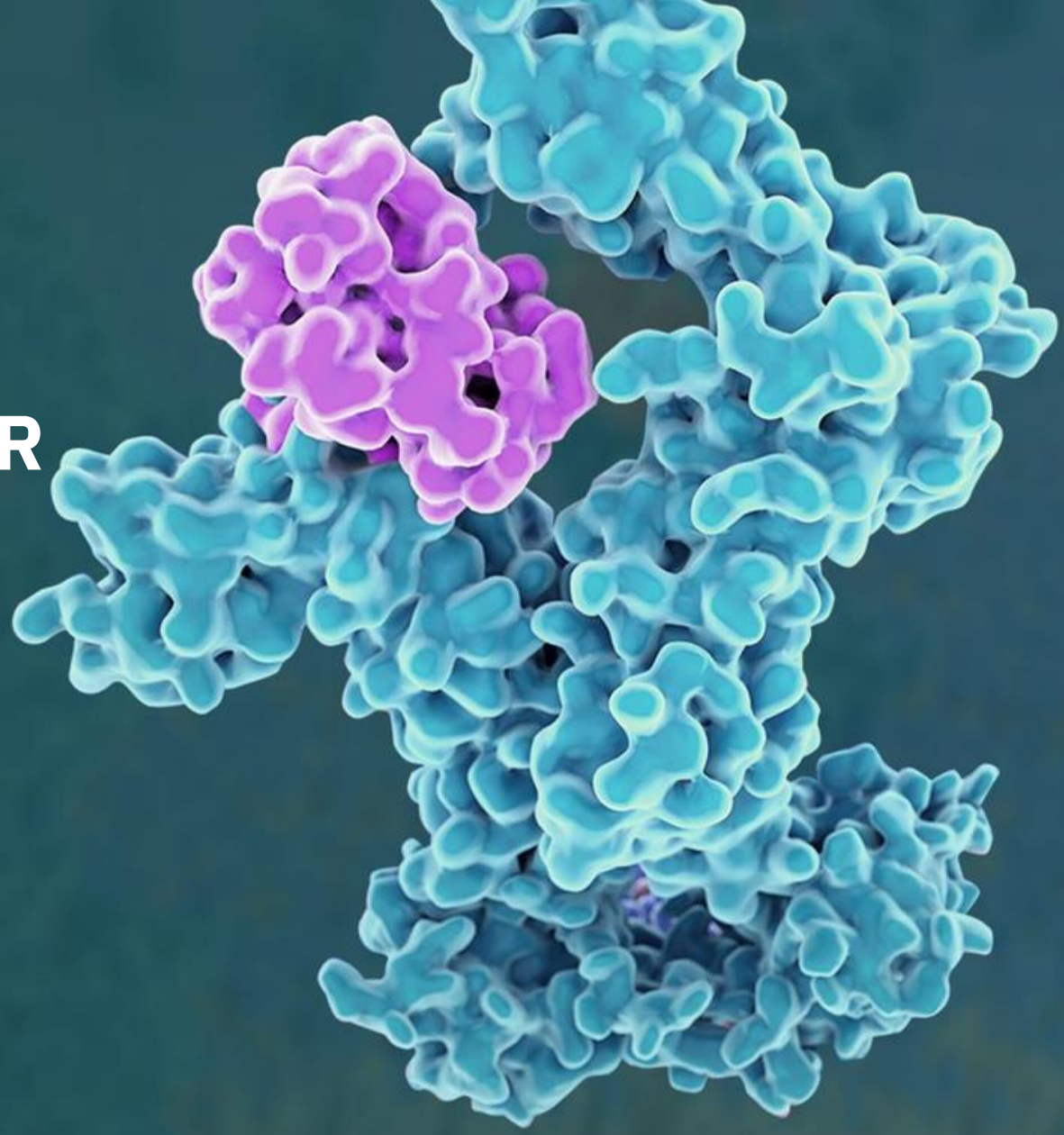
SNO 2024

Invigorating Effector Immune Cells With Highly Selective IL-2R Agonists and Potential Synergy With Tumor Targeting Therapeutics for Treatment of Glioblastomas



