

DOC1021 Cell-Based Vaccination as Adjuvant Therapy for Glioblastoma: Phase I Clinical Trial Analysis



Yoshua Esquenazi, MD

Associate Professor

Director of Neurosurgical Oncology

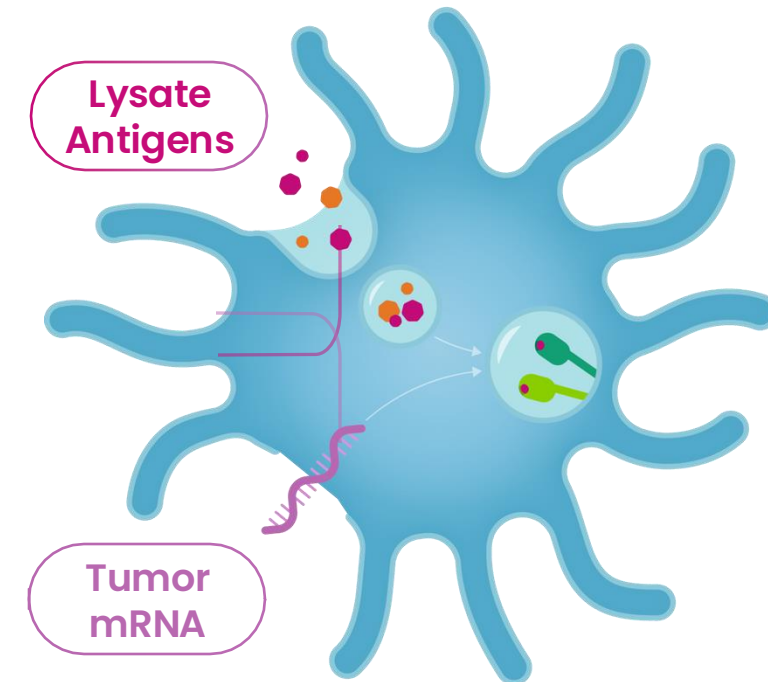
Co-Director of the Gamma Knife Radiosurgery Program

