Harnessing Immunity: A Personalised, Multi-Target Approach to Cancer

NHS Cancer Conference

6 October 2026

Northwest Biotherapeutics

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Overview

Key characteristics of dendritic cell (DC) based cancer vaccines such as DCVax® make them uniquely suited to treating solid tumors

- Solid tumors comprise 90% of all cancers
- Solid tumors are extremely heterogeneous, evade targeted therapies

Clinical evidence of the special capabilities of DC therapies seen in wide range of solid tumors

- 16 diverse types of tumors treated in DCVax clinical trials to date
- Additional diverse tumors treated in compassionate use cases

In vivo version of DC vaccine (DCVax®-Direct) already developed, specially suited for inoperable tumors, tested in clinical trial

Cancer Vaccines

a.k.a Active Immunotherapies for Cancer

- Cancer vaccines are typically given as **therapeutic treatments** rather than as preventative options
- The current focus appears to be directed towards mRNA vaccines and neoantigen peptide vaccines, which typically deliver a limited number of selected antigens
- Dendritic cell vaccines have several **unique properties** that may be advantageous:
  - **Fully personal**
  - **Broad spectrum**
  - **Less susceptible to tumour-induced immunosuppression**

Cancer Is A Personalised Disease

Solid tumours comprise ≥90% of all cancers and are extremely heterogeneous

- Extensive variation **among cancers**
- Extensive variation **among patients**, even with "same" cancer
- Significant variations **within a single patient** as disease progresses
- Extensive heterogeneity even **within a single tumour**

Personalised disease requires personalised treatment, in order to be effective

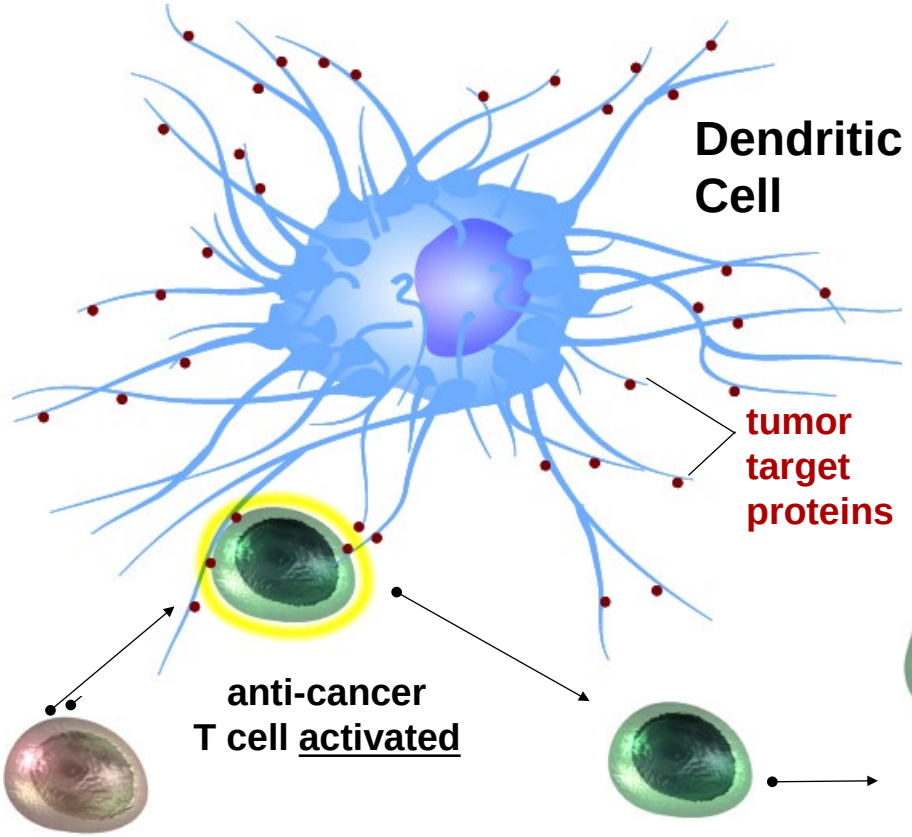
DCVax Is Fully Personal and Precision Targeted, yet also Broad Spectrum

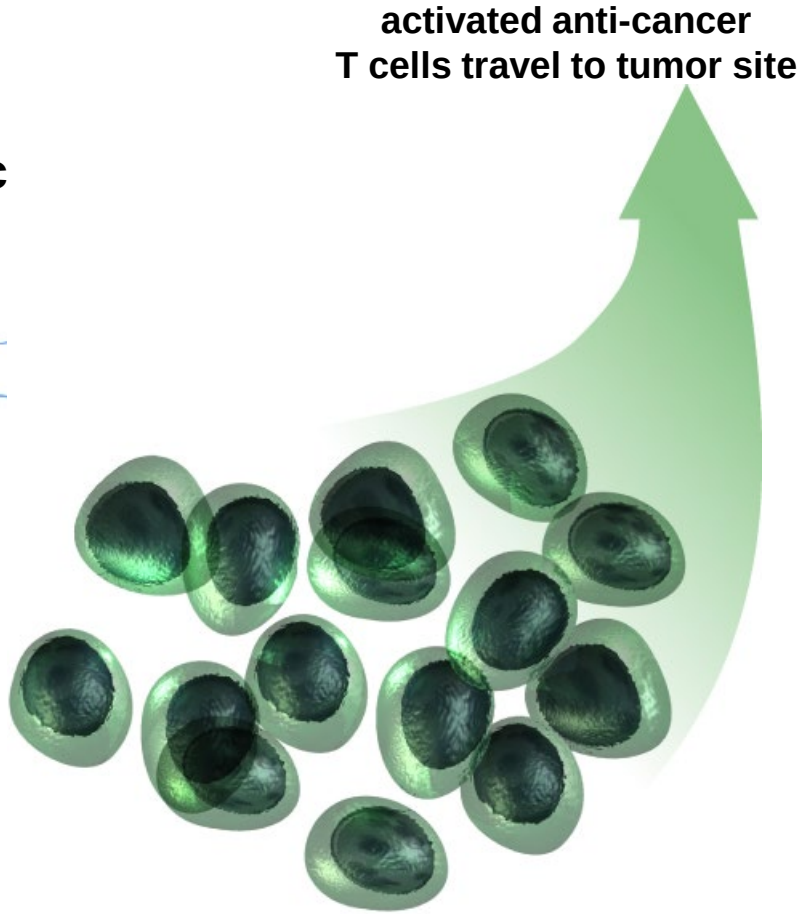
DCVax®-L is **autologous** dendritic cells (DCs) loaded with **autologous** tumour cell lysate. 3 key characteristics:

- Uses DCs, which are the **master cells of the immune system;** DCs direct both the targeting and the direction of the response, mobilise both adaptive and innate immune responses
- Uses antigens from patient's own tumour to ensure **correct targets**
- Uses whole tumor cell lysate (*full repertoire* of antigens) to ensure a **broad-spectrum immune response** against **hundreds of antigens**

- 6 doses in Year 1, then 2 doses per year for maintenance
- Simple intra-dermal injection in upper arm **in any healthcare facility**

