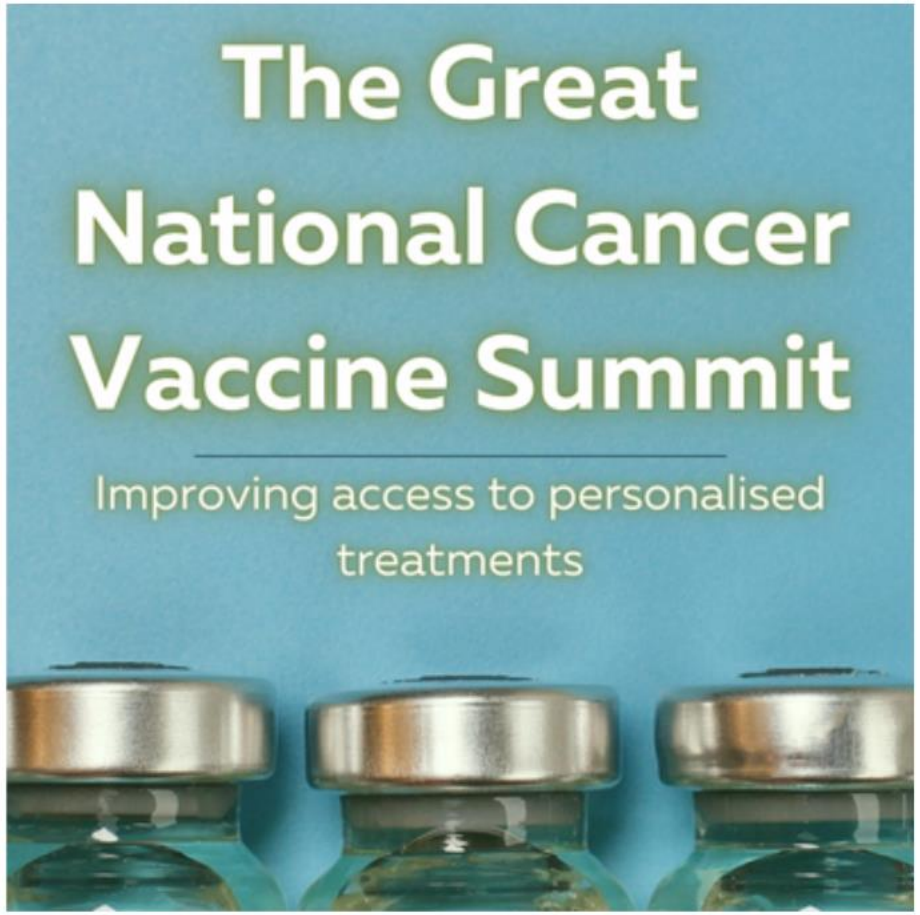
CONVENZIS

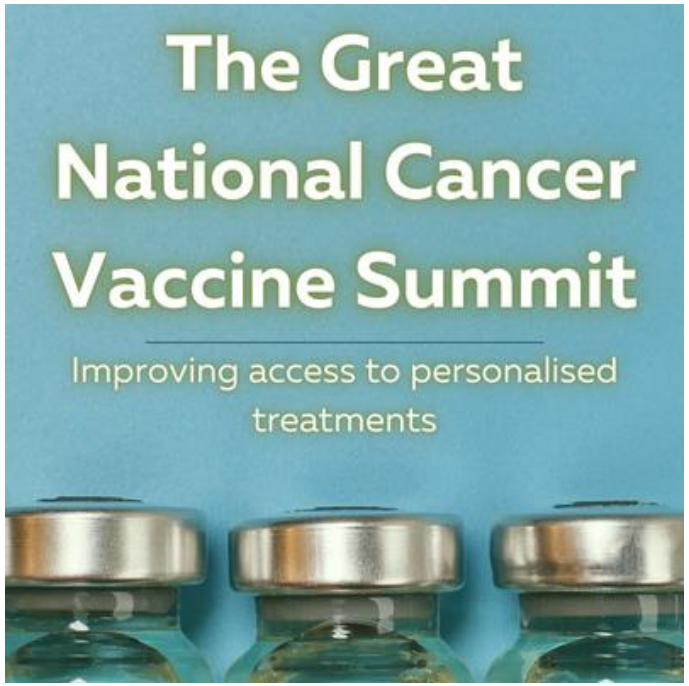


Agenda for today:

SCAN ME

Wednesday 1st May | 15Hatfields, London

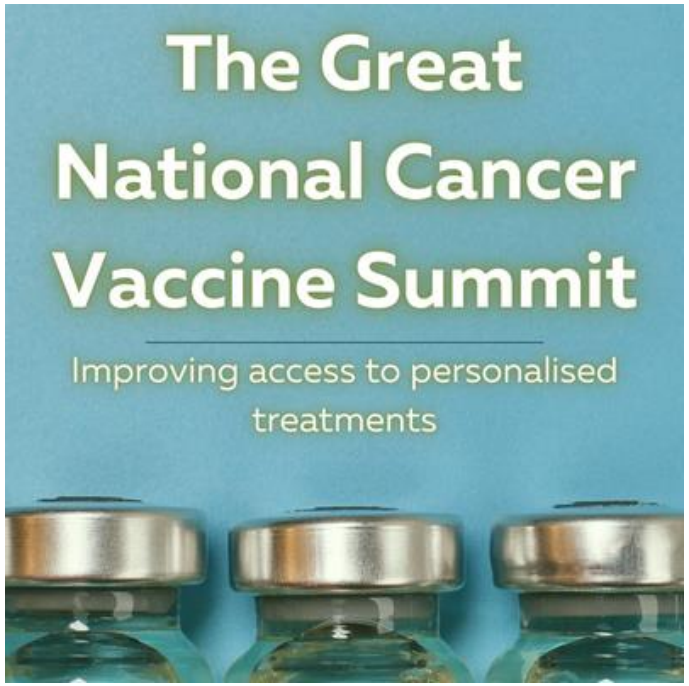
CONVENZIS



Welcome to The National Cancer Vaccine Summit!

SCAN ME

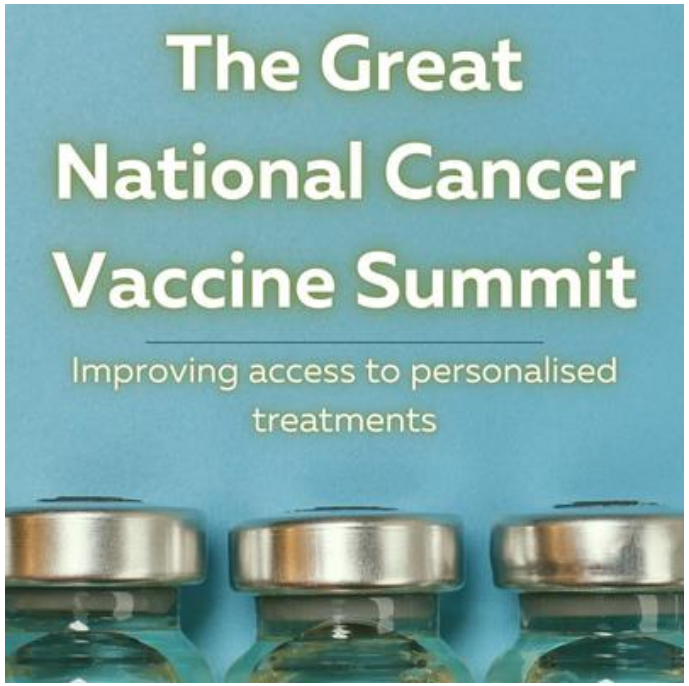
1st May 2024
9am – 5:30pm
15Hatfields, London



Slido

Please scan the QR Code on the screen. This will take you through to Slido, where you can interact with us.

SCAN ME



Chair Opening Address

Dr Lennard YW Lee
Associate Professor (University of Oxford), Medical Oncologist (NHS), National Clinical Advisor (Office for Life Sciences) - University of Oxford

The Great National Cancer Vaccine Summit

Improving access to personalised treatments

Our place in the world

The UK routinely deliver world firsts for vaccination, health and high-end technologies

In 2024, a new opportunity has opened, vaccine for cancer, generating global interest.

The summit showcases our national expert's greatest ideas for our UK strategy to potentially make an advance against cancer.

Building on the strongest foundations

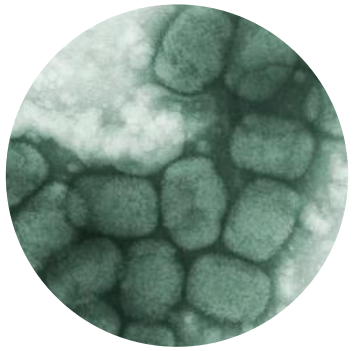
1796
Edward Jenner
St Andrews

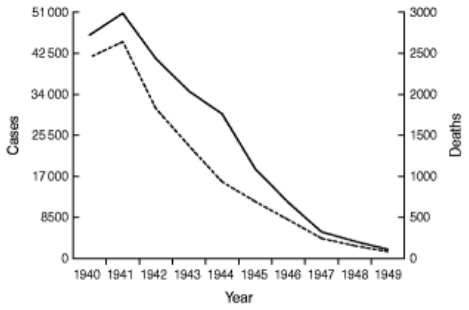
1940
Florence Horsbrugh
Edinburgh

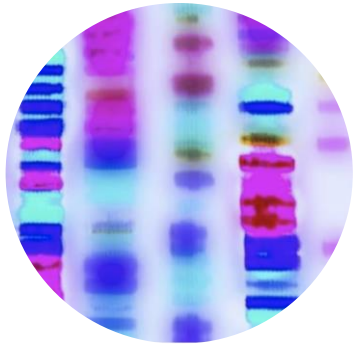
1953
Watson & Crick
Cambridge

2012-2018
100,000 genome
Pan- UK

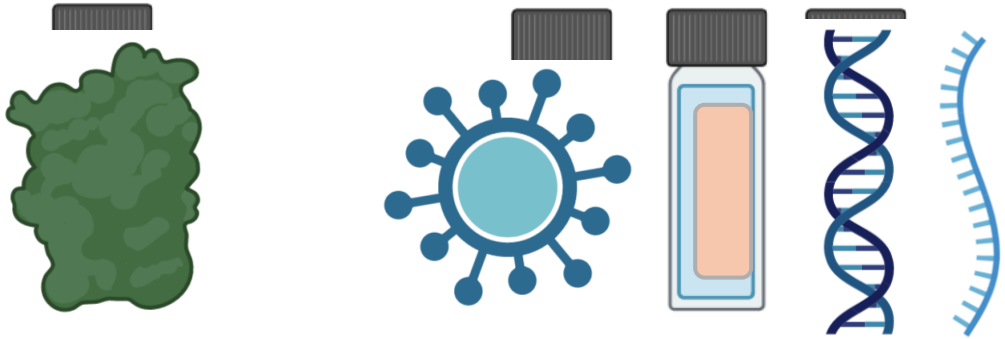
2022
COVID vaccine
Oxford







What are vaccines?



Vaccines

Personalised vaccines

Peptide vaccines

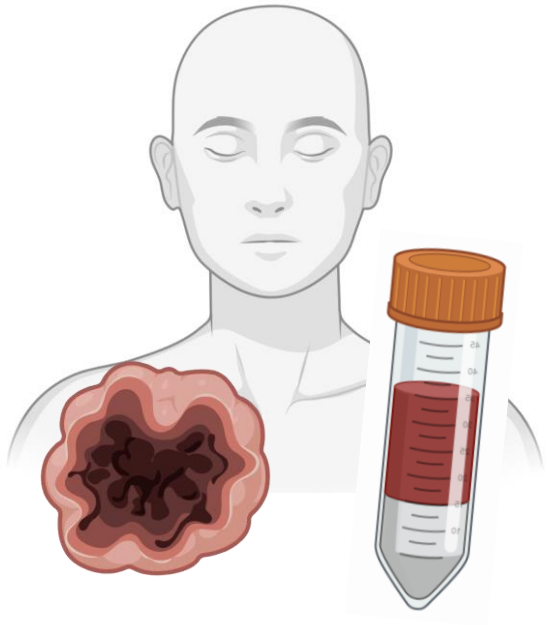
Viral vaccines

DNA/RNA vaccines

Vaccines train our immune system

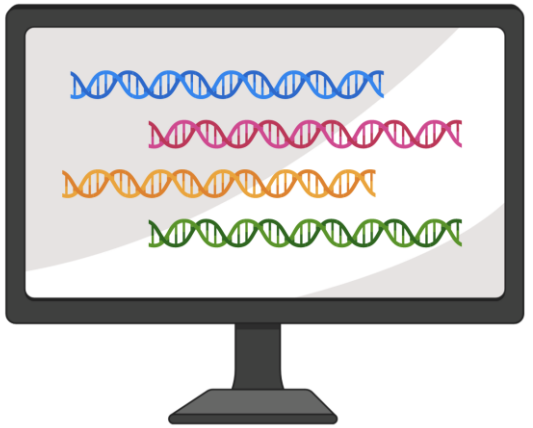
They help the immune system find abnormalities, called antigens, and remove diseased cells.

What is a cancer vaccine?



Tissue acquisition

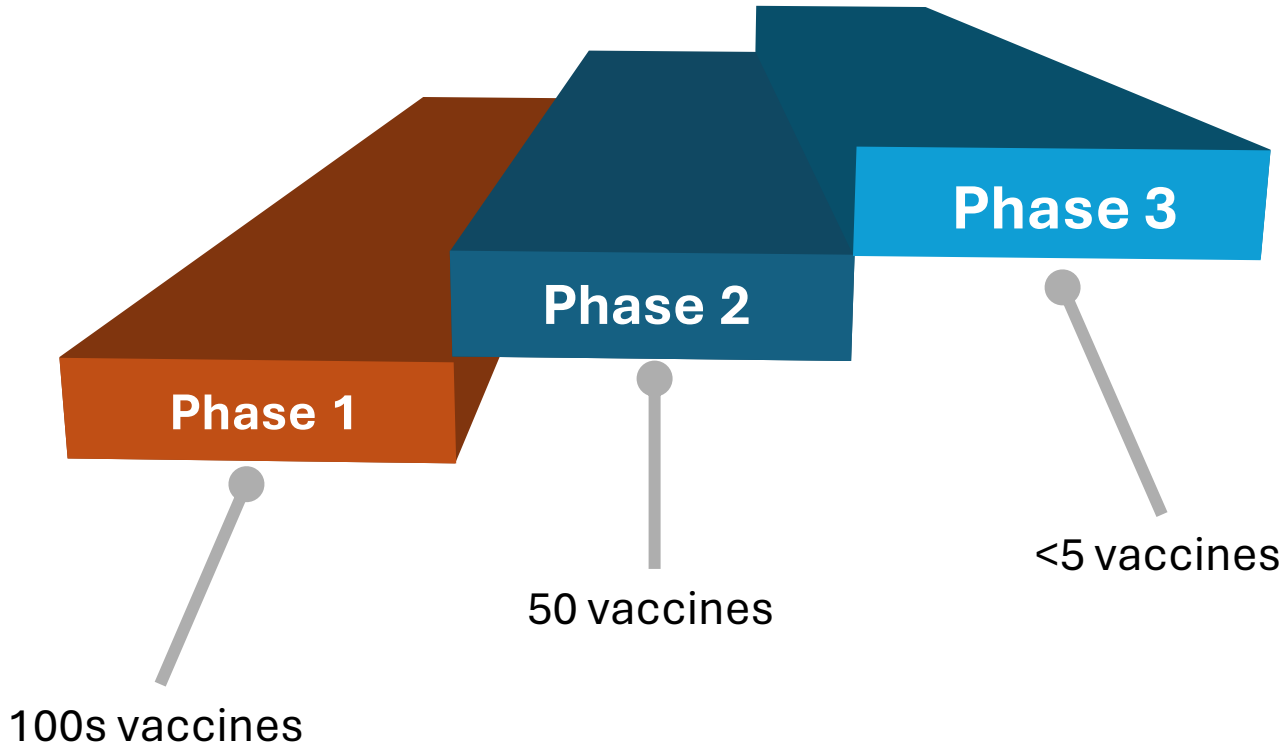
Genomic sequencing



Target identification and prioritisation

Vaccine manufacturing

A global vaccine technology race is underway



What's the plan?

1. To initiate a **global advance** of vaccines for cancer for immunity against cancer

2. Transformative benefit will be achieved across **multiple cancer subtypes**, for **early and late-stage cancers**

3. To place **10,000 people** through clinical trials **by 2030**

UK NEWS WEBSITE OF THE YEAR

The Telegraph

Dozens of NHS hospitals to offer pioneer cancer vaccines in next three months

Health chiefs sign deal with BioNTech as part of cutting-edge clinical trials

By Joe Pinkstone, SCIENCE CORRESPONDENT

8 July 2023 • 2:33pm

118

NHS
University Hospitals Birmingham
NHS Foundation Trust

UHB first to start mRNA cancer vaccine trial for colorectal cancer

University Hospitals Birmingham NHS Foundation Trust (UHB) is the first site in the UK to launch the BioNTech Messenger RNA (mRNA) cancer vaccines trial which will aim to recruit 10,000 people across the UK.

BBC NEWS

Covid vaccine research now helping cancer patients

By Gill Dummigan
Health Correspondent, BBC North West

Ten months ago, Adrian Taylor was told he had incurable cancer and there were few treatment options left.

THE TIMES

Britain jabs its way to centre stage in the mRNA revolution

INDEPENDENT

NEWS › HEALTH

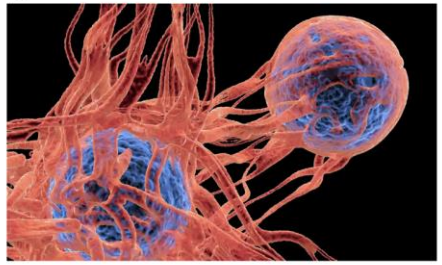
Up to 10,000 Britons could take part in cancer vaccine trials

Participants could receive groundbreaking treatment after the Government signed an agreement with a leading pharmaceutical company.

