vaccibody

Bringing Individualised Neoantigen-based Cancer Vaccines into the Clinic; Challenges, Learnings & Victories

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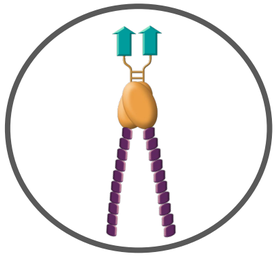
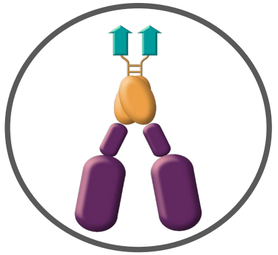
Vaccibody Product Pipeline

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		





Vaccibody – Proprietary Vaccine Technology Platform

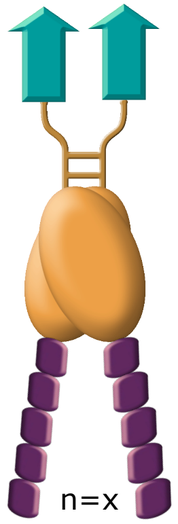
The Vaccibody Technology Platform was developed based on the concept of **targeting antigen to APC** in order to create more efficacious vaccines.

Exchangeable DNA Cassette

Vaccibody DNA Vaccine Plasmid

VB10.NEO

In vivo expression



Vaccibody in Protein Format

Target to Antigen Presenting Cell

Dimerization for crosslinking target receptor

Antigen moiety

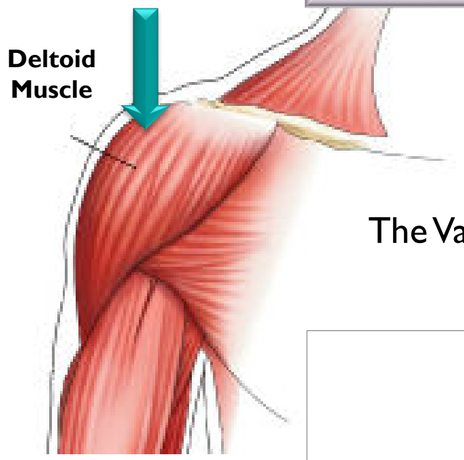
Mechanism of action: Intrinsic adjuvant for direct targeting

Administration (i.m.) of DNA plasmid

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

Attract – Deliver – Cross-present

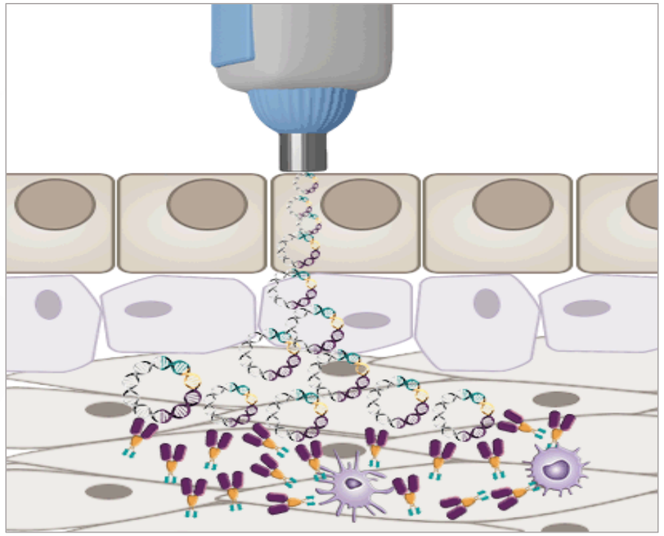
Skewing the immune system to a CD8+ killer T-Cell response

