DET SUNDHEDSVIDENSKABELIGE FAKULTET
KØBENHAVNS UNIVERSITET

REGION Herlev Hospital

Vacciner i behandlingen af lungekræft

DANSK LUNGE CANCER
GRUPPE ÅRSMØDE 2026

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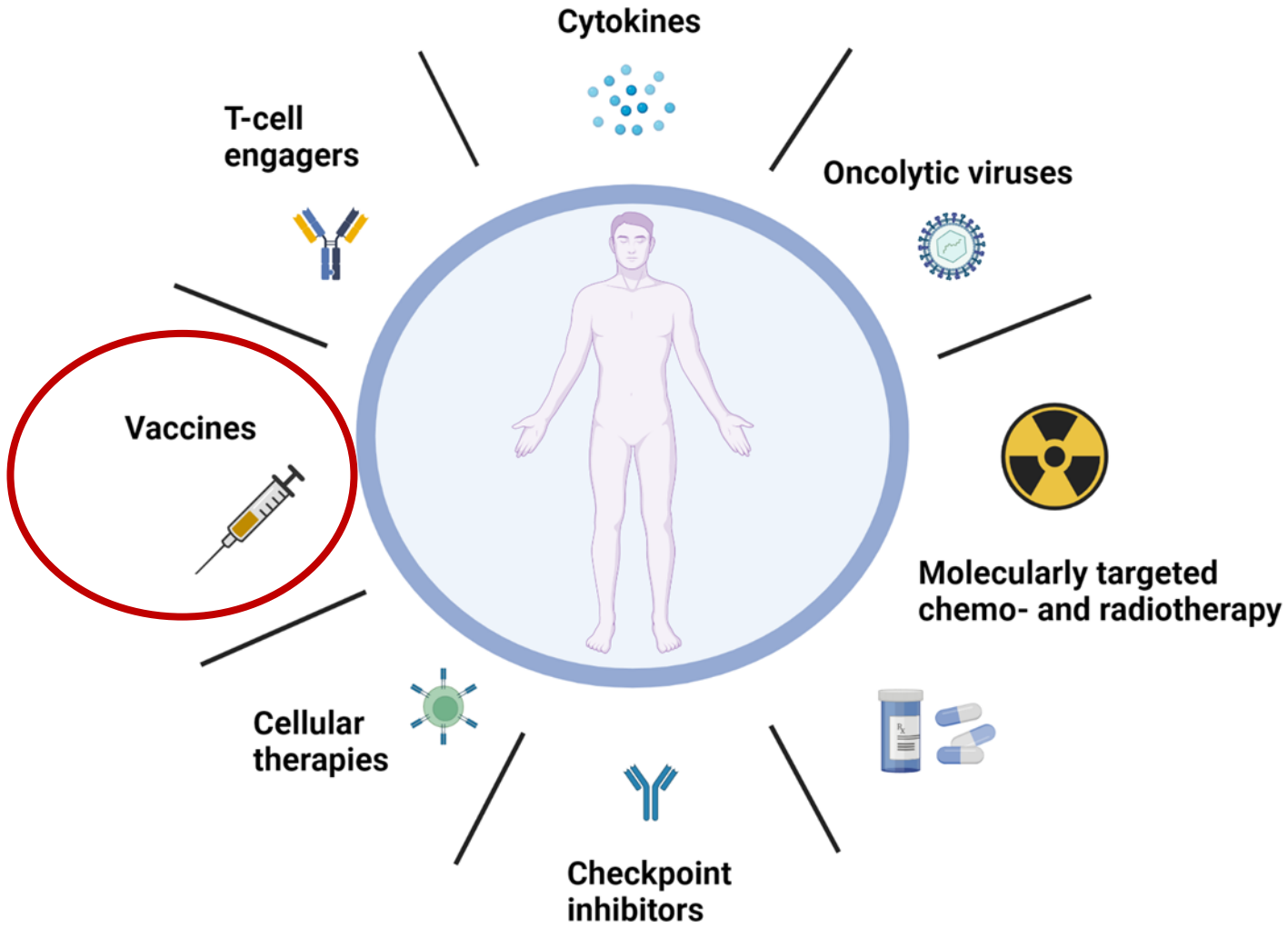
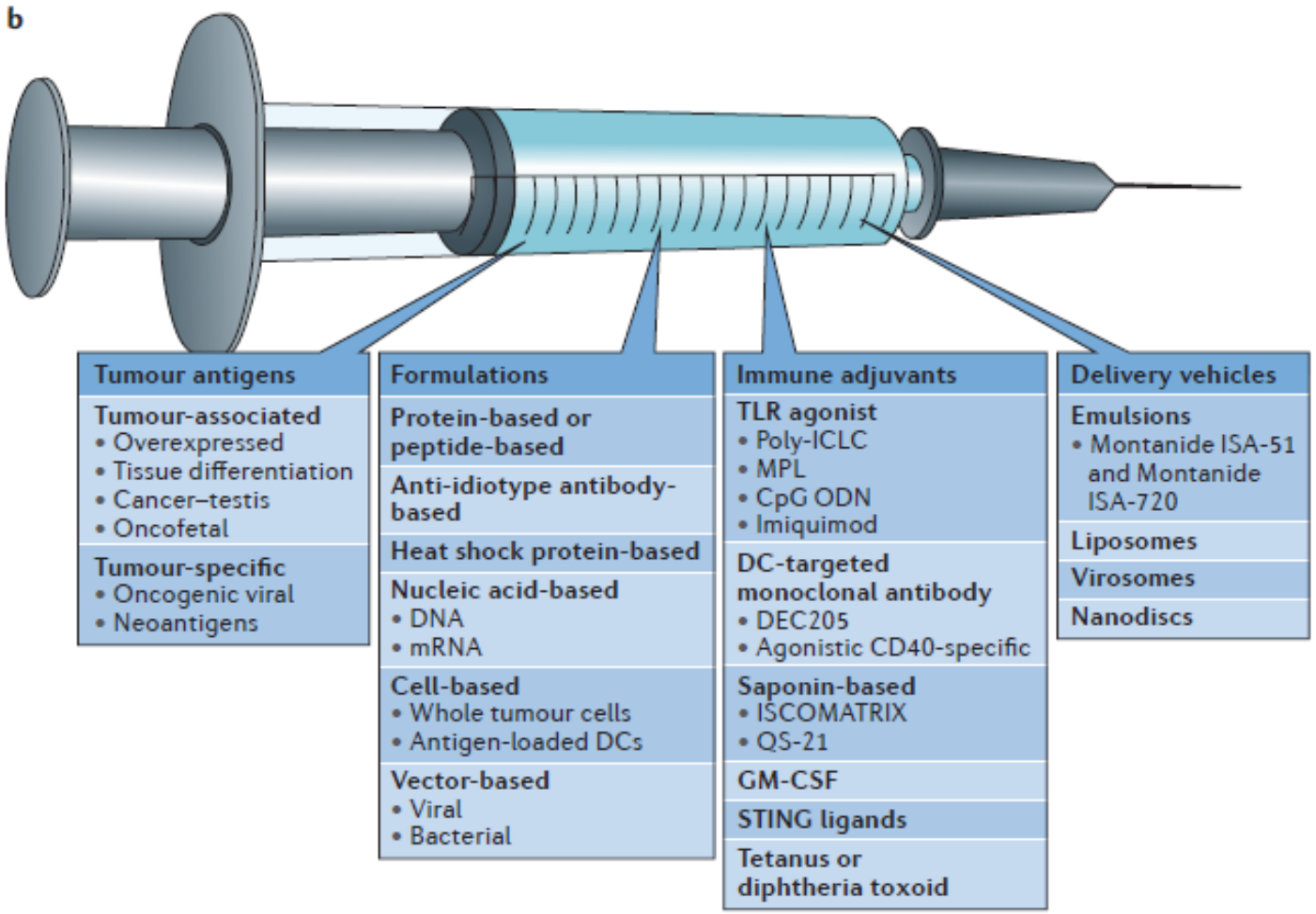
Types of Cancer Immunotherapy in clinic stage



What is a cancer vaccines ?

CANCER VACCINES

Components of cancer vaccines



Hu et al Nature Rev Immunol 2017

CANCER VACCINES

Classification of cancer vaccine types

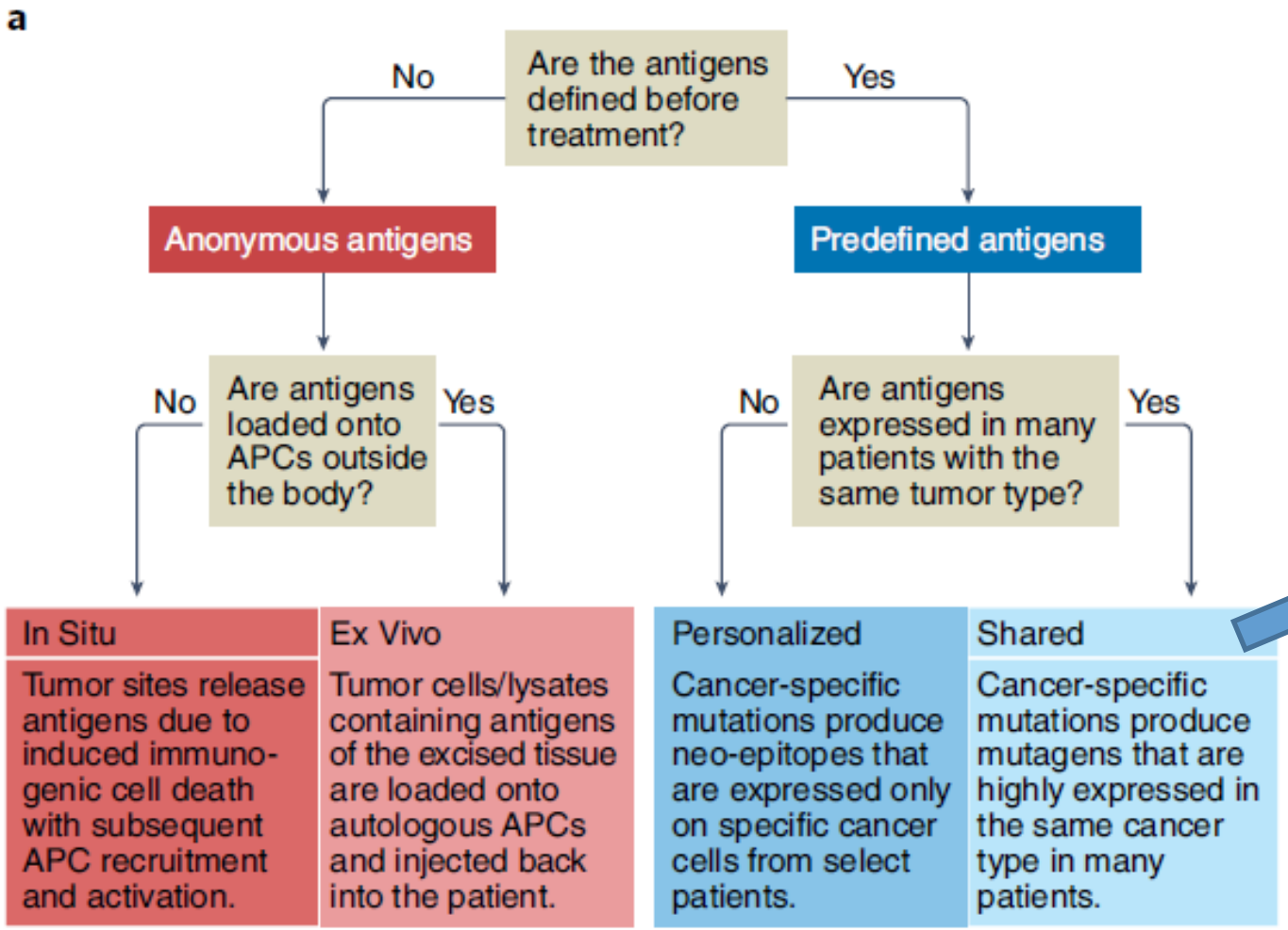


Table 1 | TSAs and TAAs classified into four groups with examples

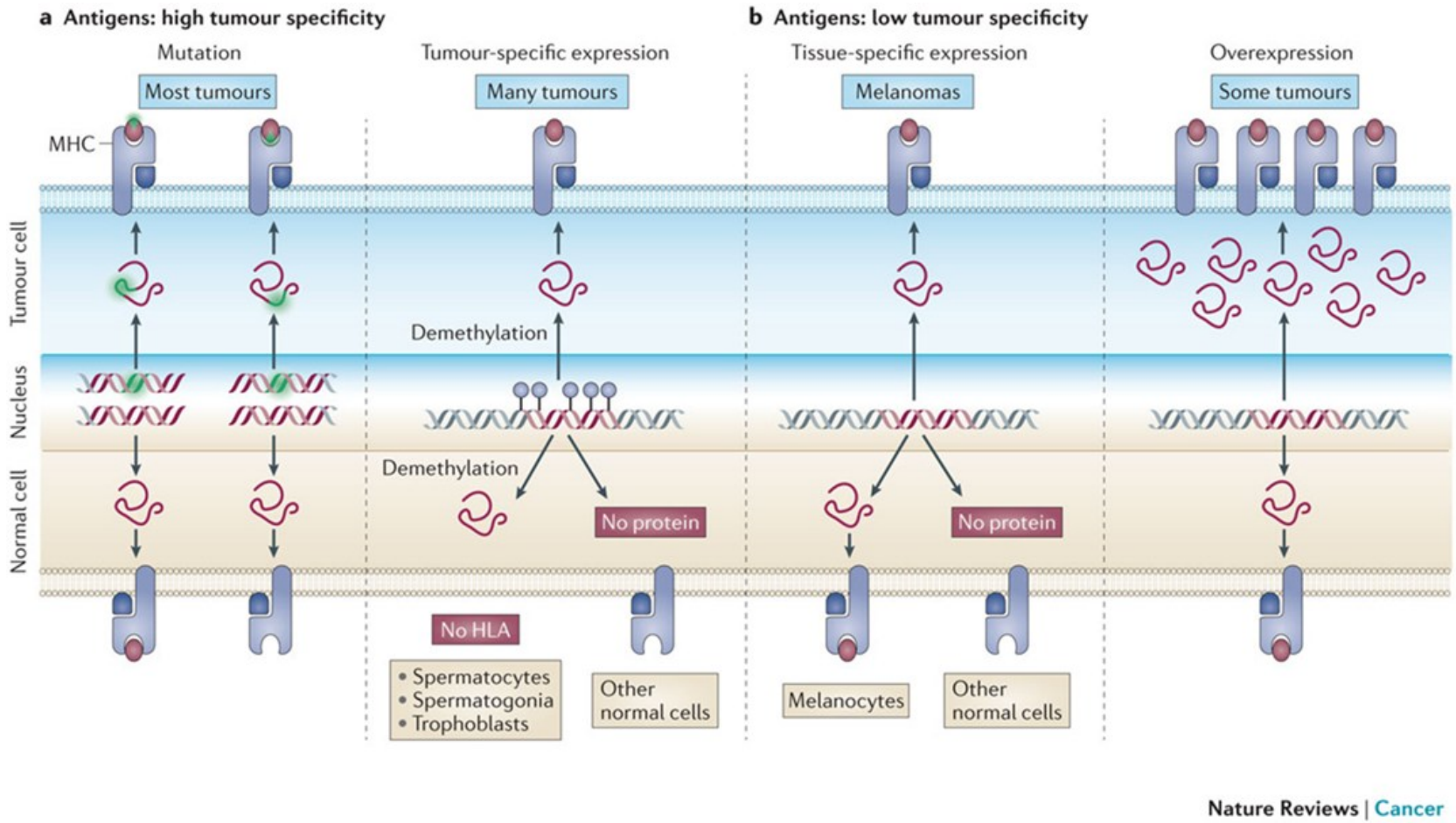
TSA		TAA	
Viral	**Mutated self**	**Development specific**	**Tissue specific**
LMP1, LMP2	EGFRvIII	WT1	HER2/Neu
HPV E6/E7	$KRAS^{G12C}$	MAGE-A3	MUC1
	$BRAF^{V600E}$	NY-ESO-1	gp100

$BRAF^{V600E}$, v-raf murine sarcoma viral oncogene homolog B1 V600E mutation; MUC1, mucin 1.

Lin et al Nature Cancer 2022

CANCER VACCINES

Different ways for tumor antigens to emerge

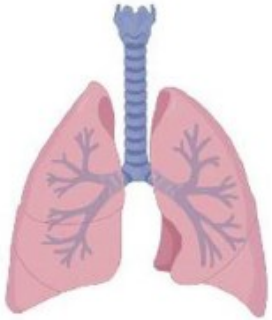


Coulie et al., Nat Rev Cancer 2013

CANCER VACCINES

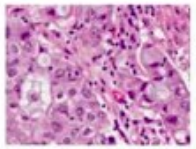
Tumor antigens in lung cancer

(A) Tissue Origin

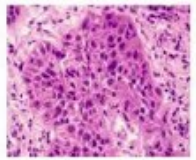


(B) Histology

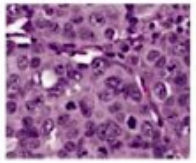
Non-Small Cell Lung Cancer or NSCLC (~85%)



Adenocarcinoma (~45%)

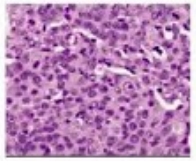


Squamous Cell (~25%)



Large Cell (~5-10%)

Small Cell Lung Cancer or SCLC (~15%)



(C) Neoantigen Targets

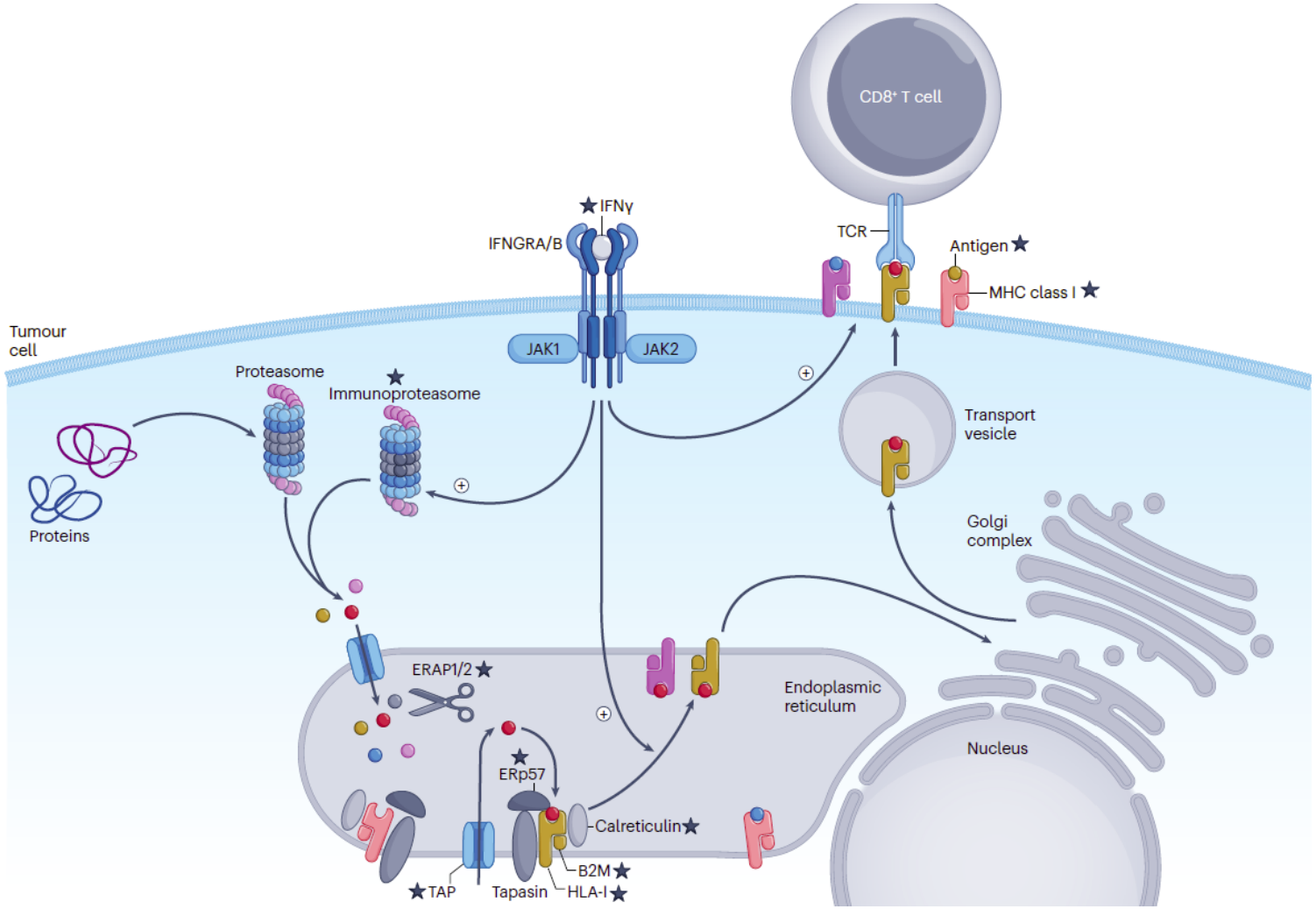
	Subsets	Targets
TAAs	Over-expressed proteins	EFGR, WT-1, MUC1, HER2, surviving, telomerase
	Cancer germline proteins	MAGE, NY-ESO-1, BAGE, GAGE
	Tissue-differentiation proteins	PSA, PAP, gp100, MART-1, CEA, TRP2
TSAs	Viral oncoproteins	HPV (E6/E7), LMP, HBsAg, EBV, HTLV
	Shared neoantigens	Mutated RAS, ALK, p53, Labyrinthin
	Individual neoantigens	Patient-specific