DCVax-L: Each DC Mobilises Hundreds of T Cells





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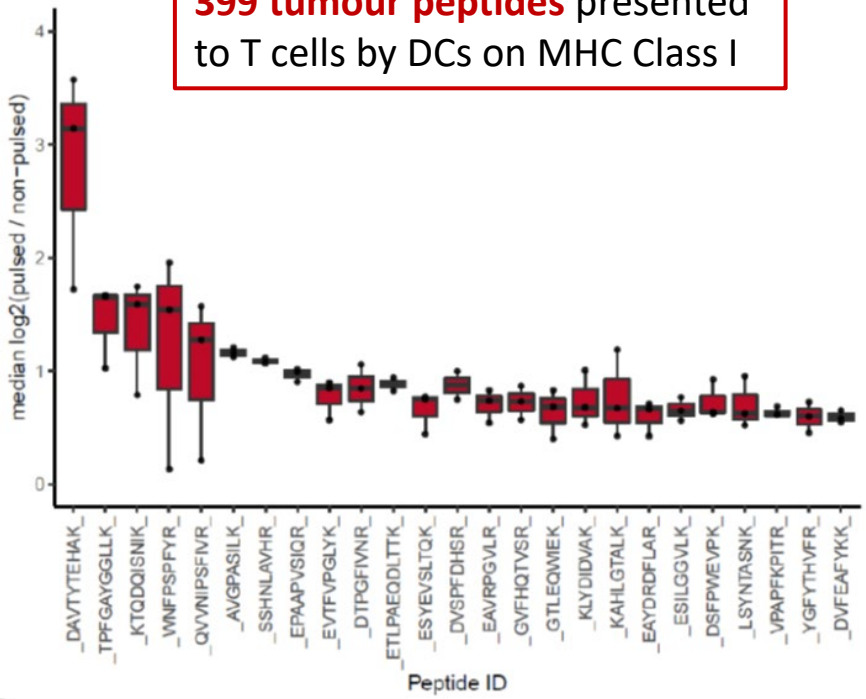
DCVax-L: DCs Mobilise Immune Response Against Many Hundreds of Personalised Tumour Targets

DCs select, process and present tumor targets (peptides) to T cells through 2 channels (MHC I & MHC II)

A single DCVax-L product can present *over 600 tumour targets* to T cells
(vs. ~1-2 targets in CAR-Ts; ~9-10 targets in peptide vaccines, ~16-20 targets in mRNA vaccines)

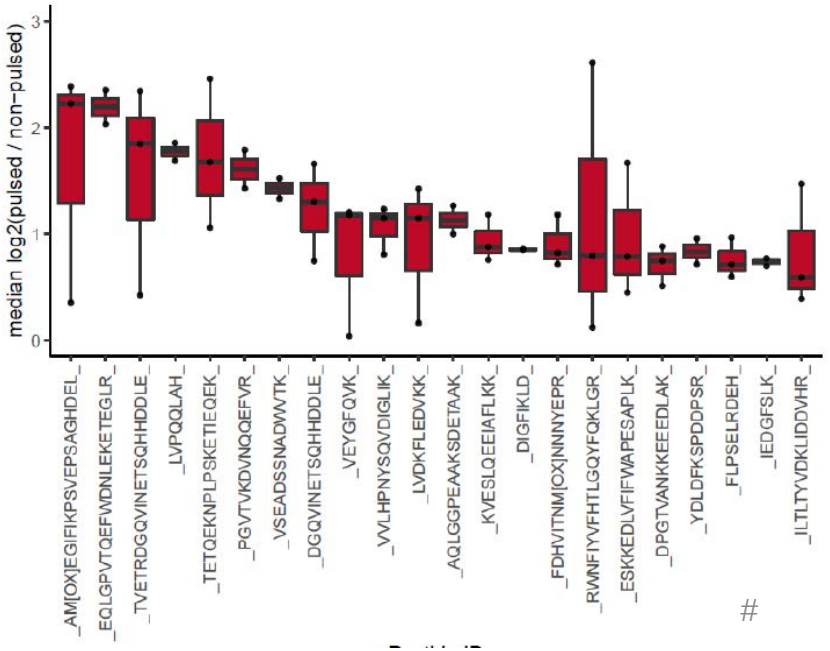
Example:

399 tumour peptides presented to T cells by DCs on MHC Class I



+

220 tumour peptides presented to T cells by DCs on MHC Class



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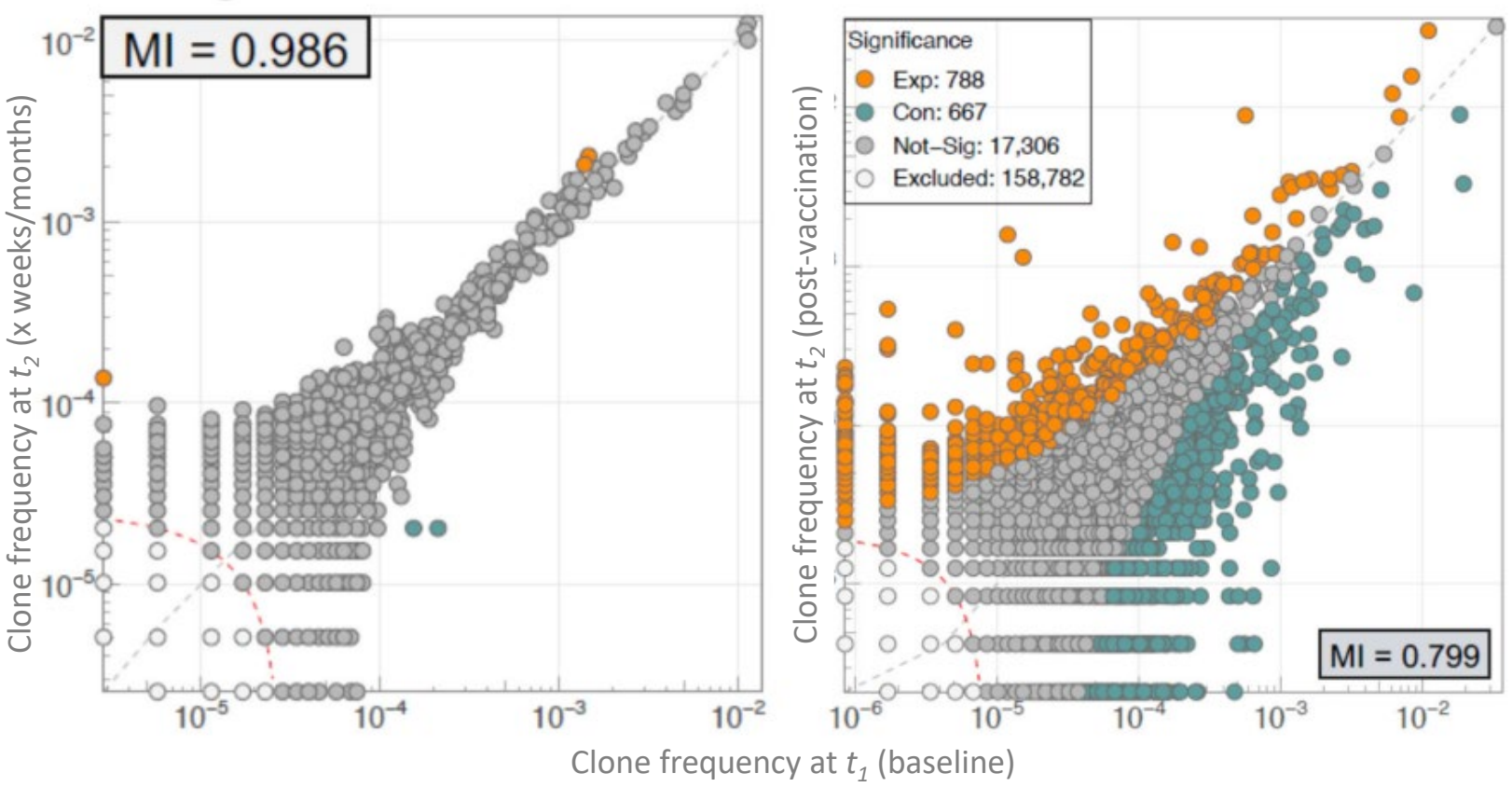
Strong T Cell Responses Are Stimulated



