A Phase 1 Trial of Intra-lymph Node Administration of a Novel Immunotherapeutic Regimen (MKC1106-MT) in Patients with Advanced Melanoma

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ABSTRACT

Target Overall Non-Target

N=7

Lesion Surgically Unresectable Stage IIIC, IV (M1a)

containing Melan-A (MEL) and tyrosinase (TYR) antigen fragments and 2 peptide (E-MEL; E-TYR) analogs corresponding to an HLA-A*0201-restricted epitopes from each. Patients were given a prime boost regimen of the plasmid (2,400 µg/dose) via ultrasound guided injections into inguinal or axillary nodes on days 1, 4, 15 and 18 followed by peptide on days 29 and 32; cycles were repeated every 43 days. Patients without disease progression progressed up to 6 cycles of treatment. Immune responses using MHC tetramer and IFN gamma ELISPOT were measured days 29 and 32 of each cycle by HLA-A*0201 tetramer stained PBMCs to either the Melan A or tyrosinase antigens, was achieved in 50% of all subjects. Most subjects over the course of treatment, indicating no systemic accumulation.

Intramuscular administration of MKC1106-MT is feasible, safe, induces objective tumor regression and correlates with baseline immunity to MEL.

Bilateral bolus injection directly into inguinal lymph nodes

Plasmid DNA-priming followed by peptide-boost y

Cycle

Trial Results

Comparison of clinical responses, as measured by the tetramer assay in PBMC to either the Melan A or tyrosinase antigens, was achieved in 50% of all subjects. Most subjects over the course of treatment, indicating no systemic accumulation.

INVESTIGATIONAL DRUG REGIMEN

1) Cytokine cocktail, such as GM-CSF, IL-2, IL-12 (8 doses)
2) Investigator-specified investigational agent (1-4 regimens)
3) Radiation (2 regimens)
4) Unspecified chemotherapy regimen
5) All 4 subjects with tumor objective response and treated for 1 year through 8 cycles with 1 subject on study for 9 cycles (> 1 year).

1. Repeat intra-lymph node administration of the MKC1106-MT regimen was well-tolerated and no difference in safety profile was observed between the low and high dose peptide cohorts.

2. Immunologic response, as measured by the tetramer assay in PBMC to either the Melan A or tyrosinase antigens, was achieved in 50% of all subjects.

3. Plasmid pMEL-TYR levels were small or not detectable in most subjects over the course of treatment, indicating no systemic accumulation.

4. Tumor objective response assessed by RECIST was achieved in 50% of all subjects.

5. All 4 subjects with tumor objective response and treated for ≥ 8 cycles had lymphatic disease and presence of Melan A specific T cells at baseline, suggesting such subjects are likely to benefit from this treatment.