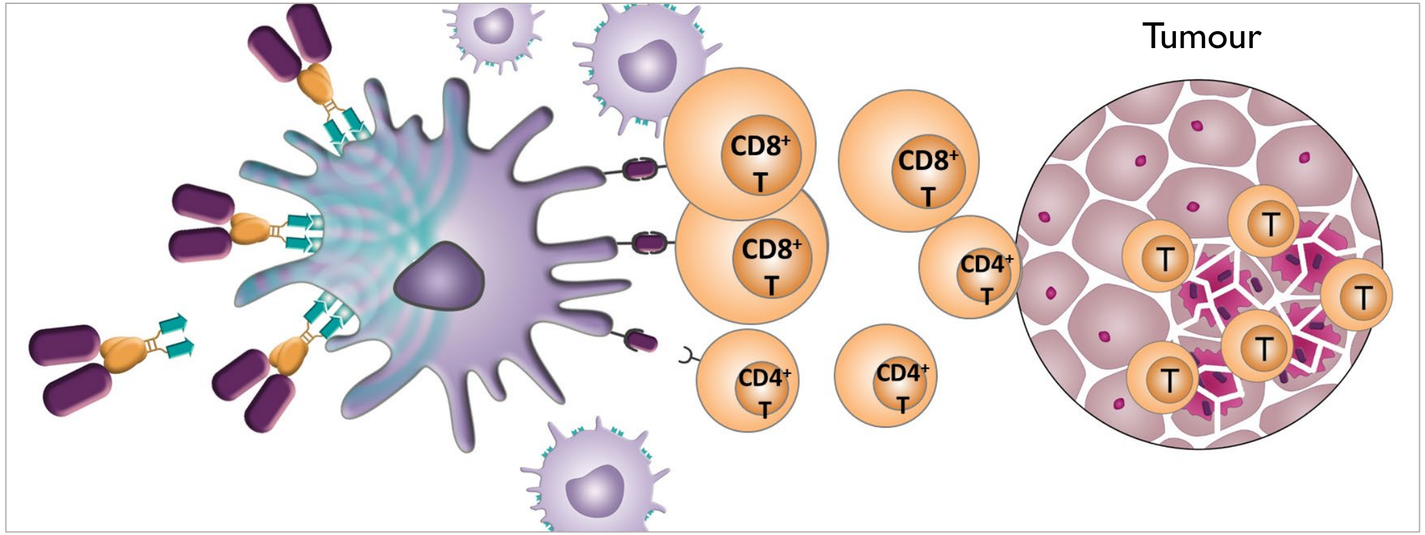


The Vaccibody uses the muscle cell as a factory

- 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**

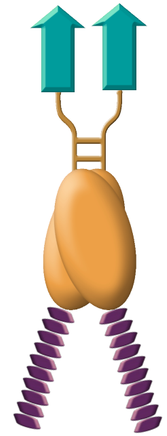
PharmaJet®



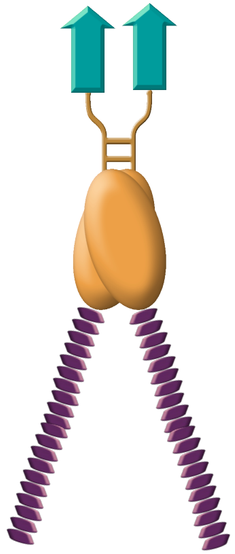


Targeting is elicited by the MIP-1α chemokine

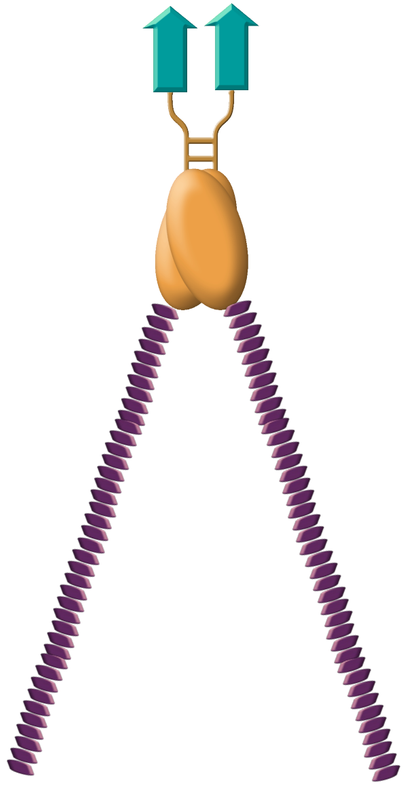
VB10.NEO – A Robust Vaccine Format



VB10.NEO-X



VB10.NEO-XX



VB10.NEO-XD

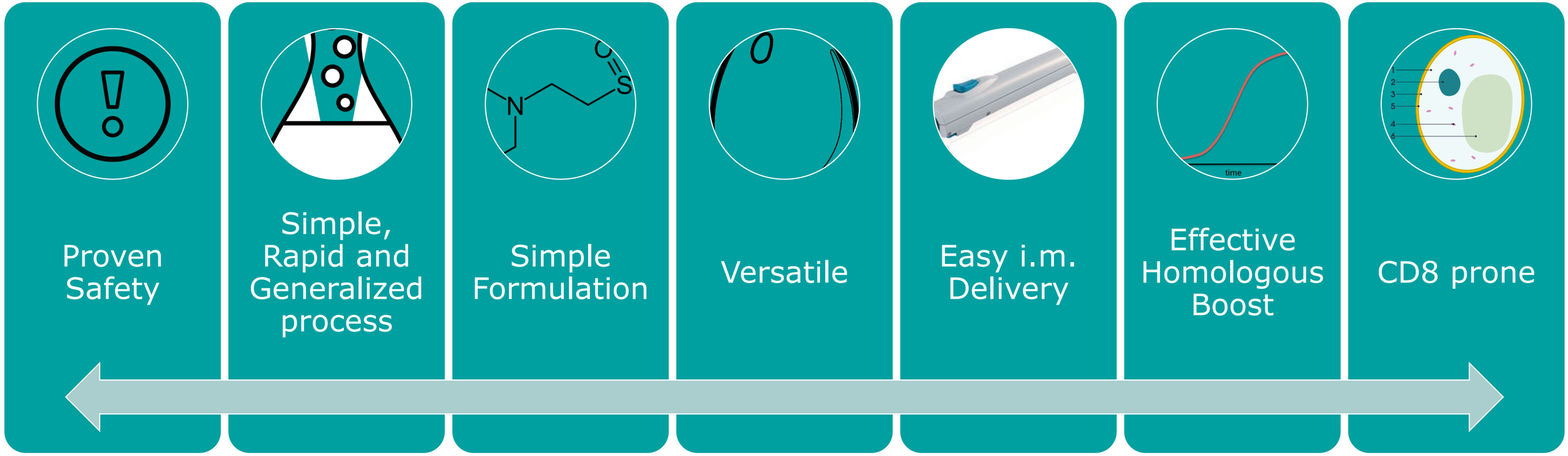
>90 different VB10.NEO constructs with >450 neoepitopes constructed to date with up to 40 neoepitopes

Patient Friendly, simple Vaccine Delivery

PharmaJet®

- ✓ Needle free injection
- ✓ Small, handy, easy to use
- ✓ Minimal pain compared to electroporation
- ✓ Cost effective
- ✓ Applicable for multiple immunizations
- ✓ High patient compliance

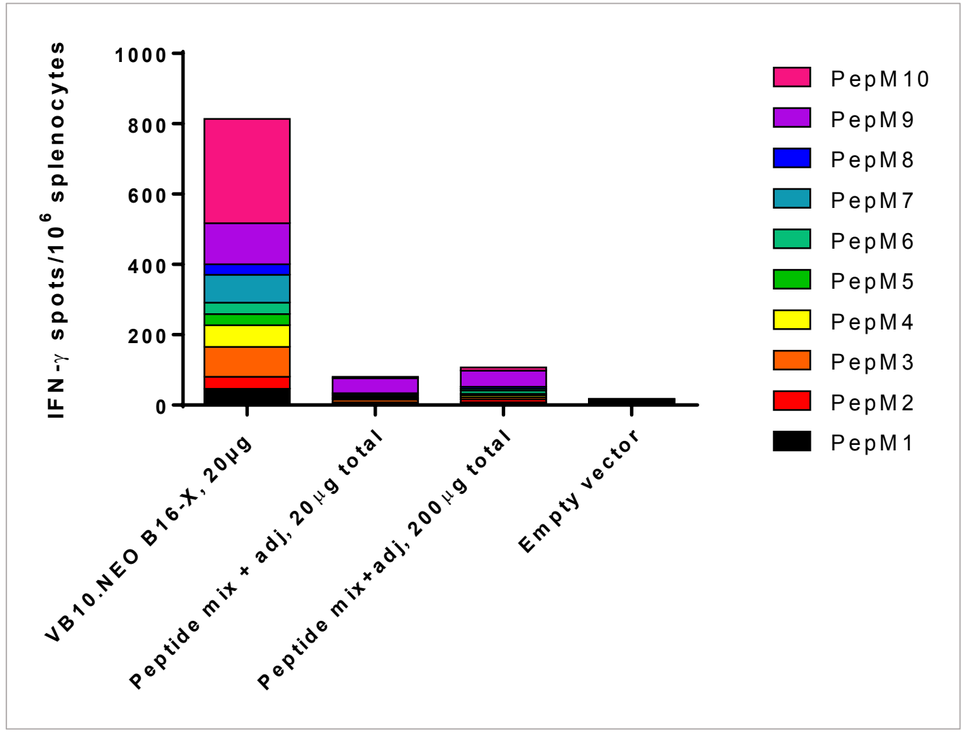
Naked DNA plasmid as IMP



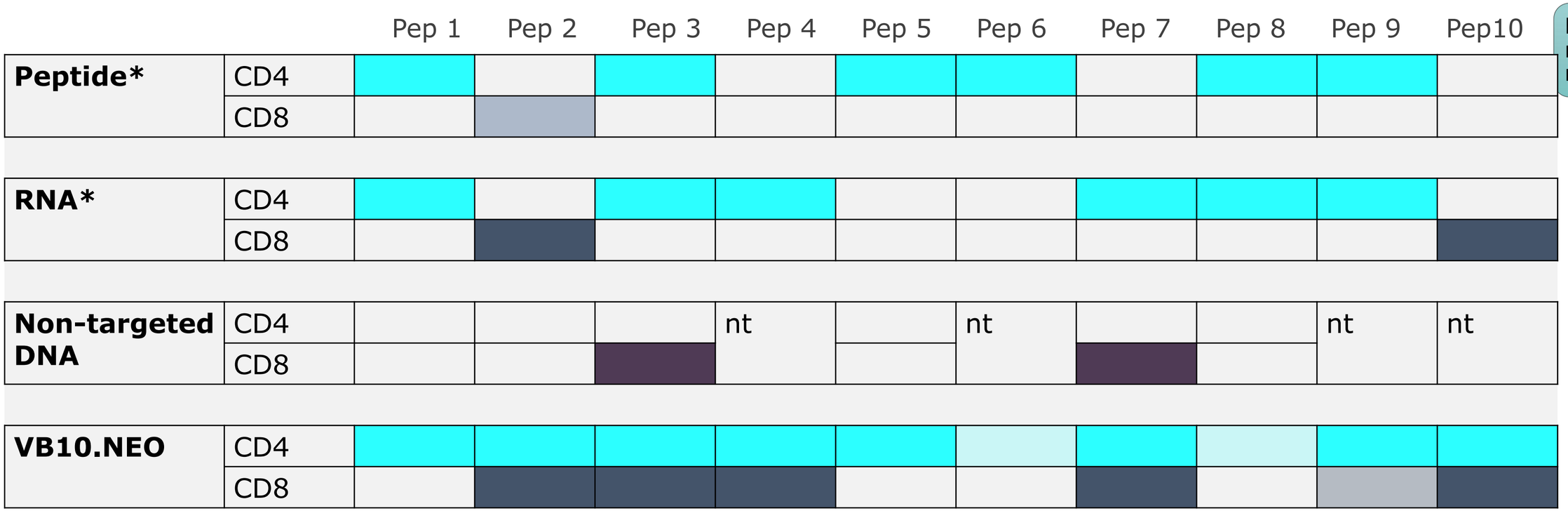
DNA plasmid is an ideal platfrom for bringing individualized neoantigen vaccines to the market as a viable product at reasonable COGS