The Guardian
Newspaper of the year

'A silver lining': how Covid ushered in a vaccines golden era

Pandemic accelerated advances in vaccine technology, opening up possibilities for combating array of diseases



CNBC

HEALTH AND SCIENCE

BioNTech says it will start cancer vaccine trials in the UK from September

PUBLISHED FRI, JAN 6 2023·8:27 AM EST | UPDATED FRI, JAN 6 2023·8:54 AM EST

Jenni Reid

SHARE

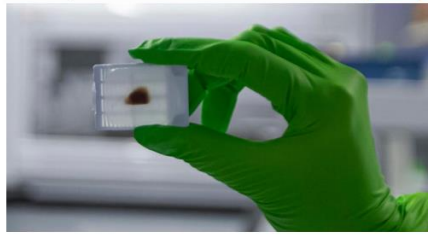
Forbes

BREAKING

Cancer Vaccine Trials—Using Same mRNA Tech Behind Covid Shots—Could Launch In U.K. This September

Robert Hart Forbes Staff
I cover breaking news.

Follow



BBC NEWS

Home | Israel-Gaza war | Cost of Living | War in Ukraine | India Election | Climate | UK | World | Business

Health

British man tests first personalised melanoma vaccine

Steve Young, 52, is one of the UK patients enrolled on the trial.

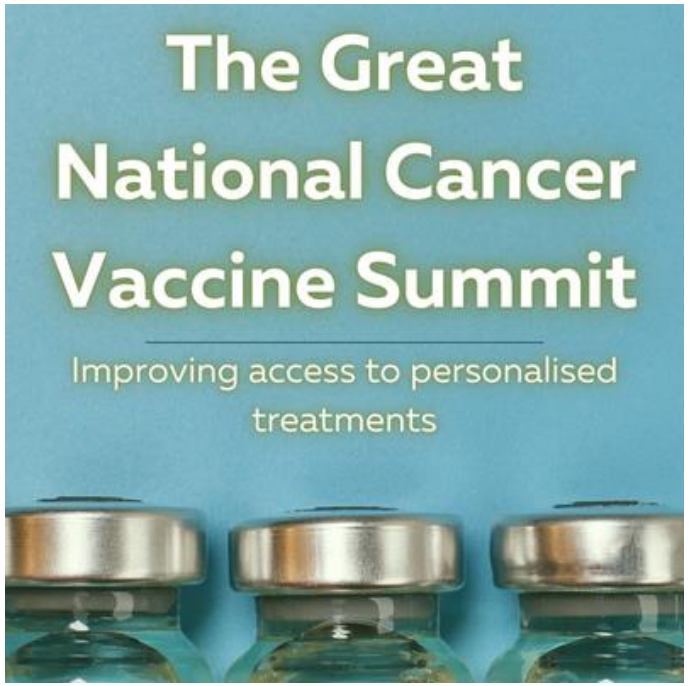
#cancervaccinesummit

How you can help?

Your support:- Being here and learning about what national experts are doing. Be vocal in support

Your insights:- Do let us know if you see any opportunities to raise awareness for this new advance against cancer vaccines.

#cancervaccinesummit



Speaking Now…

Professor Christian Ottensmeier
Professor of Immuno-Oncology, Molecular & Clinical Cancer Medicine / Consultant Medical Oncologist - University of Liverpool / Clatterbridge Cancer Centre

CAN CANCER VACCINES BE A CORE BUILDING BLOCK FOR COMBINATION IMMUNOTHERAPY?

CHRISTIAN OTTENSMEIER MD PHD

PROFESSOR OF IMMUNO-ONCOLOGY

CLATTERBRIDGE CANCER CENTER & UNIVERSITY OF LIVERPOOL

The brief answer is: YES

…and the date are accumulating at a staggering pace in randomized studies

- But there is a lot of history to consider

- After many years of failure Steve Rosenberg concluded in 2004:

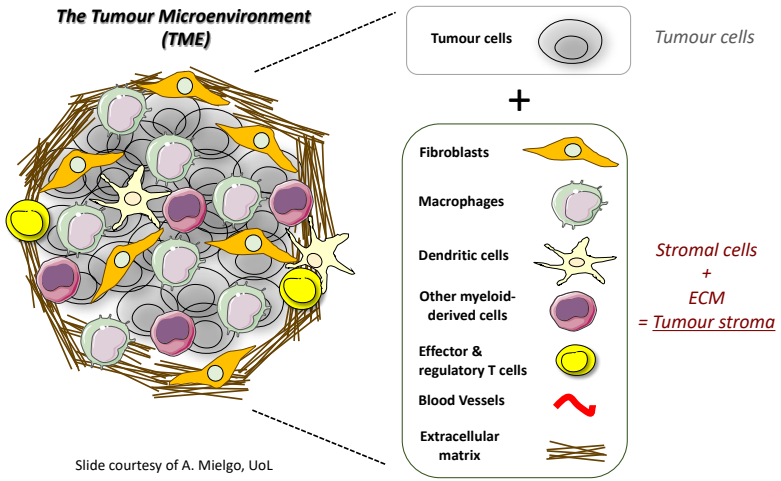
  "The ineffectiveness of cancer vaccine approaches is not commonly appreciated, however, because of the 'spin' often accompanying reports of cancer vaccines."

- So what has changed?

Rosenberg, S., Yang, J. & Restifo, N. ***Nature medicine 10 (2004).***

What has changed?

- We know more about 'immune competence' of the patient
  - A vaccine cannot work if the immune system is damaged
  - Issues:
    - more inhibitory tumour microenvironment in advanced disease
    - Global immunocompetence decays with progression
      - Not least because of the treatments we have given
- We are better at understanding the tumor microenvironment



What has changed?

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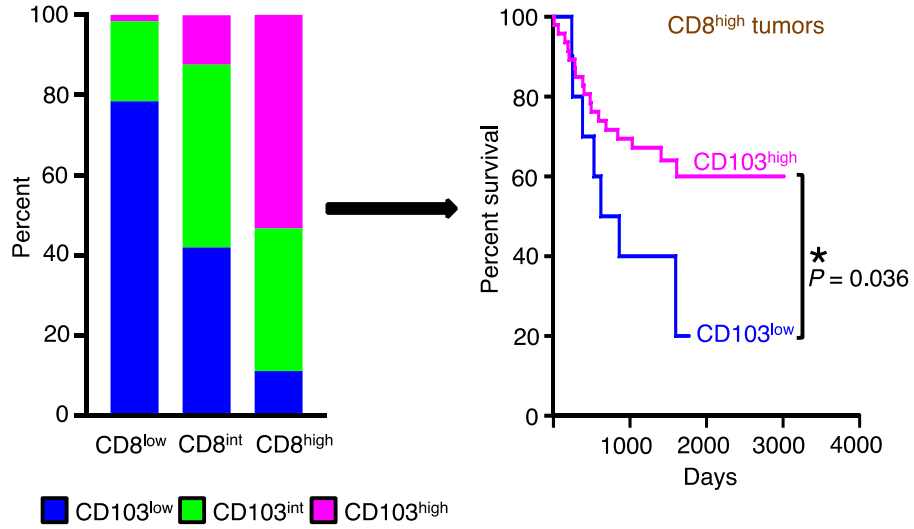
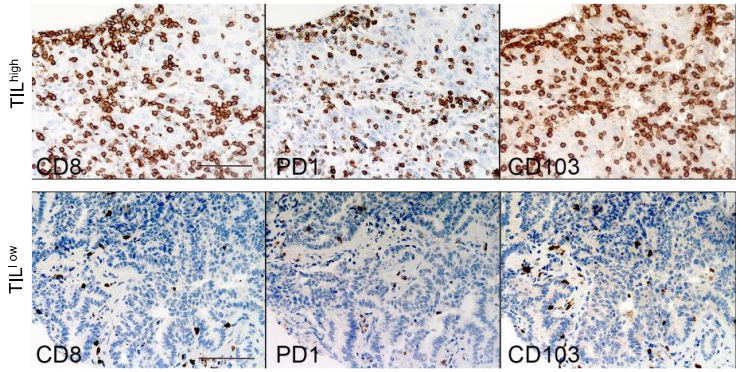
  - A vaccine cannot work if the immune system is damaged
  - Issues:
    - more inhibitory tumour microenvironment in advanced disease
    - Global immunocompetence decays with progression
      - Not least because of the treatments we have given
- We are better at understanding the tumor microenvironment
- We are doing smarter trials (efficacy endpoints in early disease)
  - as we leave drug development strategies of cytotoxics behind
- We are making better vaccines
- We are better at making IO treatment choices (well, a bit)

We understand better the correlates of protection

long lived CD8+ T tissue resident memory:

1. Presence of CD103 (IHC) predicted patient survival above that of CTLs





highly effective killers

divide in the cancer tissue

clonally expanded

express unique, actionable target profile

released by aPD1 treatment

unique actionable targets identified

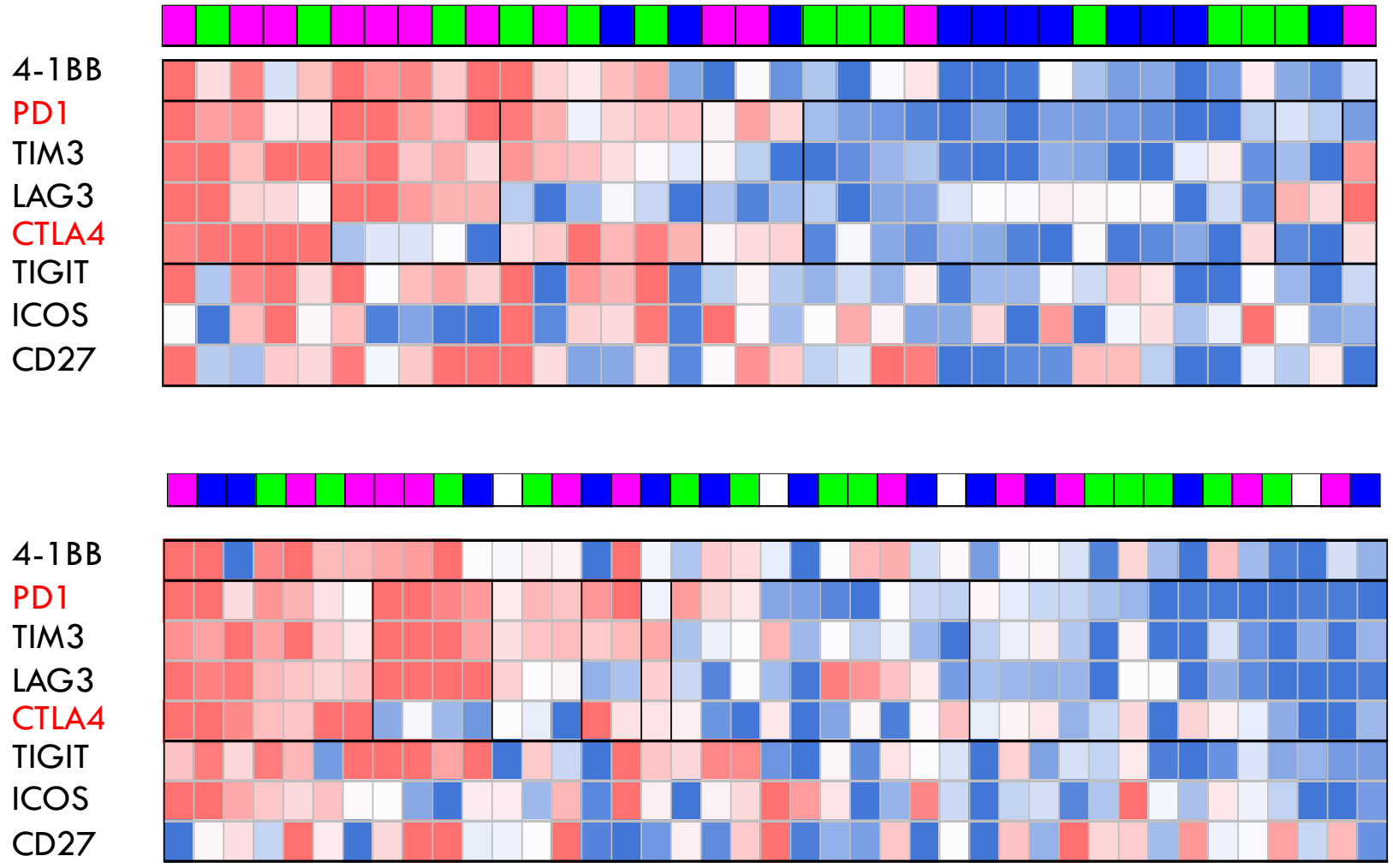
‚TRAINED' BY VACCINATION

Ganesan et al, Nat Imm 2017
Clarke et al, JEM 2019
Von Witzleben, CCR 2023

Determining which checkpoint blocks T cells

NSCLC

HNSCC

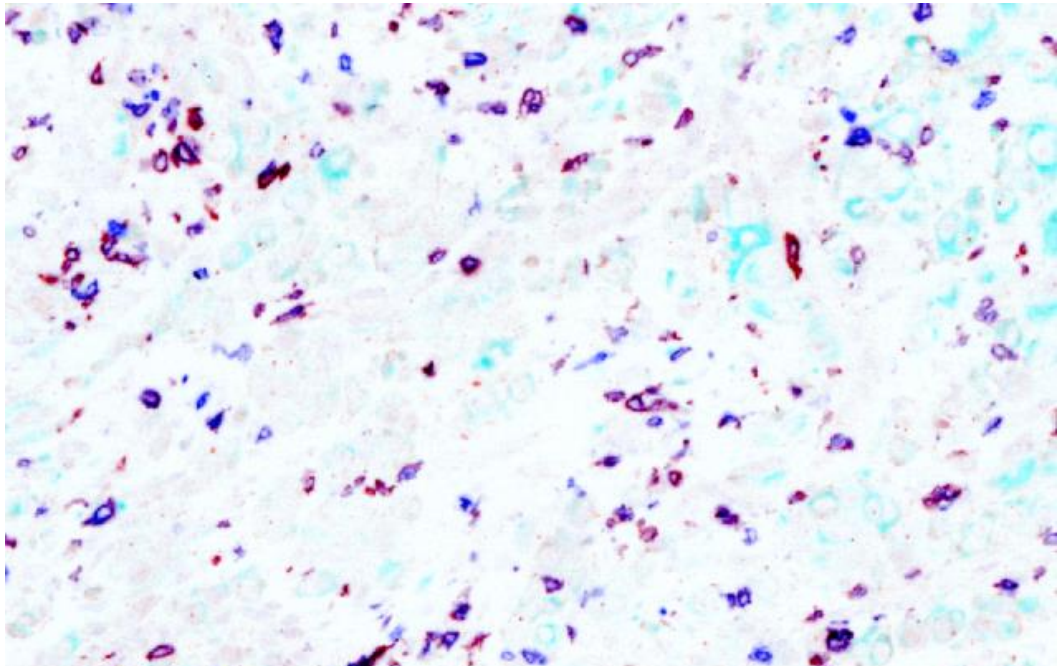


So there is no point to 'throw the kitchen sink' at the problem

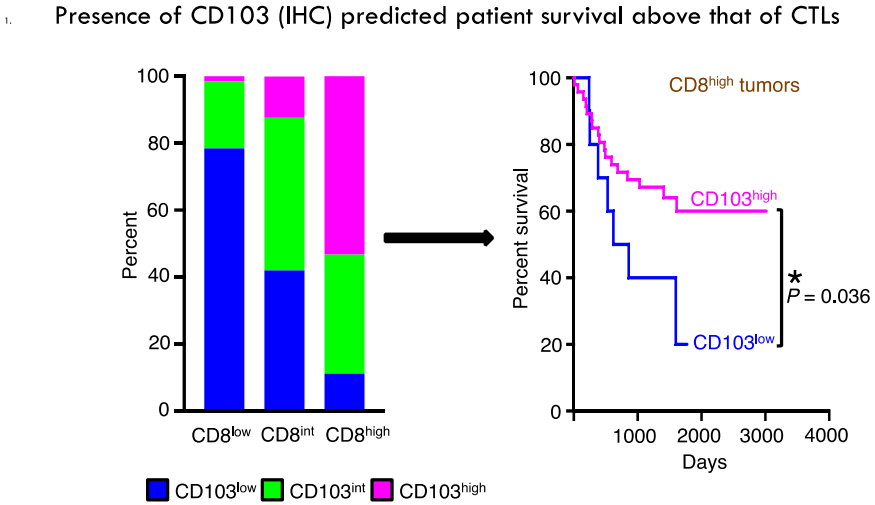
Ganesan et al. Nat Immunol 18 (8), 940-950. 2017

Conclusion:

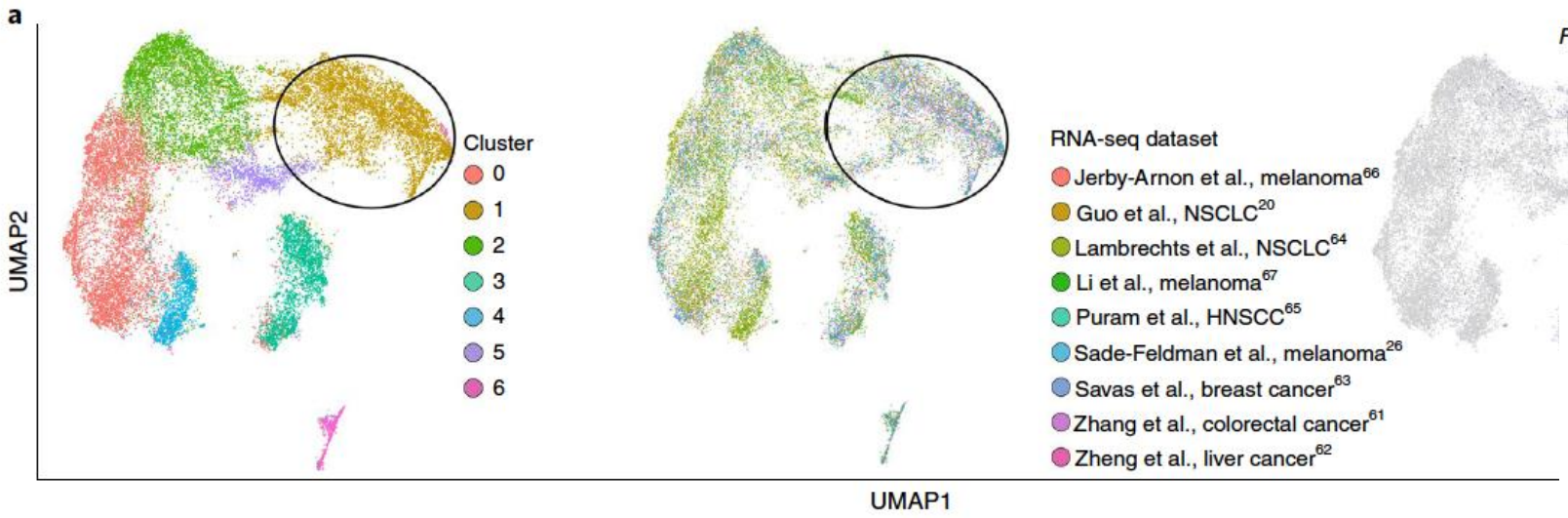
- Enough tissue resident memory cells: anti-PD1 for control sufficient
  - Selection markers:
    - ➔PDL1 expressing cells in the TME
    - PDL1 is upregulated by effector T cells that produce IFNg
    - (note: other pathways to upregulate PDL1 exist)
    - Their 'target antigen' is unknown

