Harnessing the Power of Gamma-Delta T Cells

August 2024

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Deep Experience Across Development and Biotechnology

William Ho
Co-Founder, President and Chief Executive Officer

Lawrence Lamb, PhD
Co-Founder and Chief Scientific Officer

Patrick McCall, CPA
Chief Financial Officer

Trishna Goswami, MD
Chief Medical Officer

Kate Rochlin, PhD
Chief Operating Officer

Glenn Schulman, PharmD, MPH
Head IR and Corporate Communications

IN8bio's team has deep experience in cell therapy & oncology expertise:

- Diverse leadership team brings decades of extensive background in oncology discovery, business insights, franchise creation, product development, regulatory affairs, and commercialization
- Business development and licensing expertise across biopharmaceutical and biotechnology companies
- Founding of a private healthcare investment fund and management of public investments and cross-over portfolio at leading healthcare venture capital firm, New Leaf Venture Partners
- Specialization in transplantation immunology and recognized innovation in the field of γδ T cells
- Leadership of Curadigm's spin-out from Nanobiotix and platform collaborations and partnerships
- Proven and measurable successes in bringing high-profile candidates to market, including Stemline, Immunomedics and Gilead Sciences

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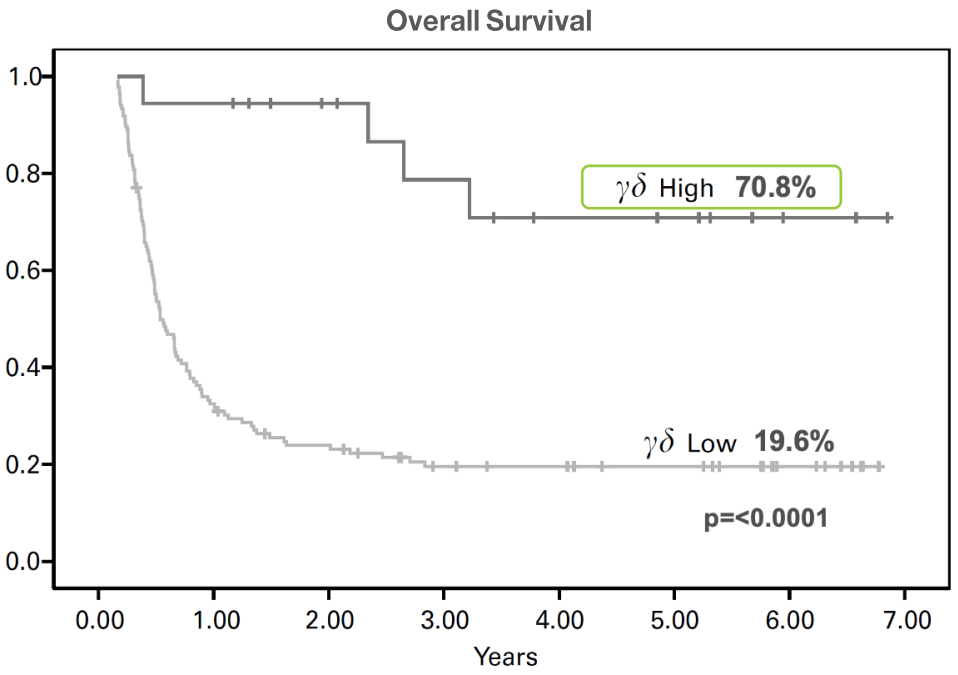
IN8bio

IN8bio Leading the Fight Against Cancer

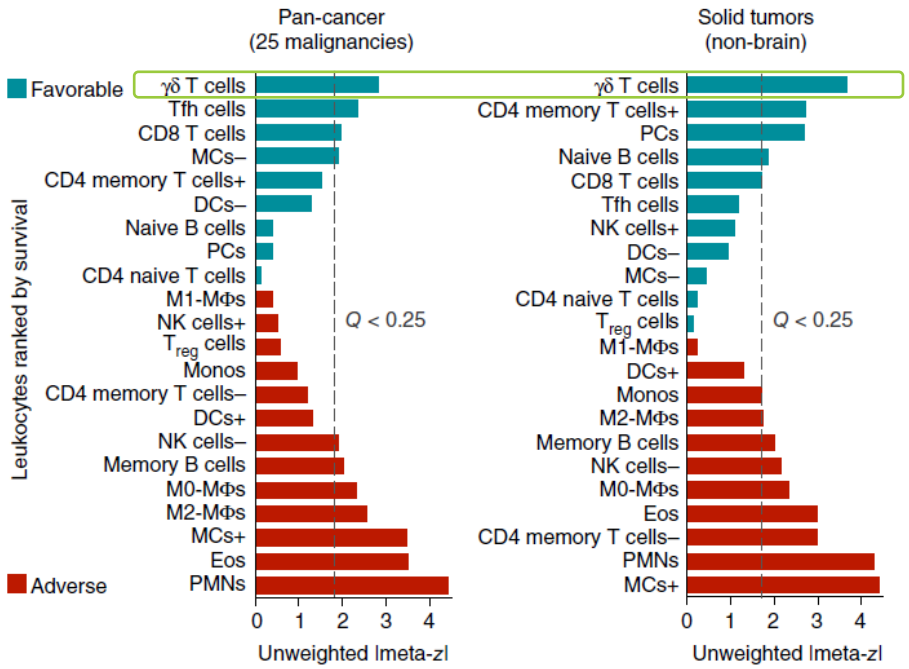
- At IN8bio, our pioneering approach has achieved long-term remissions exceeding 3 years in patients with Acute Myeloid Leukemia (AML) and Glioblastoma (GBM) through two groundbreaking clinical trials
- Unconventional Strategies in the "*War on Cancer*"
  - **Harnessing the Power of Immune Cells:** Our γδ T cells are a "Special Operations Force" that act as direct cancer killers while orchestrating a comprehensive immune response
  - **Precision and Safety:** These cells coordinate and direct the actions of the immune system and identify the locations of friendly forces, enemies, and civilians on the battlefield, which helps to reduce the risk of adverse events and toxicities
  - **Durable Remissions:** With over 30 years of expertise in γδ T cell research, we have pioneered the field; achieving long-term remissions against challenging cancers with significant unmet needs
- Mission **Cancer Zero**™ - Driven by our goal to safely eradicate residual cancer cells, we employ innovative and unconventional strategies to transform treatment outcomes
- IN8bio is redefining cancer treatment with our innovative and novel approaches. Join us in our mission to achieve **Cancer Zero**™ and transform cancer care

γδ T Cells are Key to Better Survival

Leukemia Post-HSCT:
Improved Patient Survival



Pan-Cancer:
Improved Patient Overall Prognosis



Human data demonstrate that γδ T cell levels strongly correlate with improved clinical outcomes

Source: Gentles et al. 2015, Godder et al. (Lamb), 2007 and Meraviglia et al. 2017

The Role of γδ T Cells is Starting to be Recognized

nature cancer

Review article

https://doi.org/10.1038/s43018-024-00798-x

γδ T cells as critical anti-tumor immune effectors

Received: 19 January 2024

Accepted: 29 May 2024

Published online: 26 July 2024

Check for updates

Marcel Arias-Badia [1], Ryan Chang [1] & Lawrence Fong [1,2]

While the effector cells that mediate anti-tumor immunity have historically been attributed to αβ T cells and natural killer cells, γδ T cells are now being recognized as a complementary mechanism mediating tumor rejection. γδ T cells possess a host of functions ranging from antigen presentation to regulatory function and, importantly, have critical roles in eliciting anti-tumor responses where other immune effectors may be rendered ineffective. Recent discoveries have elucidated how these differing functions are mediated by γδ T cells with specific T cell receptors and spatial distribution. Their relative resistance to mechanisms of dysfunction like T cell exhaustion has spurred the development of therapeutic approaches exploiting γδ T cells, and an improved understanding of these cells should enable more effective immunotherapies.

Our Programs Span 30+ years of Peer-Reviewed Data…

We believe that the innovative critical findings over time reduces the risk in our clinical programs

- Leukemia, Bone Marrow Transplant, and Manufacturing

- **1996** – Association between increased circulating γδ T cells and long-term survival in leukemia patients following haploidentical bone marrow transplantation. DOI: 10.1089/scd.1.1996.5.503
- **1999** – Concentrated γδ T cells are required in the graft to achieve high γδ T cell numbers and the subsequent clinical effect. DOI: 10.1080/00324720310001412 95
- **2001** – Scalable manufacturing of Vδ1 T Cells with solid phase antibody and IL-2 that do not initiate allogeneic GvHD. DOI: 10.1038/sj.bmt.1702830
- **2005** – Near-complete loss of circulating Vδ2 T Cells and reduced Vδ1 CDR3 region diversity in children presenting with leukemia prior to induction therapy DOI: 10.1007/s00262-005-0094-6
- **2007** – Association between increased circulating γδ T cells and long-term survival over eight years in leukemia patients following haploidentical bone marrow transplantation (most cited) DOI: 10.1038/sj.bmt.1705650
- **2014** – Manufacturing and characterization of of γδ T cells from iPSC. DOI: 10.1371/journal.pone.0097335
- **2018** – Clinical-scale manufacturing of Vδ2 T Cells DOI: 10.1038/s41409-018-0130-8

