vaccibody

Next Generation Cancer Immunotherapy

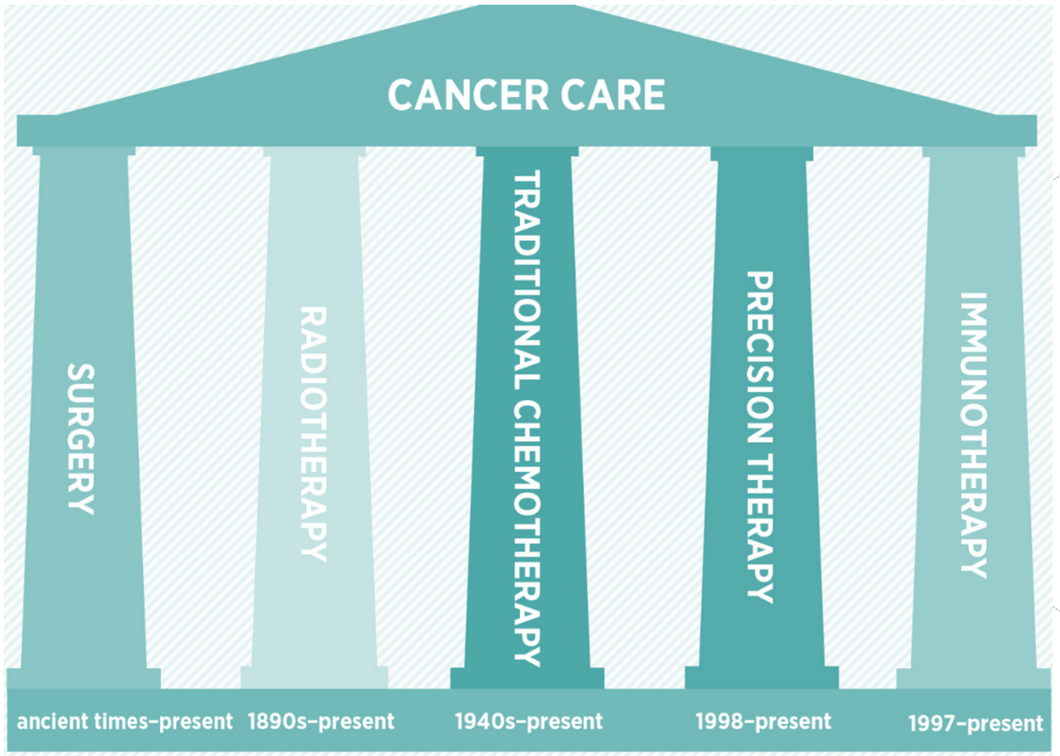
One treatment specifically designed to treat your unique tumour

Food for thought
Forskningsparken May 21, 2019

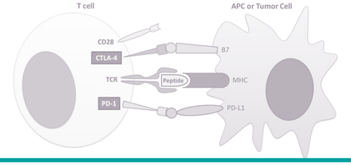
Agnete B Fredriksen
President & CSO
Vaccibody AS

abfredriksen@vaccibody.com

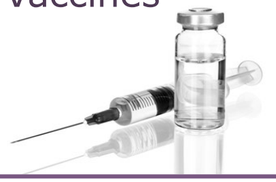
Immunotherapy: The next Wave of Cancer Therapy



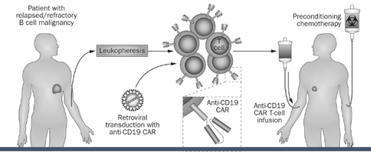
Checkpoint Inhibitors



Vaccines



Cell Therapies



Others, e.g.

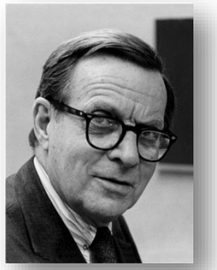
Oncolytic viruses
Cytokines
Bi-specific antibodies
Small molecules
Adjuvants

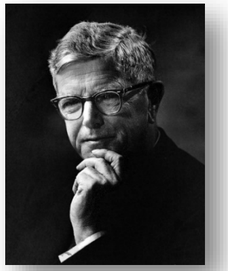
Various Immuno-Therapy Modalities

History of the Immune System and Cancer

Paul Ehrlich (1909) first conceived the idea that tumor cells can be recognized as "foreign" and eliminated by the immune system.

Lewis Thomas and Macfarlane Burnet (1959) formalized this concept by coining the term immune surveillance, which implies that a normal function of the immune system is to constantly "scan" the body for emerging malignant cells and destroy them.

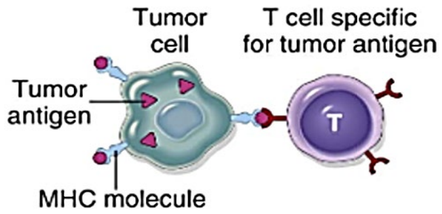
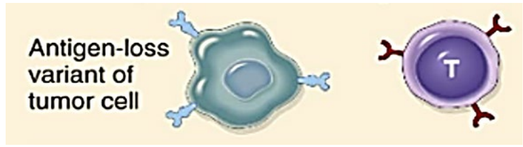
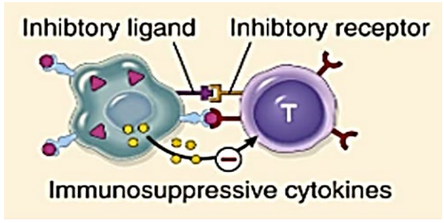




Increased frequency of cancers in the setting of immunodeficiency

- Persons with immunodeficiencies develop cancers at about 200 times the rate in immunocompetent individuals

Evasion of the Immune Response

Anti-tumour immunity		T cell recognition of tumour antigen leading to T cell activation
Immune evasion by tumours	**Failure to produce tumour antigen** 	Lack of T cell recognition of tumour
	Mutations in MHC genes or genes needed for antigen processing 	Lack of T cell recognition of tumour
	Production of immunosuppressive proteins or expression of inhibitory cell surface proteins 	Inhibition of T cell activation

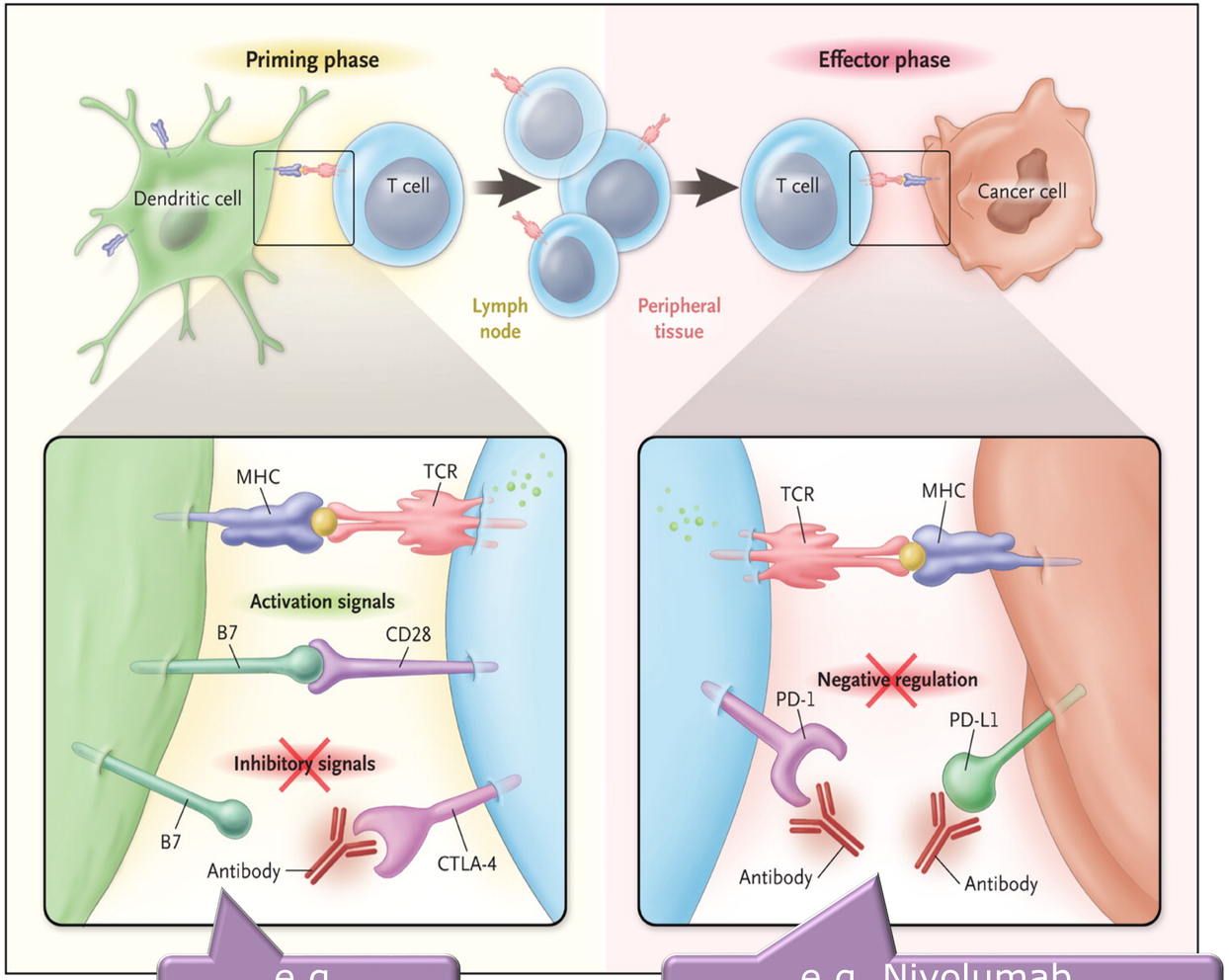
Immune Checkpoint Blockade-the success that opened the field

