Patient-Reported Outcomes in Patients Receiving Niraparib in the PRIMA/ENGOT-OV26/GOG-3012 Trial

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- Takeda
**PRIMA Trial Design**

- PRIMA is a randomized, double-blind, placebo-controlled phase 3 trial of niraparib vs placebo in patients with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube cancer with a CR or PR to 1L platinum-based chemotherapy.

**Patients with newly diagnosed OC at high risk for recurrence after response to 1L platinum-based chemotherapy**

**2:1 Randomization**

- **Niraparib**
  - Body weight- and platelet count-based dosing*
- **Placebo**

**Stratification factors**

- NACT: yes or no
- Best response to 1L platinum: CR or PR
- HRd or HRp status
- Myriad myChoice®

**Endpoint assessment**

- **Primary endpoint:** PFS by BICR
- **Key secondary endpoint:** OS

**Hierarchical PFS testing**

- Patients with HRd tumors, followed by the overall population

**PROs**

- FOSI
- EORTC QLQ-C30
- EORTC QLQ-OV28
- EQ-5D-5L

*After November 27, 2017, patients with baseline body weight <77 kg and/or platelet count <150,000/μL started at 200 mg QD; all other patients started at 300 mg QD. 1L, first-line; BICR, blinded independent central review; CR, complete response; EORTC QLQ-C30/OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire/Ovarian Cancer Module; EQ-5D-5L, EuroQol 5-Dimension 5-Level; FOSI, Functional Ovarian Symptom Index; HRd, homologous recombination deficient; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; PRO, patient-reported outcome; QD, once daily; TFST, time to first subsequent therapy.
**PRO Instruments**

**PRO measurements**

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Domains assessed</th>
<th>Score</th>
<th>Higher score indicates</th>
<th>Clinically meaningful change from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOSI</strong> Functional Ovarian Symptom Index</td>
<td>Symptoms: Fatigue, nausea, bloating, worry, pain, vomiting, cramping, QoL</td>
<td>Total 0–32</td>
<td>Better symptoms/HUI</td>
<td>± 2</td>
</tr>
<tr>
<td><strong>EORTC QLQ-C30</strong> European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire</td>
<td>Functional scale: Physical, role, emotional, cognitive, social function</td>
<td>0–100</td>
<td>Better functioning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Symptoms: Fatigue, nausea &amp; vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties</td>
<td>0–100</td>
<td>Worse symptoms</td>
<td>± 10</td>
</tr>
<tr>
<td></td>
<td>Global health status/QoL</td>
<td>0–100</td>
<td>Better QoL</td>
<td></td>
</tr>
<tr>
<td><strong>EORTC QLQ-OV28</strong> European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module</td>
<td>Functional scale: Body image, sexuality, attitude toward disease/treatment</td>
<td>0–100</td>
<td>Better functioning</td>
<td>± 10</td>
</tr>
<tr>
<td></td>
<td>Symptoms: Abdominal/GI symptoms, peripheral neuropathy, hormonal/menopausal symptoms, other chemotherapy side effects, hair loss</td>
<td>0–100</td>
<td>Worse symptoms</td>
<td></td>
</tr>
<tr>
<td><strong>EQ-SD-5L</strong> EuroQol 5-Dimension 5-Level</td>
<td>Health state for five domains: Mobility, self-care, usual activities, pain/discomfort, anxiety/depression</td>
<td>HUI 0–1</td>
<td>Better QoL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Visual analog scale (VAS)</td>
<td>VAS 0–100</td>
<td>Better QoL</td>
<td></td>
</tr>
</tbody>
</table>

EOT, end of treatment; GI, gastrointestinal; HUI, health utility index; PRO, patient-reported outcome; QoL, quality of life; VAS, visual analog scale.
High Compliance Rates by PRO Instrument

- Patient compliance rates remained consistently high (>80%) across all PRO instruments throughout the trial.
FOSI-Assessed Symptoms

- Mean FOSI HUI scores were similar in both the niraparib-treated and placebo patients.
- The overall percentage of patients with FOSI-assessed symptoms in niraparib-treated and placebo-treated patients were similar.

**FOSI HUI**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Niraparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>484</td>
<td>246</td>
</tr>
<tr>
<td>3</td>
<td>430</td>
<td>229</td>
</tr>
<tr>
<td>5</td>
<td>359</td>
<td>188</td>
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<tr>
<td>7</td>
<td>322</td>
<td>161</td>
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<td>9</td>
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<td>15</td>
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<td>24</td>
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<td>5</td>
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<tr>
<td>27</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>30</td>
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</tbody>
</table>

**Score**

- 0: Not at all
- 1: A little
- 2: Somewhat
- 3: Quite a bit
- 4: Very much

**Response**

- None
- Mild
- Severe

**Symptoms**

- I have a lack of energy
- I have nausea
- I have been vomiting
- I have cramps in my stomach area

BL, baseline; FOSI, Functional Ovarian Symptom Index; HUI, health utility index.
EORTC QLQ-C30 scores were comparable for both niraparib and placebo groups.

No difference in QoL and physical function was observed for patients receiving niraparib vs placebo.

No difference in fatigue or pain was reported for patients receiving niraparib compared with placebo.

BL, baseline; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; QoL, quality of life; SD, standard deviation.
• Ovarian specific EORTC QLQ-OV28 PRO assessments showed no difference in mean abdominal symptoms and other CT side effect scores

• EQ-5D-5L assessment revealed no meaningful difference in HUI-assessed change from baseline between niraparib and placebo

• EQ-5D-5L scores obtained with a visual analogue scale (VAS) also showed no differences between niraparib and placebo

BL, baseline; CT, chemotherapy; EORTC QLQ-OV28, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module; EQ-5D-5L, EuroQol 5-Dimension 5-Level; GI, gastrointestinal; HUI, health utility index; QoL, quality of life; SD, standard deviation; VAS, visual analog scale.
Conclusions

- Patient compliance rates were high across all PRO instruments (>80%)

- FOSI scores between niraparib and placebo were comparable
  - Percentages of patients reporting lethargy, nausea, vomiting, and abdominal cramps were similar in niraparib and placebo arms

- QoL were comparable between niraparib and placebo, as indicated by the EORTC QLQ-C30 instrument

- Abdominal/GI symptoms and other CT effects were comparable in both arms, as assessed by the EORTC QLQ-OV28 instrument

- Overall QoL was similar in patients receiving niraparib compared with those receiving placebo, as assessed by the EQ-5D-5L instrument

- Consistent with PRO results in the NOVA study, patients receiving niraparib in the PRIMA trial did not experience a decrement in QoL compared with placebo during their treatment, despite AEs including grade ≥3 hematologic toxicity
Acknowledgements

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