INB-200: Phase I Study and Characterization of Gene-Modified Autologous Gamma-Delta (γδ) T Cells in Glioblastoma Multiforme (GBM) Patients Receiving Maintenance Temozolomide (TMZ)

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Abstract #: CTIM-17

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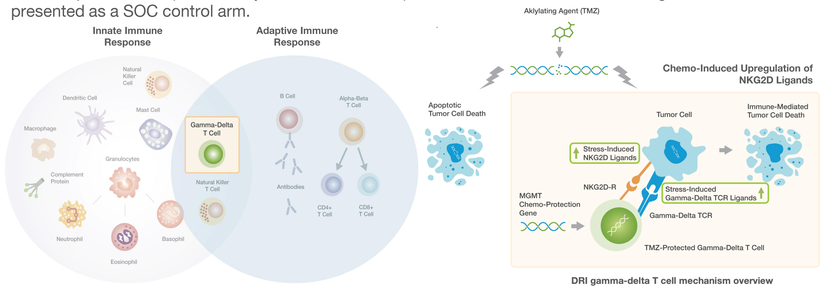
Background

Glioblastoma (GBM) is an aggressive brain tumor that has a high unmet need, an upfront treatment regimen that has remained unchanged for 20 years, and a one-year overall survival (OS) of only 53.7%[1] (mPFS 6.9m, mOS 14.6m)[2]. Gamma-delta (γδ) T cells are innate immune cells that directly recognize and kill malignant tissue through the recognition of Natural Killer Group 2D Ligands (NKG2D-L) that are highly expressed on cancer cells. Alkylating chemotherapies such as Temozolomide (TMZ) are lymphodepleting but can also force significant upregulation of NKG2D-L expression on tumor cells and tumor stem-cells. This makes them susceptible to γδ T cell mediated killing, including TMZ-resistant methylguanine-DNA methyltransferase (MGMT) unmethylated GBM cells. IN8bio's DeltEx Drug Resistant Immunotherapy (DeltEx DRI), genetically modifies γδ T cells with a MGMT expressing lentivector, rendering them TMZ resistant and permitting concomitant administration of TMZ + DeltEx DRI. This allows for greater elimination of residual GBM cells, including TMZ-resistant cells combined with standard-of-care (SOC). Here we present consolidated data from patients enrolled in the INB-200 Phase 1 IIT study and INB-400, a company sponsored Phase 2 study. Data from subjects contemporaneously enrolled and who provided consent, but not receiving DeltEx DRI cells are presented as a SOC control arm.



DRI gamma-delta T cell mechanism overview

Sources: [1]Ostrom, et al Neuro-Onc 2023; [2]Stupp,et al NEJM 2005; Hottinger, et al Neuro-Oncology 2016, * adapted with permission from Dranoff et al. Nature Rev. Can., Jan. 2004, fig 1., IN8bio, image created with biorender.com

INB-200 & 400: Study Design and Treatment Schema

Treatment Arms

Fixed dose level (Cohort) of DRI in a 3+3 design:

1. N = 3 (up to 6) patients, single dose of 1 x 10^7 cells (Cohort 1)
2. N = 3 (up to 6) patients, three doses of 1 x 10^7 cells, one dose every 28 days (Cohort 2)
3. N = 3 (up to 6) patients, six doses of 1 x 10^7 cells, one dose every 28 days (Cohort 3)*

Treatment Regimen & Timing

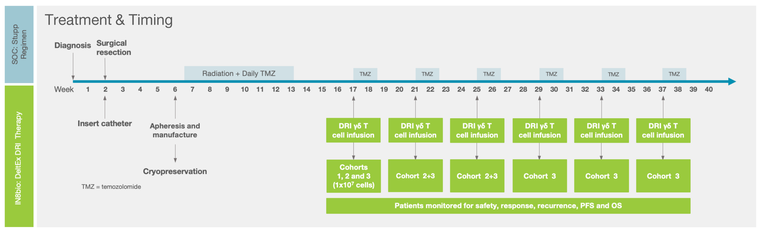
Surgical resection followed by apheresis → 6 weeks induction TMZ + radiation → 6 cycles maintenance TMZ + DRI*

Primary Endpoints

- Safety
- Maximum tolerated dose (MTD) of DRI in two dose frequencies

Secondary Endpoints

- Time to progression
- Overall survival
- Biologic response



Newly diagnosed GBM patients are enrolled and treated with DeltEx DRI in combination with the SOC Stupp regimen. A Rickham catheter is placed during surgical resection, the DeltEx DRI product is manufactured and patients received 1 (Cohort 1), 3 (Cohort 2), or up to 6 doses (Cohort 3) of DeltEx DRI, delivered intrathecally during maintenance TMZ cycles.

