



NORTHWEST
BIOTHERAPEUTICS

DCVax® Novel Personalized Immunotherapies for Solid Tumors

Phaciliate Immunotherapy World Forum

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Novel DCVax® Technology: Overview

DCVax®: Personalized DCs + personalized and full set of tumor antigens

- Avoids “Russian Roulette” and impedes tumor escape

Encouraging results to date, expanding the reach of immunotherapies

- Long tail of durable clinical responses
- Excellent safety profile

Novel Technology Aspects

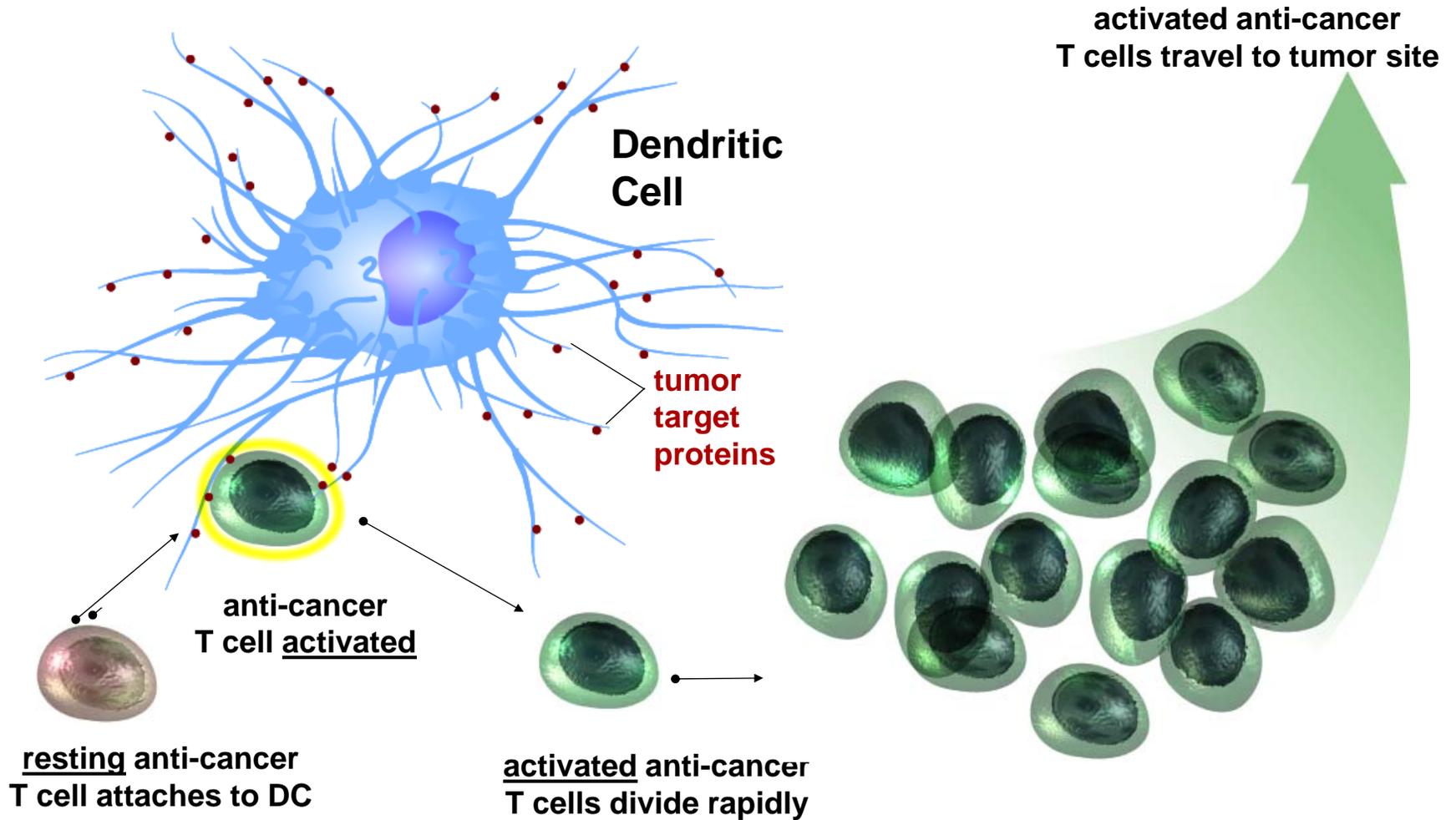
- **Robust cytokine secretion without material toxicity**
cytotoxic effects in tumors; modulation of tumor micro-environment
- **Mobilization of T cell responses:** large multiplier effect; quantity & diversity
- **Expression of PD-L1:** potential synergy with checkpoint inhibitors