Our Programs Span 30+ years of Peer-Reviewed Data…

We believe that the innovative critical findings over time reduces the risk in our clinical programs

- Glioblastoma (GBM)

- **2009** - Unique opportunities for γδ T cells in GBM DOI: 10.1215/15228517-2008-111
- **2010** – Early preclinical in vitro and animal studies support therapeutic potential of γδ T cells in GBM. DOI: 10.1007/s11060-010-0245-2
- **2013** – Successful genetic modification of γδ T cells for resistance to temozolomide (drug resistant therapy – DRI) DOI: 10.1371/journal.pone.0051805
- **2015** – Resistance of GBM to γδ T cells due to NKG2DL down-regulation in a syngeneic immune competent mouse model DOI: 10.1371/journal.pone.0122387
- **2015** – Safety of neoadjuvant allogeneic γδ T cell therapy with radiation and chemotherapy (IND-Enabling) DOI: 10.1007/s00262-015-1662-z
- **2016** – Failure of in zoledronate and IL-2 in vivo activation of γδ T cells in pediatric patients with stage IV neuroblastoma DOI: 10.1097/MD.0000000000004909
- **2021** – Efficacy and safety of temozolomide-resistant allogeneic γδ T cell therapy for primary and recurrent GBM (IND-Enabling). DOI: 10.1038/s41598-021-00536-8
- **2024** – Adoptive γδ T cell therapy of primary GBM with MGMT-modified γδ T cells in maintenance-phase (clinical trial discussion) DOI: 10.3389/fimmu2024.1299044

IN8bio's Thesis for a Successful Cellular Therapy

Our three-pronged approach to targeting cancers:

Durability

Meaningful **duration of response** can be achieved by increasing the **depth of response** through novel **synergistic combinations**.

Tolerability

Utilize **novel cell types** with a natural ability to identify and kill malignant cells while **preserving healthy tissue** to avoid toxicities seen with other cell therapy approaches.

Heterogeneity

Employ an approach that can leverage **endogenous immune mechanisms** to **cover tumor heterogeneity** and drive broader immune activation.

Robust Pipeline with Multiple Near-Term Clinical Readouts

Product Candidate	Approach	Key Indications	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone(s)^
Hematologic Malignancies (Allogeneic)							
INB-100	DeltEx	AML, MDS					• Provide LT follow-up, enroll patients and report updates in expansion cohort at DL 2 through remainder of 2024 • Potential submission of IND for Phase 2 RCT trial^ during 1H25
Solid Tumors (Autologous)							
INB-200	DeltEx DRI*	GBM (1L)**					• Additional long-term follow-up in 4Q24
INB-400	DeltEx DRI	GBM (1L)					• Data update at medical meetings in 2025
Solid Tumors (Allogeneic)							
INB-400	DeltEx DRI	GBM (relapsed & 1L)					• Potentially submit IND for Allo Phase 1b in relapsed GBM in 2025^
In Development							
INB-300	Non-signaling CAR-T (nsCAR)	TBD					• FDA guidance on pre-IND planning by 1Q25
INB-500	γδ iPSC T cells	TBD					

* DRI = Drug Resistant Immunotherapy, or a chemotherapy resistant cell therapy
** 1L = First line therapy
^ Timing of next anticipated milestones are estimates based on the successful raise of additional capital to fund our programs and are subject to change

IN8bio Possesses a Comprehensive γδ T Cell Platform

γδ T Cell Sourcing

Vδ1+

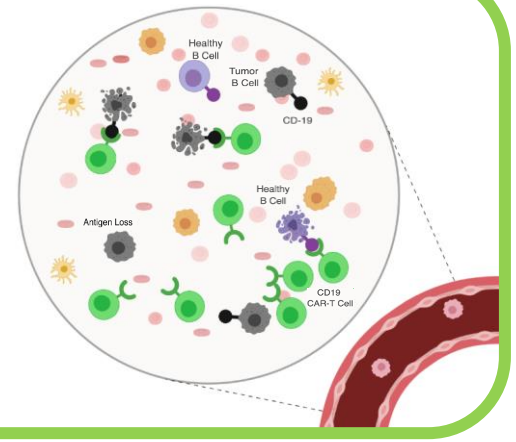
Vδ2+

iPSC

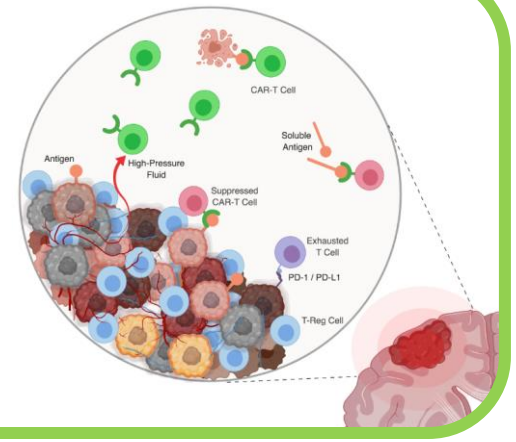
γδ

Tumor Targeting

Hematological Cancers



Solid Tumor Cancers



Source: IN8bio, image created with Shutterstock and biorender.com

INB-100

Post-Transplant Survival Supported by Outside Research

Improved Overall Survival, Relapse-Free-Survival, and Less Graft-vs.-Host-Disease in Patients With High Immune Reconstitution of TCR Gamma Delta Cells 2 Months After Allogeneic Stem Cell Transplantation

Lia Minculescu[1], Hanne Vibeke Marquart[1], Lars Peter Ryder[1], Niels Smedegaard Andersen[2], Ida Schjoedt[2], Lone Smidstrup Friis[2], Brian Thomas Kornblit[2], Søren Lykke Petersen[2], Eva Haastrup[1], Anne Fischer-Nielsen[1], Joanne Reekie[3] and Henrik Sengelov[2]*

[1] *Department of Clinical Immunology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark,* [2] *Department of Hematology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark,* [3] *Department of Infectious Diseases, PERSIMUNE, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark*

Improved Survival

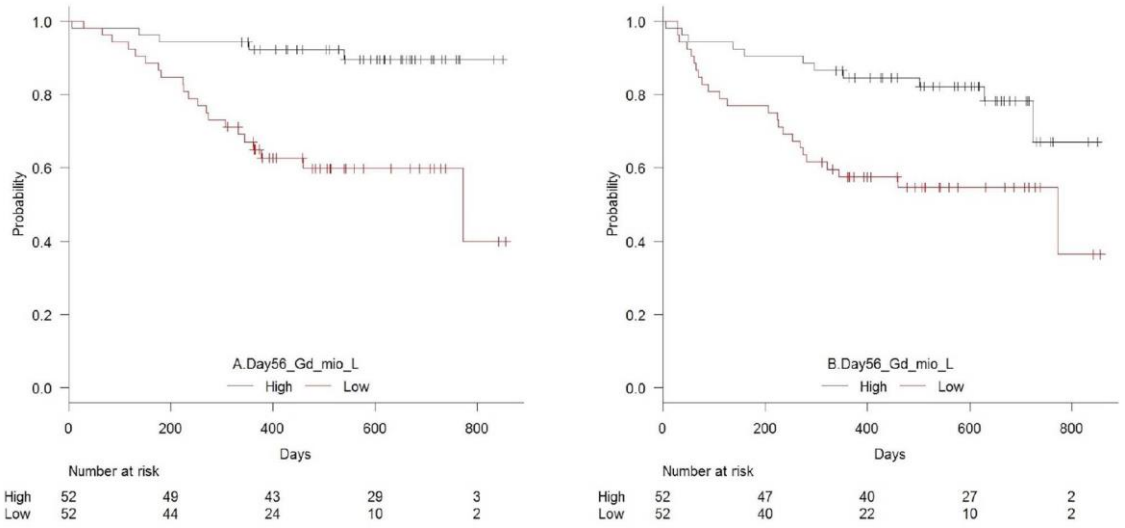


FIGURE 4 | Estimated **(A)** overall survival ($p = 0.001$) and **(B)** relapse-free survival ($p = 0.007$) in patients with high vs. low concentrations (median 21 × 10^6/L) of TCR γδ cells 56 days after transplantation, $n = 104$.

