A phase I study (E011-MEL) of a TriMix-based mRNA immunotherapy (ECI-006) in resected melanoma patients: Analysis of safety and immunogenicity

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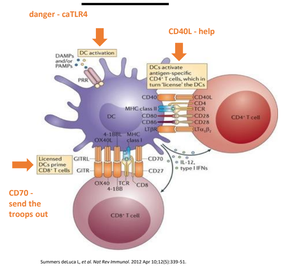
Introduction

ECI-006 is a combination of TriMix and mRNAs encoding for 5 tumor-associated antigens (TAAs)

TriMix



Summers deLuca L, *et al. Nat Rev Immunol.* 2012 Apr 10;12(5):339-51.

TAAs

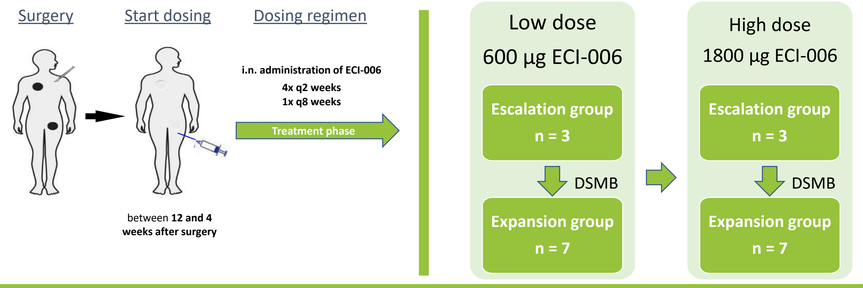
- Tyrosinase
- Gp100
- MAGE-A3
- MAGE-C2
- PRAME

DCs transfected ex vivo with TriMix and TAAs mRNAs showed significant clinical activity in combination with ipilimumab in metastatic melanoma without increasing toxicity *(Wilgenhof S et al. J. Clin. Oncol, 2016).*

Aim

To assess the safety and immunogenicity of ECI-006 vaccine administered intranodally (i.n.) in an adjuvant setting for patients with resected melanoma.

Study Design



Results

Patient Disposition

	600 µg N = 10	1800 µg N = 10	Total N = 20
Enrolled, n (%)	10 (100%)	10 (100%)	20 (100%)
Completed, n (%)	9 (90%)	10 (100%)	19 (95%)
Discontinued, n (%)*	1 (10%)	0	1 (5%)

* P00012 discontinued after 4 administrations due to relapse of melanoma

Patient Characteristics

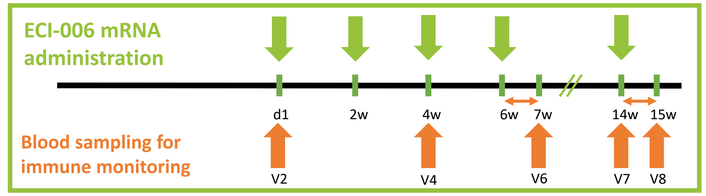
	600 µg N = 10	1800 µg N = 10	Total N = 20
Male, n (%)	4 (40%)	5 (50%)	9 (45%)
Female, n (%)	6 (60%)	5 (50%)	11 (55%)
Age, years (SD)	56.2 (12.83)	50.9 (11.10)	53.6 (11.99)
Tumor stage			
IIC, n (%)	0	1 (10%)	1 (5%)
IIIA, n (%)	7 (70%)	2 (20%)	9 (45%)
IIIB, n (%)	1 (10%)	2 (20%)	3 (15%)
IIIC, n (%)	2 (20%)	5 (50%)	7 (35%)

Most frequently reported treatment-emergent adverse events (>10% of patients)

	600 µg N = 10	1800 µg N = 10	Total N = 20
Fatigue, n (%)	2 (20%)	3 (30%)	5 (25%)
Back pain, n (%)	2 (20%)	2 (20%)	4 (20%)
Myalgia, n (%)	2 (20%)	1 (10%)	3 (15%)

Only 2 patients reported at one injection mild pain and/or hemorrhage related to the ECI-006 administration. No serious adverse events or related treatment-emergent AEs Grade 3 or higher were reported. One patient in the 1800 µg ECI-006 group was reported with the Grade 3 Treatment-emergent AE patellofemoral pain syndrome, which was judged to be not related to the study medication by the investigator.

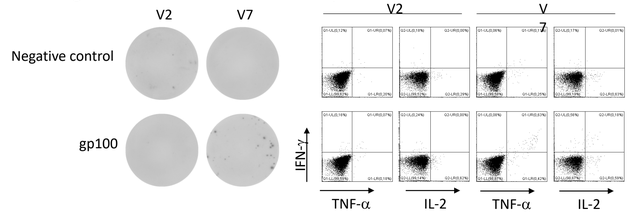
Immune monitoring



T cells isolated from the indicated samples were stimulated *in vitro*, after which the presence of vaccine-induced T-cell responses was evaluated by IFN-γ ELISPOT and intracellular cytokine staining (ICS; IFN-γ/TNF-α/IL-2).

	600 µg N = 10	1800 µg N = 10	Total N = 20
Tyrosinase, n (%)	1 (10%)	2 (20%)	3 (15%)
Gp100, n (%)	1 (10%)	0	1 (5%)
MAGE-A3, n (%)	2 (20%)	0	2 (10%)
MAGE-C2, n (%)	2 (20%)	2 (20%)	4 (20%)
PRAME, n (%)	0	0	0

Proportion of patients for which a vaccine-induced ELISPOT and/or ICS response was detected in at least one post-vaccination sample according to a pre-defined set criteria. Overall, an ECI-006 vaccine-induced immune response against at least 1 antigen was observed in 35% of all patients.



Example of vaccine-induced gp100 T cell response in P00011 detectable with ELISPOT (left) and ICS (right) at V7.

Conclusion

Among patients undergoing resection of stage IIc/III/IV melanoma, i.n. administration of ECI-006 at 600 or 1800 µg was generally well tolerated. ECI-006 provoked a vaccine-induced immune response against at least 1 TAA in 35% of the patients. These results warrant further development of ECI-006 in combination with anti-PD-1 therapy in melanoma patients.