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

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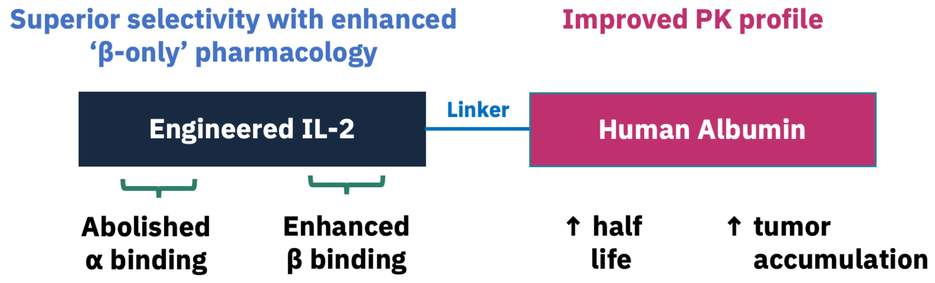
IMMU-62

MDNA11: A Long-acting 'β-enhanced Not-α' IL-2 Superkine

MDNA11 Engineered to Overcome Limitations of High Dose 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



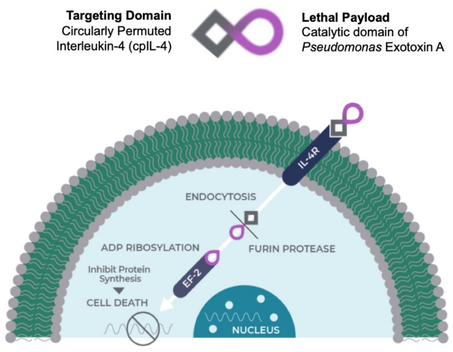
➤ MDNA11 demonstrates a **favorable safety profile** and encouraging **single-agent activity** in patients with advanced solid tumors (ongoing Phase 1/2 ABILITY study)

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

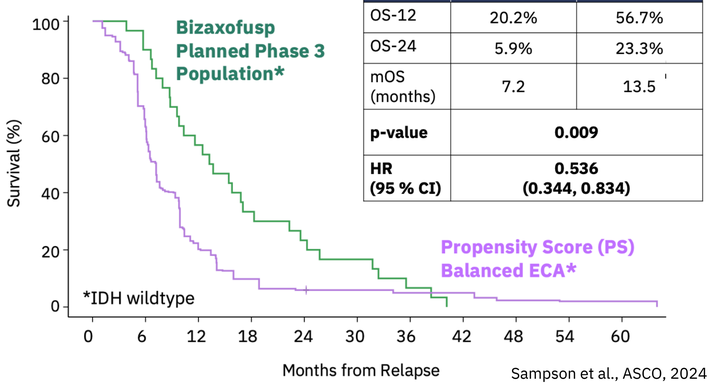
➤ Direct killing of IL-4R expressing tumor cells by inhibiting protein synthesis

➤ Kills IL-4R expressing myeloid cells to invigorate anti-tumor immunity within the TME

Mechanism of Action



Phase 2b Study: Unresectable Recurrent GBM

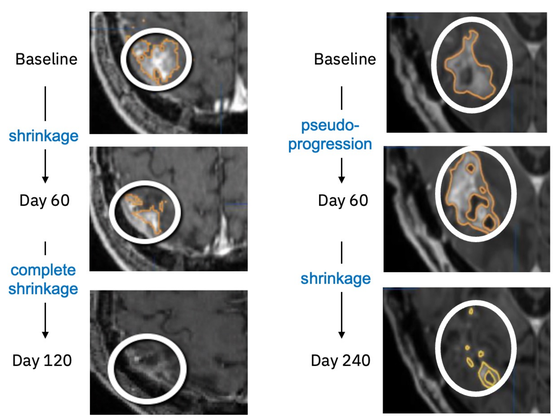


	PS Balanced ECA (N = 29.5)	Bizaxofusp (N = 30)
OS-12	20.2%	56.7%
OS-24	5.9%	23.3%
mOS (months)	7.2	13.5
p-value	**0.009**	
HR (95 % CI)	**0.536 (0.344, 0.834)**	

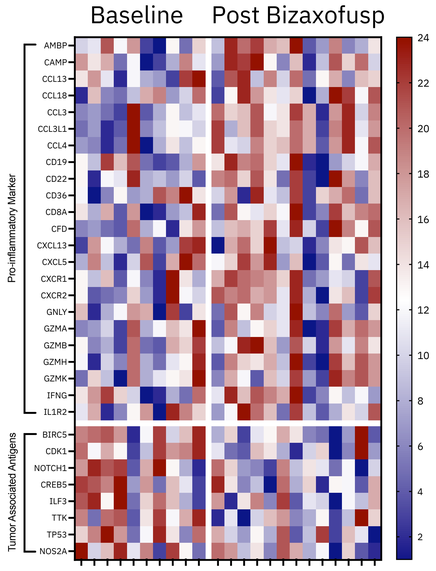
Sampson et al., ASCO, 2024

Bizaxofusp Shrinks rGBMs and Stimulates Immune Effector Cells

Tumor Response Following Single Treatment with Bizaxofusp



NanoString Gene Expression Analysis (PanCancer Immune-Profiling Panel)