T cells from the blood of an untreated person

T cells from the blood of a DCVax-L treated person

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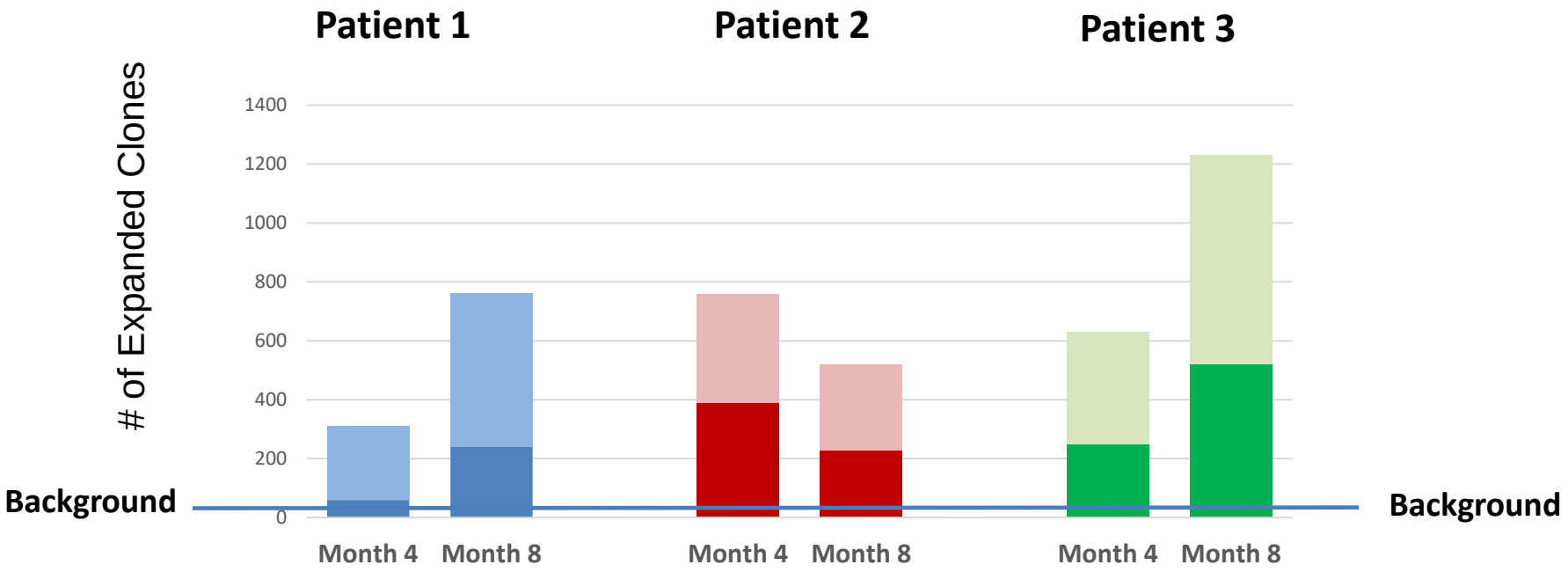
Internal report: Analysis provided by Adaptive Biosciences

Expanded T Cell Clones

compared to Baseline



- These bars represent the total number of newly expanded T cell clones (dark color) or further expanded, pre-existing clones (light color)
- Background in normal, unstimulated individuals would be 2 – 20 clones

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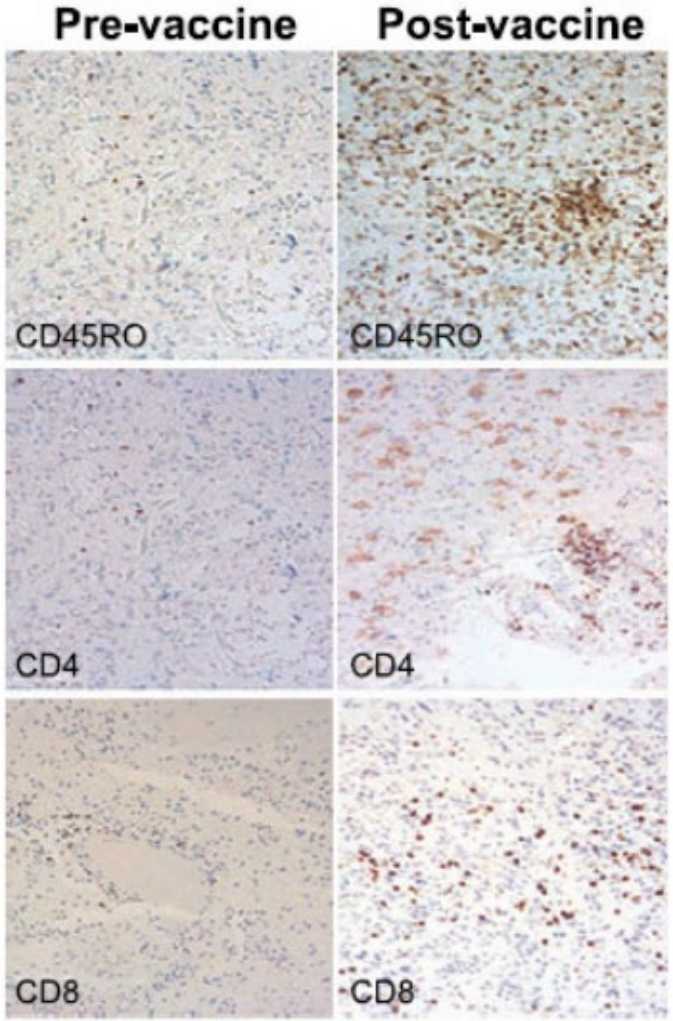
T Cell Infiltration Into Tumor Is Stimulated



Infiltration of T cells into GBM tumours is observed in patients treated with DCVax-L

Both CD4 and CD8 cells

T cells have **crossed the blood brain barrier** after being mobilised; DCVax-L doses are administered as intra-dermal injections in upper arm