DCVax Potentially Applicable to All Types of Solid Tumors

Market	Product / Administration	Composition	Lead Program
All Operable Solid Tumors	DCVax®-L Intra-dermal shot in arm	Dendritic cells + full set of tumor antigens from tumor tissue sample surgically removed	Brain cancer <i>348-patient Phase III trial underway</i> Small ovarian cancer Phase I/II trial completed
All Inoperable Solid Tumors	DCVax®-Direct Direct injection into tumor	Dendritic cells directly injected into tumor(s) + full set of tumor antigens picked up in situ in tumor	All solid tumor cancers (13 cancers treated to date) <i>60-patient Phase I/II trial under way</i>

Large Multiplier: Each Dendritic Cell Activates Hundreds of Anti-Cancer T Cells



DCVax Potential to Expand the Reach of Immunotherapy

Clinical trials/treatments of nearly 20 diverse types of cancers including:

newly diagnosed disease

- DCVax-L for newly diagnosed GBM, with SOC (Phase III trial)

late stage, heavy tumor burdens

- DCVax-L for late stage, metastatic ovarian cancer
- DCVax-L for “rapid progressor” GBM
- DCVax-Direct for inoperable metastatic tumors (13 types of cancer)
- DCVax-Direct for very large tumors (10 cm. lung; 15x19x17 cm. sarcoma)

lower grade cancers

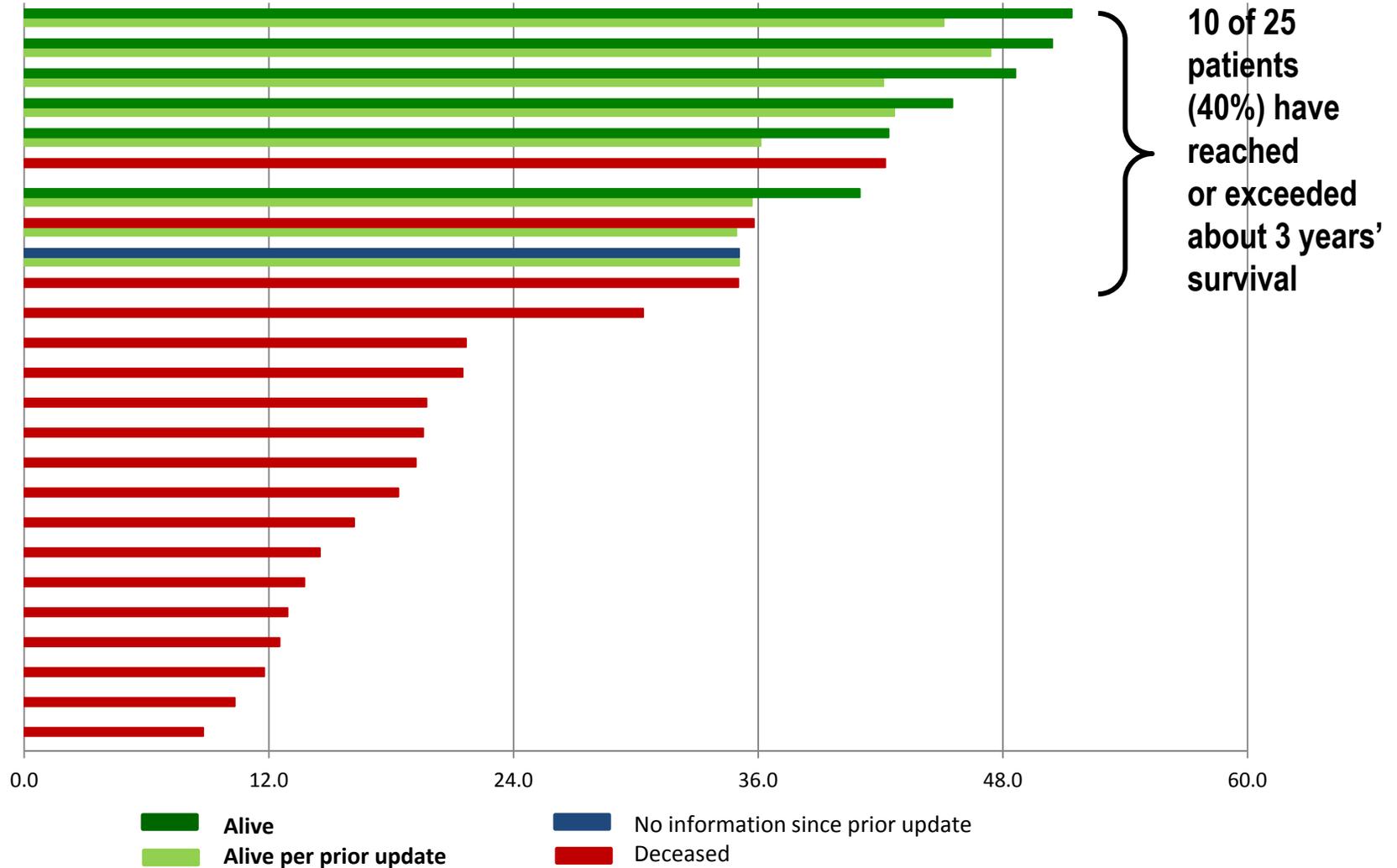
- DCVax-L for all grades of gliomas, with SOC (Hosp. Exemp., Germany)