The University of Texas Health Science Center at Houston



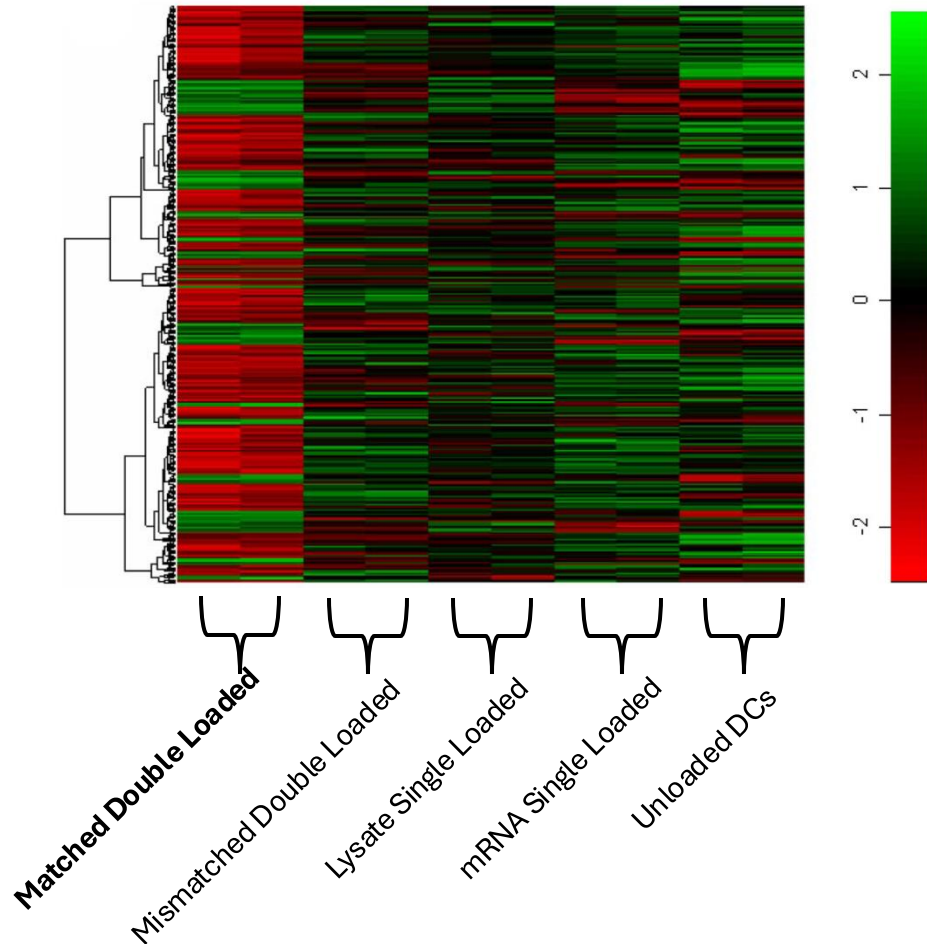
DOC1021 Dendritic Cell Immunotherapy

- Dendritic cells (DCs) are master regulators of the immune system that stimulate T cells to react to tumors and infections
- DC vaccines have shown trends towards increased survival in GBM
- DOC1021 is a unique homologous double-loaded DC vaccine, using tumor-lysate and mRNA
 - Leverages p38MAPK and mTORC1 signaling cascades to initiate cDC1-like skewing leading to downstream induction of T cells with enhanced capacity for serial killing, resistance to exhaustion, and tissue homing capacity
 - Targets whole complement of tumor antigens
 - Relatively simple manufacturing
 - Unlike Car-T cell approaches, no genetic modification or myeloablative chemotherapy required

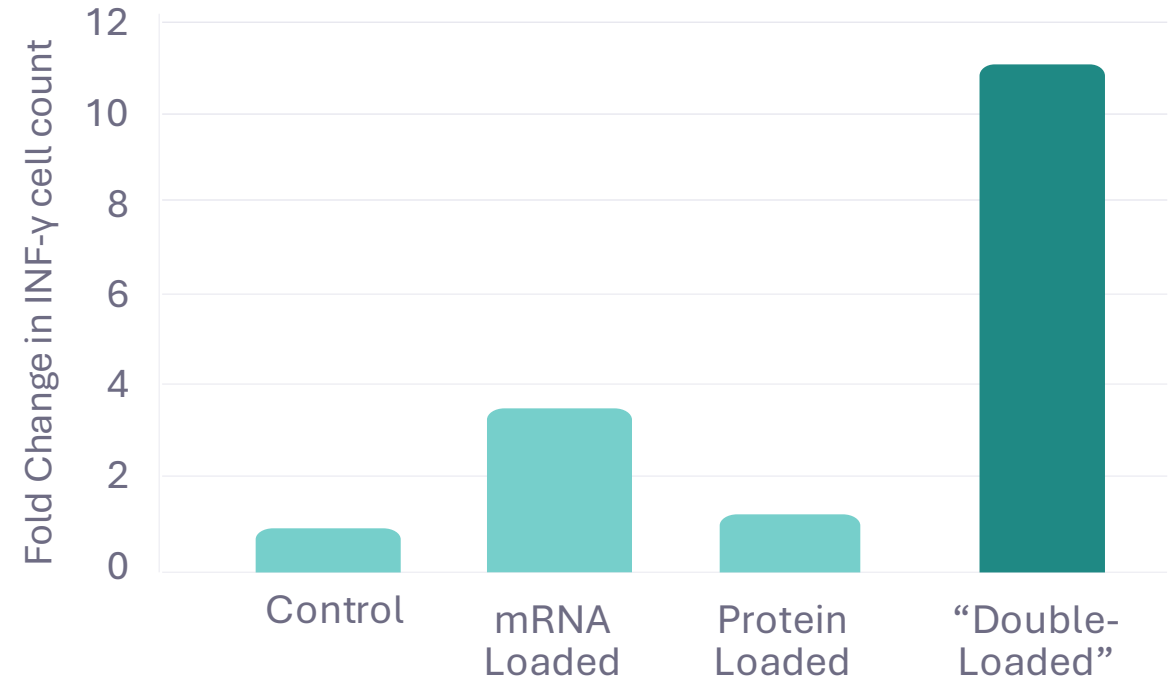


Homologous Antigenic Loading Unlocks the Potential of DCs

Unique signaling cascade, increased Th1 & decreased Th2 stimulating gene expression



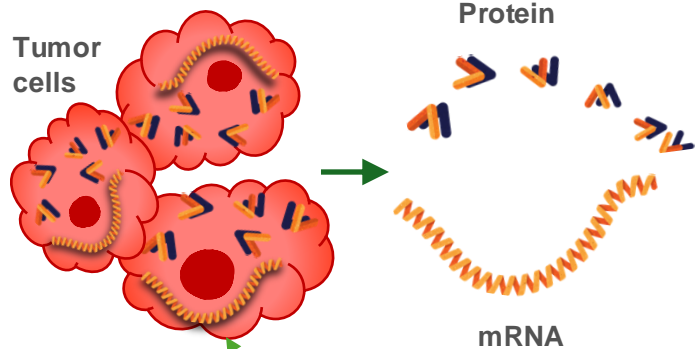
“Double Loaded” DCs generate **10x** stronger cytotoxic T cell activation



