

# Individualized APC targeted VB10.NEO cancer vaccines induce broad neoantigen-specific CD8 T cell responses in patients with advanced or metastatic solid tumors. Interim results from a phase 1/2a trial

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## BACKGROUND

VB N-01 is an open label phase 1/2a basket trial to evaluate safety, feasibility, and immunogenicity of a personalized therapeutic DNA cancer vaccine VB10.NEO in patients with locally advanced or metastatic solid cancers. Each VB10.NEO vaccine contains up to 20 patient-specific neoantigens selected by Nykode's AI platform NeoSELECT™ and is designed to target antigen presenting cells (APC) using Nykode's modular vaccine platform known as Vaccibody™.

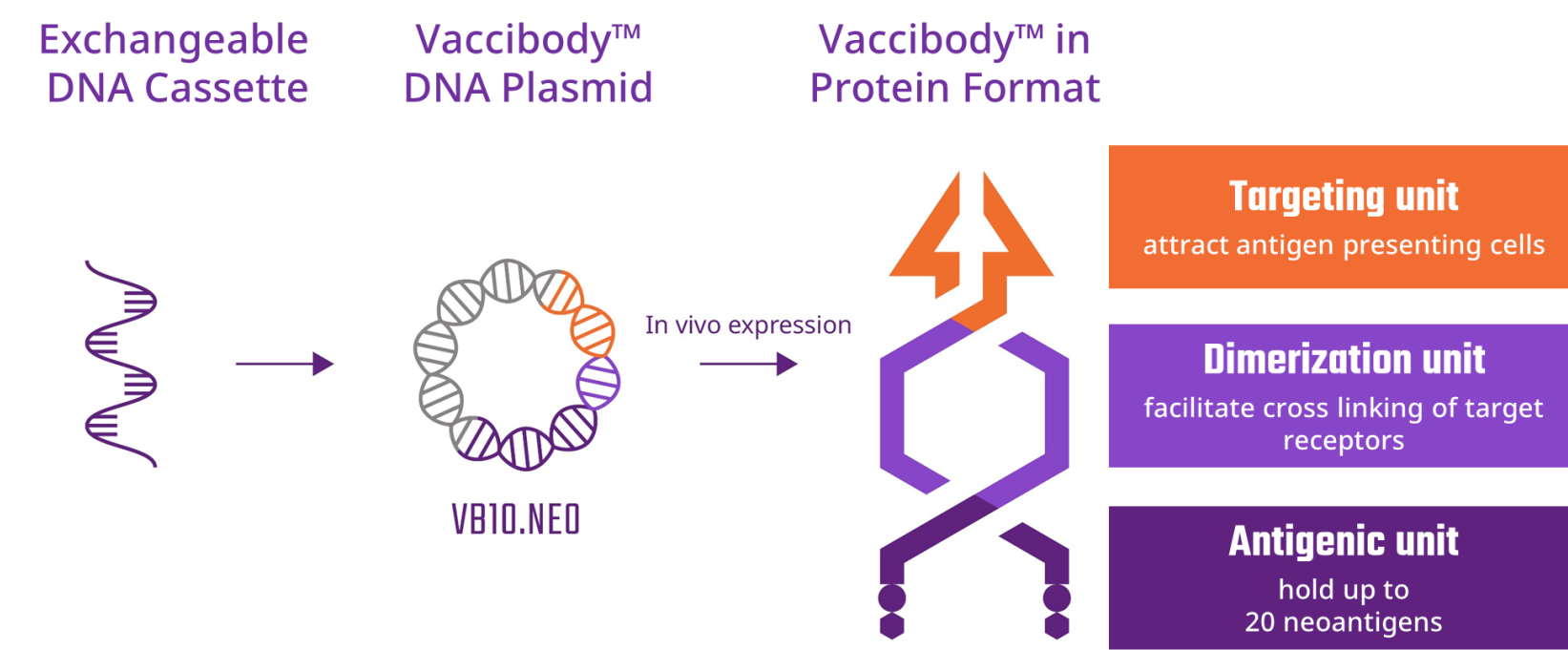


Figure 1. Nykode's modular vaccine platform known as Vaccibody™.