VB10.NEO induces Rapid, Broad and Strong responses to multiple Neoepitopes by single Vaccination

- VB10.NEO induces a broader and stronger response than Peptide + Poly (I:C) Adjuvant vaccines after a single immunization.
- VB10.NEO vaccinated animals respond to all 10 neoepitopes after a single immunization.
- Immunodominant neoepitopes differ between delivery vehicles



VB10.NEO generates a broader immune response profile dominated by CD8+ T cells than competing technologies



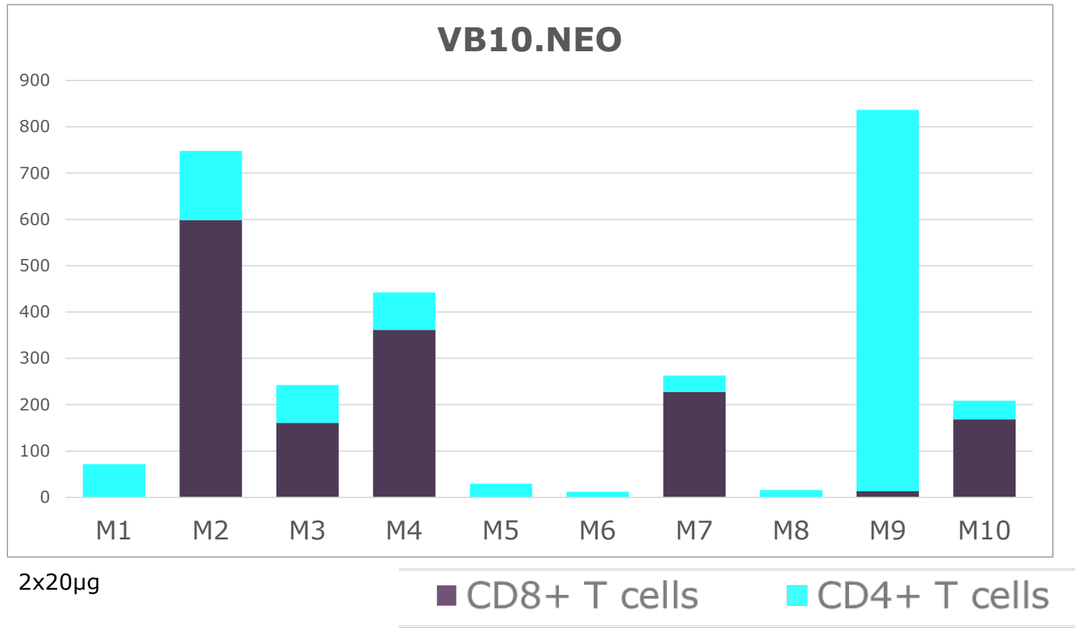
Peptide and RNA vaccines induces primarily CD4 T cell responses, while VB10.NEO induces strong, dominating CD8 responses to the identical neoepitope sequences

Non-targetd DNA vaccines induced a CD8 response towards 2 of 6 tested neoepitopes

- Castle et al., 2012 and Kreiter et al., 2015
- Aurisicchio et al., 2019

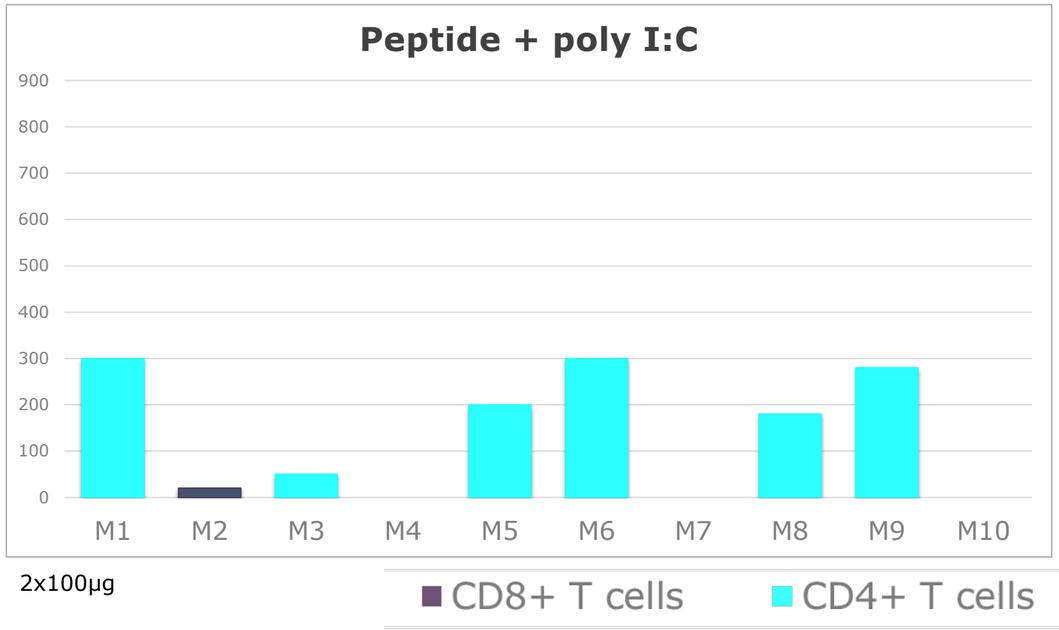
VB10.NEO leads to a unique CD8 dominated neoepitope response

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



2x20µg

Peptide + poly I:C vaccination has been reported to induce **dominantly CD4 T cell responses**



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

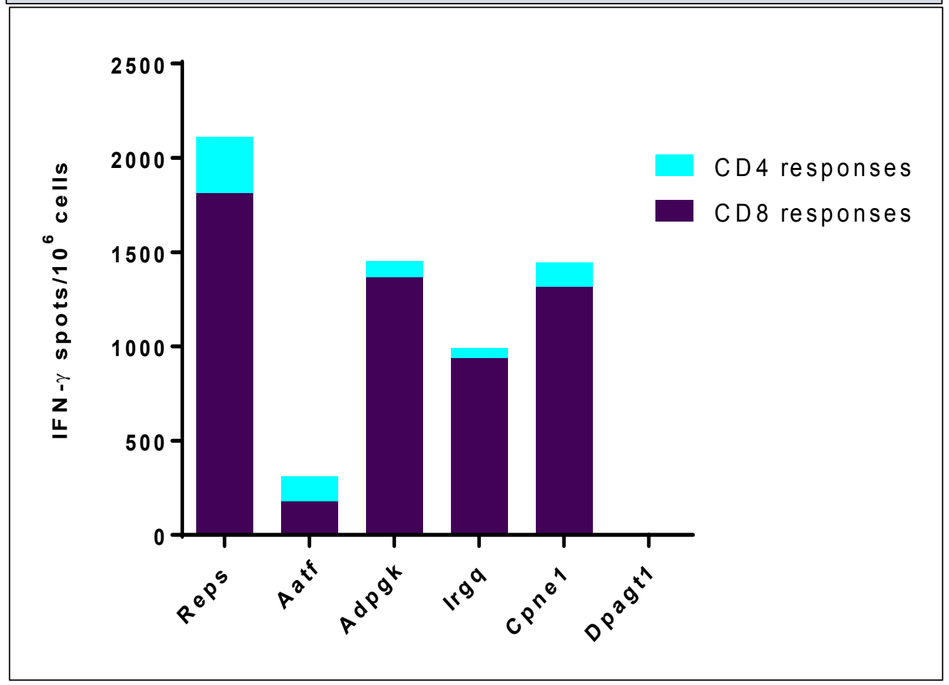
- Castle et al., 2012 and Kreiter et al., 2015-adapted figure based on B16 melanoma results

