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160P

Oral DNA vaccination targeting personalised neoantigens in immune checkpoint inhibitor treated solid tumor patients. - Interim results -

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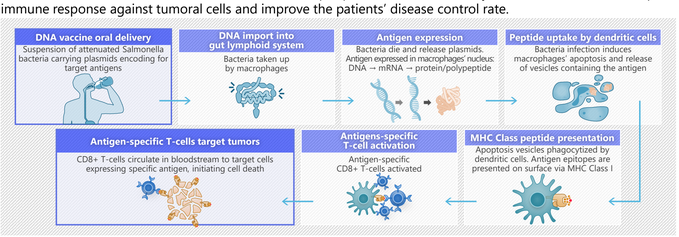
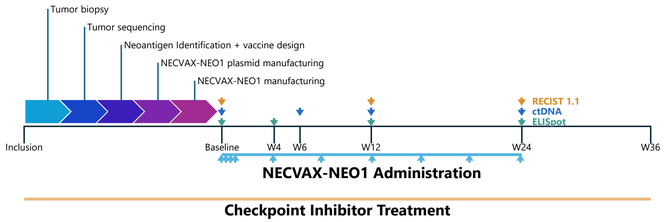
Background

Eliciting a specific immune respone against tumoral cells can be achieved by personalized cancer vaccines. NECVAX-NEO1 is a novel bacteria-based oral DNA vaccine which encodes up to 15 patient- and tumor-specific class I and class II neoepitopes predicted and ranked by the AI-based NEC Immune Profiler. The vaccine carrier Salmonella Typhi Ty21a strain (a prophylactic typhoid fever vaccine) bears an expression plasmid encoding up to 15 minimal (9-or 10-mer) and/or enriched (27-mer) epitopes. NECVAX-NEO1 may establish a cell-based adaptive immune response against tumoral cells and improve the patients' disease control rate.



Methods

NECVAX-NEO1-LT (NCT05354323) is an open-label, phase I multicenter, clinical trial of NECVAX-NEO1 in addition to anti-PD-1 or anti-PD-L1 monoclonal antibody checkpoint inhibitor monotherapy in patients with solid tumors. Based on the pharmacodynamic effects of NECVAX-NEO1 and checkpoint inhibitors, a synergistic activity of both agents in terms of immune response and clinical response is expected. The trial design is as follows:



Study Population

Inclusion criteria

- Male and female cancer patients aged 18-75 years old, with measurable disease according to RECIST 1.1, treated for at least 3 months with anti PD-1/PD-L1 as first- or second-line monotherapy for one of the following tumor types: NSCLC, cutaneous melanoma, urothelial carcinoma, RCC or SCCHN.
- Patients with adequate bone marrow, hepatic and renal function, with ECOG ≤ 2and with life expectancy of at least 6 months.

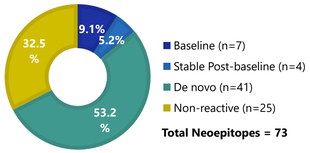
Exclusion criteria

- Patients with previous malignant diseases, active infections, organ transplantations or small intestine resection surgery.
- Patients in other clinical trials, in chronic concurrent therapies or treated with live vaccines within 30 days prior to trial treatment.
- Patients with previous reported immune-related checkpoint inhibitor side effects or hypersensitivity to the IMP or persisting toxicity related to prior therapy.

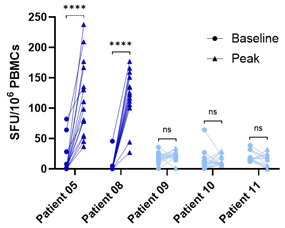
NECVAX-NEO1 Immunogenicity

NECVAX-NEO1 is immunogenic and promotes high T-cell specific responses

Positive responses to Neoepitopes

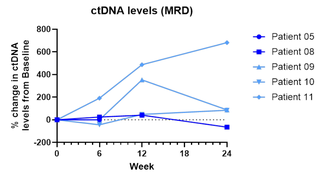


ELISpot responses to NECVAX-NEO1 administration from Baseline to Peak



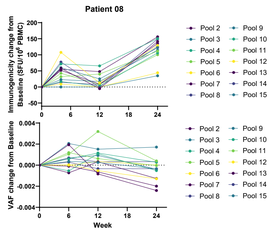
Standard Pool ctDNA Levels

ctDNA levels seem to be reduced in Immune responders vs. Immune non-responders



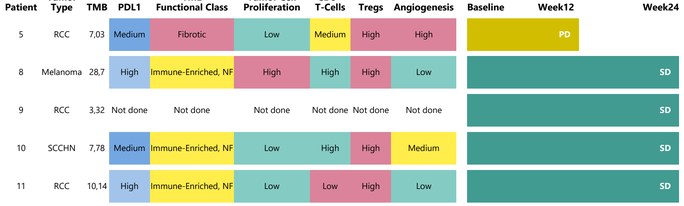
Neoantigen-Specific ctDNA and ELISpot Responses