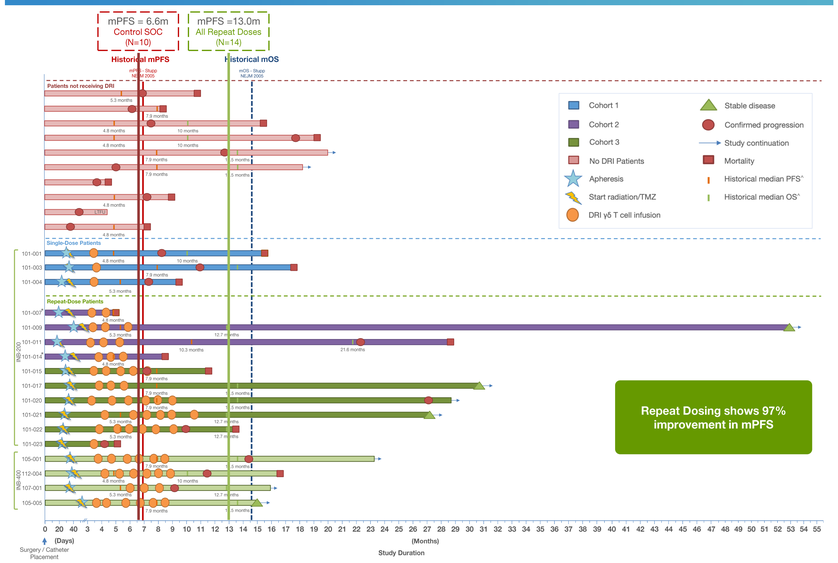
Demographics of Treated (N= 17) and Control (N= 10) Patients

Patients were enrolled in the INB-200 (Phase 1 single-center) and INB-400 (Phase 2 multi-center) trial

Treatment Arm	N	Methylation Status	Resection Type		Median Age	Gender
			Subtotal	Total		
INB-200 DL1 Patients	3	66% Unmethylated	0%	100%	68	33% Male
All Control (SOC) Patients	10	60% Unmethylated	20%	80%	67	60% Male
DL1 + Control (SOC) Patients	13	61% Unmethylated	15%	85%	64	54% Male
INB-200 Repeat Dose Patients	10	50% Unmethylated	60%	40%	62	70% Male
INB-400 Repeat Dose Patients	4	50% Unmethylated	50%	50%	66	0% Male
All Repeat Dose Patients	14	50% Unmethylated	57%	43%	64	50% Male

- 27 patients were enrolled
- 17 patients were treated with DeltEx DRI, with 14 patients receiving from 3 up to 6 doses (Repeat Dose Patients)
- 10 patients received only SOC Stupp protocol, and had consented to be tracked (Control (SOC) Patients)
- Across all patient groups there were similar methylation status distribution, gender and median age; one single patient (009) enrolled before 2021 was a grade 4, IDH-mutant glioma
- Interestingly, in the SOC Control patients, the number of Total resections was much higher (80% total) compared to the Repeat Dose patients (43% total). Patients with Total resections are generally expected to have better outcomes