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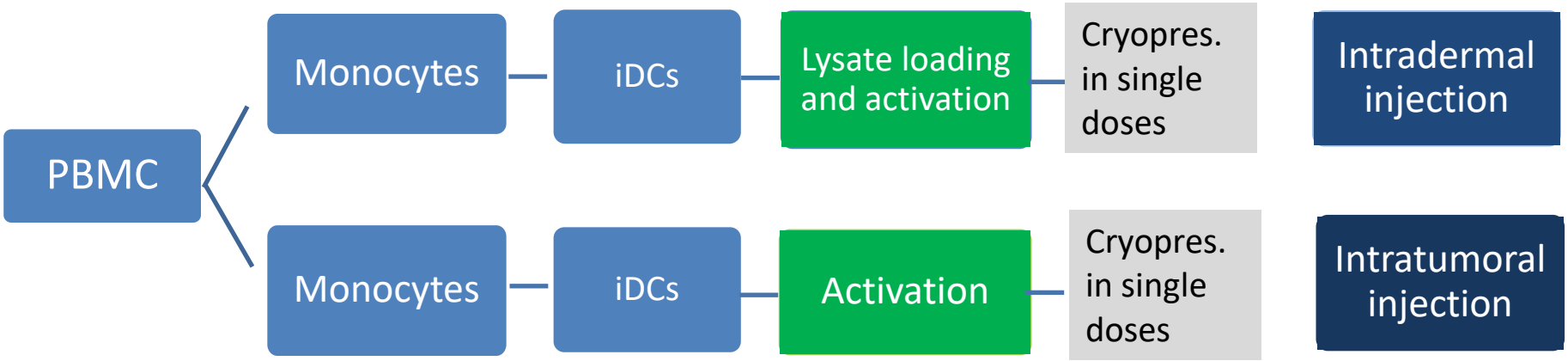
Linda Liau et al

DCVax® - Rapid Batch Manufacturing of Multi-Years of Doses; Then Off-the-Shelf

DCVax-L
for resectable tumors

8 Days
to manufacture



DCVax-Direct
for unresectable tumors

7 Days
to manufacture

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Trial Design – Phase 3 Trial of DCVax-L for GBM

Primary Endpoint: OS in newly diagnosed GBM

DCVax-L arm (n=232) vs. External controls (n=1,366)
(control arms of external studies)

Secondary Endpoint: OS in recurrent GBM

Placebo arm crossovers* (n=64) vs. External controls (n=640)
(control arms of external studies)

*(Placebo arm patients received only SOC + placebo until recurrence, then DCVax-L)

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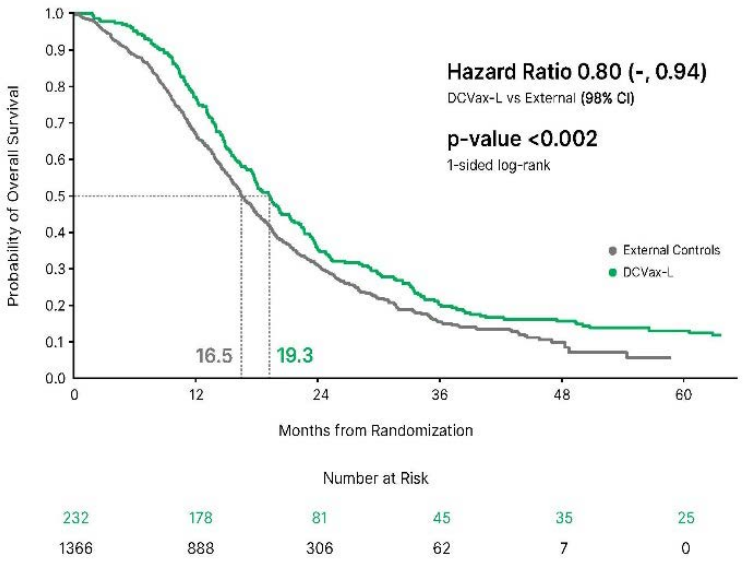
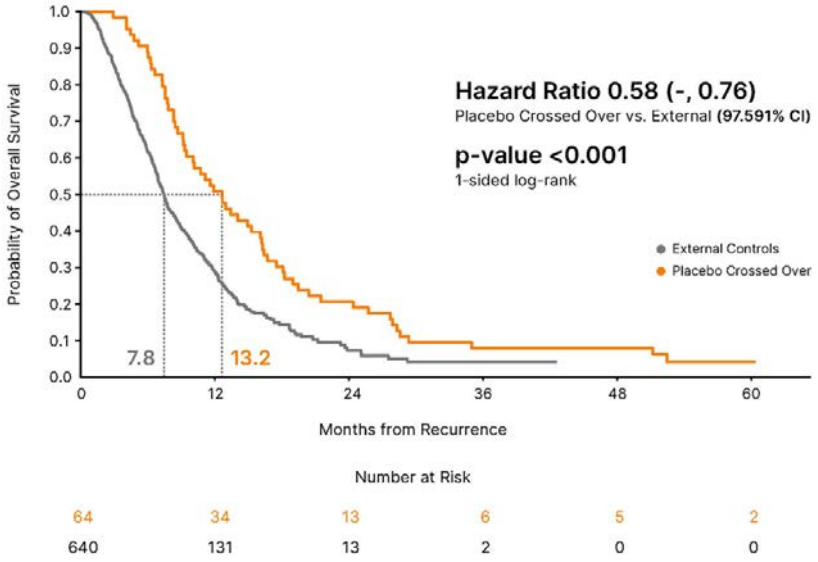
Significant Extension of Survival In Both nGBM & rGBM

Newly diagnosed GBM: mOS +2.8 months



Recurrent GBM: mOS +5.4 months



mOS of DCVax patients:
19.3 months from randomisation;
22.4 months from surgery

mOS of controls:
16.5 months from randomisation

mOS of DCVax patients:
13.2 months from recurrence

mOS of controls:
7.8 months from recurrence

*mOS = median overall survival

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'Long Tail' of Patient Survival With DCVax-L

Newly diagnosed GBM:

More than doubled 5-year survival

Recurrent GBM:

More than doubled survival 24 & 30 months *post-recurrence*

nGBM Landmark survival rate			
	ECP*	**DCVax-L**	**Relative Rate**
36 mo	15.5%	20.2%	130%
48 mo	9.9%	15.7%	159%
60 mo	5.7%	13.0%	228%
rGBM Landmark survival rate post progression			
	ECP	**DCVax-L**	**Relative Rate**
6 mo	64.0%	90.6%	142%
12 mo	30.8%	54.1%	175%
18 mo	15.9%	31.8%	200%
24 mo	9.6%	20.7%	215%
30 mo	5.1%	11.1%	217%

*ECP means External Control Population – the patients who received current standard of care (SOC) treatments, and were compared with patients who received SOC plus DCVax-L

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GBM Phase 3 Trial Results with Individual Patient Matching

Method	Delta (mo)	HR	P
Unadjusted	**2.8**	0.80	<0.002
Propensity Score Matched A	**6.3**	0.74	0.02
Propensity Score Matched B	**6.1**	0.77	0.004
Propensity Score Matched C	**4.9**	0.69	0.004
Inverse Probability Weighting 1	**3.6**		0.008
Inverse Probability Weighting 2	**4.3**		0.03
Inverse Probability Weighting 3	**4.3**		0.01
Inverse Probability Weighting 4	**3.4**		0.01
Inverse Probability Weighting 5	**4.0**		0.004
Inverse Probability Weighting 6	**3.4**		0.01
Average	**4.3 months**		

Phase I Trial in Terminal Ovarian Cancer
(Kandalaft et al. 2013)