## PATIENTS

Baseline Characteristics (N=41)	N (%)
Age	Mean (range) 62.2 years (33-81 years)
Ethnicity	White 41 (100%)
Gender	Male 25 (61%) Female 16 (39%)
ECOG	0 24 (58.5%) 1 17 (41.5%)
Prior systemic treatment lines	1 10 (24%) 2 20 (49%) 3 7 (17%) 4 4 (10%)
Cancer type	Head and neck cancer 14 (34%) Non-small cell lung cancer 5 (12%) Renal cell carcinoma 10 (24%) Melanoma 8 (20%) Urothelial carcinoma 4 (10%)
Metastatic disease	Y 37 (90%) N 4 (10%)

## STUDY

The trial enrolled patients with locally advanced or metastatic solid cancers; renal cell carcinoma (RCC), urothelial cancer (UC), non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHN), and melanoma. The patients received treatment with CPI (anti-PD-(L)1) for at least 12 weeks as standard of care prior to first VB10.NEO administration. Up to 14 VB10.NEO plasmid doses (3 mg per dose) were administered *i.m.* by PharmaJet Stratis® during a 50 weeks period in combination with CPI and/or other anti-cancer therapies at investigator's discretion. Blood samples and tumor biopsies were collected at baseline and during treatment (on-treatment biopsies optional) for evaluation of immune responses. The patients were followed for up to 2 years.

Here, we present the interim safety data for patients who received ≥1 VB10.NEO vaccinations (n=41) and interim immunogenicity data for patients who received ≥4 VB10.NEO plasmid vaccinations (n=22) at data cut-off (20<sup>th</sup> of May 2022).

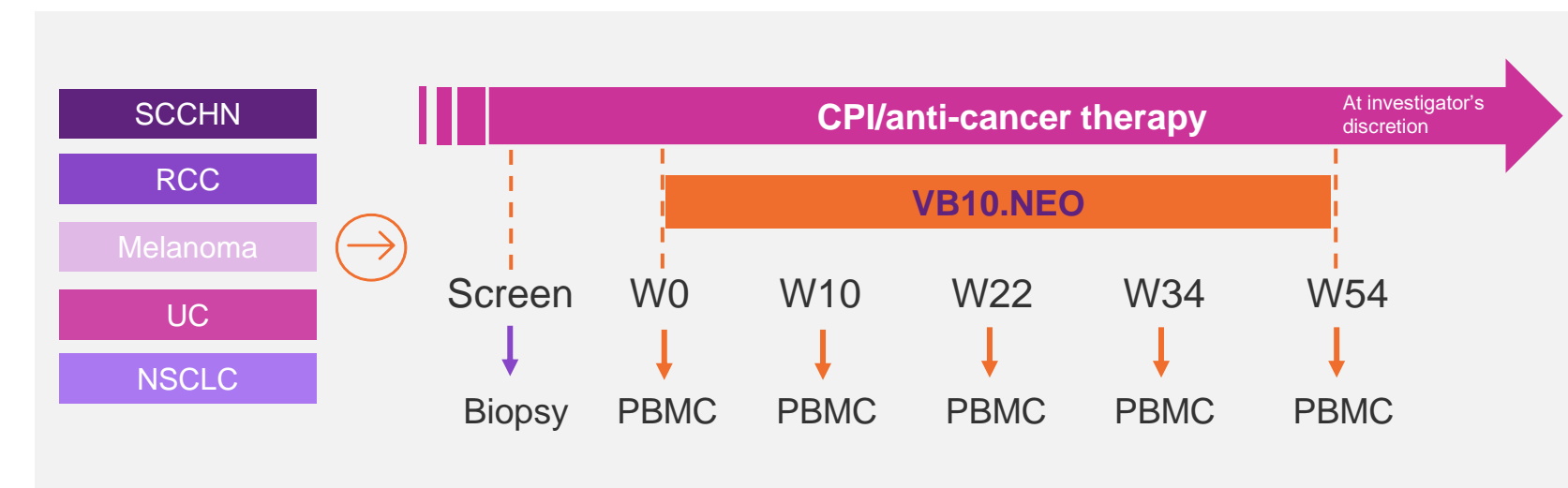


Figure 2. Trial design, timeline and sampling.

