2023 ASCO® ANNUAL MEETING

INB-200: Phase I Study of Gene Modified Autologous Gamma-delta (γδ) T Cells in Newly Diagnosed Glioblastoma Multiforme (GBM) Patients Receiving Maintenance Temozolomide

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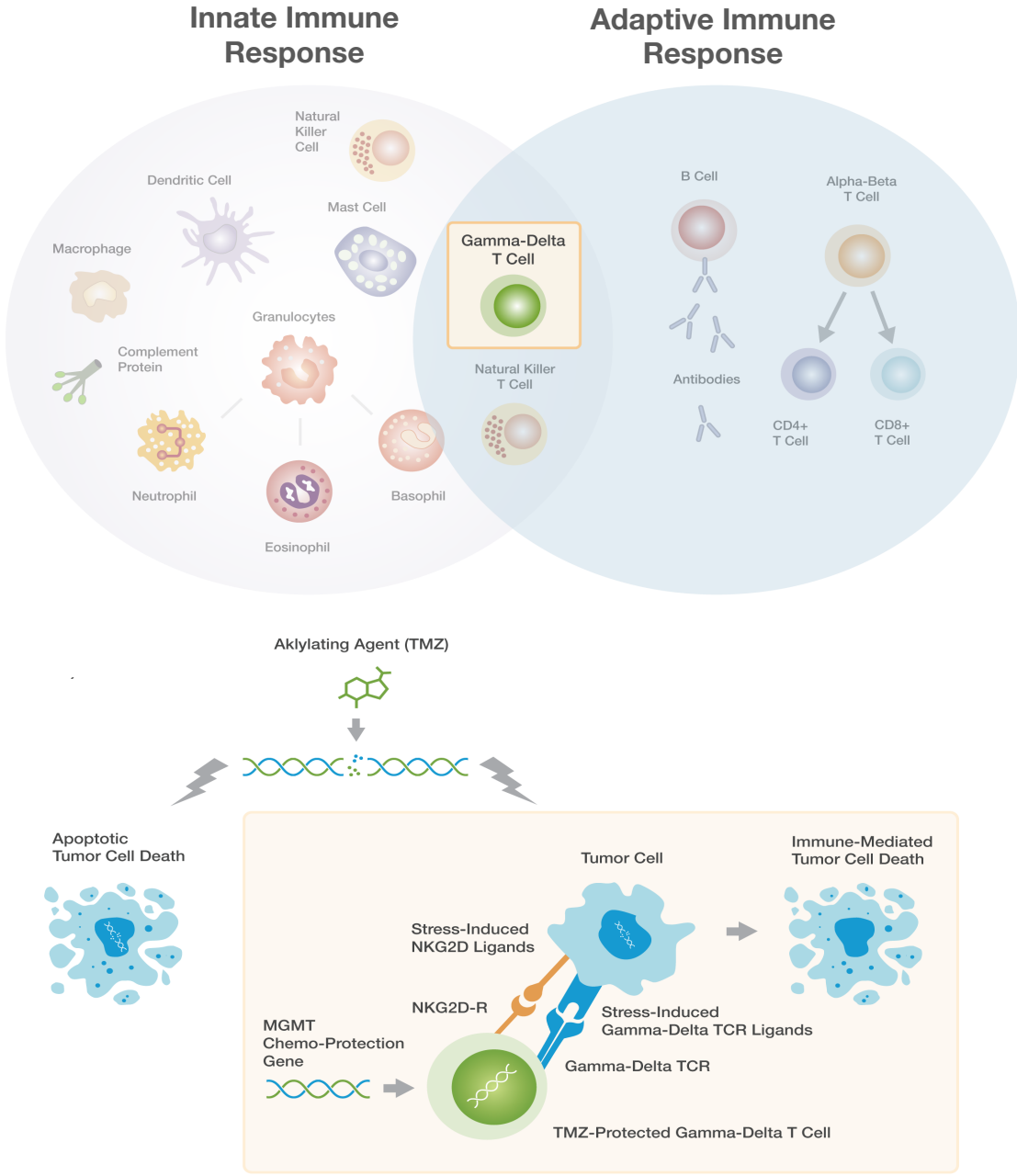
Disclosures

- None

Introduction

- Glioblastoma (GBM) 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)
- Chemotherapy can upregulate NKG2D-L expression and amplify the vulnerability of tumor cells to γδ T cell killing
- IN8bio's platform, DeltEx Drug Resistant Immunotherapy (DRI), genetically modifies γδ cells with an MGMT chemotherapy resistance gene to permit concomitant administration



