vaccibody

Generating Potent CD8-Dominated Neoantigen-Specific T Cell Responses with Novel DNA Vaccine

Molecular Med TriCon
Cancer Immunotherapy Executive Summit
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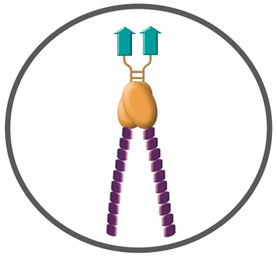
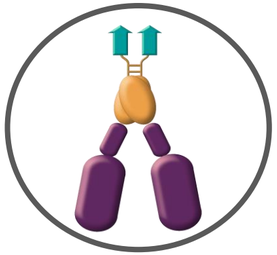
Vaccibody Product Pipeline

PROGRAM	DISCOVERY	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
MELANOMA LUNG (NSCLC) BLADDER RENAL HEAD AND NECK	VB10.NEO				
HEAD AND NECK	VB10.NEO + NKTR-214		NEKTAR®		
PRECANCEROUS CERVICAL LESIONS	VB10.16				
CERVICAL	VB10.16 + Atezolizumab (CPI)*		Roche		





**Tecentriq® (Atezolizumab) is Roche's proprietary anti-PD-L1 checkpoint inhibitor (CPI)*

The Workflow of Personalised Cancer Treatment

1. Tumour biopsy and sequencing

2. Neoepitope selection

3. Vaccine manufacturing (n=1)

4. Vaccine administration and immunogenicity/efficacy, combination therapy

Rapid, cost-effective, efficacious

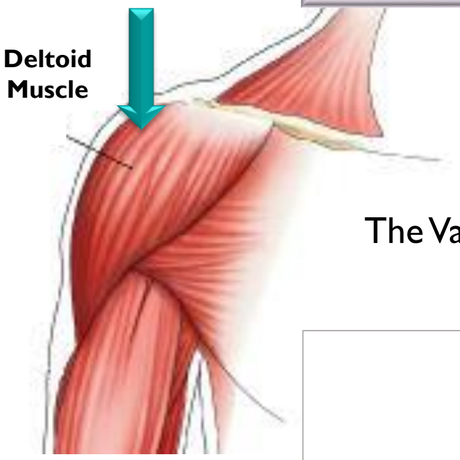
VB10.NEO: a novel DNA vaccine platform that targets antigen presenting cells

Administration (i.m.) of DNA plasmid

***In vivo* protein expression and secretion**

Target – Attract – Mature – Deliver – Cross-present

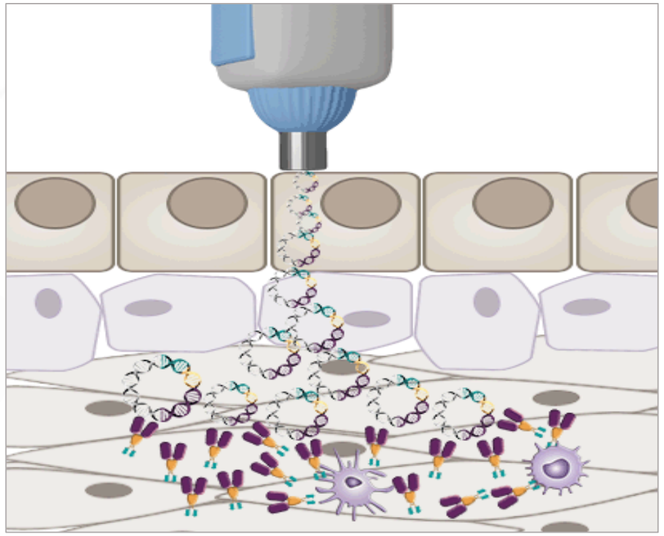
Skewing the immune system to a CD8+ killer T-Cell response