NanoString:

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

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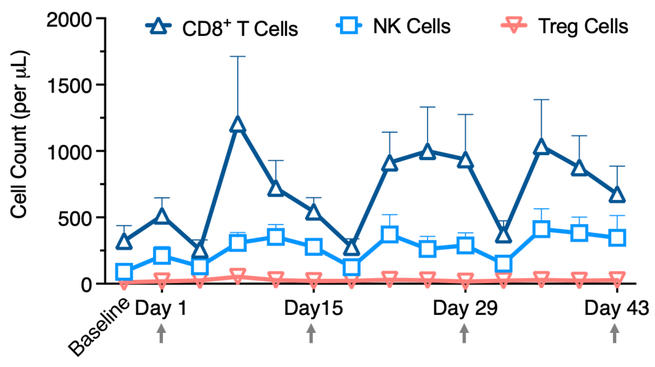
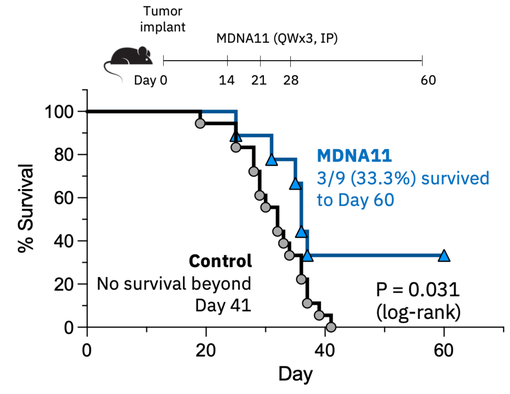
MDNA11: A Potent Immune Agonist

MDNA11 Preferentially Expands CD8⁺ T and NK Cells



MDNA11 at 90 µg/kg (IP Q2W; Recommended Dose for Expansion)
To et al., SITC (2024)

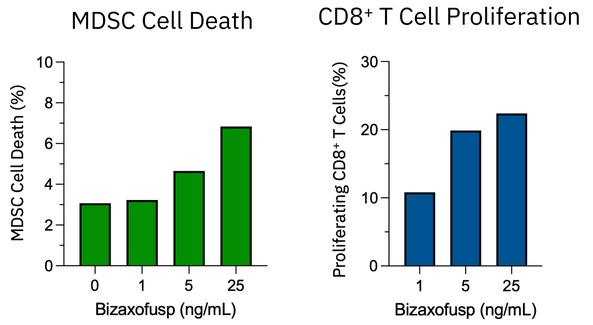
MDNA11 Significantly Extends Survival in an Orthotopic GL261 GBM Model



Liu et al., SITC (2024)

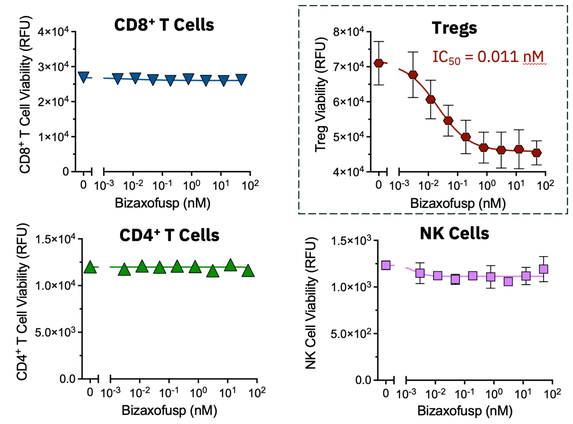
Bizaxofusp Eliminates Immune Suppressive Cells

MDSC Death Invigorates CD8⁺ T Cells in Autologous Co-cultures



PBMC derived MDSC co-cultured with autologous CD8⁺ T cells for 72 hours.
Cell viability (7AAD) and proliferation (Cell Trace Violet) evaluated cell cytometry.

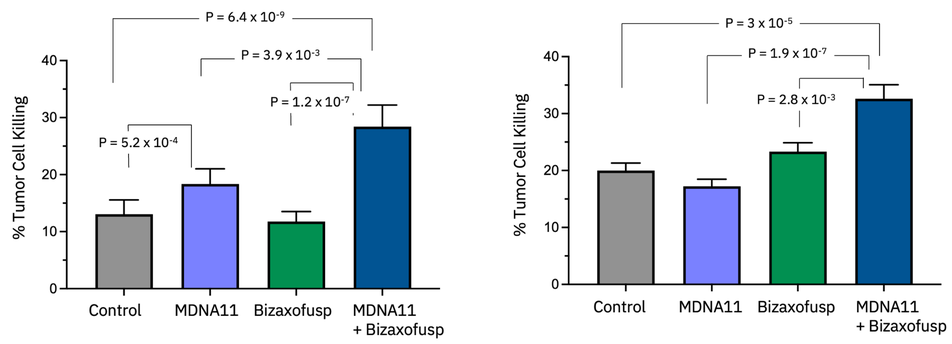
Selective Killing of Tregs



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

➤ These results underscore the promise of IL-2R stimulation together with IL-4R targeted toxin payload for treating immunologically 'cold' GBM