Source: Ostrom, et al Neuro-Onc 2023; Stupp,et al NEJM 2005; Hottinger, et al Neuro-Onc

INB-200: Study Design and Treatment Schema

Treatment Arms

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

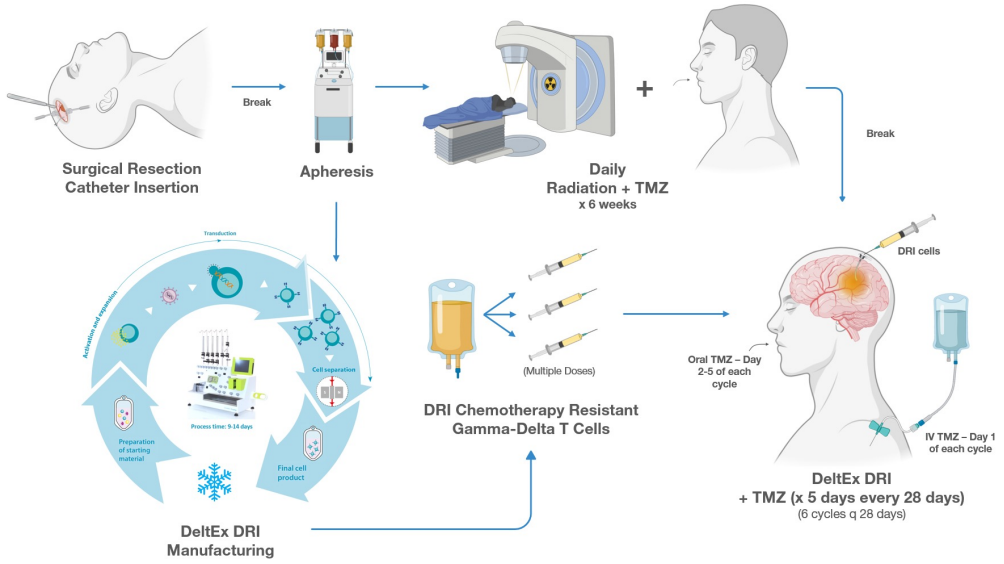
DL1: N = 3 (up to 6) patients, single dose of 1 x 10^7 cells on C1D1
DL2: N = 3 (up to 6) patients, three doses of 1 x 10^7 cells, one dose every 28 D1 of C1-C3
DL3: N = 3 (up to 6) patients, six doses of 1 x 10^7 cells, one dose every 28 days on D1 of C1-C6

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

Source: IN8bio, image created with biorender.com

O'NEAL COMPREHENSIVE CANCER CENTER
UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

UAB HEERSINK SCHOOL OF MEDICINE

Demographics and Efficacy

Subject	Age / Sex	Cytogenetics	Dose level	TMZ Maint. Cycles Received	Response	PFS (mos)	OS (mos)
001	68 / M	IDH-WT, MGMT-unmethylated	1	5	SD	8.3	15.6 Died from sepsis
003	74 / F	IDH-WT, MGMT-methylated	1	6	SD	11.9	17.7
004	21 / F	IDH-WT, MGMT-unmethylated	1	3	SD	7.4	9.6
007	74 / M	IDH-WT, MGMT-unmethylated	2	2	Unevaluable	-	5.1 Died without progression
009	32 / M	IDH-mutant, MGMT-unmethylated	2	12	SD	22.8+	Alive
011	56 / F	IDH-WT, MGMT-methylated	2	6	SD	18.8+	Alive
014	73 / F	IDH-WT, MGMT-unmethylated	2	6	SD	8.7	8.7 Died without progression
015	73 / M	IDH-WT, MGMT-methylated	3	5	SD	7.1	11.8
017	74 / F	IDH-WT, MGMT-pending	3	Await Dosing			
018	66 / M	IDH-WT, MGMT-unmethylated	3	Await Dosing			

- **18 enrolled, only four products unable to be manufactured**
- **Of 8 treated, 2 remain in follow-up**
- **2 await dosing**
- **6 deaths:**
  - 3 due to PD (003, 004, 015)
  - 3 Unrelated:
    - Sepsis (001)
    - Cardiac event (007)
    - Pulmonary embolus (014)

*As of April 30, 2023; Early trial results are not indicative of future results, including the outcome of this trial.