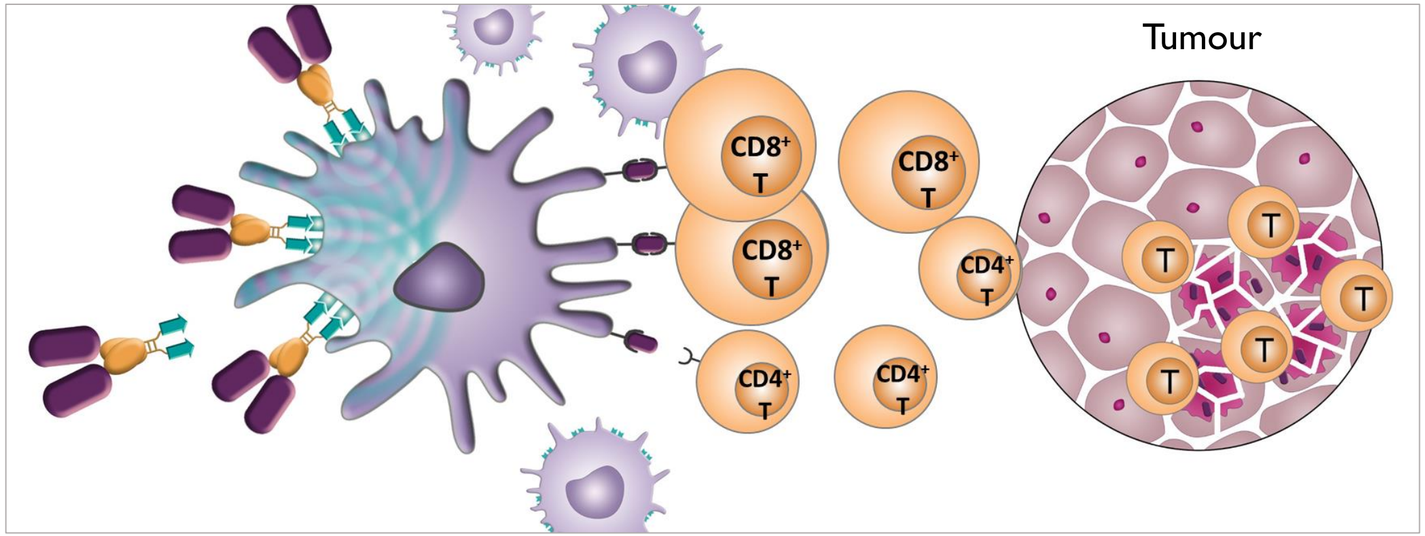


The Vaccibody uses the muscle cell as a factory

- Direct targeting & attraction of antigen presenting cells, high local vaccine concentration
- Enhanced T cell immunity obtained with fewer and lower doses
- Faster and longer lasting immune responses
- **Stronger potential to kill cancer cells**

PharmaJet®





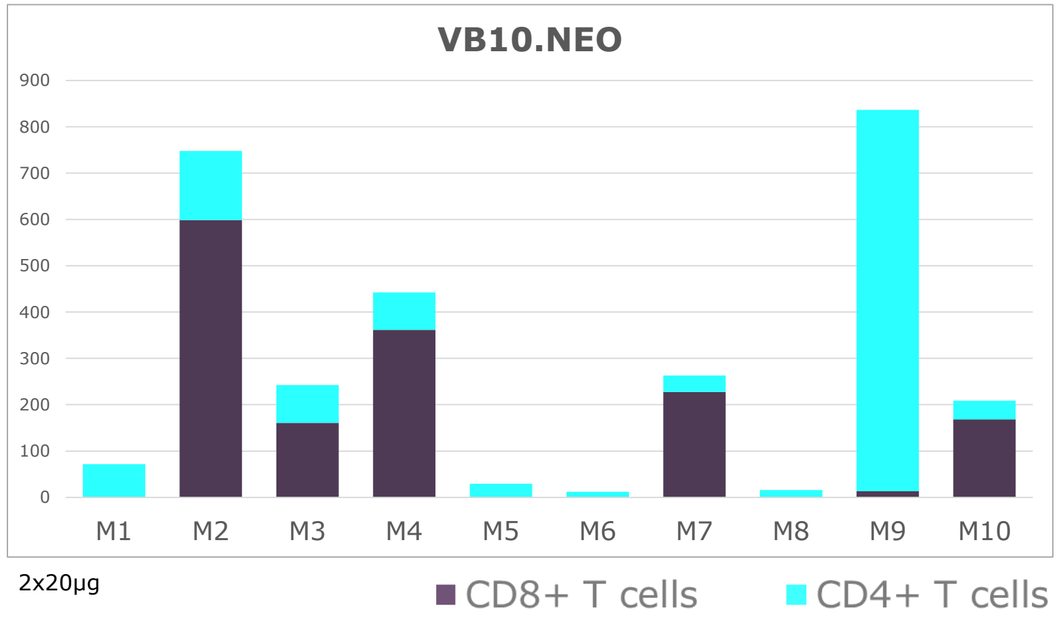
Targeting is elicited by the MIP-1α chemokine

VB10.NEO leads to a unique CD8+ dominated neoepitope response

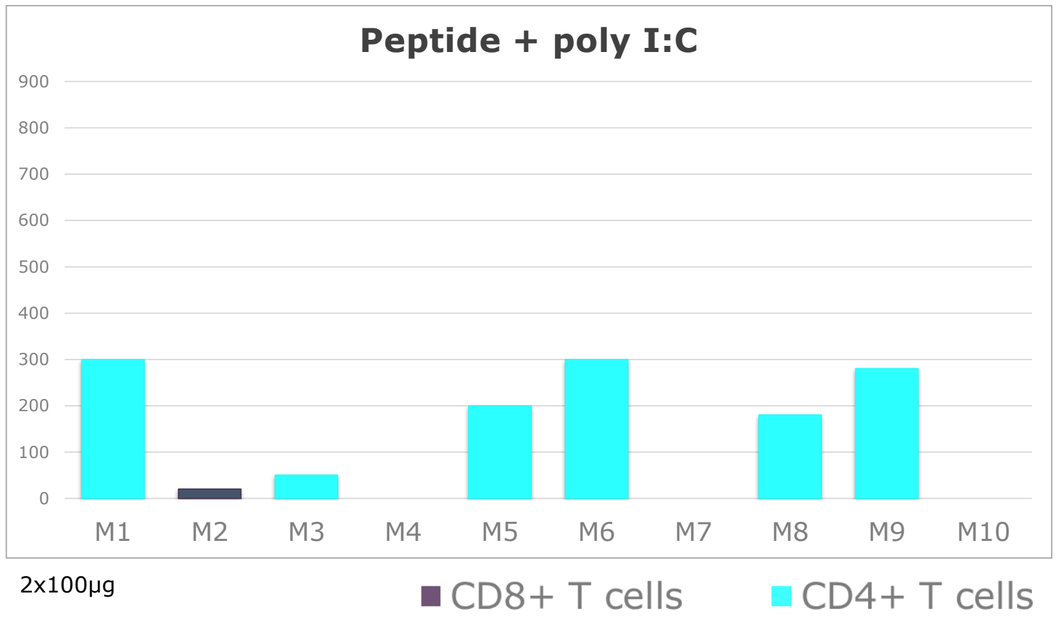
VB10.NEO induces a **strong, broad** immune response **dominated by CD8+** T cells