High level of gamma-delta T cells shown to improve survival in allogeneic transplantation

Source: Sengelov et al. Front. Immunol. 2019; DOI: 10.3389/fimmu.2019.01997

Haploidentical Stem Cell Transplantation (HSCT)

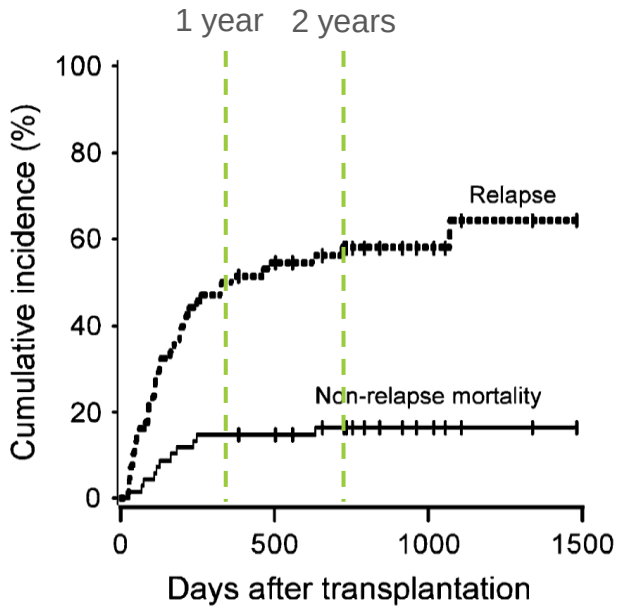
Relapse is the biggest HSCT problem

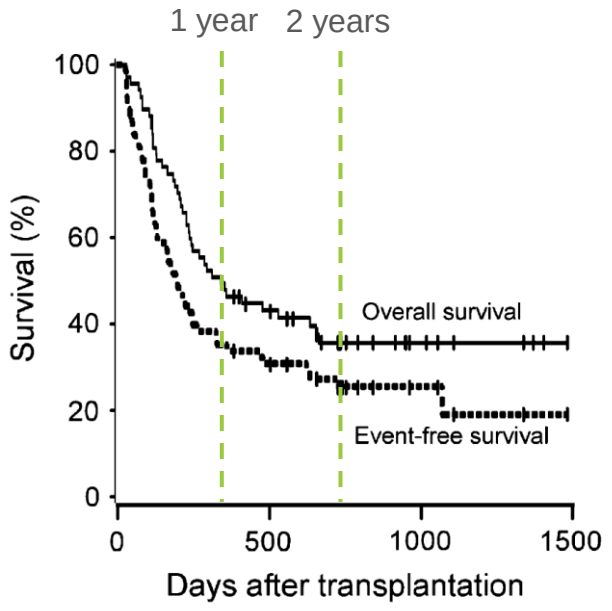
- Haploidentical transplants and reduced intensity conditioning (RIC) regimens have expanded access to stem cell transplantation
- **Relapse remains the biggest risk post-transplant with a ~51% risk of relapse at 1-year**
- Gamma-delta (γδ) T cells are an inherent anti-cancer immune cell that may be able to preempt relapse in the post-transplant setting
- γδ T cells respond to stress ligands expressed on tumor cells to eliminate residual leukemia

HLA-Haploidentical Bone Marrow Transplantation for Hematologic Malignancies Using Nonmyeloablative Conditioning and High-Dose, Posttransplantation Cyclophosphamide

Leo Luznik,[1] Paul V. O'Donnell,[2,3]* Heather J. Symons,[1] Allen R. Chen,[1] M. Susan Leffell,[1] Marianna Zahurak,[1] Ted A. Gooley,[2,3] Steve Piantadosi,[1] Michele Kaup,[1] Richard F. Ambinder,[1] Carol Ann Huff,[1] William Matsui,[1] Javier Bolaños-Meade,[1] Ivan Borrello,[1] Jonathan D. Powell,[1] Elizabeth Harrington,[2] Sandy Warnock,[2] Mary Flowers,[2,3] Robert A. Brodsky,[1] Brenda M. Sandmaier,[2,3] Rainer F. Storb,[2,3] Richard J. Jones,[1] Ephraim J. Fuchs[1]*

[1] Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland; [2] Fred Hutchinson Cancer Research Center, Seattle, Washington; and [3] University of Washington School of Medicine Seattle, Washington





Source: Luznik L,et al. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, post-transplantation cyclophosphamide. Biol Blood Marrow Transplant. 2008 Jun;14(6):641-50.

INB-100: An Allo Therapy to Reduce Leukemic Relapse

Single-center, dose-escalation trial of DeltEx Allo gamma-delta T cells post-haploidentical HSCT

Treatment Arms

Single, ascending dose levels in a 3+3 design:

1. N = 3 (up to 6) patients, single dose of 1 x 10^6 cells/kg
2. N = 3 (up to 6) patients, single dose of 3 x 10^6 cells/kg
3. ~~N = 3 (up to 6) patients, single dose of 1 x 10^7 cells/kg~~

RP2D*

Treatment Regimen & Timing

Fludarabine + cyclophosphamide + TBI = 6 days → Haploidentical HSCT* → INB-100 infusion within 7 days after engraftment

*Neutrophil engraftment is ~15-20 days following HSCT

Key Eligibility Criteria

- Adult patients with a haploidentical donor identified
- KPS ≥70
- AML in mCR with intermediate/high-risk features or relapsed disease
- CML in any chronic phase
- MDS with intermediate/high-risk features
- ALL in mCR with high-risk features or relapsed disease

Primary Endpoints

- Safety
- Maximum tolerated dose (MTD) of DeltEx Allo gamma-delta T cell infusion
- Dose limiting toxicity (DLT)

Secondary Endpoints

- Incidence of acute and chronic graft versus host disease (aGVHD), relapse, and overall survival

