Efficacy of Niraparib Therapy in Patients with Newly Diagnosed Ovarian Cancer by BRCAwt Status: PRIMA/ENGOT-OV26/GOG-3012 Study

1Elena Ioana Braicu, 2Bhavana Pothuri, 3Jose Alejandro Pérez-Fidalgo, 4David O’Malley, 5Bradley J Monk, 6Charite Medical University; 7Gynecologic Oncology Group (GOG); 8UK Medical Center; 9Royal Marsden Hospital; 10Lake City, Utah. The prespecified BRCAwt subgroup PFS analysis was performed using a stratified log-rank test and Cox prognostic hazards model and hierarchically tested in HRd patients, then the overall population. BRCA and HRd status were determined by tumour BRCA and HRd status. Patients were stratified by best response to the first-line chemotherapy (CR/PR), receipt of neoadjuvant chemotherapy (yes/no), and homologous recombination status (deficient/proficient and not determined). Patients were randomised 2:1 to receive either niraparib or placebo once daily. The primary endpoint of PFS, assessed by blinded independent central review, was analysed using a stratified log-rank test and Cox proportional hazards model and hierarchically tested in HRd patients, then the overall population. BRCA and HRd status were determined by tumour samples at screening via the myChoice test (Myriad, Salt Lake City, Utah). The prespecified BRCAwt subgroup PFS analysis was performed using a stratified log-rank test and Cox proportional hazards model and using Kaplan-Meier methodology. BRCAwt subgroups included the intention-to-treat/BRCa2wt (all patients who were homologous recombination not determined [HRnd]/BRCa2wt, HRd/BRCa2wt, and homologous recombination proficient [HRp]/BRCa2wt); subgroup analyses on the HRd/BRCa2wt and HRp/BRCa2wt were performed.

Results Of 733 randomised patients, 473 (64.5%) had BRCa2wt tumours (74 patients had unknown BRCA status). Of these 473, 150 (31.7%) had HRd/BRCa2wt tumours, 249 (52.6%) had HRp/BRCa2wt tumours, and 74 (15.7%) had HRnd/BRCa2wt tumours. Niraparib-treated patients with BRCa2wt tumours had a clinically meaningful PFS benefit regardless of homologous recombination status (table 1).
Abstract 364 Table 1

<table>
<thead>
<tr>
<th>Hazard ratio (95% CI), n=473</th>
<th>HRd/BRCAwtn=150</th>
<th>HRp/BRCAwtn=249</th>
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<tbody>
<tr>
<td>mPFS, months</td>
<td></td>
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<tr>
<td>Niraparib</td>
<td>10.9</td>
<td>19.6</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.4</td>
<td>8.2</td>
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<tr>
<td>ΔmPFS, months</td>
<td>3.5</td>
<td>11.4</td>
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<td>*Includes patients who were HRd but known to be BRCAwt.</td>
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**Conclusion**
Niraparib improved PFS when utilised as maintenance therapy after front-line treatment of OC in patients with BRCAw tumours, including in the most difficult to treat subgroup of patients with BRCAw and HRp tumours.

**Disclosures**
Dr. Braicu reports honoraria from AstraZeneca, Tesaro, GSK, Roche Pharma, Clovis and MSD; consulting or advisory roles at AstraZeneca, Tesaro, GSK, Roche Pharma, Clovis, MSD, Abbvie, Eisai, Immunogen, Takeda; institutional research funding from Roche Diagnostics and Takeda; and travel, accommodation and expenses from Astra Zeneca, Roche Pharma, Clovis, and MSD.

Dr. Pothuri reports grants, personal fees and non-financial support from GSK; Advisory Board fees from AstraZeneca and Clovis Oncology.

Dr. Alejandro Perez-Fidalgo reports speaker fees from GSK, AstraZeneca, Clovis, and Roche; advisory fees from GSK, AstraZeneca, Clovis, Abilly Pharma, CliniGen, Rocke, and Amgen; grant from GSK; and travel fees from AstraZeneca and Roche.


Dr. Graybly reports personal fees from GSK.

Dr. Dahlstrand reports personal fees from AstraZeneca and Roche.

Dr. Monk reports consulting and advisory role at Merck, GSK, Roche/Genentech, AstraZeneca, Advaxiz, Cerulean Pharma, Amgen, Immunogen, NuCana BioMed, Clovis Oncology, Pfizer, Mateon Therapeutics, Precision Oncology, Perthera, Abbvie, Myriad Pharmaceuticals, Incyte, VBL Therapeutics, Takeda, Summed, Oncomed, OncoSec, ChemID, Geistlich Pharma, Eisai and Chemocare; Speakers' bureau at Roche/Genentech, AstraZeneca, Janssen, Clovis Oncology and GSK; Honoraria from Merck, GSK, Roche/Genentech, AstraZeneca, Advaxis, Immunogen, NuCana BioMed, Clovis Oncology, Pfizer, Mateon Therapeutics, Precision Oncology, Perthera, Abbvie, Myriad Pharmaceuticals, Incyte, Janssen, Amgen, Genmab, Santumed, Takeda, VBL Therapeutics, Puma Biotechnology, Immunomedics, Conjuppo Biotherapeutics, Agenus, OncoQuest, Chemolod, Geistlich Pharma, Eisai and Chemocare; and Research funding from Novartis, Amgen, Genentech, Lilly, Janssen, Array BioPharma, GSK, Morphojet, Pfizer, Advaxis, AstraZeneca, Immunogen, Regeneron, and Nucana.

Drs. Honhon and Fabbaro have nothing to disclose.

Dr. Gupta is an employee of GlaxoSmithKline.

**FEASIBILITY STUDY OF A NETWORK META-ANALYSIS AND UNANCHORED POPULATION-ADJUSTED INDIRECT TREATMENT COMPARISON OF NIRAPARIB, OLAPARIB, AND BEVACIZUMAB AS MAINTENANCE THERAPIES IN PATIENTS WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER**

**Introduction/Background**
Although randomised controlled trials (RCTs) have demonstrated the benefit of PARP inhibitors and bevacizumab as monotherapies and combination therapies, there is limited direct head-to-head evidence of their relative clinical efficacy.

In the PRIMA study, niraparib demonstrated a clinically significant improvement in progression-free survival (PFS) compared with placebo, as a first-line (1L) ovarian cancer (OC) maintenance therapy.

The objectives of the study were to assess feasibility of an indirect treatment comparison (ITC) and a population-adjusted indirect treatment comparison (PAIC) for estimating the relative efficacy of niraparib compared with olaparib, olaparib plus bevacizumab, and bevacizumab as maintenance following 1L chemotherapy in OC. The study focused on fully powered statistical cohorts.

**Methodology**
Trials included in the ITC analysis were based on a systematic literature review conducted in February 2020.

Guidelines from the Cochrane Handbook for Systematic Reviews of Interventions were used to assess the level of heterogeneity across the studies in terms of designs, population characteristics, treatment arms and outcome measures.