B16 melanoma

Peptide + poly I:C vaccination has been reported to induce responses **dominated by CD4+** T cells



2x20µg



2x100µg

VB10.NEO induces strong, dominantly CD8+ T cell response to identical neoepitopes that induces **no or weak** immune response if delivered as peptide vaccine

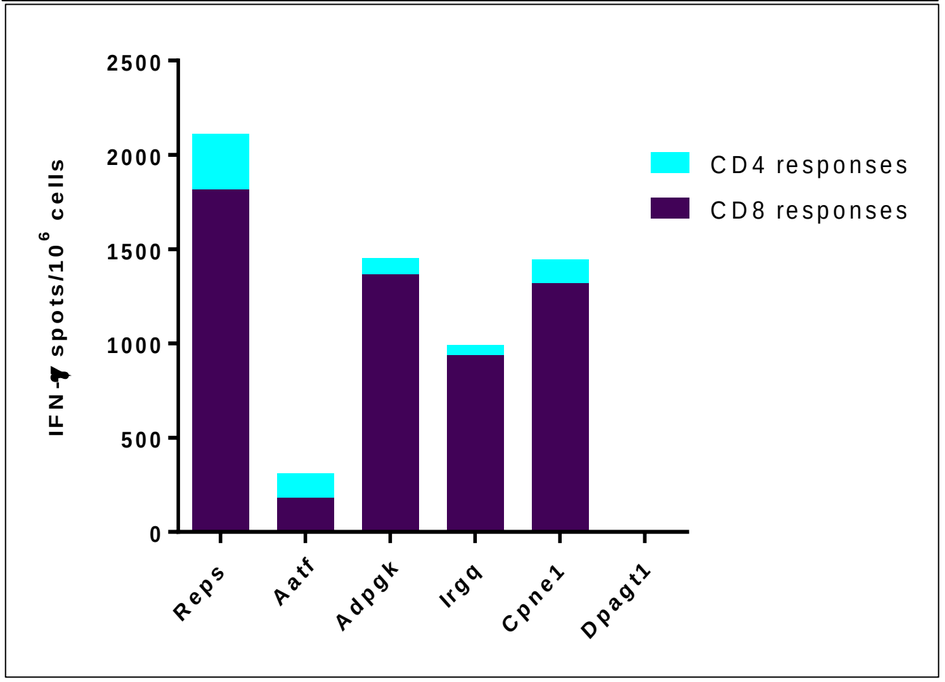
- Castle et al., 2012 and Kreiter et al., 2015-adapted figure based on B16 melanoma results

Confirmation of VB10.NEO's unique ability to induce strong neoepitope-specific CD8+ responses

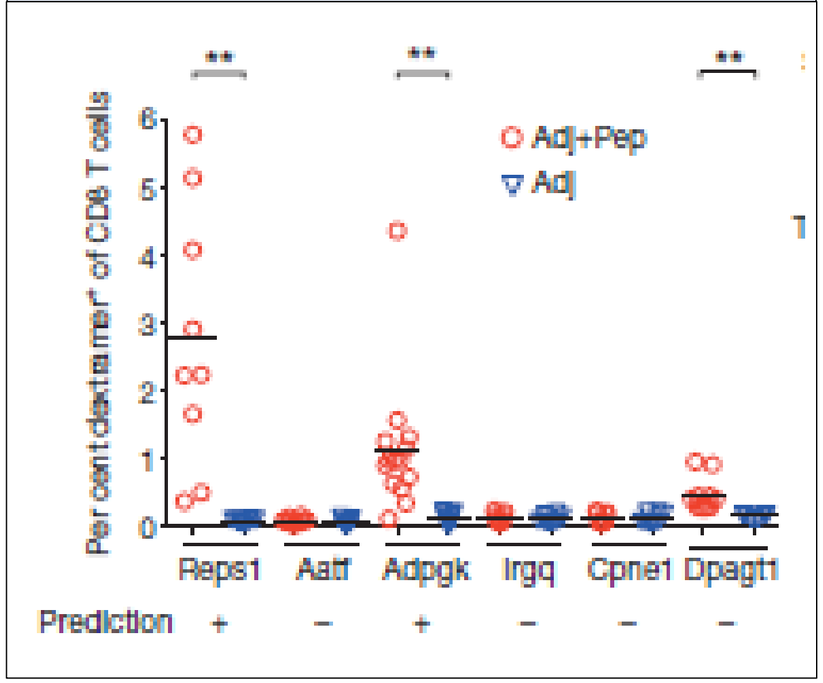
MC38 colon carcinoma

Yadav et al., 2014

VB10.NEO



Peptide + poly I:C + anti-CD40 mAb



- VB10.NEO induces a strong CD8+ T cell response, combined with a CD4+ response **to 5 of 6** MC38 neoantigens.