## SAFETY

**VB10.NEO is generally safe and well-tolerated in patients with solid tumors when administered in combination with various background therapies**

- The most common adverse events (AE) reported are fatigue (34%) and diarrhea (27%).
- 24% of patients experienced an AE of grade 3 or higher related to VB10.NEO. The most common reported was hypertension (15%). This was mostly resolving the same day without the need for medical intervention.
- 56% of patients experienced a serious AE. One case of mild somnolence was considered related to VB10.NEO. The patient was hospitalized for observation.
- 12% of patients experienced a potential immune-related AE.
- No fatal events were related to VB10.NEO.

## IMMUNOGENICITY

**Multiple vaccinations boost the breadth and magnitude of immune responses, with the majority being maintained for at least 1 year**

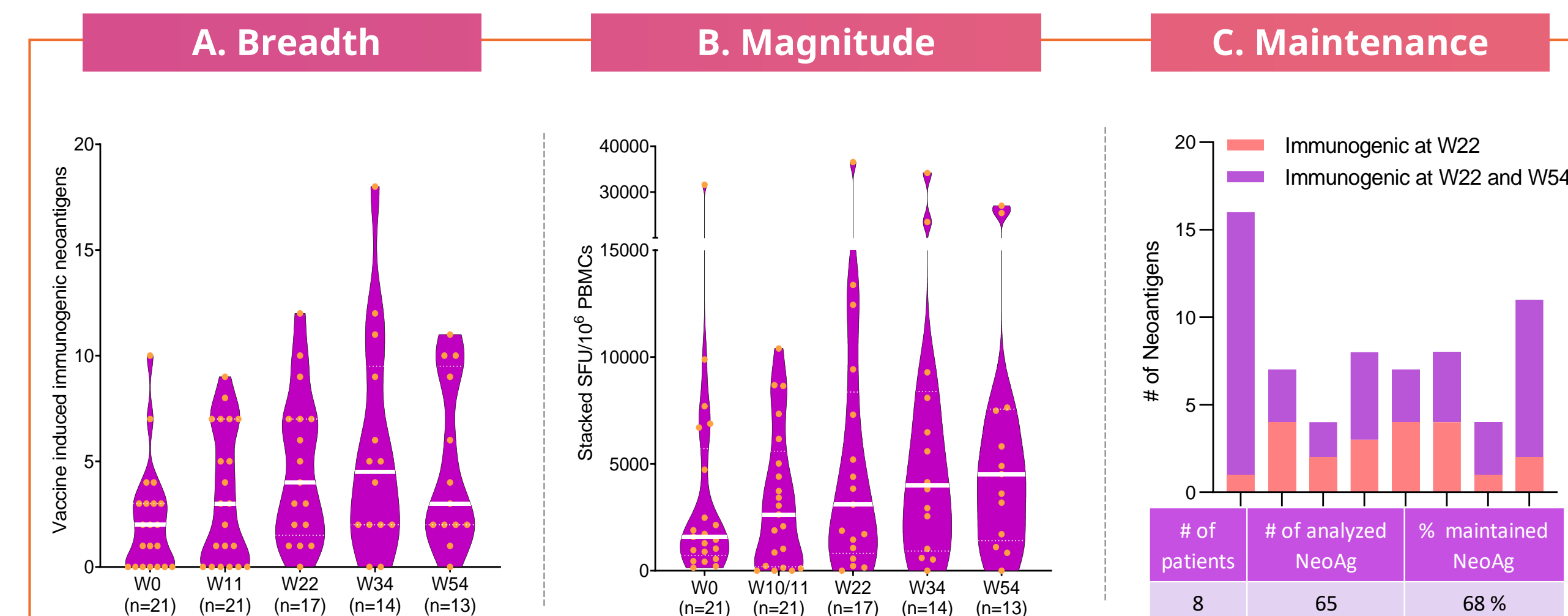


Figure 3. Temporal assessment of immunogenicity. A) The number of vaccine induced (*de novo* and amplified) immunogenic neoantigens (breadth), B) stacked IFN-γ spot forming units (SFU)/ELISpot responses (magnitude), and C) the maintenance of immune response during treatment (based on available data). Median is indicated as horizontal lines (A, B).