2016 ASCO
Advance of the Year

2011
Ipilimumab introduced for melanoma

2014
Pembrolizumab, nivolumab approved for melanoma

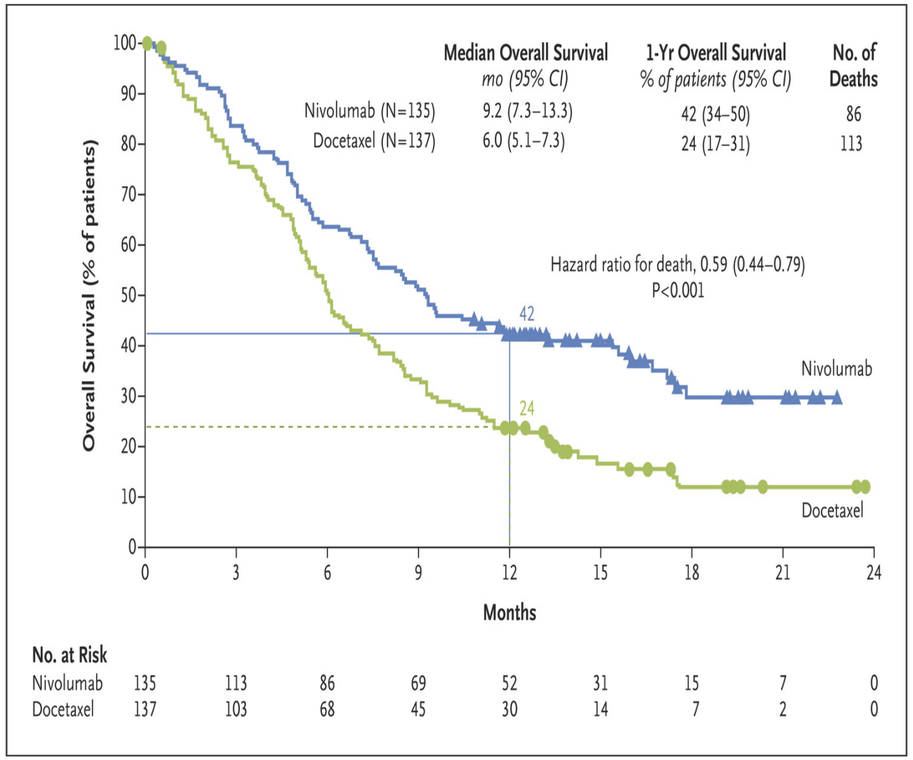
2015-2016
PD-1/L-1 drugs benefit even more of cancers