“Double-Loading” DC Preparation Protocol

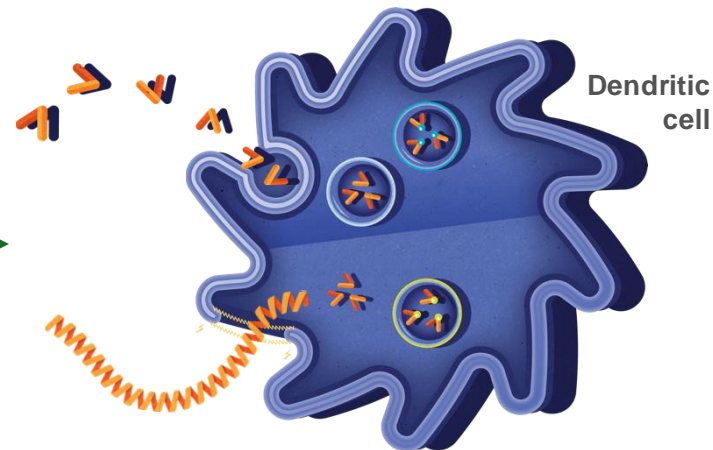
Step 1

Surgical Resection & Tumor Prep



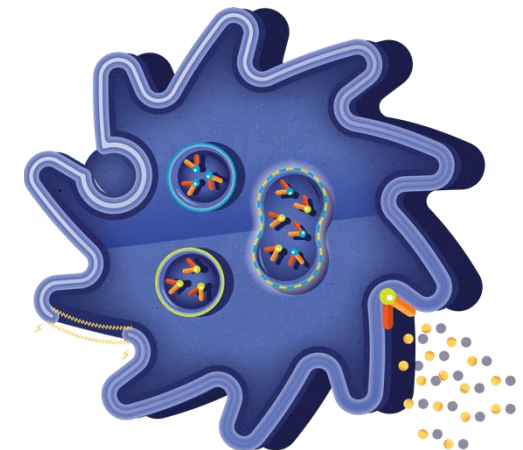
Step 2

Leukapheresis & DC Double Loading



Step 3

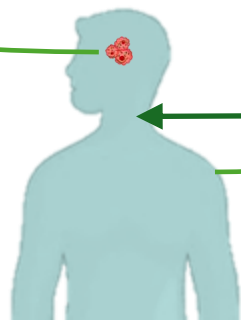
Vialed DOC1021 Shipped to Site & Injected every 2 weeks x 3



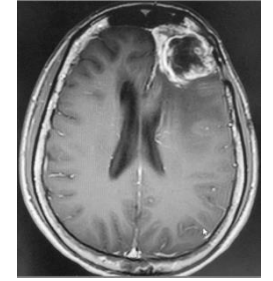
1 Surgical Resection to Collect Tumor Tissue

2 Leukapheresis to Collect Monocytes

3 US-guided DCV Injection in Cervical Lymph Nodes



Phase I Glioblastoma Trial



DOC1021 Dendritic Cell Regimen With Standard Postoperative Therapy for Adult Glioblastoma (IDHwt)

UTHealth Houston , MDAnderson Cooper, Camden NJ
NCT04552886

Enrollment & Dosing Completed:
16 newly diagnosed & 2 recurrent*

Dose Level	Patients	DLTs
Dose Level 1 (3.5M Cells)	4	0
Dose Level 2 (7M Cells)	4	0
Dose Level 3 (14M Cells)	5	0
Dose Level 4 (36M Cells)	5	0

*1 additional participant dropped out after first vaccine dose, patient choice

Surgical Resection

Neupogen,
Leukapheresis

TMZ, Radiotherapy

1st DCV Injection, IFN

2nd DCV Injection, IFN

3rd DCV Injection, IFN

Day 0

Day 9 - 14

Day 21-64

Day 64

Day 78

Day 92

PegIFN alfa2a SC weekly x 6 weeks starting with 1st DCV

Primary Outcome- Safety

Favorable Safety Observed

- No DLTs, no Grade 4 AEs
- 1 Grade 3 AE possibly related to DOC1021
- Common Grade 1 AEs: flu-like symptoms⁺ and injections site reaction[^]

Treatment-emergent > grade 1 possibly, probably or definitely related AEs			
	Grade 2	Grade 3	Grade 4
Cohort 1 - total	6	1	-
<i>Chills</i>	1	-	-
<i>Fatigue</i>	3		-
<i>Nausea</i>	1	-	-
<i>Neutropenia</i>	-	1	-
<i>Vestibular disorder</i>	1		
Cohort 2 - total	4	-	-
<i>Nausea</i>	1	-	-
<i>Lethargy</i>	1	-	-
<i>Confusion</i>	1	-	-
<i>Urticaria</i>	1	-	-
Cohort 3 - total	2	-	-
<i>Fatigue</i>	1	-	-
<i>Urticaria</i>	1		
Cohort 4 - total	2	-	-
<i>Headache</i>	1	-	-
<i>Nausea</i>	1		