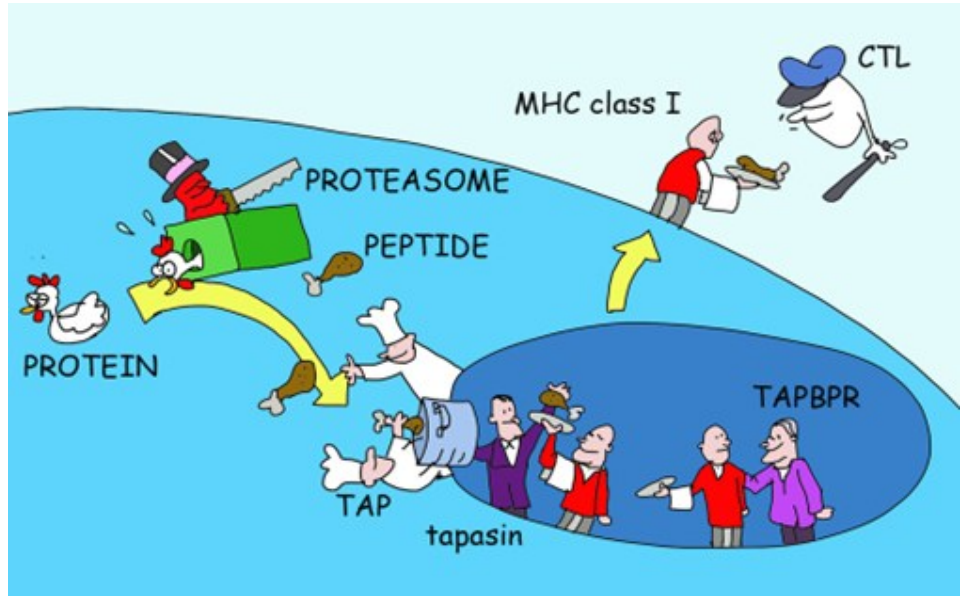
	Subsets	Targets
TAAs	Over-expressed proteins	DLL3, B7-H3, TROP2, SEZ6
	Tissue-differentiation proteins	Glycosphingolipids
TSAs	Shared neoantigens	p53
	Individual neoantigens	Patient-specific

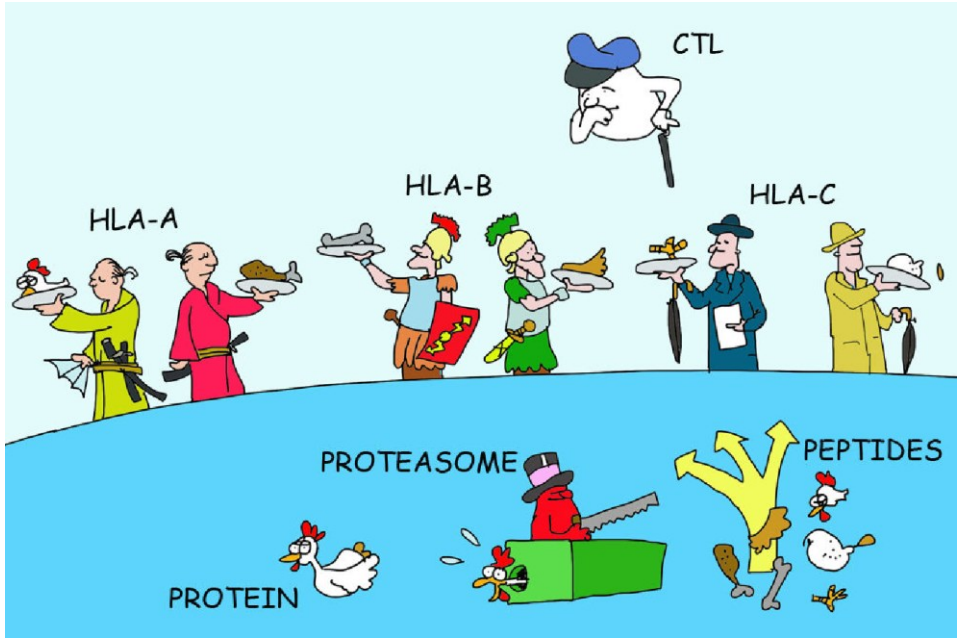
Tang et al. Journal of Hematology & Oncology 2026

CANCER VACCINES

Cancer antigen presentation



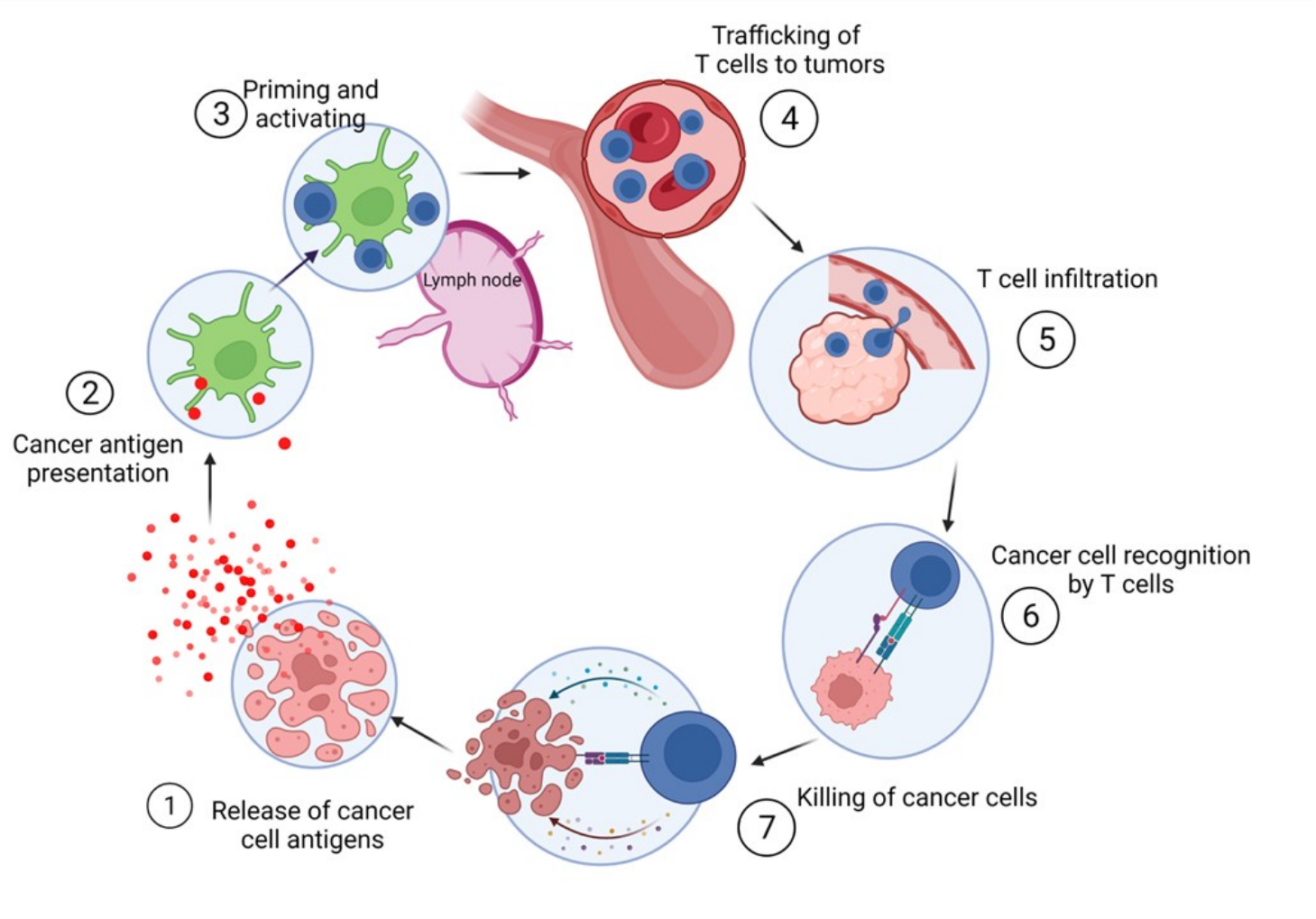




Yang et al Nature rev Clin Oncol 2023

CANCER VACCINES

The cancer immunity cycle

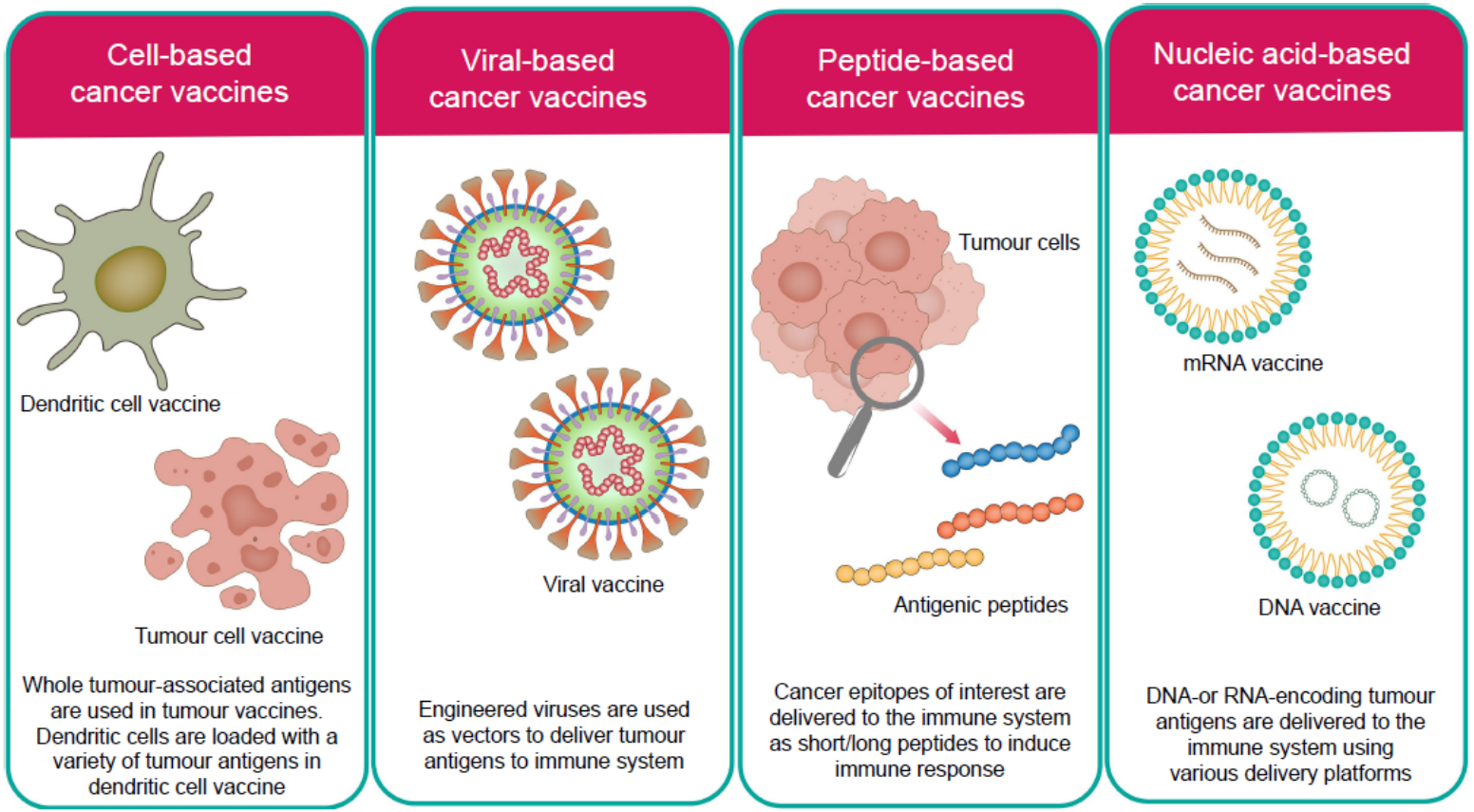


Created with biorender.com

Adapted from Chen and Mellmann, Immunity 2013

CANCER VACCINES

Components of cancer vaccines



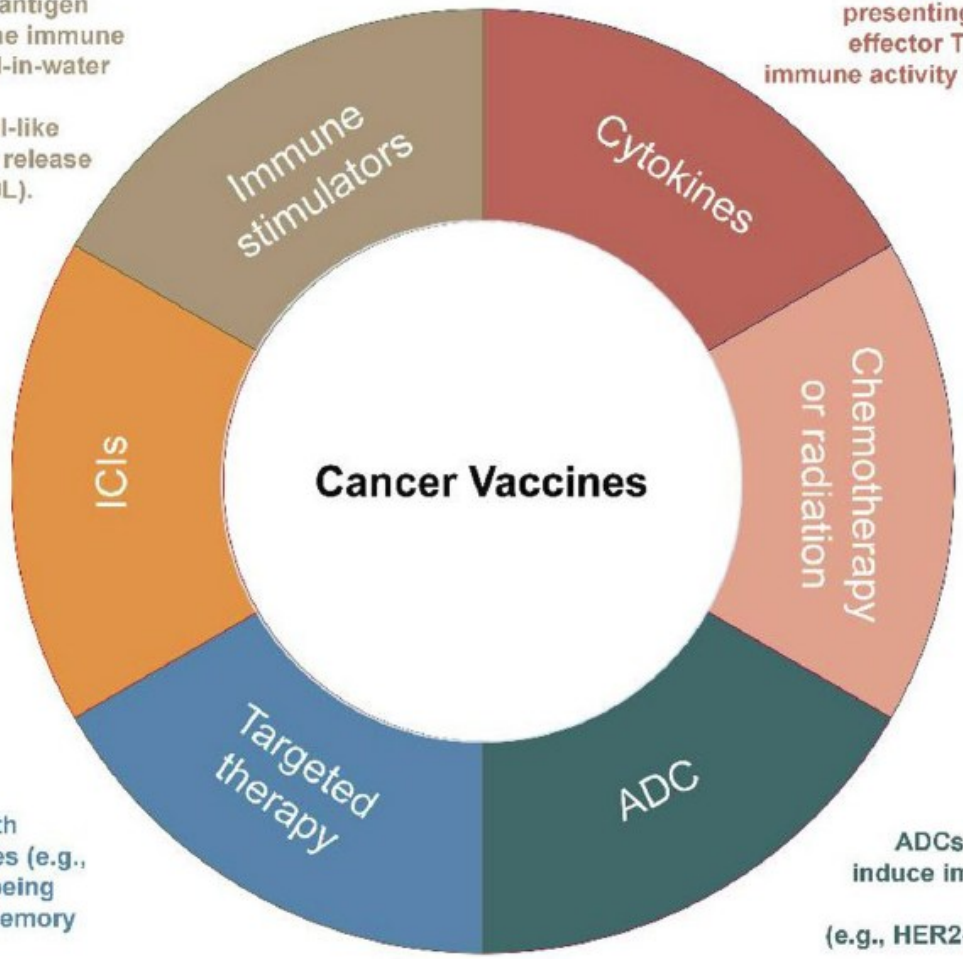
Clifford et al BJS Open 2026

CANCER VACCINES

Vaccine adjuvants and combinations

Depot-type adjuvants prolong antigen retention and release, enhancing antigen uptake by APCs and sustaining the immune response (e.g., aluminum gels, oil-in-water emulsions, liposomes).
Synthetic molecules targeting Toll-like receptors (TLRs) induce cytokine release (e.g., poly-ICLC, imiquimod, CD40L).

Cytokines recruit T cells and antigen-presenting cells to lymph nodes, support effector T-cell proliferation, and enhance immune activity in the tumor microenvironment (e.g., IL-2, IL-7, IL-15).



Combining cancer vaccines with ICIs helps overcome tumor induced immunosuppression. Vaccines prime de novo T-cell responses, which ICIs amplify and sustain.

Cytoreductive therapies like chemotherapy and radiation can reduce tumor size and achieve rapid disease control. Combining these with cancer vaccines may provide longer-term disease control. However, chemotherapy can blunt immune responses.

Targeted therapies combined with mutation-specific cancer vaccines (e.g., targeting EGFR, ALK, RAS) are being developed to promote durable memory immune responses in NSCLC.

ADCs deliver cytotoxic agents that can induce immunogenic cell death, leading to effector T-cell activation (e.g., HER2-directed, TROP2-directed ADCs).

Tang et al. Journal of Hematology & Oncology 2026

Lung cancer vaccine studies

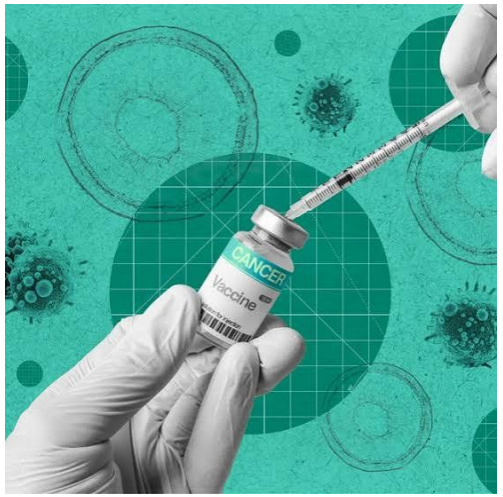
Multiple published phase I-II studies and some phase III studies.

- Several non-randomized phase II studies indicating potential benefit
- Phase III studies are either negative og terminated prematurely

Clinicaltrial.gov

- Lung cancer AND vaccine therapy: 298 trials.
  - 141 completed
  - 61 terminated/withdrawn
  - **28 recruiting**

- Recruiting clinical trials (28)
  - 19 phase I-I/II
  - 5 phase II
  - 1 phase III

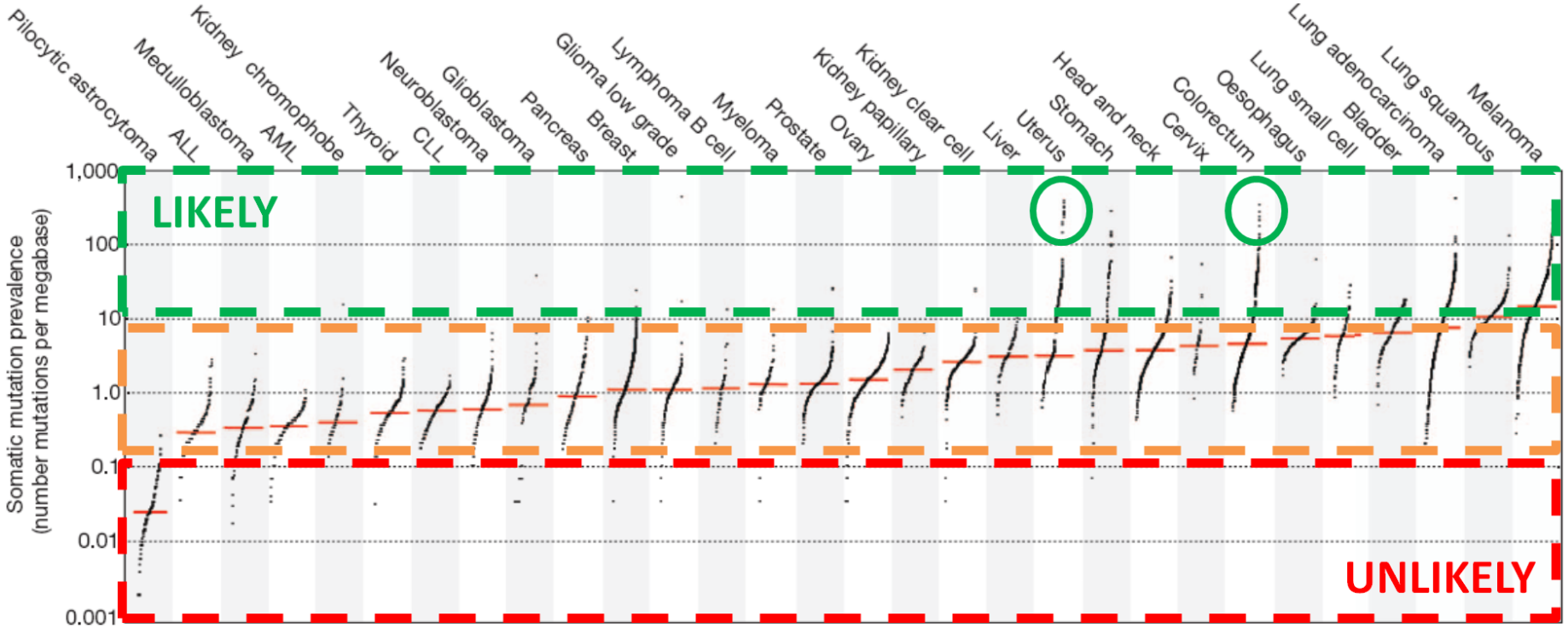


Personalized neoantigen targeting vaccines

CCIT DENMARK

NEOANTIGEN TARGETING VACCINES
Mutational load in different cancers

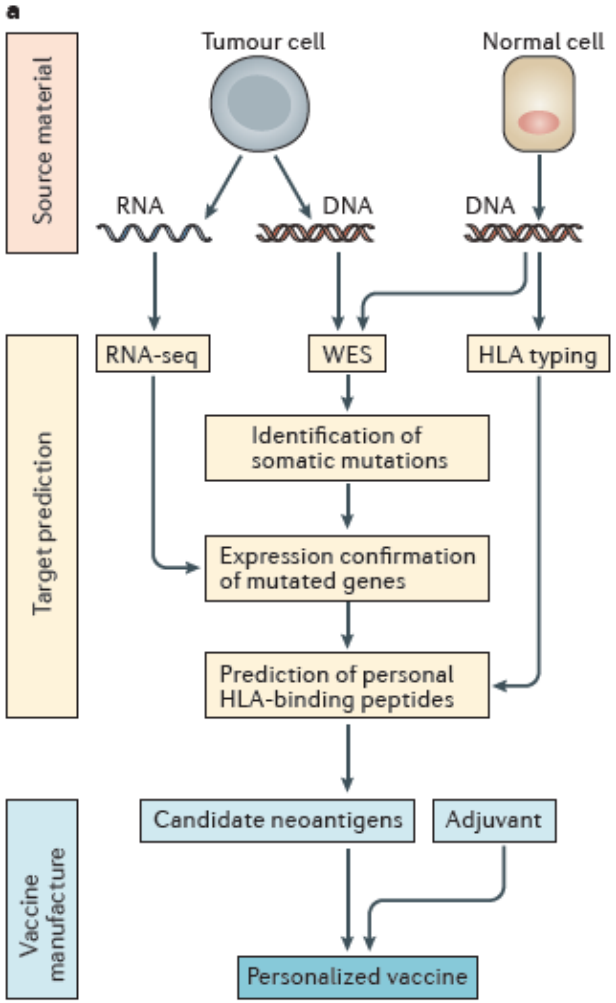
Mutations-derived neoantigens constitute important targets for immune attacks.