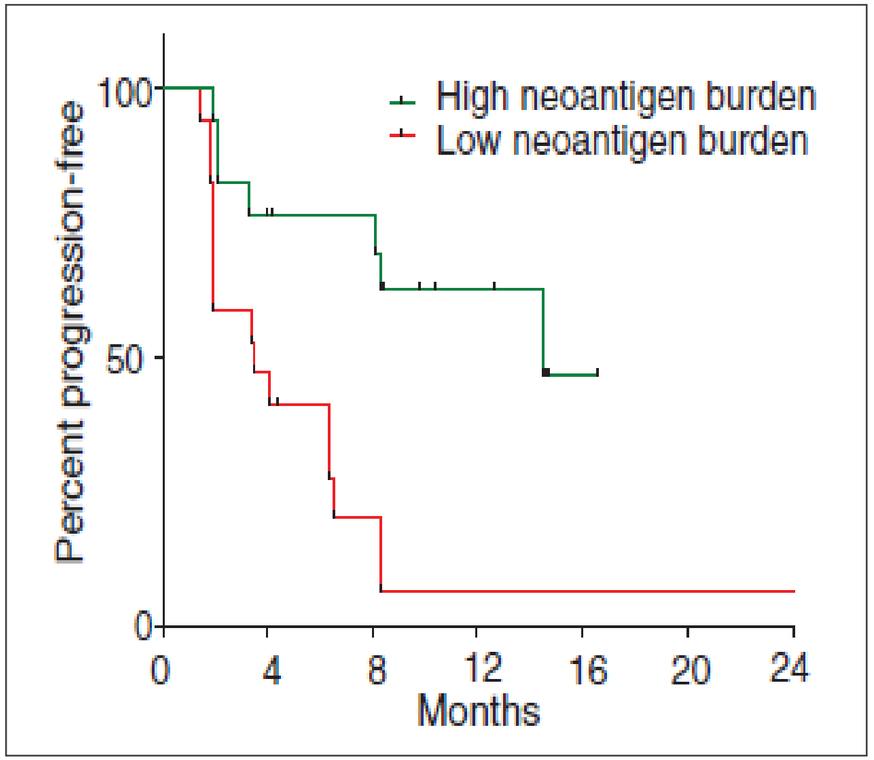


e.g. Ipilimumab

e.g. Nivolumab, Pembrolizumab

CheckPoint Inhibitors – Their Promise and their Limitations



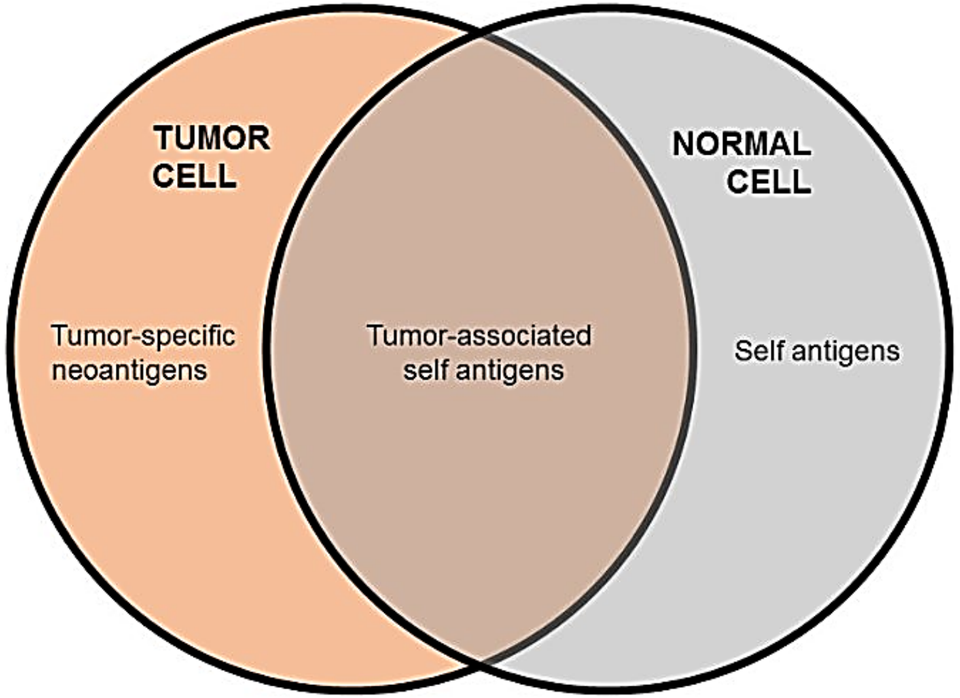


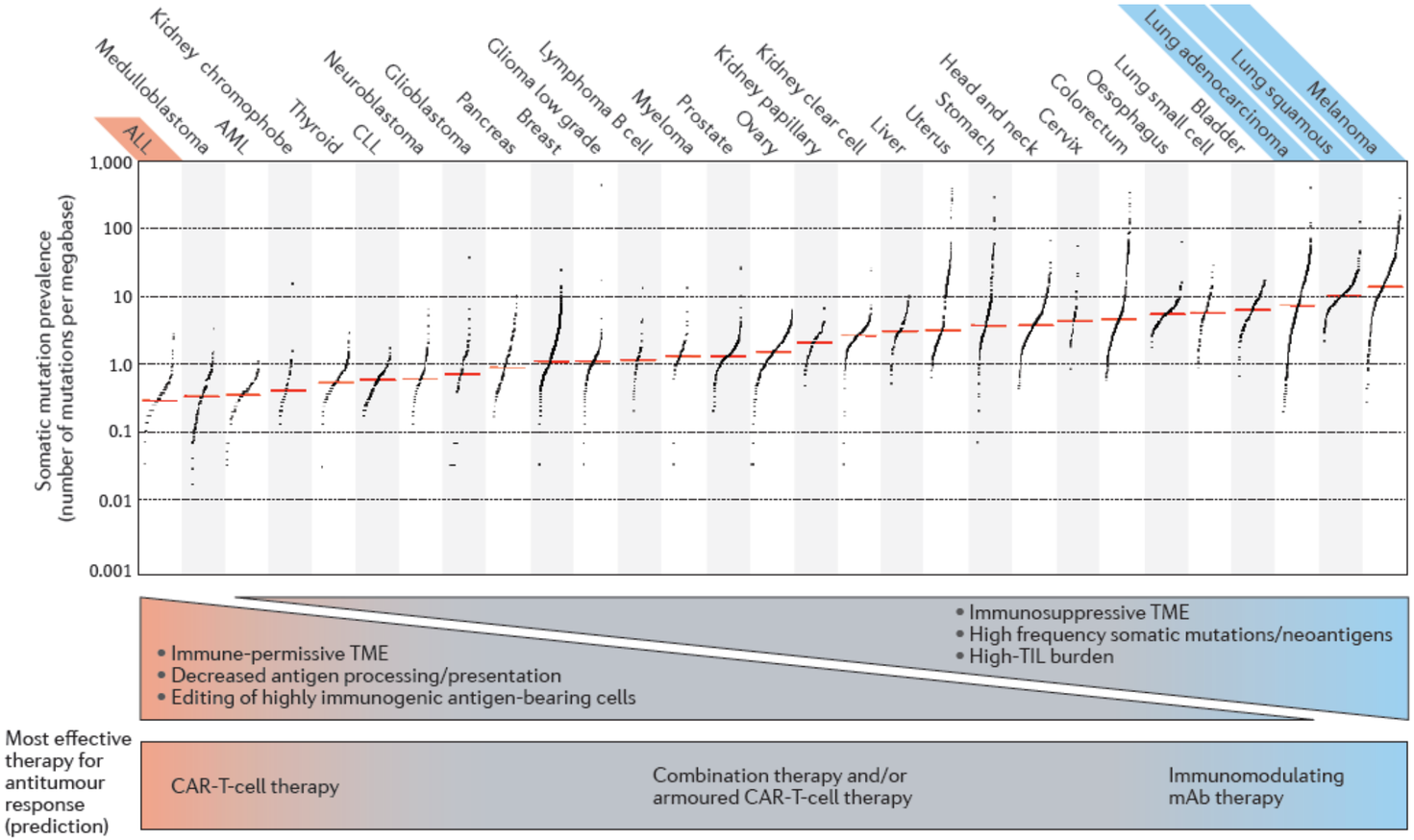
- Still modest survival rates
- Limits response to already existing T cell repertoire
- Reveals an important role of neoantigens

Question – how could we boost the immune response to elicit more effective and broader tumor neoantigen specific T cell responses?

Brahmer et al., NEJM 2015
Rizvi et al., Science 2015

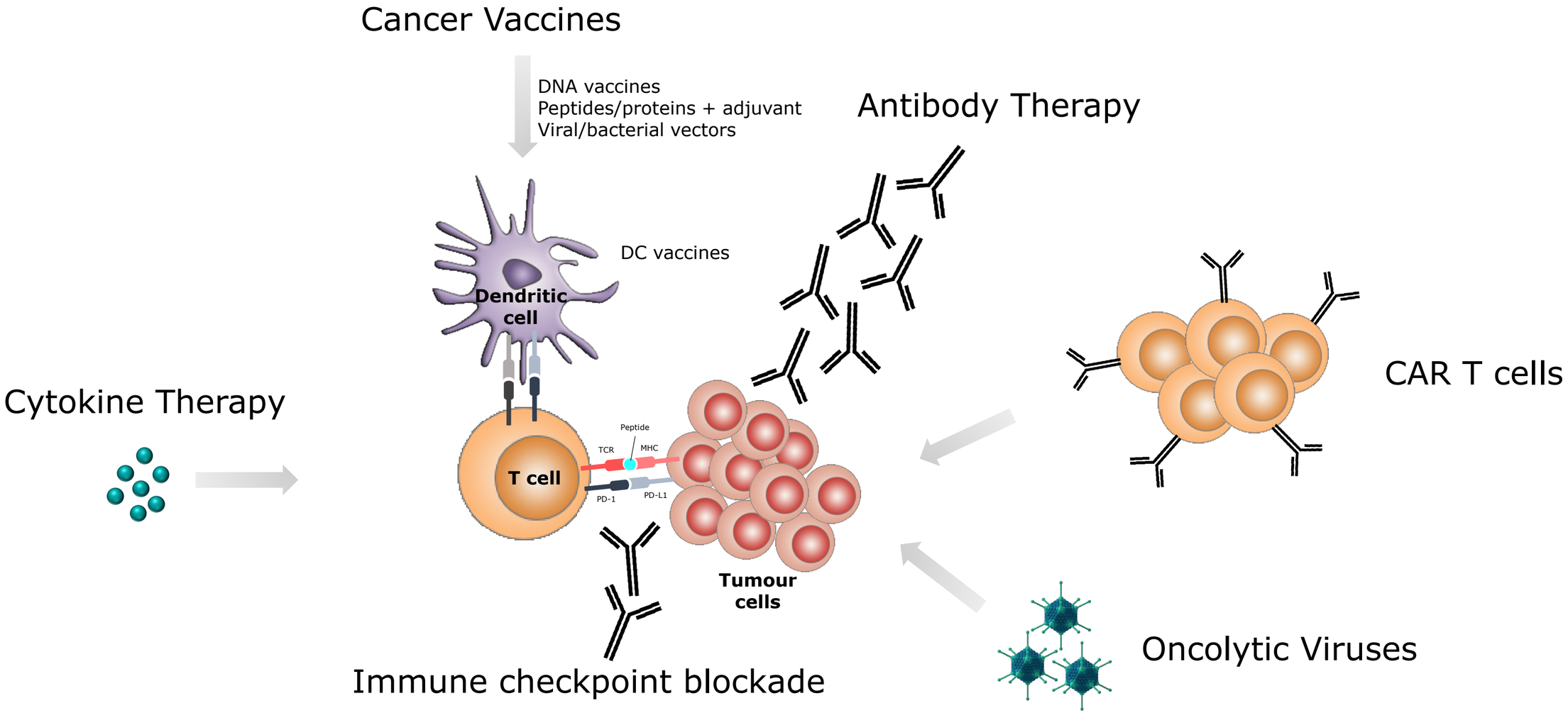
Neoantigens – Tumour-specific newly arisen Antigens





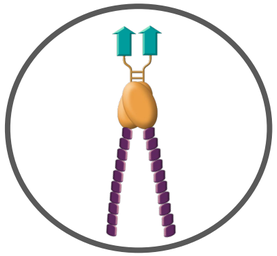
Source: Khalil DN et al., Nat Rev Clin Oncol. 2016 Mar 15

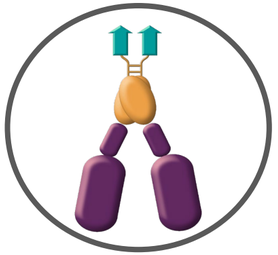
Types of Immunotherapy



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

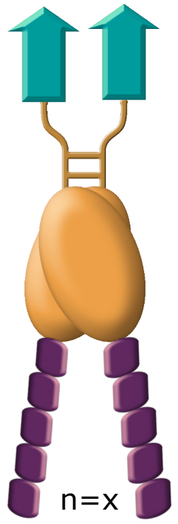
The Vaccibody Technology Platform was developed based on the concept of **targeting antigen to APC** in order to create more efficacious vaccines.

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: the multiple effect of MIP-1α as targeting unit

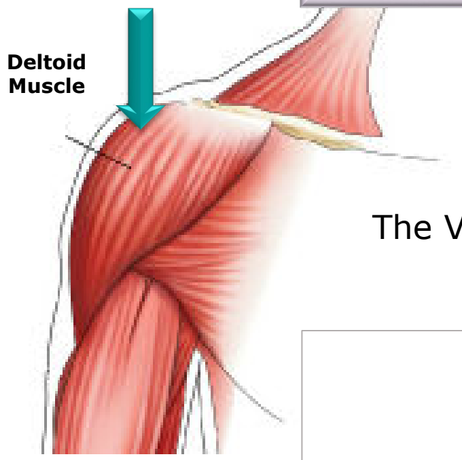
Administration (i.m.) of DNA plasmid

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

Target – Attract – Mature – Deliver – Cross-present

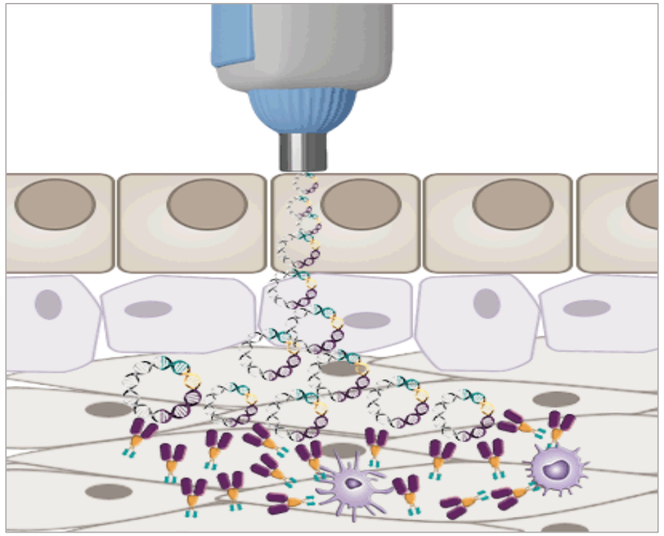
MIP-1α: Skewing the immune system to a CD8+ killer T-Cell response