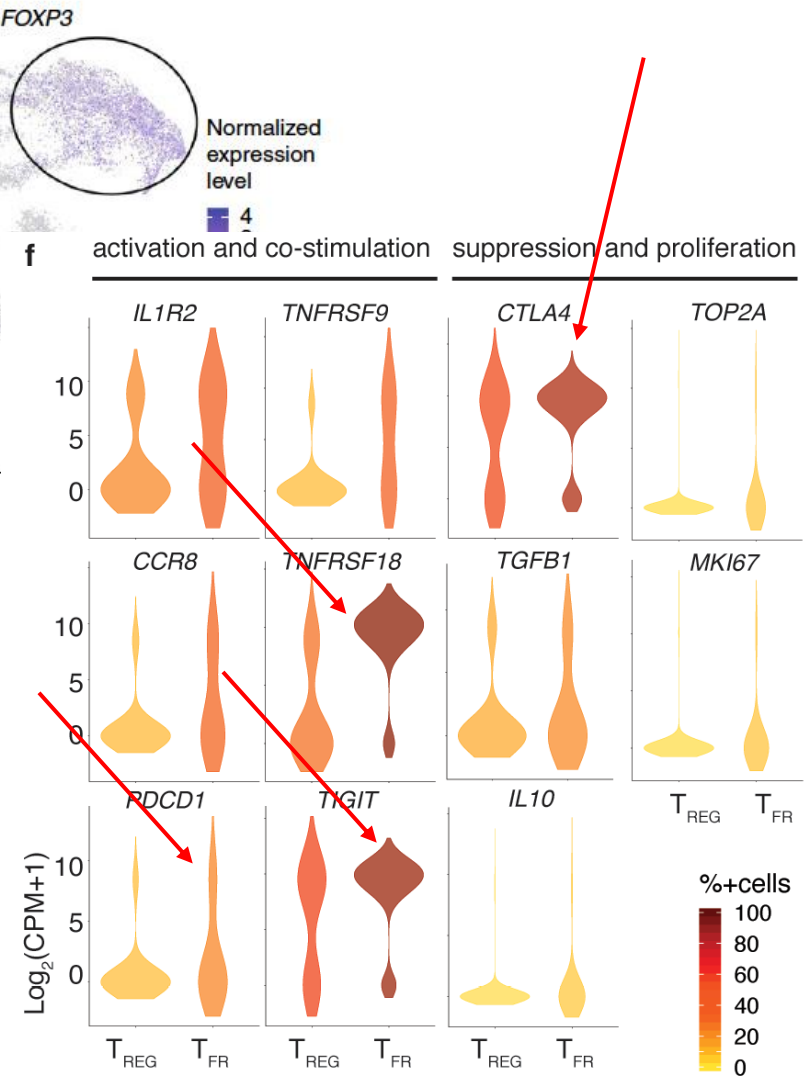


CD3 PD1
CD3+PD1=purple
cytokeratin



Inhibitory $T_{regulatory}$ cells are abundant across cancer types





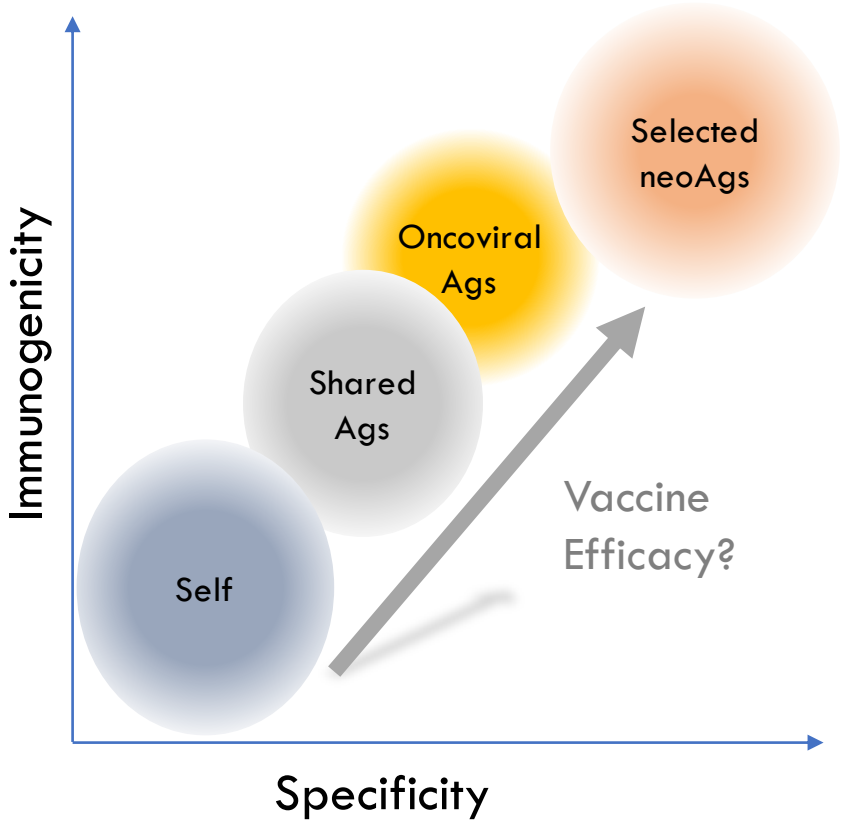
- Meta-analysis of RNA-sequencing from 6 types of cancer
- T_{FR} cells were present in all assessed studies
- T_{FR} cells highly suppressive
- T_{FR} cells activated by aPD1 antibody

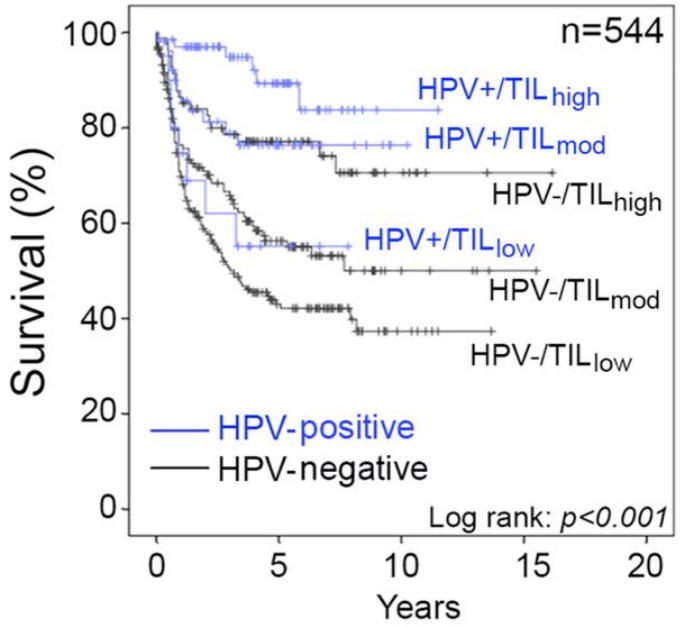
Eschweiler, Nat Immunology 2021
Eschweiler, Nature 2022

Stratification of IO treatment:

- T cells are turned off
  - by tumour cells
    - Anti-PD1 antibody or anti PDL1 antibody
  - by other T cells
    - Remove regulatory T cells (Treg/T follicular regulatory cells)
      - E.g. anti-CTLA4 antibody, PI3k delta inhibitor, anti-CCR8, anti-GITR…
  - (by myeloid cells
    - No clear strategy yet (chemotherapy?))
- Not enough T cells
  - Vaccinate to train more T cells
  - Protect them against 'being turned off'
    - Anti-PD1 antibody (as above)
    - Anti-CTLA4 antibody (as above)
- T cells cannot get to the cancer cells
  - Need to address CAF, myeloid cells

T cells recognition of tumor cells: ‘cancer cell content’ the immune system can ‘see’





Antigen recognition underpins outcome differences

Central tolerance and peripheral tolerance: limit immune attack

Multiple targets are immunogenic

The best target is unknown

Training the immune system

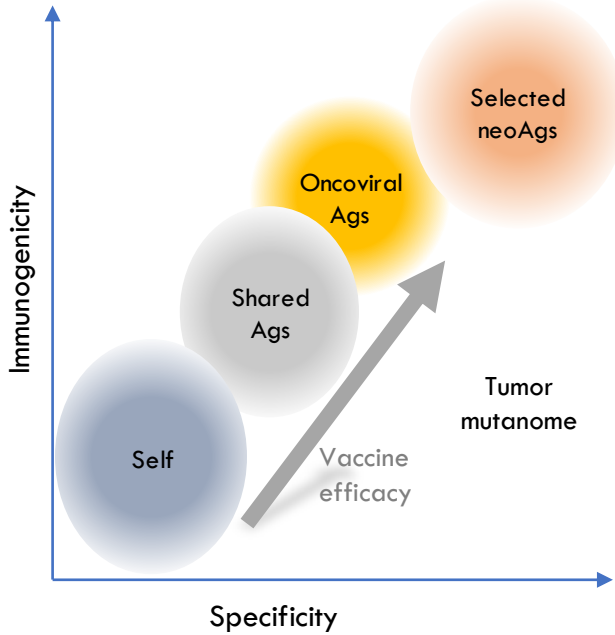
- THE PROCESS:

read out what makes a cancer different to healthy cells → turn the difference into a vaccine → vaccinate the patient

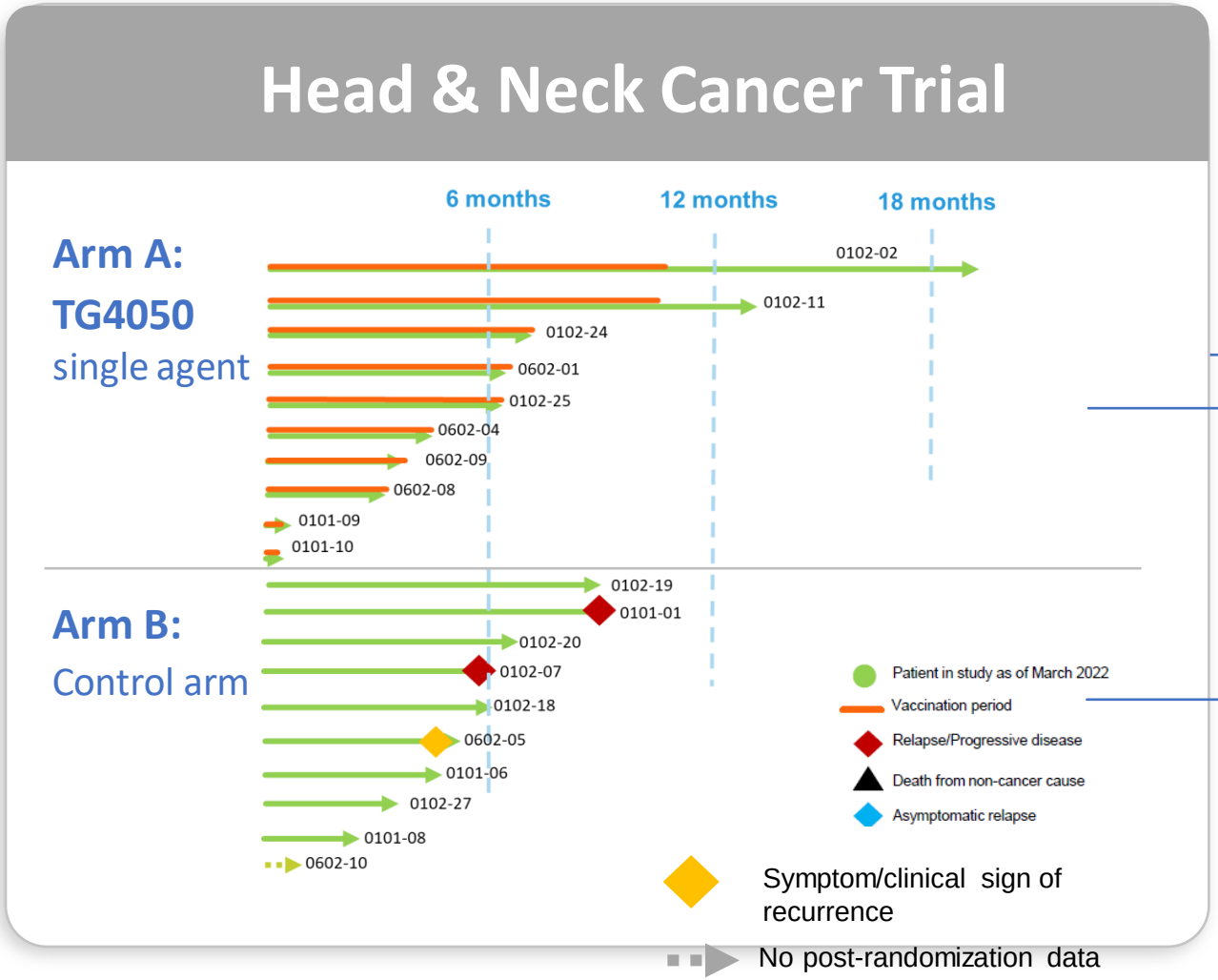
- TWO CONCEPTS:

A NEW VACCINE FOR EACH PATIENT
PERSONALISED MEDICINE

ONE VACCINE FOR MANY PATIENTS
STRATIFIED MEDICINE



Personalised cancer vaccines:
Adjuvant TG4050: early suggestion of agent clinical activity



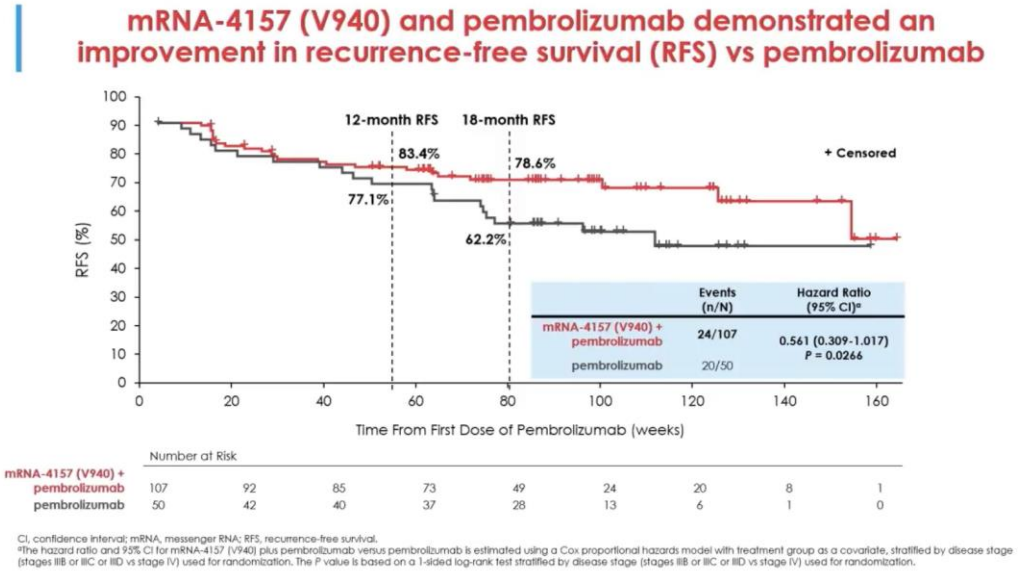
No related SAEs
Good safety profile

treated patients are stable

3 patients of the "control" arm have already relapsed

- From Repeated Injections of TG4050 as Monotherapy in Patients with Minimal Residual Disease

Randomized data: making cancer vaccines mainstream…



Multiple trials either ongoing or reported

Personalised cancer vaccines:

Nykode – DNA vaccine in advanced cancer + aPD1

BioNtech &Roche - PCV mRNA vaccine in pancreatic cancer

Nouscom – adenovirus

Transgene – in HNSCC

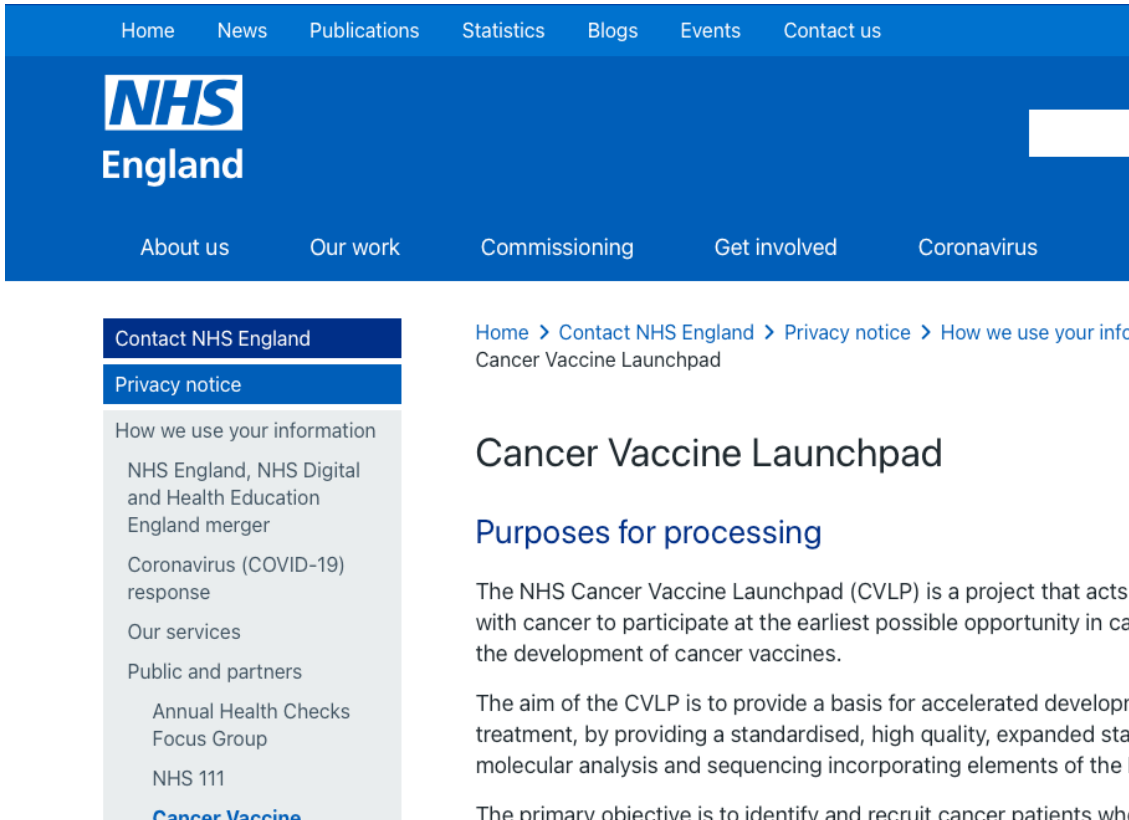
Geneos DNA vaccine+ aPD1 in HCC

Shared antigen vaccination:

Many targets and platforms

Moderna:

Adjuvant anti-PD1 +/- Personalised cancer vaccine

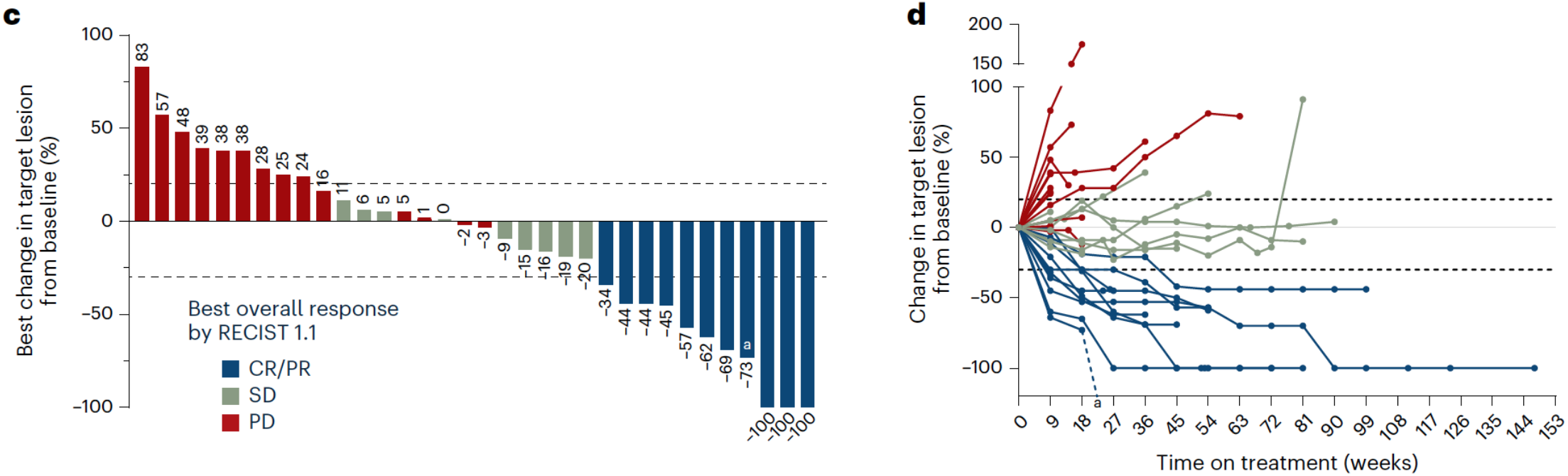


Merck V940 / Moderna rna-4157 Individualized Neoantigen Therapy (INT) Trials

Phase / Status		Treatment Setting / Stage	N, Indication	TME Modulation	Breakthrough Data
1 (8 **single arm** cohorts)	Actively recruiting to N=242	**Adjuvant**, completely resected Stage IA-IIB	**11** pts, **NSCLC** (Part A)	None (monotherapy)*	**0/11 relapses** (interim data, Sep 2023)
		Unresectable (locally advanced or metastatic)	**22** pts, CPI-naive HPV-neg **HNSCC** (Part C)	αPD-1 pembrolizumab	**6/22 (27.1%) ORR** (2 CR, 4 PR)
2b **Randomized**	Actively recruiting to N= 257	**Adjuvant**, completely resected Stage III/IV	**157** pts, **Melanoma**	αPD-1 pembrolizumab	**49% relapse reduction/delay** (Dec 2023) 1-sided p=0.0095
2b **Randomized**	Actively recruiting	**Adjuvant**, completely resected	**200** pts, **Muscle invasive bladder cancer**	αPD-1 pembrolizumab	Relapse data (DFS) expected OCT2026
2b **Randomized**	Actively recruiting	**Adjuvant**, completely resected	**272** pts, **Renal cell carcinoma**	αPD-1 pembrolizumab	Relapse data (DFS) expected JAN2028
3 **Randomized**	Actively recruiting	**Adjuvant**, completely resected Stage IIB/C, III, IV	**1089** pts, **Melanoma**	αPD-1 pembrolizumab	Relapse data (RFS) expected OCT2029
3 **Randomized**	Actively recruiting	**Adjuvant**, completely resected Stage II, IIIA, IIIB (N2)	**868** pts, **NSCLC**	αPD-1 pembrolizumab	Relapse data (DFS) expected JUN2030
2 / 3 **Randomized**	Not yet recruiting	**Neoadjuvant / adjuvant**, completely resected Stage II, III, IV(M0)	**1012** pts, **Cutaneous squamous cell carcinoma**	αPD-1 pembrolizumab	Relapse data (EFS) expected APR2029

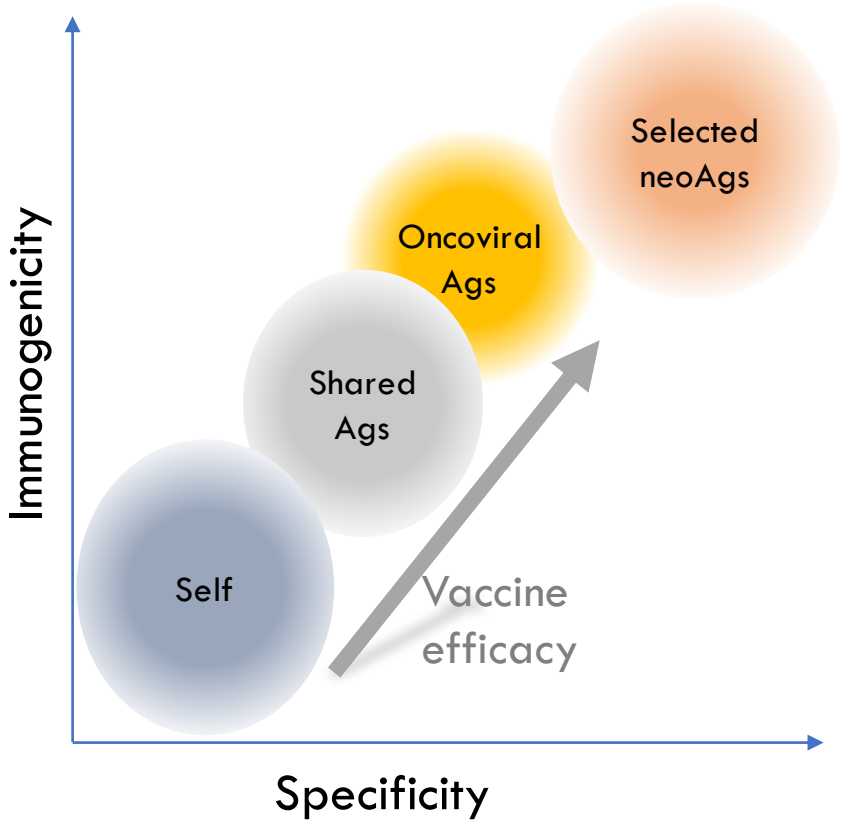
*Prior Adjuvant αPD(L)-1 permitted

PCV DNA vaccine encoding IL12 in Hepatocellular carcinoma



Yarchoan, Nature Medicine, 2024
Geneos trial, HCC – vaccine + aPD1

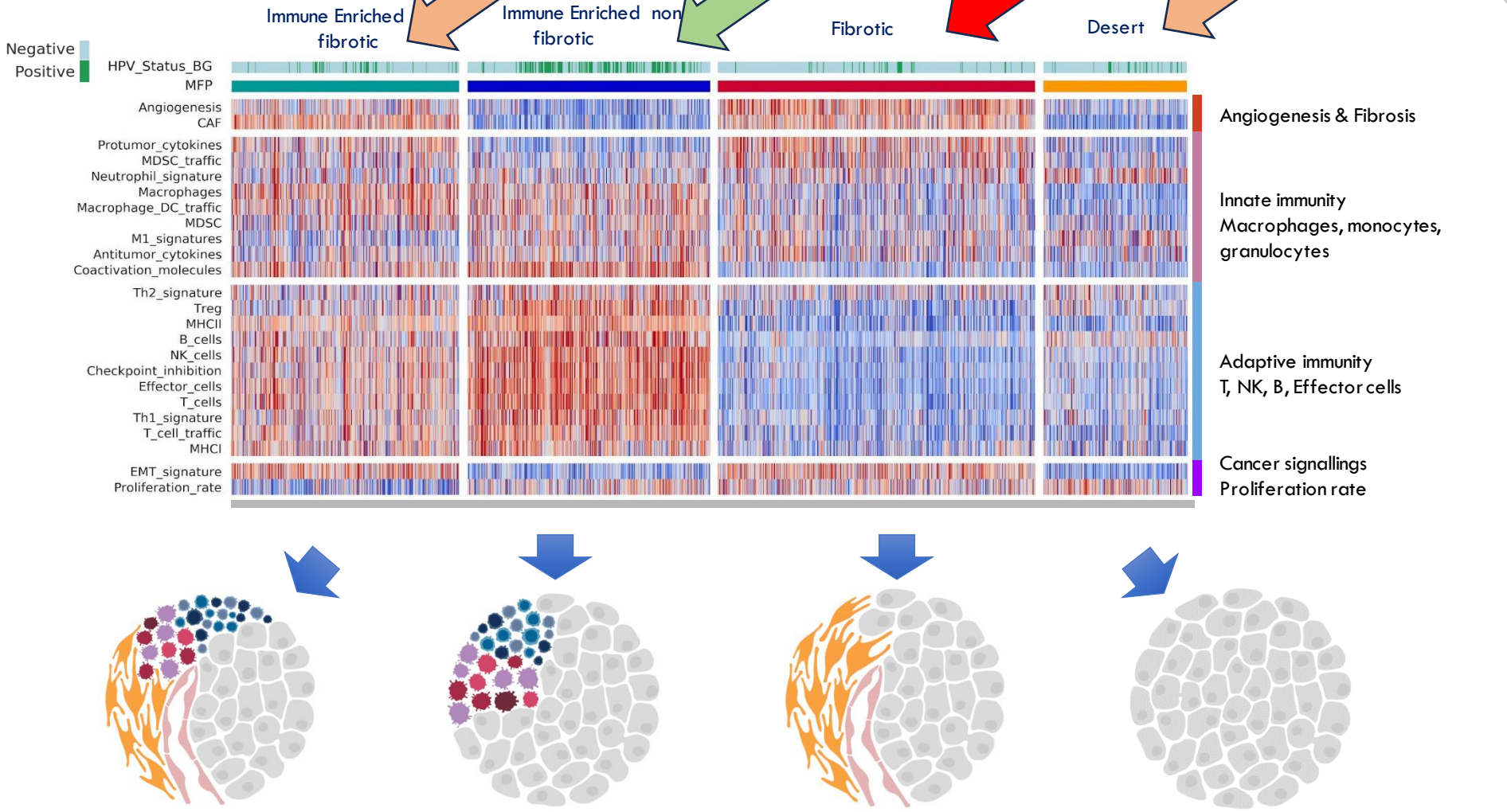
T cells recognition of tumor cells: ‘cancer cell content’ the immune system can ‘see’



We need to understand for individual vaccine targets

- Can T cells ‘see’ it
  - Only a small fraction of gene products make it into MHC molecules
- Does the immune system consider the antigen as ‘self’
  - ‘No’ is good for vaccination
    - tumour mutations
    - shared antigens can also behave like this
- How much inherent ‘regulation’ is there through CD4 regulatory cells
  - Expect this problem to be worse as the cancer progresses

Defining patient ‘strata’ based on TME classification



Bagaev A. et al. Cancer Cell, 2021.

Reference population is in line with the described literature with 50/50 fraction of immunoreactive/immusuppressive phenotypes described by other authors. (e.g. Zhang et al. 2021 (https://doi.org/10.3389%2Ffcell.2021.711348) or De Cecco et al., 2015 (https://doi.org/10.18632%2Foncotarget.3301)

1486, HNSCC

Slide adapted from
K. Bendjama, Transgene

Towards rational vaccine + IO approaches:

- Testing how the TME is set up in individual patients
- Systematic evaluation of classes of antigens for targeting with vaccines
- Tumour antigen recognition by T cells:
  - Upregulation of ‘checkpoint molecules’ is the mandatory consequence
  - Vaccination needs CPI to overcome this
- Targeting inhibitory cells
  - Regulatory T cells
  - Other cells
- For clinical testing:
  - Comparing vaccine platforms
  - Strictly standardizing immune monitoring

Barcelona:
Arriola
Cardiff:
Chester, Evans
Chester:
Vimalachandran
Edinburgh:
Symeonides, Frame
Glasgow:
Paterson
ICR/RMH:
Harrington, Melcher
Manchester:
Illidge, Metcalf
Oxford:
Middleton, Lu, Kessler
Portsmouth:
Chauhan, Ward
Ulm:
Laban, v. Witzleben

working

TIG

together

cancer research malaysia

Kue Peng Lim
Sok Ching Cheong

Amgen
BioNtech
Lineage
Merck
Neuvogen
Pfizer
Touchlight
Transgene
Verastem

CANCER RESEARCH UK

ECMC

NIH National Institutes of Health

MRC Medical Research Council

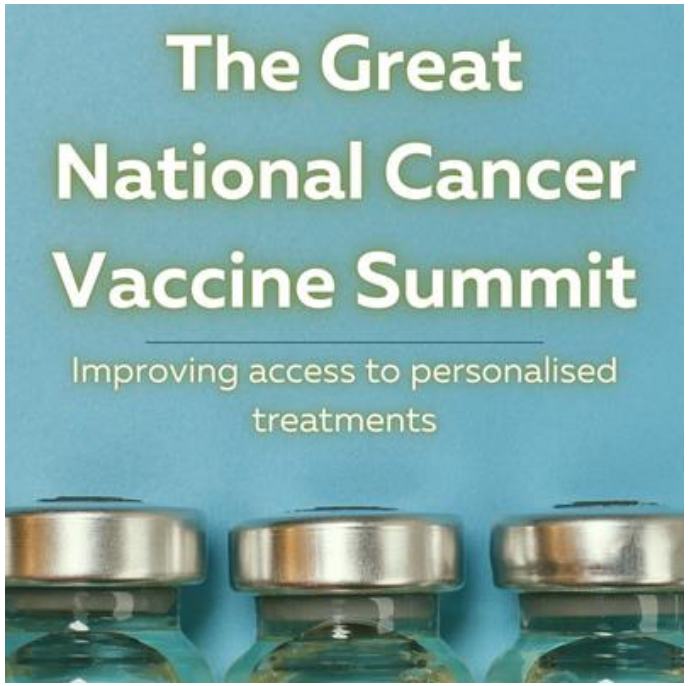
Southampton Hospitals Charity

iCURE immunotherapy: ground-breaking research in finding cures for cancer

Clatterbridge Cancer Charity

Whittaker Fund

The IOM Anticancer Association



Speaking Now…

Gary Middleton
Professor of Medical Oncology
University of Birmingham

Why and when should we use cancer vaccines?