Adapted from
Schumacher et al. Sience 2017
Alexandrov et al, Nature 2013

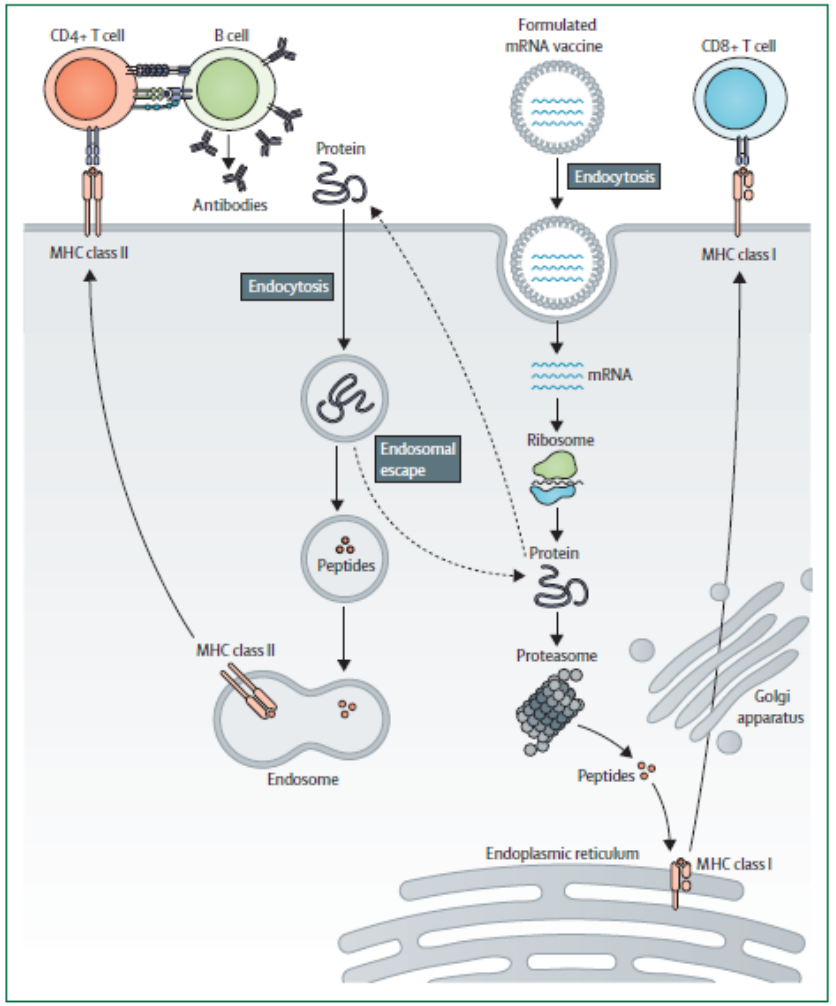
PERSONALIZED NEO-ANTIGEN VACCINES – PREDICTION AND MODE OF ACTION

Prediction of neo-antigens



Hu et al Nature Rev Immunol 2017

mRNA vaccines MOA

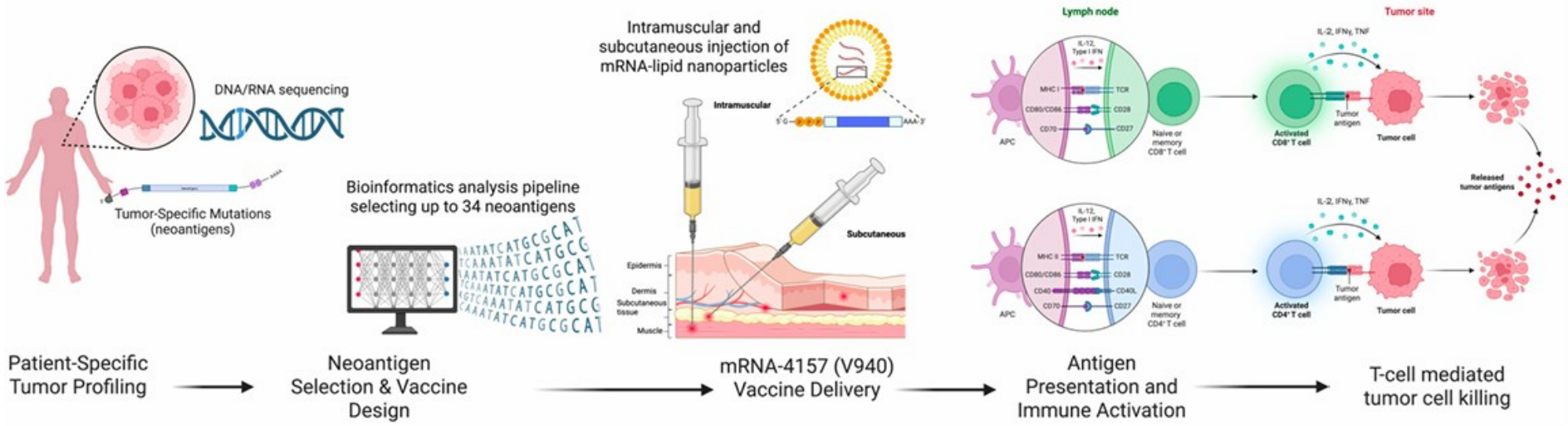


Lorentzen & Svane, Lancet Oncol 2022

PERSONALIZED NEOANTIGEN MRNA VACCINE
V940/MRNA-4157/INTISMERAN AUTOGENE

Intismeran autogene (formerly V940, mRNA-4157)

- mRNA-based individualized neoantigen therapy
- encoding ≤34 neoantigens specific to each patient's tumor
- promotes a T cell–mediated response against the neoantigens.

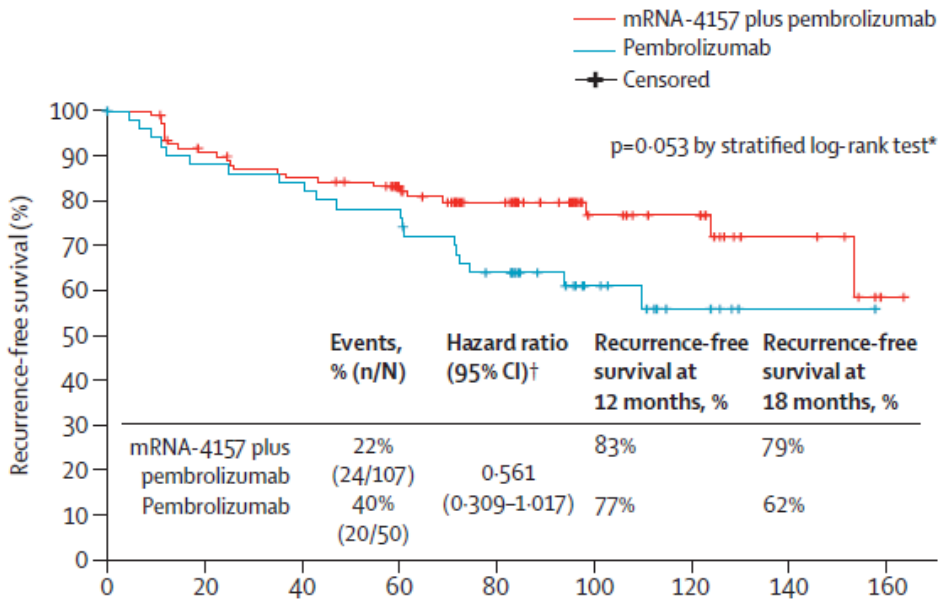


Mc Niel Cancers (2025)

PERSONALIZED NEOANTIGEN MRNA VACCINE PLUS ANTI-PD-1 IN ADJUVANT SETTING FOR MELANOMA.

RANDOMIZED PHASE II STUDY KEYNOTE-942

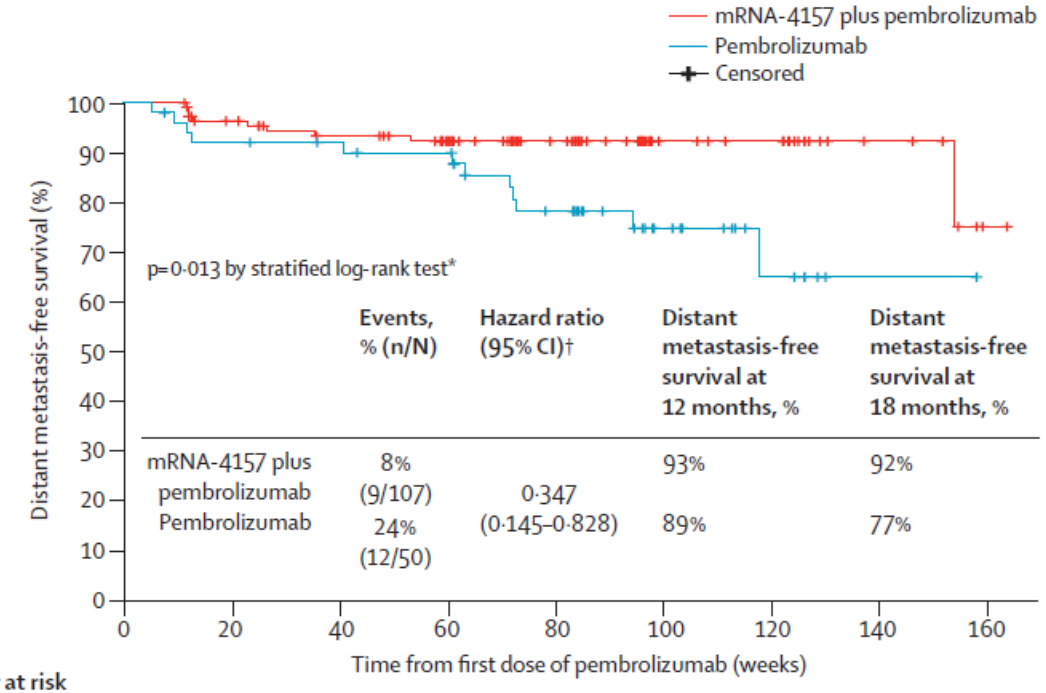
Recurrence-Free Survival



	Events, % (n/N)	Hazard ratio (95% CI)†	Recurrence-free survival at 12 months, %	Recurrence-free survival at 18 months, %
mRNA-4157 plus pembrolizumab	22% (24/107)	0·561 (0·309–1·017)	83%	79%
Pembrolizumab	40% (20/50)		77%	62%

Number at risk									
mRNA-4157 plus pembrolizumab	107 (0)	92 (5)	85 (6)	73 (16)	49 (37)	24 (61)	20 (65)	8 (76)	1 (82)
Pembrolizumab	50 (0)	42 (2)	40 (2)	37 (2)	28 (4)	13 (18)	6 (24)	1 (29)	0 (30)

Distant Metastasis-Free Survival



	Events, % (n/N)	Hazard ratio (95% CI)†	Distant metastasis-free survival at 12 months, %	Distant metastasis-free survival at 18 months, %
mRNA-4157 plus pembrolizumab	8% (9/107)	0·347 (0·145–0·828)	93%	92%
Pembrolizumab	24% (12/50)		89%	77%

Number at risk									
mRNA-4157 plus pembrolizumab	107 (0)	94 (9)	86 (14)	73 (26)	49 (50)	23 (76)	20 (79)	8 (91)	1 (97)
Pembrolizumab	50 (0)	43 (3)	41 (5)	39 (6)	29 (11)	14 (25)	6 (32)	1 (37)	0 (38)

157 pts enrolled: Due to Covid pandemic 45 pts were not randomized (the last 37 pts all allocated to vacc arm)

Weber et al, Lancet (2024)

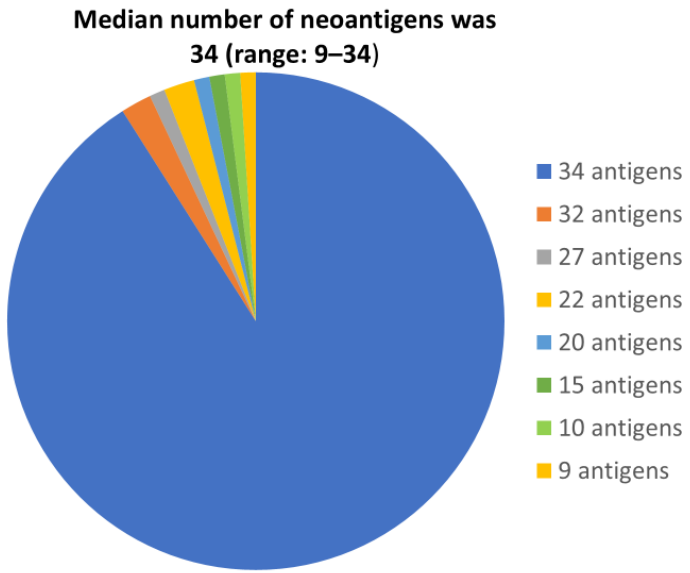
PERSONALIZED NEOANTIGEN MRNA VACCINE

Individualized Neoantigen Therapy Characteristics

>90% of patients screened had tissue of sufficient quality/quantity for mRNA-4157 (V940) manufacture

mRNA-4157 (V940) was successfully prepared for >99% of patients in the combination arm

91% of patients in the combination arm had an INT with 34 neoantigens



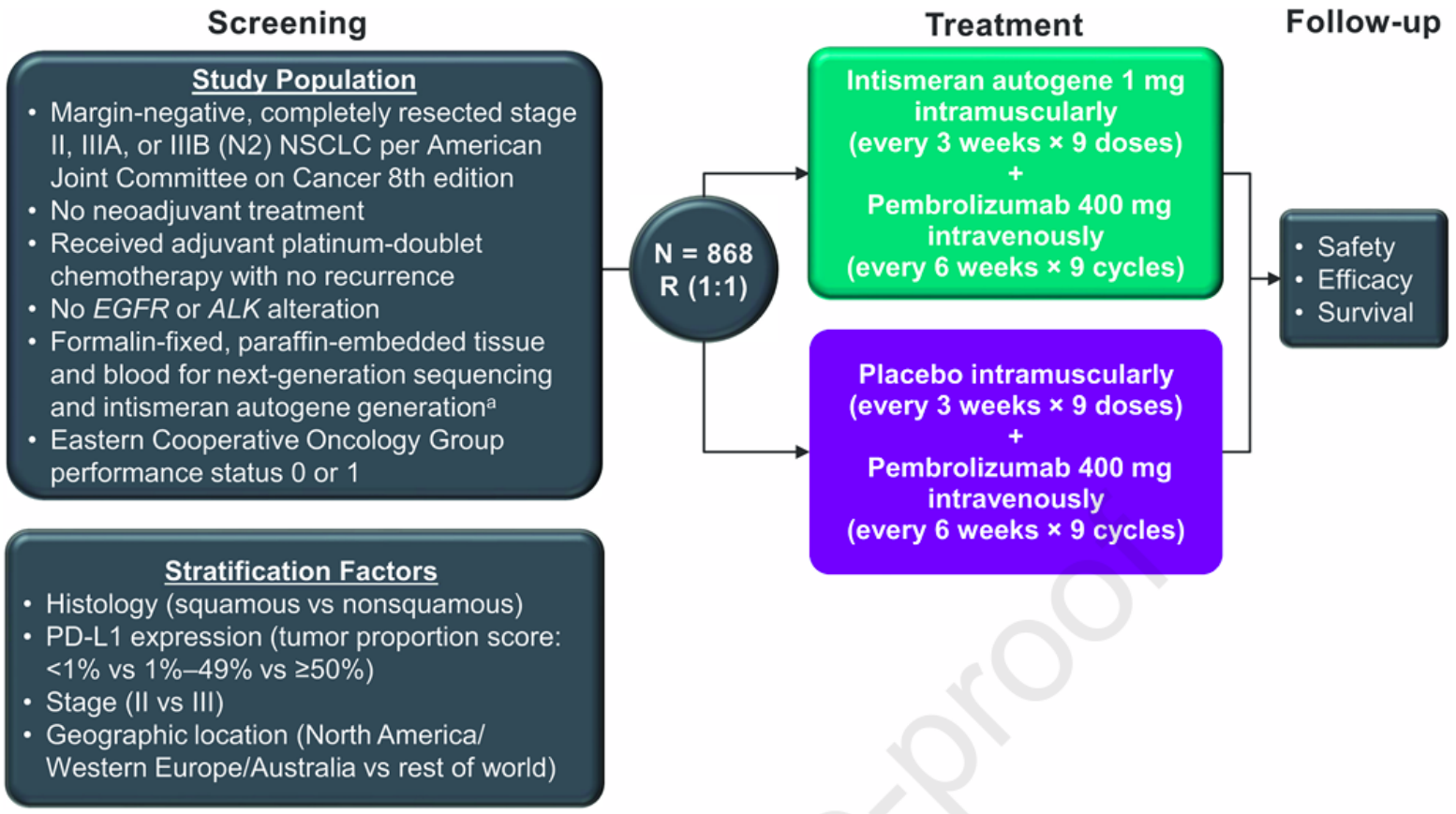
INT, individualized neoantigen therapy.
Khattak A, et al. Previously presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001.

