Background
Immunization against self-antigens can induce regulatory responses that inhibit desirable Type 1 antitumor immune responses. Deletion of epitopes that favor a regulatory phenotype may improve the efficacy of therapeutic vaccines. We have developed a novel IGFBP-2 targeting DNA plasmid vaccine that selectively induces Type 1 immunity. IGFBP-2 regulates invasiveness and metastases in ovarian cancer. Eradication of ovarian cancer cells expressing IGFBP-2 through effective immunization could prevent disease relapse or metastasis.

Methods
Twenty-five patients with advanced stage or recurrent ovarian cancer treated to complete remission after primary or salvage therapy received 3 monthly doses of an IGFBP-2 DNA vaccine in a single-arm, non-randomized study. ELISPOT and flow cytometry were used to characterize antigen specific T-cell responses. Serum antibodies were measured using ELISA and Western blot. The SEER database was reviewed to identify women diagnosed between 2006 and 2012 matched for age, year of diagnosis and stage of diagnosis. The difference between dates of diagnosis and enrollment (lead time) was calculated for each patient receiving vaccine. Only SEER patients who survived at least as long as the lead time of their matches plus an additional 6 months were kept for analysis. In cases where this resulted in no SEER matched patients, unmatched vaccine patients were excluded. Overall survival (OS) was analyzed using Cox models and the Kaplan-Meier method.

Results
206 adverse events (AE) were recorded. Fatigue (12%) and injection site reactions (12%) were the most common. 97% of AE were grades 1-2, 3% grade 3, and no grades 4 or 5. In preliminary immune analysis (16 patients), IGFBP-2 specific T-cell precursor frequencies are significantly elevated over baseline levels at 4 (p<0.01) and 6 (p<0.001) months. T-regulatory cells were not increased over the levels measured in a control reference population. We saw induction of effector memory CD4 and CD8 T cells and Tbeta+ T cells consistent with a Th1 response. Median OS for the matched SEER group (n=754) was 11 months. Matched IGFBP-2 vaccinated patients (n=20) have yet to reach median OS, but the lower 95% confidence limit is 27.3 months (p<0.0001).

Conclusions
IGFBP-2 Th1 selective immunization is well tolerated, generates significant Type 1 immunity, and may demonstrate clinical efficacy.

References/Acknowledgements
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