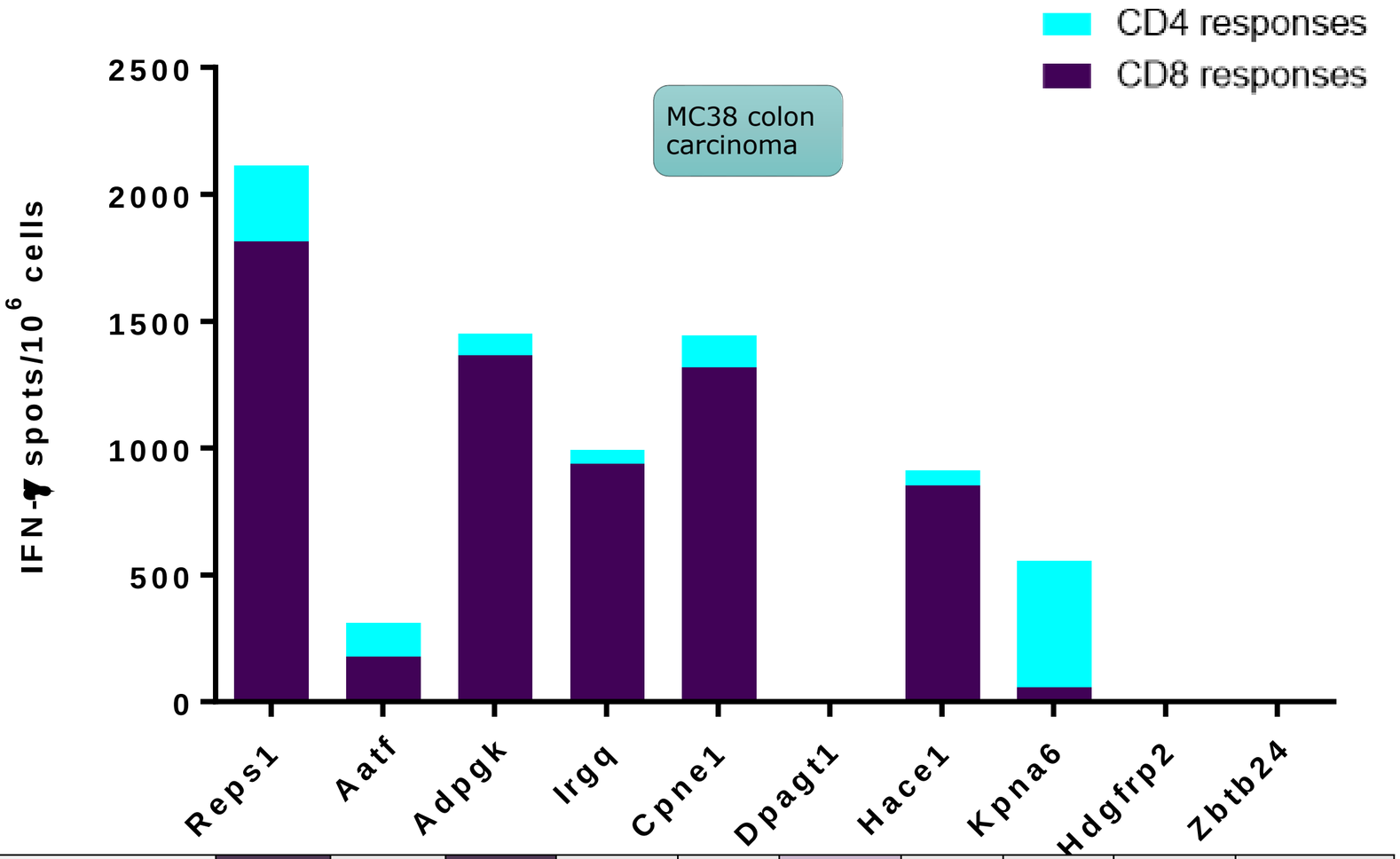
- 3 of these neoepitopes have been shown to be **non-immunogenic delivered as peptide + adjuvant**

- Confirmation of VB10.NEO's ability to induce stronger CD8+ responses to neoantigens

Targeting of VB10.NEO to chemokine receptors is important for this unique ability to induce an immune response to multiple neoepitopes

DNA vaccine delivery alone is not explaining the ability to induce strong CD8 dominated immune responses to a higher number of neoantigens.

Vaccibody's unique *targeting* mechanism is essential for this observed feature.



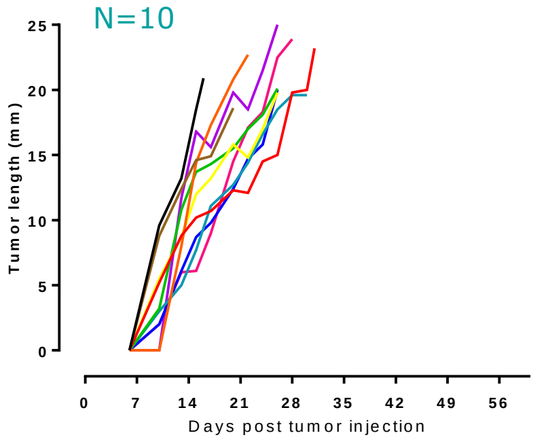
Peptide*	+	-	+	-	-	+	nt	nt	nt	nt
Non-targeted DNA	+	-	+	nt	-	nt	+	-	-	-

Yadav et al., 2014
Aurisicchio et al., 2019

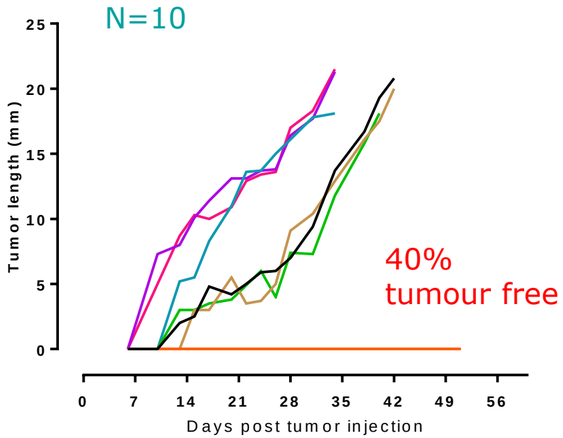
Vaccibody Induces Tumor Protection as Monotherapy