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

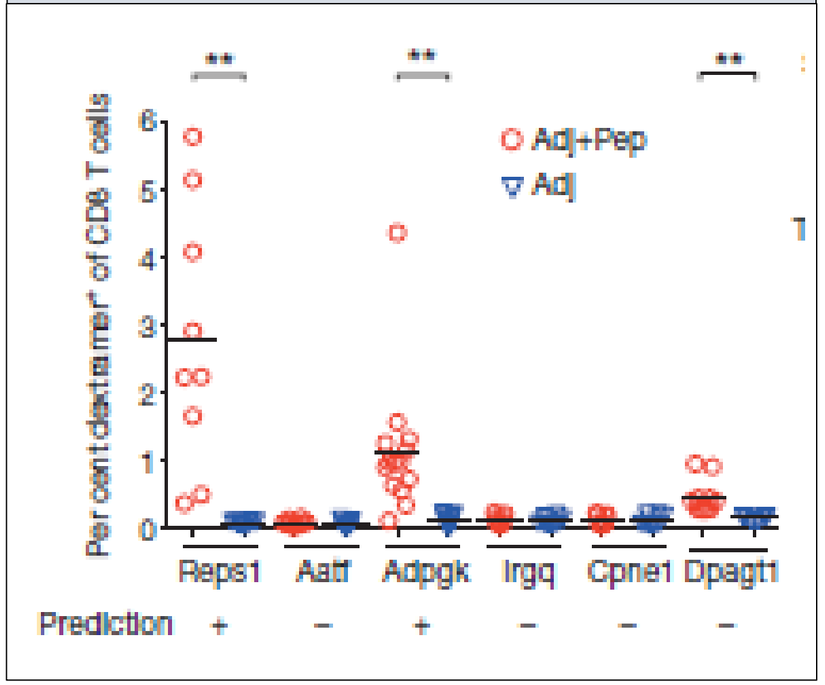
MC38 colon carcinoma

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.

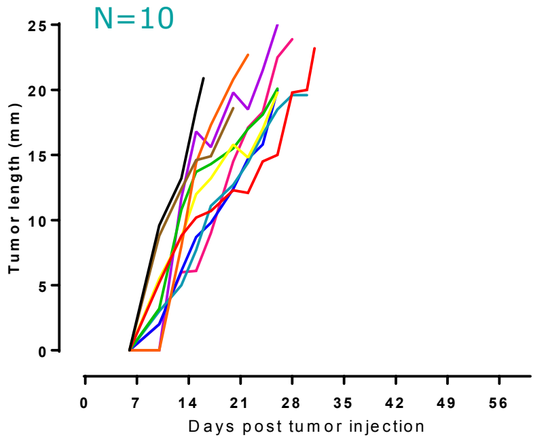
-3 of these neoepitopes have been shown to be **non-immunogenic delivered as peptide + adjuvant**

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

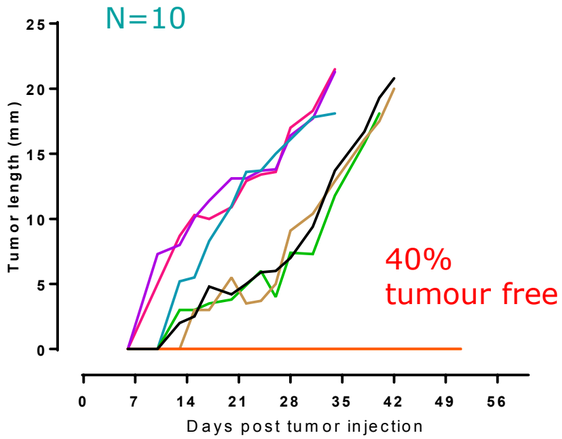
Vaccibody Induces Tumor Protection as Monotherapy

CT26 colon carcinoma model

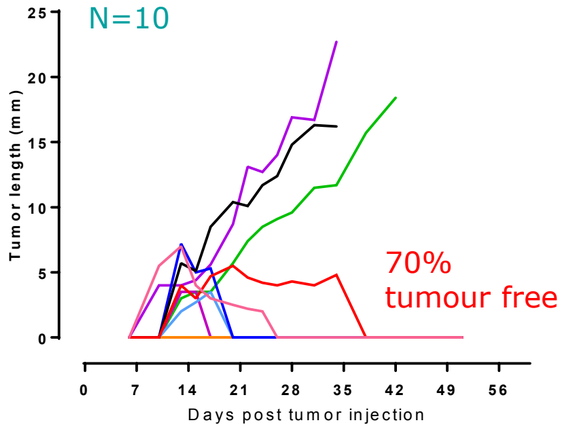
Control



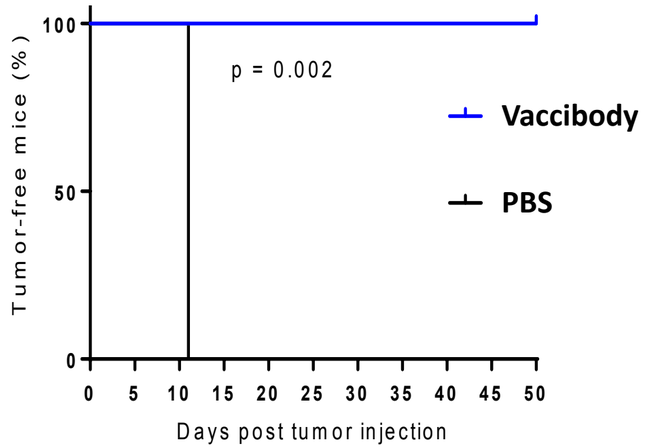
Vaccibody Monotherapy



Vaccibody Combination Therapy



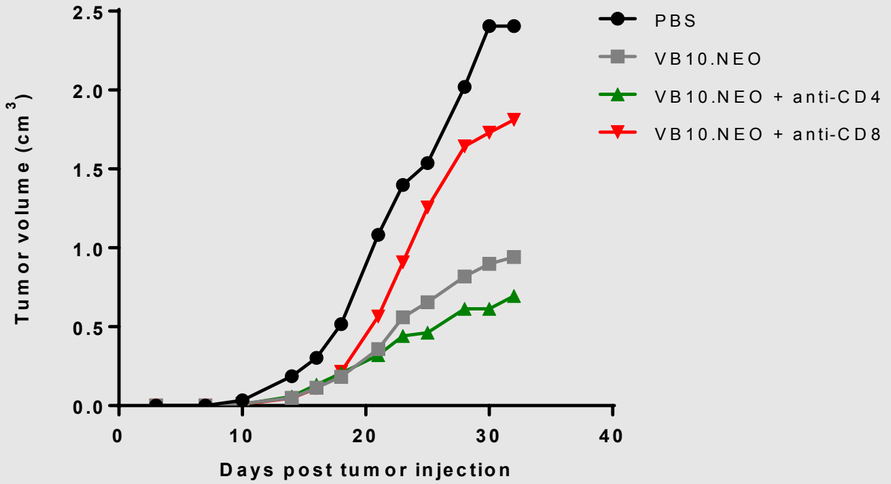
Re-challenged mice are protected



- 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

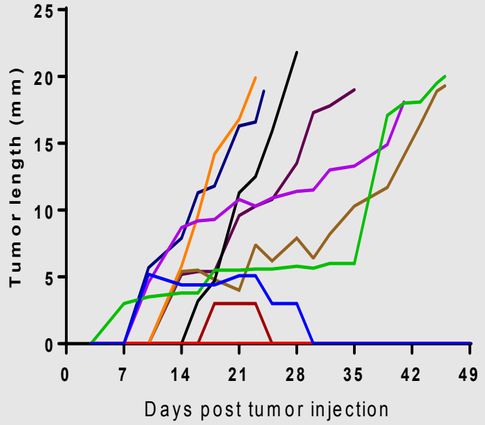
Neoepitope-specific CD8 T cells are crucial for tumour protection