MEDICENNA

Authors and Affiliations

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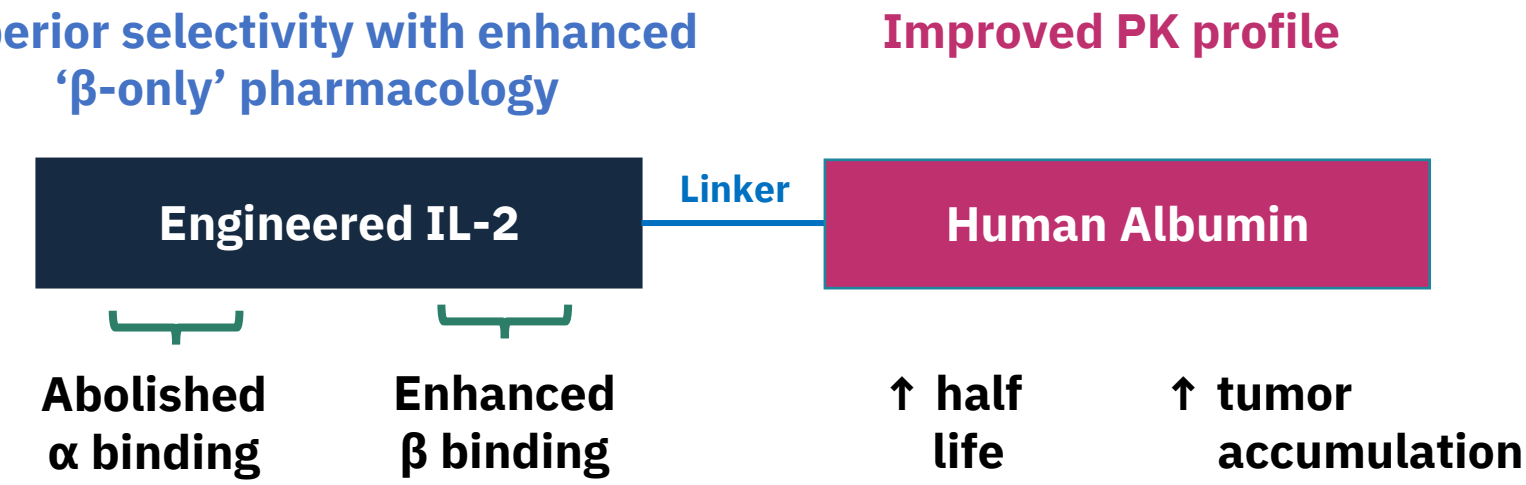
MDNA11: Long-acting ‘β-enhanced Not-α’ IL-2 Superkine



MDNA11 engineered to overcome key limitations of HD rhIL-2:

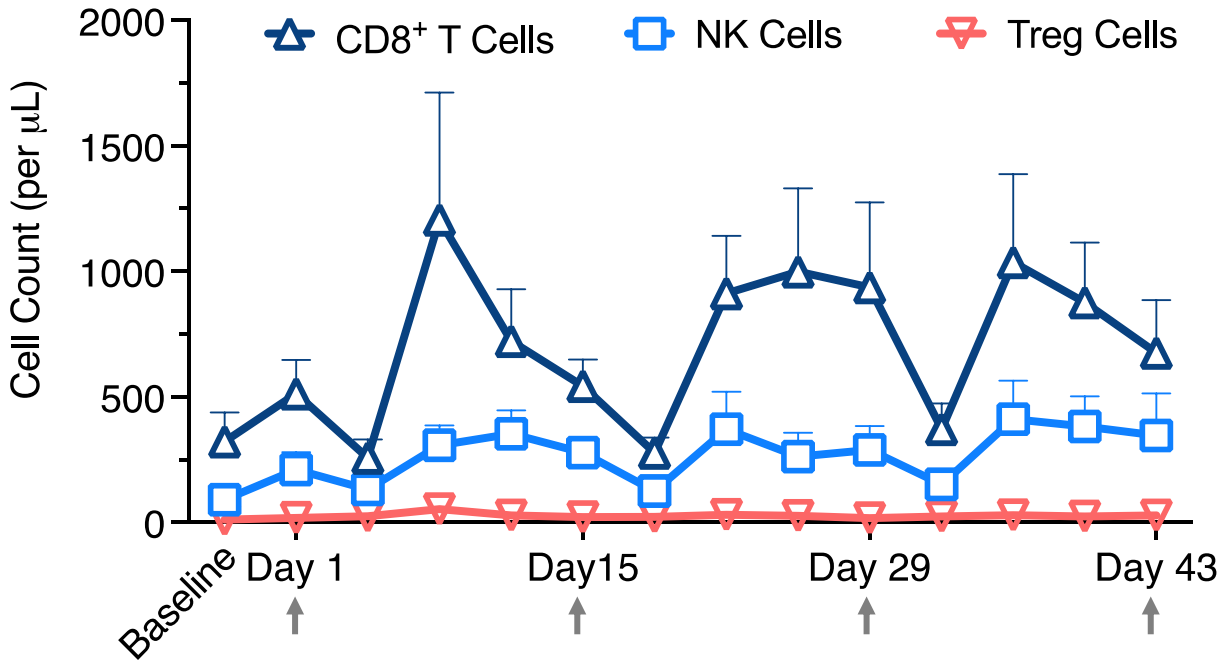
- ↑ affinity to IL-2Rβ (CD122) - Potentiate effector immune activation
- Abolish binding to IL-2Rα (CD25) – ↓Treg stimulation & associated toxicities
- Fusion to albumin increases half-life and promotes accumulation in tumors

➢ MDNA11 demonstrates a favorable safety profile and encouraging single-agent tumor response in patients with advanced solid tumors (ongoing Phase 1/2 ABILITY study)

