, further validation using other methods to identify predictors (including LASSO and Ridge regression) should also be considered. Additionally, this analysis used a more conservative significance threshold to decrease the probability of a type

1 error without overfitting. This choice was subjective, and adoption of a less conservative approach in future analyses may be warranted.

Implications for Practice and Future Research

This analysis indicates that the established risk factors for disease progression with advanced ovarian cancer of *BRCA1/2* mutation/homologous recombination-deficiency status and FIGO stage at diagnosis may also predict long-term progression-free survival with first-line maintenance niraparib. Other risk factors of interest included the number of baseline non-target lesions and primary tumor location. Assessment of these risk factors in patients with advanced ovarian cancer may help inform treatment decisions by facilitating identification of those who are more likely to experience long-term progression-free survival with niraparib first-line maintenance. Future analyses including real-world patients with ovarian cancer treated with niraparib who may have been ineligible for PRIMA are required to confirm the applicability of the observed associations to the wider ovarian cancer patient population. Analyses of predictors of overall survival in PRIMA may also properly contextualize the results of this study.

CONCLUSIONS

This post hoc analysis suggests that progression-free survival of ≥2 years in patients with advanced ovarian cancer treated with niraparib may be associated with *BRCA1/2* mutation/homologous recombination-deficiency status, FIGO stage at diagnosis, and number of baseline non-target lesions.

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