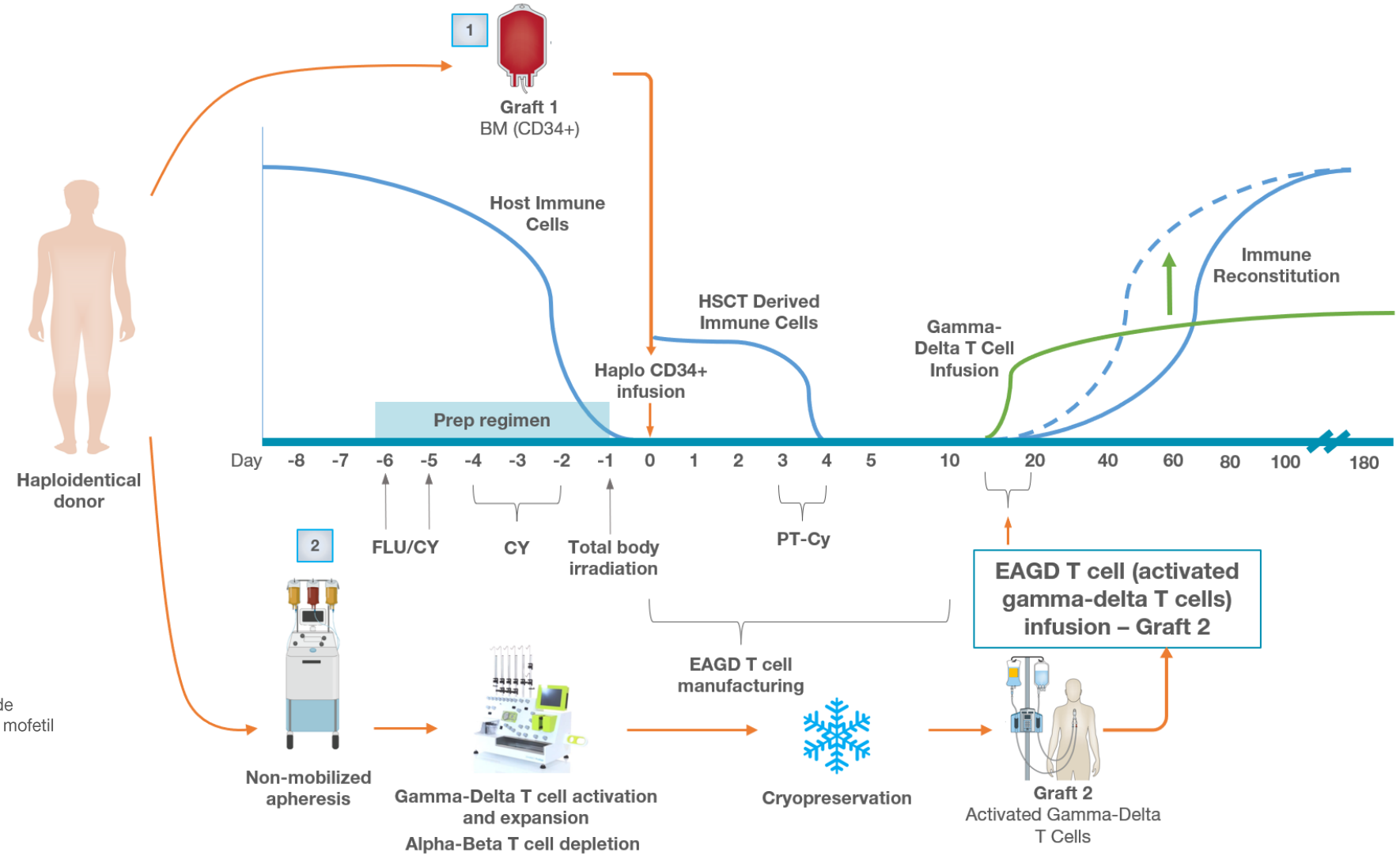
Site

THE UNIVERSITY OF KANSAS CANCER CENTER

*RP2D = Recommended Phase 2 Dose

Potential to Provide Protection During a Vulnerable Period

Expanded + activated gamma-delta T cells (EAGD) to prevent leukemic relapse



FLU = Fludarabine
CY = Cyclophosphamide
MMF = Mycophenolate mofetil

Patient Demographics and Summary

Patient	Dose Level	Age / Sex	Prior Therapies	Disease	Acute / Chronic GvHD	CR (mos)	OS (mos)
002	1	63 / female	Idasanutlin + 7+3	**High-risk AML trisomy 8+ and del7, FLT3 TKD**	Acute G2 skin GvHD Chronic limited mild skin GvHD	**51.6+**	**Alive**
003	1	44 / female	7+3	**High-risk AML trisomy 8+ and del7, IDH2**	Acute G2 GI, Acute G2 rash GvHD	**42.4** **LTFU**	**Alive**
006	1	66 / male	7+3 IDAC	**High-risk relapsed AML**	Acute G2 rash GvHD Chronic extensive GvHD	**37.6+**	**Alive**
007	1	71 / male	Ven/Aza+Pembrolizumab	AML	Acute G2 rash GvHD Chronic limited mod GvHD	**15.5**	**15.5 died due to IPF**
009	2	68 / male	R-CHOP Blinatumomab Inotuzumab Flu/Mel/TBI Vincristine/steroids Flu/cy/brentuximab **CAR-T with Tecartus**	**Relapsed Ph- ALL; TP53 mutated**	Acute G2c rash GvHD	**14.7**	**Alive at 21.2+**
010	2	63 / female	7 cycles Venetoclax/Aza	AML	Acute G2b rash - GvHD	**20.9+**	**Alive**
011	2	68 / male	Hydrea/Peg-IFN	ET with **MDS/MPN overlap; TP53 mutated**	Acute G1 rash - not GvHD Acute G1 diarrhea - not GvHD	**12.5**	**Alive at 18.0+**
012	2	69 / male	2 cycles Venetoclax/Aza	AML		**14.6+**	**Alive**
013	2	71 / female	1 cycle Ven/aza/gliteritinib 2 cycles Venetoclax/Aza	AML, **FLT3**	Acute G1 diarrhea - not GvHD Oral sensitivity- not GvHD	**14.3+**	**Alive**
014	2	71 / male	Venetoclax/Dacogen	AML, del20, -Y	Acute G1 diarrhea - not GvHD Acute G1 rash - not GvHD	**13.8+**	**Alive**

Average patient age ~68 y/o

Majority have AML

Received up to 7 prior therapies

14 enrolled, n=10 dosed and evaluable for safety

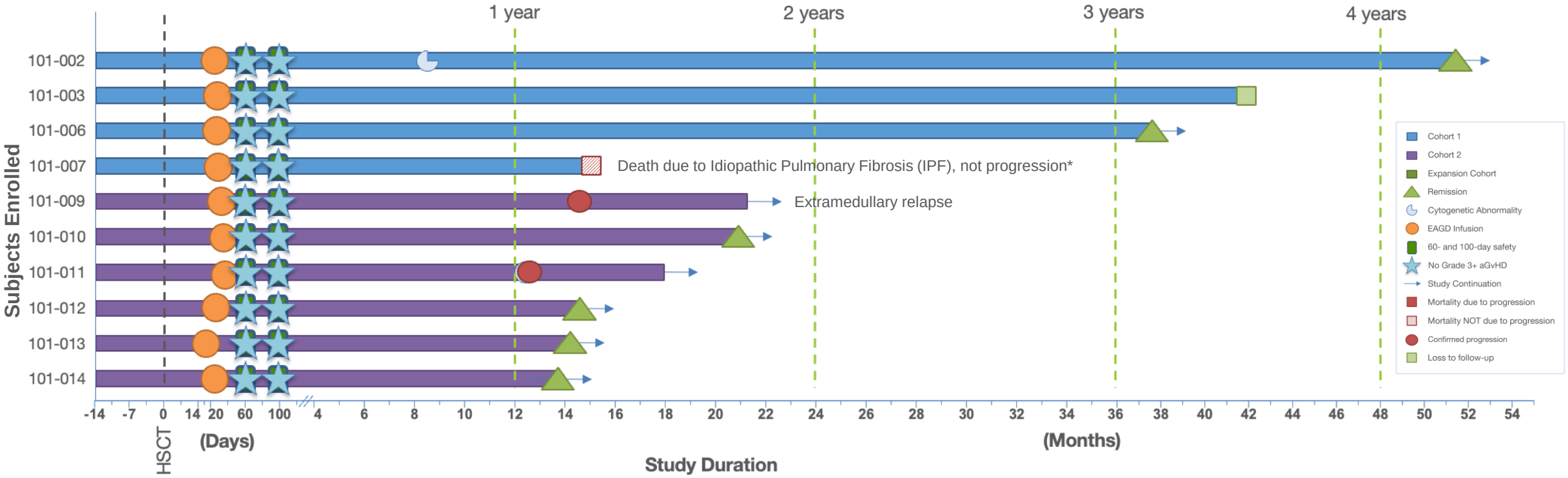
- 1 patient expired prior to dosing
- 1 patient received an out of specification product at 6 x 10^5 EAGD/kg
- 1 manufacturing failure
- 1 screen failure due to relapse prior to treatment

Median follow-up = 19.5 mos

Note: As of August 1, 2024; Early trial results are not indicative of future results, including the outcome of this trial.

100% Patients Remained in Morphologic CR ≥ 12 Months*

Three patients with high-risk disease remain relapse free for > 3 years with median follow-up 19.5 months;
No AML patients have relapsed to date



Note: *POD = progression of disease;
*As of August 1, 2024; Early trial results are not indicative of future results, including the outcome of this trial.

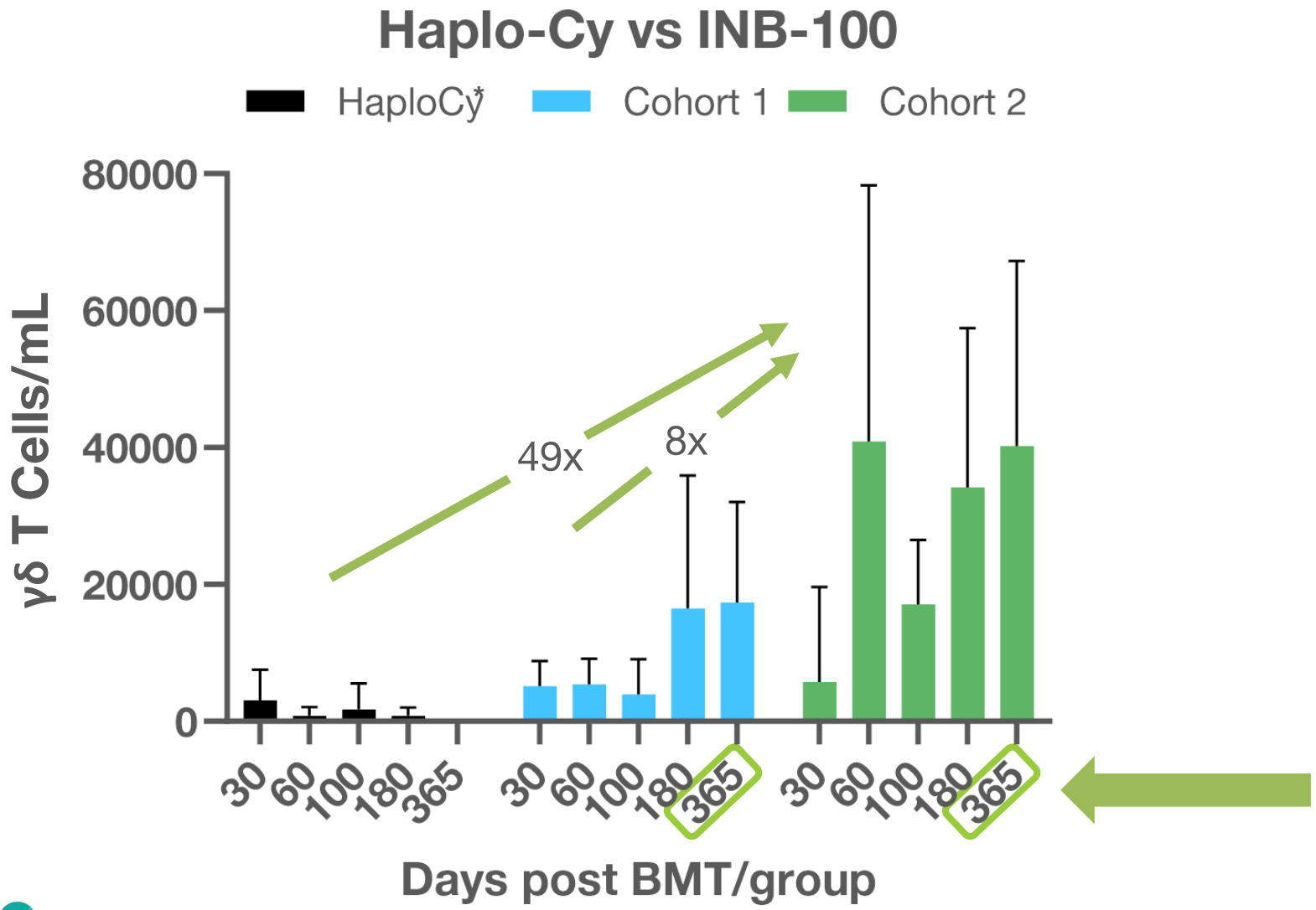
Chimerism Data Confirms 1-year RFS for 10/10 Patients

	Dose Level 1				Dose Level 2 - RP2D					
	101-002	101-003	101-006	101-007	101-009	101-010	101-011	101-012	101-013	101-014
Infusion	●	●	●	●	●	●	●	●	●	●
Day 30	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Day 60	✓	✓	✓	✓	✓	✓	✓	✓	na	✓
Day 100	✓	✓	na	✓	✓	na	✓	✓	✓	✓
Day 180	⬢	na	✓	✓	✓	✓	✓	✓	✓	✓
Day 365	✓	na	✓	✓	✓	✓	⬢	✓	✓	✓
Morphologic CR @ 1yr	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