Safety and Adverse Events

All Adverse Events in > 1 Subject (n=8)

Adverse Events	Grade 1/2	Grade 3	Grade 4
WBC decreased	25%	12.5%	
ALC decreased	12.5%	12.5%	
ANC decreased			12.5%
Platelet count decreased		37.5%	12.5%
Nausea	50%		
Vomiting	25%		
Constipation	25%		
Anorexia	25%		
Asthenia/lethargy/fatigue	50%		
Headache	37.5%		
Fever/pyrexia	50%		
Urinary tract infection	12.5%	12.5%	
Seizures	12.5%		
Sepsis	12.5%		12.5%
Hydrocephalus	12.5%	12.5%	
Dehydration	12.5%	12.5%	
Incision site pain	37.5%		

TEAE in > 1 Subject (n=8)

Adverse Events	All Grades	≥ Grade3
Balance Disorder	25%	
Headache	25%	
Hydrocephalus	25%	12.5%
Platelet count decreased	37.5%	37.5%
WBC count decreased	37.5%	12.5%
Lymphocyte count decreased	12.5%	12.5%
Neutrophil count decreased	12.5%	12.5%
Asthenia	25%	
Urinary tract infection	25%	

- 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**
- **Repeat dosing DOES NOT demonstrate change in toxicity profile to date**

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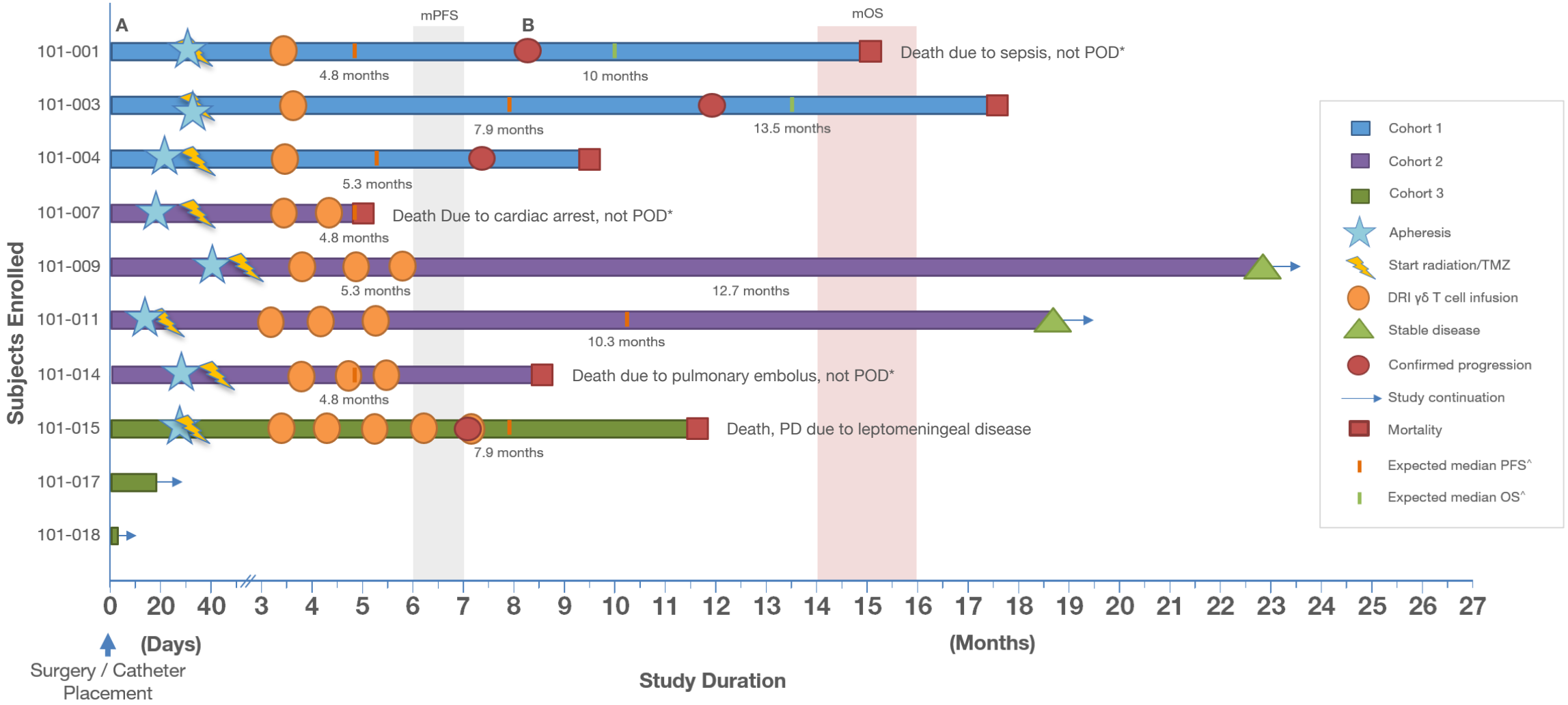
INB-200: Long-term Durability Observed