Lung Cancer as an exemplar

Gary Middleton

University of Birmingham

“I am going to tell you a thing that will make you wish yourself here. The small-pox, so fatal, and so general amongst us, is here entirely harmless, by the invention of engrafting, which is the term they give it. There is a set of old women, who make it their business to perform the operation, every autumn, in the month of September, when the great heat is abated. People send to one another to know if any of their family has a mind to have the small-pox; they make parties for this purpose, and when they are met (commonly fifteen or sixteen together) the old woman comes with a nut-shell full of the matter of the best sort of small-pox, and asks what vein you please to have opened. She immediately rips open that you offer to her, with a large needle (which gives you no more pain than a common scratch) and puts into the vein as much matter as can lie upon the head of her needle, and after that, binds up the little wound with a hollow bit of shell, and in this manner opens four or five veins”

Lady Mary Wortley Montagu to her friend, Sarah Chiswell

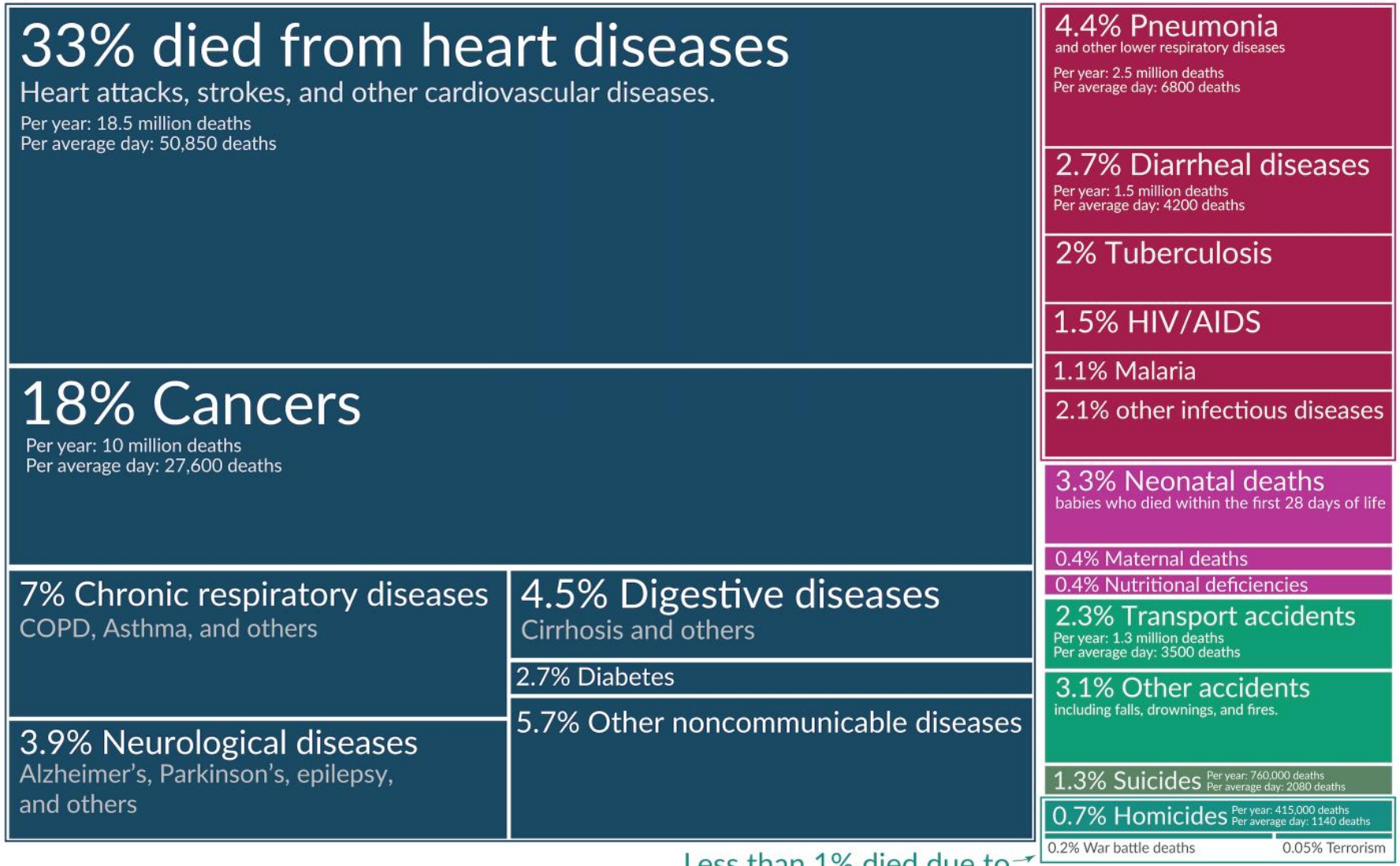
What do people die from? Causes of death globally in 2019

The size of the entire visualization represents the total number of deaths in 2019: 55 million.
Each rectangle within it is proportional to the share of deaths due to a particular cause.

Our World in Data

74% died from noncommunicable diseases

14% died from infectious diseases



Less than 1% died due to interpersonal violence

Data source: IHME Global Burden of Disease and Global Terrorism Database

OurWorldinData.org – Research and data to make progress against the world's largest problems.

Global					
		2019			
Rank	Cause	Deaths (000s)	% of total deaths	Cumulative % of total deaths	CDR (per 100 000 population)
0	All Causes	55,416	100.0	100.0	718.9
1	Ischaemic heart disease	8,885	16.0	16.0	115.3
2	Stroke	6,194	11.2	27.2	80.4
3	Chronic obstructive pulmonary disease	3,228	5.8	33.0	41.9
4	Lower respiratory infections	2,593	4.7	37.7	33.6
5	Neonatal conditions	2,038	3.7	41.4	26.4
6	*Trachea, bronchus, lung cancers*	*1,784*	*3.2*	*44.6*	*23.1*
7	Alzheimer disease and other dementias	1,639	3.0	47.6	21.3
8	Diarrhoeal diseases	1,519	2.7	50.3	19.7
9	Diabetes mellitus	1,496	2.7	53.0	19.4
10	Kidney diseases	1,334	2.4	55.4	17.3
11	Cirrhosis of the liver	1,315	2.4	57.8	17.1
12	Road injury	1,282	2.3	60.1	16.6
13	Tuberculosis	1,208	2.2	62.3	15.7
14	Hypertensive heart disease	1,149	2.1	64.4	14.9
15	Colon and rectum cancers	916	1.7	66.0	11.9
16	Stomach cancer	831	1.5	67.5	10.8
17	Self-harm	703	1.3	68.8	9.1
18	Falls	684	1.2	70.0	8.9
19	HIV/AIDS	675	1.2	71.2	8.8
20	Breast cancer	640	1.2	72.4	8.3

The Global Health Observatory: World Health Organisation. Downloaded 22.4.24

International Agency for Research on Cancer
https://www.iarc.who.int/
World Health Organization

GLOBAL CANCER OBSERVATORY

CANCER TODAY
GLOBOCAN 2022

LUNG

Incidence

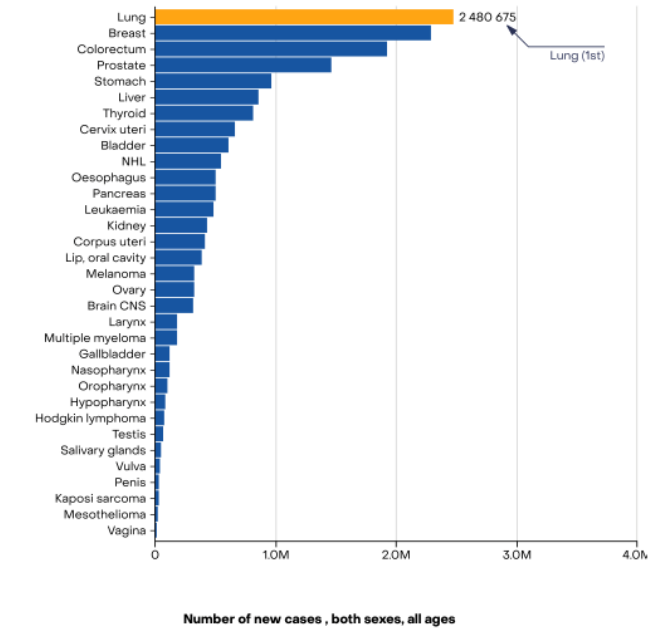
Rank	Cases	ASR (World)
1	2 480 675	23.6

Mortality

Rank	Deaths	ASR (World)
1	1 817 469	16.8

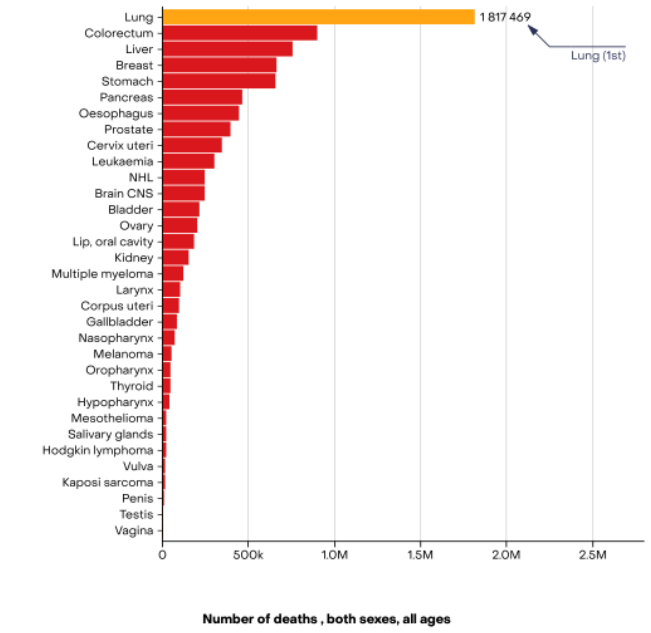
Cancer site ranking

Incidence



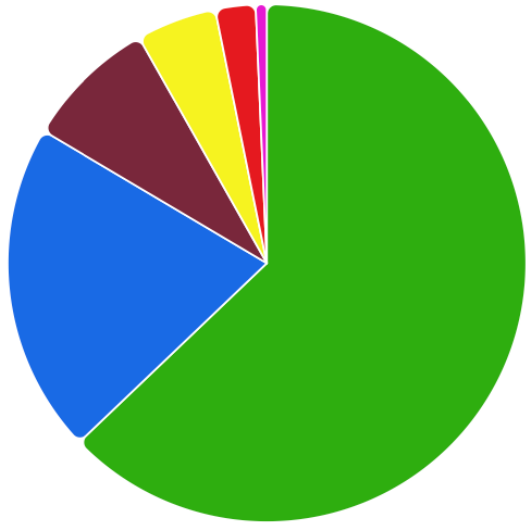
Number of new cases , both sexes, all ages

Mortality



Number of deaths , both sexes, all ages

Mortality



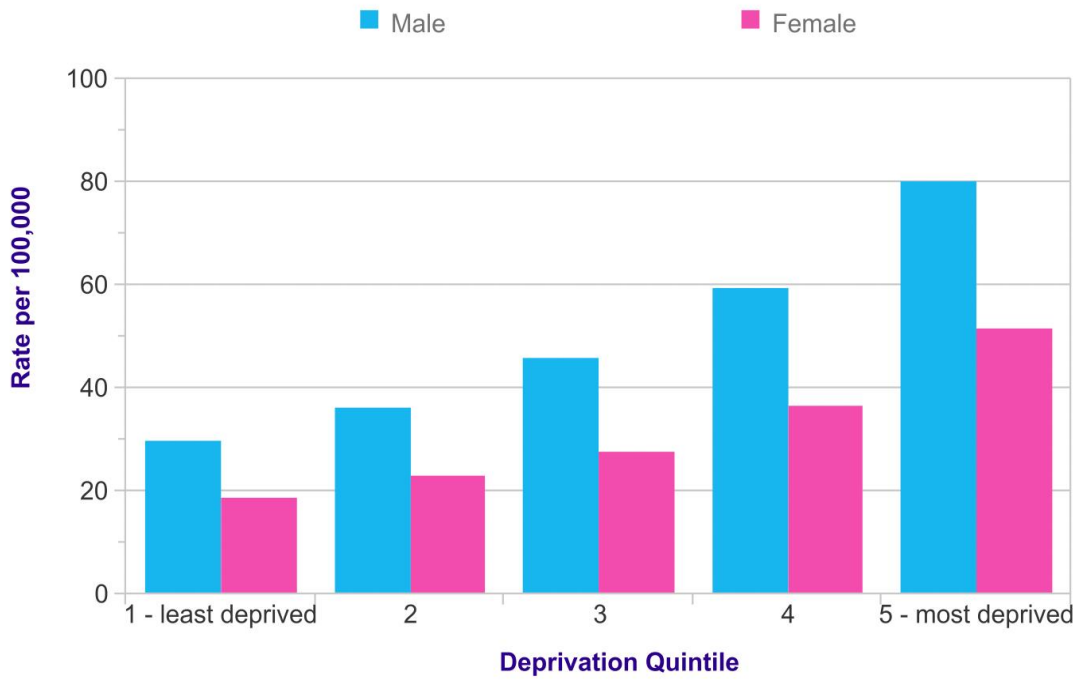
Continent	Deaths	Percent
Asia	1 142 397	62.9%
Europe	375 569	20.7%
Northern America	150 675	8.3%
Latin America and the Caribbean	90 846	5.0%
Africa	45 464	2.5%
Oceania	12 518	0.69%

Mortality, both sexes

Lung Cancer (C33-C34): 2007-2011

European Age-Standardised Mortality Rates by Deprivation Quintile, England

	Male	Female
1 - least deprived	29.6	18.6
2	36.1	22.9
3	45.7	27.4
4	59.1	36.3
5 - most deprived	80.1	51.3



CANCER RESEARCH UK

The LungVax study

Prof Sarah Blagden – Director of Oncology Clinical Trials Office (OCTO), Oxford

What do we know about premalignant cancer?

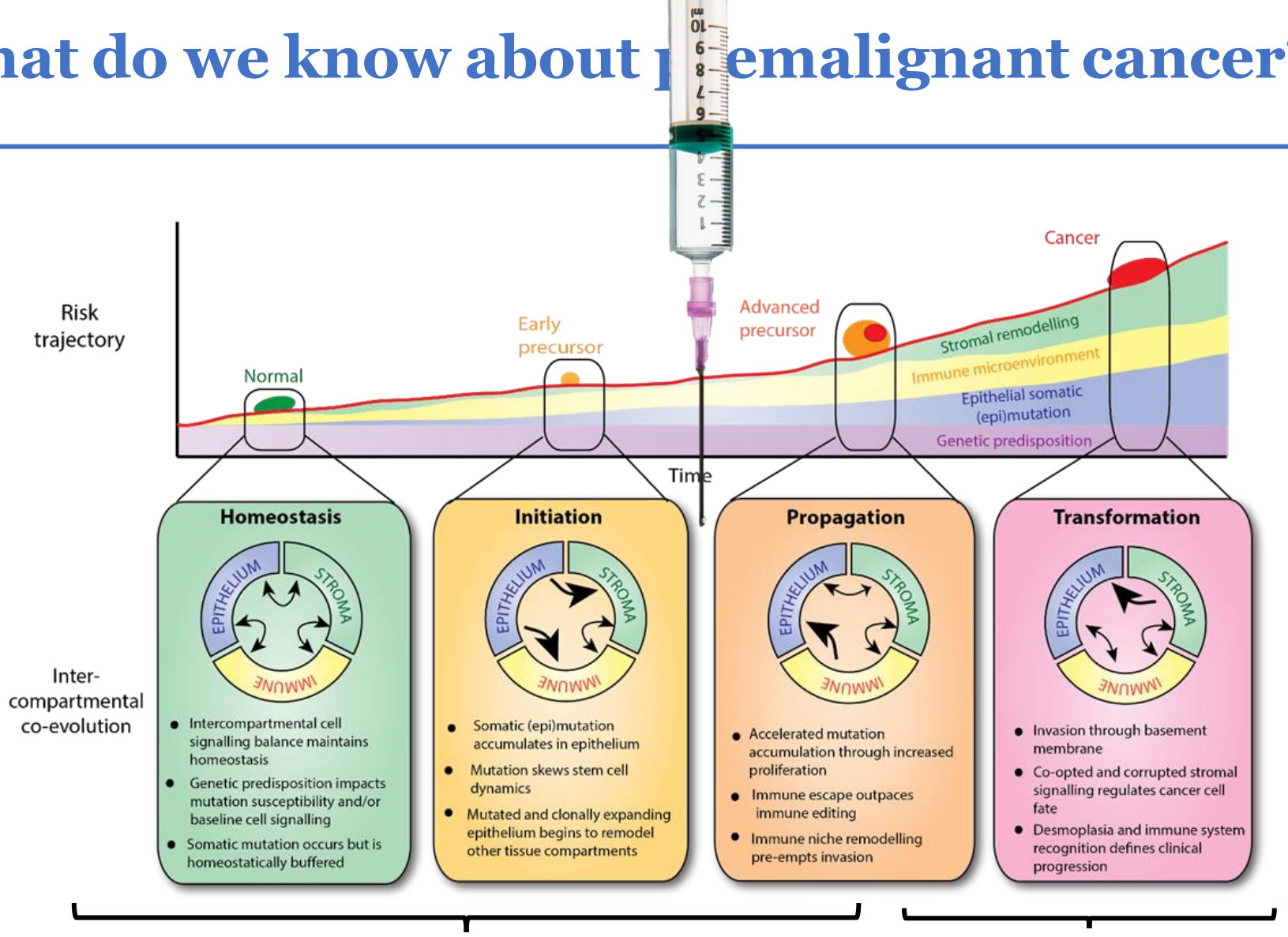
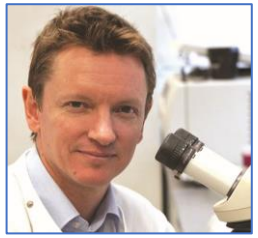


Figure from Simon Leedham

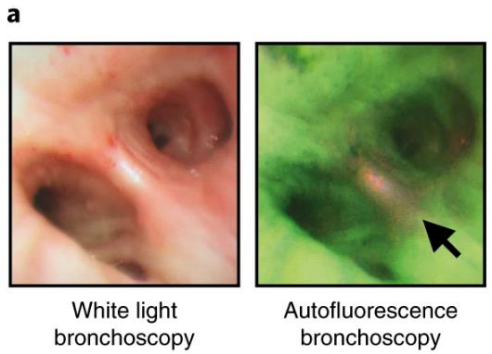
Premalignant phase: reversible

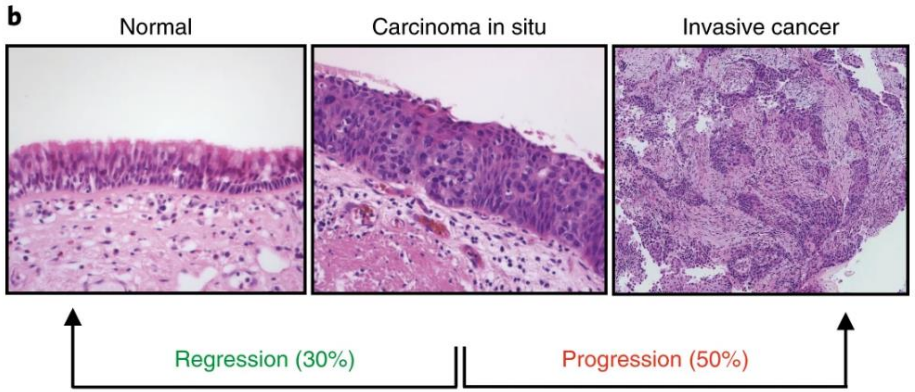
Invasive cancer: irreversible, obeys cancer hallmarks.