- Cohort 1
- Cohort 2
- EAGD Infusion
- Cytogenetic CR
- Morphologic CR
- Mixed chimerism requiring clinical intervention

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

One-Year *In Vivo* Persistence and Expansion of γδ T Cells



- Comparison of γδ T cell count recovery between patients who received haploidentical BMT + post-BMT Cy without γδ T cell infusion and INB-100 patients from Cohort 1 and Cohort 2
- Dose dependent increase of circulating γδ T cells at Days +60, +100, +180 and +365 for INB-100 treated patients
- Despite Cohort 2 patients receiving 3x the γδ T cell dose as Cohort 1, an 8x increase in γδ T cells was observed at 60 days
- Continued presence at 365 days suggests **in vivo expansion AND persistence** of cells

Source: IN8bio, Inc. and UAB *previously unpublished data from laboratory of Dr. Lawrence Lamb; as of August 1, 2024

Registrational Trial Design

Registrational Phase 2 Trial

γδ T Cells Maintenance Therapy in AML Patients Undergoing Haploidentical Transplant

AML
N~287

- Adult AML patient with high risk features in CR1
- Adult AML patients with relapse
- KPS≥70
- Hematopoietic cell transplant comorbidity index (HCT-CI) ≤ 3
- Prior allotransplant excluded
- Exclude CrCL<50mL/min
- No active CNS involvement
- Exclude CBL or APL, biphenotypic leukemia, MDS, MPN

2:1

Arm A: Experimental n=191

RIC Haploidentical transplant with post-transplant cyclophosphamide with $3x10^6$ cells/kg unmodified γδ T cells administered at engraftment

Arm B: SOC n=96

RIC Haploidentical transplant with post-transplant cyclophosphamide with NO maintenance

Stratification Factors:

- Age (<65, ≥65)
- Poor risk cytogenetics: *defined by ELN 2022 criteria*
- *Presence of MRD+ peri-transplant*

Powering:

- Target Hazard Ratio (HR) = 0.667
- 80% Power

Primary Endpoint:

- **Relapse Free Survival**

Secondary Endpoints:

- AE's including GvHD
- Time to relapse
- OS
- QoL

Targeting Solid Tumor Cancers

Shortfalls of Conventional Cell Therapies in Solid Tumors

CAR-Ts have demonstrated efficacy in blood cancers but have not had similar results in solid tumors

Tumor heterogeneity

Tumor cells harbour distinct molecular signatures with varying treatment sensitivity

T Cells unable to penetrate tumor

Unrecognizable and impenetrable; malignant cells turn off antigens and receptors for immune evasion

Few targets that can be ablated

Unfavorable therapeutic profile of conventional immunotherapy with off-target recognition

Immune-suppression

T_{Regs} of the tumor microenvironment (TME) suppress $T_{Effector}$ function and anti-tumor response

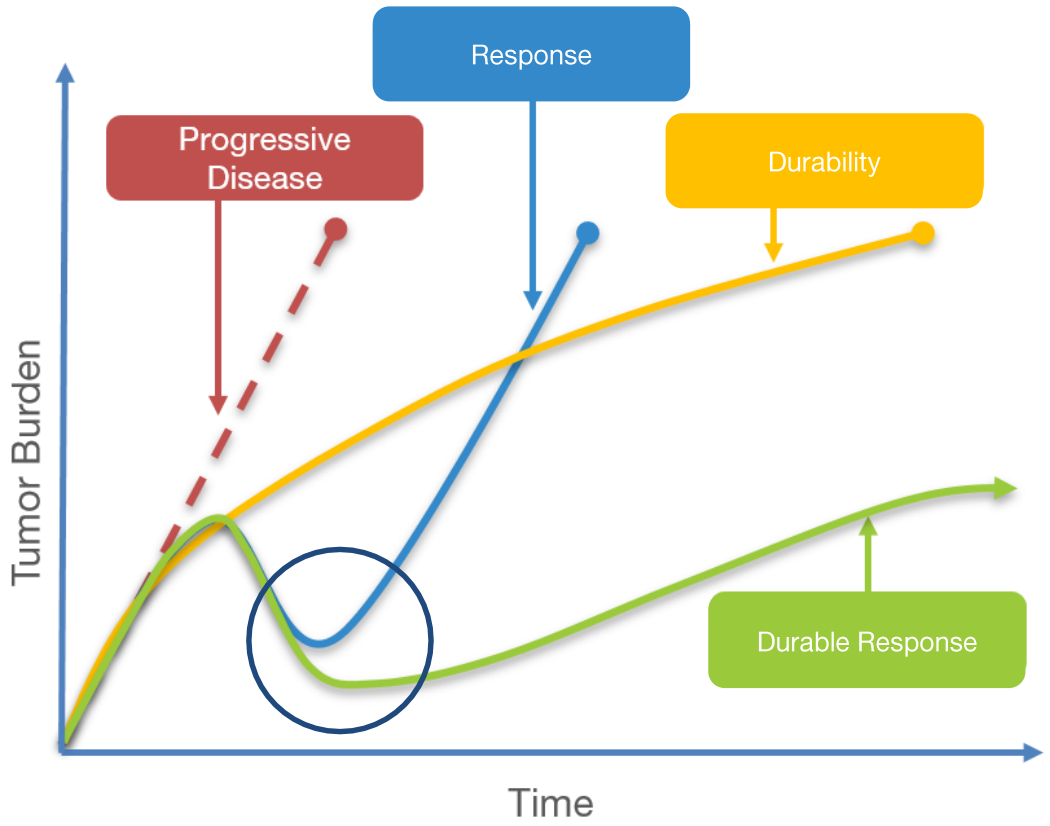
Trafficking of T cells into Tumors

Effective immunotherapy requires concerted and abundant T cell migration to the disease site

Chemotherapy kills immune cells

Non-selective cytotoxicity kills immune cells required for tumor surveillance and targeting

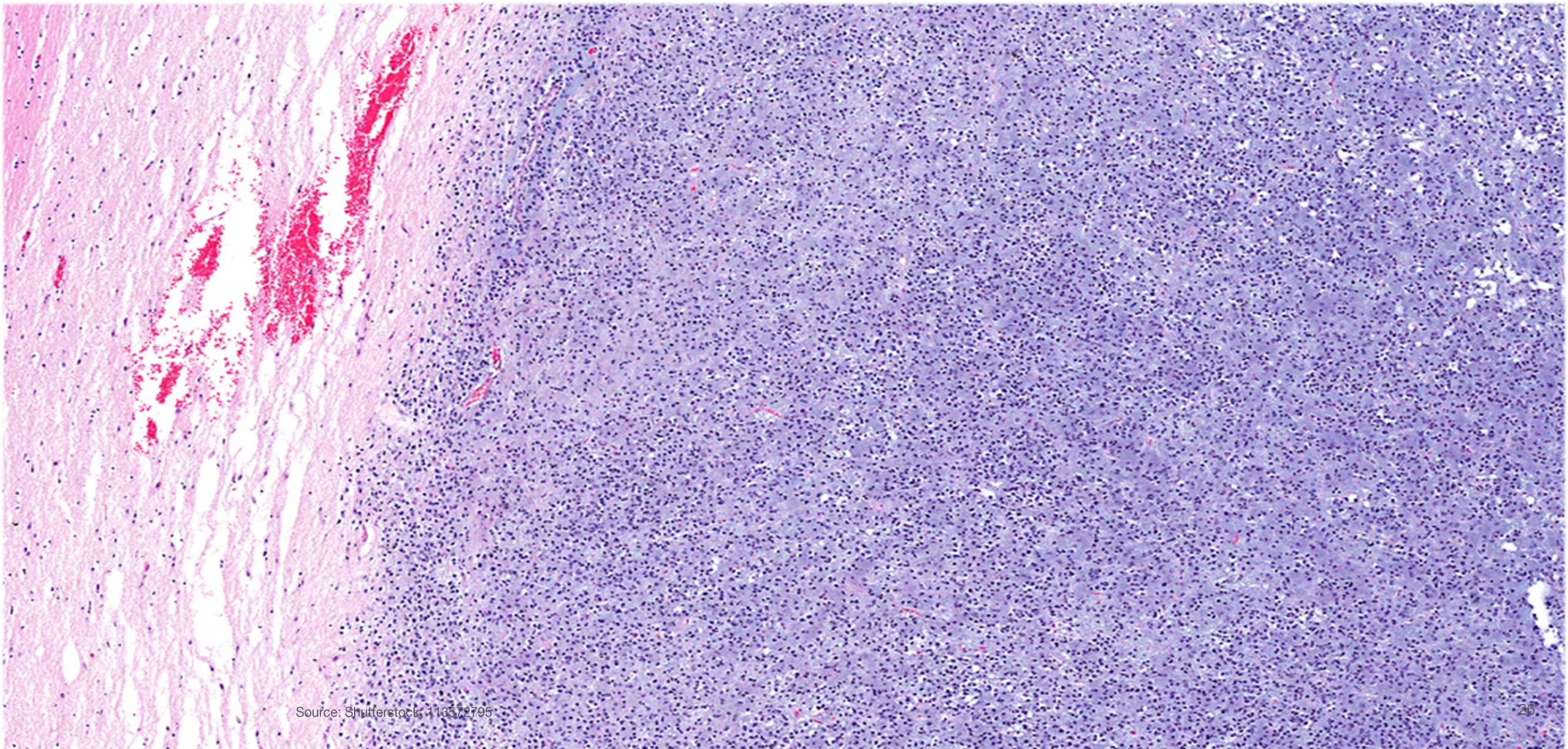
Targeting Cancers by Driving Deeper Responses