Weber et al, Lancet (2024)

PERSONALIZED VACCINES – ONGOING ADJUVANT STUDIES IN NSCLC

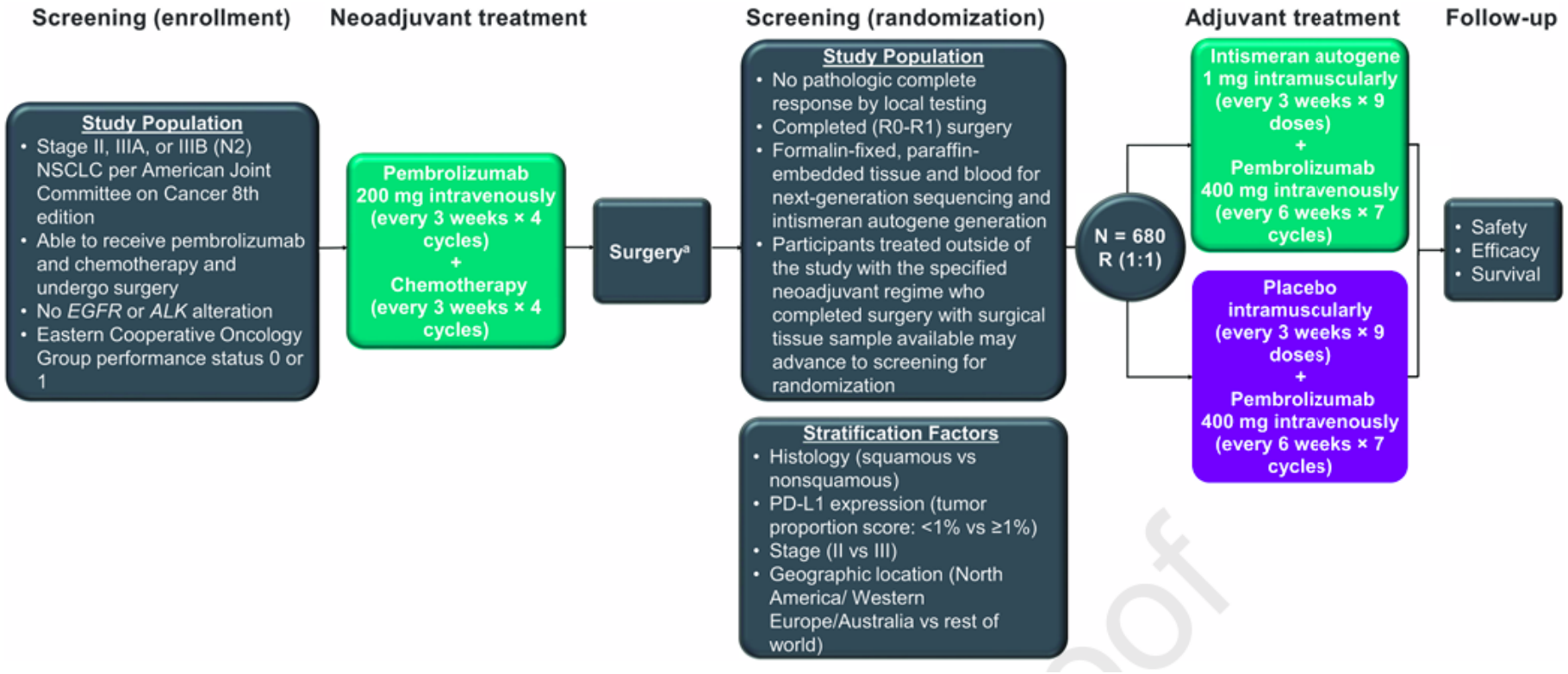
INTISMERAN

INTerpath-002: phase 3 study evaluating adjuvant intismeran autogene plus pembrolizumab for completely resected, stage II–IIIB (N2) NSCLC following adjuvant platinum-based chemotherapy



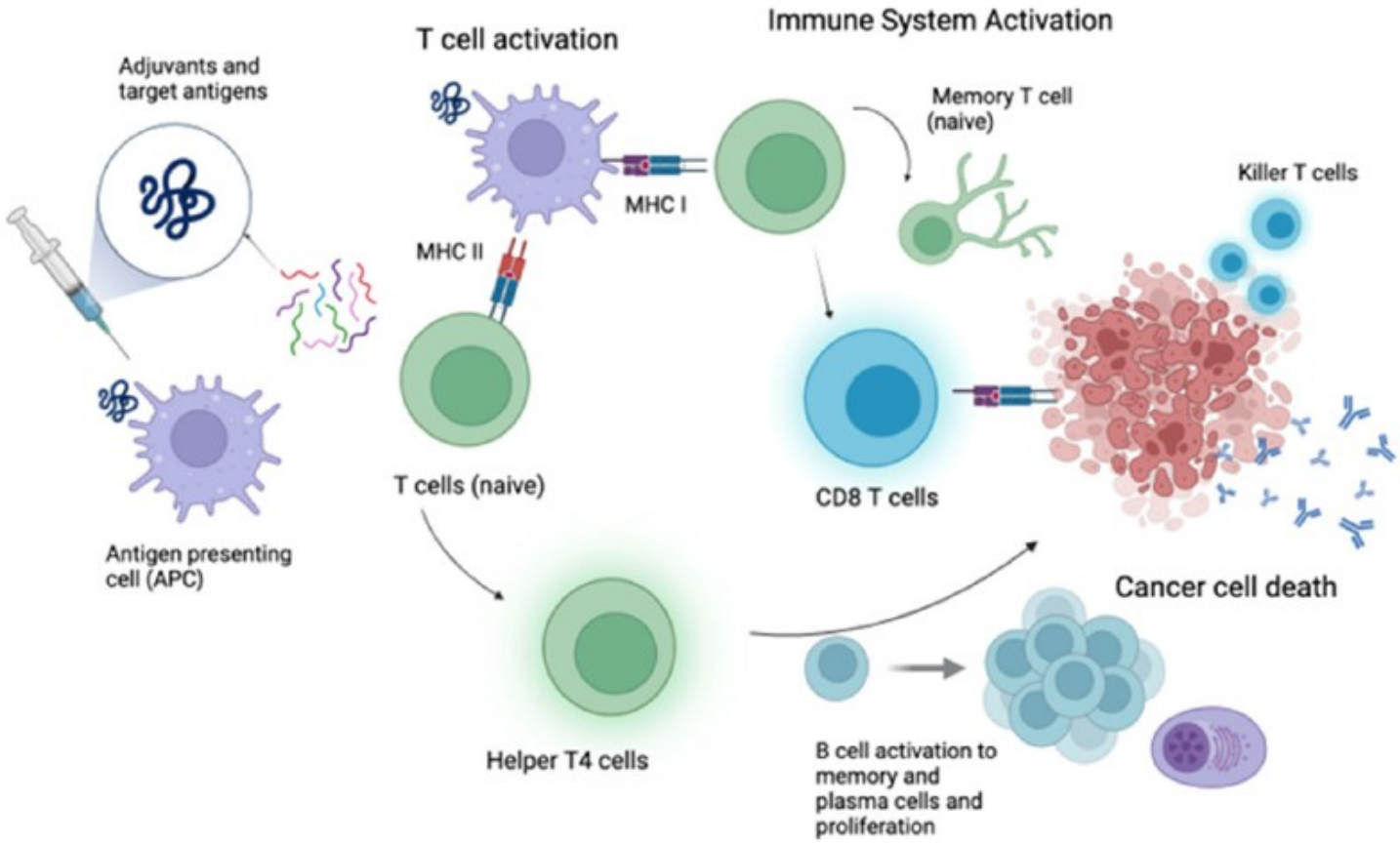
PERSONALIZED VACCINES – ONGOING ADJUVANT STUDIES IN NSCLC
INTISMERAN

INTerpath-009: phase 3 study evaluating adjuvant intismeran autogene plus pembrolizumab in participants with R0–R1 resected stage II–IIIB (N2) NSCLC who did not achieve pathologic complete response following neoadjuvant pembrolizumab plus chemotherapy



PEPTIDE VACCINES –MODE OF ACTION

Antigen presentation and T cell activation



Banda et al, Vaccines (2025)

Personalized Neoantigen Peptide Vaccine Plus Anti-PD-1 in Patients with Advanced Melanoma, Non-small Cell Lung Cancer, or Bladder Cancer

Clinical efficacy

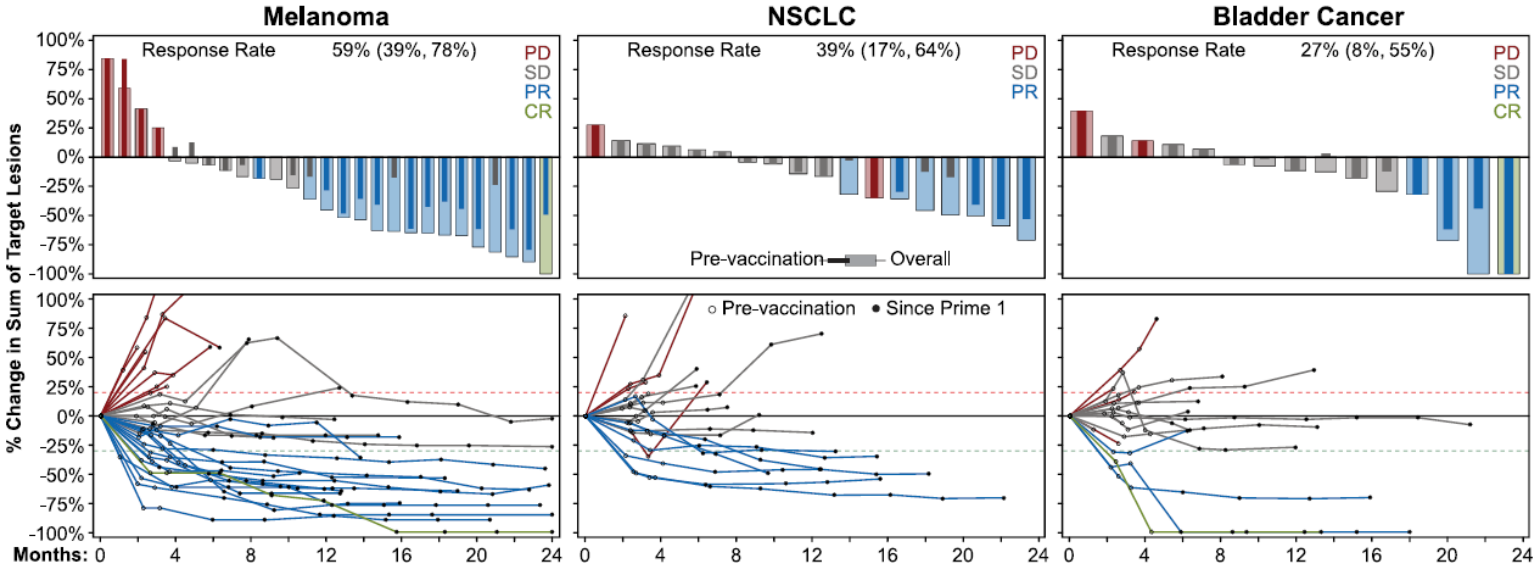


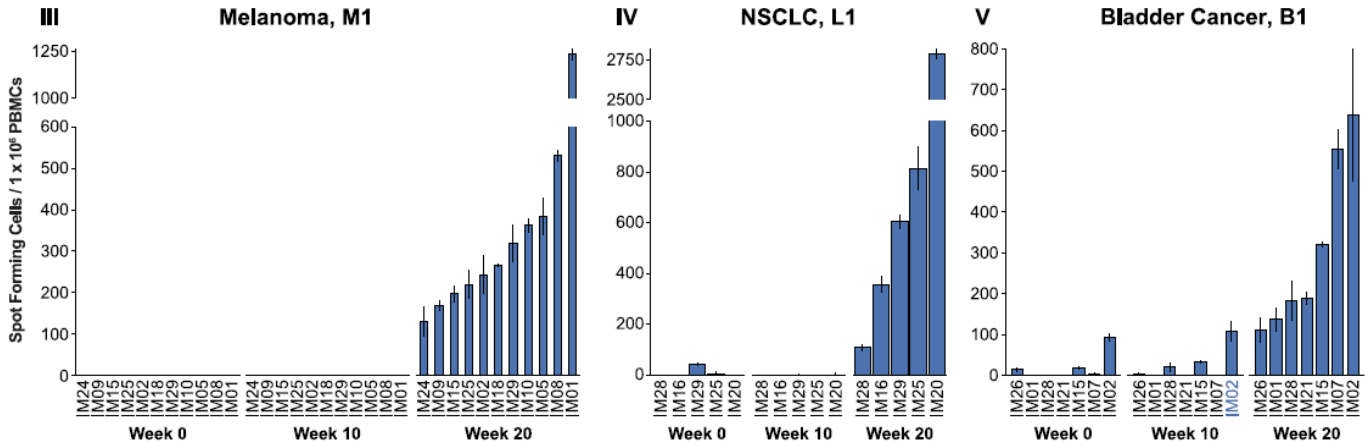
Figure 2. Rates and Durability of Responses Following Treatment with NEO-PV-01 Plus Anti-PD-1

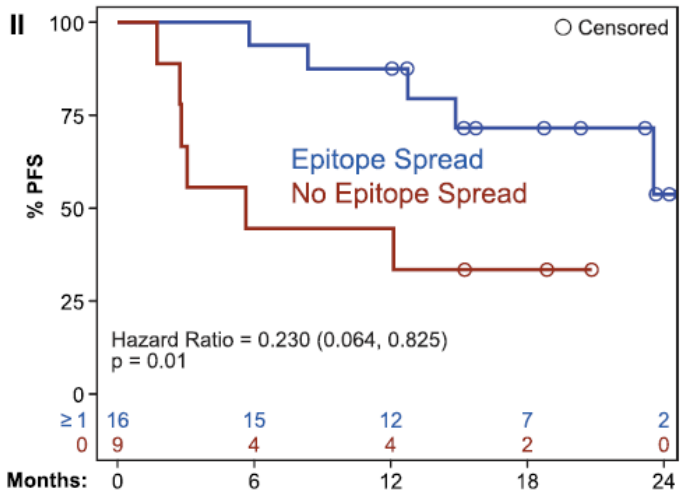
Top: best radiographic change (%) in sum of target lesions for each patient. The dark shade narrow bars represent best change pre-NEO-PV-01; the light shade wide bars represent the overall best change in study for patients who received at least 1 dose of NEO-PV-01 plus anti-PD-1. Red indicates progressive disease, blue indicates partial response, and green indicates complete response. Bottom: radiographic changes (%) in target lesions from the initiation of nivolumab treatment for each patient. The colors are the same as in the top panel.

Ott et al, Cell 2020

Personalized Neoantigen Peptide Vaccine Plus Anti-PD-1 in Patients with Advanced Melanoma, Non-small Cell Lung Cancer, or Bladder Cancer

Vaccine induced immunity





CENTER FOR CANCER IMMUNE THERAPY

Ott et al, Cell 2020

ONCOIMMUNOLOGY
2022, VOL. 11, NO. 1, e2023255 (15 pages)
https://doi.org/10.1080/2162402X.2021.2023255

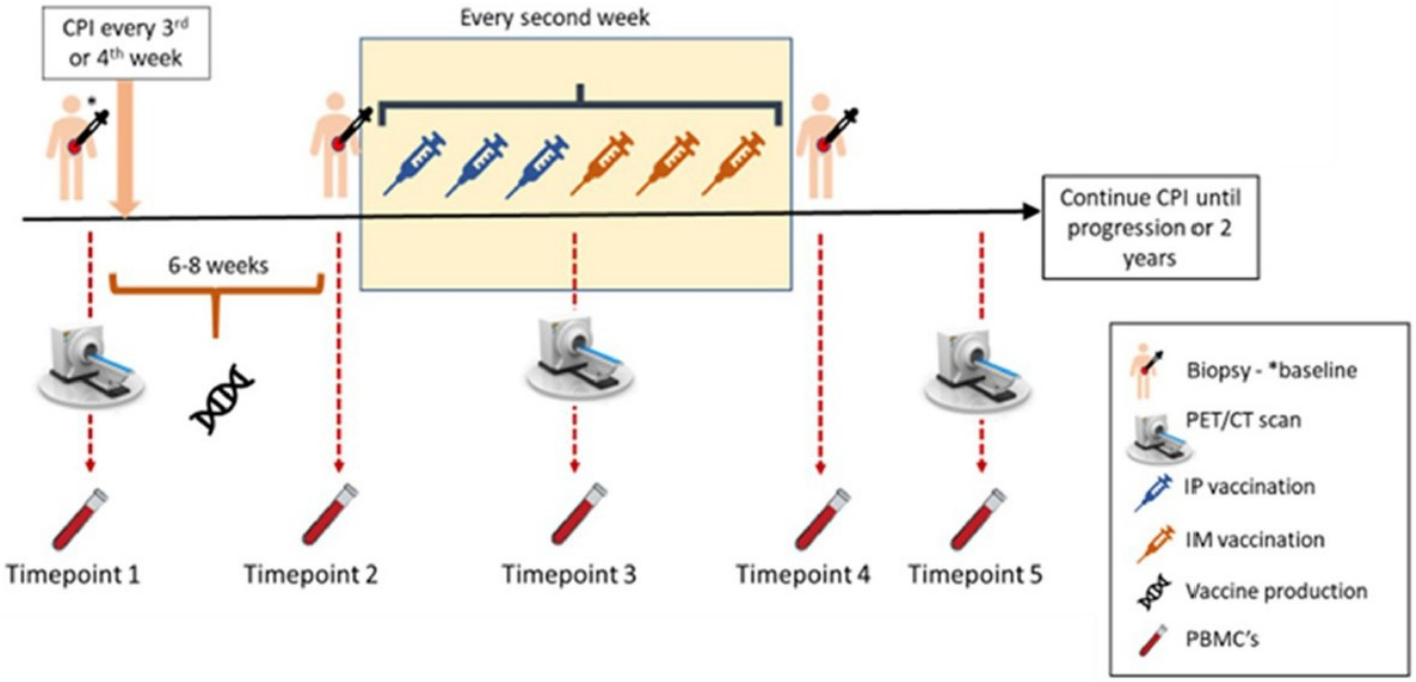
Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

OPEN ACCESS Check for updates

Personalized therapy with peptide-based neoantigen vaccine (EVX-01) including a novel adjuvant, CAF®09b, in patients with metastatic melanoma

Sofie Kirial Mørk[a], Mohammad Kadivar[b], Kalijn Fredrike Bol[a*], Arianna Draghi[a], Marie Christine Wulff Westergaard[a], Signe Koggersbøl Skadborg[b], Nana Overgaard[b], Anders Bundgård Sørensen[c], Ida Svahn Rasmussen[d], Lars Vibe Andreasen[d], Christina Westmose Yde[e], Thomas Trolle[c], Christian Garde[c], Jens Friis-Nielsen[c], Nis Nørgaard[f], Dennis Christensen[d**], Jens Vindahl Kringelum[c**], Marco Donia[a**], Sine Reker Hadrup[b**], and Inge Marie Svane[a]



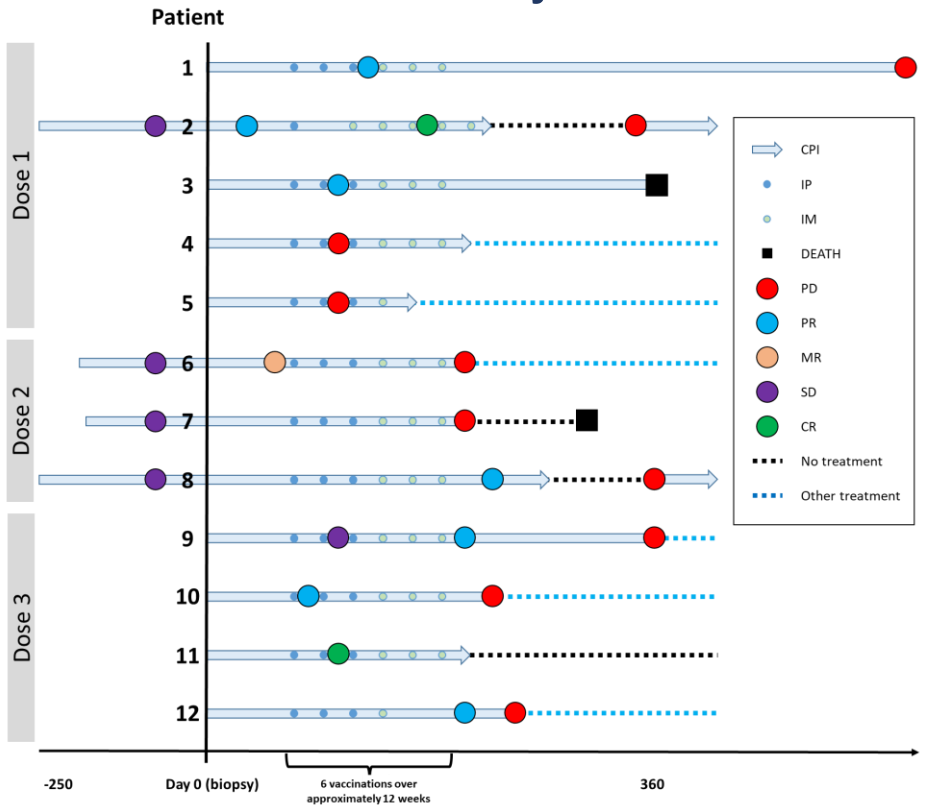
interim analysis reports the results from the first dose-level

- Short vaccine manufacturing time of 48–55 days which enabled the initiation of vaccine treatment within 60 days from baseline biopsy.
- No severe adverse events were observed.
- EVX-01 elicited long-lasting vaccine specific T-cell responses in all patients.