**Majority of VB10.NEO neoantigens activate polyfunctional T cells dominated by CD8 T cells**

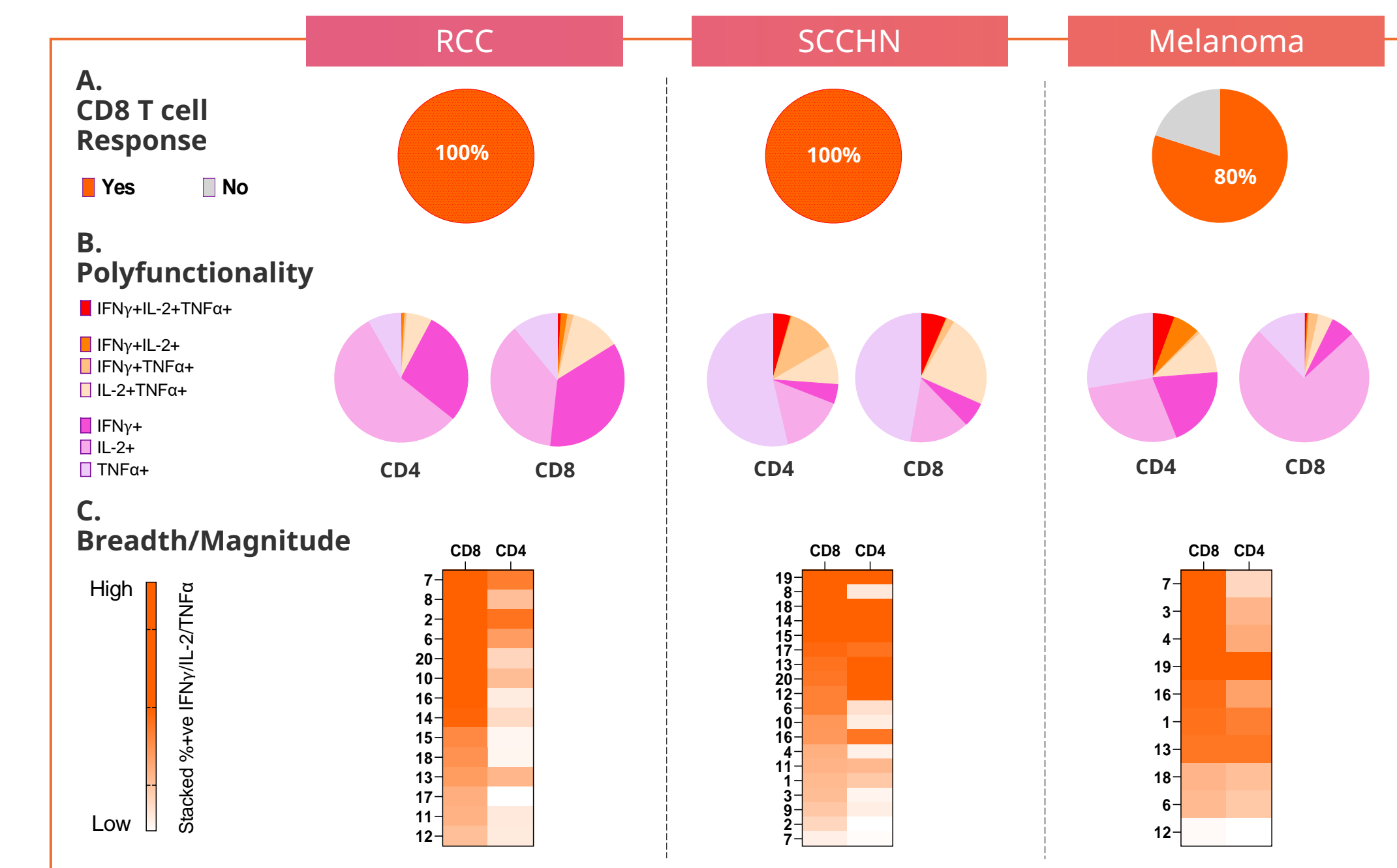


Figure 4. Phenotyping performed by *in vitro* stimulated intracellular cytokine staining of PBMCs collected at week 22 (n=7, 3 shown as example). A) Percentage of neoantigens inducing CD8 T cell responses. B) Cytokine profile of responding CD4 and CD8 T cells. C) The magnitude of response (stacked) to the individually tested neoantigens are displayed. T cell responses are defined as ≥0.2% above DMSO background. Numbers on the heatmap indicate individual neoantigen ID in VB10.NEO.