higher grade cancers

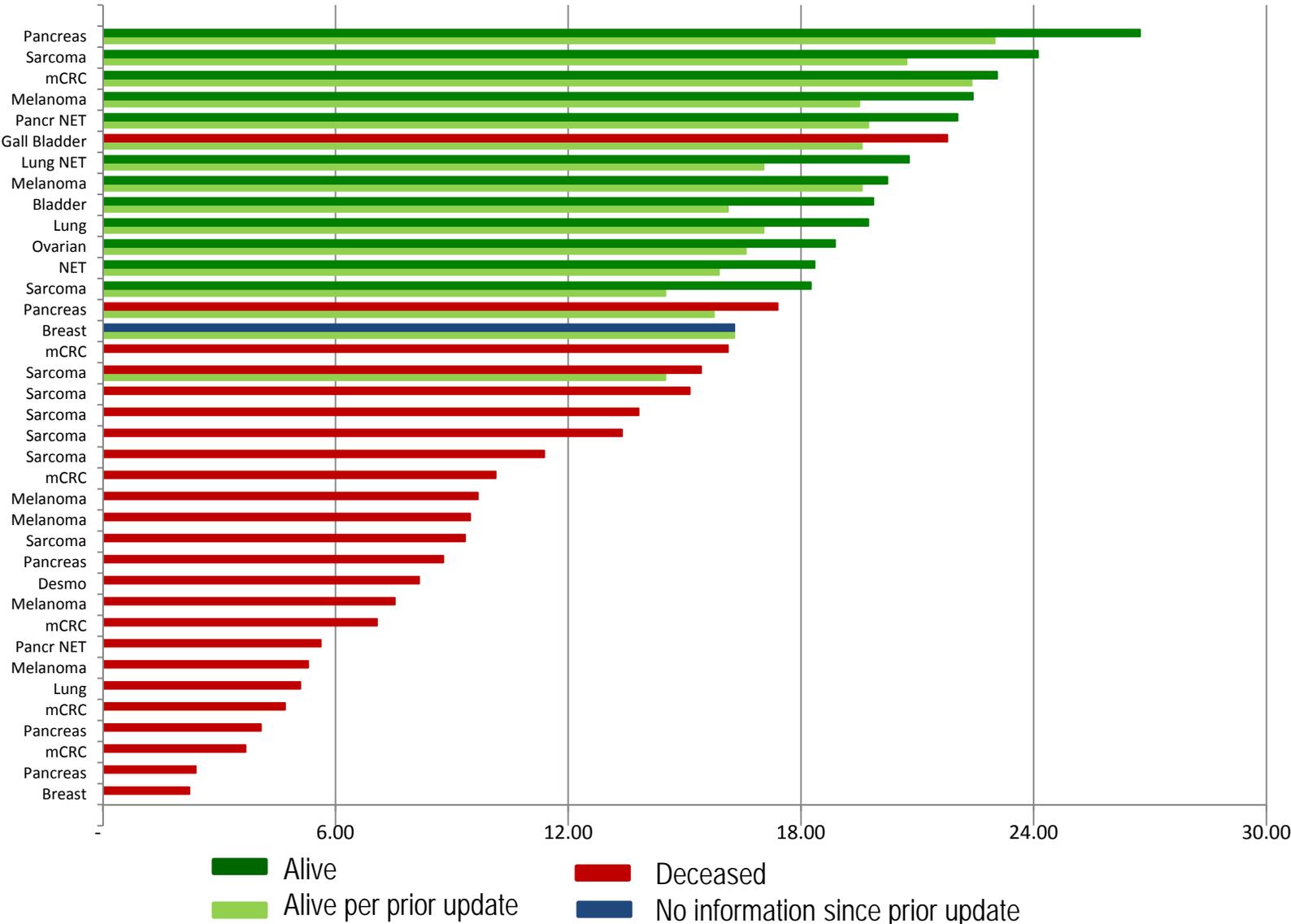
- DCVax-L for high-grade/GBM (Phase III trial)



