INB-200: Fully Enrolled Phase 1 Study of Gene-Modified Autologous Gamma-Delta (γδ) T Cells in Newly Diagnosed Glioblastoma Multiforme (GBM) Patients Receiving Maintenance Temozolomide (TMZ)

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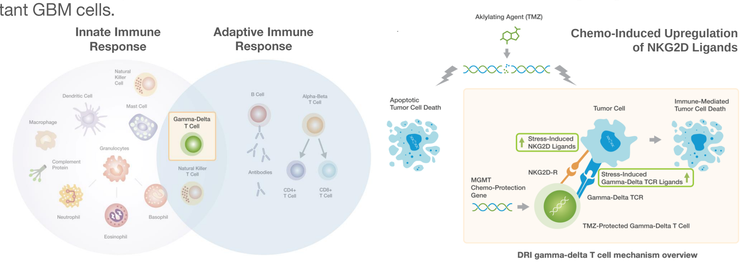
Background

Glioblastoma (GBM) is an aggressive brain tumor that has a high unmet need with one-year overall survival (OS) of 53.7%. Gamma-delta (γδ) T cells are innate immune cells that directly recognize and kill malignant tissue through recognition of Natural Killer Group D Ligands (NKG2D-L) that are expressed on cancer cells. Alkylating chemotherapies such as Temozolomide (TMZ) are lymphodepleting but can also upregulate NKG2D-L expression and amplify the vulnerability of tumor cells to γδ T cell mediated killing, even on TMZ-resistant methylguanine-DNA methyltransferase (MGMT) unmethylated GBM cells. IN8bio's DeltEx Drug Resistant Immunotherapy (DRI), genetically modifies γδ cells with an MGMT chemotherapy resistance gene to permit concomitant administration and the additional targeting of residual TMZ-resistant GBM cells.



DRI gamma-delta T cell mechanism overview

Sources: Ostrom, et al Neuro-Onc 2023; 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: Study Design and Treatment Schema

Treatment Arms

Fixed dose level (DL) of DRI in a 3+3 design (N=18):

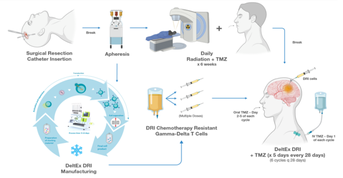
DL1: N = 3 (up to 6) patients, single dose of 1 x 10^7 cells on C1D1
DL2: N = 3 (up to 6) patients, three doses of 1 x 10^7 cells, one dose every 28 D1 of C1-C3
DL3: N = 3 (up to 6) patients, six doses of 1 x 10^7 cells, one dose every 28 days on D1 of C1-C6

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 DeltEx DRI in two dose frequencies

Secondary Endpoints

- Time to progression
- Overall survival
- Biologic response

Site

O'NEAL COMPREHENSIVE CANCER CENTER, UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM; HEERSINK SCHOOL OF MEDICINE

Source: INIBbio, image created with biorender.com

Safety and Adverse Events (n=13)

Serious Adverse Events	All Grades	≥ Grade3
Cardiac Arrest	7.7%	7.7%
Cardiac Disorder	7.7%	7.7%
Platelet Count Decreased	15.4%	15.4%
WBC Count Decreased	7.7%	7.7%
Hydrocephalus	15.4%	7.7%
Dysarthria	7.7%	7.7%
Pulmonary Embolus	7.7%	7.7%
Cyst Drainage	7.7%	7.7%
Deep Vein Thrombosis	7.7%	7.7%
Fall	7.7%	7.7%

Adverse Events	All Grades	≥ Grade3
Decreased Appetite	15.4%	
Balance Disorder	15.4%	
Headache	15.4%	
Hydrocephalus	15.4%	7.7%
Platelet count decreased	23.1%	23.1%
WBC count decreased	23.1%	7.7%
Lymphocyte count decreased	7.7%	7.7%
Neutrophil count decreased	7.7%	7.7%
Asthenia	15.4%	
Fatigue	15.4%	
Urinary tract infection	15.4%	
Deep Vein Thrombosis	15.4%	

- No DRI-related toxicity
- **No DLT's to date**
- **No ICANS/CRS**
- Majority of toxicities are grade 1 or 2 and attributable to TMZ
- Unrelated TESAE's of cardiac arrest, pulmonary embolus, temporal cyst drainage, dysarthria, hydrocephalus
- **No treatment-related deaths**
- **No change in safety profile observed to date following repeat administration of up to six doses**

*As of May 1, 2024; Early trial results are not indicative of future results, including the outcome of this trial.