CT26 colon carcinoma model

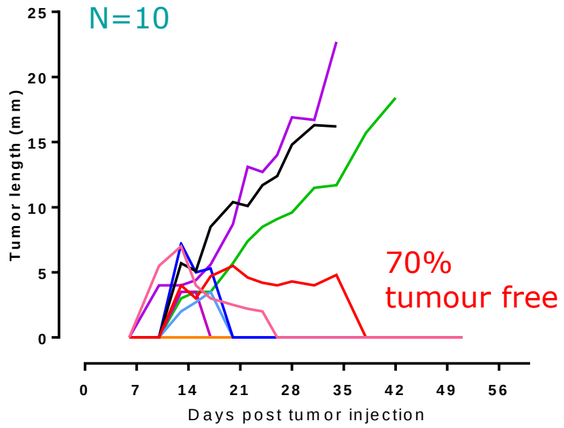
Control



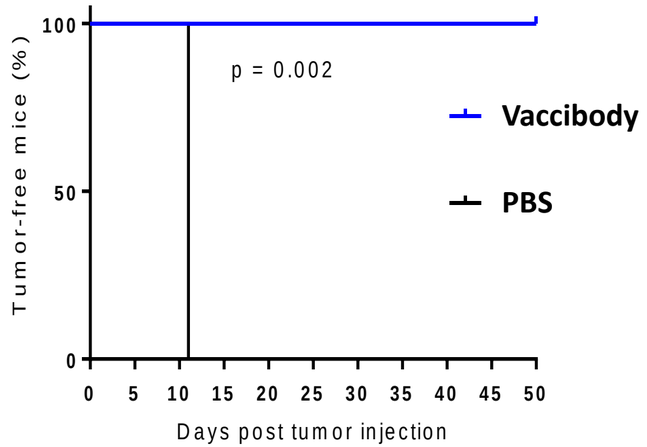
Vaccibody Monotherapy



Vaccibody Combination Therapy



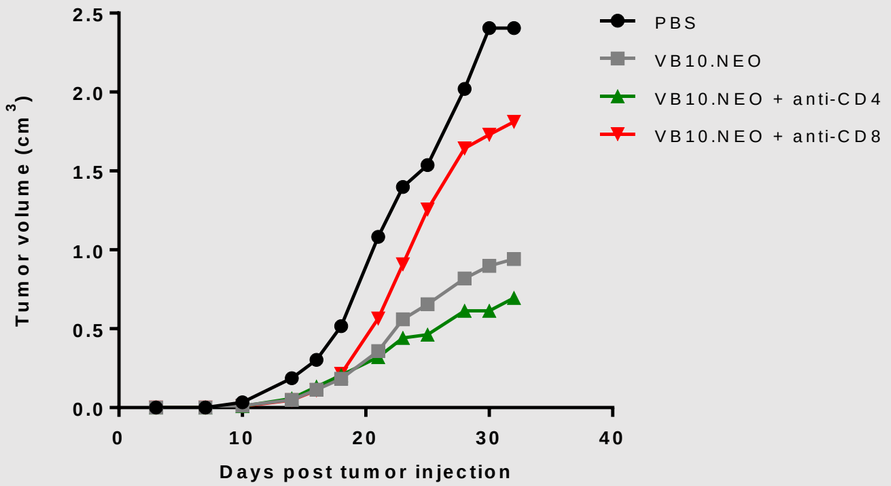
Re-challenged mice are protected



- Vaccibody vaccination induces strong CD8+ T cell responses and **tumor protection as Monotherapy**
- Combination with anti-PD-1 immunotherapy induced enhanced anti-tumour responses in mice involving **complete tumour regression** of large, established tumours
- **Long-term memory responses** ensure effective anti-tumour responses after a 2nd tumour challenge in surviving mice with no sign of tumour growth

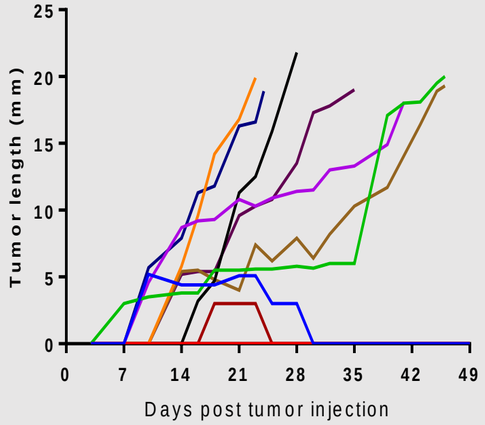
Neoepitope-specific CD8 T cells are crucial for tumour protection