Patients Treated with Repeated Doses have Extended mPFS, mOS



Repeat Dosing shows 97% improvement in mPFS

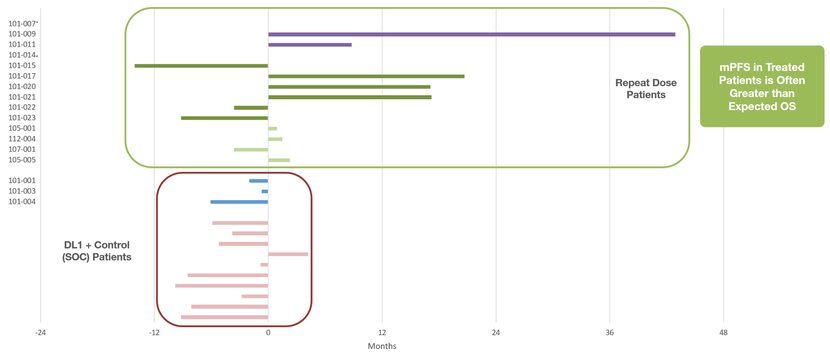
Note: As of October 31, 2025; Source: ^NEJM 2005; 352:987-996 & 352:997-1003 DOI: 10.1056/NEJMoa043330, DOI: 10.1056/NEJMoa043331; NEJM 2017; 376:1027-1037 DOI: 10.1056/NEJMoa1611977; Early trial results are not indicative of future results, including the outcome of this trial.

Strong Treatment Effect Observed in Repeated Dose Patients

Treatment Arm	Median PFS (m)	Median OS (m)	Pts without progression or PFS Exceeding Expected OS (%)
Historical NEJM Data	6.9	14.6	NA
INB-200 DL1 Patients	8.0	15.7+	(0/3) 0%
All Control (SOC) Patients	6.6	11.0	(1/10) 10%
DL1 + Control (SOC) Patients	7.2	13.3	(1/13) 8%
INB-200 Repeat Dose Patients	16.1	20.4+	(5/10)* 50%
INB-400 Repeat Dose Patients	13.0	16.4+	(3/4) 75%
All Repeat Dose Patients	13.0	16.4+	(8/14) 57%

Patients that received repeated doses of DeltEx DRI in INB-200/400 show a significant improvement in median progression-free survival (mPFS = 13.0m) over enrolled control patients from the same centers who only received SOC Stupp Regimen (mPFS = 6.6m), which is inline with historical Stupp controls (mPFS 6.9m). INB-200/400 repeated dose patients have not yet reached mOS, which continues to climb at 16.4+ mOS, while control patients have reached mOS at 11.0m.

Comparison to Control Group Highlights Improved Outcomes



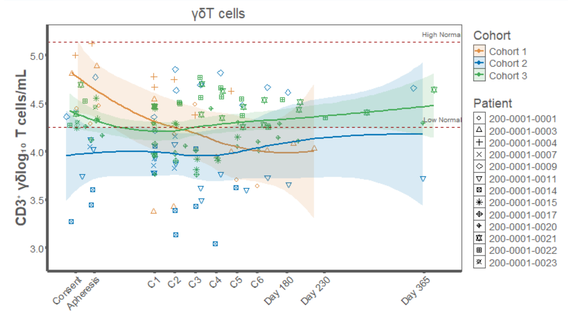
mPFS in Treated Patients is Often Greater than Expected OS

*Pts 007 and 014 passed of CV events without progression; Note: As of October 31, 2025

Timepoint 0 is expected OS based on individual patient demographics from Stupp NEJM study (age and MGMT status). Bars to right show PFS exceeding expected OS, bars to the left represent PFS less than expected OS.

Multiple patients that received repeated doses of DeltEx DRI in INB-200/400 have PFS exceeding expected OS (N=8, 57%) including two MGMT-unmethylated patients (one Total and one Subtotal resection), compared to SOC Control patients (N=1). To date, four repeated dose patients have exceeded 2-years progression-free with one patient (IDH-mut, MGMT-methylated, grade 4) almost 4.5-years without progression. PFS exceeding expected OS is rare in newly diagnosed GBM but occurred in 57% of repeated dose DeltEx DRI patients.

