**Olaparib as Maintenance Treatment Following First-line Platinum-based Chemotherapy
(PBC) in Patients With a Germline BRCA Mutation and Metastatic Pancreatic Cancer
(mPC): Phase III POLO trial**

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**Background:** PC patients with a germline *BRCA1* and/or *BRCA2* mutation (gBRCAm) have shown response to the PARP inhibitor olaparib (Kaufman 2015). POLO(NCT02184195) is the first Phase III trial to evaluate efficacy of maintenance treatment with a PARP inhibitor in mPC.

**Methods:** POLO is an international, randomized, double-blind, placebo-controlled trial of patientswith a gBRCAm and pancreatic adenocarcinoma who had received ≥16 weeks of first-line PBC for metastatic disease without progression. Patients were randomized 3:2 to maintenance olaparib tablets (300 mg bid) or placebo. Treatment began 4–8 weeks after last PBC dose, continuing until investigator-assessed progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS) by blinded independent central review (modified RECIST 1.1).

**Results:** We screened 3315 patients, identified 247 with a gBRCAm, randomized 154 (olaparib 92, placebo 62), and treated 151 (olaparib 90, placebo 61). Patient characteristics (olaparib/placebo): age, median (range) 57 (37–84)/57 (36–75); male, 58%/50%; ECOG performance status 0, 71%/61%. With 104 events, PFS was significantly improved with olaparib versus placebo (HR 0.53; 95% CI 0.35–0.82; *P*=0.0038; median 7.4 vs 3.8 months) and consistent irrespective of response to prior PBC (complete/partial HR 0.62; stable disease HR 0.50). At 2 years, 22.1% of olaparib-arm patients versus 9.6% of placebo-arm patients were free from disease progression. At the interim overall survival analysis (46% maturity), HR was 0.91 (95% CI 0.56–1.46; *P*=0.68). Grade ≥3 adverse events occurred in 40% of olaparib- and 23% of placebo-treated patients; 5.5% and 1.7%, respectively, discontinued treatment due to an adverse event.

**Conclusions:** Maintenance olaparib provided a statistically significant and clinically meaningful improvement in PFS in mPC patients with a gBRCAm who had not progressed on PBC. Safety was consistent with the known profile for olaparib. POLO is the first Phase III trial to validate a biomarker-driven treatment in PC.