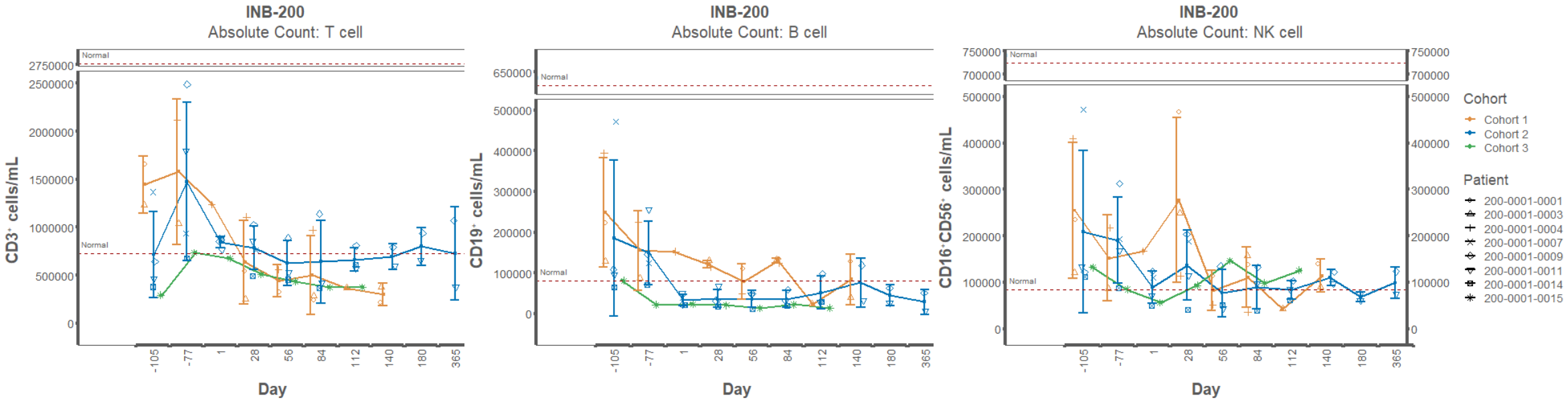
Median Follow-up of 15.5 months



Note: ***POD = progression of disease***; As of April 30, 2023; 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.

Peripheral Immunophenotyping

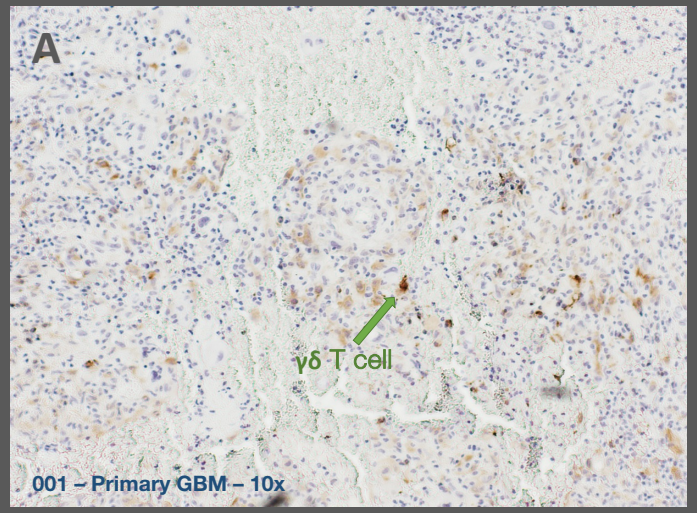
TMZ is an effective lymphodepleting agent for cell therapy