Long Tail of Durable Responses: **DCVax-L** Info Arm Study of Apparent Rapid Progressor (Recurrent) GBM Patients



Long Tail of Durable Responses: DCVax-Direct Phase I Trial; 13 Cancers



Excellent Safety Profile

DCVax-L:

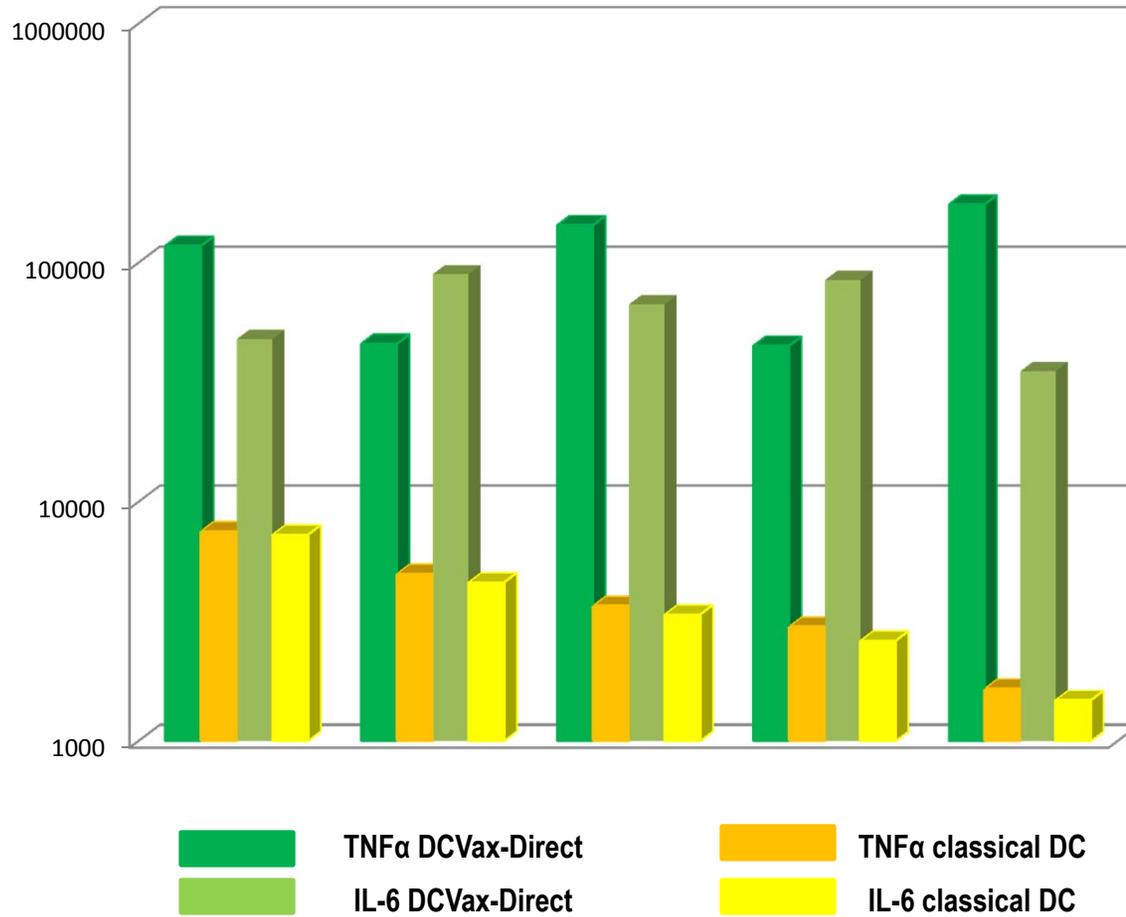
- **Over 400 patients treated, with over 2,800 treatment cycles: only 7 “possibly or probably related” SAEs**
- **Generally, AEs are related to underlying disease or other treatments (e.g., temozolamide).**