⁺flu-like symptoms included chills, fatigue, headache, nausea

[^]injection site reaction included neck pain, pruritus and urticaria

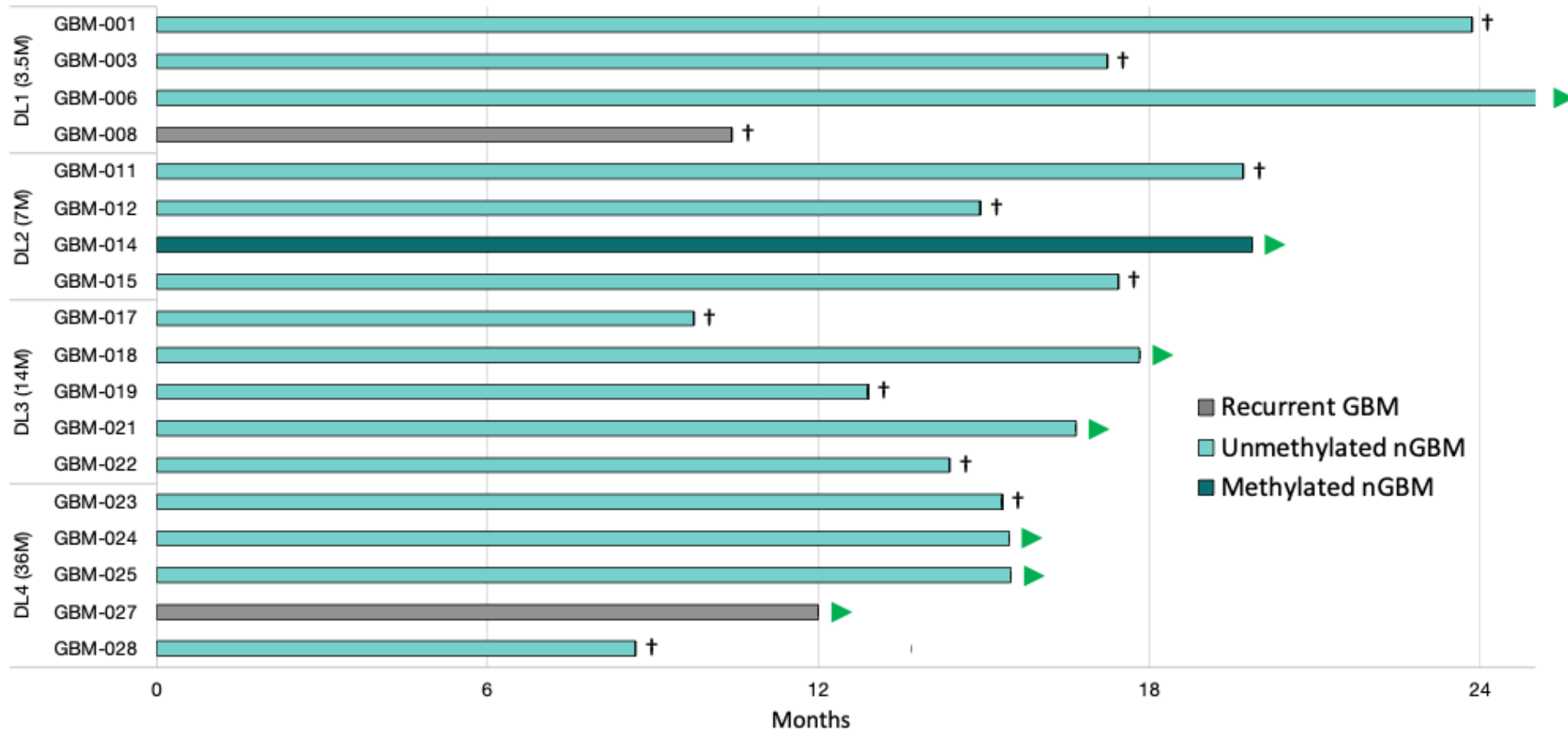
Phase 1 GBM Patient Status

16 nGBM (IDHwt) patients:

- **12-month survival:** 88% vs expected ~60% for SOC alone
- **Median OS:** estimated 19.7mo vs expected 12-14mo for SOC alone in this poor prognostic group

Prognostic factors:

- **MGMT unmethylated:** 94% vs expected 60%
- **Resection:** 33% subtotal
- **Progression prior to treatment:** allowed to continue



Data Cut-off Date October 24, 2024

† Deceased ► Alive

T cells Stimulated in Tumor and Peripheral Blood

- Histology of post-treatment resections **confirmed the presence of cytotoxic immune responses** in patient tumors.
- Flow cytometry analysis **showed increases in circulating CD8 and CD4 central memory and CD8 memory precursor effector cells**