Personalized Neoantigen Peptide Vaccine Plus Anti-PD-1 in Patients with Advanced Melanoma

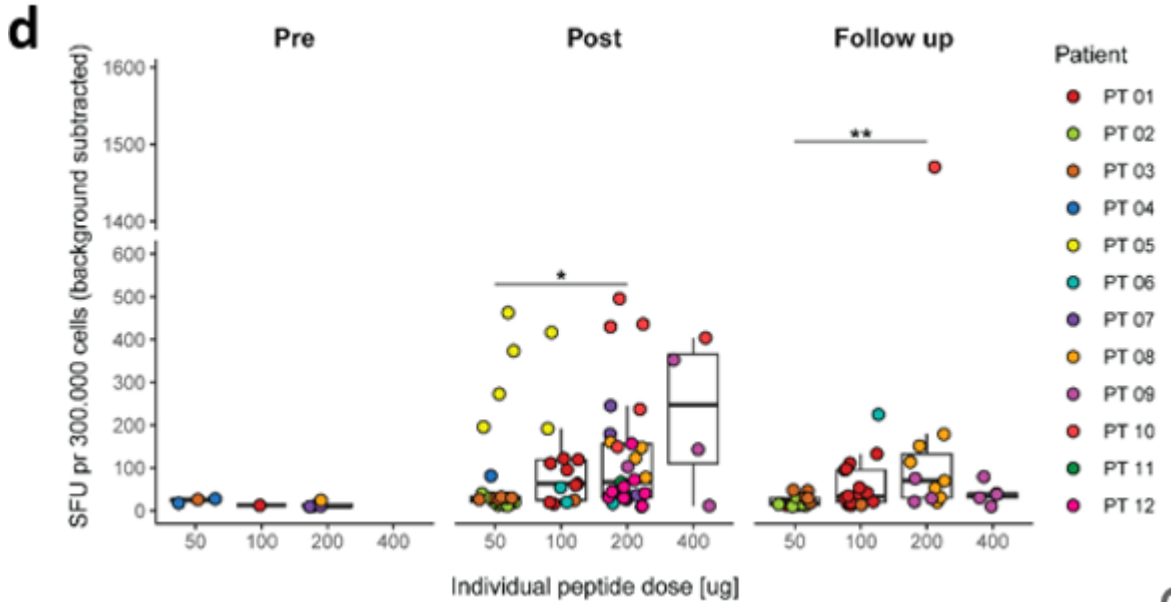
Clinical efficacy and vaccine response

Clinical efficacy



8 out of the 12 patients had objective clinical responses (6 PR and 2 CR) including all patients at the highest dose level

Vaccine response



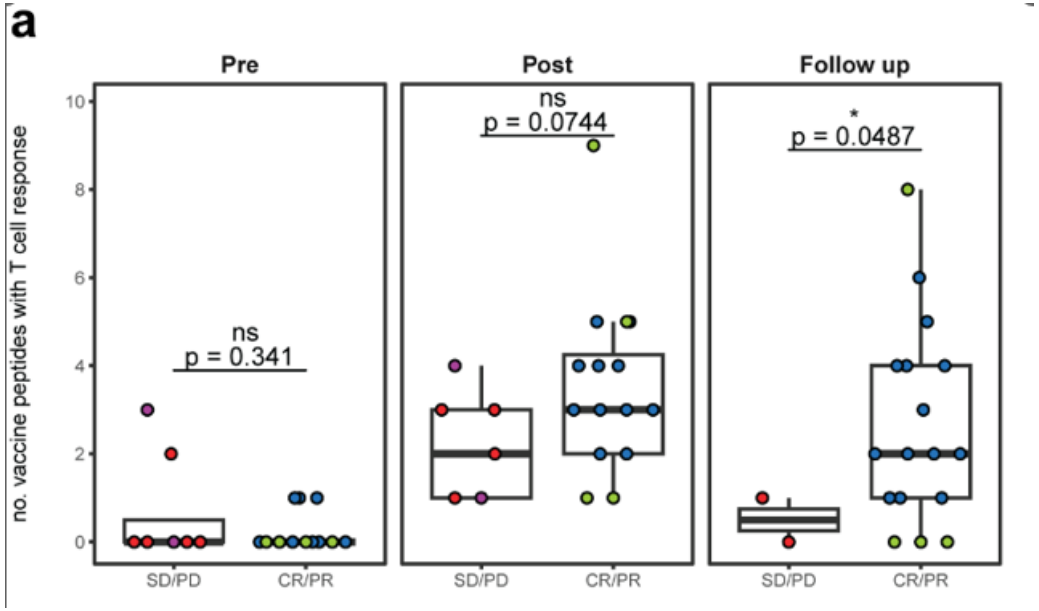
- Vaccine specific responses in all treated patients, with CD4+ T cells as the dominating responses.
- The magnitude of immune responses measured by IFN-γ ELISpot assay correlated with individual peptide doses.

Mørk et al manuscript in resub JITC 2024

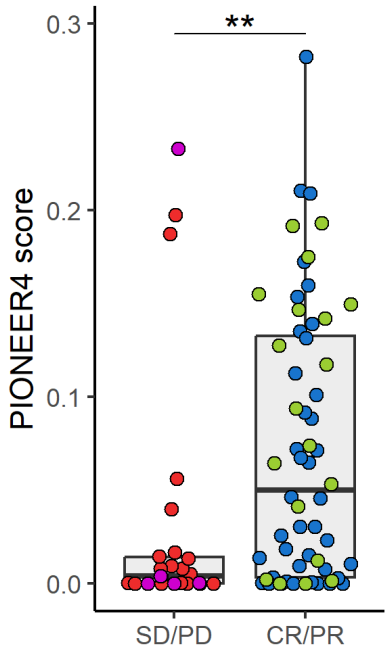
Personalized Neoantigen Peptide Vaccine Plus Anti-PD-1 in Patients with Advanced Melanoma

Prediction of response

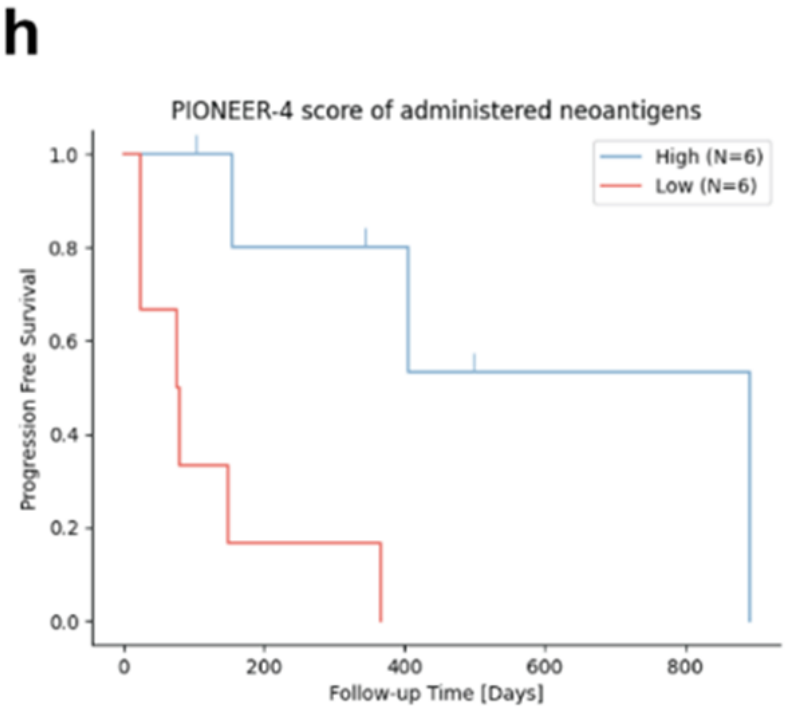
Vaccine response and OR



Neo-Ag quality score and OR



Neo-Ag quality score and PFS



CENTER FOR CANCER IMMUNE THERAPY

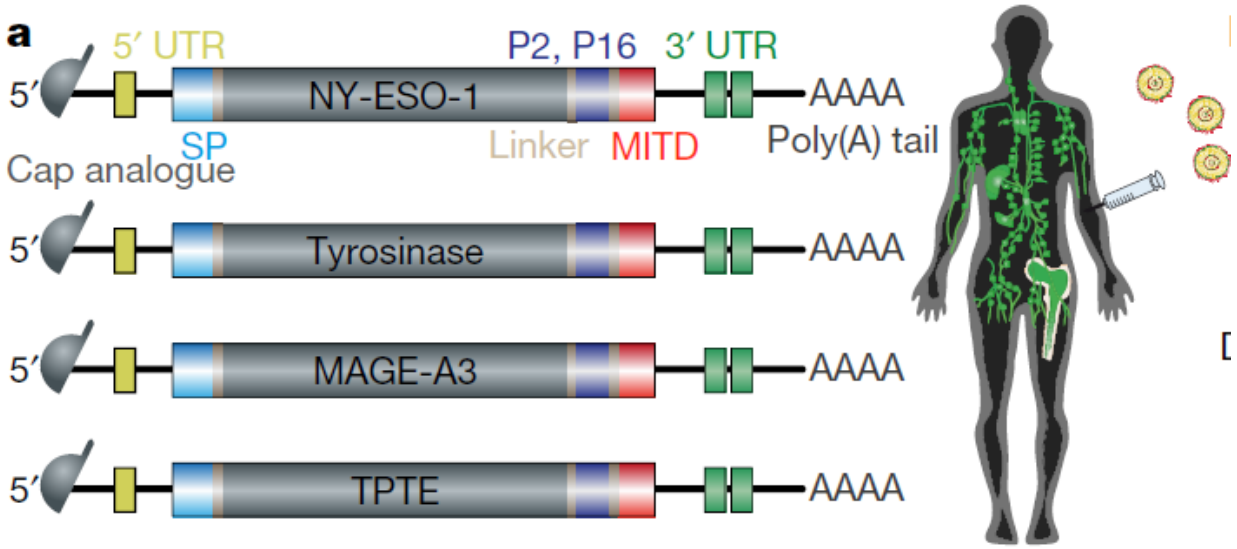
Mørk et al manuscript in resub JITC 2024

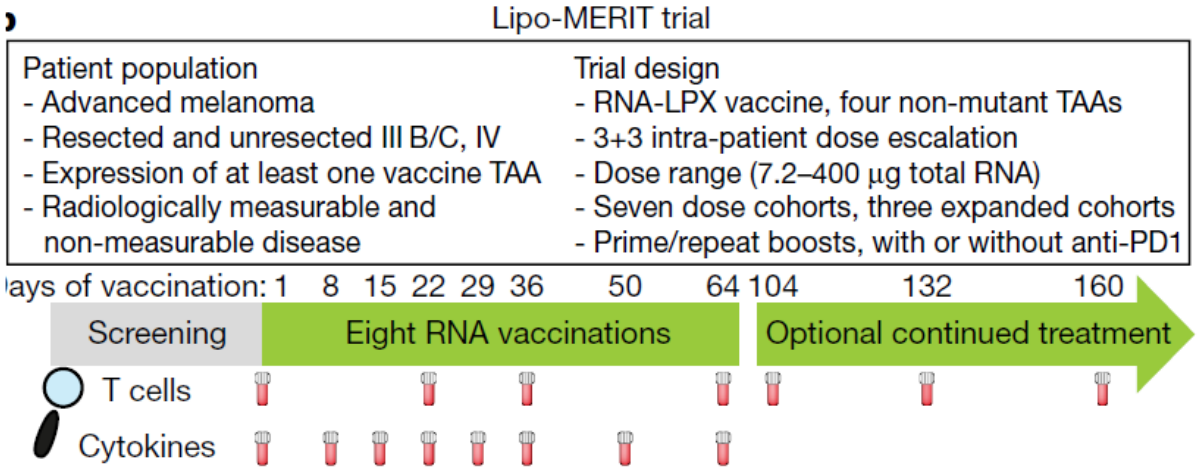
Shared antigen targeting vaccines

CCIT DENMARK

Melanoma FixVac (BNT111) - an intravenously administered liposomal mRNA (RNA-LPX) vaccine

Targeting four non-mutated, tumour-associated antigens prevalent in melanoma

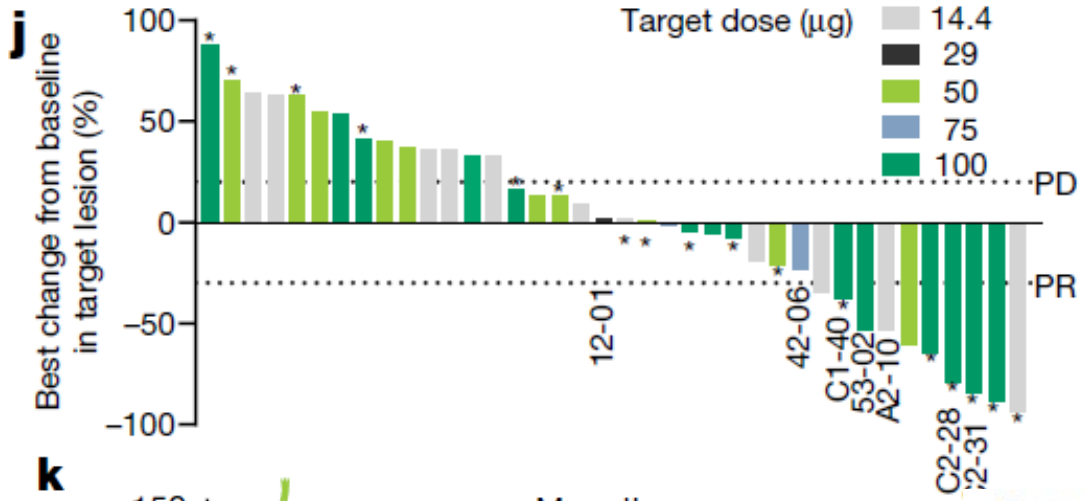


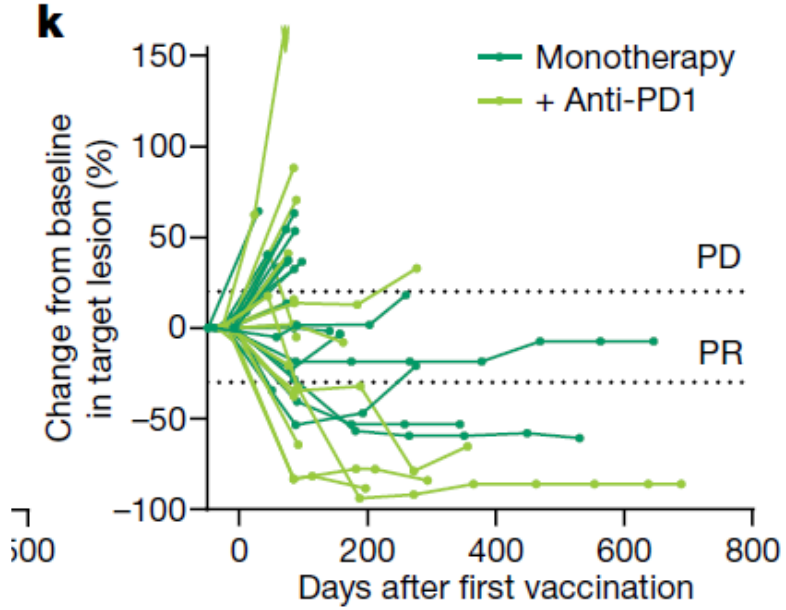


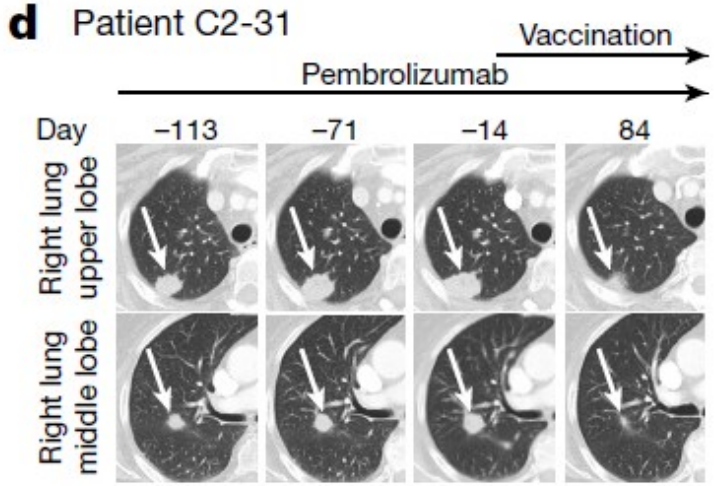
Sahin et al Nature 2020

Melanoma FixVac (BNT111) - an intravenously administered liposomal RNA (RNA-LPX) vaccine

Clinical efficacy with and without anti-PD1







Sahin et al Nature 2020

SHARED ANTIGEN VACCINE – LUNG CANCER
BNT116

BNT116, an intravenously administered, unmodified RNA-based lipoplex cancer vaccine

Composed of six mRNAs (CLDN6, KK-LC-1, MAGE-A3, MAGE-A4, MAGE-C1, PRAME)

Each encoding a tumor-associated antigen (TAA) frequently expressed in NSCLC

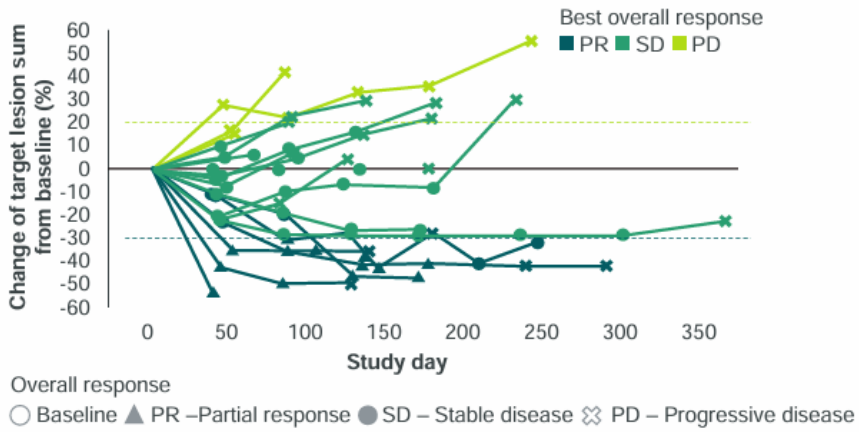
SHARED ANTIGEN VACCINE – LUNG CANCER
BNT116

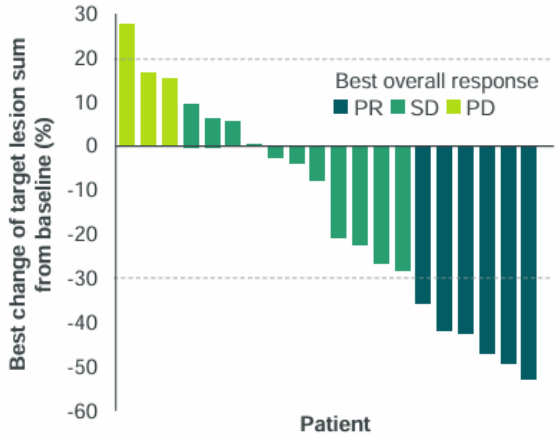
Preliminary Results of BNT116 Show Encouraging Antitumor Activity and Manageable Safety Profile in Combination with Docetaxel

Phase 1 FIH study (NCT05142189): Clinical activity and tolerability

Öven BB. et al. Presented at AACR 2024. #CT051.

	Cohort 3
	BNT116 + docetaxel (n=20)
ORR, n (%)	6 (30)
DCR, n (%)	17 (85)
mPFS, m	4.4





BNT116 + docetaxel shows activity in heavily pretreated patients with NSCLC

Safety:

- Manageable safety profile, comparable to other FixVac candidates
- No signs of the combination treatment increasing the severity or duration of the adverse events were observed.

Historical efficacy of docetaxel monotherapy (Garon et al. Lancet. 2014):

- ORR ~10%
- mPFS ~ 3 months
- mOS ~ 9 months

FIH = first in human; ORR = objective response rate; DCR = disease control rate; (m)PFS = (median) progression-free survivial; (m)OS = (median) overall survival; PR = partial response; SD = stable disease; PD = progressive disease; NSCLC = non-small cell lung cancer.

BIONTECH

SHARED ANTIGEN VACCINE – LUNG CANCER
BNT116

Abstract CT013: Phase I trial evaluating BNT116, a TAA-encoding mRNA vaccine, in combination with cemiplimab in frail patients with advanced non-small cell lung cancer (NSCLC) FREE

Rafal Dziadziuszko; Dániel Deme; Rodryg Ramlau; Erdem Göker; Bulent Yalcin; Neru Munshi; Janet L. Markman; Victoria Chen; Manas Kumar Rout; Chiara Dalle Fratte; Tobias Burkard; Iryna Tsyhankova; Chris D. Hermann; Michael Wenger; Israel Lowy; Frank Seebach; Patrick Forde; Akin Atmaca; Özlem Türeci; Uğur Şahin; Patrick Brueck

Phase I LuCa-MERIT-1 clinical trial aims to determine the safety and clinical activity of BNT116, alone or in combinations.

This cohort evaluate BNT116 in combination with cemiplimab (anti-PD1) in frail pts (ECOG PS 0-2) who are not candidates for first-line chemotherapy and had a PD-L1 tumor proportion score (TPS) ≥1% on tumor cells.

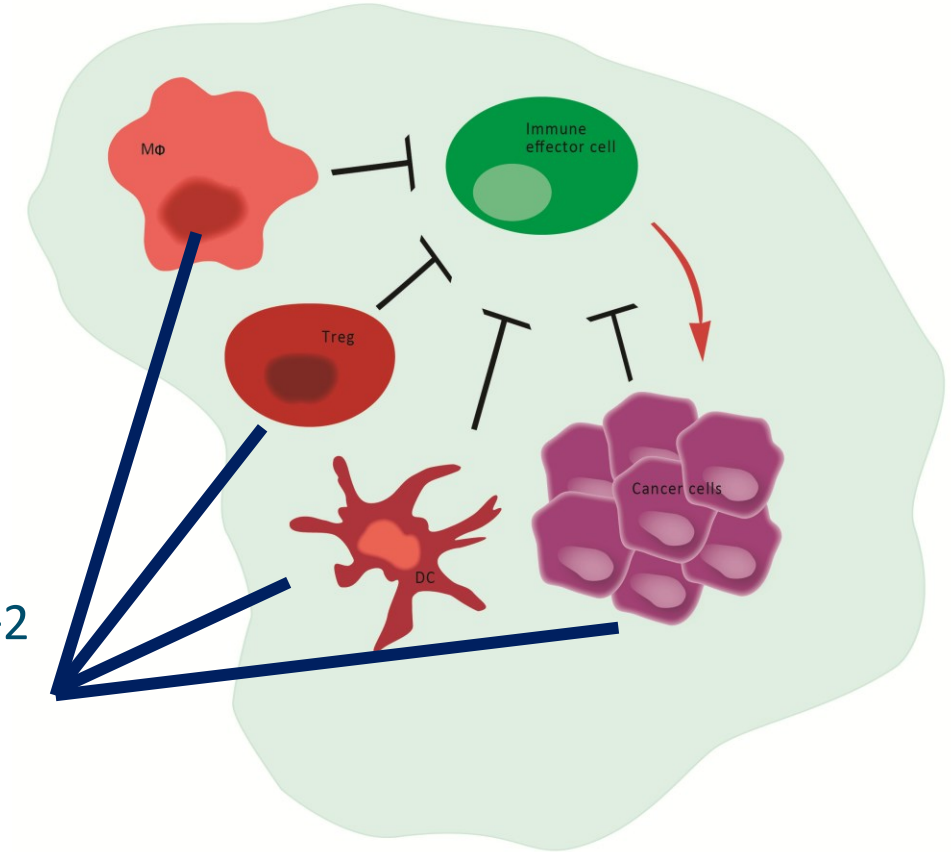
The best overall response was a partial response (PR) in 9 of 20 pts (45%), and stable disease in 7 of 20 pts (35%). Of the 9 PR pts, 2 had a PD-L1 TPS <50%.
The confirmed objective response rate was 45%, the disease control rate was 80%, and median progression-free survival was 9.9 months (95% CI: 2.4, not estimable).