Preinvasive squamous cell lung cancer has clonal mutations

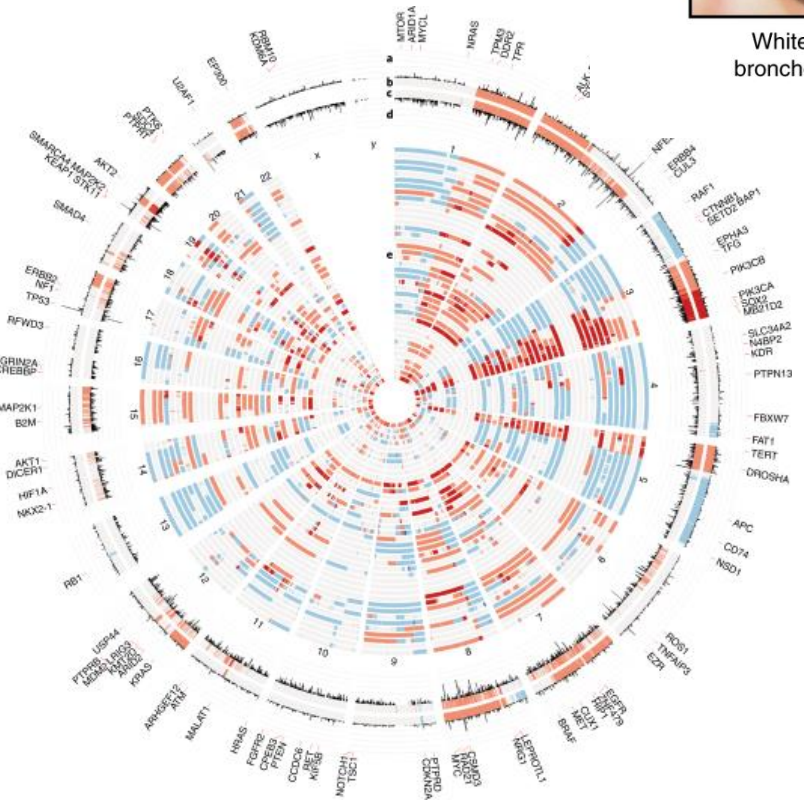


Prof Sam Janes, UCL





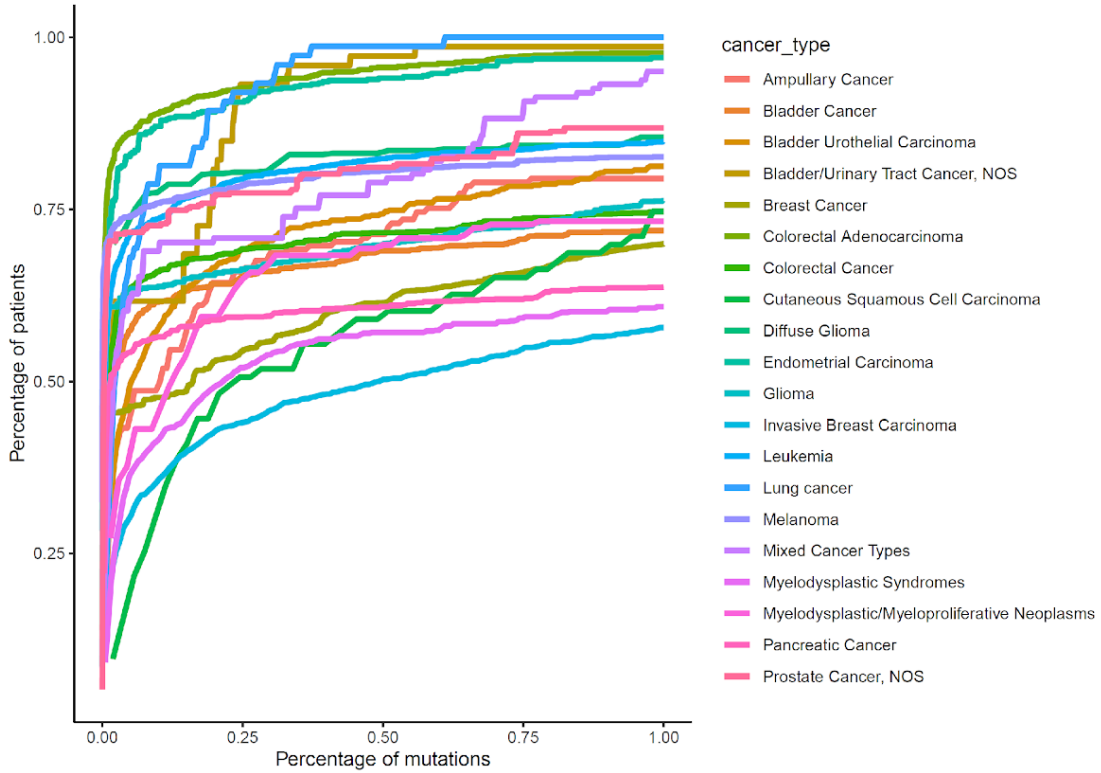
Teixeira et al, Nat Med 2019



Hotspot mutations include TP53, KRAS, EGFR and others (same nucleotide positions as late stage).

Lung cancer has shared "public" mutations

Kevin Litchfield, UCL



Top 20 cancer types ranked by % of patients captured by 10 most common hotspot mutations:

Cancer type	% of Patients
Diffuse Glioma	80.2%
Lung cancer	64.0%
Glioma	56.6%
Melanoma	53.7%
Myelodysplastic Neoplasms	53.5%
Pancreatic Cancer	53.0%
Mixed Cancer Types	50.3%
Colorectal Adenocarcinoma	48.8%
Ampullary Cancer	48.6%
Bladder/Urinary Tract Cancer, NOS	47.9%
Bladder Cancer	47.0%
Bladder Urothelial Carcinoma	45.9%
Endometrial Carcinoma	44.6%
Cutaneous Squamous Cell Carcinoma	44.6%
Colorectal Cancer	40.1%
Myelodysplastic Syndromes	37.1%
Leukemia	36.5%
Invasive Breast Carcinoma	32.7%
Breast Cancer	32.6%
Prostate Cancer, NOS	29.4%

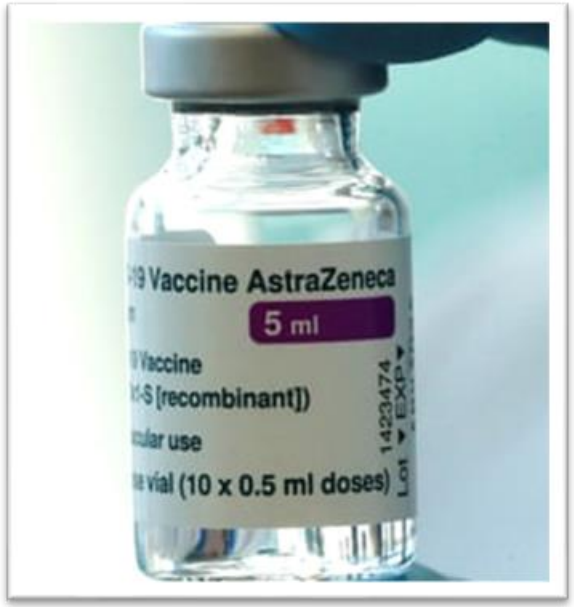
Concentration curve analysis on >61,000 cancer genomes (cBioportal) including >8,000 lung cancers shows high concentration of hotspot shared mutations in lung cancer. For fixed cocktail of the 10 or 20 most common mutations, lung cancer is second most attractive for "off the shelf" targeting.

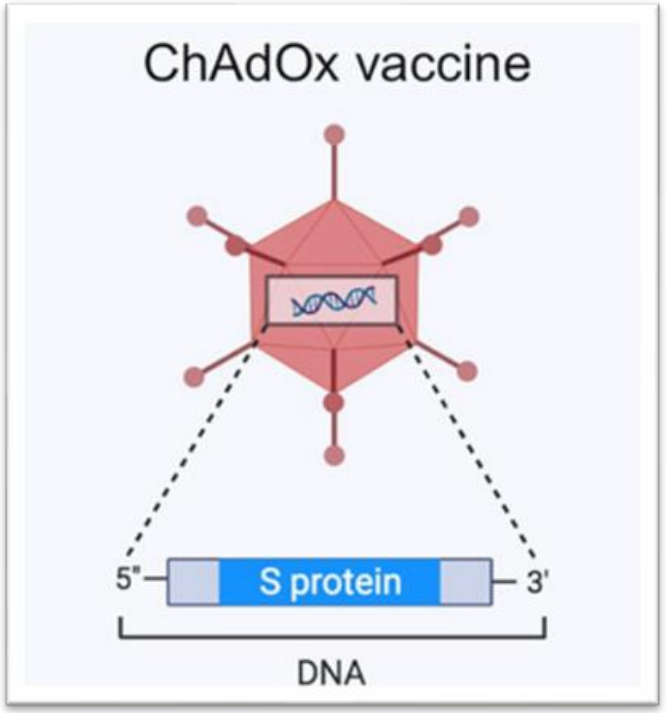
LungVax - the strategy

Life savers: the amazing story of the Oxford/AstraZeneca Covid vaccine

A year ago, two scientists began work on the response to a new virus. Now, as their vaccine is being given to millions, they tell of their incredible 12 months

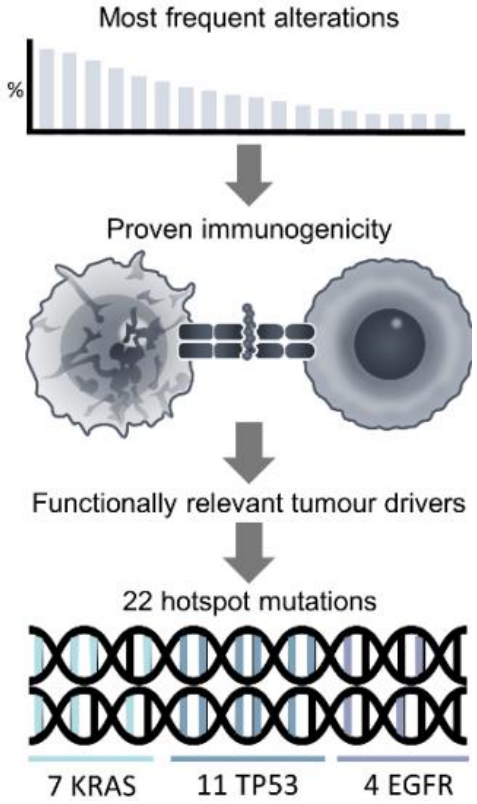
Professor Sarah Gilbert and Professor Andrew Pollard, who were key figures in the development of the Oxford AstraZeneca vaccine. Composite: Christian Sinibaldi/The Observer; John Cairns/Oxford University





Saved 6.3 million lives in the first year of the pandemic

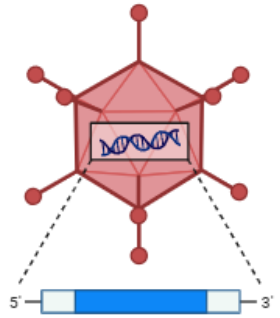
We are testing 4 variations (V1-V4) of ChAdOx2-LungVax

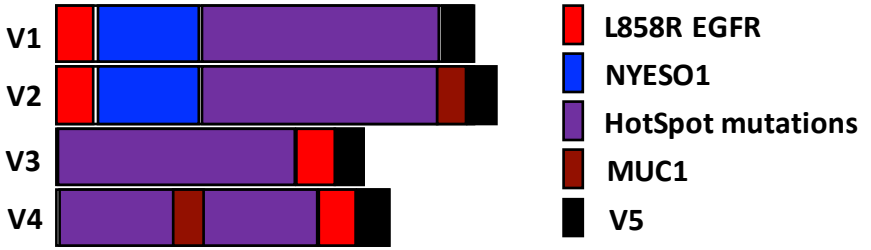


+/-

MUC1 and NY-ESO-1

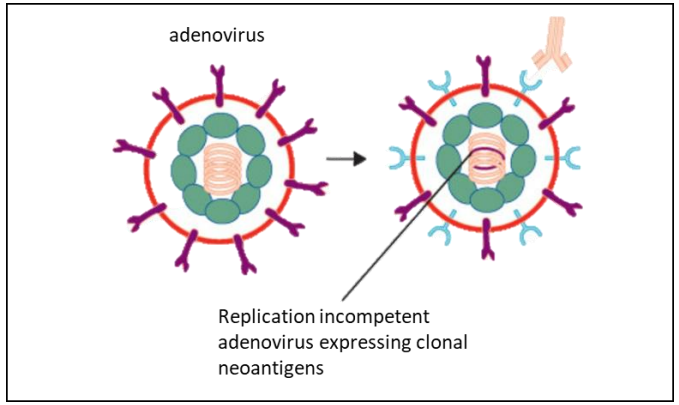
ChAdOx2

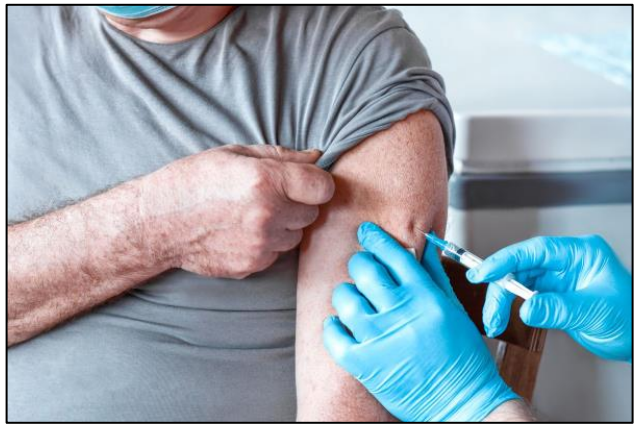




LungVax - the strategy

Vaccinate people at high risk of lung cancer with ChAdOx2 + DNA encoding shared clonal lung cancer neoantigens





ChAdOx2 taken up by macrophages and dendritic cells. Neoepitope DNA incorporated into host DNA, expressed, presented by HLA as peptides

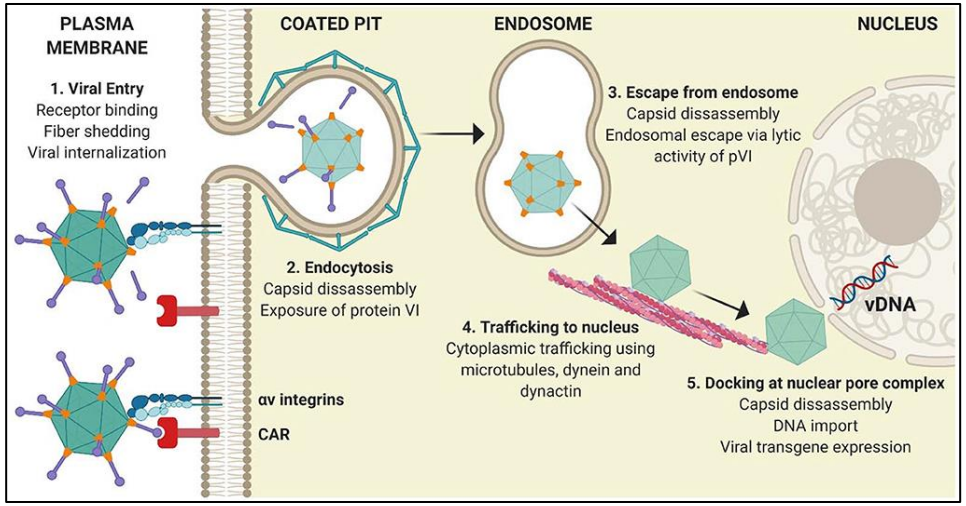
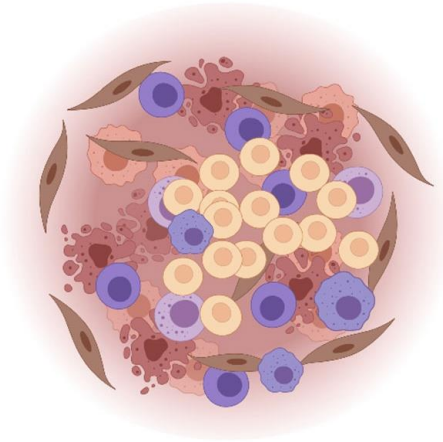


Figure from Coughlan, Frontiers in Immunology, 2020

To elicit lasting tissue resident memory T cells – long term lung surveillance

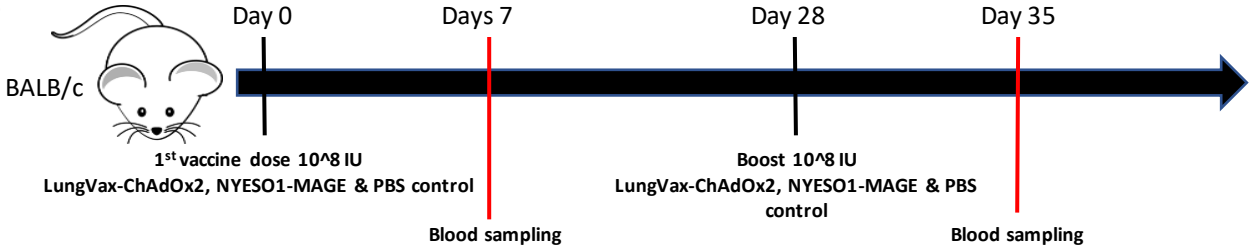


Elimination of neoantigen expressing precancer cells

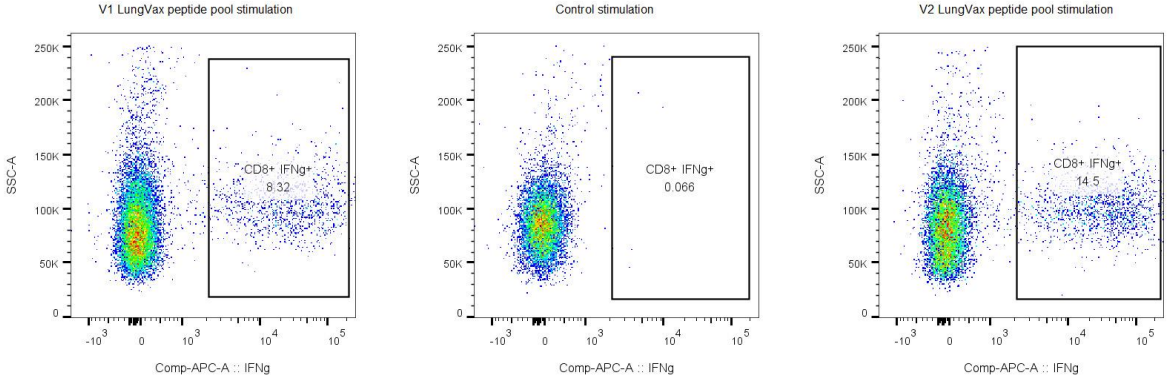
BALB/C mice show strong immunogenicity to two LungVax ChAdOx2 vaccines.