MDNA11: Potent Immune Agonist

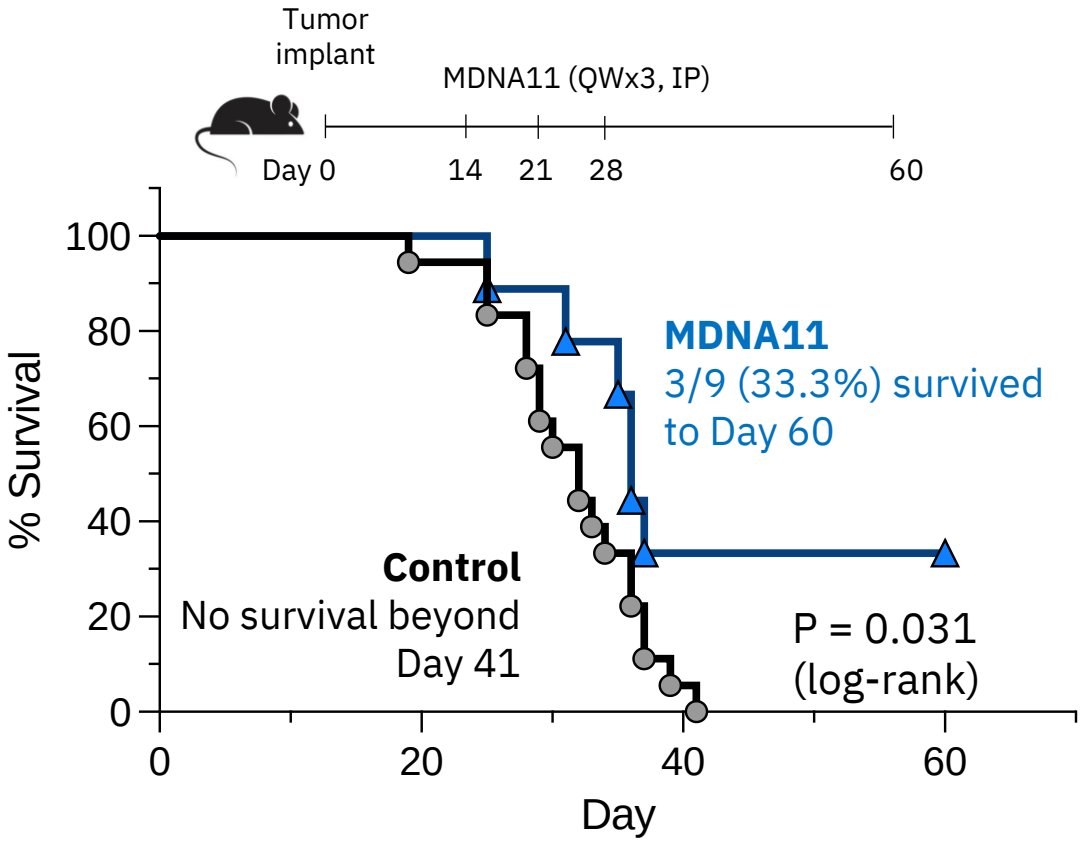
MDNA11 Preferentially Expands CD8⁺ T and NK Cells

MDNA11 at 90 µg/kg (IP Q2W; Recommended Dose for Expansion)



To et al., SITC (2024)

MDNA11 Significantly Extends Survival in an Orthotopic GL261 GBM Model

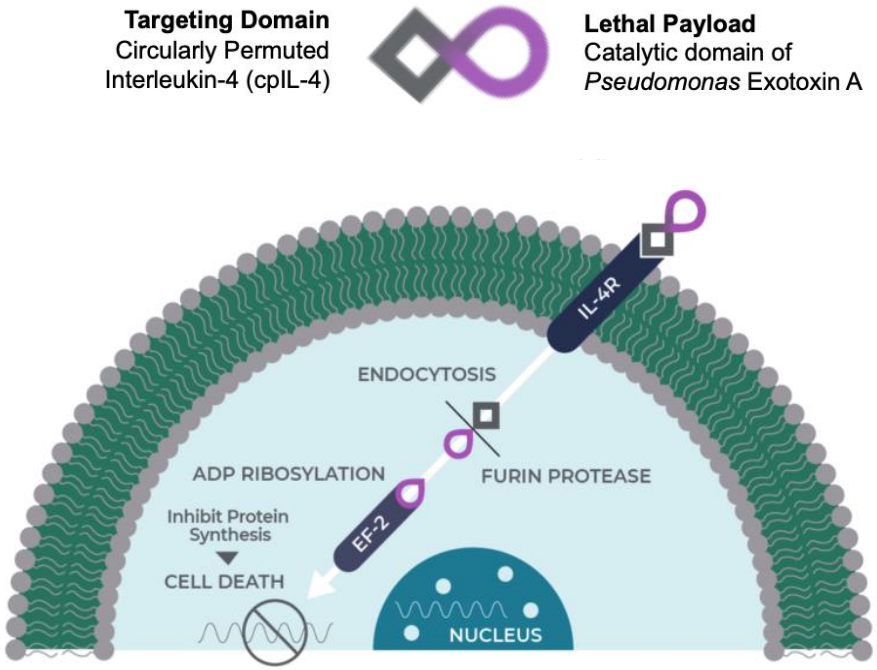


Liu et al., SITC (2024)

