Ad-RTS-hIL-12 + Velelimex Regulation of IL-12 Expression in Advanced Breast Cancer and Melanoma

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Abstract

Aim: To evaluate the safety and tolerability of intratumoral injections of Ad-RTS-hIL-12 + veledimex in patients with advanced breast cancer and melanoma.

Methods: 27 patients (18 breast, 9 melanoma) were enrolled in cycle 1. 617 – 12 subjects enrolled on 21 day cycle, for up to 6 cycles; intratumoral injection of Ad-RTS-hIL-12 + veledimex followed by oral veledimex dose escalation. 11 female breast cancer and melanoma subjects. Multiple treatment cycles up to 3 or 6 cycles, based on RECIST 1.1. Serum IL-6, IL-12, IL-18, and IFN-γ measured with a quantitative sandwich immunoassay. IFN-γ was measured in serum cytokines in melanoma patients. Changes in tumor burden and change from baseline in cytokine levels were measured. Data was analyzed descriptively and summarized with the use of Kaplan-Meier plots and statistical tests. The study enrolled 12 subjects to Cycle 1, and an additional 25 subjects for a total of 72 subjects.

Results: The average number of cycles per patient was 2.6. One patient developed Grade 4 neutropenia requiring hospitalization. On average there were 2 lesions per patient, with a range of 1 to 10. On the left, waterfall plot of best overall response on a per lesion basis expressed as a percent change from the baseline imaging performed 0 weeks after initiation of therapy.

Conclusions:

• Expression of IL-12 in humans by direct intratumoral injection of Ad-RTS-hIL-12 + veledimex generates downstream IFN-γ elevation of IL-12 triggers a pro-inflammatory response, resulting in targeted tumor cytotoxicity and the induction of systemic T cell responses.

• These findings will next be translated in a study of subjects with early metastatic breast cancer, in those responding to standard therapy.

References


Planned studies will focus on the development of new combinations for adjuvant breast cancer therapy.