**VB10.NEO induces *de novo* as well as amplification of pre-existing T cell responses**

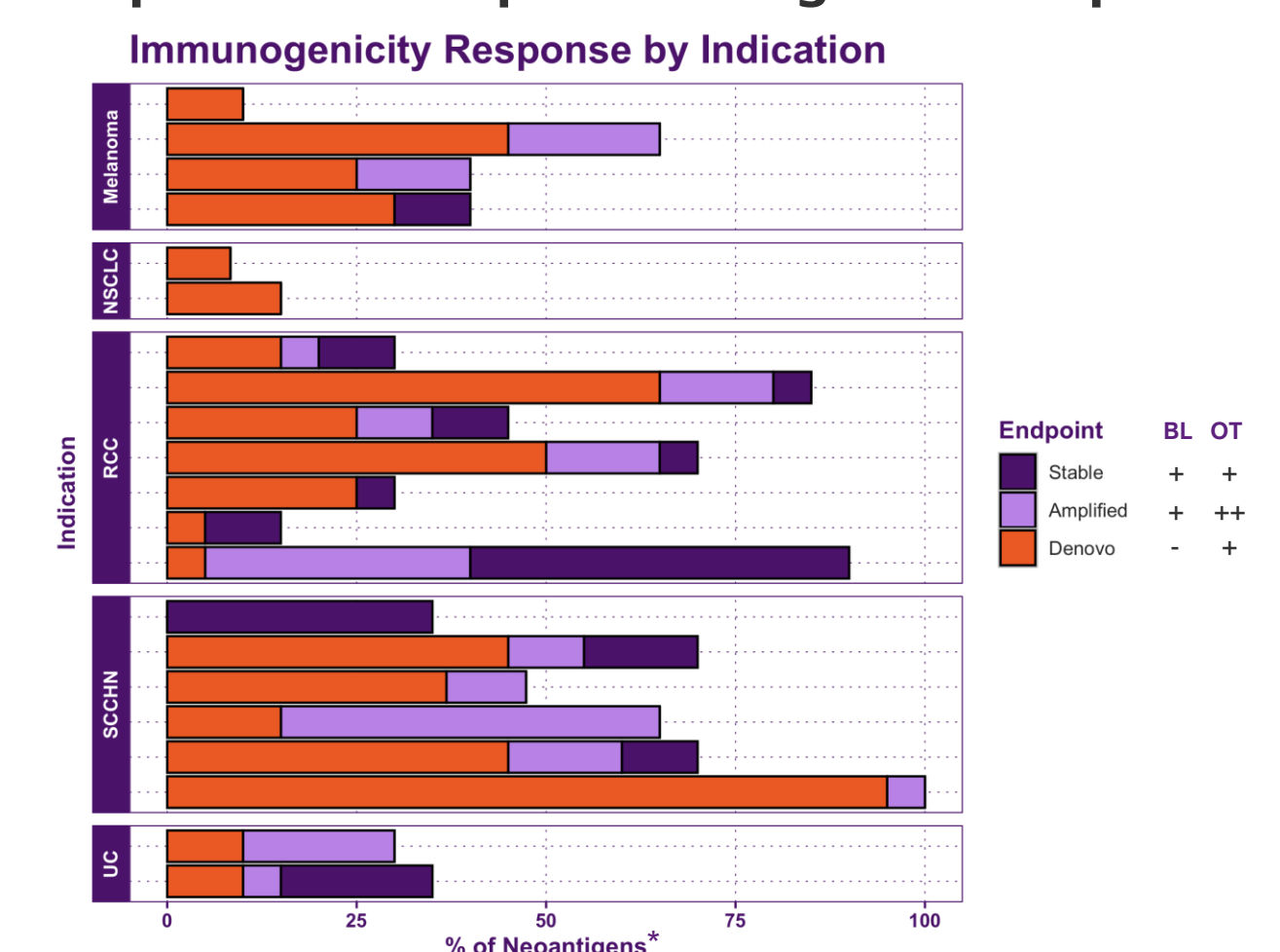


Figure 5. *In vitro* stimulated IFN-γ ELISpot performed on patient PBMCs (n=21; one patient without baseline sample excluded). Colors indicate response type. Positive responses are defined based on DFR1.3x method. BL= Baseline, OT= On treatment. +/- indicates presence/lack of immunogenic response \*Includes tested neoantigens having baseline samples.