Average, all groups

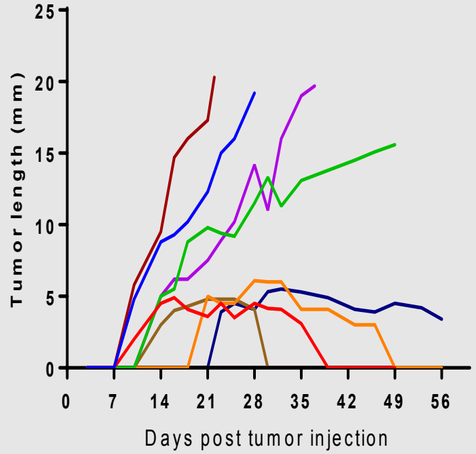


Individual growth curves

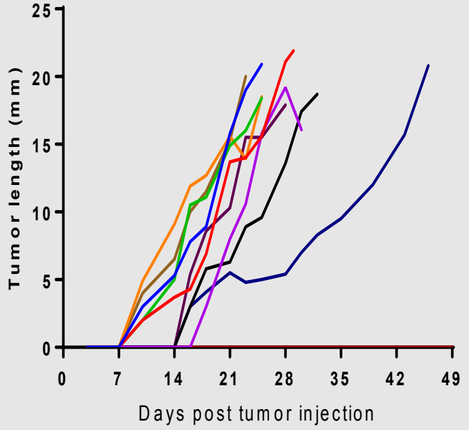
VB10.NEO



VB10.NEO + anti-CD4

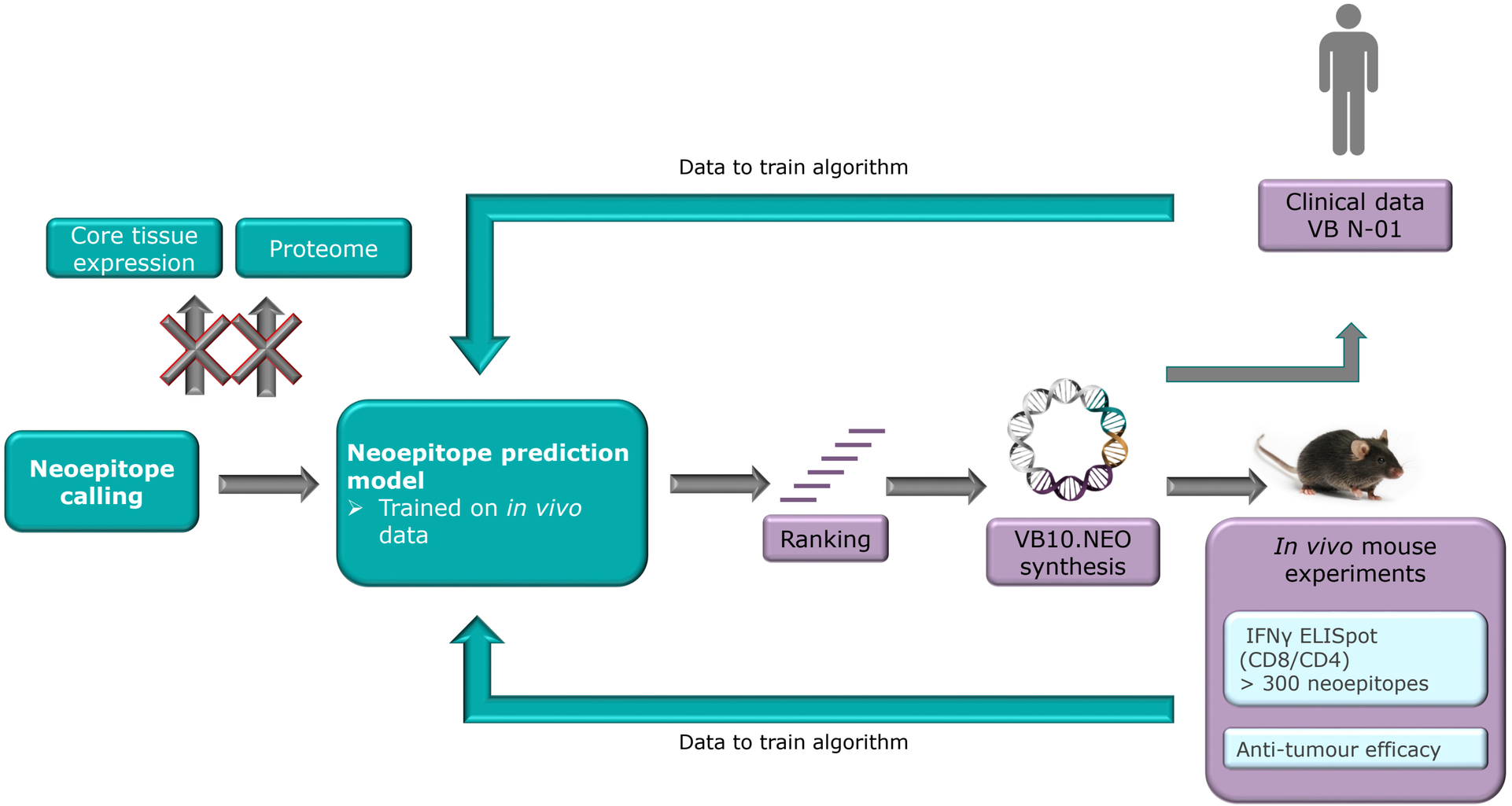


VB10.NEO+ anti-CD8

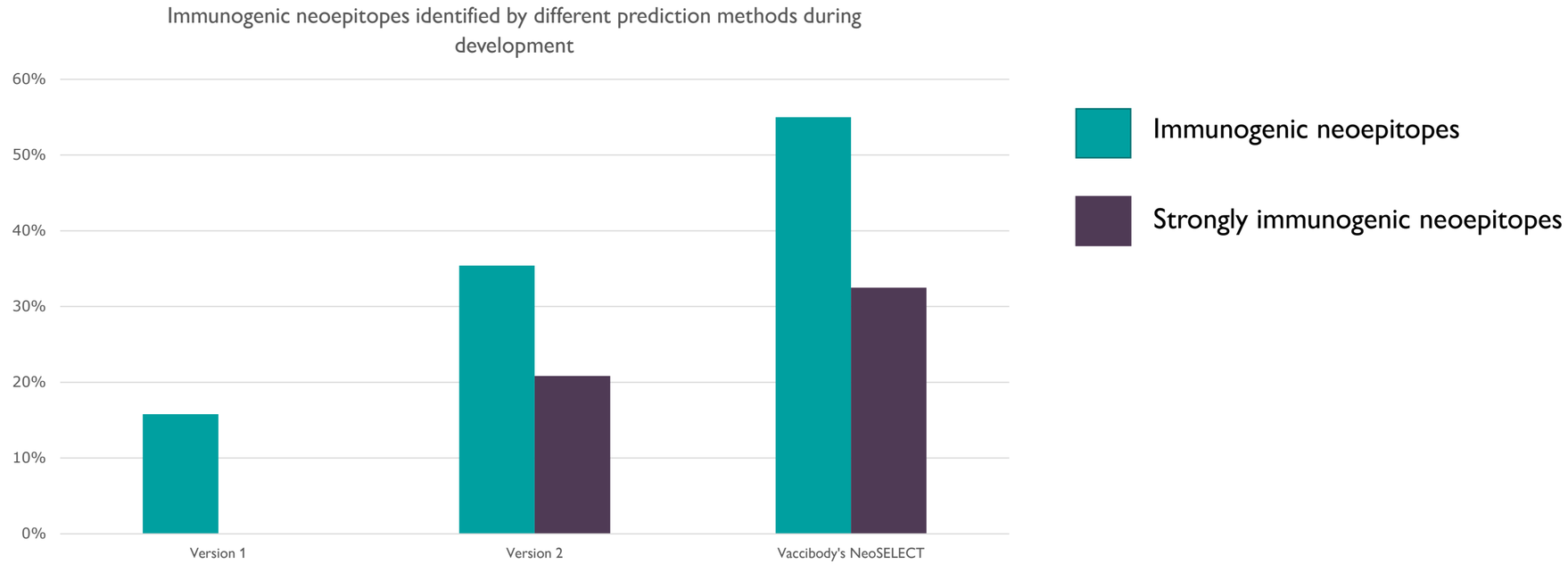


Depletion of CD8 T cells prohibit tumour protection in VB10.NEO vaccinated mice, indicating a crucial role of neoepitope-specific CD8 T cells for anti-tumour efficacy