Tumor Microenvironment Antigens as vaccine targets

Suppressive immune cells and tumor cells in the TME express Tumor Microenvironment Antigens (TMAs)

TMAs include:

- Metabolic enzymes
- Checkpoint molecules
- Cytokines



Arginase-1+2
IDO, TDO
PDL1, PDL2
TGF-beta

CLINICAL EXAMPLES

IDO VACCINE IN LUNG CANCER (NSCLC)

First-in-man phase I trial

15 patients included June 2010 – May 2012

(Before CPI)

Inclusion criteria

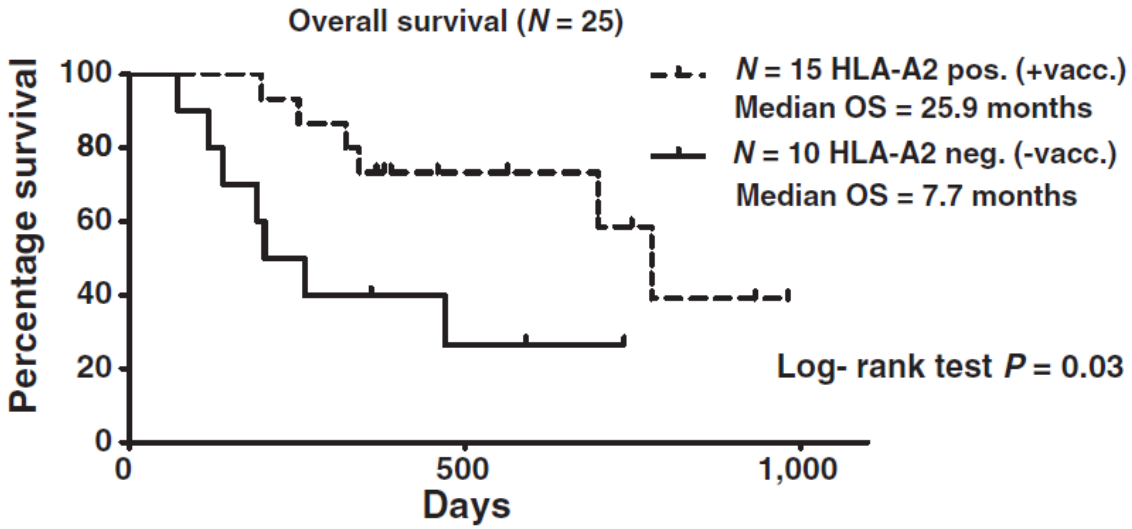
- Stage III/IV metastatic NSCLC
- > 18 years
- Stable disease after standard therapy
- PS 0-1
- HLA-A2 positive

Treatment plan

Patients were vaccinated q2w x 6 and thereafter monthly with the HLA-A2 restricted IDO peptide vaccine (maintenance therapy)

PR: 1/15 and SD (>8.5 mo.): 6/15

Clinical benefit rate: 47%



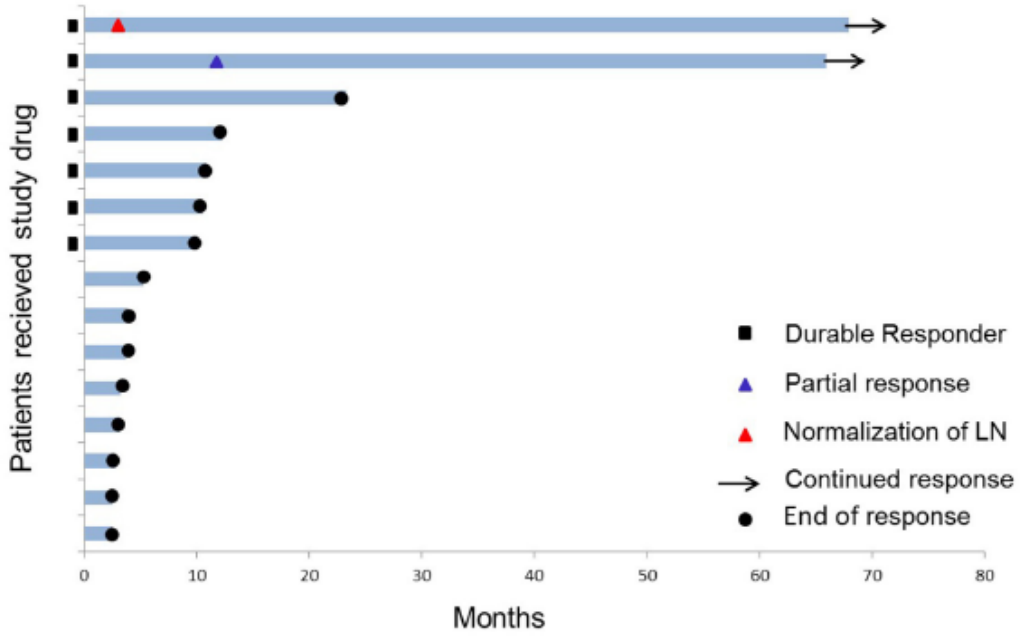
Iversen et al, Clin Cancer Res, 2013

CLINICAL EXAMPLES

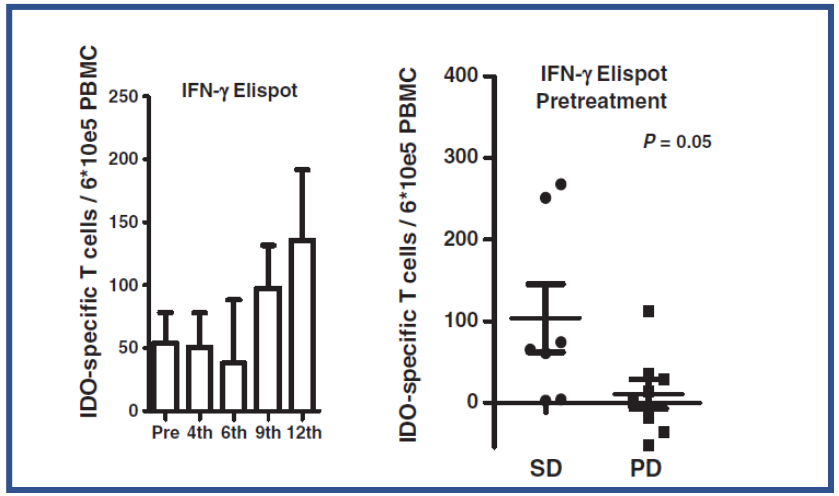
IDO VACCINE IN LUNG CANCER (NSCLC)

2 pts without disease progression beyond 6 years.

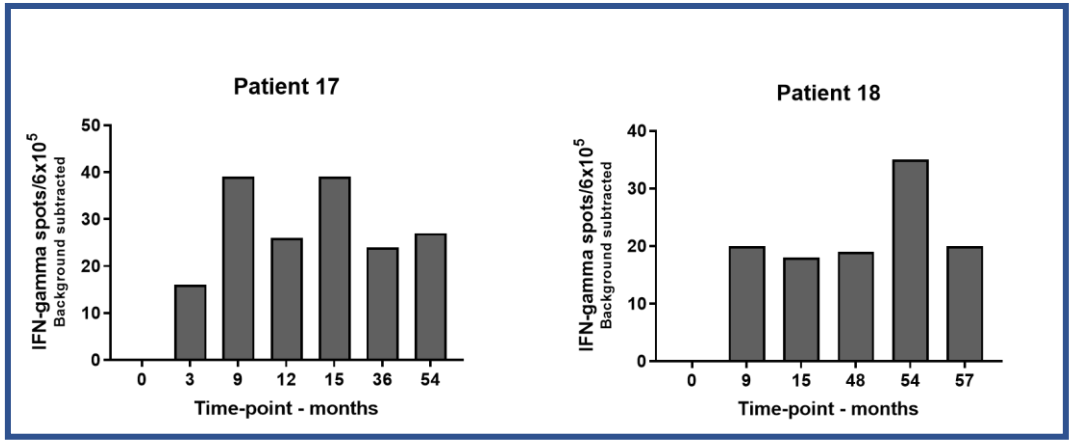
Of these 1 pt with liver metastases in PR



IDO response baseline and during vaccination with IDO-targeting vaccine



Sustained IDO responses over years.



Lorentzen et al, Front. Immunol., 2018

Iversen et al, Clin Cancer Res, 2013

CLINICAL EXAMPLES

IDO + PDL1 VACCINE IN COMBINATION WITH ANTI-PD1 IN NSCLC and SCCHN

Study design

IOB-022/KN-D38: Phase 2, non-comparative, open-label, basket trial

Eligibility criteria

- N = up to 30 per cohort
- Previously untreated metastatic solid tumors
- No prior 1st line therapy
- Measurable disease
- ECOG PS 0 or 1

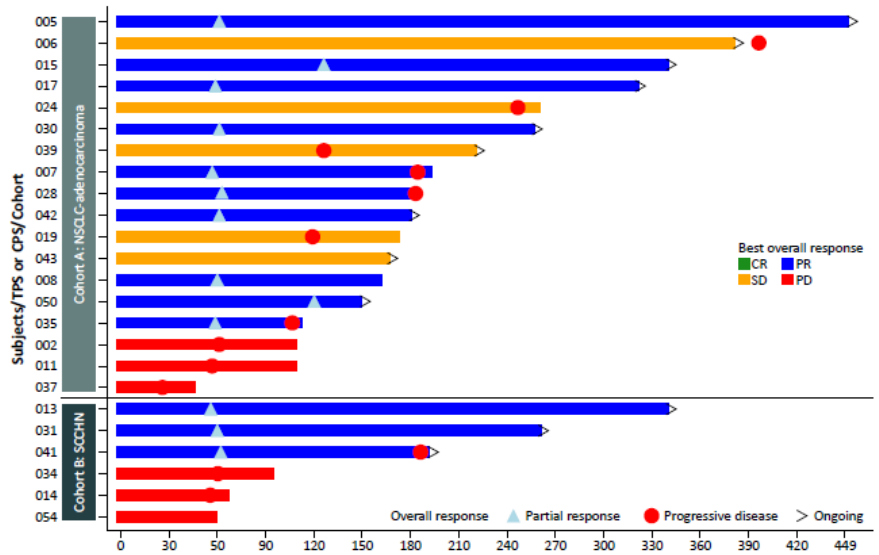
Cohorts

- NSCLC PD-L1 TPS ≥ 50%
- SCCHN (HPV +/-) PD-L1 CPS ≥ 20

IO102-IO103 and Pembrolizumab 200mg q3w

For up to 35 cycles

Preliminary efficacy data



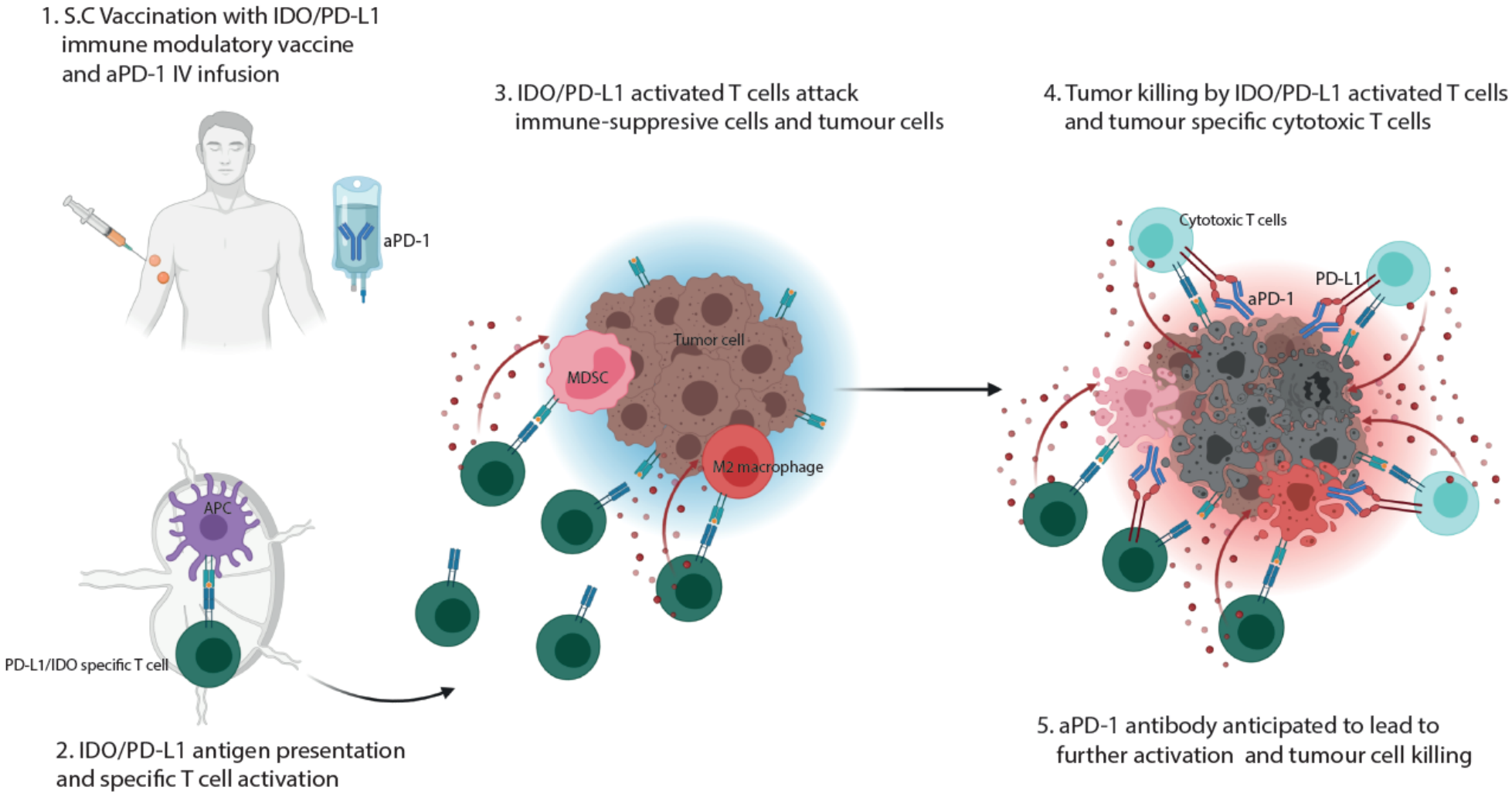
NSCLC Best overall response	N = 18
ORR (95% CI)	10 (56%) [30.8; 78.5]
Partial Response (PR)	10 (56%)
Stable Disease (SD)	5 (28%)
Progressive Disease (PD)	3 (17%)

SCCHN Best overall response	N = 6
ORR	3 /6
Partial Response	3
Stable Disease	0
Progressive Disease	3

Riess et al. 1038P
ESMO 2023

IDO & PDL1 VACCINE IN MELANOMA

A VACCINE TARGETING IMMUNE REGULATION

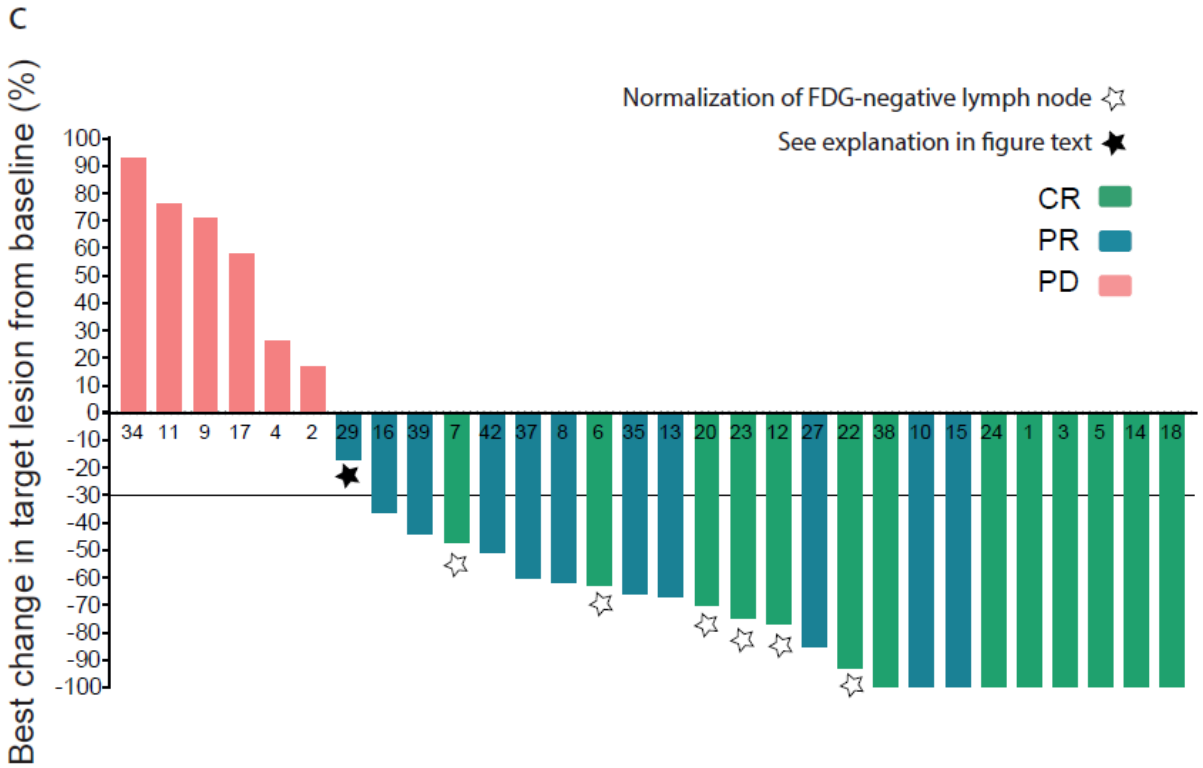


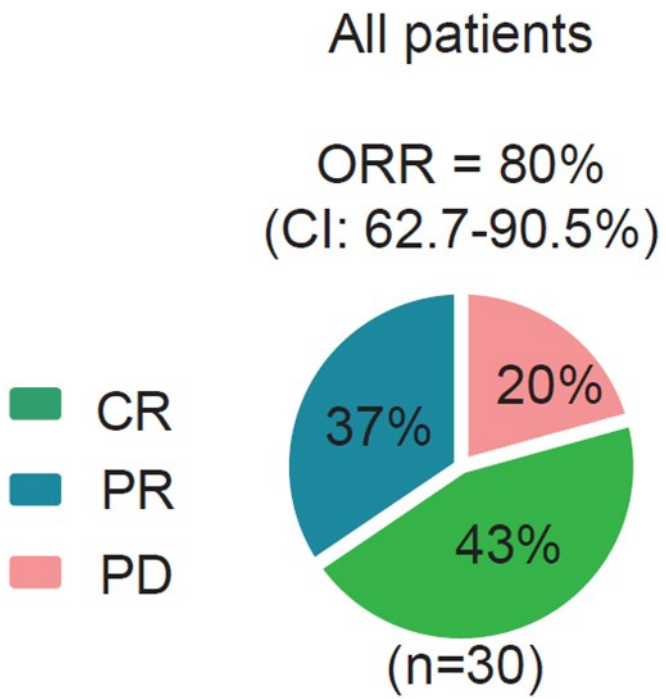
Kjeldsen & Svane Nature Med 2021

IDO & PDL1 VACCINE + anti-PD1 IN MELANOMA

CLINICAL EFFICACY

Waterfall plot: Deep tumor responses





Kjeldsen & Svane Nature Med 2021

BERLIN 2025 ESMO congress

IO102-IO103 cancer vaccine plus pembrolizumab for first line advanced melanoma: primary results from a randomized phase 3 trial (IOB-013/KN-D18)

JC Hassel[1], A Arance[2], MS Carlino[3], P Ascierto[4], S Sandhu[5], I Puzanov[6], A Eggermont[7], O Hamid[8], L Mortier[9], P Rutkowski[10], C Coetzee[11], SB Karaca[12], S Grabbe[13], A Poklepovic[14], A Vedel[15], B Wang[15], Q Ahmad[15], F. Ringeisen[15], C Robert[16], IM Svane[17]

[1]Heidelberg University, Department of Dermatology and National Centre for Tumour Diseases (NCT), NCT Heidelberg, a partnership between DKFZ and University Hospital Heidelberg, Germany; [2]Department of Medical Oncology, Hospital Clínic of Barcelona, University of Barcelona, Spain; [3]Westmead and Blacktown Hospitals, Melanoma Institute Australia and the University of Sydney, Australia; [4]Istituto Nazionale Tumori IRCCS Fondazione Pascale, Naples, Italy; [5]Peter MacCallum Cancer Centre, Sir Peter MacCallum Department of Oncology, The University of Melbourne, Australia; [6]Roswell Park Comprehensive Cancer Center, Buffalo, New York, United States; [7]University Medical Center Utrecht, Netherlands and the Comprehensive Cancer Center Munich of the Technical University Munich and the Ludwig Maximilians University, Germany; [8]The Angeles Clinic and Research Institute, a Cedars Sinai Affiliate, Los Angeles, USA; [9]INSERM U 1189, Lille University, CHU Lille, Hôpital Huriez, Lille, France; [10]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [11]Cape Town Oncology Trials, Cape Gate Oncology Centre, Kraaifontein, South Africa; [12]Ege University Faculty of Medicine, T. Aktas Oncology Hospital, Bornova İzmir Turkey; [13]Department of Dermatology, University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [14]Department of Internal Medicine, Division of Oncology, Massey Comprehensive Cancer Center, Virginia Commonwealth University, Richmond, USA; [15]IO Biotech, Copenhagen, Denmark; [16]Gustave Roussy Cancer Center, Villejuif, France; [17]National Center for Cancer Immune Therapy, CCIT-DK, Department of Oncology, Copenhagen University Hospital, Herlev, Denmark.