γδ T cells Genetically Engineered to Survive Chemotherapy Induced Cell Death

Source: Adapted from Madan et al. Sem in Onc. 2012, Vol 39, No 3 and Ribas et al. Clin Canc Res, 18(2), Jan. 2012

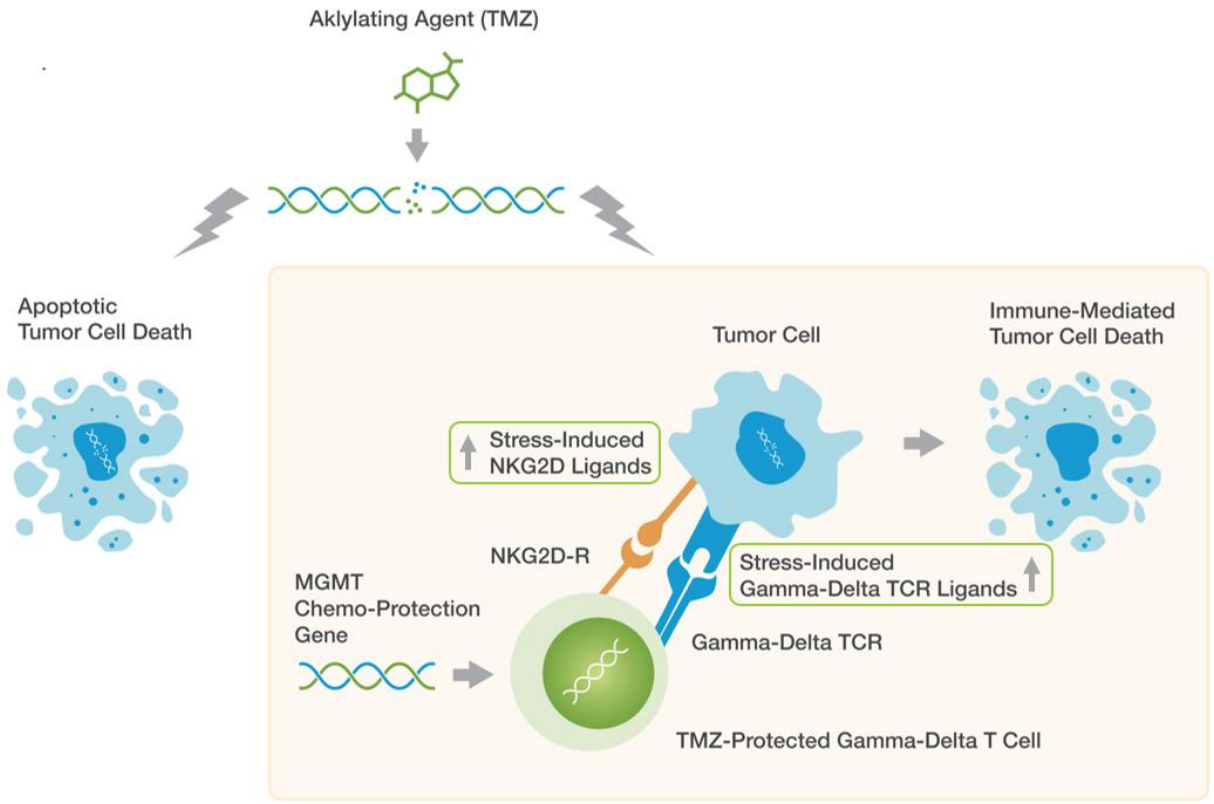
Overcoming Challenges to Targeting Solid Tumors



Source: Shutterstock, 113572795

Targeting the DNA Damage Response (DDR) to Kill Tumors

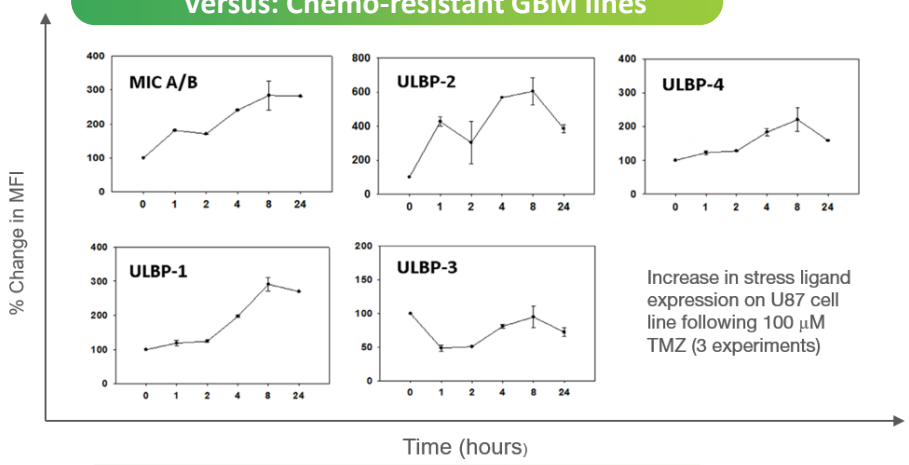
DDR is a biological process that can detect and eliminate cells with DNA damage through increased avidity



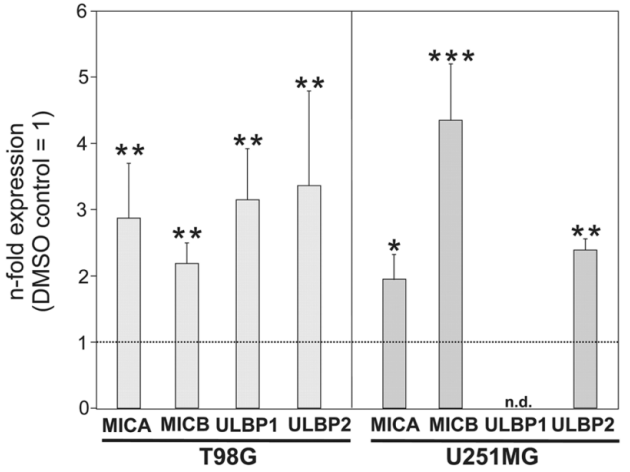
DRI gamma-delta T cell mechanism overview

TMZ Increases NKG2D-L Expression:

Versus: Chemo-resistant GBM lines



Versus: Glioma stem-like cells



Source: IN8bio, Lamb et al. Plos One, (2013) Vol 8., Issue 1, Held-Feindt et al. Histochemistry and Cell Biology, (2018) 149: 2019-233; https://doi.org/10.1007/s00418-018-1633-5

Peer Reviewed Pre-Clinical Data for INB-200/400 Published

scientific reports

Check for updates

OPEN

A combined treatment regimen of MGMT-modified γδ T cells and temozolomide chemotherapy is effective against primary high grade gliomas

Lawrence S. Lamb[1]✉, Larisa Pereboeva[1], Samantha Youngblood[1], G. Yancey Gillespie[2], L. Burton Nabors[3], James M. Markert[2], Anindya Dasgupta[4], Catherine Langford[2] & H. Trent Spencer[4]

Chemotherapeutic drugs such as the alkylating agent Temozolomide (TMZ), in addition to reducing tumor mass, can also sensitize tumors to immune recognition by transient upregulation of multiple stress induced NKG2D ligands (NKG2DL). However, the potential for an effective response by innate lymphocyte effectors such as NK and γδ T cells that recognize NKG2DL is limited by the drug's concomitant lymphodepleting effects. We have previously shown that modification of γδ T cells with a methylguanine DNA methyltransferase (MGMT) transgene confers TMZ resistance via production of O^6-alkylguanine DNA alkyltransferase (AGT) thereby enabling γδ T cell function in therapeutic concentrations of TMZ. In this study, we tested this strategy which we have termed Drug Resistant Immunotherapy (DRI) to examine whether combination therapy of TMZ and MGMT-modified γδ T cells could improve survival outcomes in four human/mouse xenograft models of primary and refractory GBM. Our results confirm that DRI leverages the innate response of γδ T cells to chemotherapy-induced stress associated antigen expression and achieves synergies that are significantly greater than either individual approach.