Immune response to the targeted neoepitopes decreases ctDNA levels at week 24 in melanoma



TME Features and Clinical Follow-up

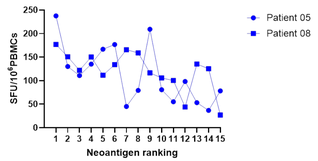
Disease Control Rate of 80%.



Melanoma patient #08 shows the most favourable pre-treatment tumor immune biomarker pattern.

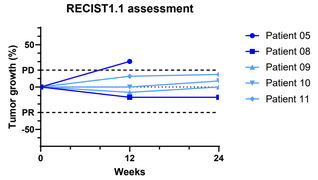
Neoantigen ranking

Higher ranked epitopes promote stronger immune responses



Tumor size progression

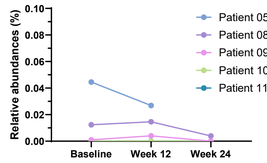
NECVAX-NEO1 responders present tumor size reduction at week 24.



Microbiome Assessments

The vaccine vector is not affecting *S. enterica* population in the gut microbiome.

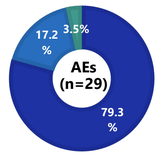
Relative abundance of *S.enterica* species in the gut microbiome



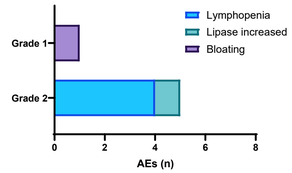
Safety of NECVAX-NEO1

NECVAX-NEO1 is safe and well tolerated.

Relation of Adverse Events to NECVAX-NEO1

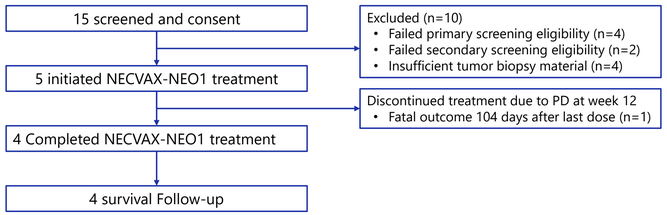


Types of Adverse Events related to NECVAX-NEO1 administration



Trial characteristics

Trial flowchart:



Trial participants characteristics at screening and at the time of NECVAX-NEO1 start of administration:

Characteristics		Screening (n=15)	NECVAX-NEO1 (n=5)
Age at diagnosis	Median (range)	63.0(54.0, 65.0)	65.0 (52.5, 73.5)
	Mean (SD)	60.4 (9.16)	63.4 (12.54)
Sex	Male (n)	13	5
	Female (n)	2	0
Race	White (n)	15	5
Height	Median (range)	177.0 (170.0, 182.0)	175.0 (171.0, 184.0)
	Mean (SD)	176.8 (6.75)	177.0 (7.87)
Weight	Median (range)	85.5 (79.3, 94.7)	88.0 (75.0, 133.0)
	Mean (SD)	91.3 (20.2)	100.8 (31.09)
ECOG	Level 0 (n)	9	2
	Level 1 (n)	6	3
Cancer type	RCC (n)	7	3
	Melanoma (n)	5	1
	NSCLC (n)	1	0
	SCCHN (n)	2	1
SoD at Screening	Median (range)	41.0 (20.0, 67.8)	38.0 (23.0, 63.5)
	Mean (SD)	44.8 (26.2)	42.2 (25.43)

Key Messages

- **NECVAX-NEO1 is safe and well tolerated.**
- **NECVAX-NEO1 is immunogenic and promotes high T-cell specific responses with higher ranked neoepitopes promoting higher immune responses.**
- **NECVAX-NEO1 does not affect *S. enterica* population in the gut microbiome.**