Patient 11 CD8+ T cell Staining

Pre-Treatment Resection

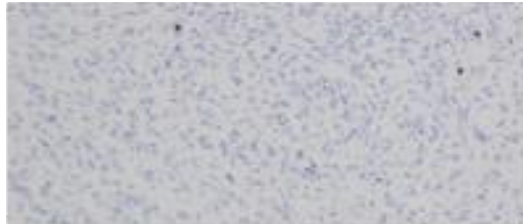


Post-Treatment Resection



Patient 12 CD8+ T cell Staining

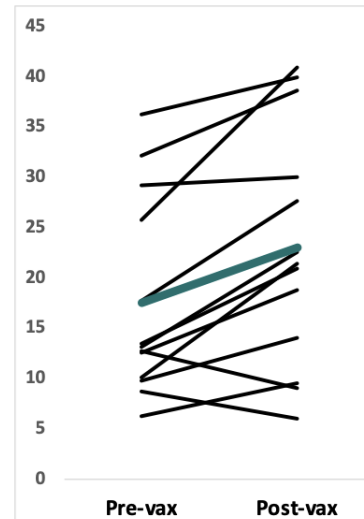
Pre-Treatment Resection



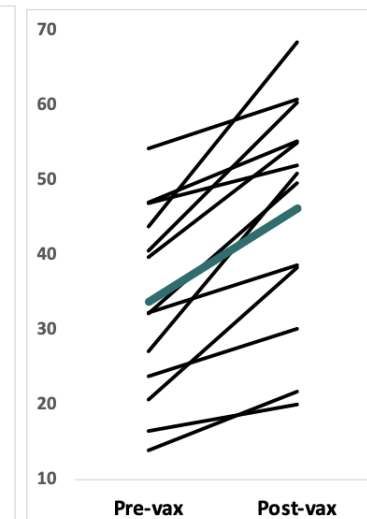
Post-Treatment Resection



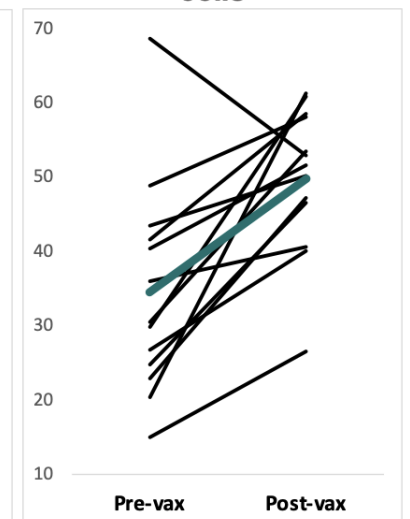
Frequency
Central Memory
CD8+ T cells



Frequency
Central Memory
CD4+ T cells

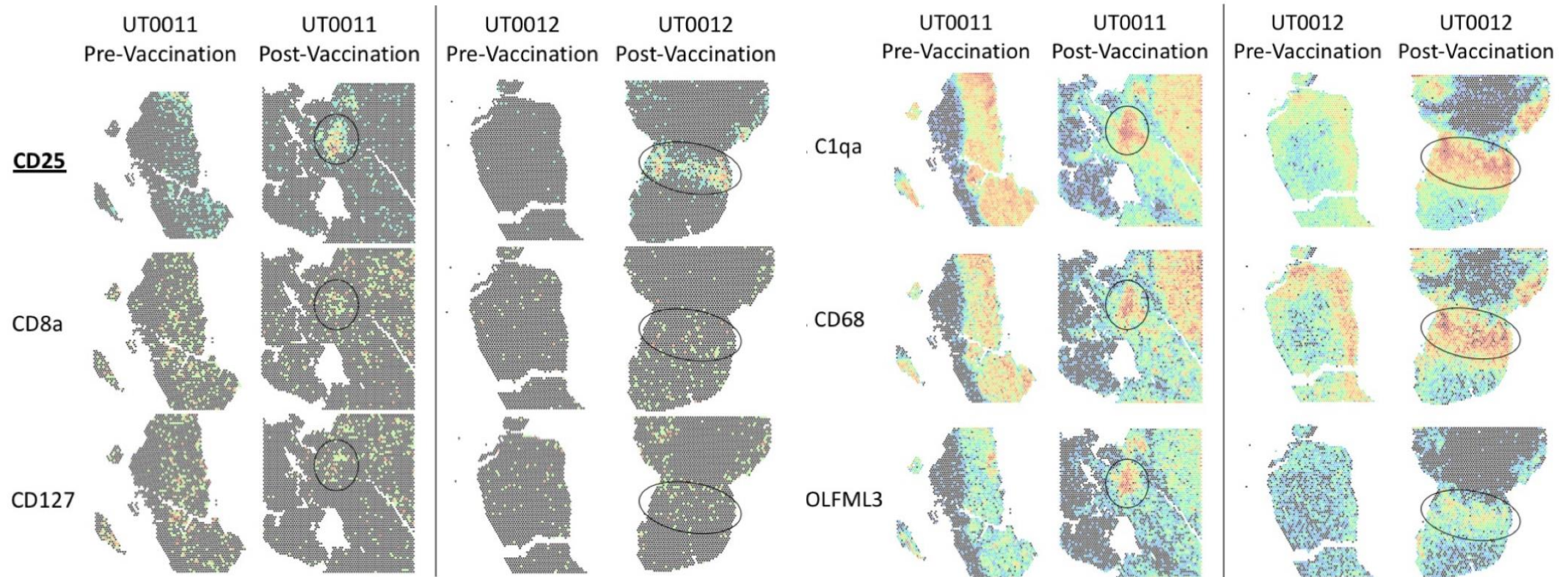


Frequency
CD127+
CD8+ MPEC T
cells



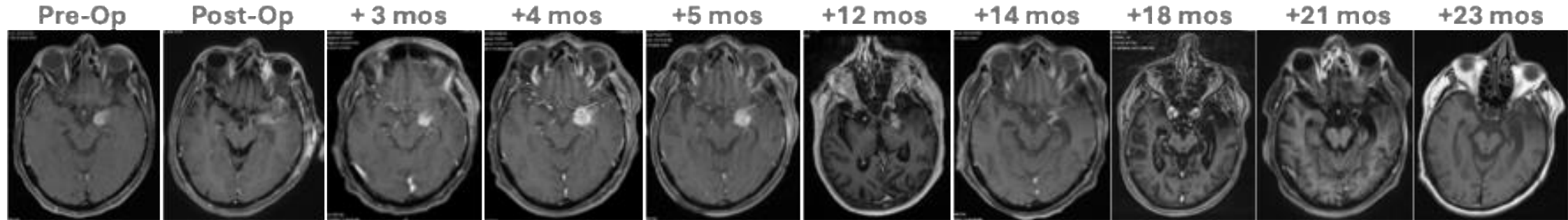
Spatial Transcriptomics Confirms Robust Cytotoxic Immune Activation Post-Vaccination

- CD25 foci are clusters of activated CD8 T cells and migratory microglial-like cells
- seen after but not before vaccination

