ONCOLYTIC VACCINIA (OLVI-VEC) PRIMED IMMUNOCHEMOTHERAPY IN PLATINUM-RESISTANT/REFRACTORY OVARIAN CANCER

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Introduction Intraperitoneal oncolytic vaccinia virus (Olvi-Vec) was administered to heavily pretreated patients with platinum-resistant/refractory ovarian cancer (PRROC) followed by intravenous carboplatin-doublet (CD) ± bevacizumab (Bev) in a Phase-2 trial (NCT02759588). Primary objectives: RECIST overall response rate (ORR) & progression-free survival (PFS).

Methods Patients with PRROC who progressed after most recent therapies received 2 days of Olvi-Vec followed by CD ± Bev, then maintenance with single-agent therapies ± Bev. Pre- & post-virotherapy tumor biopsies were obtained for translational analyses.

Results 27 patients enrolled: median 4 prior regimens, 82% prior Bev, 52% platinum-refractory and 48% platinum-resistant. Mean cycles of CD±Bev were 6(±3). Median follow-up was 26.5 months. RECIST ORR was 54% (95% CI: 33–74%): 2(8%) complete response, 11(46%) partial response; 8(33%) stable disease. Median duration of response was 7.6 months (95% CI: 3.7–9.6). Clinical benefit rate was 88%. Median PFS was 11.0 months (95% CI: 6.7–13.0), and PFS-6-month was 77%. CA-125 ORR was 85% (95% CI: 63–96%). There were no Grade 4 adverse events with virotherapy. Performance status was preserved/improved in 24 (89%) patients while on CD±Bev. Post-virotherapy intra-tumoral infiltration of CD8+
T-cells and upregulation of STAT1 expression (p=0.008) were demonstrated.

**Conclusions** Despite PRROC, prior bevacizumab, and progression on last therapy, the majority of patients achieved RECIST response with median PFS exceeding their prior line of therapy. Virus-induced changes in the tumor microenvironment may explain the apparent clinical reversal of platinum resistance.

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**Efficacy on Individualized Starting Dose (ISD) and Fixed Starting Dose (FSD) of Niraparib Per Investigator-Assessment (IA) in Newly Diagnosed Advanced Ovarian Cancer (OC)**

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**Introduction** Niraparib is a poly(ADP-ribose) polymerase inhibitor approved for maintenance treatment of patients with newly diagnosed or recurrent OC that responded to platinum-based chemotherapy and treatment in heavily-pretreated recurrent OC. Here we report efficacy in patients receiving the FSD and ISD in the PRIMA/ENGOT-OV26/GOG-3012 trial (NCT02655016).

**Methods** This double-blind, placebo-controlled, phase 3 study randomized 733 patients to receive niraparib or placebo for 36 months or until disease progression/toxicity. A protocol amendment introduced ISD: 200 mg in patients with body weight <77 kg or platelets <150,000/μL, or 300 mg in all others. The primary endpoint was PFS by blinded independent central review (BICR). IA PFS was a sensitivity analysis. At the primary analysis data cut, follow-up was 11.2 months and 17.1 months in the ISD and FSD subgroups, respectively. An ad hoc analysis of IA PFS was performed using an updated data cut with additional 6 months follow-up.

**Results** BICR and IA PFS were highly concordant in the overall population. Efficacy of niraparib based on IA PFS in FSD vs ISD subgroups for each data cut were similar (table 1). Dose interruptions, modifications, and hematologic toxicity were lower with the ISD. Exposure–response data supported the clinical data.

**Conclusions** The 200- or 300-mg ISD by baseline body weight and platelet counts demonstrated comparable efficacy while improving the safety profile of niraparib. Use of this regimen for first-line maintenance of advanced OC patients is approved by the US FDA. Funded by: GlaxoSmithKline

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Plenary V

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**Phase II Trial Evaluating Efficacy and Safety of Standard of Care with or Without Bevacizumab in Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer**

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**Introduction** There are no ongoing clinical trials investigating bevacizumab efficacy beyond disease progression in platinum-resistant OC. Patients who are refractory to platinum and bevacizumab are not eligible for Phase III BEYOND trial. Here, we report Phase II efficacy and safety of standard of care plus or minus bevacizumab as third-line chemotherapy for patients who have platinum-resistant OC.

**Methods** This was a single-institution, open-label, single-arm, Phase II trial (JCOG1604) in patients with platinum-resistant OC after at least two prior regimens and/or a platinum-free interval of <24 weeks. The efficacy endpoints were progression-free survival (PFS) in the overall population and the ISD and FSD subgroups, HR (95% CI).

**Results** A total of 32 patients were enrolled between May 2016 and December 2018 after at least two prior regimens and/or a platinum-free interval of ≥24 weeks. The median PFS was 7.8 months (95% CI, 6.1–13.0 months) and the 12-month PFS rate was 37.5% (95% CI, 22.0–52.9%). The median OS was 30.9 months (95% CI, 15.4–38.3 months). The incidence of adverse events was manageable. This study demonstrates the efficacy of standard of care plus or minus bevacizumab as third-line chemotherapy for patients with platinum-resistant OC.

**Conclusions** EFS and OS in patients with platinum-resistant OC were prolonged by adding bevacizumab to standard of care chemotherapy. This study also demonstrated the feasibility of third-line chemotherapy in patients with platinum-resistant OC after at least two prior regimens and/or a platinum-free interval of ≥24 weeks.