Clinical Summary

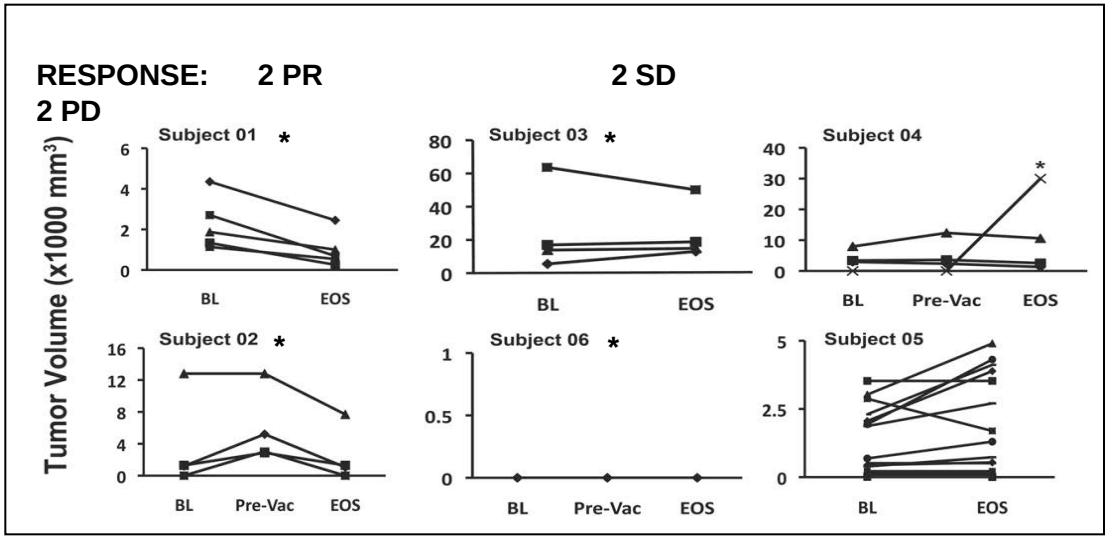
Patient ID #	DC Dose *10^6	Response[1] (RECIST)	Survival[2] (months to Nov 2012)	Status per Nov 2012[2]
01	5	PR	48.0	Dead
02	7.5	PR	13.2	Dead
07	7.5	SD	>50.0	Alive
14	7.5	SD	>41.7	Alive
15	9.5	PD	>38.8	Alive
16	7.5	PD	>38.4	Alive

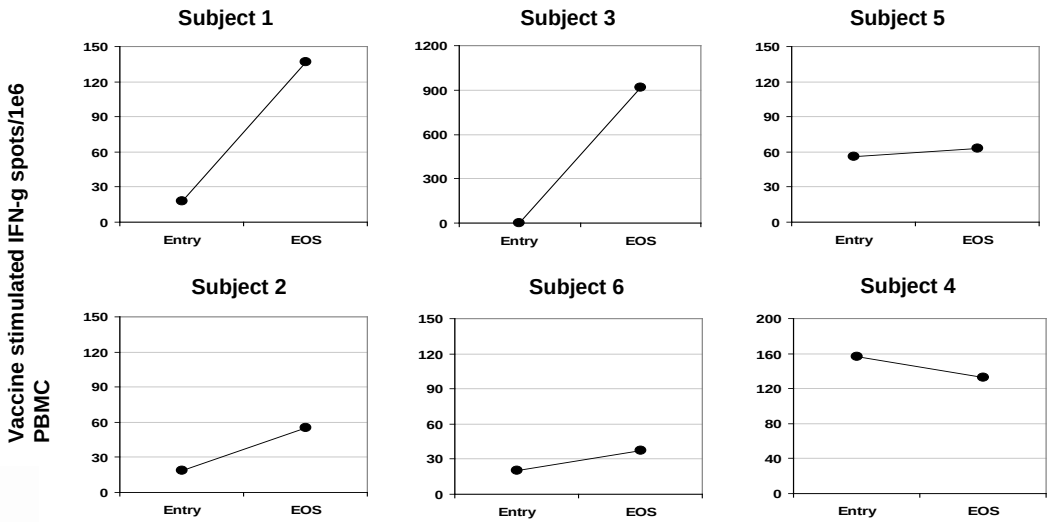
1) Tumor response post DCVax-L vaccination, and prior to T cell infusion
2) Three patients (01, 02, 07) received T cell infusions post DCVax-L treatment

Immunological Summary

Patient ID#	DC Dose *10^6	Increase in T cell responses to DCVax-L	Increase in Her-2-specific CD8+ T Cells after vaccination	Antibody responses to human proteins
01	5	+	+	+
02	7.5	+	n.d.	+
07	7.5	+	n.d.	n.d.
14	7.5	+	n.d.	n.d.
15	9.5	-	n.d.	n.d.
16	7.5	-	n.d.	n.d.

Immunological Results in Ovarian Cancer





George Coukos, Lana Kandalaft, Dan Powell, Bruce Levine, Carl June et al.

Next Steps: Combination Approaches

- Given that DCVax-L works through the induction of an anti-tumour immune response, one would expect that **combining DCVax-L with immune enhancers** such as adjuvants, TLR agonists and checkpoint inhibitors (CPIs) could enhance the survival extension.
- A recent paper demonstrated meaningful enhancements of survival seen by combining DCVax-L with **Hiltonol®, a TLR-3 agonist**.[1]
- To date, CPIs have failed to extend survival in GBM[2], likely due to insufficient active immune response to 'take the brakes off of'. Combining DCVax-L with **CPIs** would overcome that initial hurdle.

Rational design of trials to test combination therapies centered around DCVax-L may lead to further dramatic enhancements of survival in GBM patients

1) *Everson et al. 2024*
2) *Fioletova et al. 2026*

DCVax-L Summary

- DCVax-L has a well-established mechanism of action
- DCVax-L induces **clonal expansion of hundreds of diverse T cells** in vivo and those T cells infiltrate the tumor
- In glioblastoma, DCVax-L treatment is associated with clinically meaningful and statistically significant **extension of life**
- Early results in **other indications** such as ovarian cancer are promising
- DCVax-L is currently under review by the MHRA for a **marketing authorization** for the treatment of glioblastoma

DCVax®-Direct
for
Inoperable Solid Tumours

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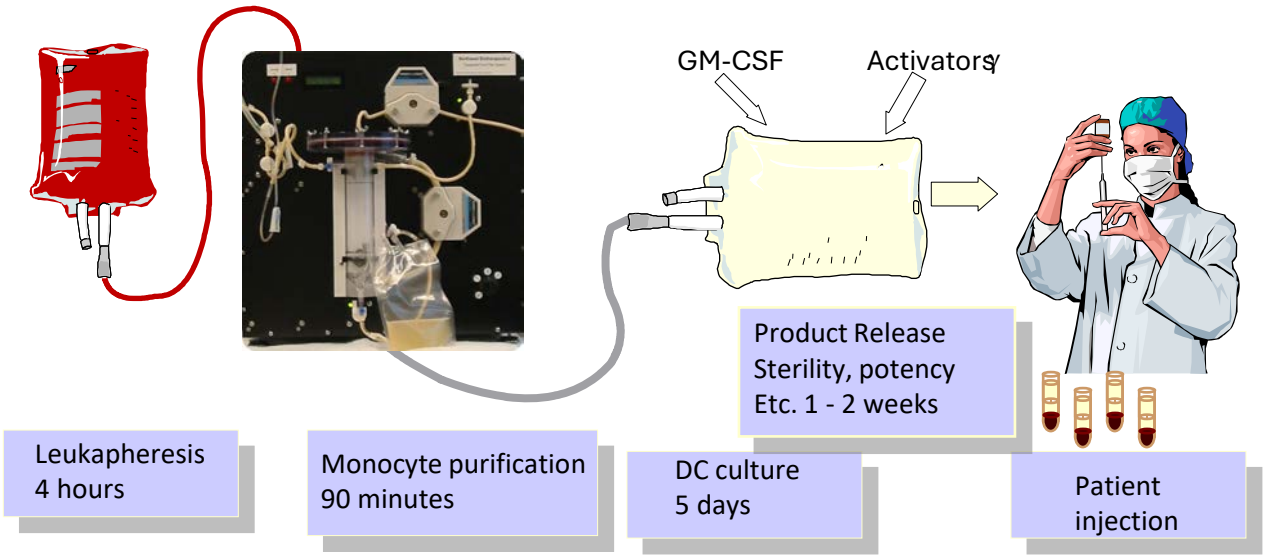
What is DCVax®-Direct?