Developing VB10.NEO specific Neoepitope Selection



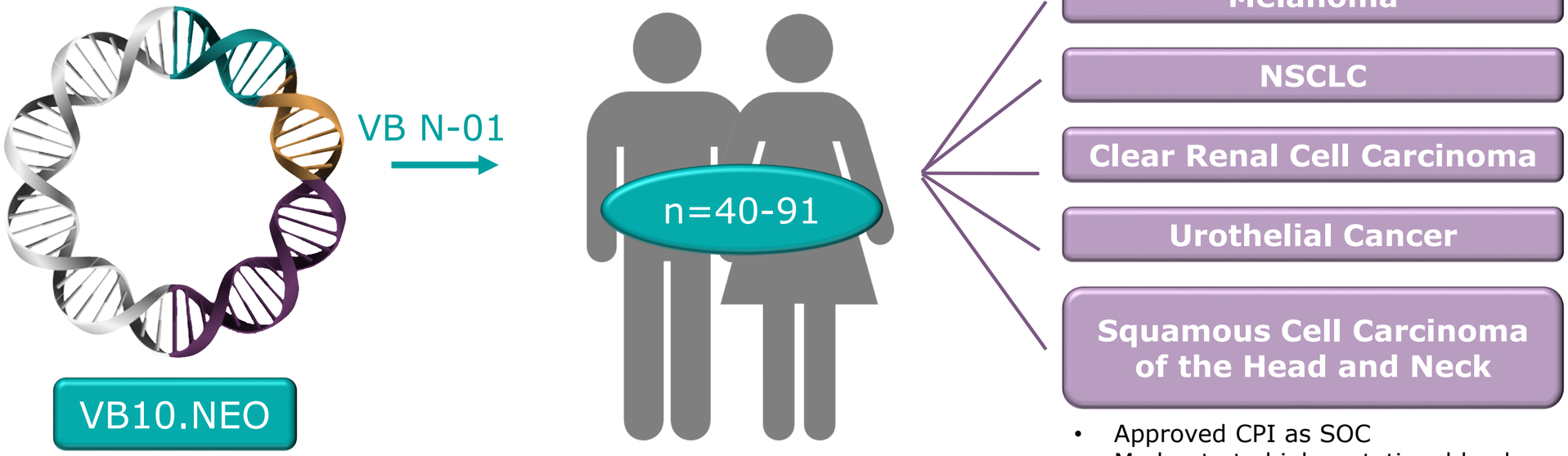
Successful development of a strong proprietary neoepitope selection method NeoSELECT™



- Vaccibody has since 2017 successfully developed a proprietary neoepitope selection method able to identify a high number of immunogenic neoepitopes when used in VB10.NEO vaccines
- Majority of the induced responses are CD8 restricted (measured ex vivo) with latest version
- This method, NeoSELECT, is used in the VB N-01 clinical trial

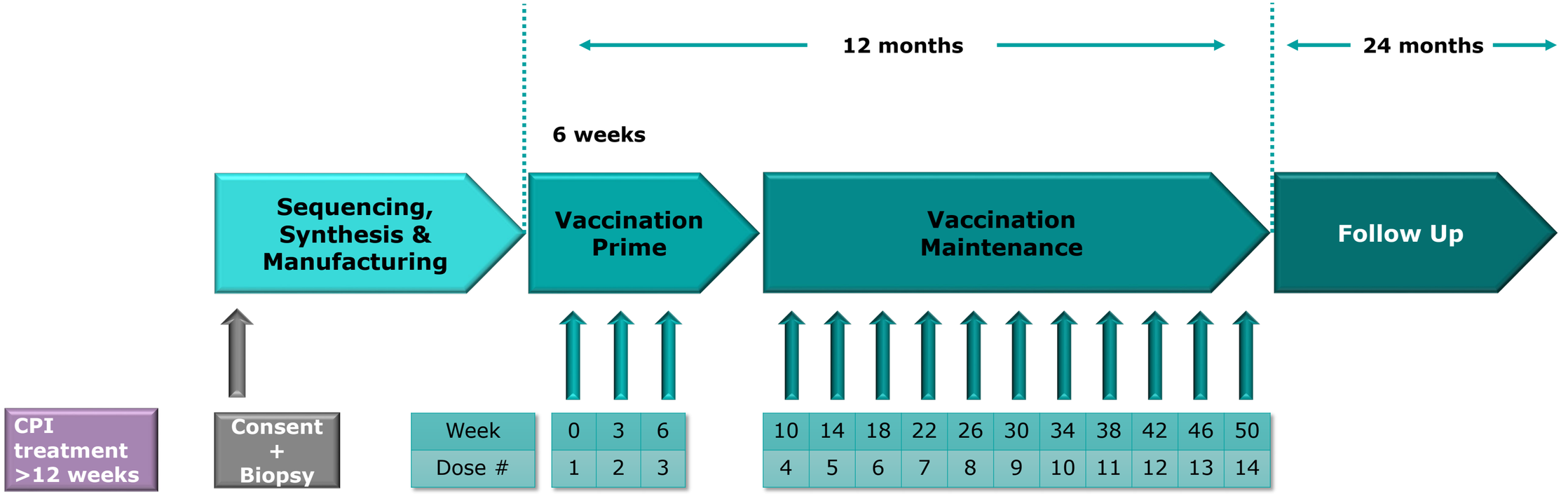
Clinical Trial VB N-01

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

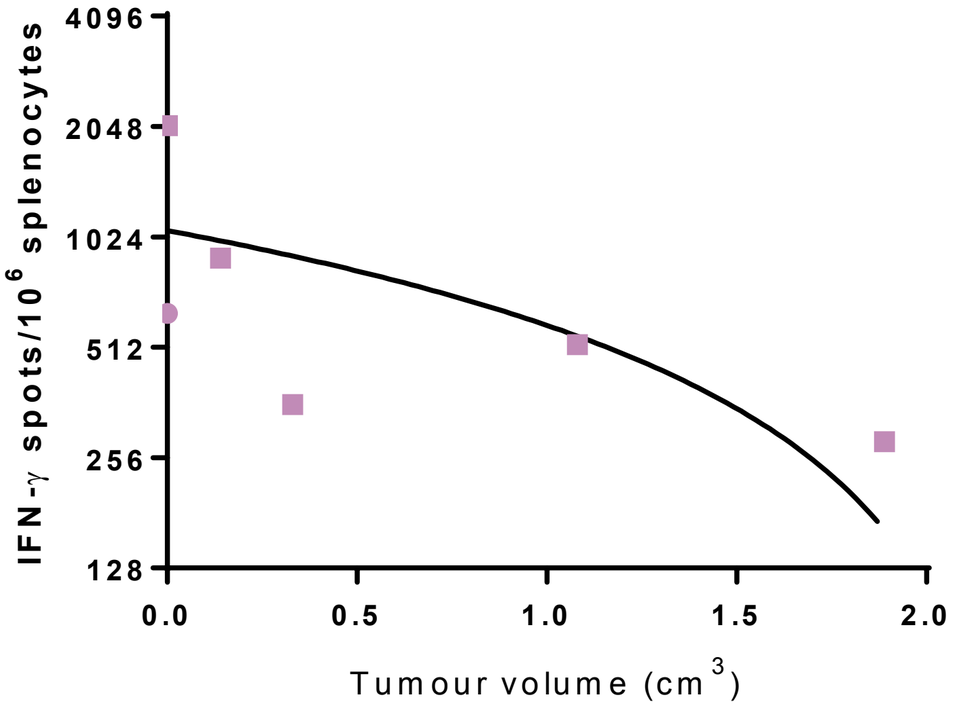
Study Design and Treatment Schedule VB N-01



One year into the VB N-01 clinical study

Challenges	• Biopsies • Multiple providers in manufacturing chain
Learnings	• Quality of neoepitopes versus predicted immunogenicity • Implication of different indications • Inclusion criteria >12 weeks on CPI
Successes	• 100% success in manufacturing VB10.NEO for all patients with positive biopsy • 100% successful with top 20 neoepitope choice • DNA vaccine manufacturing proven to be ideal for PCV