Bizaxofusp (aka MDNA55): A Potent IL-4R Targeted Toxin Payload

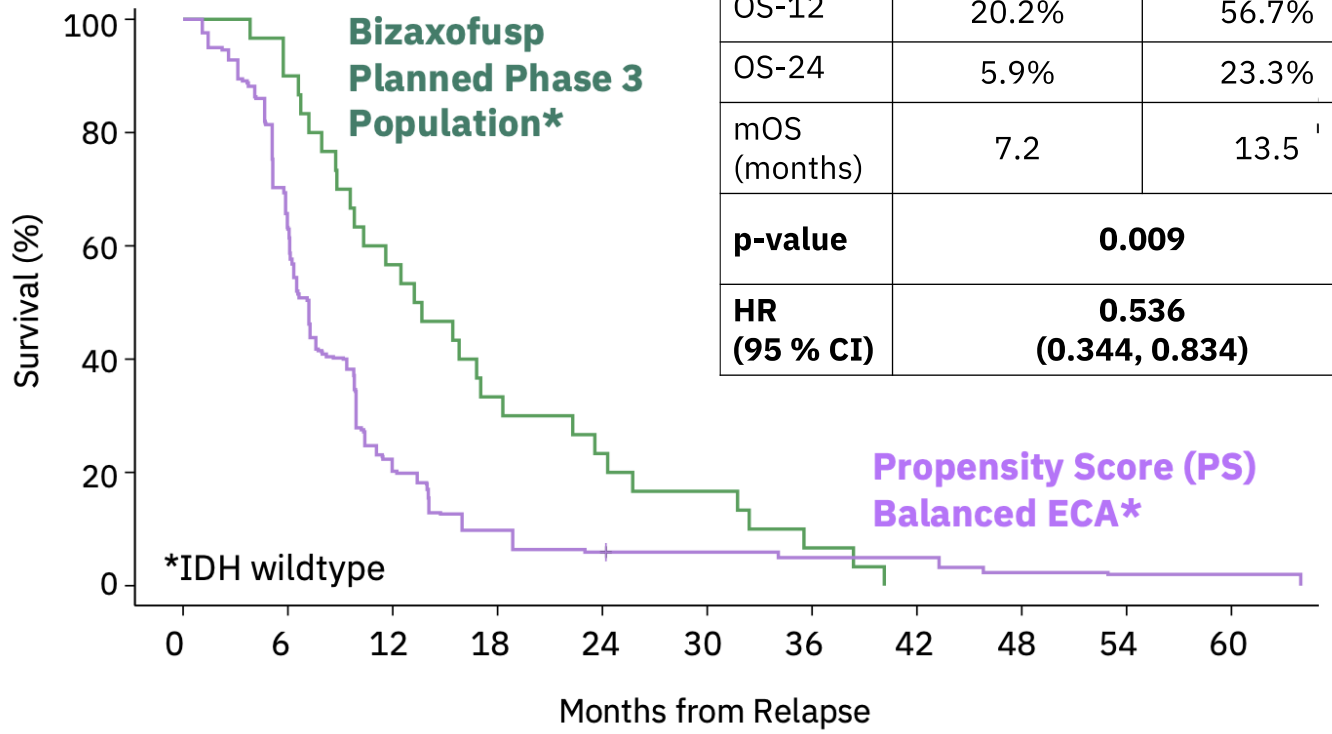
- Direct killing of IL-4R expressing tumor cells by inhibiting protein synthesis
- Kills IL-4R expressing myeloid cells to invigorate anti-tumor immunity within the TME

Mechanism of Action



Phase 2b Study: Unresectable Recurrent GBM (rGBM)

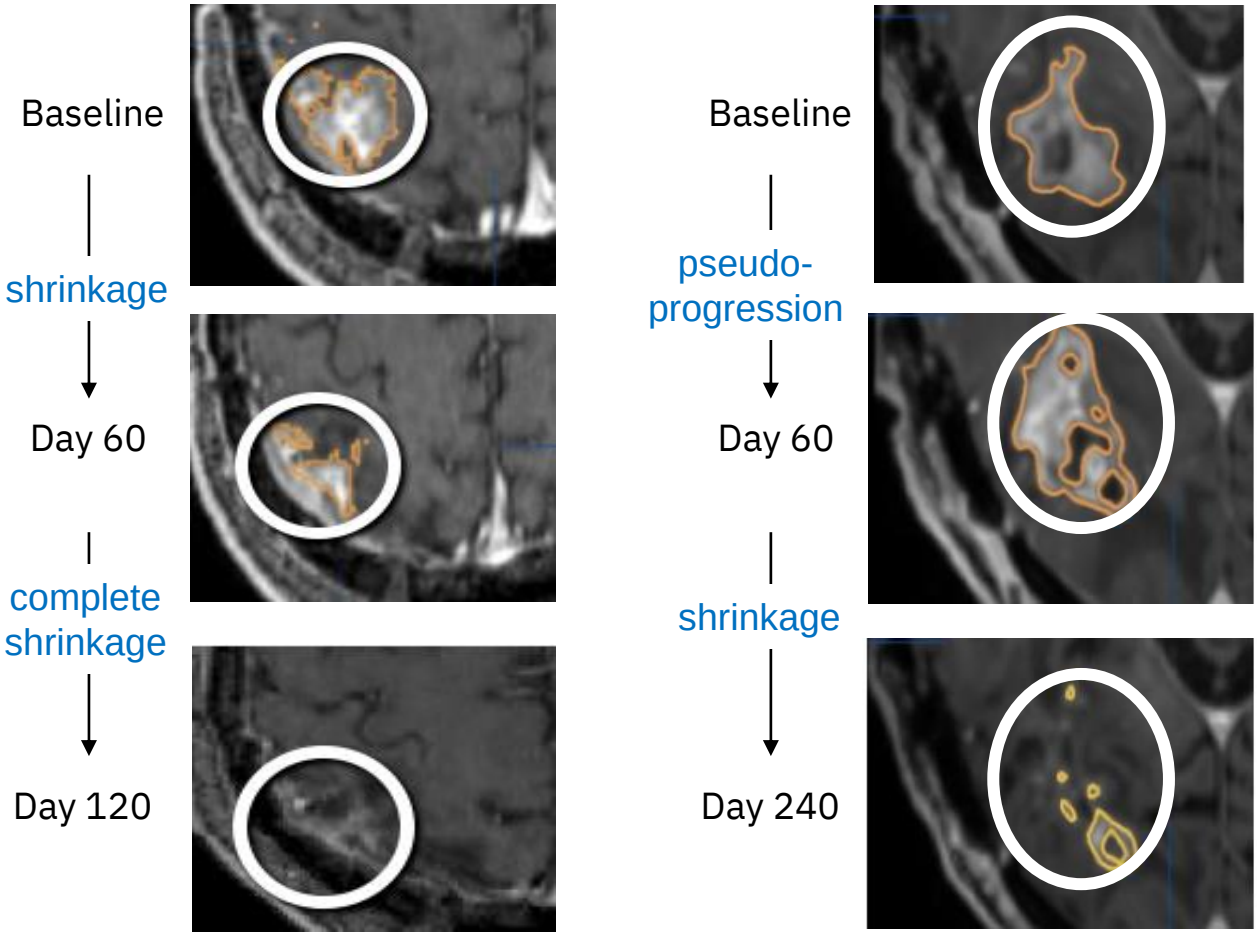
	PS Balanced ECA (N = 29.5)	Bizaxofusp (N = 30)
OS-12	20.2%	56.7%
OS-24	5.9%	23.3%
mOS (months)	7.2	13.5
p-value	**0.009**	
HR (95 % CI)	**0.536 (0.344, 0.834)**	