Source: Lamb et al., Scientific Reports, 2021) 11:21133 - https://doi.org/10.1038/s41598-021-00536-8

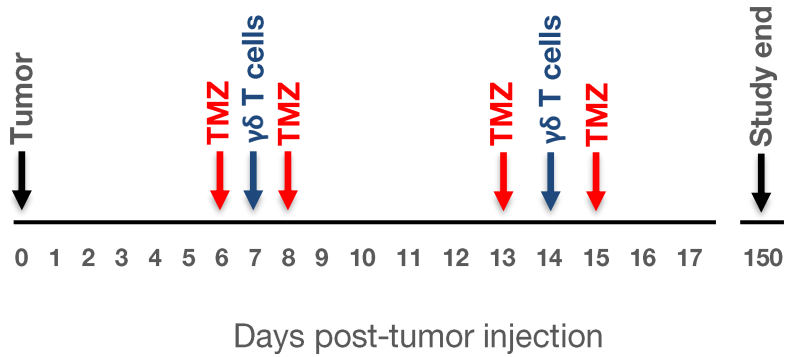
Dosing to Optimize DRI Therapy

- Optimal dosing for DRI combinations either to:
  - Sequence to preserve maximal number of gamma-delta T cells; or
  - Dose together to maximize expression of NKG2D ligands on the tumor surface
- TMZ has a $T_{1/2}$ of ~1.8 hours, a T_{max} of ~1 to 2.3 hours and remains in the plasma for 8+ hours
- TMZ has 100% oral bioavailability and availability of ~30 to 40% across the blood brain barrier
- NKG2DL on chemo-resistant tumors reach peak between 4 to 24 hours after chemo infusion

Dosing Regimen

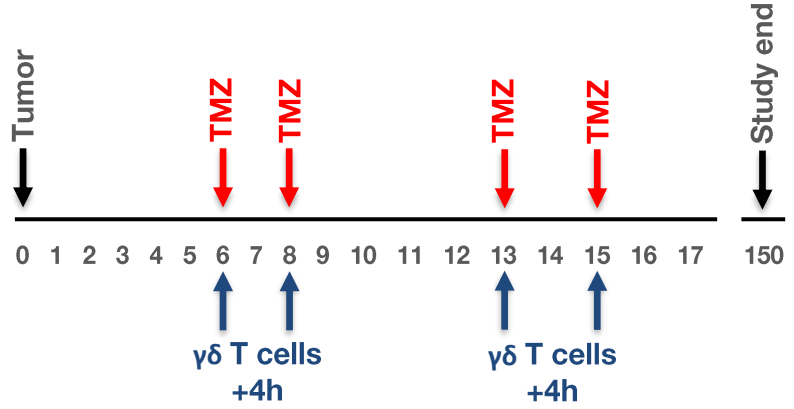
Condition 1

(preserves maximal number of γδ T cells)



Condition 2

(takes advantage of maximum NKG2DL expression)



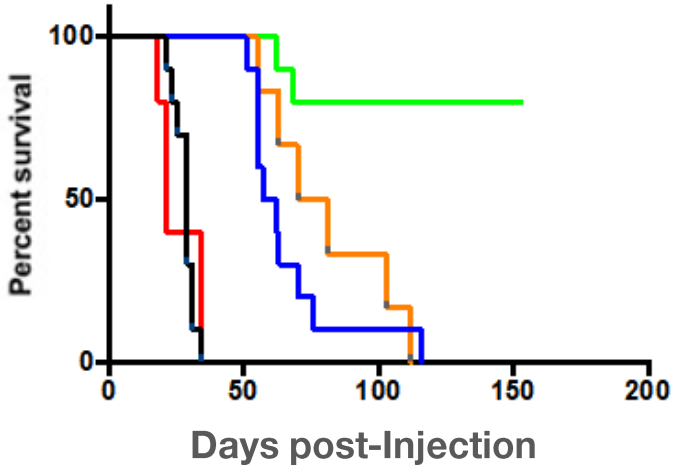
Source: Lamb et al. Scientific Reports (2021) 11:21133 - https://doi.org/10.1038/s41598-021-00536-8

DRI in a Preclinical GBM Model

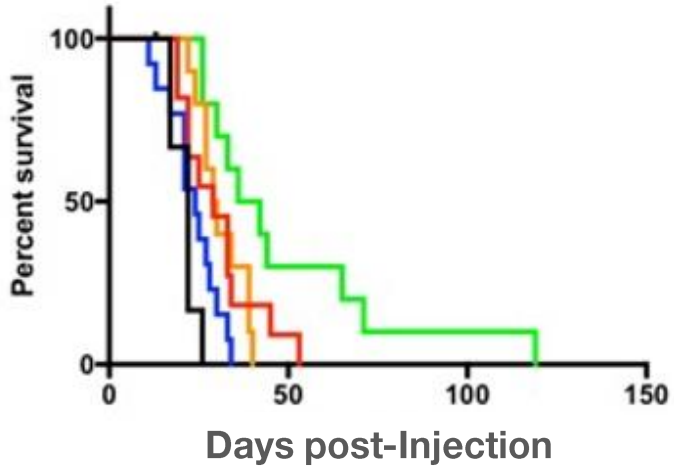
80% of animals show survival beyond 150-days with DRI combination in GBM

- DRI = TMZ + TMZ Resistant γδ T cells dosed together
- Temodar (TMZ) increases cell surface expression of NKG2D ligands and sensitizes GBM cells to γδ T cell lysis^
- In animals with TMZ resistant tumors, DRI showed 41% increased survival (38 vs. 27 days, p=0.017) confirming targeting via cell stress
- Data presented at EBMT 2017 (https://goo.gl/16qPgs)

TMZ vs. DRI+TMZ*
(primary patient glioma; classical)



TMZ vs. DRI+TMZ*
(TMZ-**Resistant** glioma)

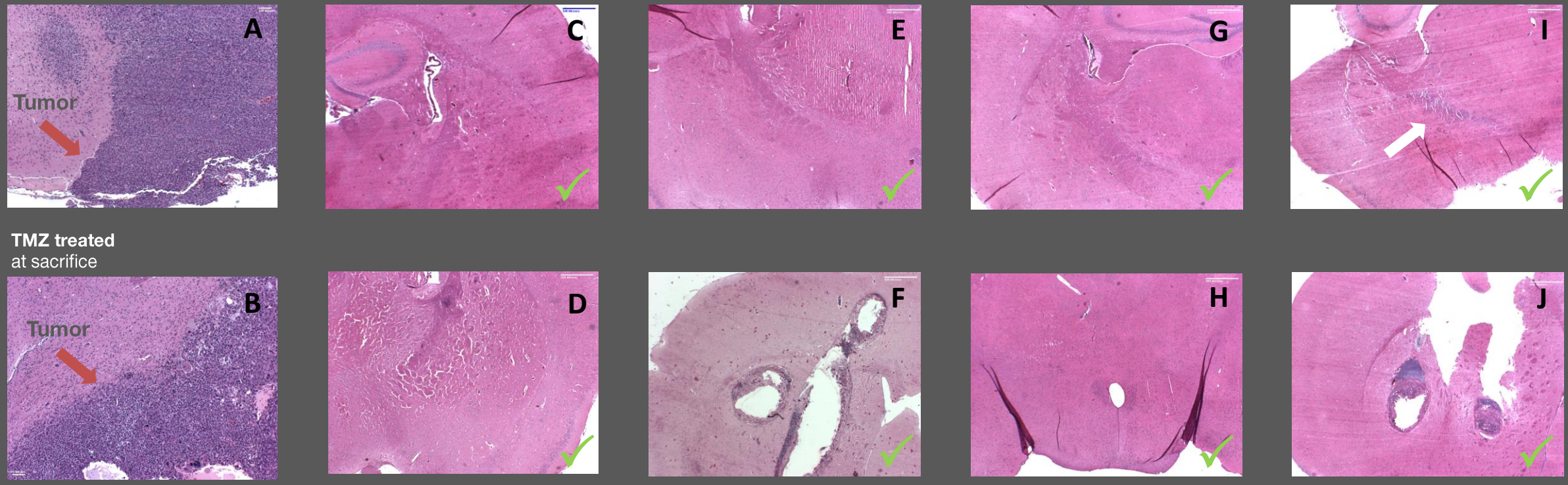


Source: Lamb et al. Scientific Reports (2021) 11:21133 - https://doi.org/10.1038/s41598-021-00536-8

Targeting the DDR Pathway Eliminates Residual GBM

Untreated
+14 days

TMZ + DRI gamma-delta T cells treated - surviving mice (n=8)



✓ - Long-Term Survival (+150 days)

Figure 1: Digital light microscopic images from athymic nude mice that received intracranial injection of 5 x 10^5 GBM tumor cells derived from classical human patient GBM xenograft JX12P. Images (A) show hematoxylin and eosin (H&E) staining of tumor growth (dark purple - noted by red arrow) from untreated mice at +14 days following stereotactic tumor placement in the left caudate nucleus (4x); (B) was obtained at euthanasia following fatal tumor progression from a mouse treated with temozolomide (TMZ) (4x); (Images: C - J) surviving mice treated with TMZ + DRI γδ T cells, 80% (n=8) demonstrated long-term survival (+150 days) following tumor placement, at the time of euthanasia these mice demonstrated improved survival with no observable neurologic dysfunction and are negative for H&E staining and the white arrow (I) points to scarring where residual necrotic tumor has been cleared.

IN8bio

Source: Lamb et al. Scientific Reports (2021) 11:21133 - https://doi.org/10.1038/s41598-021-00536-8

INB-200

DeltEx DRI Auto for GBM

Pursuing Treatment in GBM: Following the Biology

The biology shows us the multiple advantages of γδ T cells in the solid tumor setting, particularly in glioblastoma, where patients have **very limited available treatment options.**

The brain offers a separate compartment that allows direct delivery of cells through a catheter directly to the site of the tumor, increasing E:T ratio and reducing the variable of cell trafficking.

As we move towards allogeneic cell therapy in the solid tumor setting it simplifies the challenges around dealing with host-versus-graft (HvG) effect and the persistence of the delivered cells.

The advantage of going into the brain is that it is one of three organ centers in the body historically considered immune-privileged.