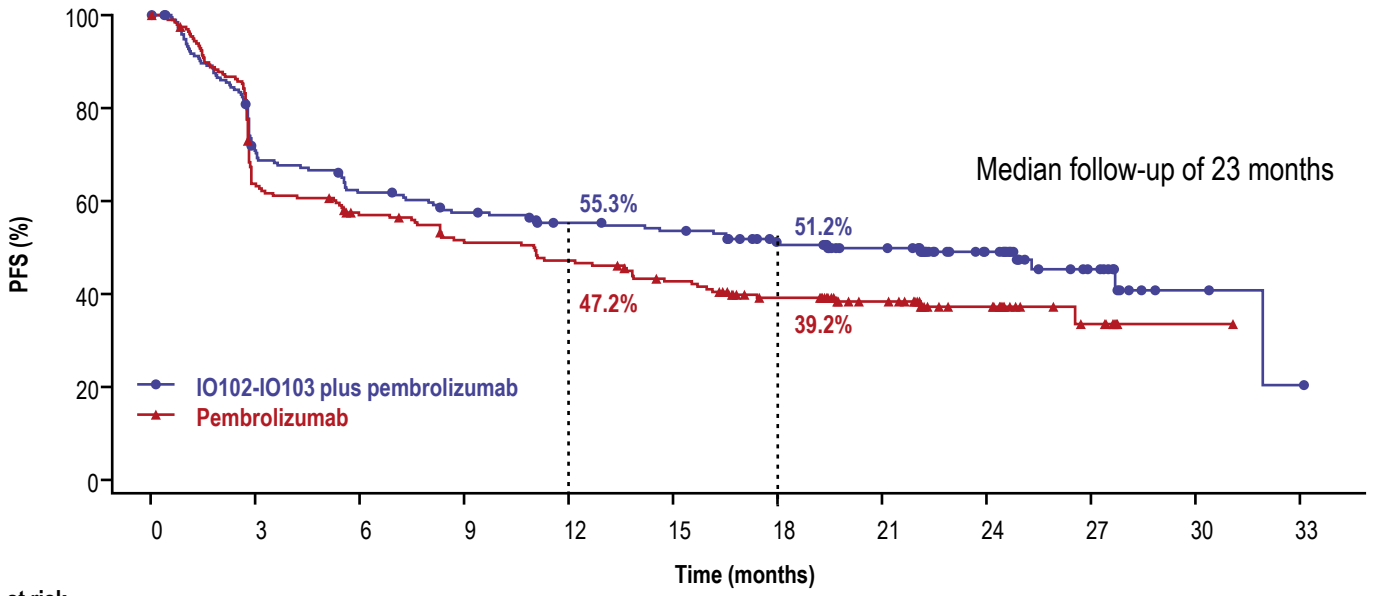
20 October 2025

50 YEARS ESMO

Primary endpoint: PFS

Blinded independent central review

Kaplan–Meier estimate of PFS in ITT determined by BICR per RECISTv1.1 and stratified by PD-L1 status and disease stage



Patients at risk

IO102-IO103 plus pembrolizumab	203	134	116	106	97	93	79	68	39	18	3	1
Pembrolizumab	204	124	107	94	86	75	59	44	22	8	1	0

	IO102-IO103 plus pembrolizumab N=203	Pembrolizumab N=204
Events	99	119
PFS, months, median (95% CI)	19.4 (9.7 to NR)	11.0 (6.0 to 14.8)
HR (95% CI)	0.77 (0.58 to 1.00)	
Log-rank P	0.0558	

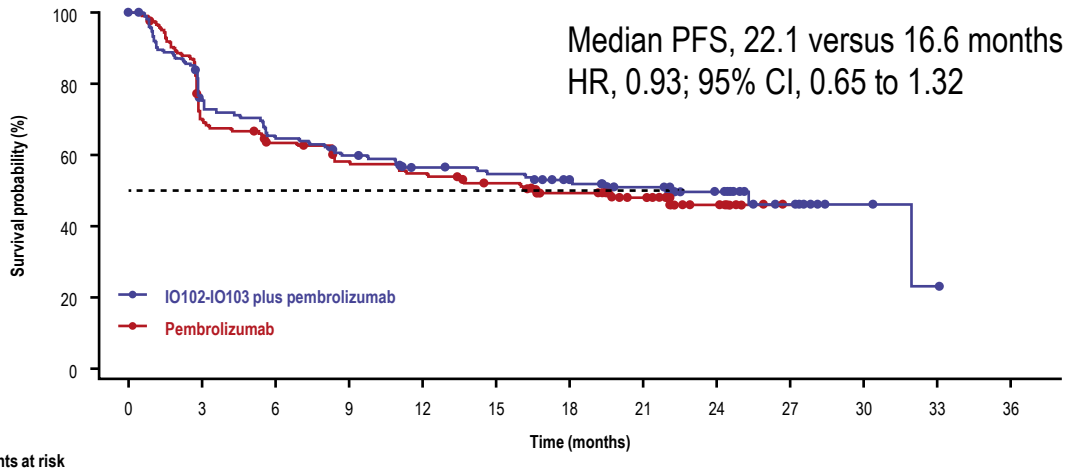
*Statistical significance threshold for this study was p=0.045.

Jessica C. Hassel

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat population; NR, not reached; P, p-value; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

Pre-specified analysis: PFS per PD-L1 status*

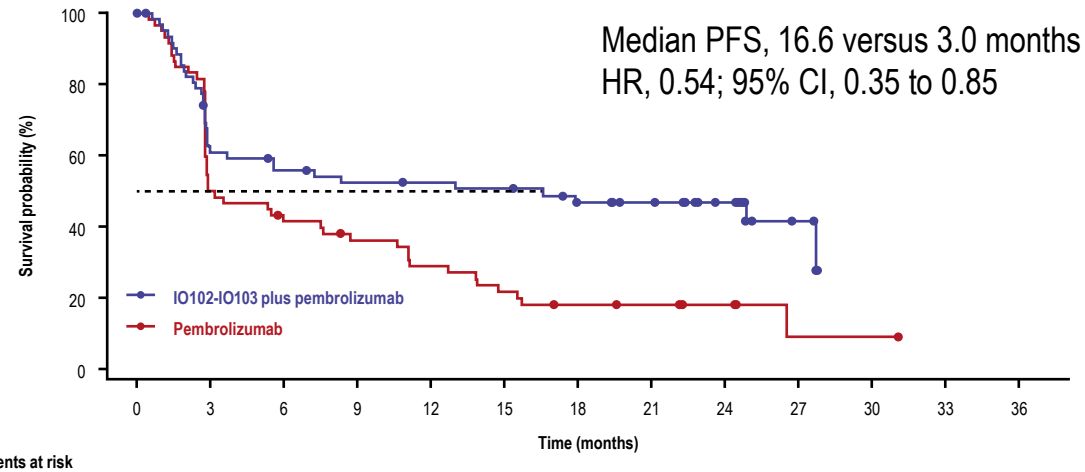
PD-L1 positive tumors



Patients at risk													
IO102-IO103 plus pembrolizumab	129	93	80	73	65	62	53	46	23	11	3	1	0
Pembrolizumab	127	86	75	67	63	57	47	33	15	6	0	0	0

ORR, 47.3% in IO102-IO13 plus pembrolizumab vs 48.8% in pembrolizumab

PD-L1 negative tumors



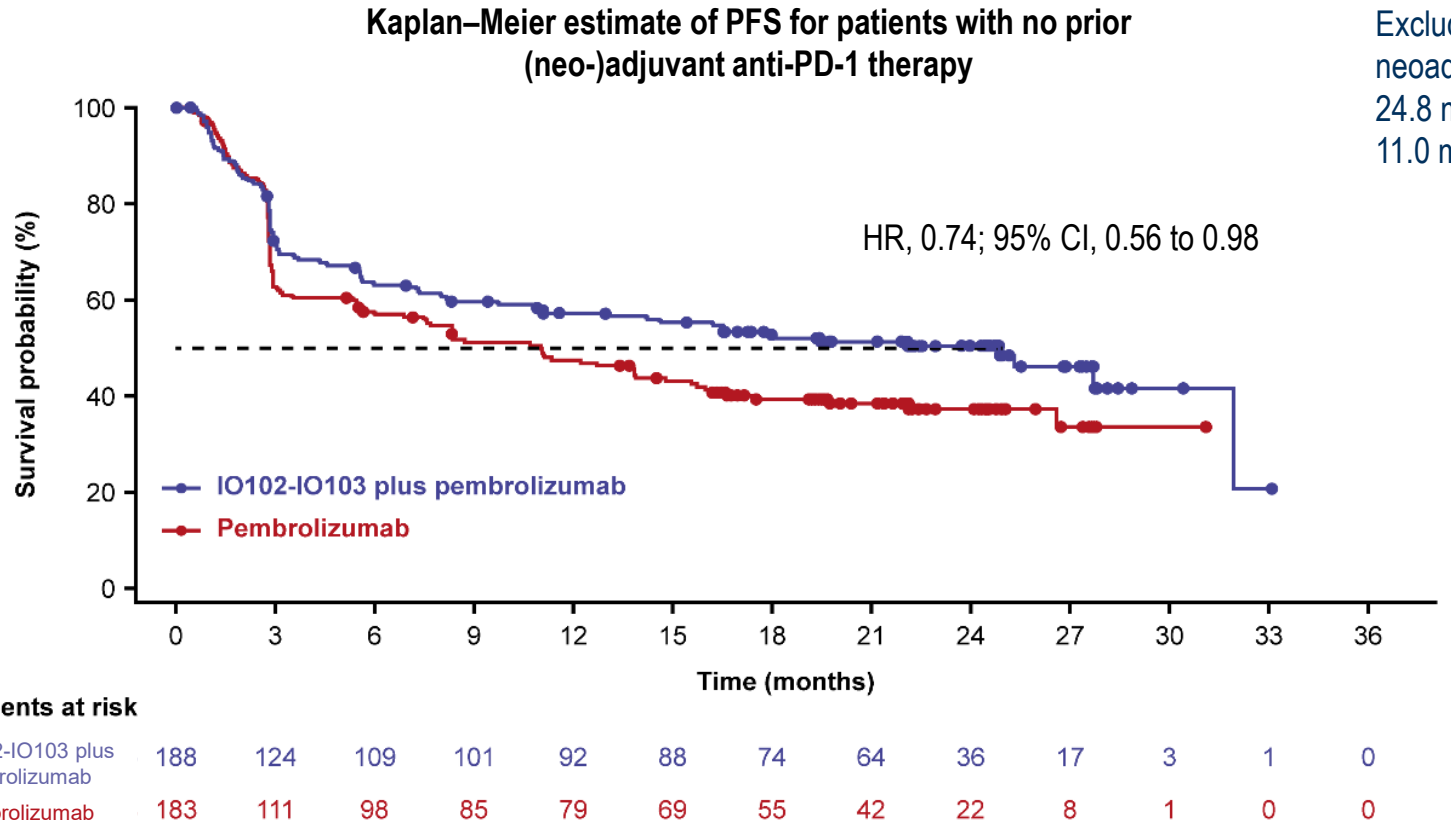
Patients at risk													
IO102-IO103 plus pembrolizumab	67	37	33	30	29	28	23	19	13	5	0	0	0
Pembrolizumab	63	30	24	20	16	12	9	8	5	1	1	0	0

ORR, 43.3% in IO102-IO13 plus pembrolizumab vs 25.4% in pembrolizumab

Jessica C. Hassel

*PD-L1 expression in tumor tissue was assessed at a central laboratory by IHC with clone 22C3; based on the MEL Score approach as per Duad et al. J Clin Oncol 2016 using a ratio of tumor and associated immune cells expressing membranous PD-L1 at any intensity (weak, moderate, or strong staining), relative to all viable tumor cells. Positive PD-L1 reflects a MEL score of 2 or greater (e.g. of greater than or equal to 1% of PD-L1 cells as calculated above).
CI, confidence interval; HR, hazard ratio, MEL, melanoma; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival.

Post-hoc analysis: PFS for patients with no prior (neo-)adjuvant anti-PD-1 therapy



Excluding patients with prior anti-PD-1 therapy as neoadjuvant/adjuvant therapy, median PFS was 24.8 months with IO102-IO103 plus pembrolizumab versus 11.0 months with pembrolizumab alone

Jessica C. Hassel

Kaplan–Meier estimate of PFS determined by BICR per RECISTv1.1. CI, confidence interval; HR, hazard ratio, PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival.

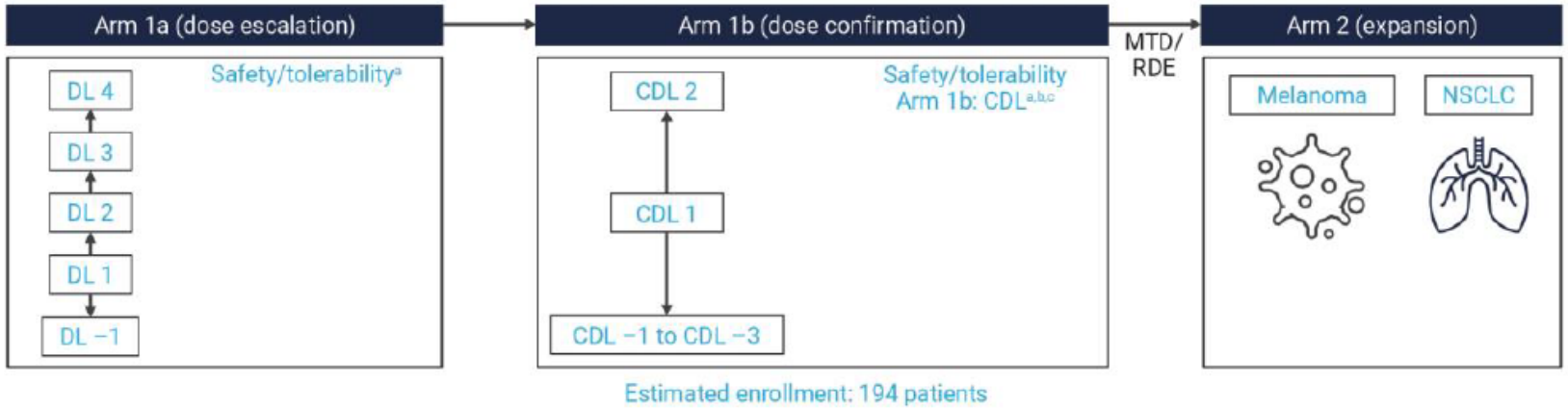
1. Kjeldsen J.W., et al. Nat Med 2021;27:2212–23. Erratum in: Nat Med 2022;28:87. 2. Lorentzen C.L., et al. J Immunother Cancer 2023;11:e006755

IMMUNE MODULATORY VACCINES -mRNA

TARGETING IDO AND PDL1

Phase 1/2 study of mRNA-4359 administered alone and in combination with immune checkpoint blockade in adult participants with advanced solid tumors

Figure 1. mRNA-4359-P101 (NCT05533697) study design



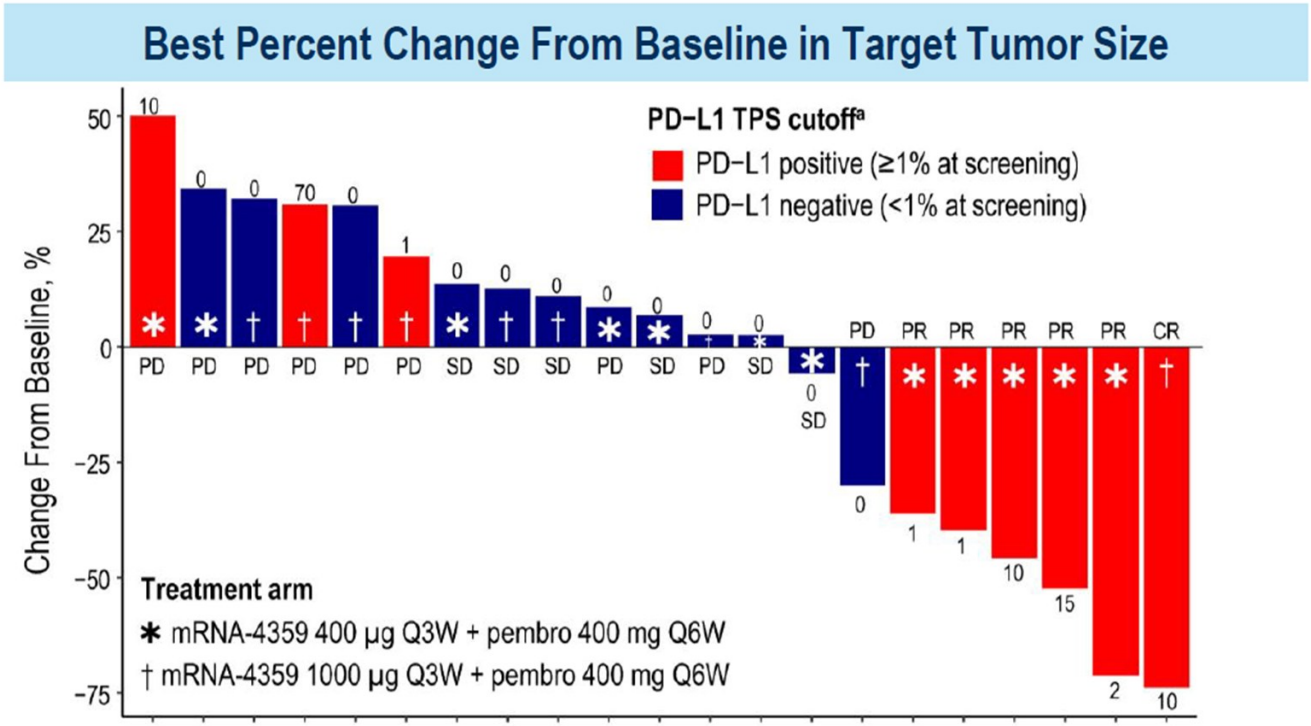
mRNA-4359 is a lipid nanoparticle encapsulated mRNA-based cancer vaccine encoding for PD-L1 and IDO1 antigens given as an intramuscular injection.