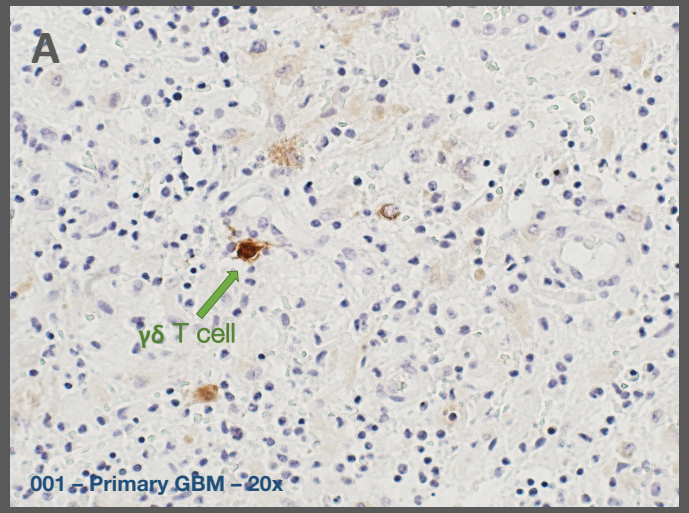


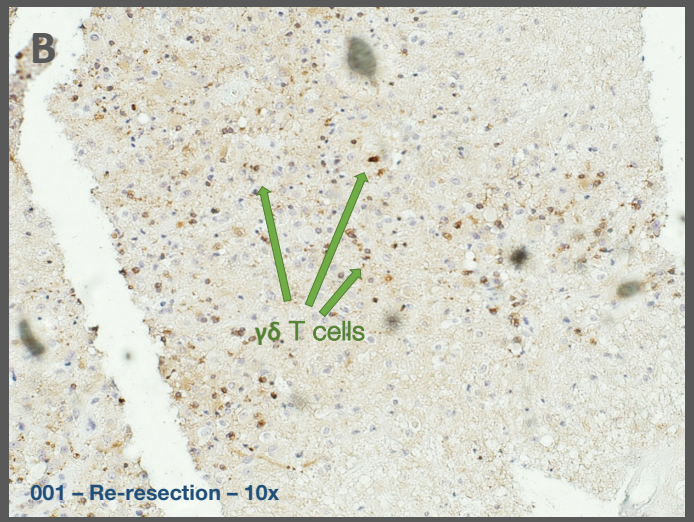
- During TMZ treatment, as expected T, B and NK levels drop to low normal or below low normal values
- The main CD8+ T cells profile is Naïve and Central Memory

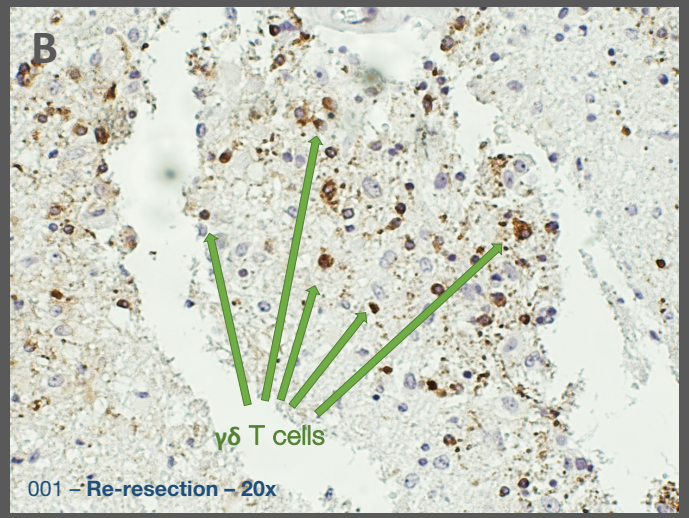
001: γδ T Cells Infiltrating and Persisting in Tumor Tissue

Biopsies - A) at diagnoses and B) 148 days following a single infusion of INB-200 despite TMZ lymphodepletion