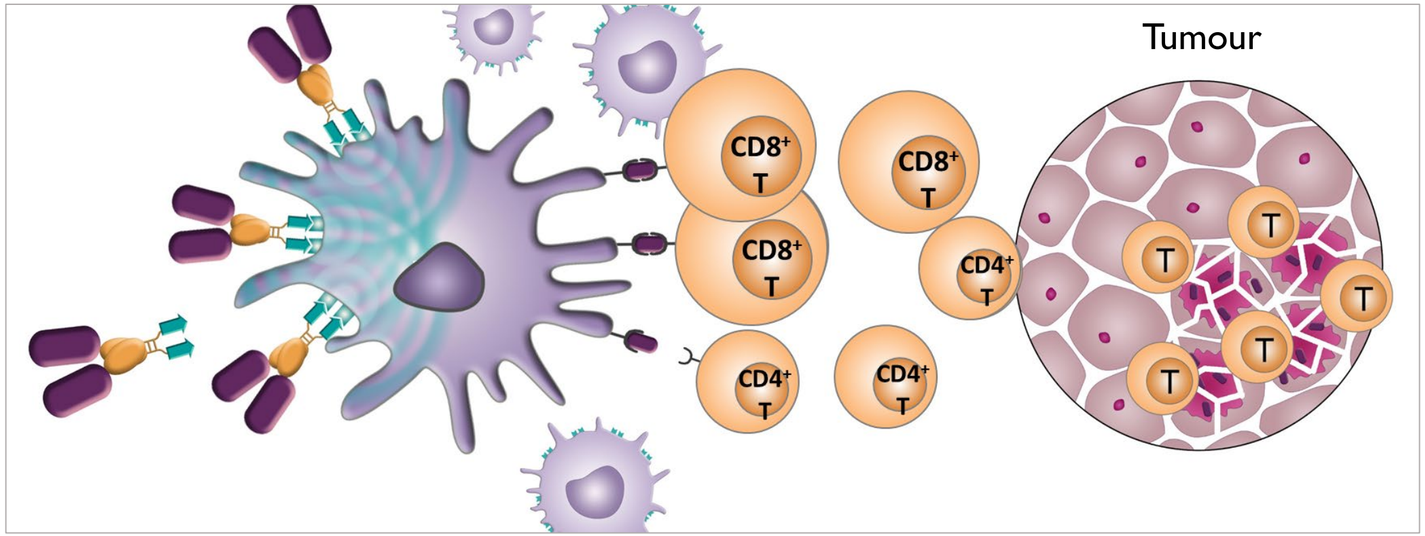
- Direct targeting & attraction of antigen presenting cells, high local vaccine concentration
- Enhanced T cell immunity obtained with fewer and lower doses
- Faster and longer lasting immune responses
- **Stronger potential to kill cancer cells**



The Vaccibody uses the muscle cell as a factory

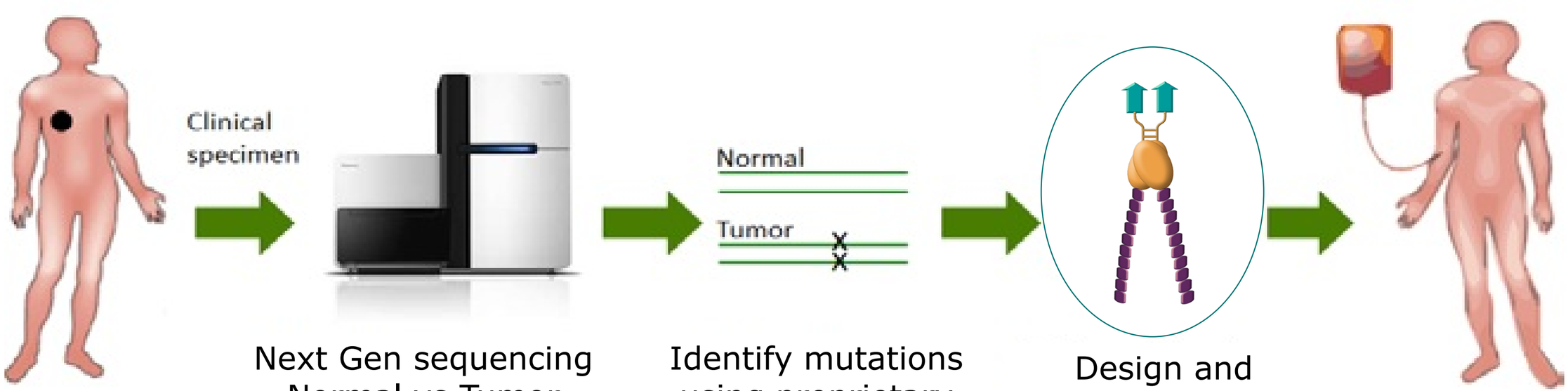
PharmaJet®





Targeting is elicited by the MIP-1α chemokine

A Personalised Cancer Neoantigen Vaccine Designed per Patient

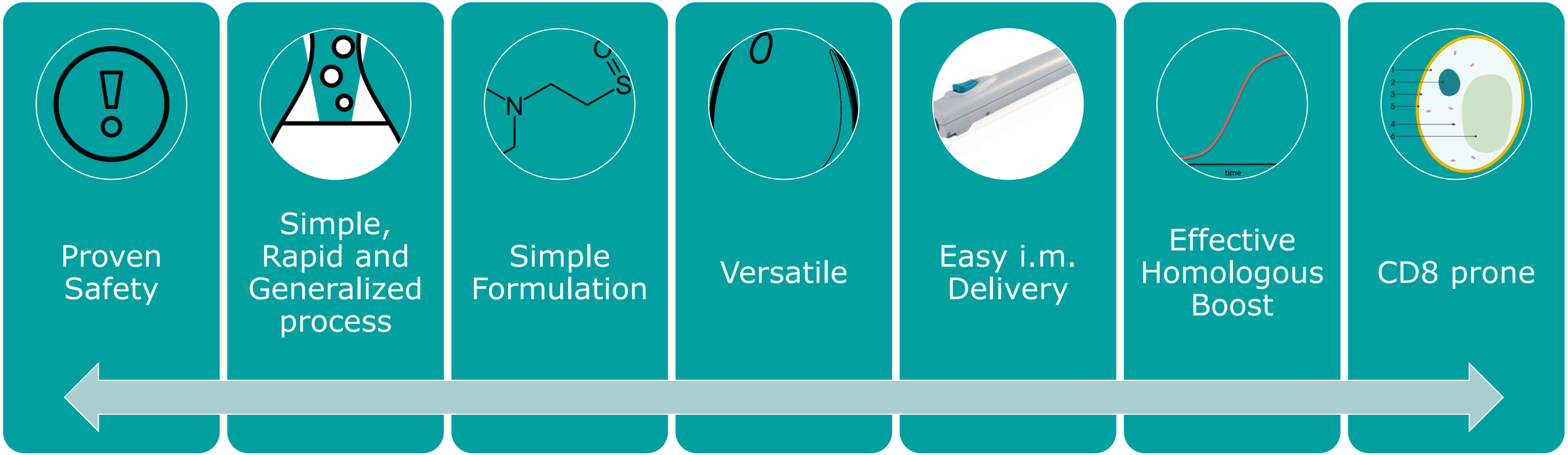


Next Gen sequencing
Normal vs Tumor

Identify mutations using proprietary bioinformatics

Design and manufacture neoantigen vaccine

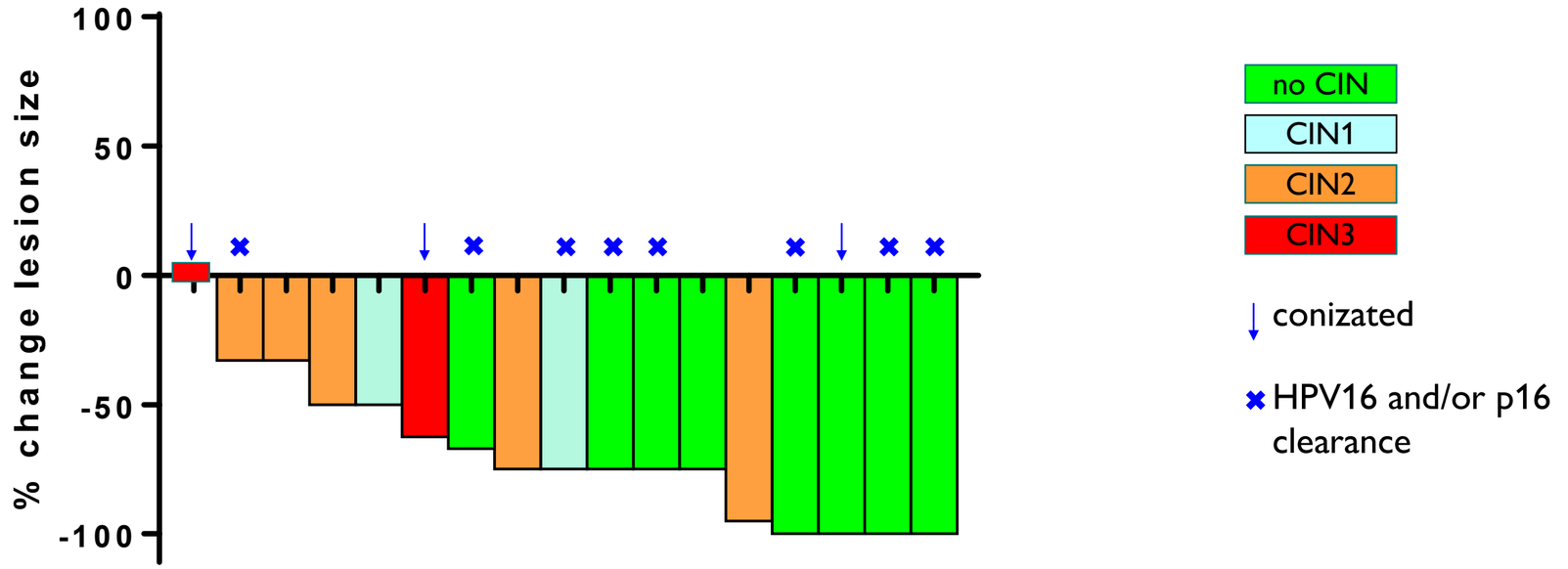
Naked DNA plasmid ideal for personalized manufacturing