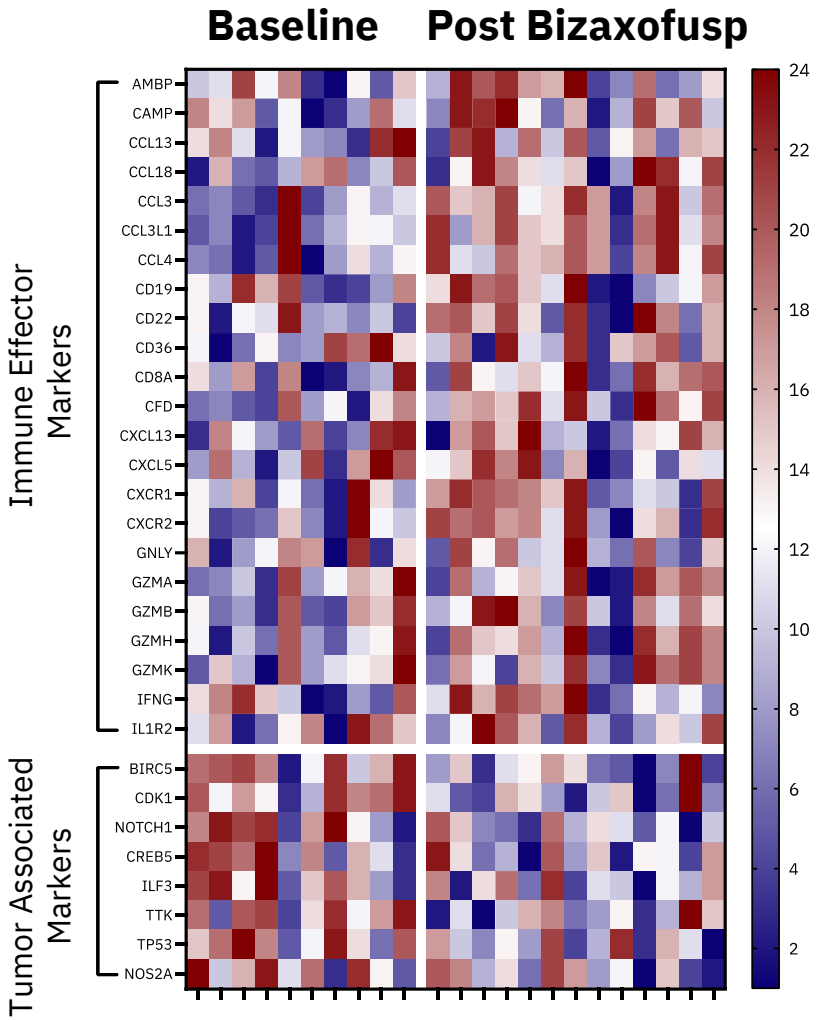
Sampson et al., ASCO 2024

Bizaxofusp Shrinks rGBMs and Stimulates Immune Effector Cells

rGBM Following Single Treatment with Bizaxofusp



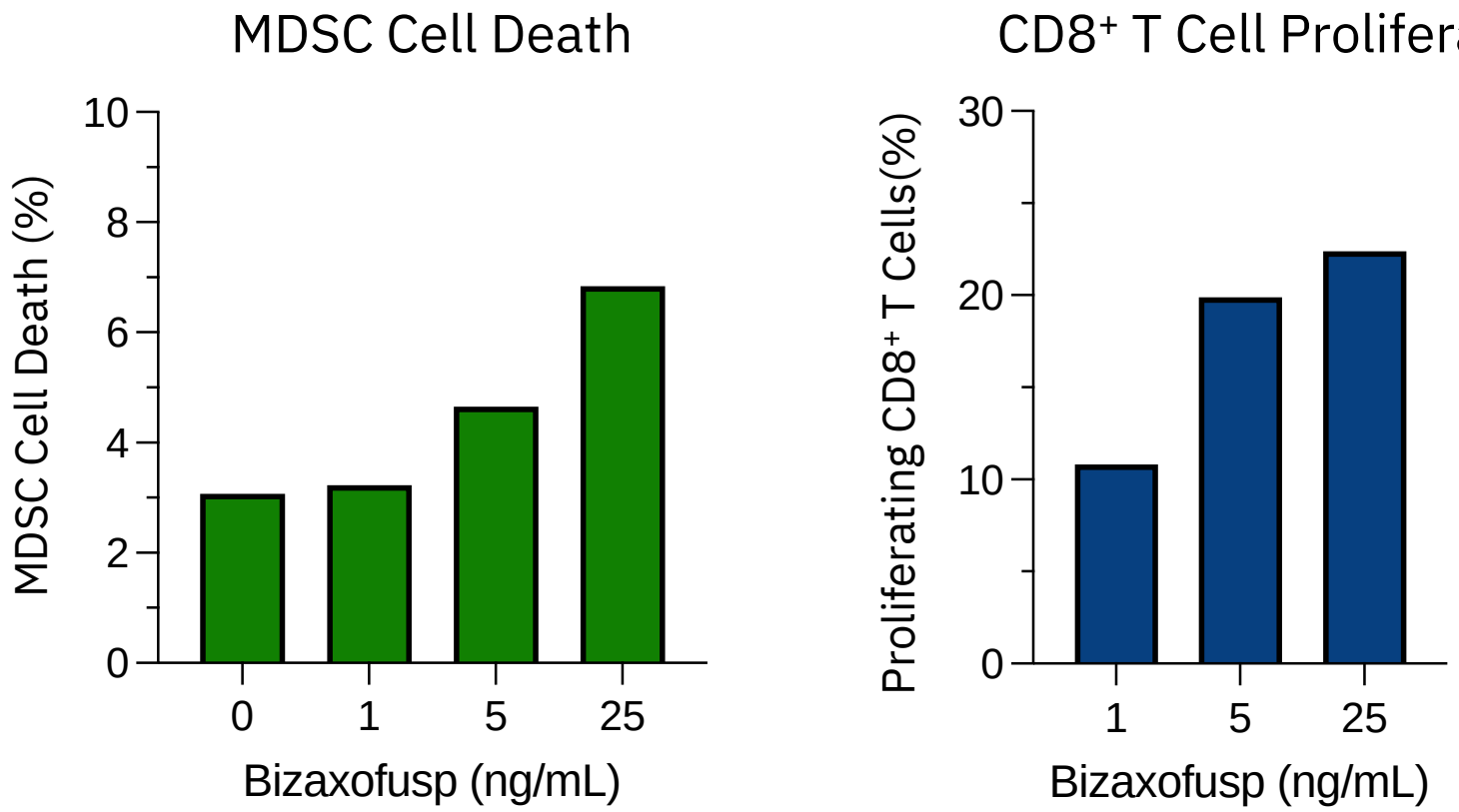
NanoString Gene Expression Analysis



- Baseline samples from initial diagnosis
