Abstracts

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A PHASE IB STUDY OF INDIRECT IMMUNIZATION WITH OREGOVOMAB AND TLR3 STIMULATION WITH HILTONOL® (H) IN PATIENTS WITH RECURRENT PLATINUM RESISTANT OVARIAN CANCER (PROC)

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Objectives This phase IB study assessed safety of Oregovomab (O) indirect immunization (monoclonal antibody for CA125) and TLR3 stimulation with H (polyICLC) in PROC. Secondary endpoints were RECIST response, immune response, response to subsequent therapies, and overall survival.

Methods Patients with PROC (median 3 prior Rx) received 4 IV infusions with 2 mg O followed by 2 mg H IM 30 min & 48 hours post-O at weeks 0, 3, 6 and 9. Week 12, imaging was performed, and elective chemotherapy was allowed post-progression. A final O infusion was given at week-16 and patients were followed.

Results 17 patients were enrolled at 2 centers; 15 were dosed and 13 completed the minimum 3 infusions. Treatment phase safety analysis is complete & post IT follow-up is ongoing. Local site reactions to H and mild fatigue/flulike symptoms were reported in 13(87%) patients. Serious adverse events were reported in 5 (33%) patients, attributed to underlying disease. No new safety signals were observed. Six (40%) had stable disease through the 12-week immunization period. Four patients with persistent/progressive disease stopped IT prior to infusion 4. Early humoral response by week-6 was observed in 7 of 9 (77%) patients with the available time points. 14 patients with persistent/progressive disease stopped Rx, 5 died of disease and 5 with persistent/progressive disease are stable on Rx.

Conclusions Safety, compatibility of combining O with H, and early humoral responsiveness to indirect immunization by week-6 have been established. The potential to enhance activity of chemotherapy using O indirect immunization is proposed.

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A NOVEL BIOMARKER FOR EARLY STAGE OVARIAN CANCER, AND A NEW TARGET FOR IMMUNOTHERAPY?

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Objectives Ovarian cancer (OC) is the eighth most commonly occurring cancer worldwide. One of the most effective ways to improve patient survival would be an earlier diagnosis when survival rates are highest. However, diagnosis tends to be in the later stages of disease when patients present with pelvic or abdominal pain, urinary frequency or urgency, increased abdominal size or bloating. A diagnosis of OC is usually confirmed by a pelvic examination, transvaginal ultrasoundography and detection of carbohydrate antigen 125 (CA125). However, the value of CA125 in early stage disease is limited due to a lack of sensitivity.

Methods Using immunohistochemistry we examined the expression of a panel of tumour antigens including ovarian cancer protein (OCP), as well as the standard biomarkers for OC, CA125, HE4 and WT1, in paraffin-embedded OC microarrays containing 208 samples. Scoring was performed in a single blinded fashion.

Results We found OC to be expressed at an intensity and frequency that exceeded that of CA125, HE4, WT1 or PASD1 in stage I and II OC. To confirm this expression we used two additional commercially-available antibodies that recognised OCP and demonstrated that this expression was reproducible and restricted to OC with little or no expression in adjacent, healthy ovarian or endometrial tissues, or indeed disease or inflamed endometrial tissue.

Conclusions We have identified a cancer-testis antigen that is more frequently expressed in presentation OC Stage I and II OC than CA125, HE4 and WT1. We are now examining the impact of siRNA treatment targeting OCP on OC cell survival in vitro.