**VB10.NEO induces T cell responses in hard-to-treat low-TMB patients**

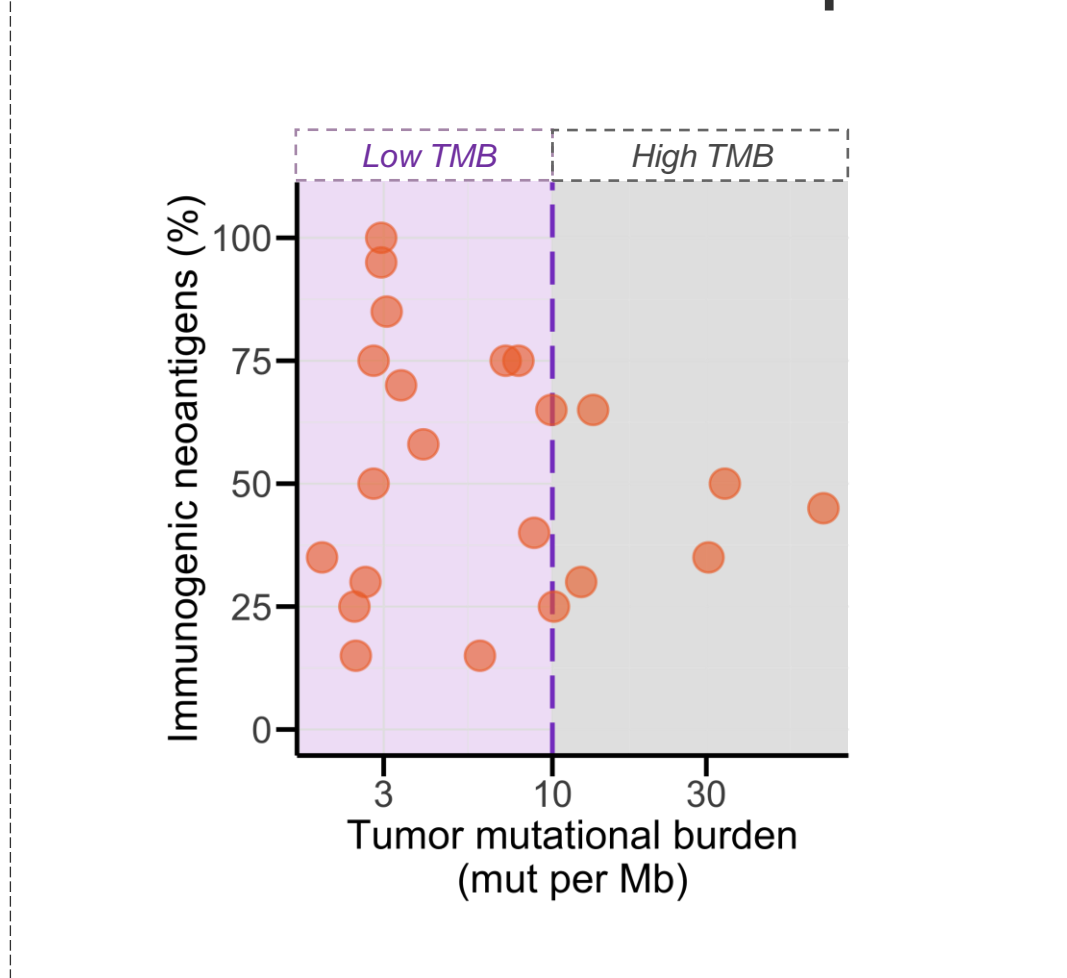


Figure 6. The percentage of immunogenic neoantigens versus tumor mutational burden (TMB) demonstrating a high immune reactivity in a hard-to-treat population of low TMB patients (<10 mut/Mb).