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

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:

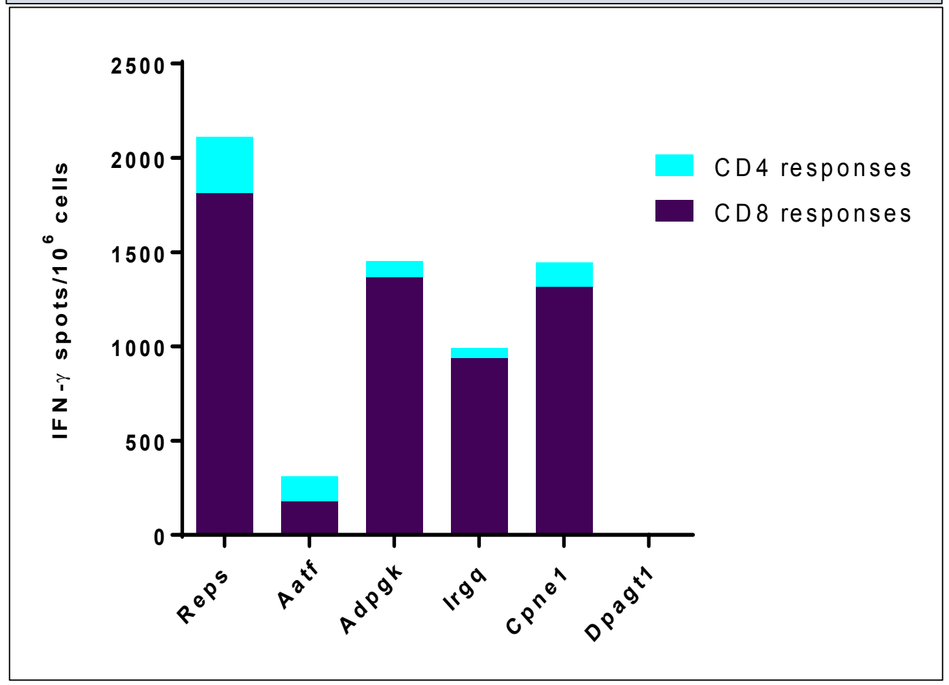
- Lesion size reduction in all patients followed >4 months
- CIN regression to CIN1 or no CIN in 10 patients
- HPV16 and/or p16 clearance in 8 patients

VB10.NEO has a unique ability to induce strong neoepitope-specific CD8 responses due to crosss-presentation

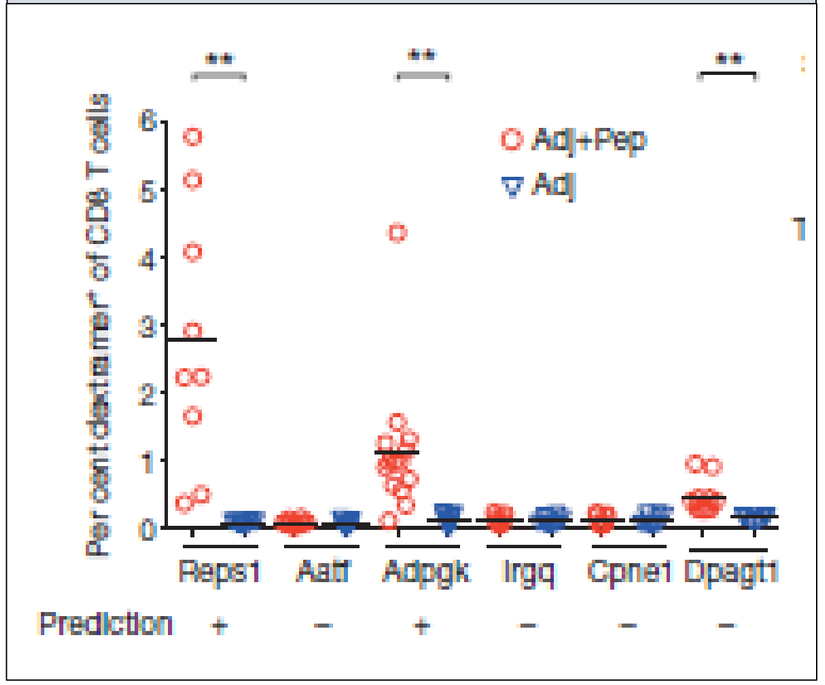
MC38 melanoma model

Yadav et al., 2014

VB10.NEO



Peptide + poly I:C + anti-CD40 mAb

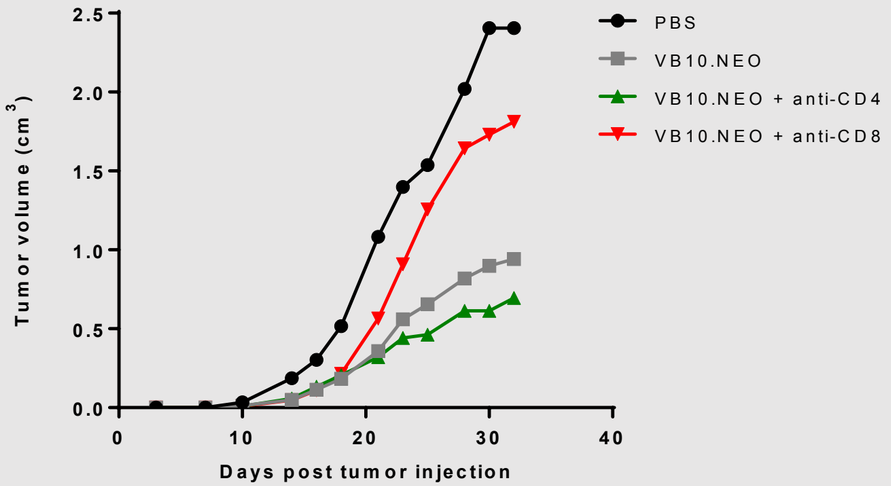


-VB10.NEO induces a strong CD8 T cell response, combined with a CD4 response **to 5 of 6** MC38 neoantigens.

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

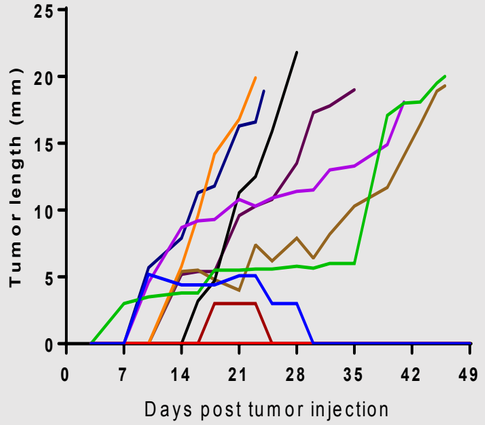
Neoepitope-specific CD8 T cells are crucial for tumour protection

