

Title

Evaluation of immunity and clinical outcome in a phase 1 trial, of an investigational active immunotherapy (MKC1106-PP) in patients with PRAME and PSMA positive solid tumors

Authors

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Abstract

Background: PRAME (Preferential Antigen of Melanoma) and PSMA (Prostate Specific Membrane Antigen) are potential targets for active immunotherapy in cancer. MKC1106-PP is an investigational agent consisting of three components: a plasmid (pPRA-PSM) and two peptide analogues (E-PRA and E-PSM).

Methods: The patients enrolled had advanced cancer, were HLA-A2 and tumor antigen positive. The plasmid dose for bilateral injection was fixed at 1,200ug / injection and two peptide doses were used: 'low dose' of 22.5 and 30 ug, and 'high dose' of 150 and 300 ug of peptide / injection, for E-PRA and E-PSM, respectively. All components were administered separately into lymph nodes under ultrasound guidance. Subjects were evaluated clinically after two therapeutic cycles (12 weeks). Those determined to be non-progressors, continued on therapy and could receive up to 6 cycles of treatment. Immune response was assessed by tetramer and ELISPOT analysis.

Results: A total of 26 patients with various tumor types have been dosed (13 in each dose cohort). The treatment regimen was safe and well tolerated. Seven patients showed evidence of clinical response and completed four or more cycles of therapy: 4 out of 12 prostate carcinoma patients; both kidney cancer patients, and 1 out of 10 melanoma patients. To date, the best clinical outcomes include: a prostate carcinoma patient with objective tumor regression and PSA decline (30+ weeks), two prostate carcinoma patients with stable disease (36+ weeks) accompanied by PSA velocity change, a kidney cancer patient with no evidence of disease, post-resection, in a neo-adjuvant setting (72+ weeks) and a metastatic melanoma patient (M1c stage) with stable disease at 72+ weeks. Twelve out of 19 evaluable patients showed transient or persistent expansion of T cells for the immunizing antigens, after treatment. The patients who showed evidence of clinical benefit demonstrated early expansion of specific T cells in the blood, in a larger proportion (5 out of 6 evaluable patients) compared to only 7/14 patients with disease progression.

Conclusion: Intranodal immunization against PRAME and PSMA, induced immune responses and clinical benefit in patients with solid tumors, with minimal toxicities – laying the foundation for phase II testing in select cancers.

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