Average, all groups

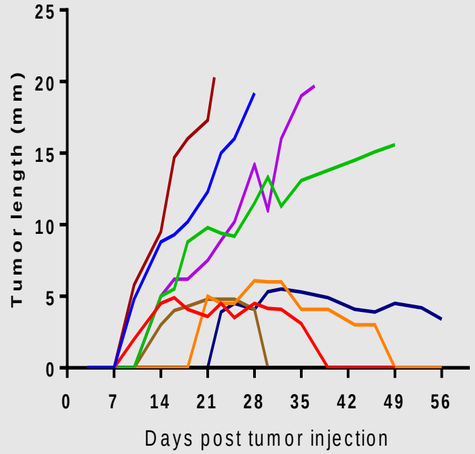


Individual growth curves

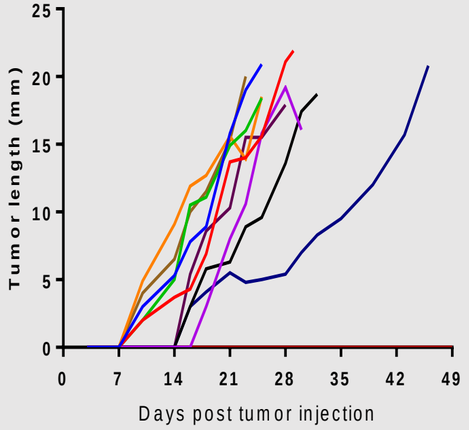
VB10.NEO



VB10.NEO + anti-CD4



VB10.NEO+ anti-CD8



Depletion of CD8 T cells prohibit tumour protection in VB10.NEO vaccinated mice, indicating a crucial role of neoepitope-specific CD8 T cells for anti-tumour efficacy

Vaccibody Product Pipeline

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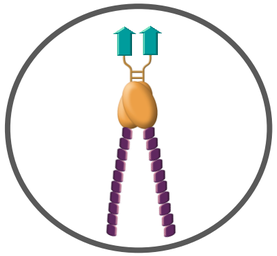
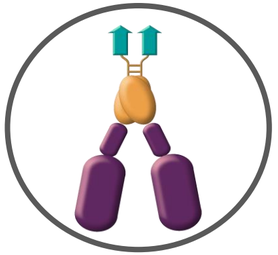
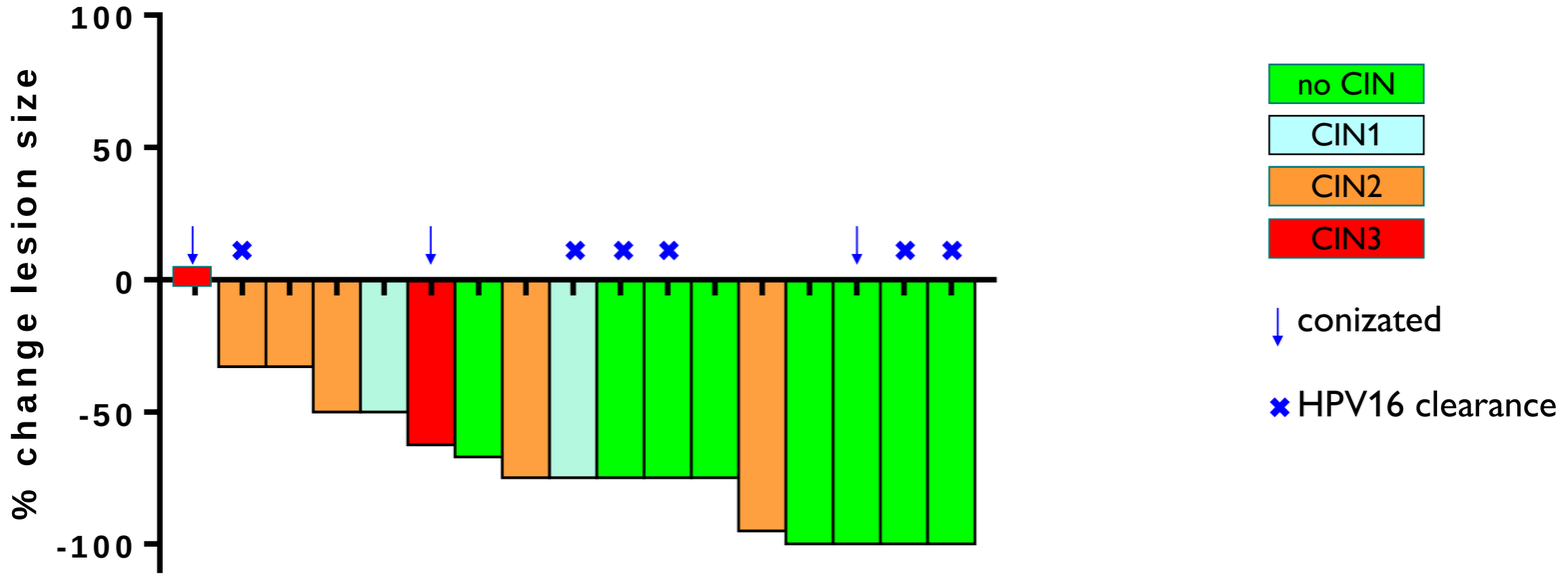




Tecentriq® (Atezolizumab) is Roche's proprietary anti-PD-L1 checkpoint inhibitor (CPI)

Promising clinical efficacy with excellent safety, VB C-01

Best response data
(At enrollment: 10 CIN3 and 7 CIN2 patients)