- Post treatment rGBM collected ≥ 52 days after a single intra-tumoral dose of bizaxofusp

Bizaxofusp Kills MDSCs to Invigorate CD8⁺ T Cells

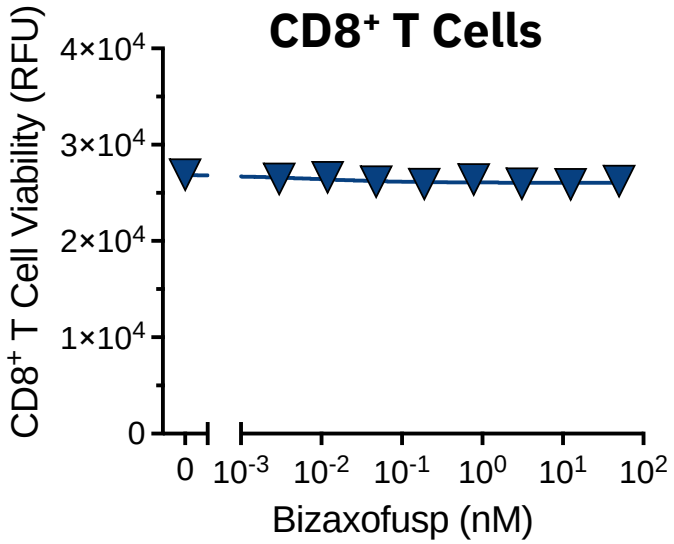
Autologous co-cultures of MDSC / CD8⁺ T cells treated with increasing concentrations of bizaxofusp