DCVax-Direct:

- **40 patients treated, with over 140 treatment cycles: only 3 “related” SAEs**
- **Generally, Grade 1 and occasionally Grade 2 fevers related to treatment**



Robust Cytokine Secretion

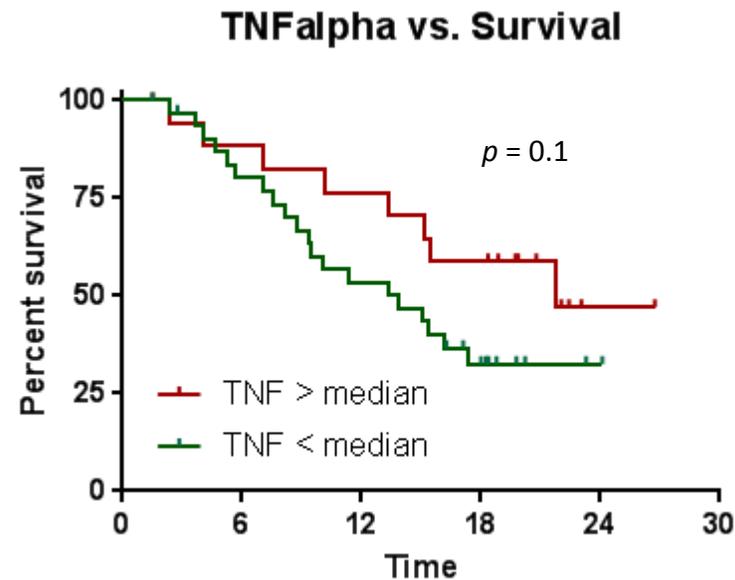
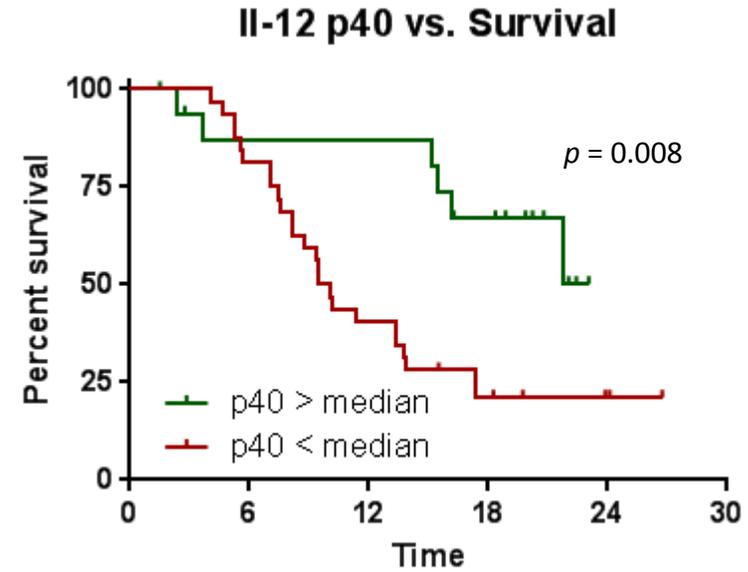
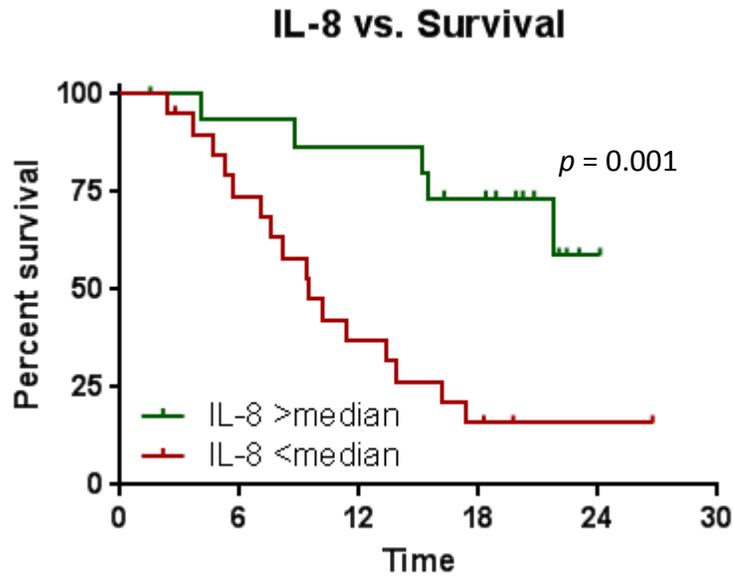