Demographics and Efficacy

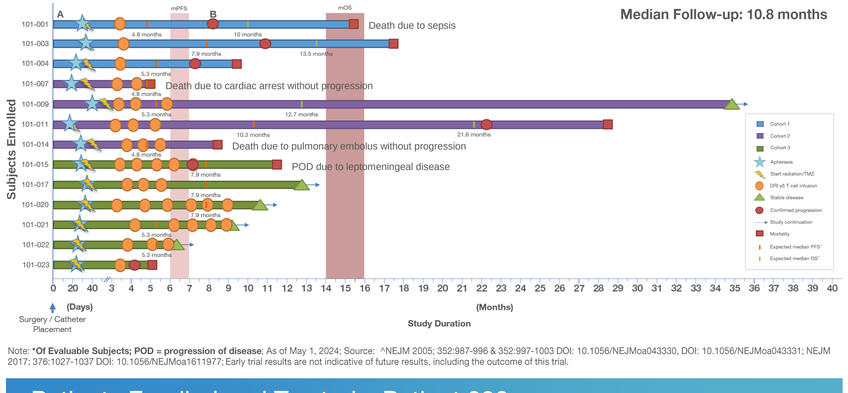
Subject	Age / Sex	Cytogenetics	Dose level	Resection	TMZ Maint. Cycles Received	Response	PFS (mos)	OS (mos)
001	68 / M	IDH-WT, MGMT-unmethylated	1	Total	5	SD	8.3	15.6 Died from sepsis
003	74 / F	IDH-WT, MGMT-methylated	1	Total	6	SD	11.9	17.7
004	21 / F	IDH-WT, MGMT-unmethylated	1	Total	3	SD	7.4	9.6
007	74 / M	IDH-WT, MGMT-unmethylated	2	Total	2	Unevaluable	-	5.1 Died w/out progression
009	32 / M	IDH-mutant, MGMT-methylated	2	Total	12	SD	34.9+	Alive
011	56 / F	IDH-WT, MGMT-methylated	2	Total	6	SD	22.2	28.6
014	73 / F	IDH-WT, MGMT-unmethylated	2	Subtotal	6	SD	8.7	8.7 Died w/out progression
015	73 / M	IDH-WT, MGMT-methylated	3	Subtotal	5	SD	7.1	11.8
017	74 / F	IDH-WT, MGMT-methylated	3	Subtotal	3	SD	12.7+	Alive
020	66 / M	IDH-WT, MGMT-methylated	3	Subtotal	6	SD	10.8+	Alive
021	57 / M	IDH-WT, MGMT-unmethylated	3	Total	5	SD	9.2+	Alive
022	53 / M	IDH-WT, MGMT-unmethylated	3	Subtotal	3	SD	6.4+	Alive
023	52 / M	IDH-WT, MGMT-unmethylated	3	Subtotal	1	PD	4.2	5.4

*As of May 1, 2024; Early trial results are not indicative of future results, including the outcome of this trial.

- **Median Age: 68**
- **Unmethylated: 54%**
- **23 enrolled, five products unable to be manufactured of 13 treated, five remain in follow-up**
- **Deaths: Eight**
  - **Seven due to PD or disease-related issues**
  - **One Unrelated:**
    - Cardiac event (007)

INB-200: Durability Observed

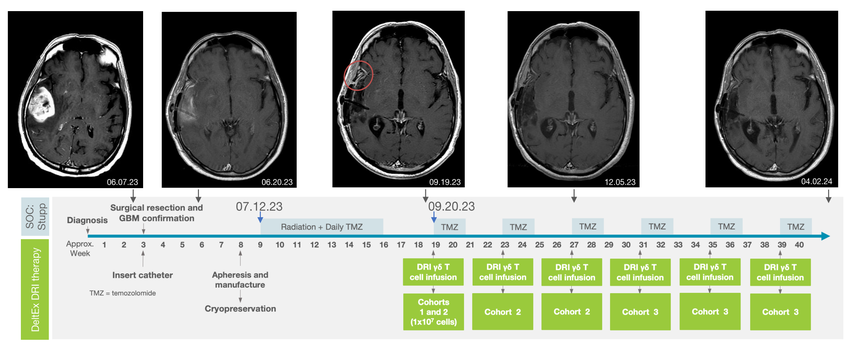
83%* Exceeding Stupp Regimen Median PFS of 7 months



Note: ***Of Evaluable Subjects; POD = progression of disease**; As of May 1, 2024; 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.