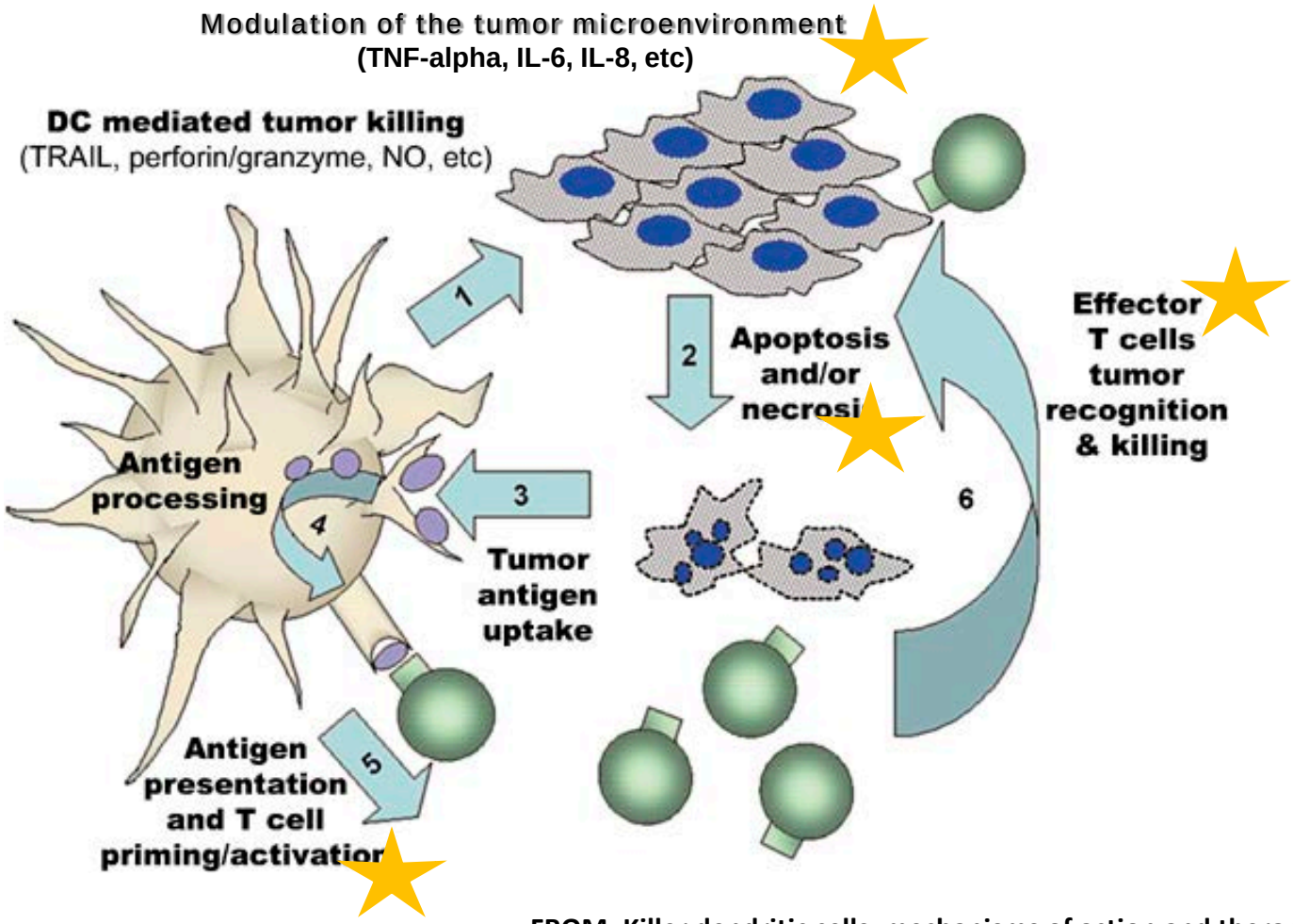
- DCVax-Direct is autologous, unloaded, partially activated dendritic cells for intratumoral injection
- DCVax-Direct is manufactured in a **closed and automated system** that is specifically designed to maximize therapeutic effects:
  - The resulting DCs are uniformly immature
  - Activation of these immature DCs to **partial maturation** is tightly controlled to ensure antigen uptake as well as subsequent DC maturation following injection
  - This also results in **large-scale, local production of cytokines** that appear to be essential for clinical effectiveness

Automated Manufacturing



This system has been used to produce clinical-grade dendritic cells for intratumoral injection, with encouraging clinical results.
Vivek Subbiah et al., Clin. Cancer Res. 24 (16): 3854-3858 (2018)

DCVax-Direct Mechanism of Action



FROM: Killer dendritic cells: mechanisms of action and therapeutic implications for cancer A K Wesa and W J Storkus

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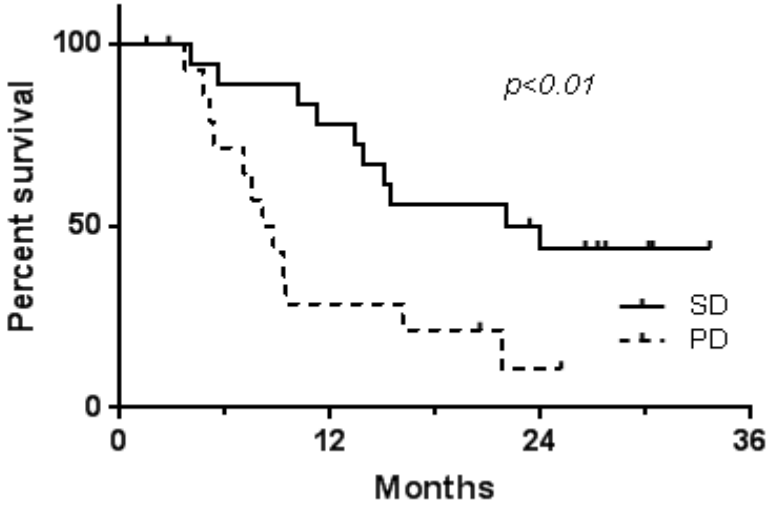
Phase I Trial Summary

- The trial treated 40 patients with 13 types of **locally advanced or metastatic** cancer
- All patients were heavily pre-treated, had **failed all other treatments**, and had progressive disease at study entry
- 75.8% of evaluable study subjects **exceeded their expected survival time**, by an average of 14.3 months.



