THE POTENTIAL OF ANTI-TIM3 IN AN OVARIAN CANCER MOUSE MODEL

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Introduction/Background The immune system has proven to be involved in ovarian cancer (OC) disease, yet, clinical immunotherapeutic trials have not resulted in convincing successes. Innate immunosuppression is currently left untackled. Anti-TIM3 (T-cell immunoglobulin and mucin-domain containing-3) has a potential advantage for OC immunotherapy, since it can manipulate the function of innate (macrophages and dendritic cells) and adaptive (CD4+, CD8+ and regulatory T-cells) immune cells.

Methodology Female C57BL/6 mice were inoculated intraperitoneally (IP) with 5x10^6 ID8-fluc OC cells. Treatment was initiated 20 days post inoculation and consisted of carboplatinum-paclitaxel (C/P) chemotherapy (100mg/kg and 10mg/kg initiated 20 days post inoculation and consisted of carboplatinum-paclitaxel (C/P) chemotherapy (100mg/kg and 10mg/kg respectively) through a single IP injection with or without biweekly IP administration of anti-TIM3 (InVivoMAB anti-mouse TIM3 (CD366)) (350μg/injection) for three or four weeks in different schedules. Survival was recorded using predefined humane endpoint criteria. The immune system was analysed at predefined time-points using fluorescence activated cell sorting on peritoneal washings.

Results Anti-TIM3 monotherapy did not induce changes in disease progression. Moreover, addition of C/P to anti-TIM3 treatment did not prolong the survival of OC bearing mice compared to mice treated with C/P alone. However, adapting the sequence from sequential administration, with first C/P and one week later anti-TIM3 administration, to simultaneous administration of both treatments improved the survival of tumor bearing mice (p=0.0287). From an immunological perspective, we observed a significant reduction in the percentages of regulatory T-cells in the cohort receiving the sequential combination treatment compared to the mice receiving the simultaneous treatment. Additionally, prolonging the anti-TIM3 treatment duration from three to four weeks in combination with simultaneous C/P resulted in significantly increased survival (p=0.0151).

Conclusion Overall, we show that anti-TIM3 does not improve the survival of OC-bearing mice in monotherapy or in combination with C/P compared to C/P alone, however our results highlight the importance of the order and duration when combining immunotherapeutic treatments with chemotherapy.

Disclosures AC is a contracted researcher for Oncoinvent AS and Novocure and a consultant for Sotio a.s. and Epics Therapeutics SA.

Efficacy and safety of Senaparib as maintenance treatment in patients with newly diagnosed advanced ovarian cancer (FLAMES study): a randomized, double-blind, placebo-controlled, phase 3 trial

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Introduction/Background Ovarian cancer (OC) is the most lethal gynecologic cancers. The first-line (1L) treatment of newly diagnosed advanced OC is surgery and platinum-based chemotherapy, up to 85% of patients (pts) may experience a recurrence. Poly ADP-ribose polymers (PARP) inhibitors are recommended as maintenance therapy to prolong the benefit of platinum. Senaparib (IMP4297) is a novel, high potency PARP inhibitor. The phase 3 study FLAMES is to confirm the efficacy and safety of Senaparib as 1L maintenance therapy in Chinese pts with newly diagnosed advanced OC.

Methodology Eligible pts are those with high-grade serous or endometrioid tumors staged FIGO (International Federation of Gynecology and Obstetrics) III or IV, who completed 1L platinum-based chemotherapy with complete response (CR) or partial response (PR). Pts were randomized 2:1 to receive senaparib (Sena) or placebo (PBO) 100 mg/day orally, stratified by CR/PR and breast cancer susceptibility gene (BRCA) mutation positive/negative. Primary endpoint was progression-free survival (PFS) evaluated according to RECIST v1.1.

Results As of Mar of 16 ,2023, 404 pts have been randomized. 268 and 135 pts received Sena and PBO with median follow-up x months. Sena significantly improved PFS (mPFS x vs x mo; HR 0.26, p<0.01) over placebo. Subgroup analysis demonstrated consistent benefit. Incidence rates of grade ≥3 treatment emergent adverse events (AEs) were x% vs x%, AEs leading to dose reduction and discontinuation were x% vs x% and x% vs x%, No AE leading to death. The most common grade ≥3 TEAEs were anaemia (x%), thrombocytopenia (x%), and neutropenia (x%).

Conclusion Pts who received Sena had a meaningful and significant improvement in PFS compared to those who received PBO and the PFS is much longer than other PARP inhibitors, regardless of biomarker status. Sena was well tolerated, no new safety signals were identified.

Disclosures All of the authors have no conflict of interest to report.