Complete response in first-in-human immunotherapy targeting lymphopenia in recurrent Glioblastoma Multiform (GBM): NAI and PD-L1 t-haNK plus bevacizumab

Simon Khagi[1], Jose Carrillo[2], David Park[3], Leylah Drusbosky[4], Paul Bhar[4], Hui Zhang[4], Lennie Sender[4], Sandeep Reddy[4], Santosh Kesari[2], Patrick Soon-Shiong[4]
[1]Hoag Cancer Center, Newport Beach, USA, [2]Providence Medical Foundation, Fullerton, CA, [3]Department of Neurosurgery, Stanford University, Palo Alto, CA, [4]ImmunityBio, Inc., San Diego, CA

BACKGROUND

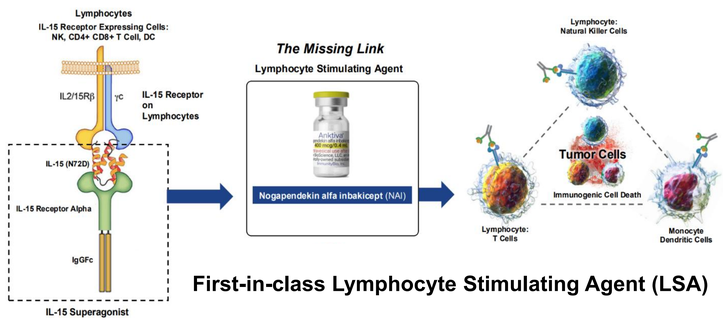
- Treatment options for recurrent GBM are limited and associated with high mortality.
- We hypothesize that the **current standard of care treatment for GBM induces severe lymphopenia** and, by treating lymphopenia, overall survival (OS) can be prolonged.
- **Prior to the approval of Nogapendekin alfa inbakicept (NAI),** an IL-15 receptor superagonist which stimulates lymphocytes important in immunogenic cell death (natural killer cells, CD4+ CD8+ T cells and memory T cells)[1], **no treatment existed to address lymphopenia** as measured by the absolute lymphocyte count (ALC) in the CBC differential. Given the MOA, **NAI represents a novel agent with the ability to either prevent of reverse lymphopenia**.[1]
- Confirmation of causation that **reversing the immune deficit represented by low ALC** induced by chemotherapy, radiation, and checkpoint inhibitors may prolong survival across tumor types.[2,3]
- NAI administered in combination with PD-L1 targeted high-affinity CAR-NK cells (PD-L1 t-haNK) and bevacizumab was hypothesized to elicit tumor response in patients with recurrent GBM through activation of NK and T cells.
- ResQ378 is a randomized Phase III trial in recurrent GBM to be initiated.

METHODS

- QUILT-3.078 (NCT06061809): 14 participants received NAI, PD-L1 t-haNK, and bevacizumab, every two weeks, as outpatients.[4]
- 5 participants also received concurrent tumor treating fields (TTF).
- Mean ALC levels over time were measured through data cutoff (Oct 20, 2025).

RESULTS

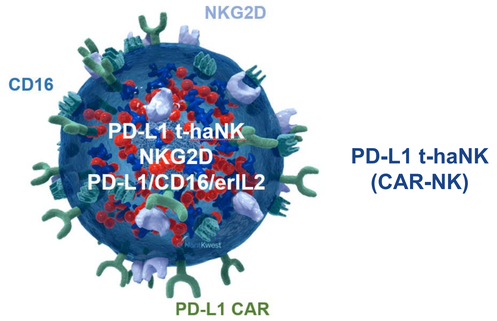
Figure 1: Nogapendekin alfa inbakicept (NAI) Structure & MOA



First-in-class Lymphocyte Stimulating Agent (LSA)

Package Insert: Binding of nogapendekin alfa inbakicept-pmln to its receptor results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immuno-suppressive Treg cells.[1]

