1031P OCTAVE: A phase I study of enadenotucirev, an oncolytic group B adenovirus, in combination with weekly paclitaxel in platinum-resistant epithelial ovarian cancer

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Background: Enadenotucirev (EnAd) is a tumor selective Ad11/Ad3 group B adenovirus that has demonstrated pre-clinical activity in a model of platinum-resistant ovarian cancer. Synergy has also been reported between oncolytic adenoviruses and microtubule manipulating drugs such as paclitaxel (Pxl). This study aims to establish the tolerability and preliminary efficacy of EnAd delivered in combination with Pxl. Here we present data from the intravenous (IV) dose expansion group.

Methods: Patients with platinum-resistant or refractory ovarian cancer received a minimum of two 28-days cycles of IV infusional EnAd ($1x10^{12}$ viral particles) on days 1, 3 and 5, and IV Pxl ($80mg/m^2$) on days 9, 16 and 23. Baseline and on-treatment biopsies were taken. Primary endpoint was safety and tolerability; additional endpoints included, response rate (RECISTv1.1/GCIG CA125 criteria) and duration of response.

Results: Twenty patients, median age 60.5 years (range 37-78) who had received a median of 4 prior lines of therapy (range 1-12) were enrolled. Adverse events reported from the combination of EnAd and Pxl were as previously described (for both agents individually), with 'flu-like symptoms reported in the majority of patients following EnAd administration. Hematological changes including neutropenia, previously identified at higher doses of EnAd IV monotherapy, were reported at the dose level tested in this study population. Virus kinetics, cytokine and anti-virus antibody responses were consistent with previous results with EnAd. As of 03May19, Investigator-assessed ORR is 37.5% (6/16), with median DoR of 16 weeks (range 8-32). Reductions in CA125 broadly follow the pattern of tumor regression, with 36% (4/11) achieving response according to GCIG CA125 criteria. Disease control rate (RECIST CR, PR, SD) is 75% (12/16). To date, matched biopsies (N = 2) have been analysed for pharmacodynamic markers, providing preliminary evidence of increased CD8 T cell infiltration in on-treatment tumour biopsies.

Conclusions: The combination of EnAd and Pxl has manageable tolerability. Favorable disease control is noted in this recurrent platinum-resistant population, which is worthy of further investigation.

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