ENGOT-OV65/KEYNOTE-B96: PHASE 3, RANDOMIZED, DOUBLE-BLIND STUDY OF PEMBROLIZUMAB VERSUS PLACEBO PLUS PACLITAXEL WITH OPTIONAL BEVACIZUMAB FOR PLATINUM-RESISTANT RECURRENT OVARIAN CANCER

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Introduction/Background Despite therapeutic advances in ovarian cancer, platinum-resistant recurrent ovarian cancer remains an area of high unmet clinical need and there is an urgent need for new treatments to further improve clinical outcomes. ENGOT-ov65/KEYNOTE-B96 (NCT05116189) compares the efficacy and safety of pembrolizumab plus weekly paclitaxel (± bevacizumab) versus placebo plus weekly paclitaxel (± bevacizumab) in patients with platinum-resistant recurrent ovarian cancer.

Methodology In this randomized, placebo-controlled, double-blind, phase 3 study, eligible patients are aged ≥18 years with histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal carcinoma with 1–2 prior lines of systemic therapy, including at least 1 prior platinum-based therapy with ≥4 cycles in first line. Patients must have platinum-resistant disease (radiographic evidence of disease progression ≥6 months after last platinum-based therapy dose), be eligible for disease (radiographic evidence of disease progression ≥C21 cycles in first line). Patients must have platinum-resistant therapy, including at least 1 prior platinum-based therapy with ≥4 cycles in first line. Patients must have platinum-resistant disease (radiographic evidence of disease progression ≥6 months after last platinum-based therapy dose), be eligible for disease (radiographic evidence of disease progression ≥C21 cycles in first line). Patients must have platinum-resistant therapy, including at least 1 prior platinum-based therapy with ≥4 cycles in first line. Patients must have platinum-resistant disease (radiographic evidence of disease progression ≥6 months after last platinum-based therapy dose), be eligible for disease (radiographic evidence of disease progression ≥C21 cycles in first line).

Primary endpoint is PFS per RECIST version 1.1 by investigator review. Secondary endpoints are OS, PFS per RECIST version 1.1 by blinded independent central review, safety, and patient-reported outcomes. Enrolment is ongoing.

Results N/A

Conclusion N/A

INTRODUCTION/BACKGROUND

MIRVETUXIMAB SORAVTANSINE (MIRV) is a first-in-class antibody-drug conjugate comprising a folate receptor alpha (FRα)-binding antibody, cleavable linker, and the maytansinoid payload DM4, a potent tubulin-targeting agent that has demonstrated significant antitumor activity in this difficult-to-treat ovarian cancer population. The objective was to characterize the patients with FRα-positive recurrent ovarian cancer who achieved extended treatment benefit (ETB); progression-free survival for >12 months) with MIRV monotherapy.

Methodology Retrospective pooled analysis included patients enrolled across three trials: phase 1 first-in-human, phase 3 FORWARD I, and phase 3 SORAYA. Analysis included patients with low, medium, and high FRα expression by immunohistochemistry. All patients received intravenous MIRV at 6 mg/kg, adjusted ideal body weight, every three weeks until disease progression or unacceptable toxicity.

Results Of the 464 patients included in the analysis, 40 ETB patients were identified: median age 63 years, median of one prior therapy, 52.5% with prior PARPi, and 60% with prior bevacizumab. ETB patients had an overall response rate of 75.0%, with 9 (22.5%) achieving a complete response and 21 (52.5%) achieving a partial response by RECIST v1.1 and demonstrated a median duration of response of 22.1 months (95% CI, 13.8–60.0; interquartile range 13.5–60.0). The most common treatment-related adverse events (TRAEs) (all grade, grade 3+) included blurred vision (60%, 0%), fatigue (50%, 2.5%), nausea (50%, 0%), and keratopathy (40%, 2.5%). Peripheral neuropathy was present in 35% (no grade 3+) and pneumonitis was present in 20% (no grade 3+). TRAEs led to dose delay or reduction in 65% and 47.5% of ETB patients, respectively, and discontinuation in six patients.