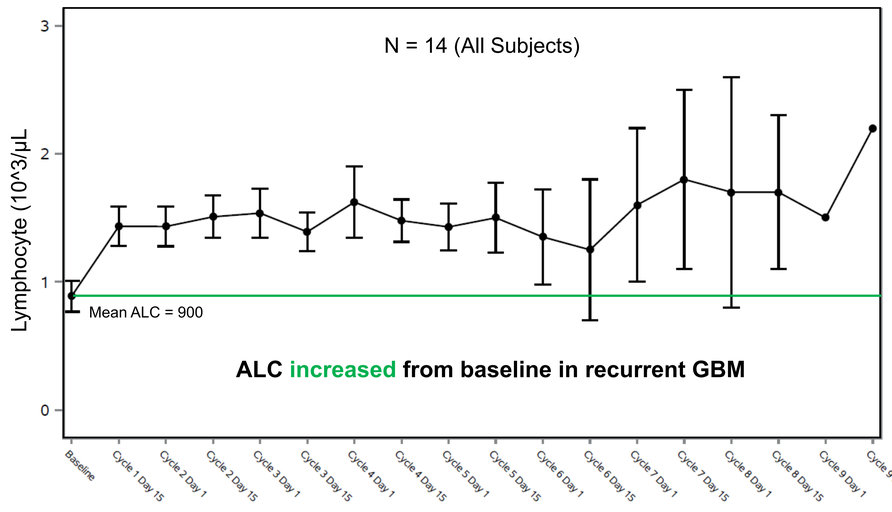
Figure 2: PD-L1 targeted high-affinity CAR-NK



PD-L1 t-haNK (CAR-NK)

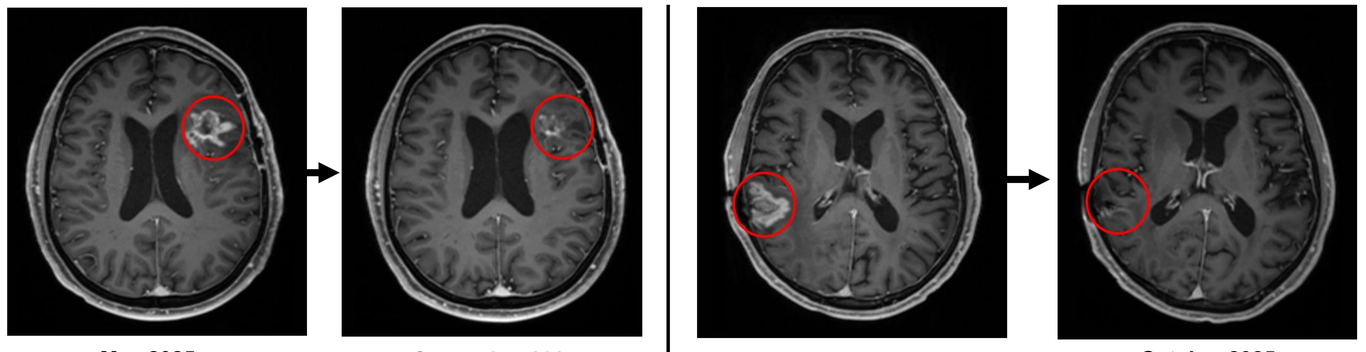
CAR NK cell therapy (PD-L1 t-haNK) is a human, allogeneic, natural killer (NK) cell line that has been shown to induce direct anti-tumor effects.[5]

Figure 3: Mean Absolute Lymphocyte Count (ALC) Over Time by Median Baseline ALC (0.9x10^3/uL)



- 14 participants received 122 total doses of combination immunotherapy, **with 8/14 (57.1%) remaining on therapy**. **Median OS is not reached**
- In 14 evaluable participants, **ALC count increased and maintained** from baseline ALC (900 ALC) through cycle 9.
- Median follow-up time is 141 days (20 weeks, 4.6 months) with 3 deaths on-study (**median OS is not reached**).
- 2 participants had SAEs related to the experimental therapy. No CRS or ICANS was observed.

Figure 4: Imaging Studies and ALC Trends in Select Participants with Recurrent GBM with a Complete Response



May 2025
ALC: 1,100 cells/μL

September 2025
ALC: 1,400 cells/μL ↑

March 2025
ALC: 500 cells/μL

October 2025
ALC: 1,100 cells/μL ↑

CONCLUSIONS

- These findings provide support that **treating lymphopenia and reconstituting lymphocytes** (NK & T cells) results in positive response including CR in recurrent GBM.
- This is the first report of disease response in participants with recurrent GBM who received **orchestrated systemic immunotherapy** with CAR-NK cells combined with an IL-15 superagonist and bevacizumab.
- The potential of reversing lymphopenia induced by SOC treatment, and prolonging survival, and improving prognosis across tumor types, may be a **paradigm change in cancer care**.

REFERENCES

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