**T cell clones were expanded in tumor tissue after vaccination and were also found in blood**

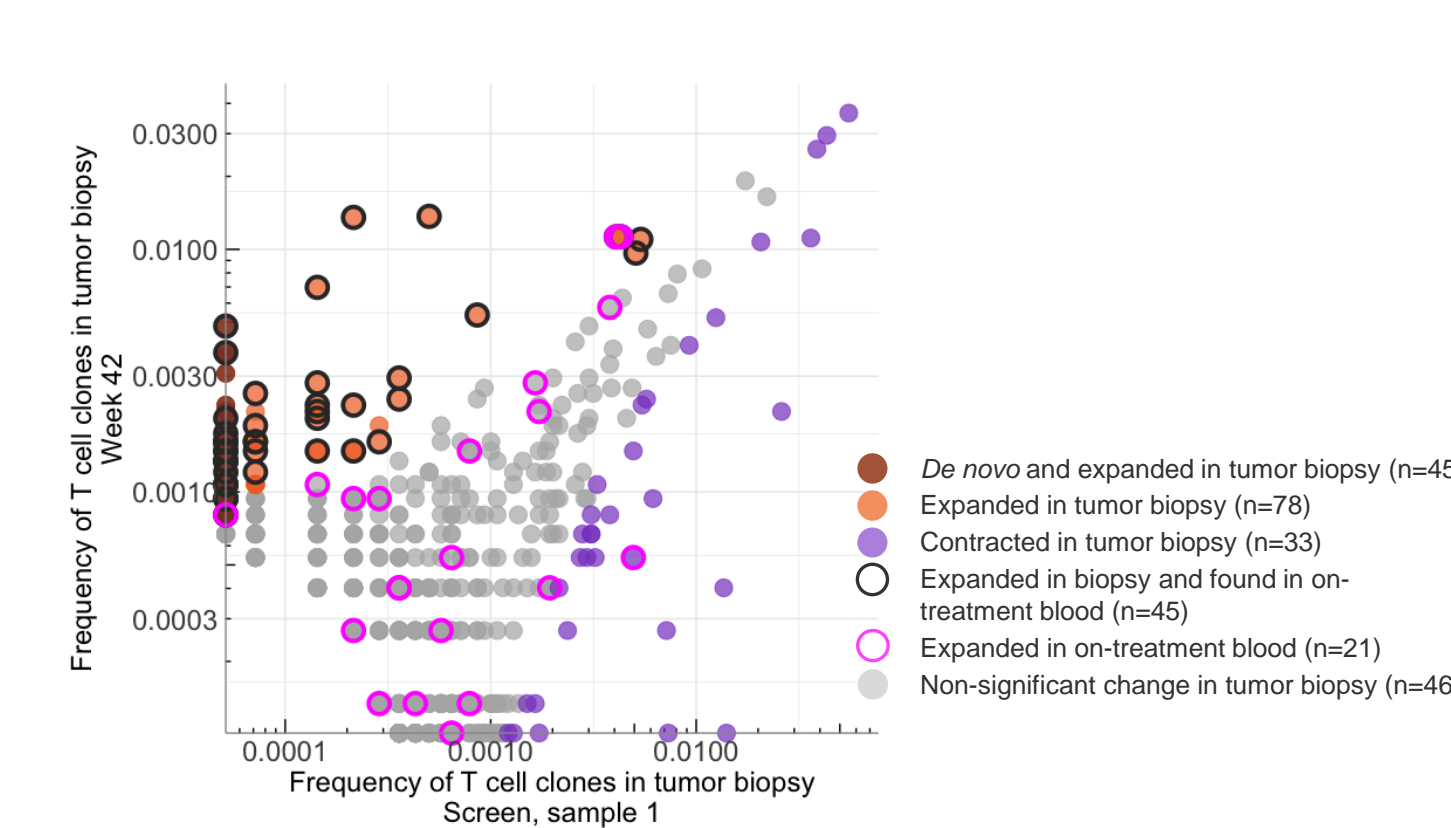


Figure 7. TCR analysis of screen and on-treatment biopsies. Data from four patients revealed expansion of T cell clones in the tumor when comparing baseline with on-treatment biopsies taken from the same tumor site (range 7-152 clones, a representative example is shown). Frequency of T cell clones in baseline biopsy (x-axis) versus frequencies of T cell clones in on-treatment biopsy (y-axis) are shown; T cell clones expanded in the tumor (orange) also found in on-treatment PBMC are shown with a black circle. T cell clones in the tumor (grey) expanded in post-vaccination PBMC are shown with a pink circle.

## SUMMARY

- VB10.NEO was generally well tolerated in patients with various pre-treated and advanced cancers.
- Assessment of neoantigen-specific T cell reactivity demonstrated VB10.NEO-induced broad and long-lasting T cell responses, and the majority of tested neoantigens activated polyfunctional CD8 T cells.
- T cell responses were elicited in both TMB high and low patients indicating selection of high quality neopeptides in a hard-to-treat population.
- T cell clones expanded in the tumor post-vaccination were also found in on-treatment blood providing proof-of-concept that vaccine-induced neoantigen-specific T cells in the periphery are able to infiltrate tumors.