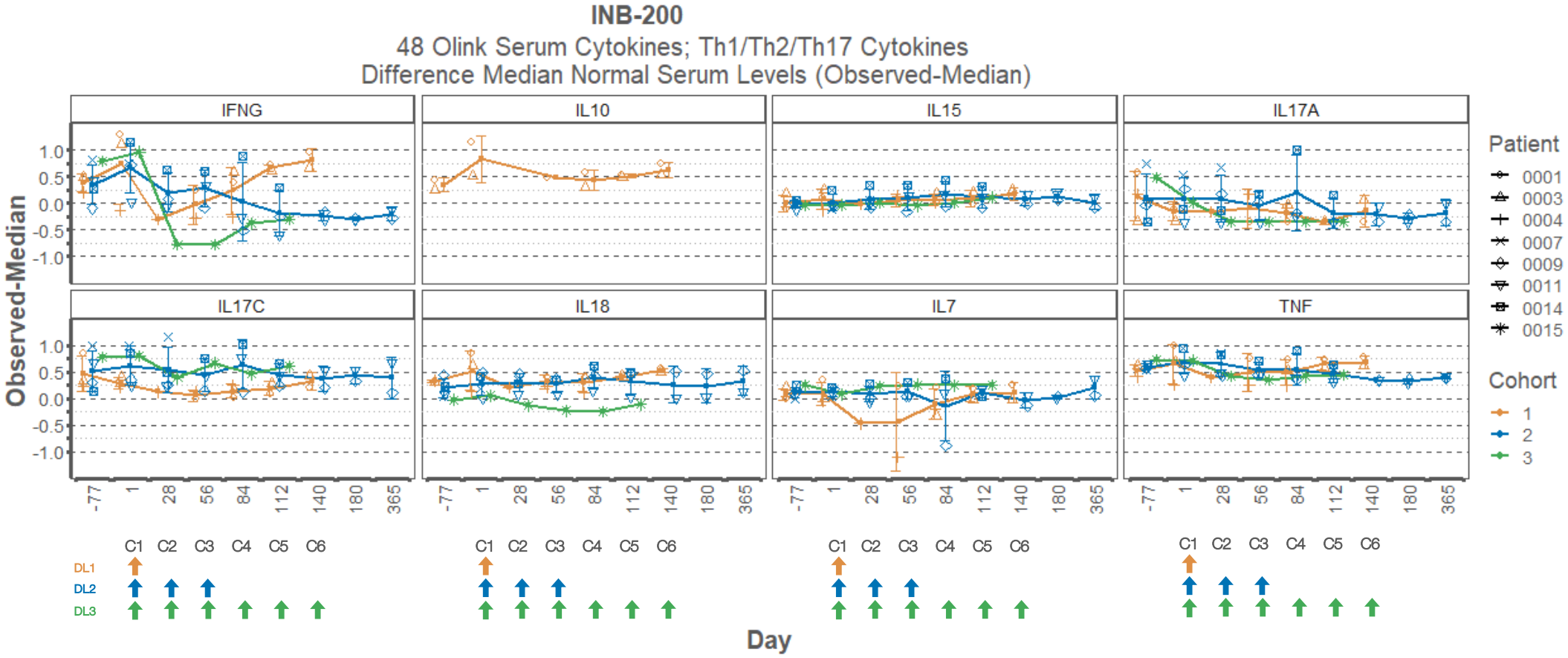




Source: * UAB and IN8bio

Serum Cytokines

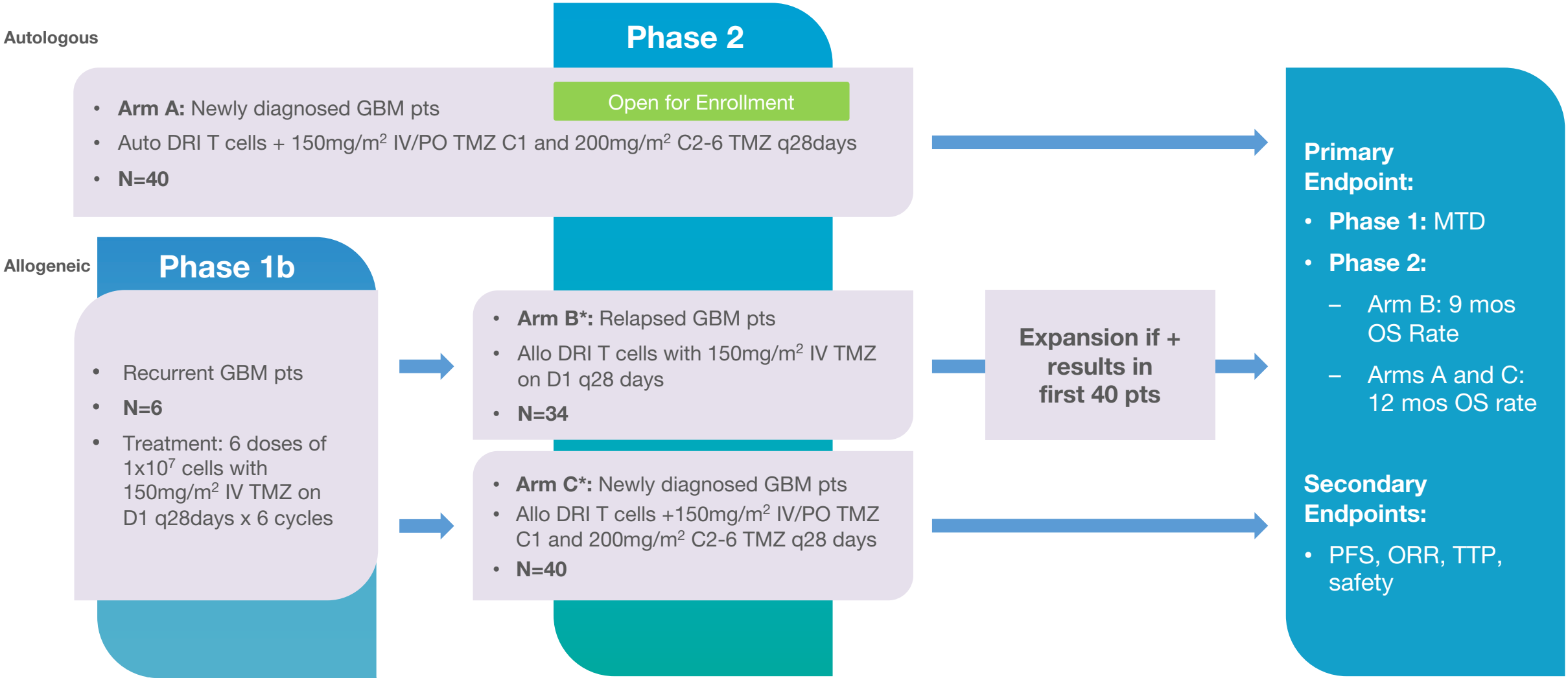
No significant increase in inflammatory cytokines with repeat dosing



Conclusions

- First study evaluating safety and efficacy of genetically modified γδ T cells
- First study demonstrating tolerable safety of repeat dosing of γδ T cells
    - No CRS or ICANS observed despite intra-cavitary infusion
- **All treated patients surpassed a median PFS of 7 months, with most exceeding their expected PFS based on age and MGMT status of their tumors**
- TMZ is an effective lymphodepleting regimen for cellular therapy
- Promising results indicate γδ T cells could open new avenues for treating GBM and was granted Orphan Drug Designation by the FDA
- Phase 1b/2 trial underway to confirm and validate autologous AND allogeneic γδ T cell therapy in GBM, with the autologous arm now open for enrollment

INB-400: NCT05664243



*Arm B and C subject to additional IND for allogeneic drug product (INB-410) as per FDA Guidance for Industry updated Nov. 2022, IND expected in 2H 2023 (https://clinicaltrials.gov/ct2/show/NCT05664243)