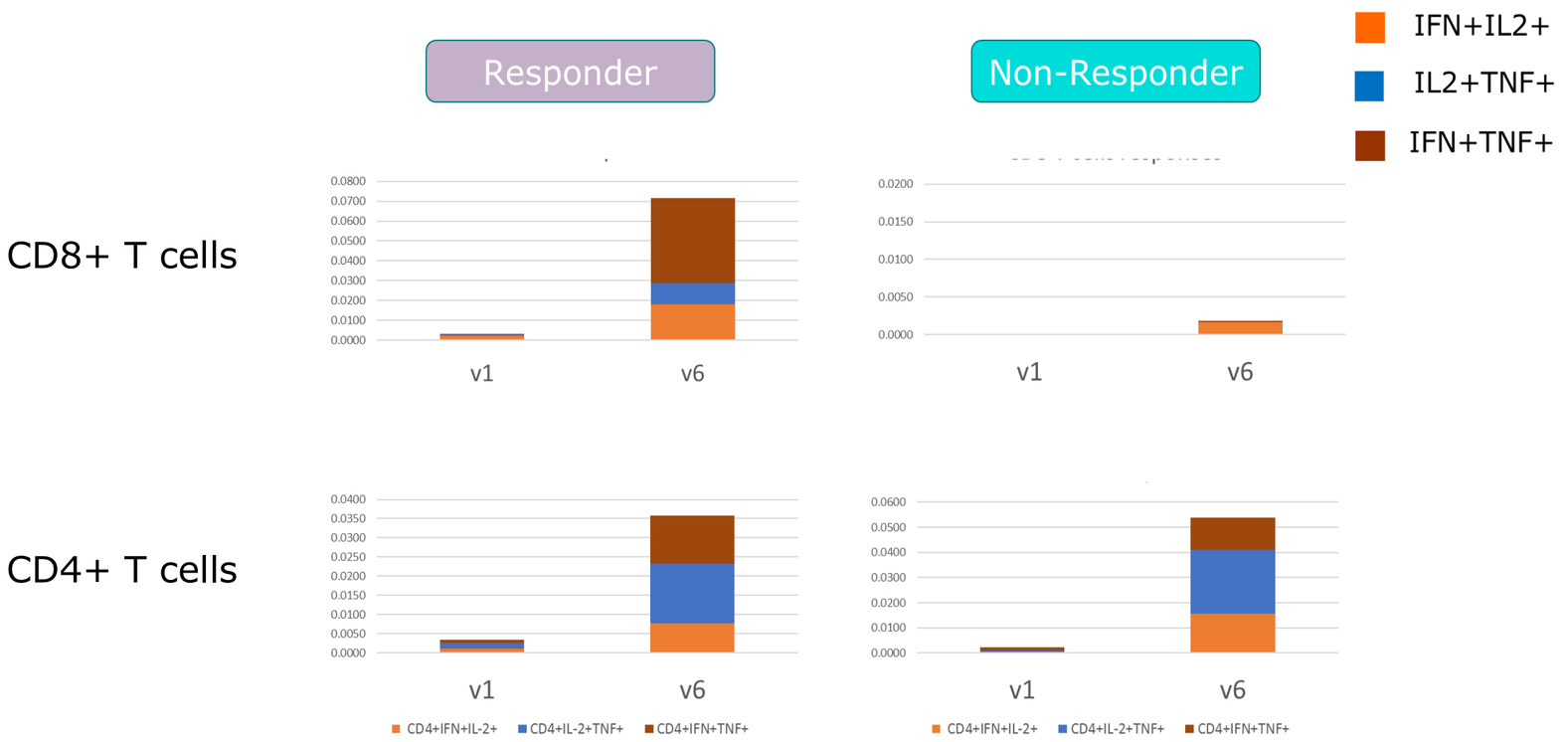


VB10.16 as a monotherapy in HPV16-positive, precancerous cervical lesions induces:

- Lesion size reduction in all patients followed >4 months
- CIN regression to CIN1 or no CIN in 10 patients
- HPV16 clearance in 6 patients

VB C-01: Strong multi-functional CD8+ and CD4+ T cell responses induced

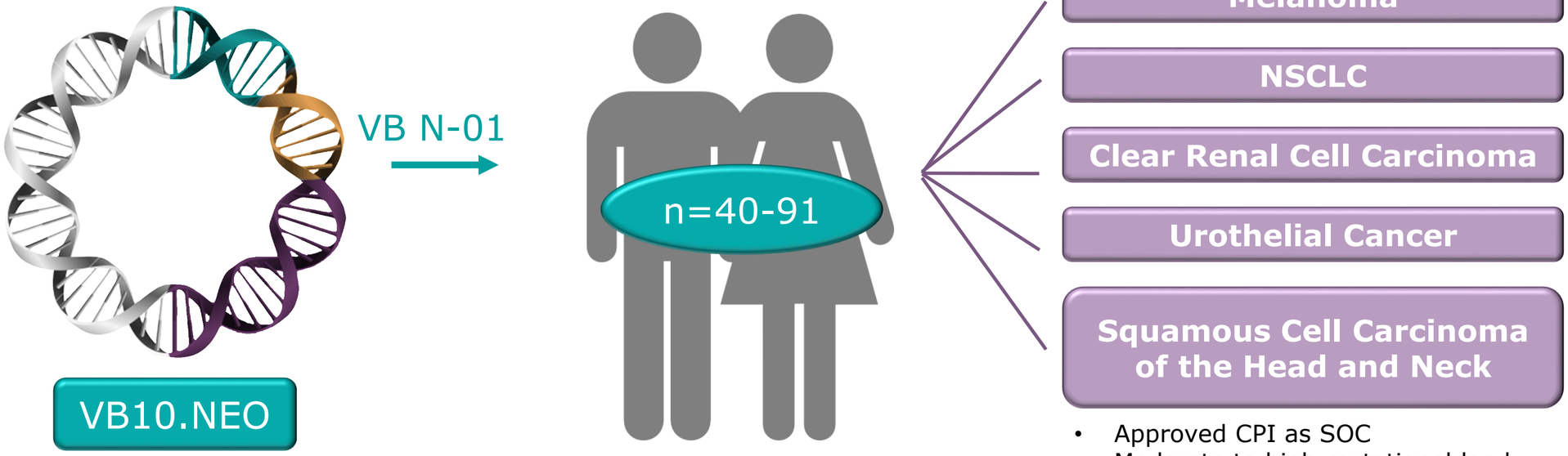
CD8+ T cell responses linked to clinical benefit



- In patients with CIN regression and HPV clearance, induction of multi-functional CD8+ T cells were significantly induced compared to non-responders.
- In contrast, CD4+ responses were similarly induced in all patients tested.