- 23 of 37 (62%) of evaluable patients achieved SD at week 8
- SD at wk8 is predictive of longer survival

- The treatment is well tolerated. Most frequent adverse event is **mild to moderate fever** for <48 hours

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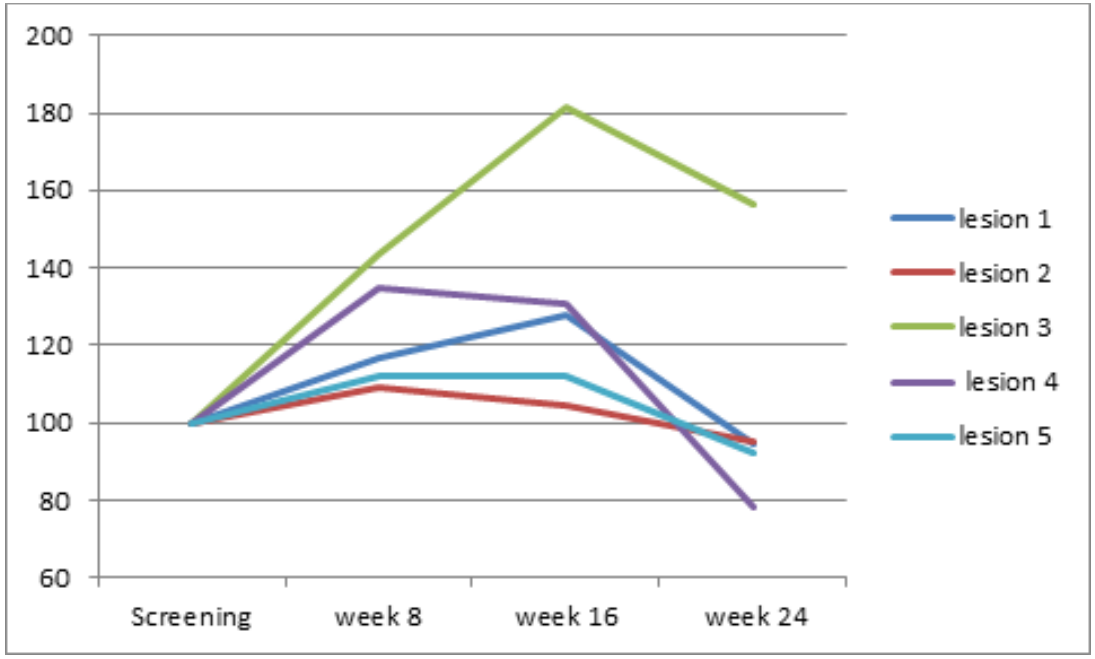
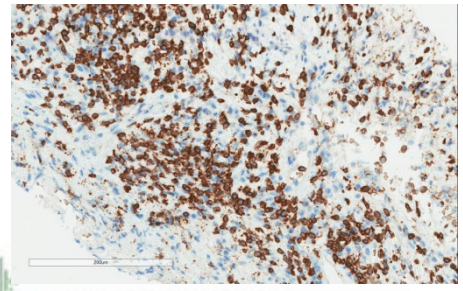
Local and Systemic Effects on Tumour Growth

- Clear cell sarcoma
- Patient failed multiple other treatments
- Only single lesion injected
- 5 measurable tumours

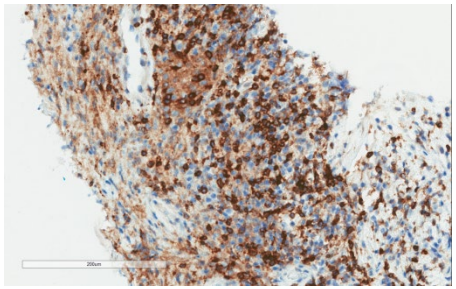


Substantial T-cell infiltration (week 8):

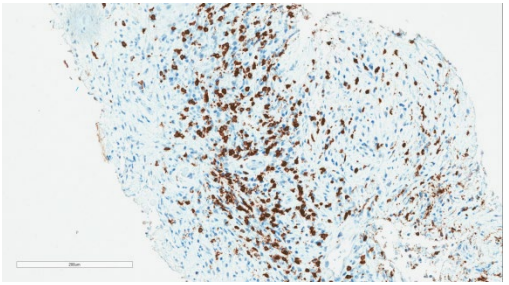
CD3 cells



CD4 cells



CD8 cells



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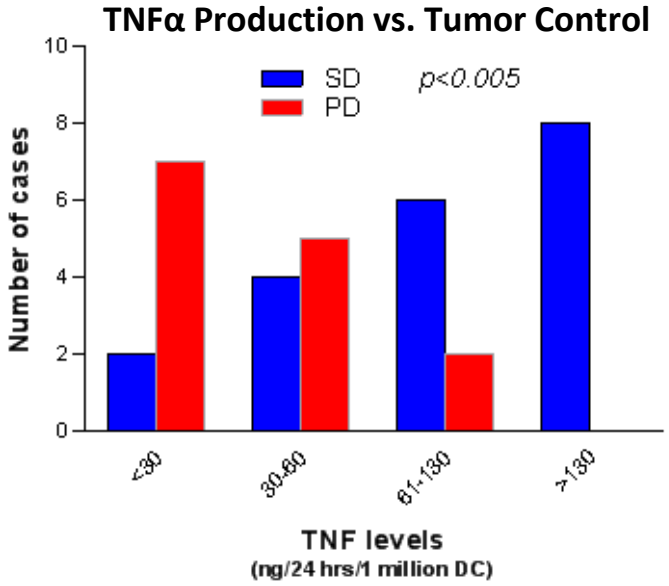
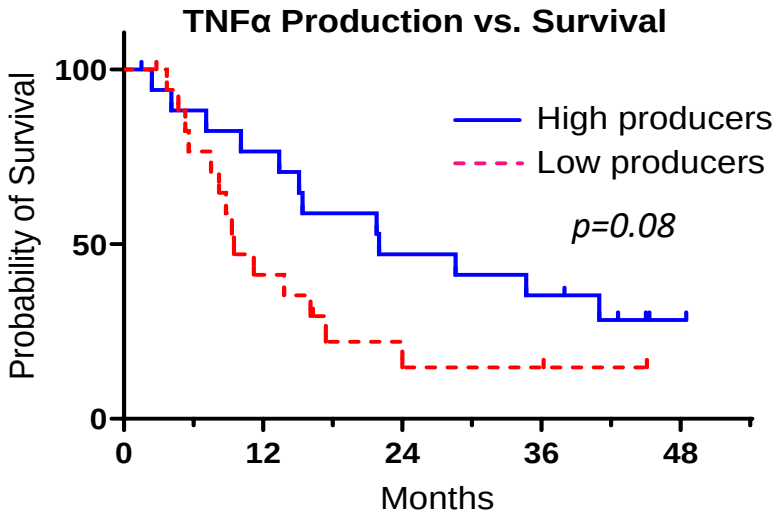
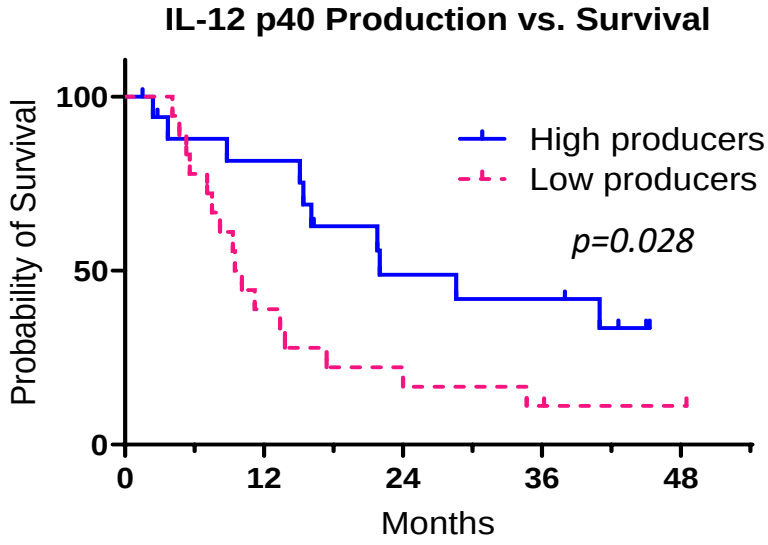
Correlations Between Cytokine Production and Survival