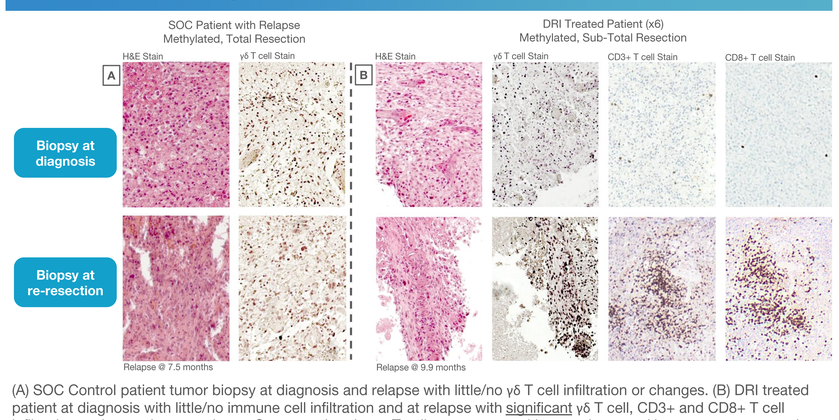
Repeat Dose Patients: Improved Peripheral Immune Reconstitution



Assessment of the peripheral immune system demonstrated that there is a dose-dependent response in DeltEx DRI treated patients.

Cohort 1 (single dose) demonstrated a transient increase, then decline in peripheral γδ T cells while Cohort 2 & 3 (repeated dose), show sustained peripheral γδ T cell reconstitution. Demonstrates a dose-dependent positive systemic immune response in patients from local intrathecal administration of the DeltEx DRI therapy, despite multiple rounds of lymphodepleting TMZ.

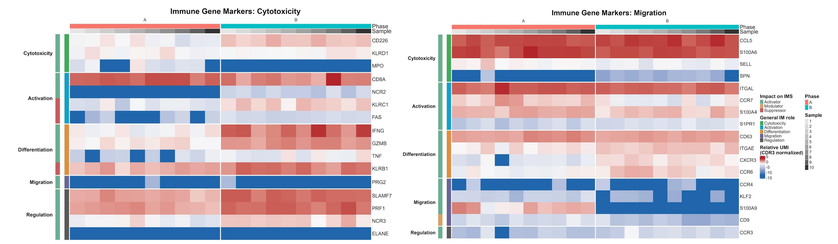
Persistent Active γδ T cells Observed in Treated Patients



(A) SOC Control patient tumor biopsy at diagnosis and relapse with little/no γδ T cell infiltration or changes. (B) DRI treated patient at diagnosis with little/no immune cell infiltration and at relapse with significant γδ T cell, CD3+ and CD8+ T cell infiltration and necrotic tumor tissue. Suggests that the γδ T cells are present with an orchestrated immune response at the site of the GBM, which is typically considered a "cold" tumor without appreciable immune infiltrate.

*IN8bio and UAB

Manufactured γδ T cells are Activated, Cytotoxic and Migratory



Expression of hundreds of genes were analyzed from DeltEx DRI manufactured clinical products. Expression levels are shown as a heatmap (red = high, blue = low), between each donor's Starting material (A) and Clinical Product (B).

The data shows an upregulation of genes involved in immune cell activation, stimulation, cytotoxicity, trafficking and migration, demonstrating that the manufacturing platform is generating a robust, reproducible and cytotoxic cell therapy product.

Conclusions

- Intracranially delivered DeltEx DRI gamma-delta T cell therapy was well-tolerated in patients, showing no dose-limiting toxicities (DLTs), no neurotoxicities (ICANs) and no cytokine release syndrome (CRS)
- Patients receiving repeated doses have a mPFS of 13.0m with a mOS of 16.4m+ and climbing. A notable improvement that surpassed Control patients receiving only SOC with mPFS of 6.6m and mOS of 11.0m
- Significantly, 8/14 (57%) patients receiving repeated DRI doses exhibit a mPFS exceeding their expected OS, compared to only 1/10 (10%) in the Control SOC group, an important milestone
- Repeated dose patients show a dose-dependent systemic immune response. Sustained circulating peripheral T cell numbers and elevated gamma-delta T cells demonstrate that the local administration of the DeltEx DRI is promoting broader immune stimulation and reconstitution that is critical in patients receiving lymphodepleting chemotherapy
- This data demonstrates the power of using γδ T cell based cellular therapy (DeltEx DRI) synergistically with the SOC in frontline GBM. The intent of this therapy is to drive deeper tumor cell elimination through repeated dosing to extend PFS and provide meaningful time to newly diagnosed GBM patients