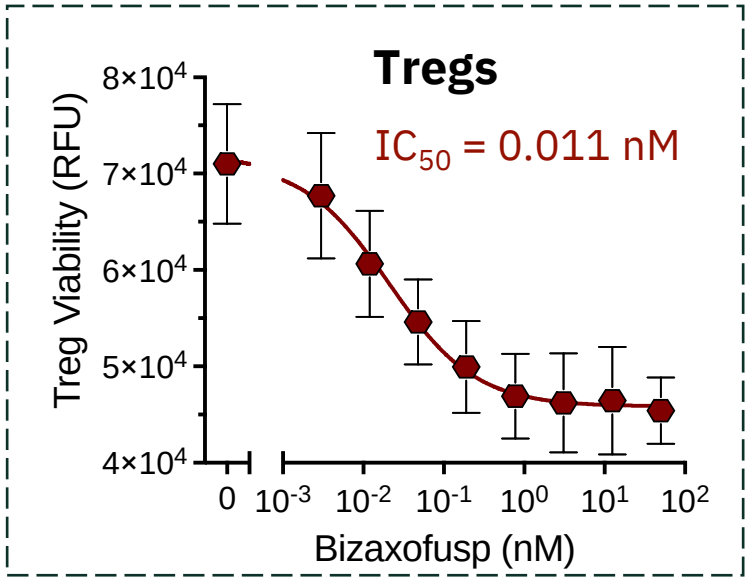


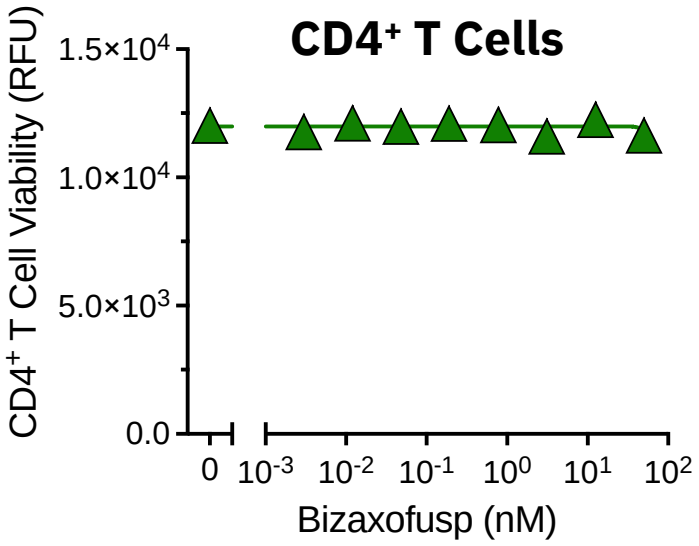
PBMC derived MDSC co-cultured with autologous CD8⁺ T cells in 1:2 ratio (Lechner et al., J Immunology, 2010).
Treatment for 3 days; cell viability (7AAD) and proliferation (Cell Trace Violet) evaluated cell cytometry.

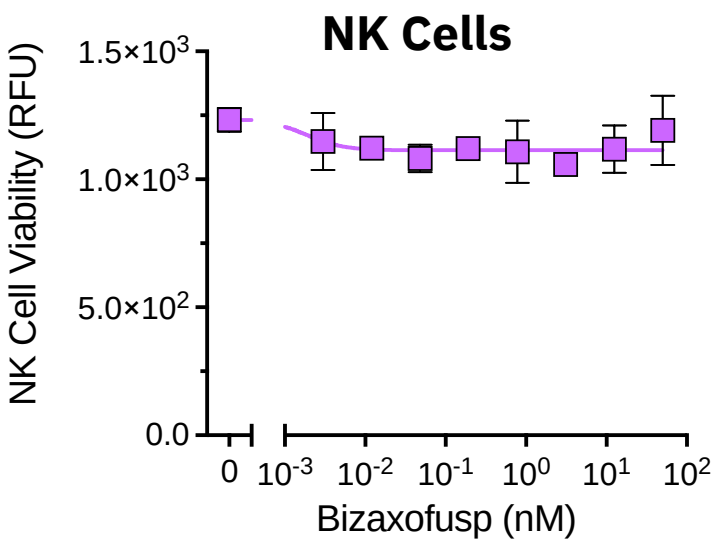
Bizaxofusp Selectively Kills Immune Suppressive Tregs