Average, all groups

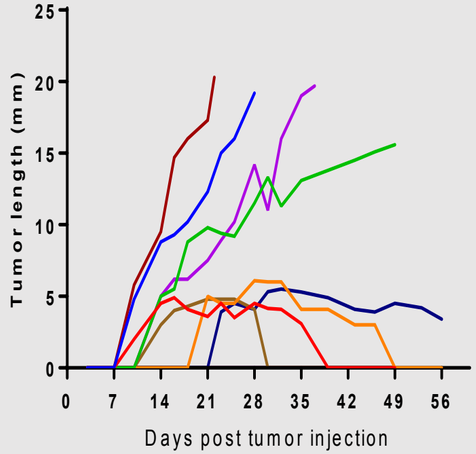


Individual growth curves

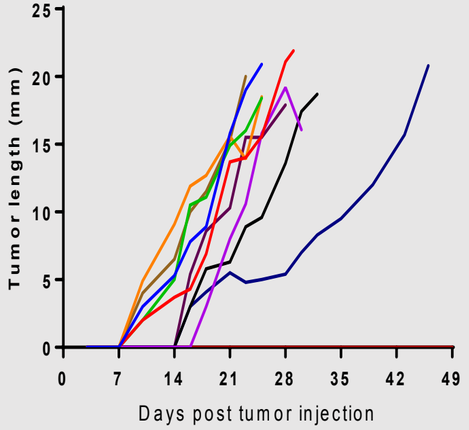
VB10.NEO



VB10.NEO + anti-CD4

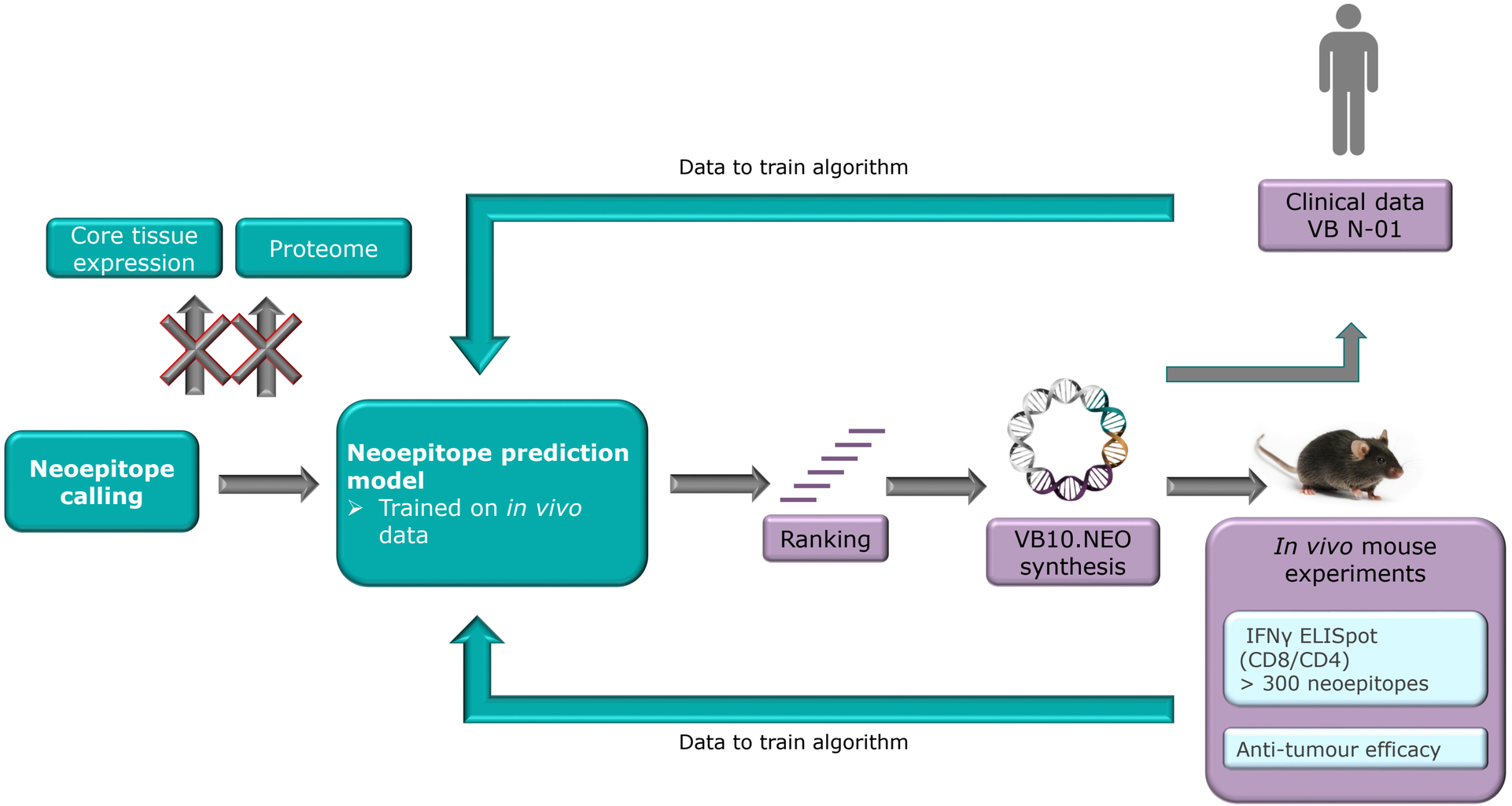


VB10.NEO+ anti-CD8



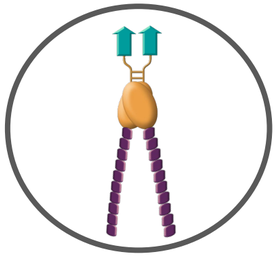
Depletion of CD8 T cells prohibit tumour protection in VB10.NEO vaccinated mice, indicating a crucial role of neoepitope-specific CD8 T cells for anti-tumour efficacy

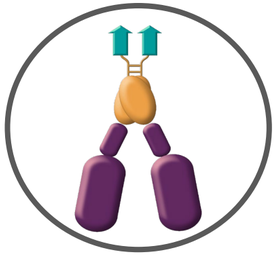
Development of proprietory Neoepitope Selection NeoSELECT™ matching VB10.NEO delivery



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		

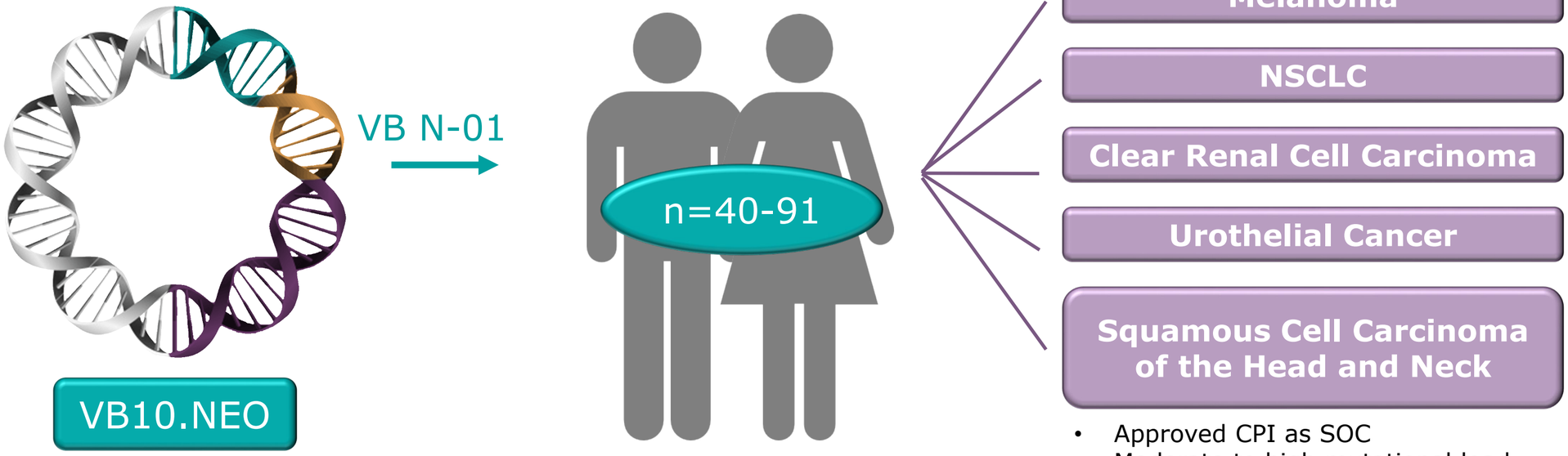




Tecentriq® (Atezolizumab) is Roche's proprietary anti-PD-L1 checkpoint inhibitor (CPI)

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

Careful Selection of Experienced Clinical Sites

Active sites

Prof. Dr. med. Jürgen Krauss*
National Centre for Tumour Diseases (NCT), Medical Oncology