Patients Enrolled and Treated – Patient 020

Patient 020 – Male 66y, IDH-wt, MGMT-methylated; Remains alive and relapse-free at 10.8+ months; anterior and medial portion of R temporal lobe showing enhancement suggestive of post-treatment change at off-treatment scan

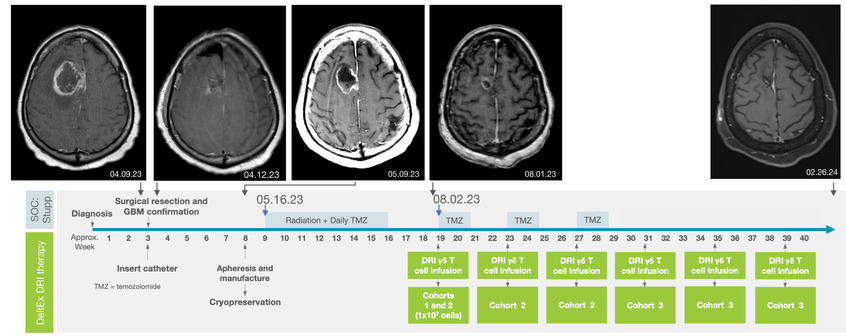


Results from one patient are not indicative of future results including the outcome of this trial

Source: IN8bio and UAB

Patients Enrolled and Treated – Patient 017

Patient 017 – Female 77y, IDH-wt, MGMT-methylated; Remains alive and relapse-free at 12.7+ months; demonstrated continued slight decrease in size of heterogenous enhancing lesions and decrease in size of nodular enhancing component

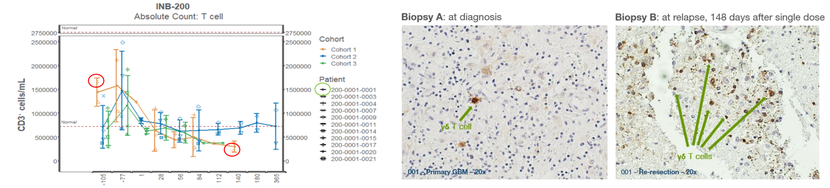


Results from one patient are not indicative of future results including the outcome of this trial

Source: IN8bio and UAB

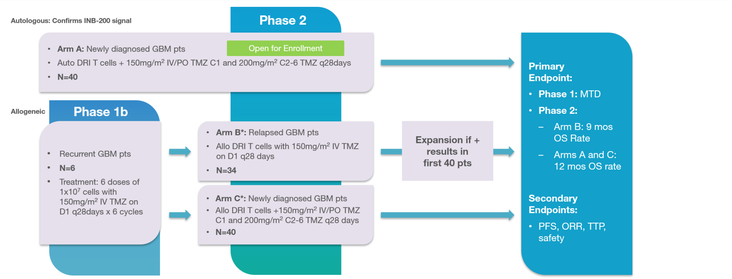
γδ T Cells are Infiltrating and Persisting in Tumor Tissue

Preserved γδ cells in relapsed tumor 148 days post-DRI infusion despite significant peripheral lymphodepletion in patient 001



Source: INBbio and UAB

INB-400: NCT05664243



*Arm B and C subject to additional IND for allogeneic drug product (INB-400) as per FDA Guidance for Industry updated Nov. 2022 (https://clinicaltrials.gov/ct2/show/NCT05664243)

Conclusions

- **In our study, gamma-delta T cells appear to provide promising PFS improvement.**
- **83% (10/12) evaluable subjects have exceeded median PFS of 7 months expected with Stupp regimen with 1 subject awaiting longer follow-up**
- **First study evaluating safety and efficacy of genetically modified γδ T cells in all tumors**
- **Genetically modified γδ T cells demonstrated a tolerable safety profile with no CRS or ICANS observed**
- **TMZ is an effective lymphodepleting regimen for cellular therapy with DeltEx DRI technology preserving γδ T cells despite significant peripheral lymphodepletion**
- **Early data suggests that repeat doses result in longer time to progression**
- **Evidence of post-treatment changes in several scans suggest immune activity from γδ T cell infusions**
- **DeltEx DRI γδ T cell therapy offers promising results to GBM patients warrants further follow-up in ongoing Phase 1b/2 trial, INB-400**
- **Autologous INB-400 ARM A has dosed its first patient and is actively enrolling**

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