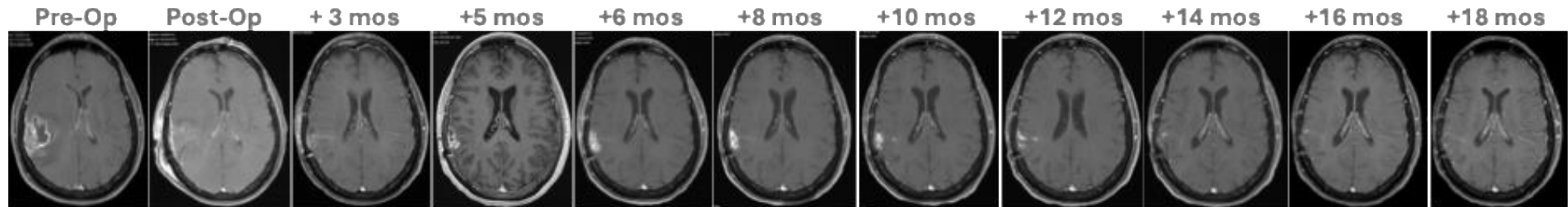


Imaging responses after presumed pseudo-progression

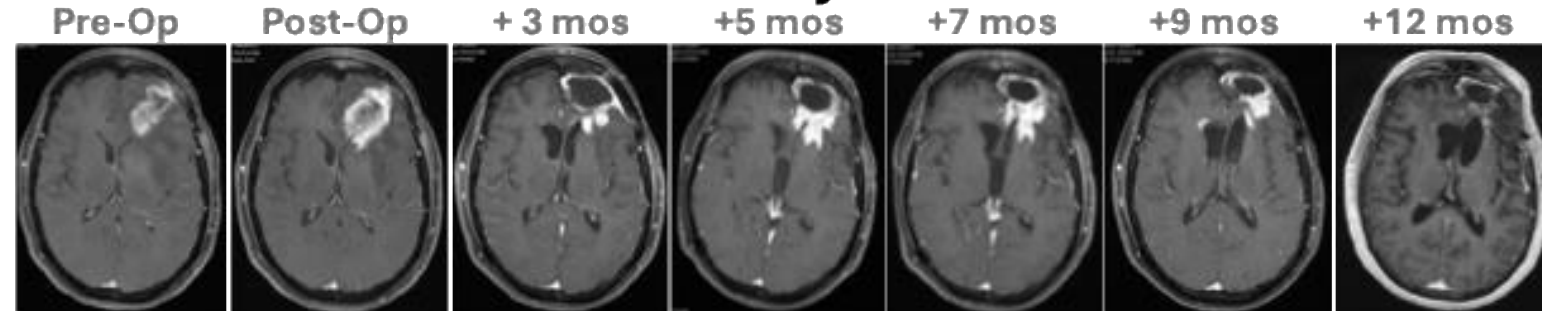
006 nGBM MGMT unmethylated



