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ARIEL4: An International, Randomised Phase 3 Study of the PARP Inhibitor Rucaparib vs Chemotherapy for the Treatment of *BRCA*-Mutated, Relapsed, High-Grade Ovarian Cancer

Background: Approximately 18% of patients (pts) with high-grade epithelial ovarian cancer (OC) harbour a deleterious germline *BRCA1* or *BRCA2* (*BRCA1/2*) mutation, and ≈7% harbour a somatic *BRCA1/2* mutation (Pennington et al. *Clin Cancer Res.* 2014;20:764-75). The poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib is approved in the United States for the treatment of pts with deleterious *BRCA* mutation (germline and/or somatic) associated advanced OC who have been treated with ≥2 chemotherapies. Data comparing PARP inhibitors to standard of care (SOC) treatment for relapsed OC are limited. Randomised studies are needed to assess the benefit-risk profile of PARP inhibitors vs SOC as treatment for *BRCA1/2*-mutated, relapsed, high-grade OC.

Trial Design: ARIEL4 (EudraCT 2016-000816-14; NCT02855944) is evaluating rucaparib vs SOC chemotherapy as treatment for pts (n≈345) with relapsed, high-grade OC (regardless of histology) and a deleterious germline or somatic *BRCA1/2* mutation who received ≥2 prior chemotherapy regimens. Pts stratified by progression-free interval after their most recent platinum regimen will be randomised 2:1 to receive rucaparib (600 mg BID) (n≈230) or chemotherapy (n≈115). Pts with platinum-resistant (progressive disease [PD] ≥1 to <6 mo after last platinum) or partially platinum-sensitive disease (PD ≥6 to <12 mo after last platinum) will receive rucaparib or weekly paclitaxel; pts with platinum-sensitive disease (PD ≥12 mo after last platinum) will receive rucaparib or platinum-based therapy (single-agent or doublet, per investigator discretion). Pts receiving chemotherapy have the option to cross over to rucaparib upon radiographic disease progression. The primary endpoint is investigator-assessed progression-free survival (RECIST version 1.1). Secondary endpoints include overall survival, objective response rate, RECIST/CA-125 response, duration of response, and patient-reported outcomes. Safety will be summarised descriptively using standard adverse event reporting.