Zinaida Dedeic

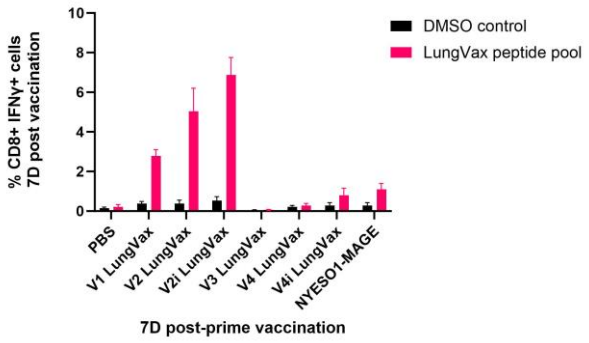
a.



b.



c.



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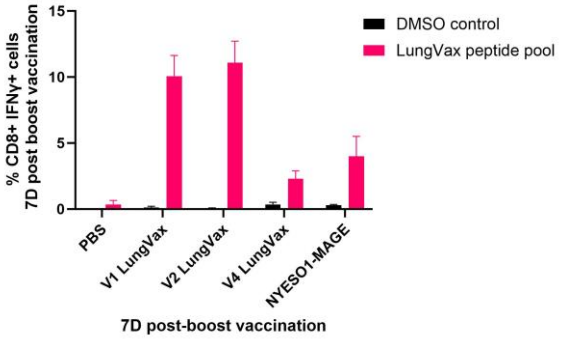
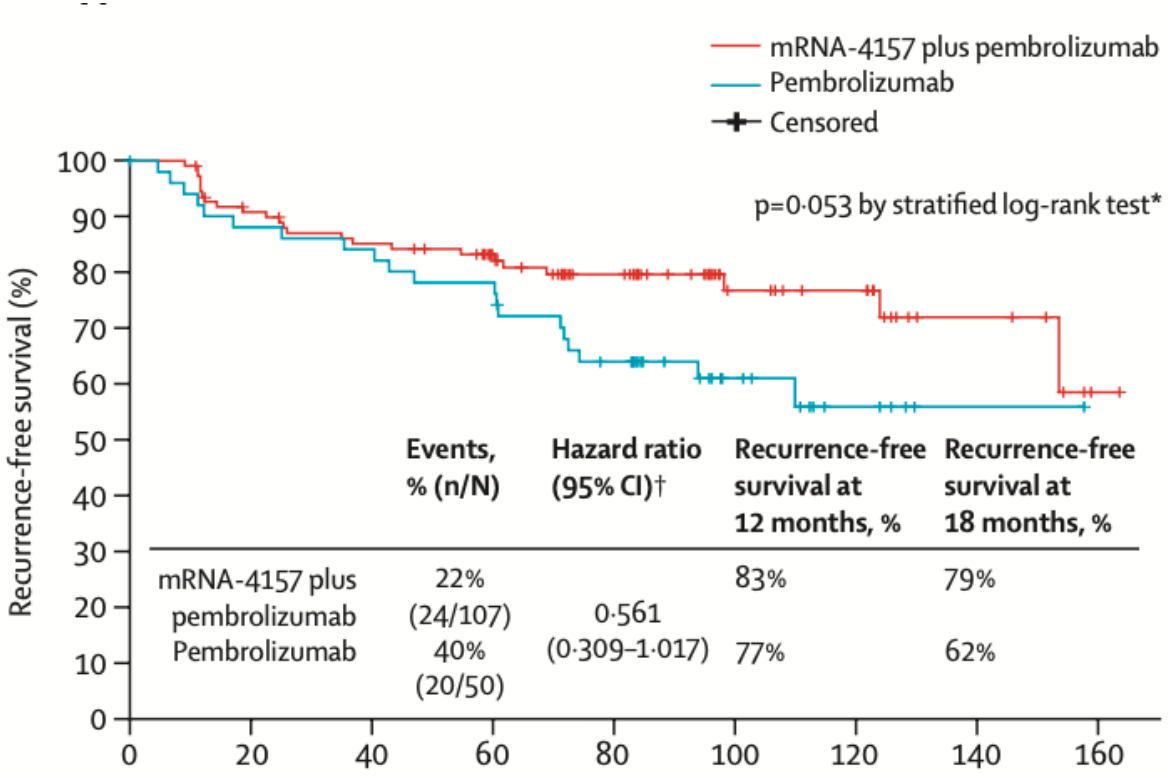


MRD and the INTerpath-002 trial in resected stages II, III_A and III_B NSCLC

Building on Individualised neoantigen therapy mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab monotherapy in resected melanoma (KEYNOTE-942): a randomised, phase 2b study

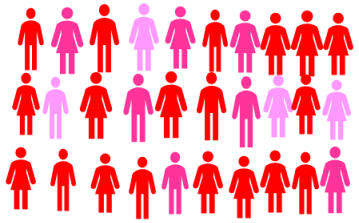


Weber JS et al. Lancet. 2024 Feb 17;403(10427):632-644.

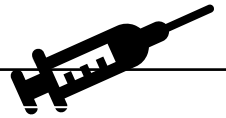
Lung Vax Precision Prevention trial

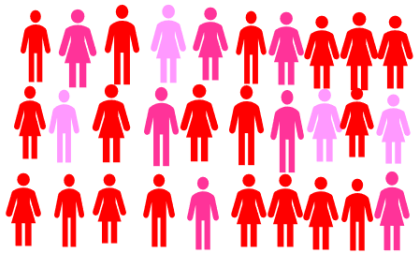
At risk group:
590 who have had **primary stage IA/1B** NSCLC resected – have 30-40% risk of recurrent or new cancer within 2 years

Part 1: 30 patient safety run in



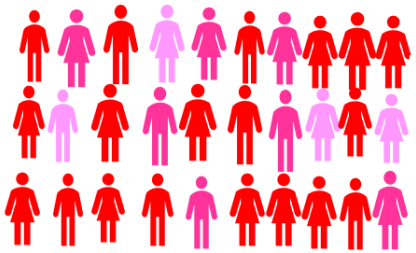
Part 2:
Randomised





Intervention (280):
ChAdOx2-LungVax.
Probably homologous Prime-Boosting schedule.
Routine surveillance imaging

versus



Control (280):
Routine surveillance imaging only

Endpoints:
Does vaccine work?
Disease-free survival, cancer incidence, safety and Quality of Life

Biological Endpoints:

How does vaccine work?
Correlations between immunogenicity and disease response

How does lung cancer start?
Correlations between cfDNA, PBMC sequencing, plasma biomarkers/methylation profiling and disease emergence and response

LungVax programme overview

Work Completed to Date:

- Patented off-the-shelf vaccine design
- Potential to prevent up to 96% lung cancers
- Designed inserts containing 21 hotspot driver mutations and tumour associated antigens
- Selected ChAdOx2 for superior T cell priming
- Non-GMP vaccine manufacture
- Clinical study drafted

PreClinical:

- Validated vaccine insert expression and immunogenicity *in vivo*
- GMP manufacture of 3K doses of vaccine for clinical study
- Validated tissue resident T cell priming in lung
- Regulatory toxicology
- Applied for clinical trial funding

Phase 1/2 Clinical Trial:

- Trial accepted onto OCTO portfolio
- Enrolling 590 participants with recently resected Stage 1A/1B NSCLC
- Safety run in, then 560 randomised to LungVax versus no treatment
- Endpoints: prevention of recurrence or new primary cancer, QoL, immunogenicity

Phase 3 Clinical Trial:

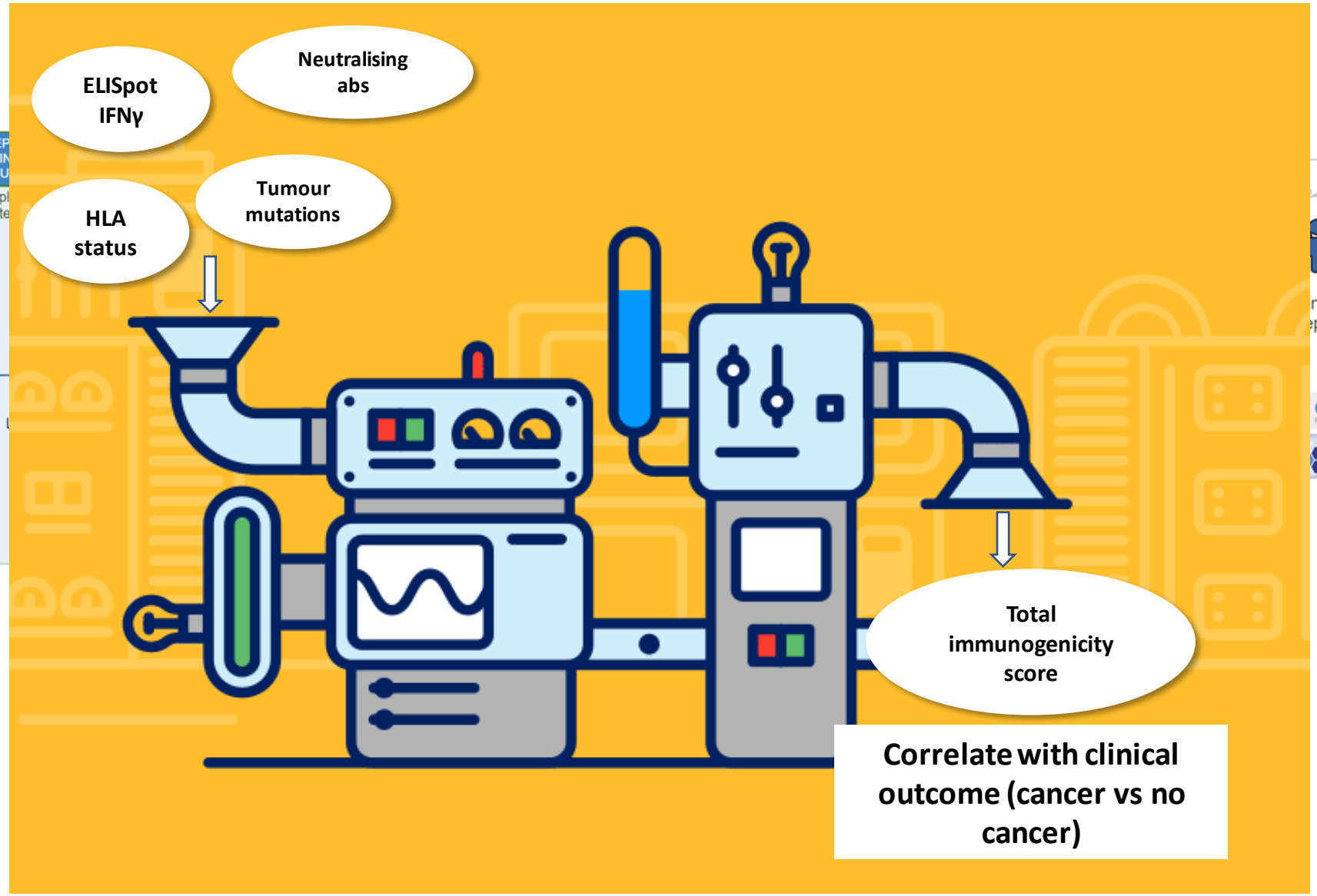
- Future Phase 3 study will be in people undergoing Lung Health Checks at risk of NSCLC
- High risk smokers without cancer
- Study will explore impact of vaccine on smoking/vaping behaviours as well as overall cancer risk reduction

Cris cancer foundation

CANCER RESEARCH UK

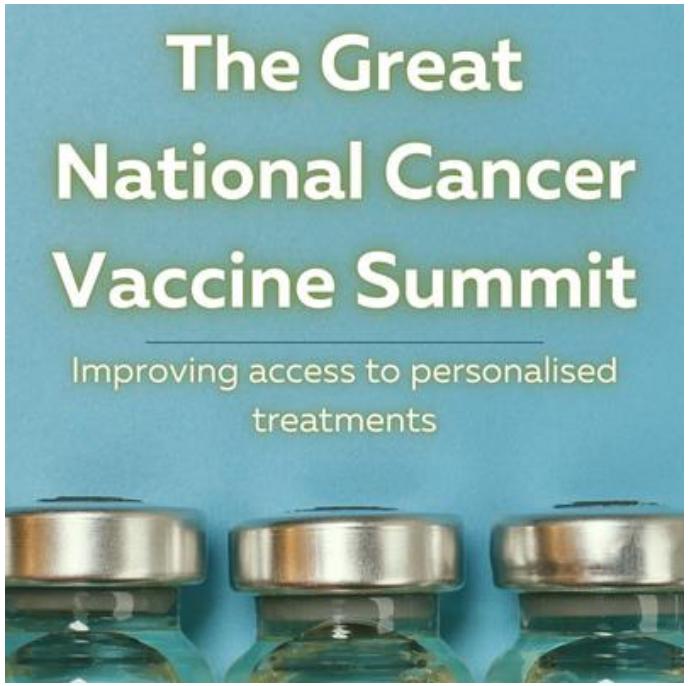
Funding application submitted

Translational Data Platform



Summary

- **Preinvasive cancer** predates emergence of cancer by years or decades and represents a therapeutic window
- Lung cancer expresses some **clonal and shared neoantigens** from preinvasive to advanced cancer
- Vaccines designed to target neoantigens is an emerging personalised strategy for adjuvant treatment and an “off the shelf” primary preventative strategy
- LungVax, based on findings from TRACERx, **is world’s first neoantigen-based lung cancer prevention vaccine**
- Clinical study to open Jan 2026



Speaking Now…

Dr Nangi Lo
Consultant Medical Oncologist - Torbay and South Devon NHS Foundation Trust

Can we deliver big vaccine trials in smaller centres?

Dr Nangi Lo
Consultant Medical Oncologist
Torbay and South Devon NHS Foundation Trust

Disclosures

I have no disclosures

Why are *you* here?

Barcelona, 2019

Why do research?

Patients	Healthcare professionals	Department	NHS systems
Improving outcomes through early diagnosis, effective treatments, disease prevention	Keeping up to date, improving care and job satisfaction	Benchmarking and quality assurance, rapid adoption of treatments and technologies	Research active hospitals have lower mortality rates and improved quality of care, not limited to research participants (Jonker et al 2020)
Levelling inequalities	Gold standard treatment is clinical trial		

Our smaller centre

- Geographically remote district general hospital
- Catchment population 290000

Wide variance

- Rural and urban
- Wealth and deprivation

Our smaller centre

- Elderly, fit population
- No ivory tower in Southwest Peninsula
- Smallest radiotherapy facility in the UK, delivering IMRT + SABR

- CAN DO mindset
- Work-life balance

Can small centres do research?

2019

Small non-income generating research department under threat

Can small centres do research?

2019

Small non-income generating research department under threat

2020 Pandemic

- Reduce/stop chemotherapy
- Impact on clinical research

Can small centres do research?

2019

Small non-income generating research department under threat

2020 Pandemic

- Reduce/stop chemotherapy
- Impact on clinical research

Torbay

- Move chemotherapy unit and ward to remote ‘green’ site
- Protect Cancer Trials team
- Continued to recruit to clinical trials

Can small centres do research?

2019

Small non-income generating research department under threat

2024

414% increase in recruitment

- Second highest recruiter to KEYNOTE 859
- One of two trusts to open B15 trial
- First recruit in to 8 national trials this year

Second to the Christie in recruitment to commercial trials

Benefits to a department

- Rapid adoption and safe delivery of new standards of care

- Income generation £750k
  - Radiology
  - Chemotherapy delivery
  - Pharmacy
  - Medical physics

- Benefits to a small department are proportionately larger
  - Attract and retain Oncology staff in a challenging recruitment climate

BNT-122 trial

A multi-site, open-label, Phase 2, randomized controlled trial to compare efficacy of RO7198457 versus watchful waiting in resected Stage II (high risk) and Stage III colorectal cancer patients who are ctDNA positive following resection

The 4 P's for achieving success

- Purpose
- Planning
- Perseverence
- Passion

Purpose: why do we want to do this?

- Exciting – Pioneering approach in management of cancer
- Equity – Important to bring this study to our rural, deprived and under-served population
- Future – Position for future vaccine trials

Planning: can we deliver?