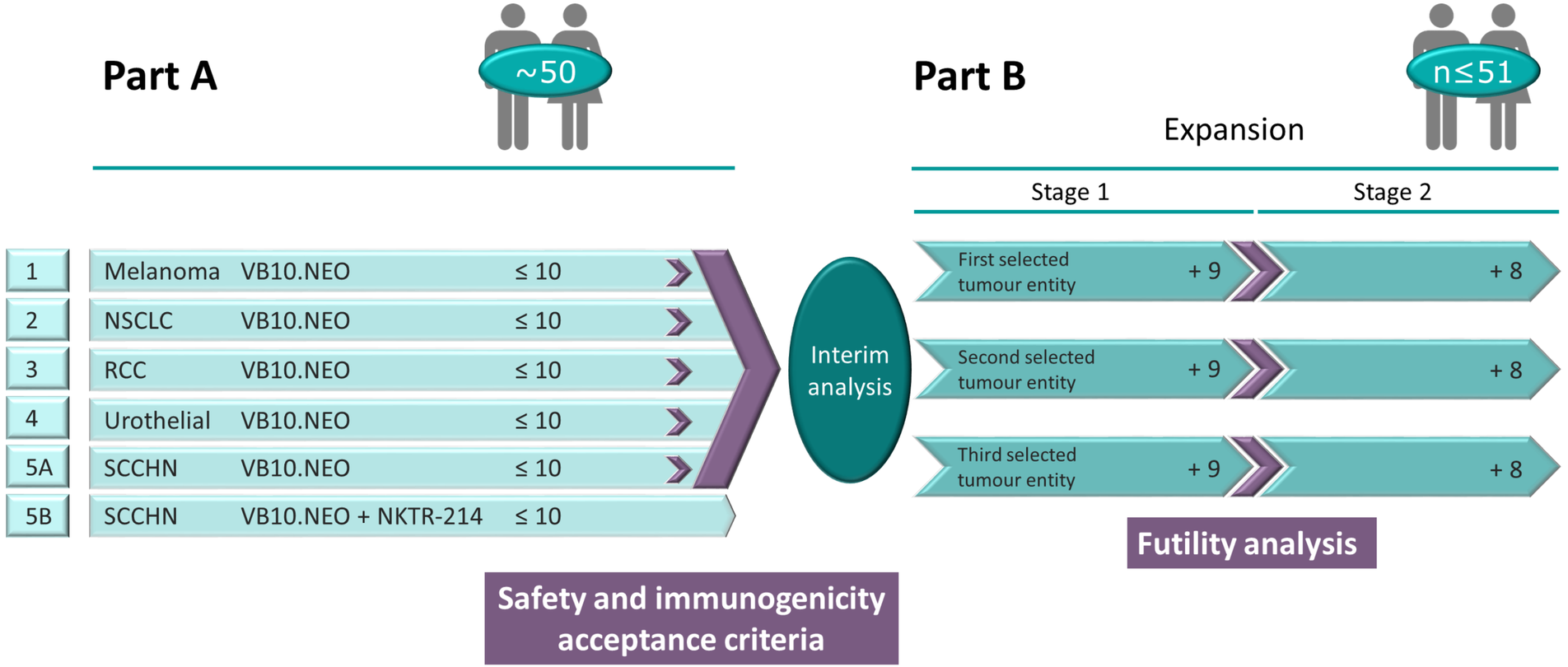
Clinical Trial VB N-01

VB N-01: An open labelled first human dose phase 1/2a study to evaluate safety, feasibility and efficacy of multiple dosing with individualised VB10.NEO immunotherapy in patients with locally advanced or metastatic melanoma, NSCLC, clear renal cell carcinoma, urothelial cancer or squamous cell carcinoma of head and neck, who did not reach complete responses with current standard of care immune checkpoint blockade



- Approved CPI as SOC
- Moderate to high mutational load

Clinical Trial VB N-01 at a a glance



- 100% vaccine manufacturing success for all patients with a successful biopsy so far
- 20 neoepitopes selected for all patients in the trial
- Jan 2019: 14 patients enrolled
- First expansion cohort to be initiated in H2, 2019

Vaccibody's Solution to Personalised Cancer Treatment

1. Tumour biopsy and sequencing

2. Neoepitope selection (TSNA)

NeoSELECT™

3. Vaccine manufacturing (n=1)

-DNA: Robust, rapid, cost-effective, stable, safe, up to 40 neoepitopes

4. Vaccine administration and immunogenicity

-Needle-free

-Target, Attract, Mature, Deliver, Cross-present

-Rapid, strong, long-lasting

-unique CD8 dominated responses

Vaccibody provide a Rapid, Cost-effective and Efficacious solution

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