Vaccination Targeting Insulin-Like Growth Factor Binding Protein-2 (IGFBP-2) in Advanced Ovarian Cancer: Safety and Immunogenicity

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Background

Immunization against self-antigens can induce regulatory responses that inhibit the development of desirable Type I antitumor immune responses. Removing epitopes that bias toward a regulatory phenotype may enhance vaccine efficacy. We developed a novel IGFBP-2 targeting DNA plasmid vaccine capable of selectively inducing Type I immunity. IGFBP-2 is an important regulator of ovarian cancer invasiveness and metastases. Eradication of cancer cells expressing IGFBP-2 through effective immunization could prevent disease relapse or metastatic spread.

Methods

In a single-arm non-randomized study of advanced stage (III/IV) or recurrent ovarian cancer patients treated to complete remission after primary or salvage therapy, 25 patients received 3 monthly doses of an IGFBP-2 DNA vaccine by intradermal injection. All adverse events (AE) were reported using the Common Terminology Criteria for Adverse Events Version 4.0. Overall survival (OS) was analyzed using the Kaplan-Meier method. ELISPOT and flow cytometry were used to characterize antigen specific T-cell responses and T-cell populations. Serum antibodies recognizing IGFBP-2 were measured by ELISA and Western blot against recombinant protein.

Results

To date, there have been 206 AE in the enrolled patients. Fatigue (12%) and injection site reactions (12%) were the most common. 97% of AE were grades 1-2, 3% grade 3, and there were no grade 4 or 5 AE. 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. No patients developed new IGFBP-2 specific antibody responses after immunization suggesting a lack of Th2 augmentation. IGFBP-2 vaccinated patients have yet to reach median OS over a median follow-up period of 23.5 months. The OS rate at 2 years was 62%.

Conclusions

IGFBP-2 Th1 selective immunization has a well tolerated safety profile and generates significant Type I immunity.

References/Acknowledgements

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