Heidelberg, Germany 01

Prof. Dr. med. Angela Krackhardt
Klinikum Rechts der Isar, TUM

Munich, Germany 02

Prof. Dr. med. Elke Jäger
Clinic Nordwest

Frankfurt am Main, Germany 03

Approved, but not yet activated

PD Dr. med. Sebastian Ochsenreither
Charité Campus Benjamin Franklin

Berlin, Germany 04

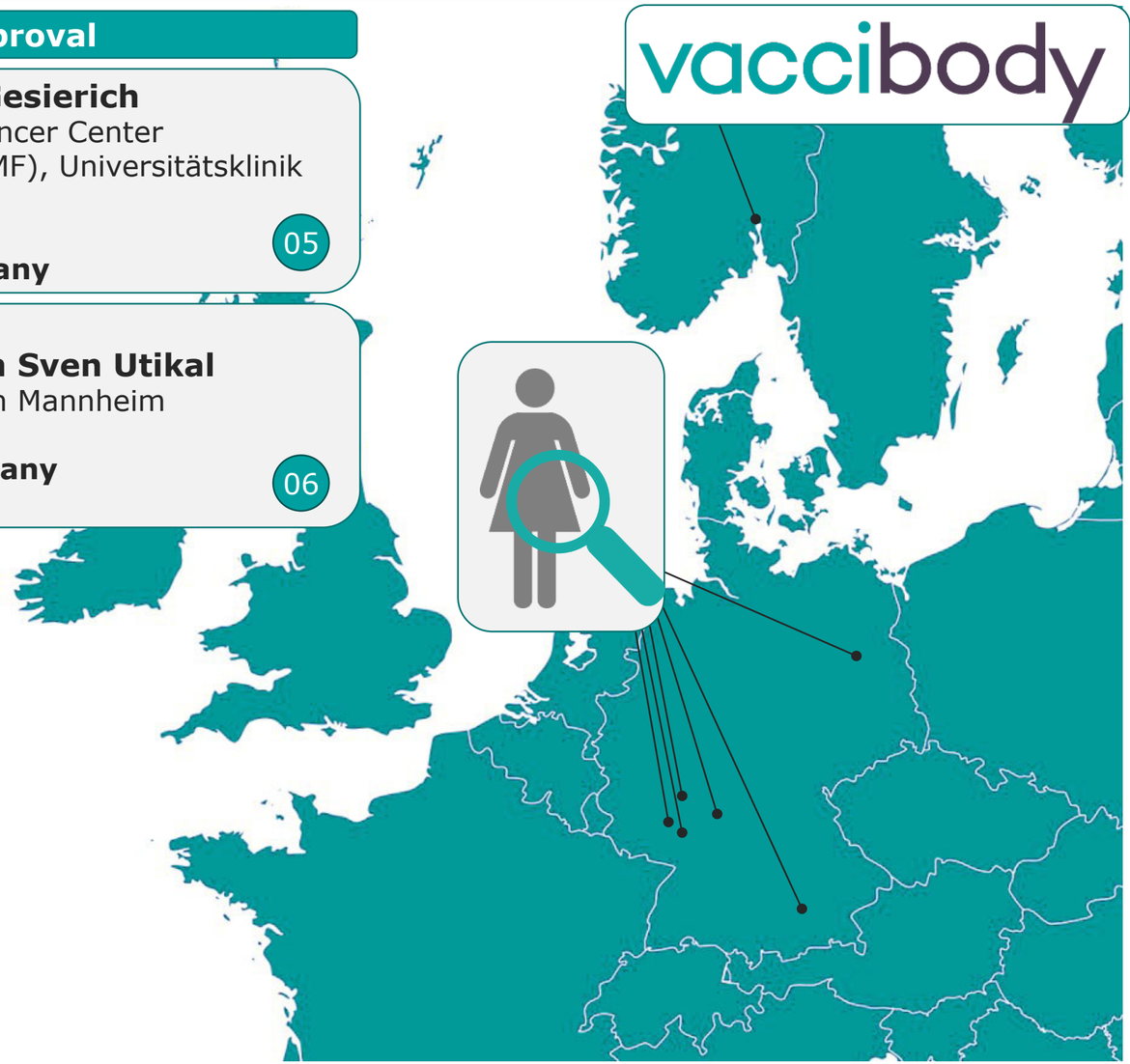
Awaiting approval

Dr. med. Anja Gesierich
Comprehensive Cancer Center Mainfranken (CCCMF), Universitätsklinik Würzburg

Würzburg, Germany 05

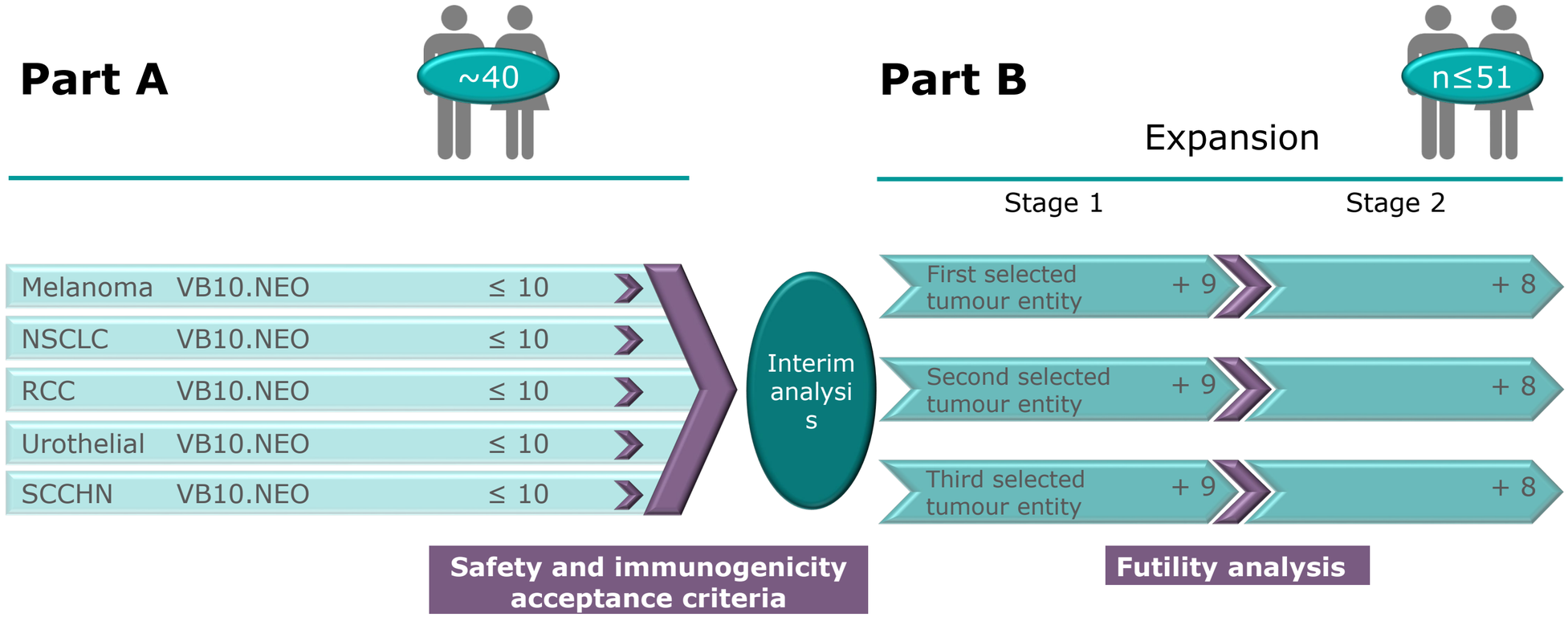
Prof. Dr. Jochen Sven Utikal
Universitätsmedizin Mannheim

Mannheim, Germany 06



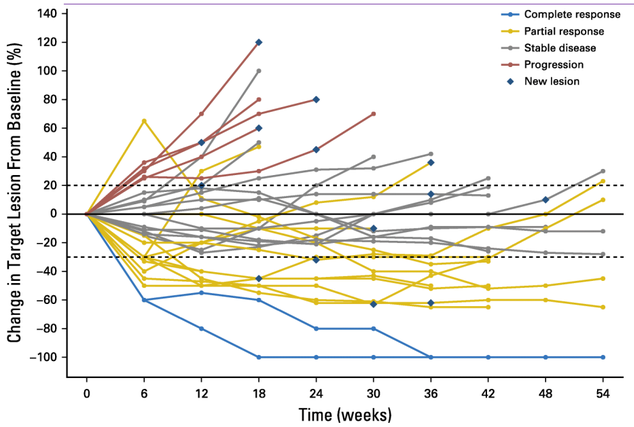
* Coordinating Investigator

Study Design and Current Status, VB N-01



- 100% vaccine manufacturing success for all patients with a successful biopsy so far
- 20 neoepitopes selected for all patients in the trial

Study Design and Treatment Schedule VB N-01



12 months

24 months

6 weeks

Sequencing, Synthesis & Manufacturing

Vaccination Prime

Vaccination Maintenance

Follow Up

CPI treatment >12 weeks

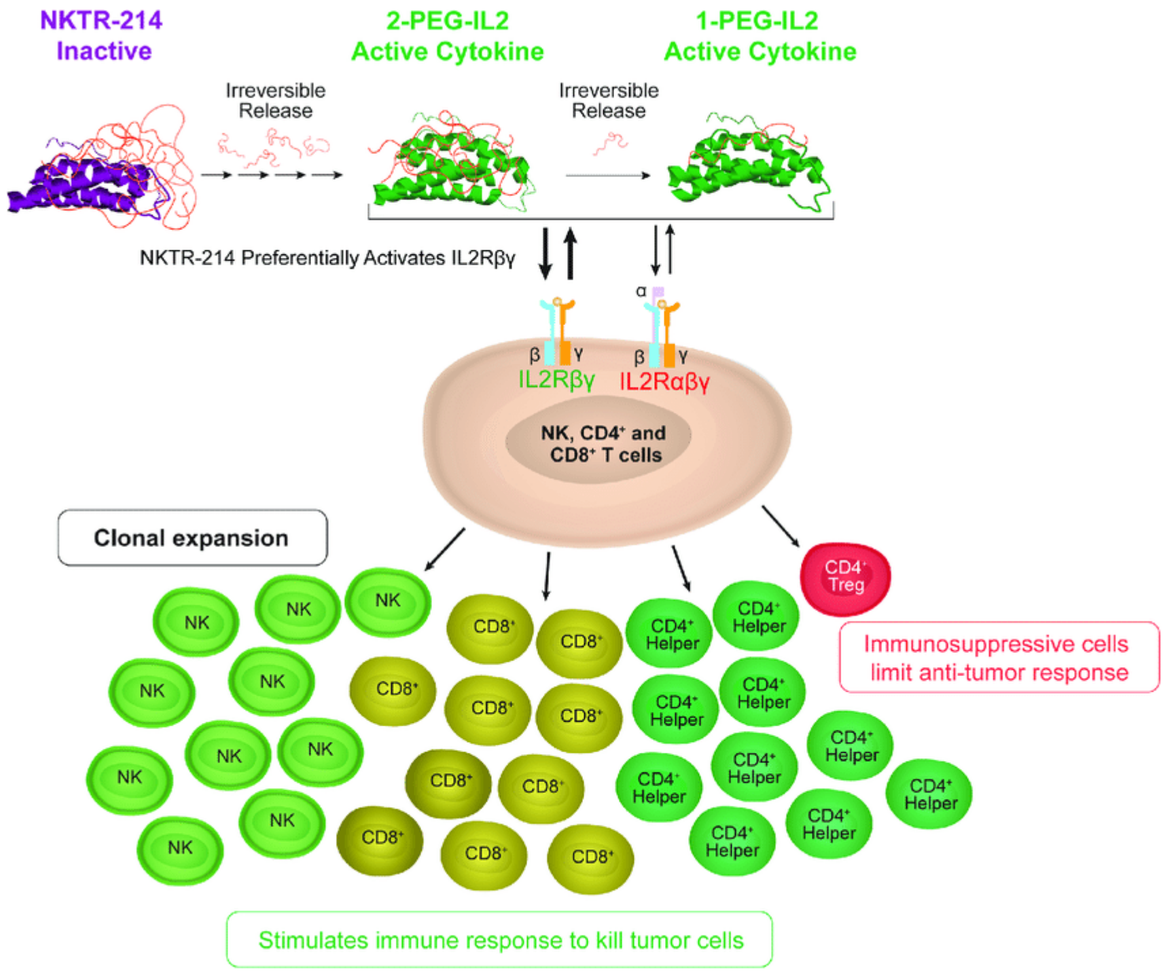
Consent + Biopsy

Week	0	3	6	10	14	18	22	26	30	34	38	42	46	50
Dose #	1	2	3	4	5	6	7	8	9	10	11	12	13	14