014 nGBM MGMT methylated



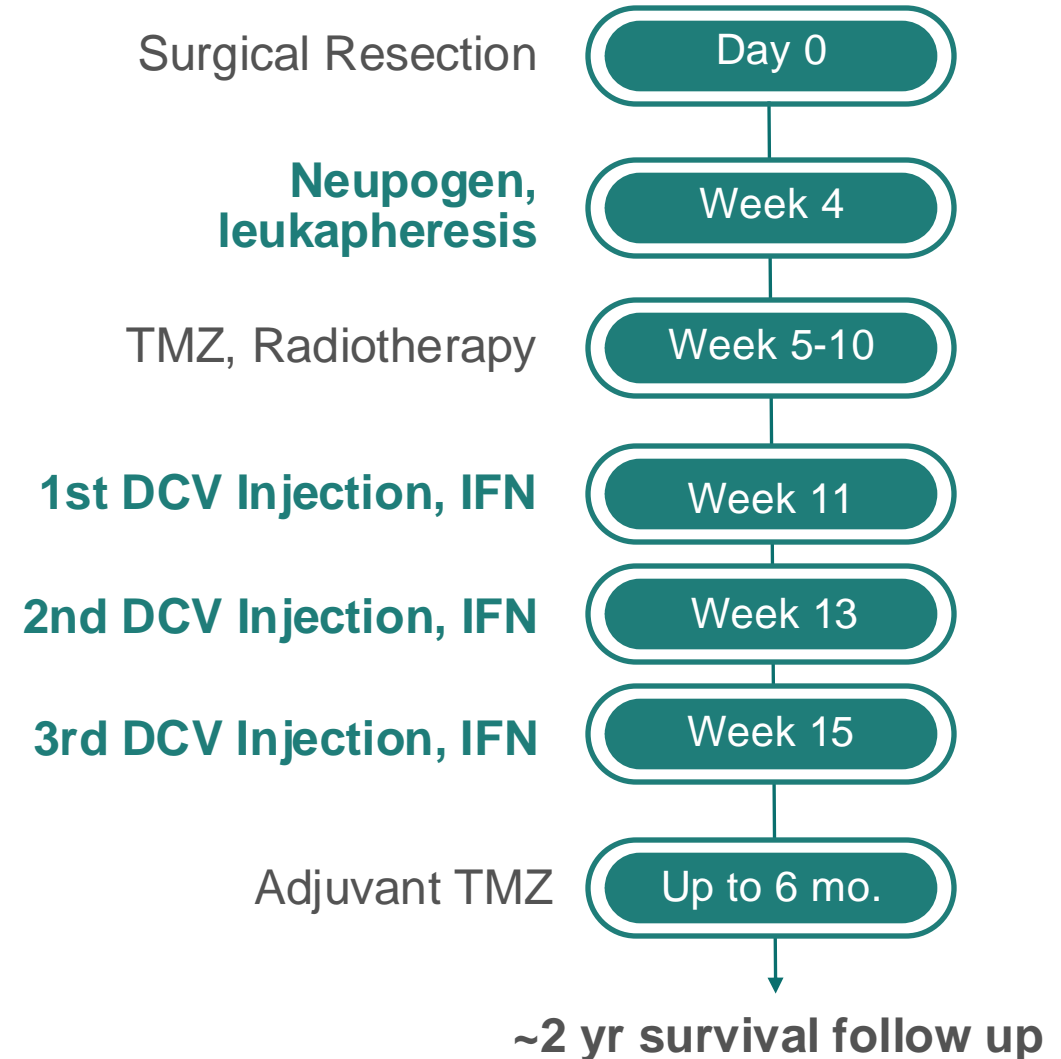
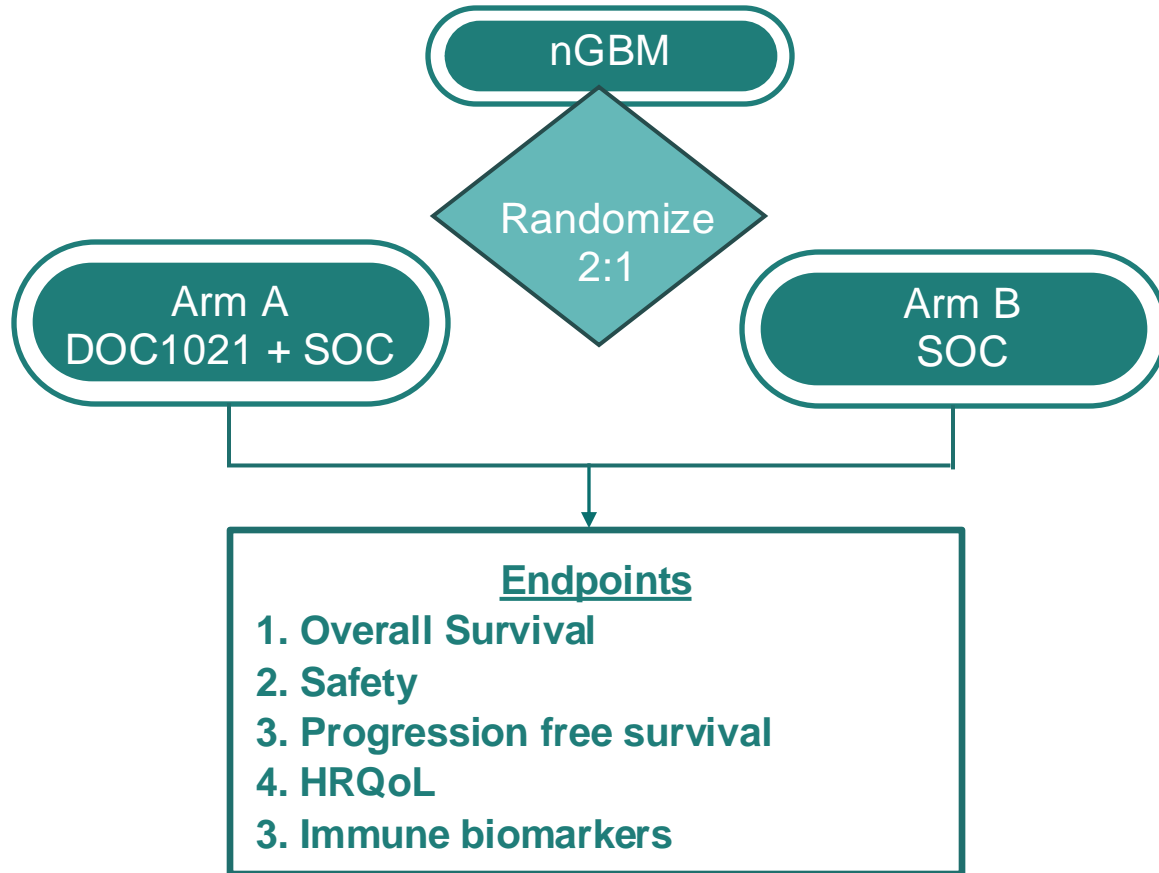
027 recurrent MGMT unmethylated