No impact on viability of key anti-tumor immune cells





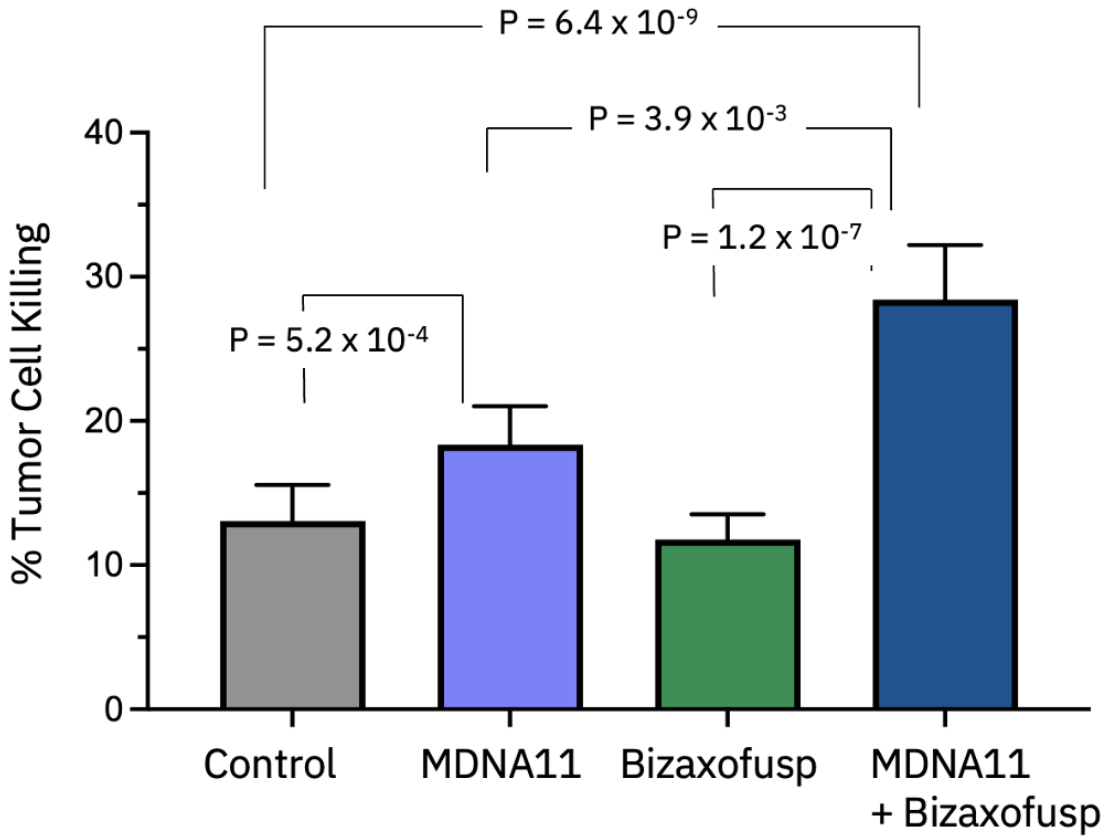


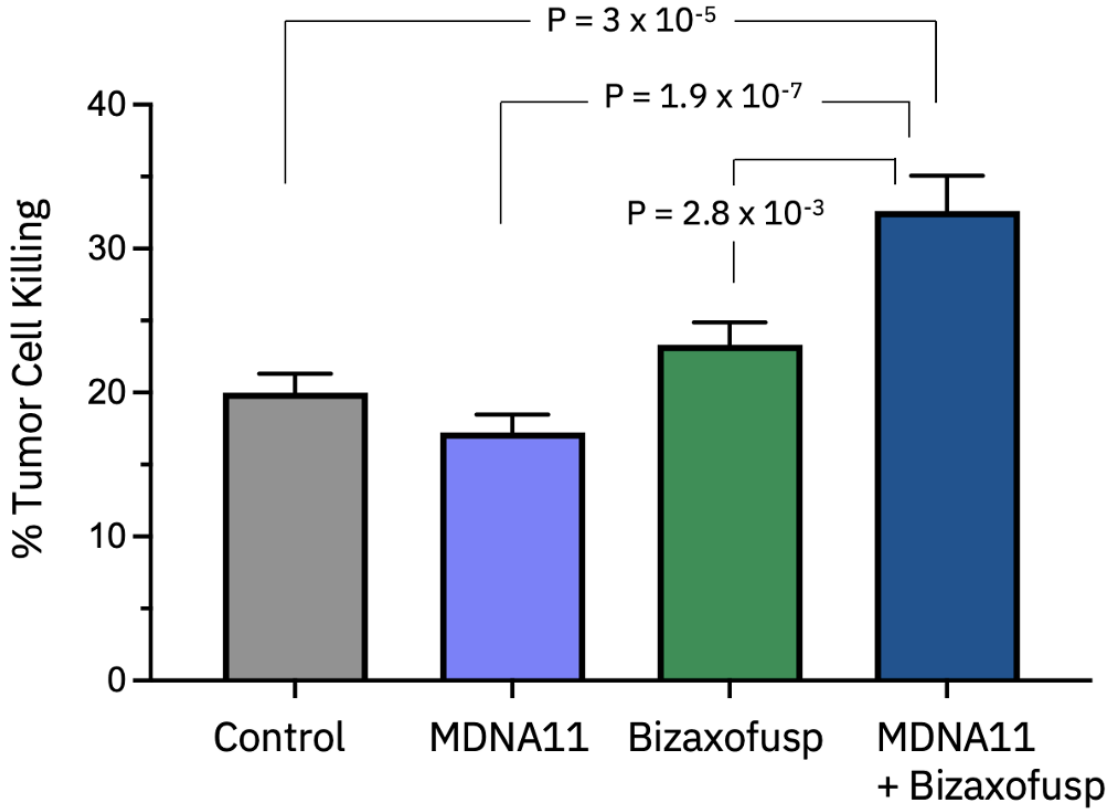


Treatment for 48 hours;
Cell viability measured by Cell TiterBlue

MDNA11 and Bizaxofusp Synergize to Enhance Tumor Cell Killing

GBM tumoroids maintain original architecture of tumor and resident immune cells.





>51 tumoroids per condition; treatment for 5 days.
Tumor cell killing measured by high resolution microscopy based on size and nuclear morphology.
P-values calculated using Mann-Whitney test

Summary

- MDNA11 showed significant survival benefit in an orthotopic model of GBM
- Single intra-tumoral treatment with bizaxofusp induced tumor shrinkage and stimulated immune effector response within the TME of rGBM patients
- Bizaxofusp kills immune suppressive MDSC and Tregs to invigorate immune effector cells (i.e., $CD8^+$ T cell proliferation)
- MDNA11 and bizaxofusp synergize to elicit tumor cell killing in patient derived GBM tumoroids
- Results underscore the promise of IL-2R stimulation together with IL-4R targeted toxin payload for treating immunologically ‘cold’ GBM.

Acknowledgments

Support from the Cancer Prevention and Research Institute of Texas (CPRIT)

Our deepest gratitude to the patients and their families