Greater Cytokine Secretion May Help Improve Outcomes

- **Cytokine secretion while product still in manufacturing process**
- **A measure of dendritic cell potency/functionality**
- **A potential indicator of patient's immune competence**
- **A potential indicator of whether patient is more likely or less likely to respond to immunotherapies**
- **Cytotoxic effects, tumor necrosis**
- **Correlation with improved survival**

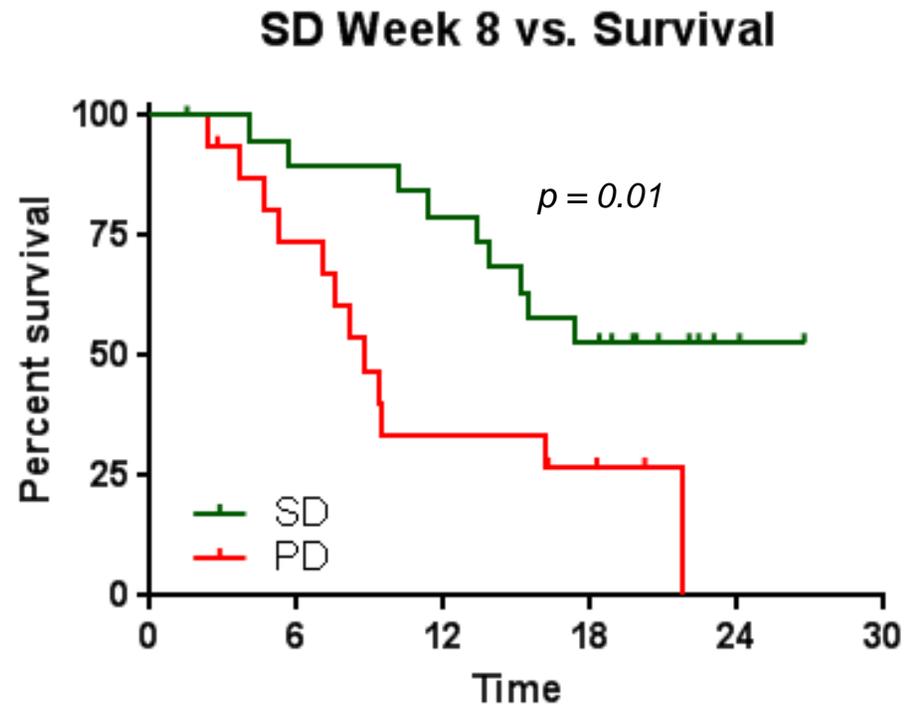
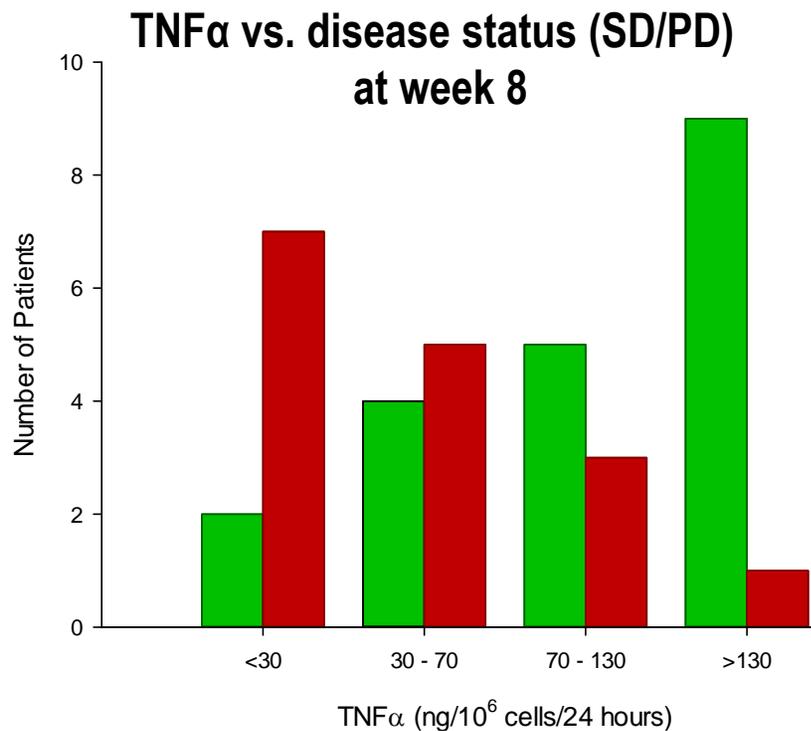