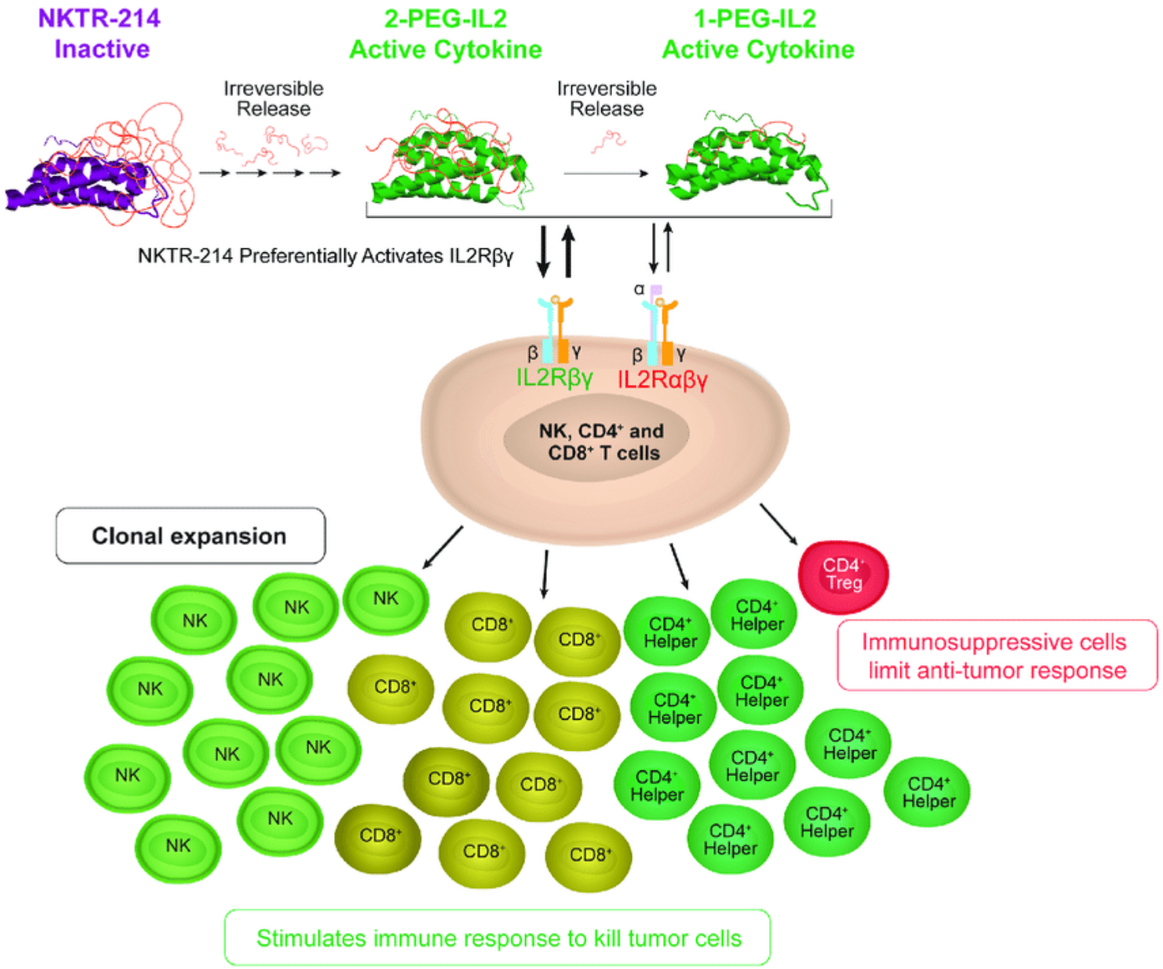
Strength of the neoepitope-specific T cell response is important for anti-tumour efficacy



Individual tumour-bearing mice vaccinated with the same VB10.NEO vaccine have different level of neoepitope-specific T cell response.

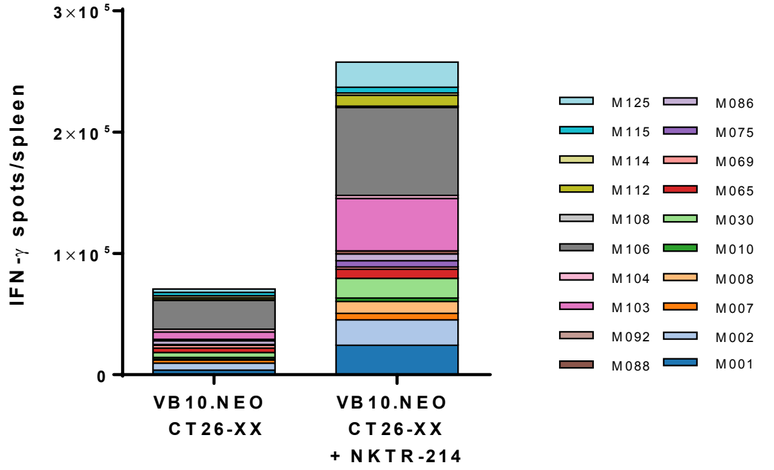
The neoantigen-specific T cell response tends to correlate with size of the tumour.