Powderly et al. TPS2676 ASCO 2023

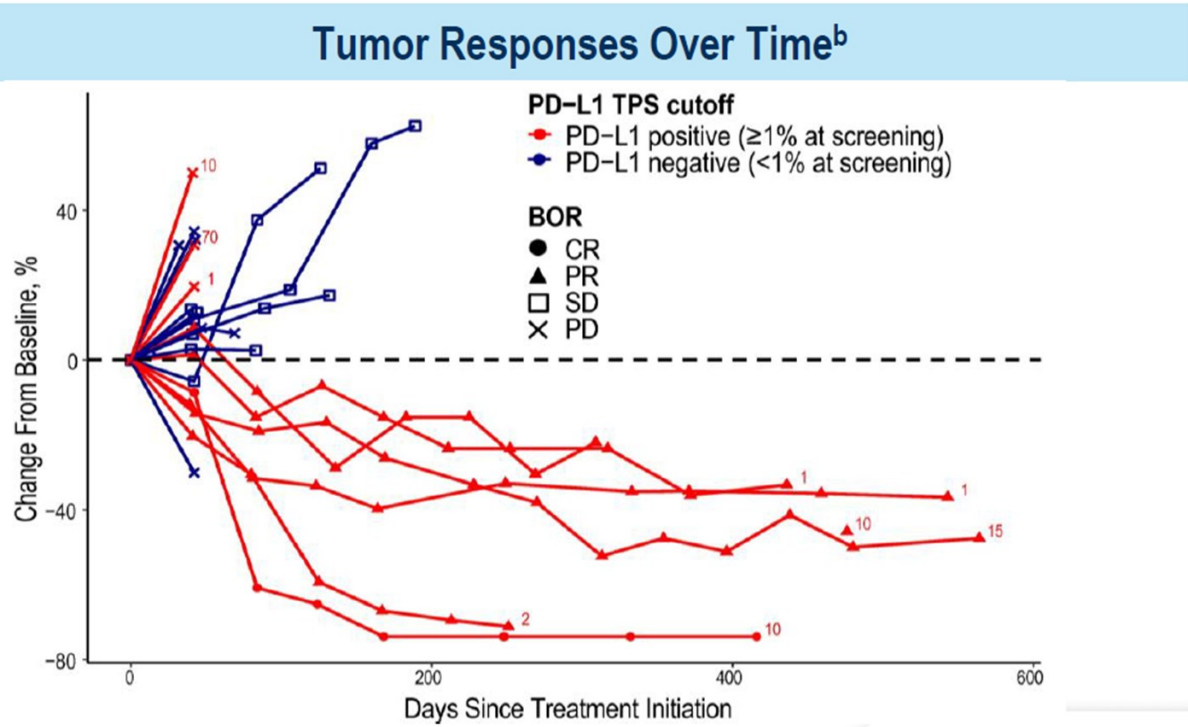
2. line mRNA vaccine + anti PD1

Phase II trial, mRNA immune modulatory vaccine targeting IDO and PD-L1

Objective responses in PDL1+



Durability of response in PDL1+



BOR, best overall response. [a]Baseline PD-L1 TPS scores are displayed above or below each bar. [b]Baseline PD-L1 TPS scores in patients with PD-L1 positive tumors are displayed at the end of the line.

Pinato et al, ESMO 2025

Seasonal viral vaccines

Influenza vaccination

Association with survival of patients with advanced cancer receiving CPI therapy

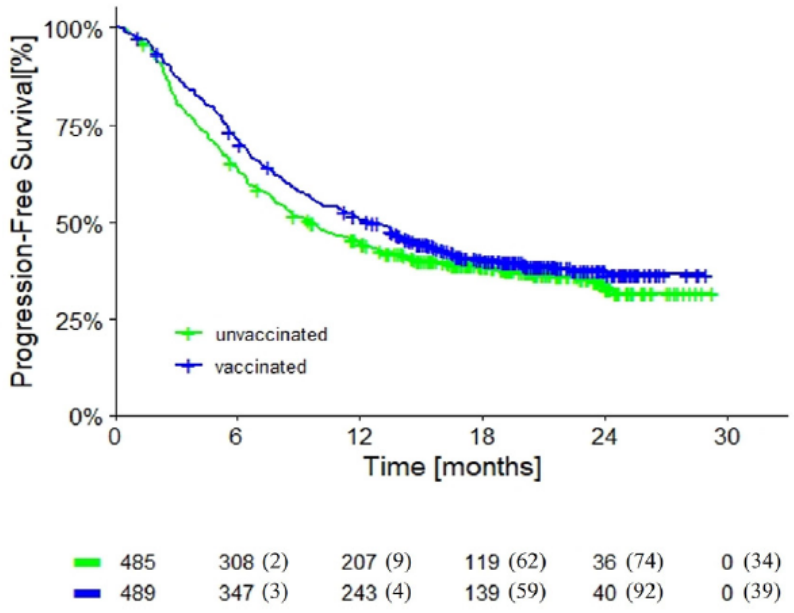


Fig. 3: **Progression-free survival of patients by vaccination status in the propensity-matched population.** (The numbers show the

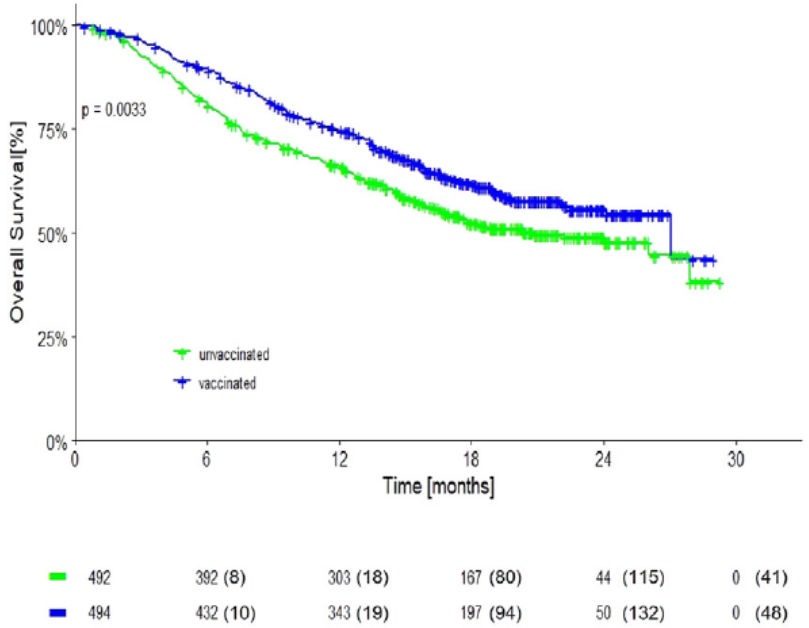


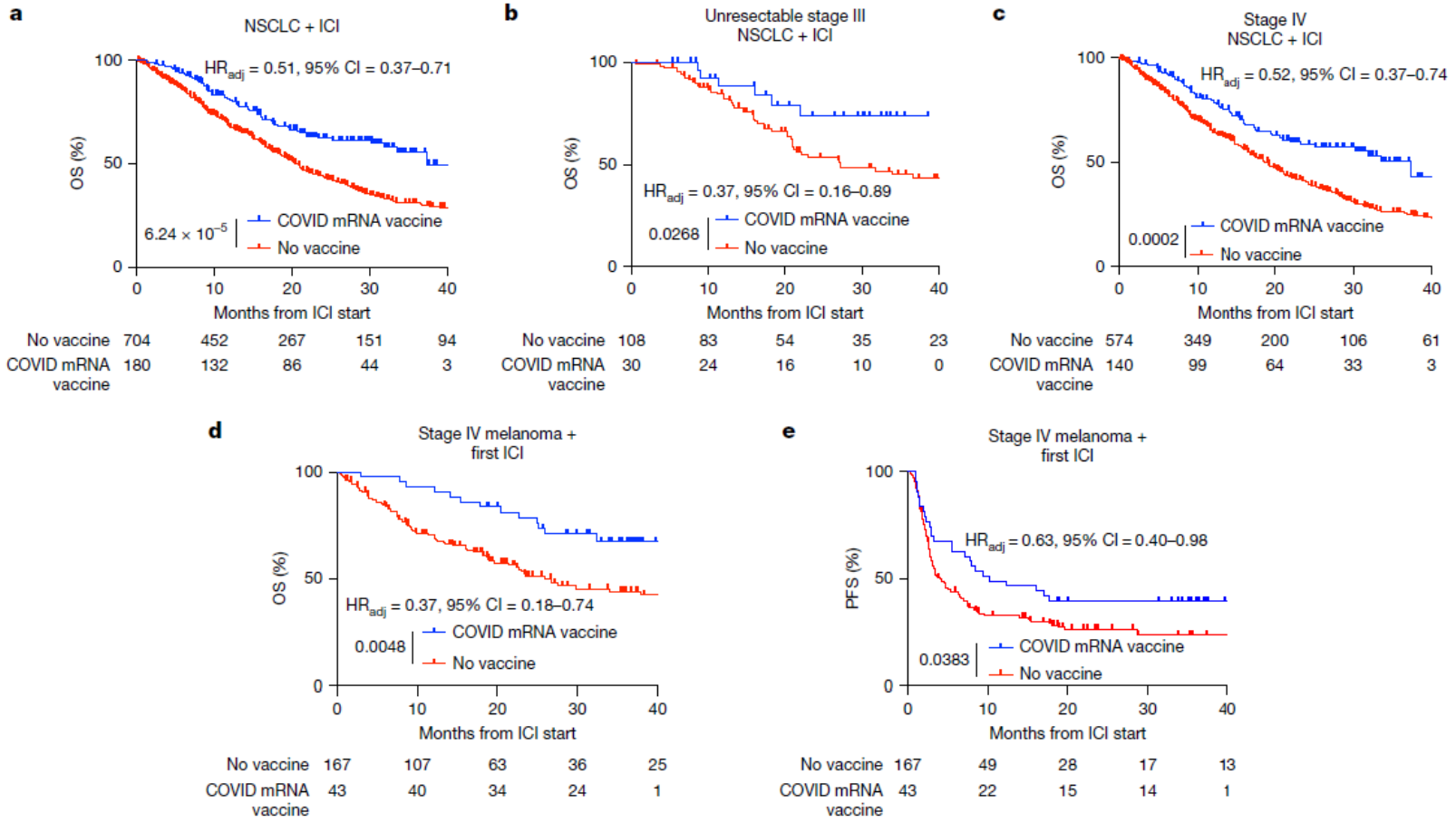
Fig. 2: **Overall survival of patients by vaccination status in the propensity-matched population.** (The numbers show the numbers

The INVIDIa-2 study results suggest a favourable immunological impact of influenza vaccination on the outcome of cancer patients receiving ICI immunotherapy

Bersanelli. The Lancet 2023

Covid vaccination

Association with efficacy of 1. line CPI therapy

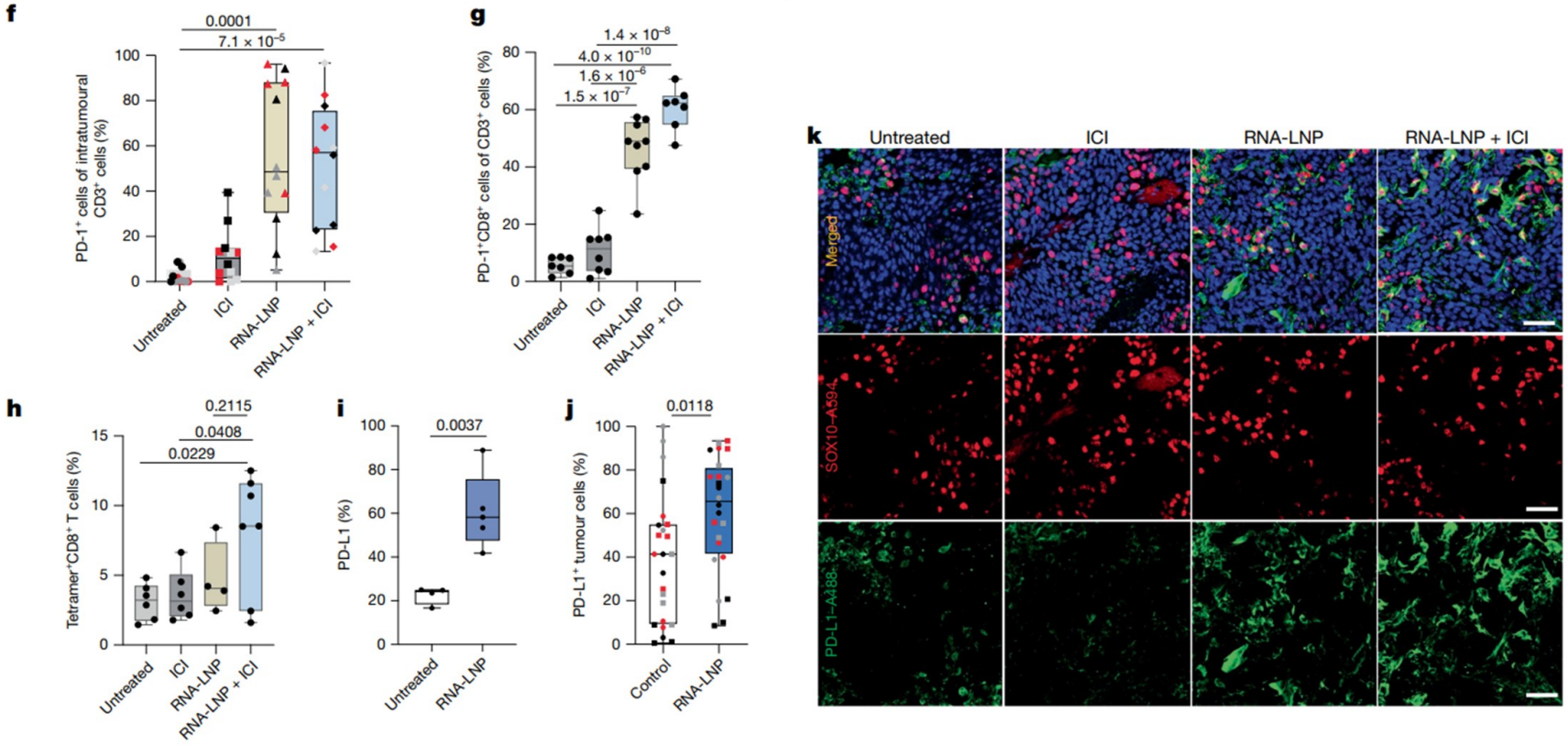


Grippin et al, Nature 2025

Inge Marie Svane

Covid vaccination

Impact on immune tumor microenvironment in murine model

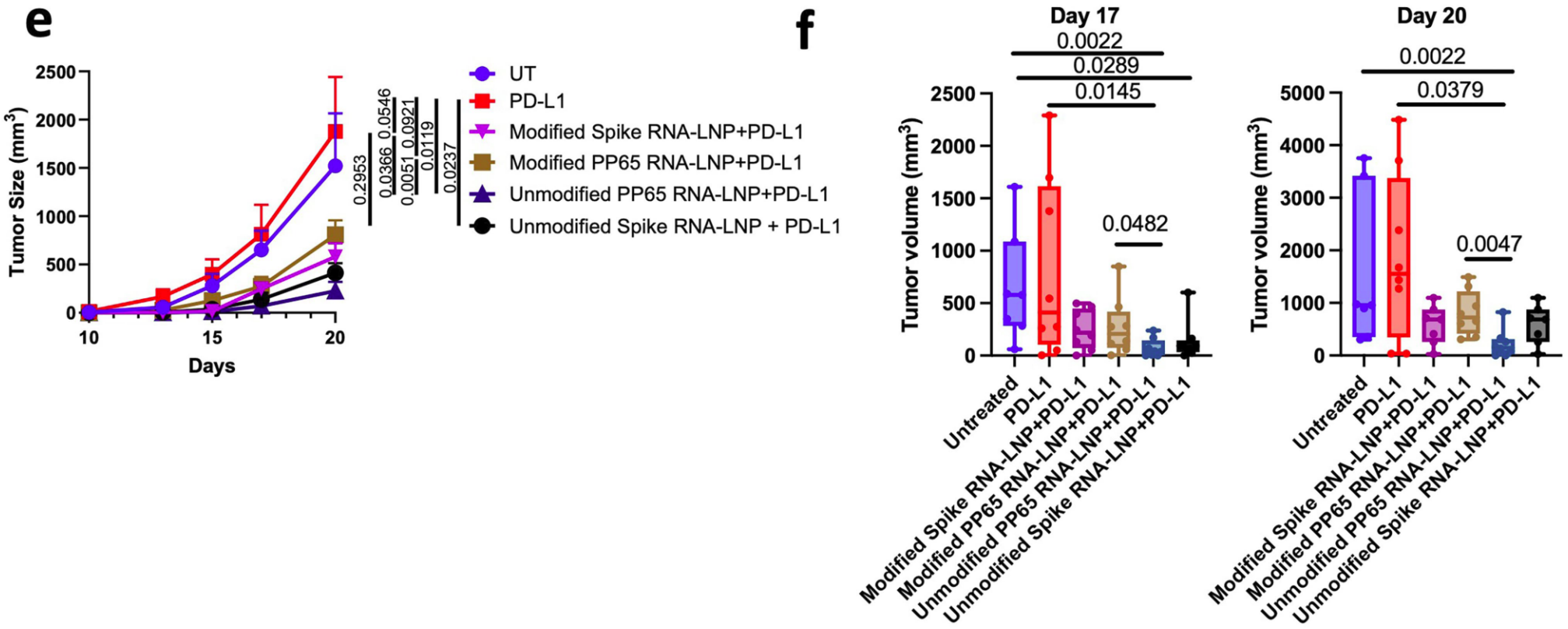


Grippin et al, Nature 2025

Inge Marie Svane

Covid vaccination

Antigen- independent immune stimulation by mRNA

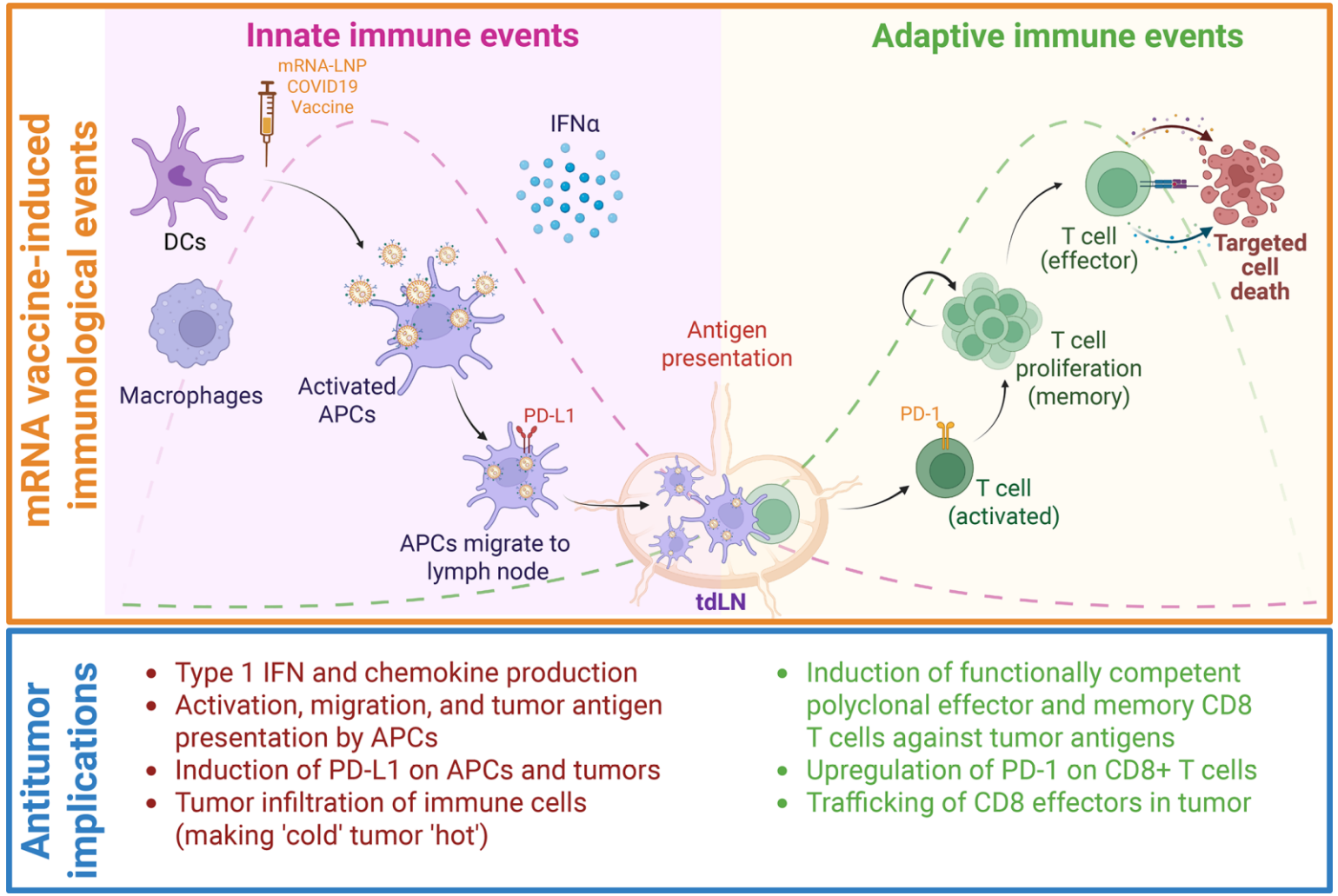


No difference in antitumour activity between mRNA encoding the spike protein compared to mRNA encoding the cytomegalovirus, suggesting that innate immune sensing of the mRNA itself is the primary driver of antitumour activity from mRNA vaccines

Grippin et al, Nature 2025

Covid vaccination

Antitumor mechanisms induced by COVID-19 mRNA vaccines and potentiating the efficacy of ICIs.



Gujar S, et al. J Immunother Cancer 2026

Inge Marie Svane

KEY POINTS

Lung cancer vaccines

- Some early phase encouraging results but no phase III evidence for efficacy of a lung cancer targeting vaccine.
- Ongoing clinical trials utilize various delivery platforms to target a wide range of tumor antigens in non-small cell lung cancer (NSCLC) patients.
- The recent pandemic accelerated the development of novel manufacturing technologies for RNA cancer vaccines.
- Combining cancer vaccines with checkpoint inhibitors seems to have encouraging results in treating NSCLC.
- A new era in treating early-stage NSCLC is being established with novel cancer vaccines

QUESTIONS ?