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Title: Long-term safety and secondary efficacy endpoints in the ENGOT-OV16/NOVA phase III trial of niraparib in recurrent ovarian cancer

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Objectives: In the ENGOT-OV16/NOVA study, maintenance therapy with niraparib significantly prolonged progression-free survival (PFS) in patients (pts) with platinum-sensitive recurrent ovarian cancer (PSROC) regardless of germline BRCA mutation (gBRCAm) or homologous recombination deficiency (HRd) biomarker status. This analysis updates long-term safety and available data on secondary efficacy outcomes.

Methods: In this randomized, double-blind, placebo-controlled, phase III trial, pts with PSROC were enrolled into 1 of 2 independent cohorts by gBRCAm status (gBRCAm or non-gBRCAm). Stratification factors were PFS after the penultimate platinum therapy (6 to <12 months vs >=12 months), best response to the last platinum-based therapy (complete or partial), and prior bevacizumab (Y/N). Pts were randomized 2:1 to niraparib 300 mg QD or placebo. The primary endpoint was PFS as assessed by blinded independent central review. Progression-free survival 2 (PFS2) and overall survival (OS) were exploratory secondary endpoints.

Results: A total of 553 pts were randomized in the NOVA study. Median follow-up was 66 months at the time of the current analysis.Hematologic treatment-emergent adverse effects (TEAEs) primarily occurred in the first year of niraparib treatment: incidence of grade ≥3 thrombocytopenia decreased from 33.8% to 2.8%, anemia decreased from 25.6% to 0.7%, and neutropenia decreased from 19.3% to 2.1% from year 1 to year 2–3, respectively. A total of 13 (3.5%; 9 gBRCAm, 4 non-gBRCAm) pts who received niraparib developed MDS/AML vs 3 (1.7%) placebo pts. Survival status could not be obtained for ~15% of pts. Data on post-progression therapy, including PARP inhibitors, were not available for 25% of the study pts. Based on data cut-off on October 2020, 127 and 238 deaths occurred in the gBRCAm and non-gBRCAm cohorts, respectively. For pts with available data, placebo pts received subsequent PARP inhibitor therapy (crossover) after disease progression: 46% (30/65) in the gBRCAm cohort and 13% (15/116) in the non-gBRCAm cohort. Hazard ratios for PFS2 were 0.67 (95% CI: 0.48, 0.95) in the gBRCAm cohort and 0.81 (95% CI: 0.62, 1.05) in the non-gBRCAm cohort. Restricted mean survival time analyses for OS up to 72 months were 43.2 months in placebo vs 45.9 months in niraparib (Δ of 2.7m, 95% CI: -4.1, 9.5) in the gBRCAm cohort and 39.1 months in placebo vs 38.5 months in niraparib (Δ of -0.6m, 95% CI: -6.0, 4.7) in the non-gBRCAm cohort.

Conclusions: These final data support the safe long-term use of niraparib for maintenance treatment in pts with PSROC. PFS2 analysis indicates that the benefit of niraparib maintenance therapy extends beyond first progression. No difference in survival was observed. The NOVA study was not powered for OS, and analysis is confounded by a high rate of crossover and missing data thus limiting its interpretation.Sponsor: GlaxoSmithKlineClinical Trial Registration: NCT01847274