INB-400: NCT05664243 (continued)

	Company/Hospital/ Institution	City (Investigator)
1	Board of Regents of the University of Wisconsin	Madison, WI
2	UCLA-Neuro-Oncology	Los Angeles, CA
3	University of Louisville Health Care - James Graham Brown Cancer Center	Louisville, KY
4	OSUWMC--James Cancer Hospital	Columbus, OH
5	The Preston Robert Tisch Brain Tumor Center (Duke)	Durham, NC
6	H. Lee Moffitt Cancer Center and Research Institute	Tampa, FL
7	Cleveland Clinic Foundation	Cleveland, OH
8	University of Alabama at Birmingham UAB - The Kirklin Clinic	Birmingham, AL
9	University of Minnesota	Minneapolis, MN
10	Yale University/Yale New Haven Hospital	New Haven, CT
11	UCSD Medical Center	La Jolla, CA
12	City of Hope	Duarte, CA

*UAB is lead center and UofL is first center to be activated; other centers have been identified, screened and in process of site activation

Acknowledgements

- Patients and their families!
- Burt Nabors, MD
- Kristen O. Riley, MD and UAB Neuro-surgery Team
- Thiru Pillai and UAB Research Staff
- Antonio Di Stasi, MD
- Amber McKell and the Cell Therapy Laboratory at UAB
- IN8bio Team

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