Greater Cytokine Production Correlates With Survival



3 outliers (based on cytokine production profile) removed prior to analyses

Cytokines Correlate with Stable vs. Progressive Disease And Stable Disease Correlates With Survival



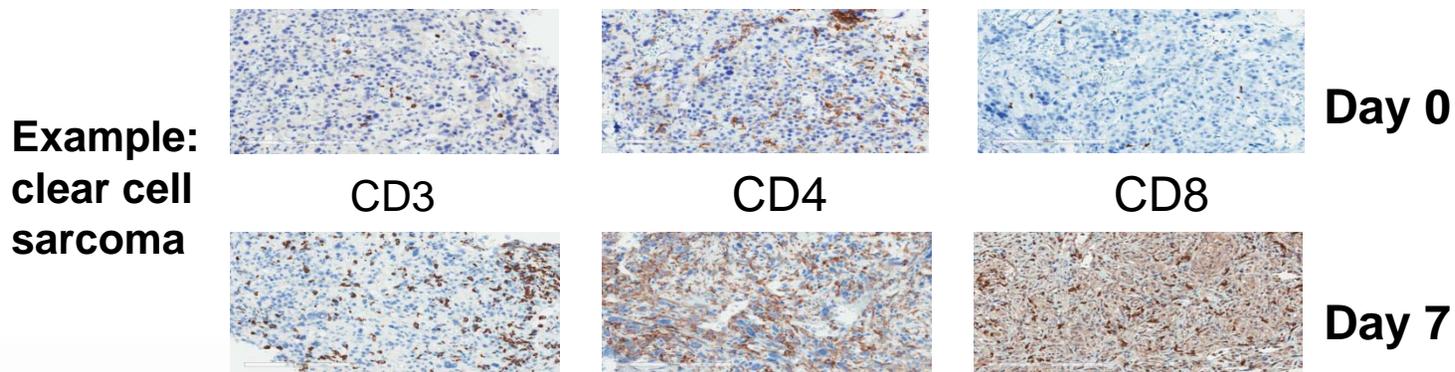
Mobilizing T Cell Responses

Overall, both CD4+ helper T cells and CD8+ killer T cells increased materially from baseline in at least 20 of 28 assessed patients (71%) in DCVax-Direct Phase 1.

Early Effects:

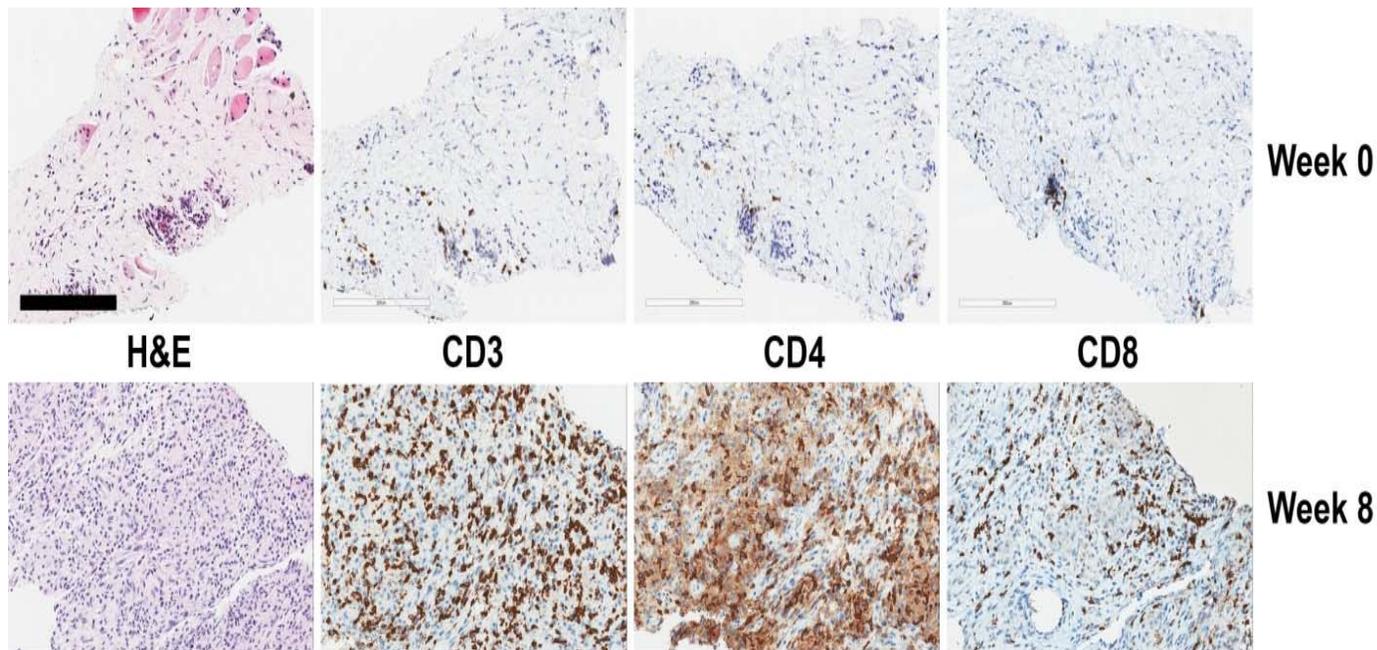
In some patients, influx of T cells into tumor was apparent within days of first DCVax-Direct administration, suggesting:

- A pre-existing immune response which was being blocked in the TME
- A modulation of TME and rapid breakdown of tumor defensive barriers



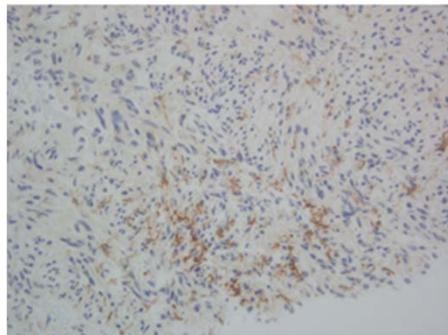
Mobilizing T Cell Responses: Longer Timeframe, De Novo Responses

- Observed more frequently than early effects of T cell responses
- Wide range of CD4 and CD8 T cell ratios observed
- Preliminary analysis suggests full T cell functionality



Induction of Checkpoint Expression (PD-L1)

- 20 of 25 evaluable patients (80%) in DCVax-Direct Phase I trial, showed either *de novo* or significantly increased expression of PD-L1 following DCVax-Direct treatment
- Patient to patient variation in timing of when PD-L1 expression appears



De novo PDL-1 staining on sarcoma tissue, 8 weeks after initiation of DCVax-Direct treatment

- At least in some types of cancers, PD-L1 expression is correlated with (and may predict) patient responsiveness to checkpoint inhibitors
(e.g., gastric cancers)



Conclusions

- DCVax products are capable of inducing immune responses in a wide variety of cancers and wide range of patients
- DCVax product potency appears likely to predict for clinical outcome (to be substantiated in further trials)
- Patients treated with DCVax-Direct exhibit both de novo or increased T cell responses and de novo or increased PD-L1 expression
- DCVax-Direct may help increase percentage of patients responding to checkpoint inhibitors
- Early identification of patients likely to respond can increase chances of success