Conclusions

- Novel cell-based vaccination methodology for the adjuvant treatment of GBM.
- Treatment demonstrated to be **both safe, feasible** and easily integrated with standard of care.
- Evidence of ongoing in situ T-cell responses at the time of reoperation seen in 3 patients.
- Multiple complete resolutions on MRI including unmethylated, methylated and recurrent
- Current data support additional investigation, including initiation of a randomized Phase 2 trial.

GBM Phase 2 Randomized Trial Design



DCV dose 12M cells per course x 3 courses (36M total)
PegIFN alfa2a SC weekly x 6 weeks starting with 1st DCV
Current design is for 135 patients, 20 sites

Acknowledgements

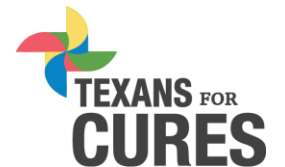


Decker Lab

Vanaja Konduri, PhD
Akshar Trivedi, MS, MS
Madhuri Namekar, MS, MS
Wei Lu, MD
Damilola Oyewole-Said, MS
Nalini Bisht, MS
Sharon Amany, MS
Briana Burns, BS
Jonathan Vasquez-Perez, BS
Giselle De La Torre Pinedo, BS
Zaniqua Bullock, BS
Keenan Ernst, BS
Yishen Shen, BS
Jon Levitt, PhD (memoriam)
Matthew Halpert, PhD (emeritus)
Vivian Liang, PhD (emeritus)
Arnav Murthy (Rice University)

Clinical Collaborators

Robert Arceci, MD, PhD (memoriam)
Alan Turtz, MD
Vinod Ravi, MD, MBA
Nitin Tandon, MD
Joseph Georges, MD
Eva Schumann, BS
Mia Vu, BS
Lindsey Coleman, MS
Lynne Koehler, MS
Ali Baaj, MD
Peter Nakaji, MD



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