Conclusion: patients whose DCs produce **high levels** of the relevant cytokines have **better tumour control** and **better survival**



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DCVax-Direct Phase I Trial: Excellent Safety Profile

- >140 treatments administered to 40 patients in Phase I trial
- 4 SAEs "related" or "possibly related" to DCVax-L treatment
  - Fevers (n=2), fever and chills (n=1), systemic inflammatory response syndrome (n=1)
- Most patients developed **mild to moderate fevers** following DCVax-Direct injections
  - ➢ Typically ≤ 2º C, and typically ≤ 2 days
- **No dose limiting toxicities** were observed at any of the dose levels (2 million, 6 million or 15 million DCs per injection)

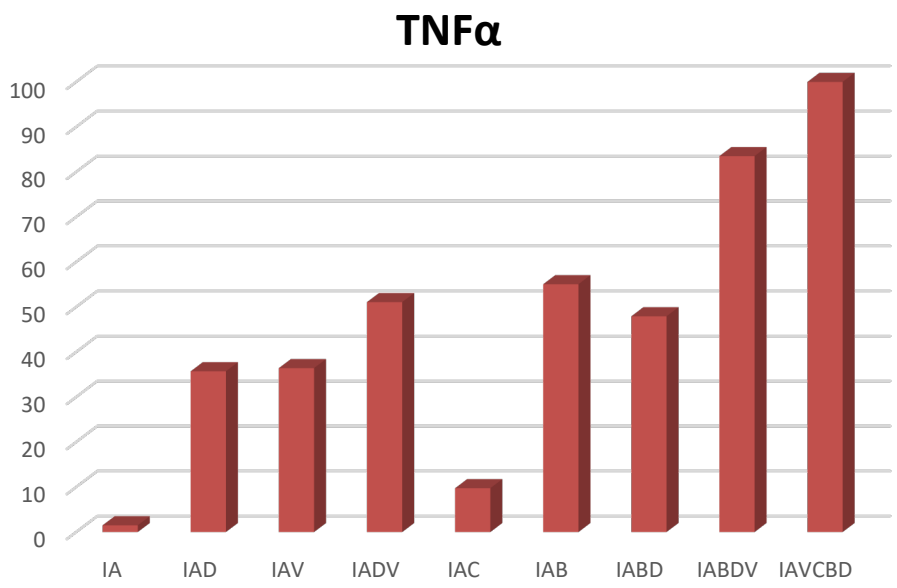
Supercharging Dendritic Cells

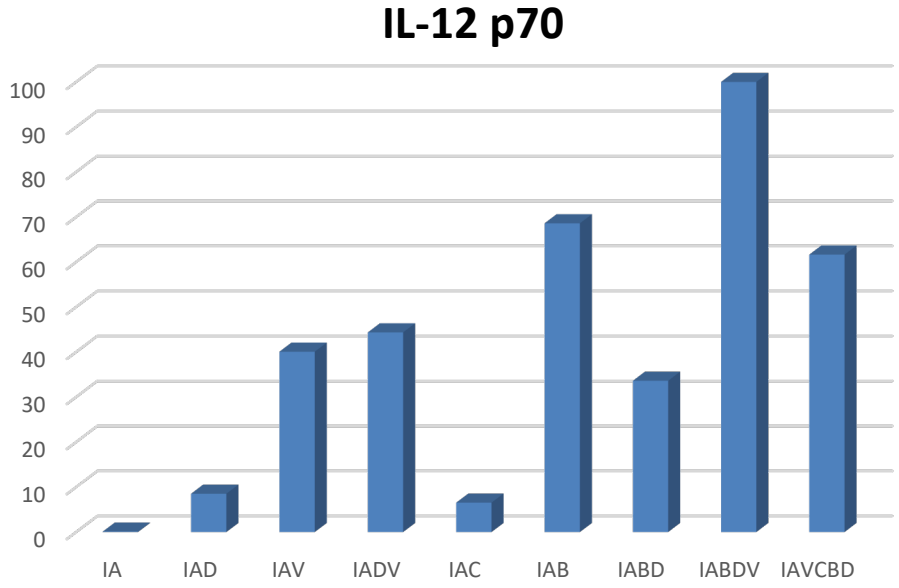
1. Judicious combinations of DC booster agents can be combined to **supercharge the DCs** prior to injection. These agents include:
   - TLR agonists (A, B, C[1])
   - biological response modifiers (I[1])
   - activators of antiviral pathways (V[1])
   - danger signals (D[1])
2. The ensuing **increase in the level and breadth of cytokines** produced by DCs for intratumoral injection can enhance both local and systemic effects
3. This enhancement can result in an even **higher rate of clinical responders**, and **longer survival**

1) These codes are used in subsequent description of the experimental results

Increasing Production of Relevant Cytokines:
TNFα and IL-12 p70

- In the Phase I trial, both TNFα and IL-12 were found to be **associated with tumour control and improved survival**
- Production of e.g. TNFα and IL-12 p70 can be **increased by 1 – 2 orders of magnitude** in response to additional booster agents
- This effect alone is expected to <u>meaningfully enhance efficacy</u>





DCVax-Direct Phase I Trial: Key Observations

- DCVax-Direct is a **multi-modal, broad-spectrum** immunotherapy for solid tumours
- DCVax-Direct can be **safely administered intratumorally** in patients with unresectable cancer
- Clinical benefit is associated with levels of cytokines produced by the DCs
- Next generation **Supercharged DCs** are in development

Cancer Vaccines – a New Era

- Cancer vaccines provide a **new therapeutic option** for cancer patients
- Due to the overall excellent safety profile, dendritic cell-based cancer vaccines can be **supplemented** with immune activators, and with checkpoint inhibitors (CPIs)
- Cancer vaccines can be applied to:
  - Blood cancers
  - Solid tumours
  - CPI naïve patients as well as CPI refractory cases
- The personalised, broad-spectrum approach of dendritic cell-based cancer vaccines ensures induction of an immune response that is **fully tailored with greater efficacy potential**
- This potential applies to both **genetically and epigenetically driven cancer**

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