Bempegaldesleukin (NKTR-214) has the potential to significantly expand T cells

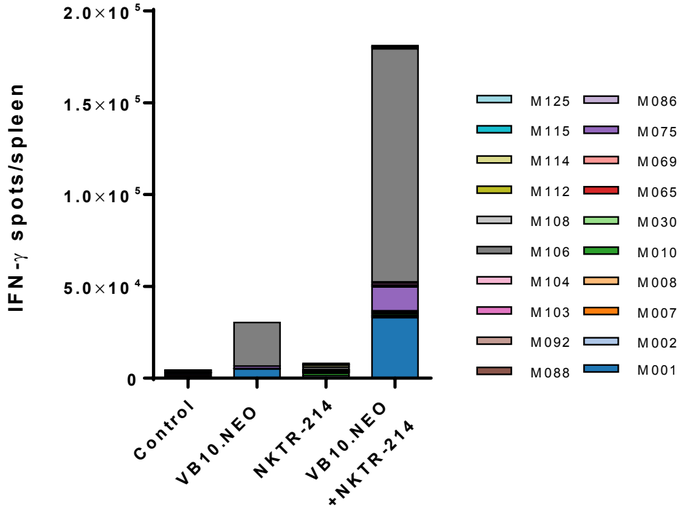


Combination of VB10.NEO and NKTR-214 greatly synergizes

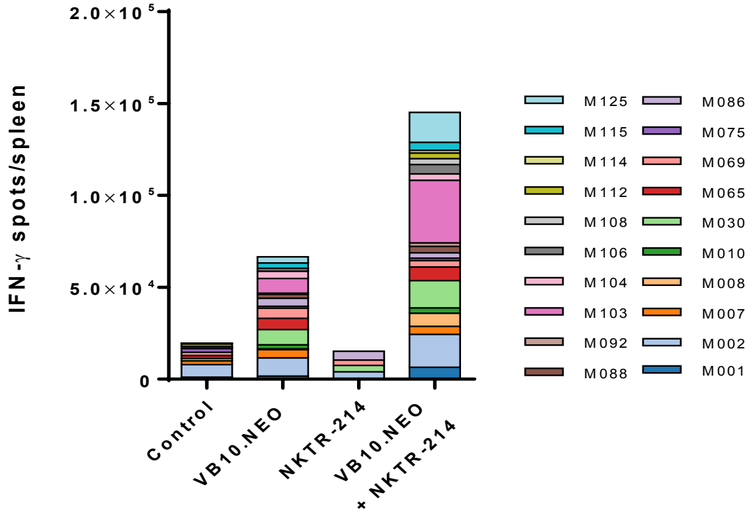
Total T cell response per spleen



CD8 responses

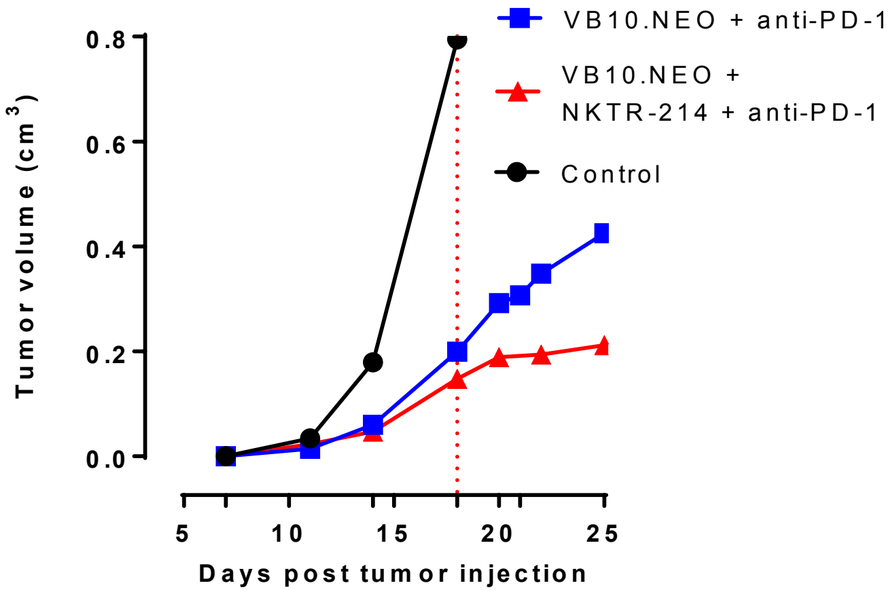


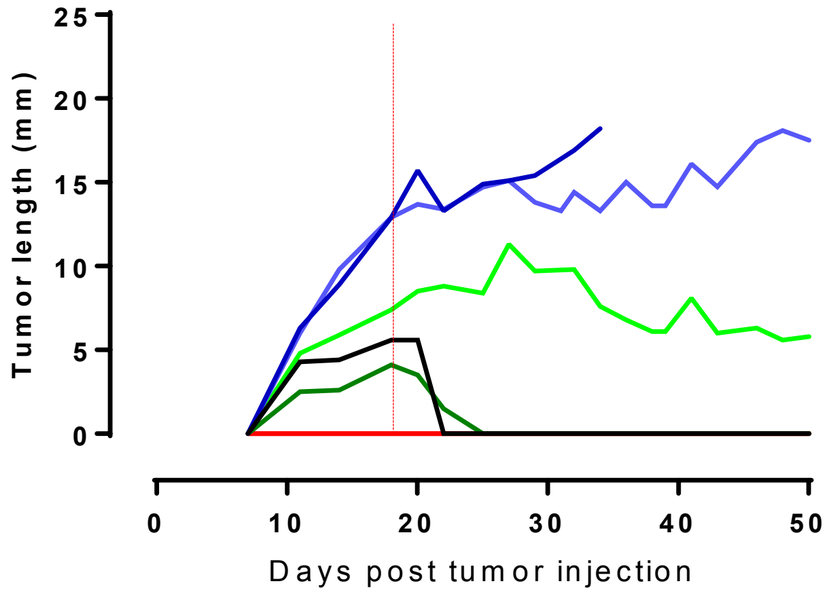
CD4 responses



- Combination of VB10.NEO and bempegaldesleukin (NKTR-214) synergizes to elicit greater breadth and depth of neoantigen-specific T cell responses than each individual treatment
- The synergistic effect was observed in both CD4 and CD8 cells. Most pronounced on CD8 T cell responses.

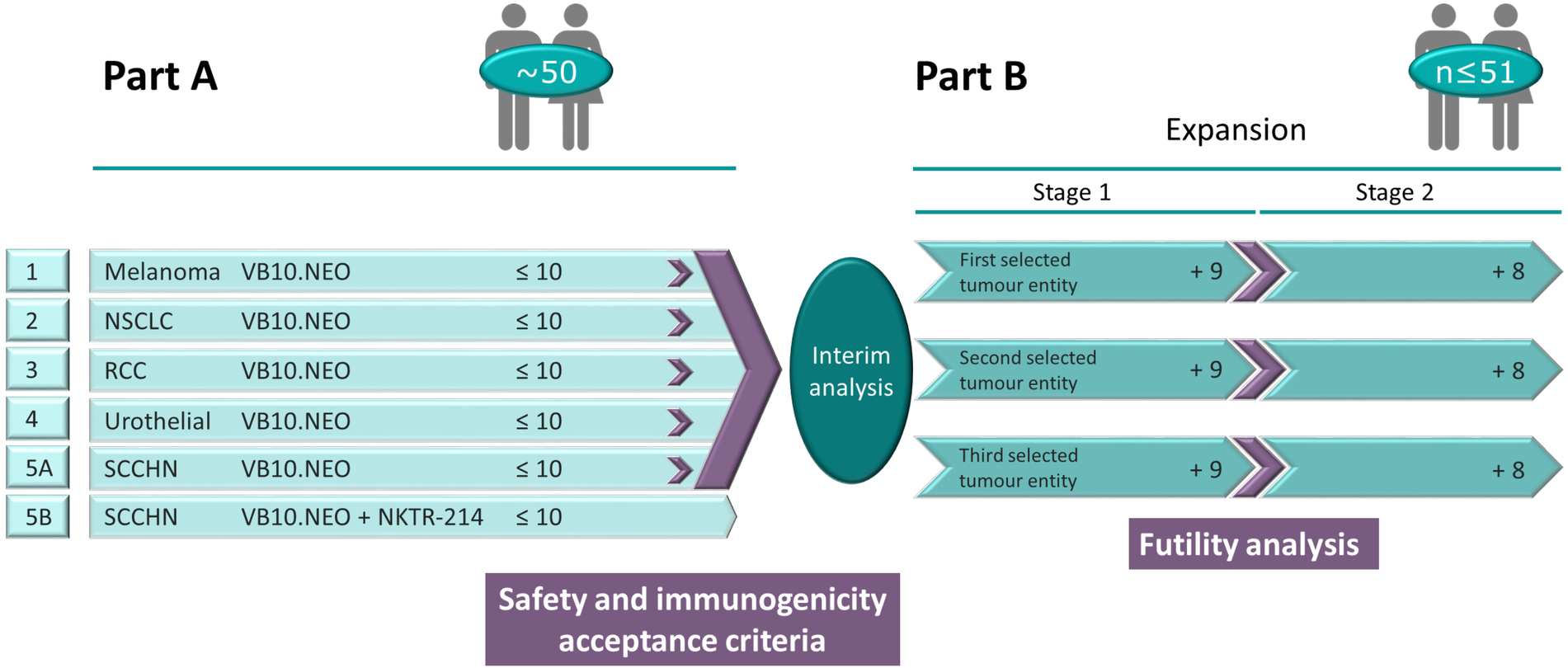
Striking immediate improvement of anti-tumour efficacy when addding bempegaldesleukin (NKTR-214) to VB10.NEO and anti-PD-1 treatment





Adding NKTR-214 (from day 18) to a VB10.NEO and anti-PD-1 treatment induce rapid, complete and durable tumour regression of small tumours and long-lasting stabilization of large tumours.

Plan to expand the VB N-01 clinical trial in 2019



- Adding an arm to treat >10 SCCHN patients with NKTR-214 plus VB10.NEO and anti-PD-(L)1
- In addition, first expansion cohort(s) may be initiated in H2, 2019

Vaccibody's Solution to Personalised Cancer Treatment

1. Tumour biopsy and sequencing

NeoSELECT™

2. Neoepitope selection (TSNA)

-DNA: Robust, rapid, cost-effective, stable, safe

-up to 40 neoepitopes

3. Vaccine manufacturing (n=1)

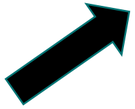
-Needle-free

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

-Rapid, strong, long-lasting

-CD8 dominated

4. Vaccine administration and immunogenicity



Vaccibody provide a Rapid, Cost-effective and Efficacious solution

Vaccibody Dreamteam!

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