Don't just do it, but do it well

- Good quality data
- Meet target

Resources

- Research staff
- Medical staff

- Pharmacy
- Space

ATIMPs: Reinventing the wheel

Vaccines are classed as ATIMPs and require an ATIMP committee to review before trial sign-off

Torbay is on the small-end of medium sized hospitals and is not resourced to have an ATIMP committee in place

Pharmacy had to conduct bespoke risk assessments mirroring those that would normally be conducted by an ATIMP committee

This allowed our pharmacy to bring this study to Torbay

Planning: Space

- Low numbers proceed to be treated
- Low level of intervention but long observation times

Options

- Colorectal day unit: blood transfusions, mAbs
- ICU: keen to collaborate, have space, all have GCP

- Portacabin in supermarket carpark
- Campervan

Chemotherapy Day unit: space in exchange for research nurse time on treatment days

Planning: Staff

- Maximise efficiency
- Get the right people to the right place at the right time

- Flexibility around whole oncology research portfolio
- Alteration of jobs plans
- Training up middle grades and SpR

- Dedicated research clinic

Perseverance: Arrival of the CVLP

CVLP referral site for the whole of the Southwest

- Team – Build a team that could flex to accommodate large numbers of patients

- Space – Maintain exposure/experience on day unit without overwhelming our small chemotherapy day unit

Planning (rapidly)

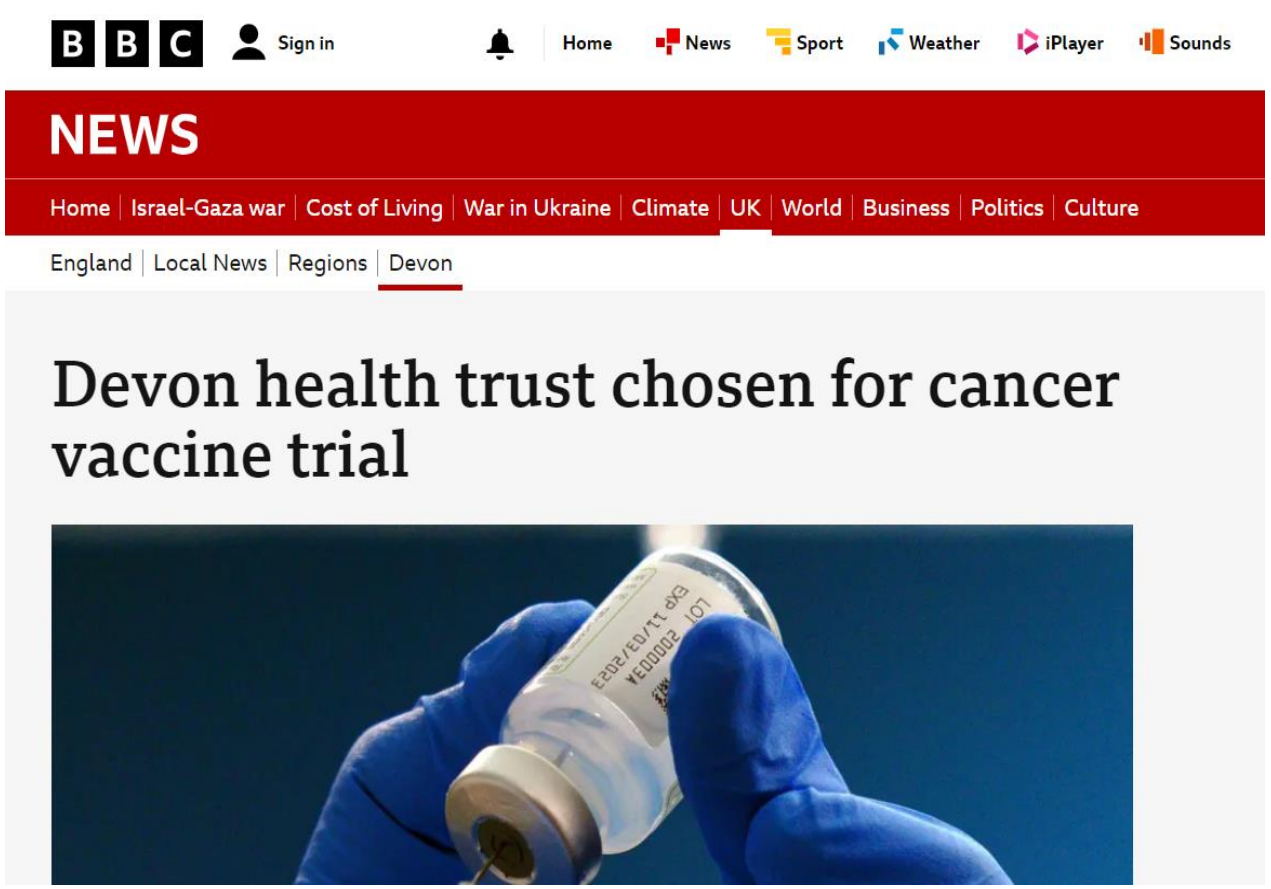
- Develop trial delivery team that could flex and accommodate surges in referrals
  - Lead nurse, 3 extra nurses on standby
  - Support team of data managers, research HCAs and specialty research doctor
  - Training to allow capacity within SpR and middle grade team
- Business case for Research SACT nurse
  - Future-proofing in order to manage full research portfolio without impacting on standard of care service
- Research fellow post

Passion

Strong feeling of enthusiasm or excitement…feeds the desire to go above and beyond

6 months on

- Capacity to screen 40+/month
- Recruiting well locally
- Referrals coming in via the CVLP
- Research SACT nurse and research fellow in post
- Dedicated research treatment space on the chemotherapy day unit



Benefits of being small

- Agile
  - Fewer links in the chain
  - Quicker turnaround
  - More control/influence
  - Better quality

- Benefits for small centres are disproportionately large

Tips

- Build the right team
- Innovate, think laterally
- Negotiate, barter

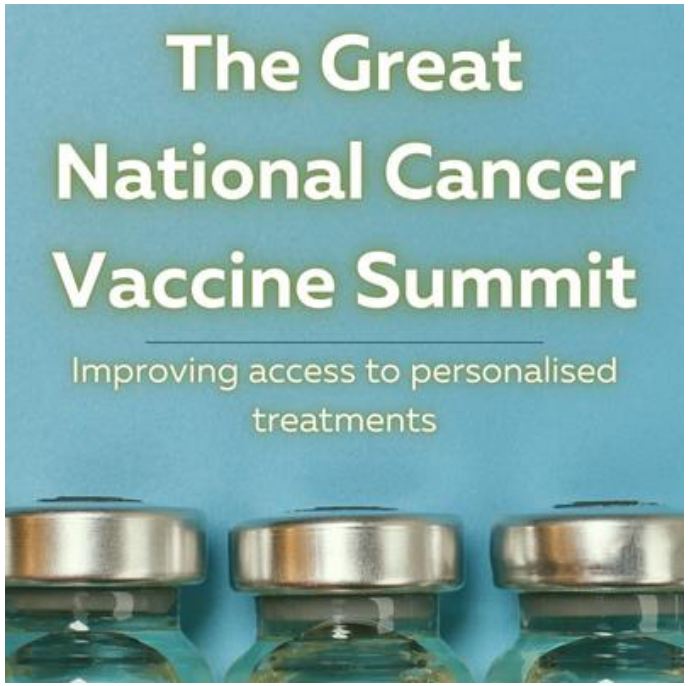
- Perfect your elevator pitch

Why are you here?

London, 2024

ADVANCING CARE
THROUGH RESEARCH*

Thank you



NHS cancer vaccine launchpad...

Dr Benjamin Moxley-Wyles
National Medical Director's Clinical Fellow - NHS England

Dr Gillian Rosenberg
Innovation Transformation Lead - NHS England

Nicola Chapman-Hart
Senior Programme Manager - NHS England

Cancer Vaccine Launch Pad (CVLP)

Dr Gillian Rosenberg, Innovation Transformation Lead, NHS England
Dr Benjamin Moxley-Wyles, Clinical Fellow, NHS England
Nicola Chapman-Hart, Senior Programme Manager, NHS England

Cancer vaccines: an opportunity to transform cancer care

- The UK has for centuries been a leader in vaccine development, research and deployment, recently exemplified through our Covid-19 response.

- Vaccinology is entering a new era with the advent of mRNA vaccine technology – offering broad benefits in terms of personalisation, modularity and deployment.

- Using these recent advances to accelerate the development of personalised therapeutic cancer vaccines could drive transformative benefit across multiple cancer subtypes.

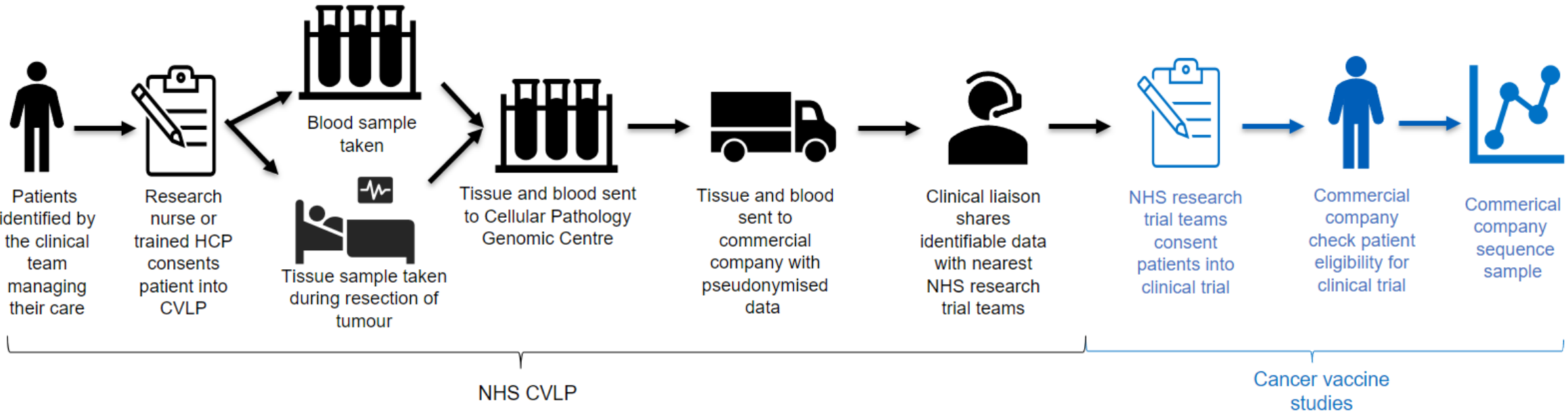
Challenges developing mRNA cancer vaccines

- Access to patients: large pre-screening patient pools can be required (eg because of significant drop-off at ctDNA analysis step)
- Logistics and capacity for genomic sequencing of tumour/blood samples
- Referral of patients into trials depends heavily on willingness/awareness of clinicians (cancer vaccines being unchartered territory)
- A need to build public trust and support for this novel approach to treatment

The Cancer Vaccine Launch Pad (CVLP)

- National research platform to support the recruitment of patients into personalised cancer vaccine trials.
- Provides a coordinated tissue pathway to enable high quality nucleic extraction and genetic sequencing of a patient's tumor.
- Provides a mechanism to identify and recruit patients at scale from multiple Trusts across the country and refer them to research trial sites.

The CVLP pathway

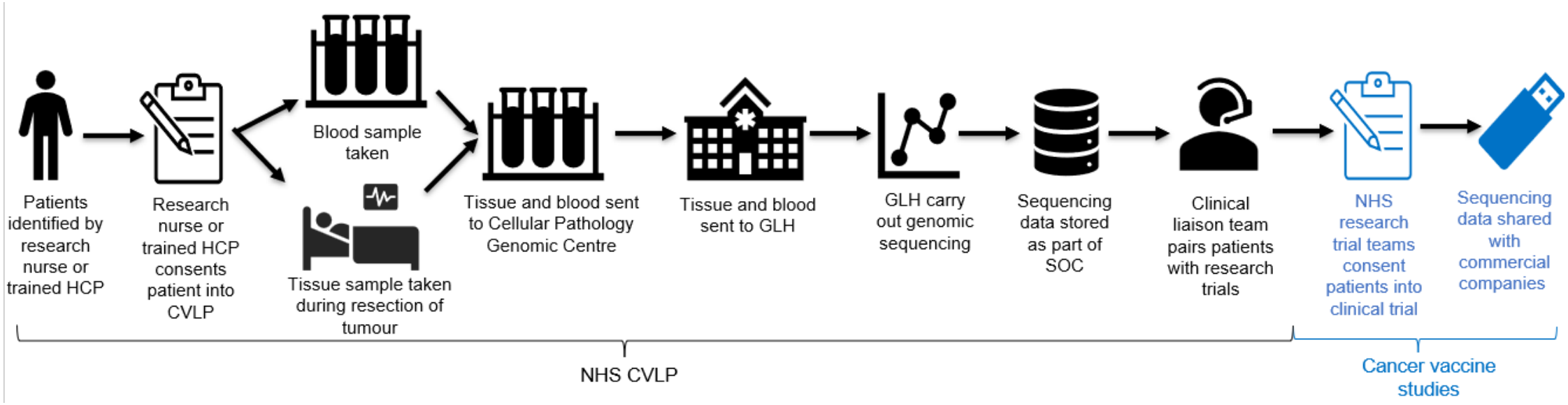


Cellular pathology and tissue processing

- Tissue quality is vital for sequencing and vaccine manufacture success.
- Molecular diagnostics has not been as streamlined as it should be.
- We are putting specific resource into cellular pathology to improve tissue pathways and expedite tissue transfer to industry partners.
- Investment for personalised cancer vaccines but will have wider benefits for molecular diagnostics.

- Through the CVLP, we can provide tumour block curls & slides ready for DNA/RNA extraction in:
  - 5 days (initial set)
  - 3 days (second set, if required)

Future pathway for the CVLP



Government strategic partnership

NHS England

Genomics England

Department of Health & Social Care

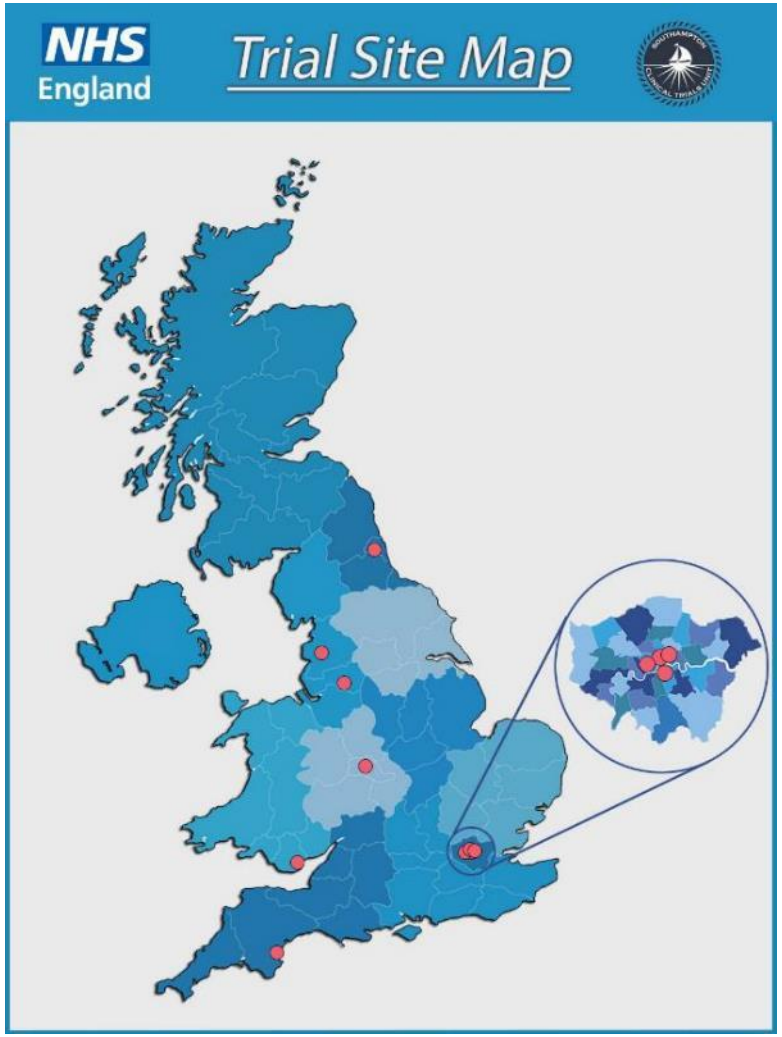
NHSE Cancer Programme &
NHSE Genomics Medicine Service

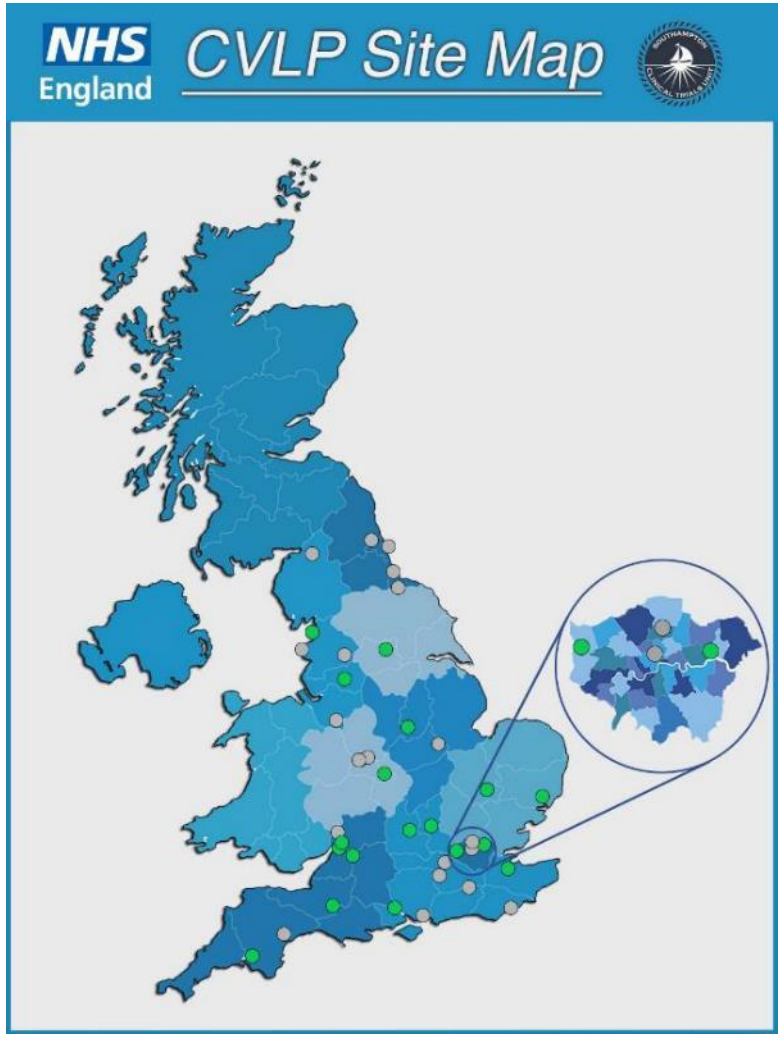
Office for Life Sciences

NIHR National Institute for Health and Care Research

BIONTECH

Active CVLP sites across England





Future ambition of the CVLP

- National platform with all suitable NHS Trusts signed up.
- Multiple cancer vaccine trials covering different cancer indications run by multiple commercial companies are part of the CVLP portfolio.
- Nucleic extraction and genetic sequencing carried out within the NHS.
- The NHS is prepared to roll-out cancer vaccines should they prove to be effective and cost-effective.

Thank You

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