- Inclusion criteria: previous treatment with CPI for >12 weeks and stable disease (or partial response or mixed response) at enrollment. Limited tumour reduction expected from continous CPI treatment only

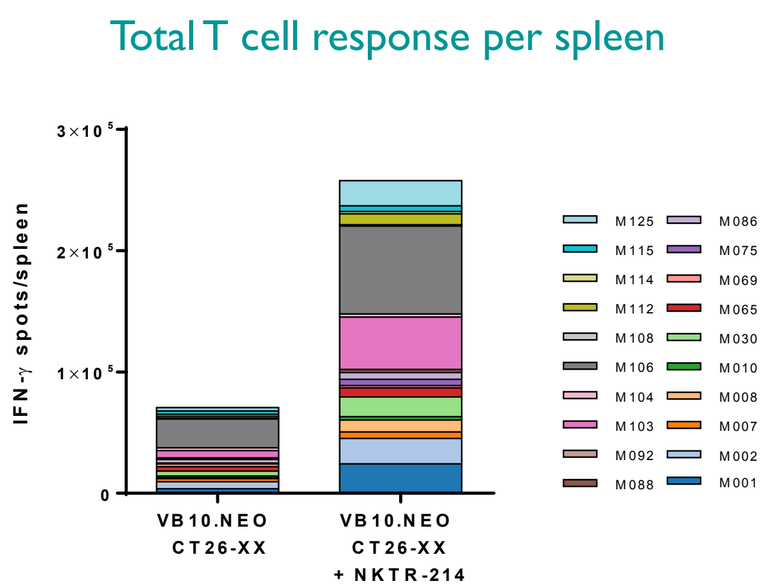
Tsimberidou et al., 2018

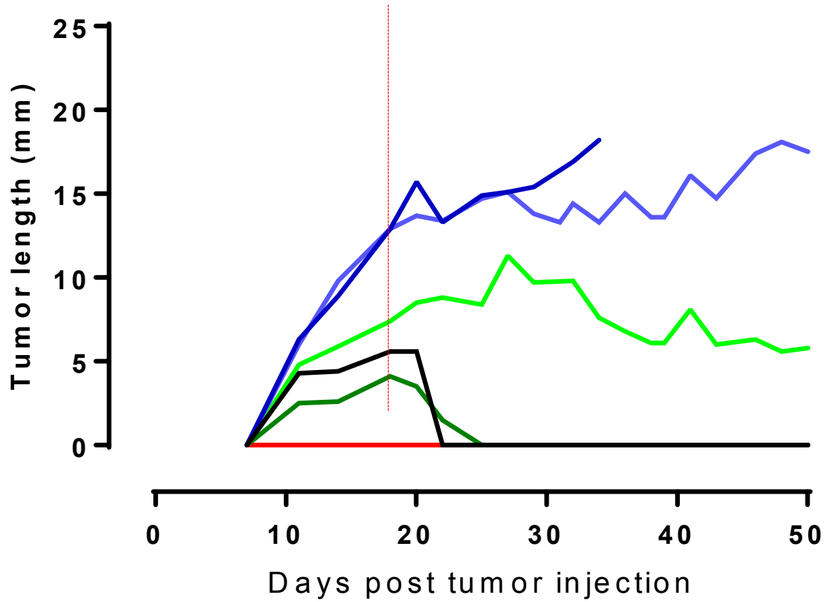
Stategic Collaborations: Bempegaldesleukin (NKTR-214) has the potential to significantly expand neoantigen-specific CD8+ T cells



NEKTAR®

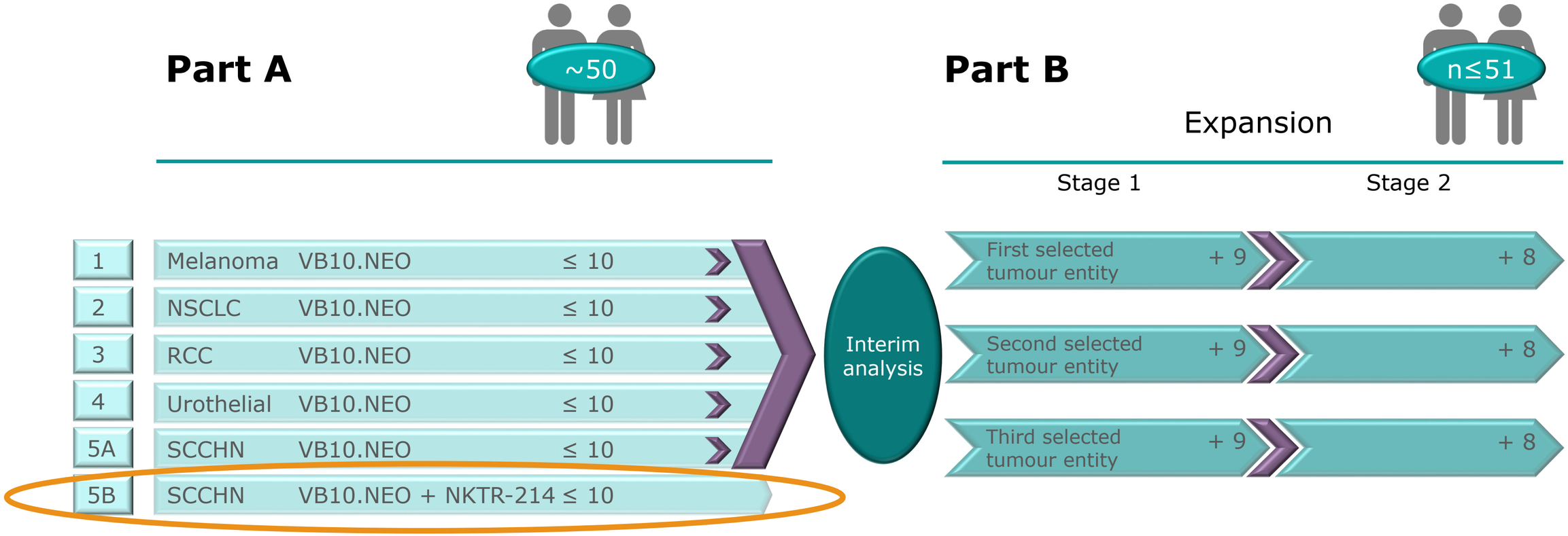
Combination of VB10.NEO and NKTR-214 greatly synergizes





- Stronger neoepitope-specific T cell responses leading to improved anti-tumour efficacy is observed when adding NKTR-214 to VB10.NEO and checkpoint inhibitor treatment

Expansion of the study planned in 2019– add NKTR-214 and expansion cohorts



- First patient enrolled planned mid 2019
- Prepare for interim analysis first indication to trigger expansion-end 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)

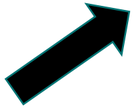
-Needle-free

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

-Rapid, strong, long-lasting

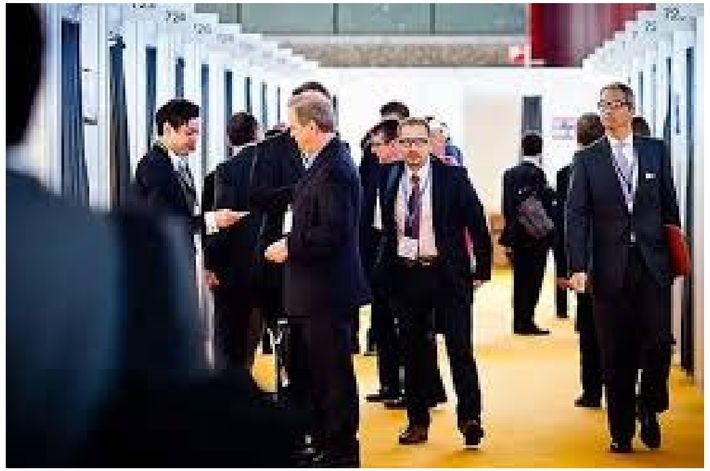
-CD8 dominated

4. Vaccine administration and immunogenicity



Vaccibody provide a Rapid, Cost-effective and Efficacious solution

Success Factors



Vaccibody team –carefully recruited!

vaccibody

www.vaccibody.com