In neuro oncology, the standard of care, Temodar, is lymphodepleting in itself. A separate lymphodepleting protocol such as Flu/Cy is not necessary.

INB-200: Study Design and Treatment Schema

Treatment Arms

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

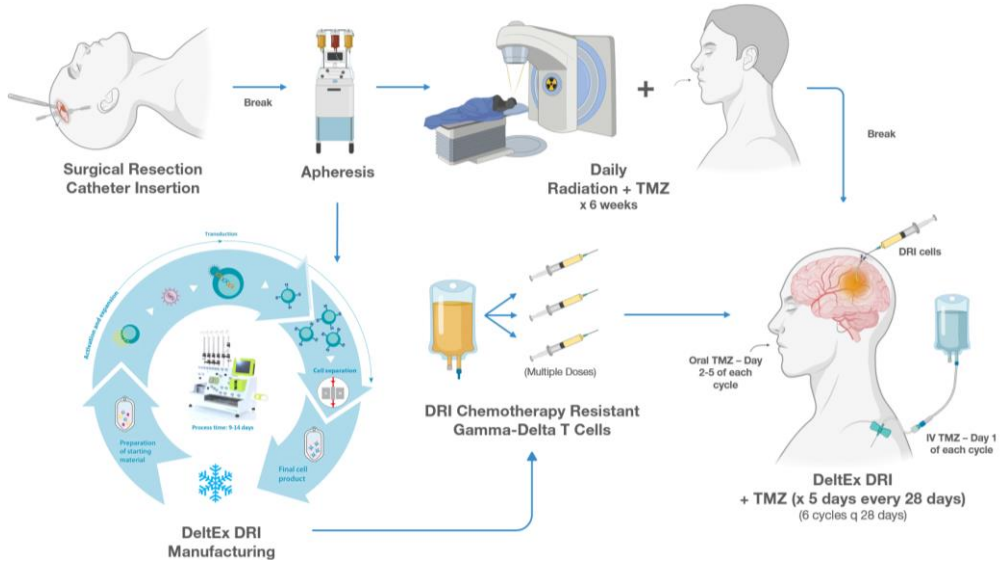
DL1: N = 3 (up to 6) patients, single dose of 1 x 10^7 cells on C1D1
DL2: N = 3 (up to 6) patients, three doses of 1 x 10^7 cells, one dose every 28 D1 of C1-C3
DL3: N = 3 (up to 6) patients, six doses of 1 x 10^7 cells, one dose every 28 days on D1 of C1-C6

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

Source: IN8bio, image created with biorender.com

Poor Survival and Standard of Care Hasn't Changed in 18 Years

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma

Roger Stupp, M.D., Warren P. Mason, M.D., Martin J. van den Bent, M.D., Michael Weller, M.D., Barbara Fisher, M.D., Martin J.B. Taphoorn, M.D., Karl Belanger, M.D., Alba A. Brandes, M.D., Christine Marosi, M.D., Ulrich Bogdahn, M.D., Jürgen Curschmann, M.D., Robert C. Janzer, M.D., et al., for the European Organisation for Research and Treatment of Cancer Brain Tumor and Radiotherapy Groups and the National Cancer Institute of Canada Clinical Trials Group*

- N = 573
- Median age 56 (range 19-71)
- PS 2 only 12%
- RT+TMZ median OS 14.6 months
- RT+TMZ median PFS 6.9 months (95% CI 5.8-8.2)
  - MGMT methylated 10.3 months
  - **MGMT unmethylated 5.3 months**

ORIGINAL ARTICLE

Short-Course Radiation plus Temozolomide in Elderly Patients with Glioblastoma

James R. Perry, M.D., Normand Laperriere, M.D., Christopher J. O'Callaghan, D.V.M., Alba A. Brandes, M.D., Johan Menten, M.D., Claire Phillips, M.B., B.S., Michael Fay, M.B., Ch.B., Ryo Nishikawa, M.D., J. Gregory Cairncross, M.D., Wilson Roa, M.D., David Osoba, M.D., John P. Rossiter, M.B., B.Ch., et al., for the Trial Investigators*

- N = 562
- Median age 73 (range 65-90)
- PS 1 – 54%; PS 2 – 23%
- RT+TMZ median OS 9.3 months
- RT+TMZ median PFS 5.3 months
  - MGMT methylated 7.9 months
  - **MGMT unmethylated 4.8 months**

IN8bio

Source: NEJM 2005; 352:987-996 DOI: 10.1056/NEJMoa043330; NEJM 2017; 376:1027-1037 DOI: 10.1056/NEJMoa1611977

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	37.9+	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	15.7+	Alive
020	66 / M	IDH-WT, MGMT-methylated	3	Subtotal	6	SD	13.8+	Alive
021	57 / M	IDH-WT, MGMT-unmethylated	3	Total	5	SD	12.3+	Alive
022	53 / M	IDH-WT, MGMT-unmethylated	3	Subtotal	3	SD	9.5+	Alive
023	52 / M	IDH-WT, MGMT-unmethylated	3	Subtotal	1	PD	4.2	5.4

- **Median age: 68**
- **54% unmethylated**
- **23 enrolled, five products unable to be manufactured**
- **Of 13 treated, 5 remain in follow-up**
- **8 deaths:**
  - 7 due to PD or disease-related issues
  - Other:
    - Cardiac event (007)

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

Patient 009 – Surpassing Expectations for IDH-mut Glioma

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

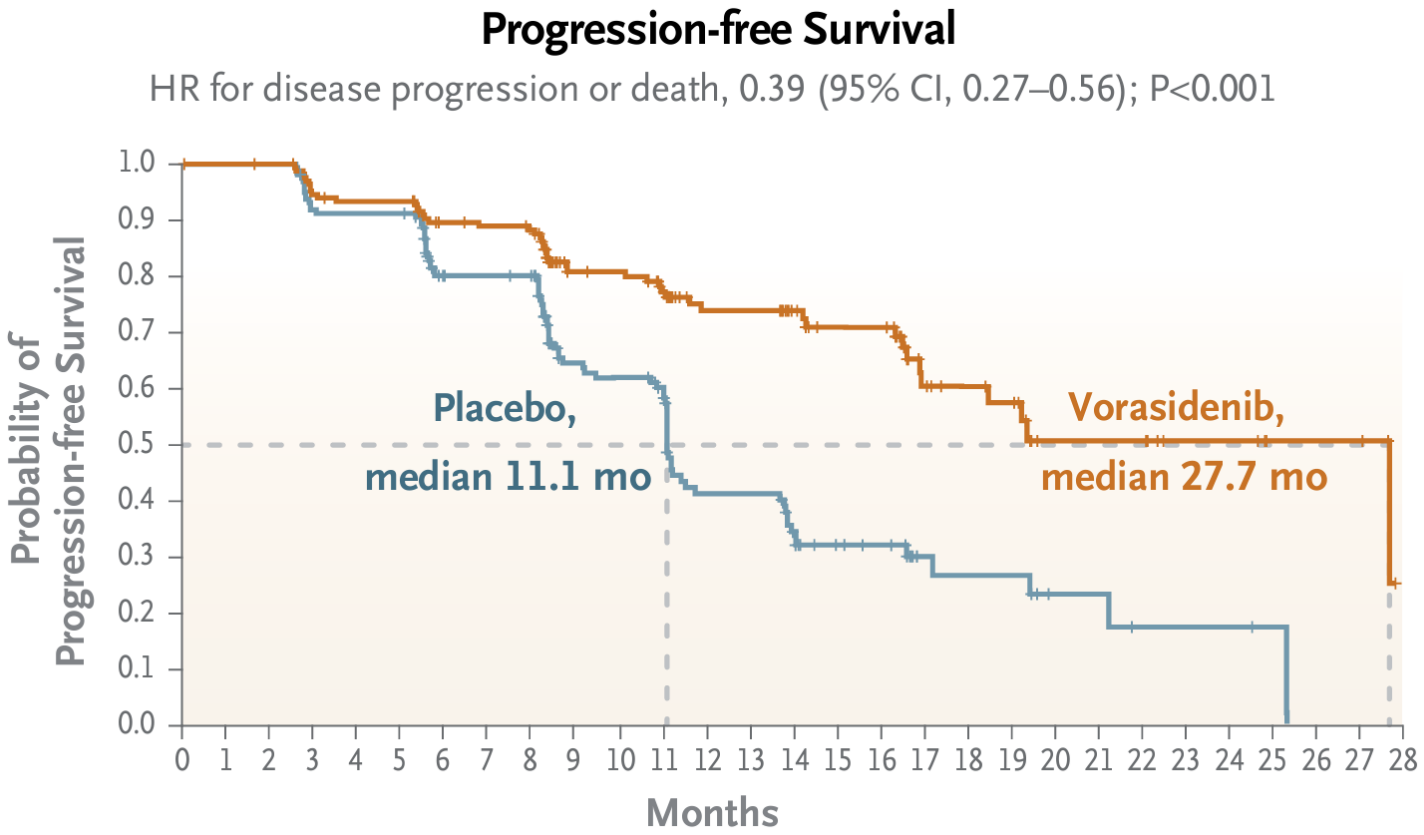
Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma

Mellinghoff IK et al. DOI: 10.1056/NEJMoa2304194

CLINICAL TRIAL

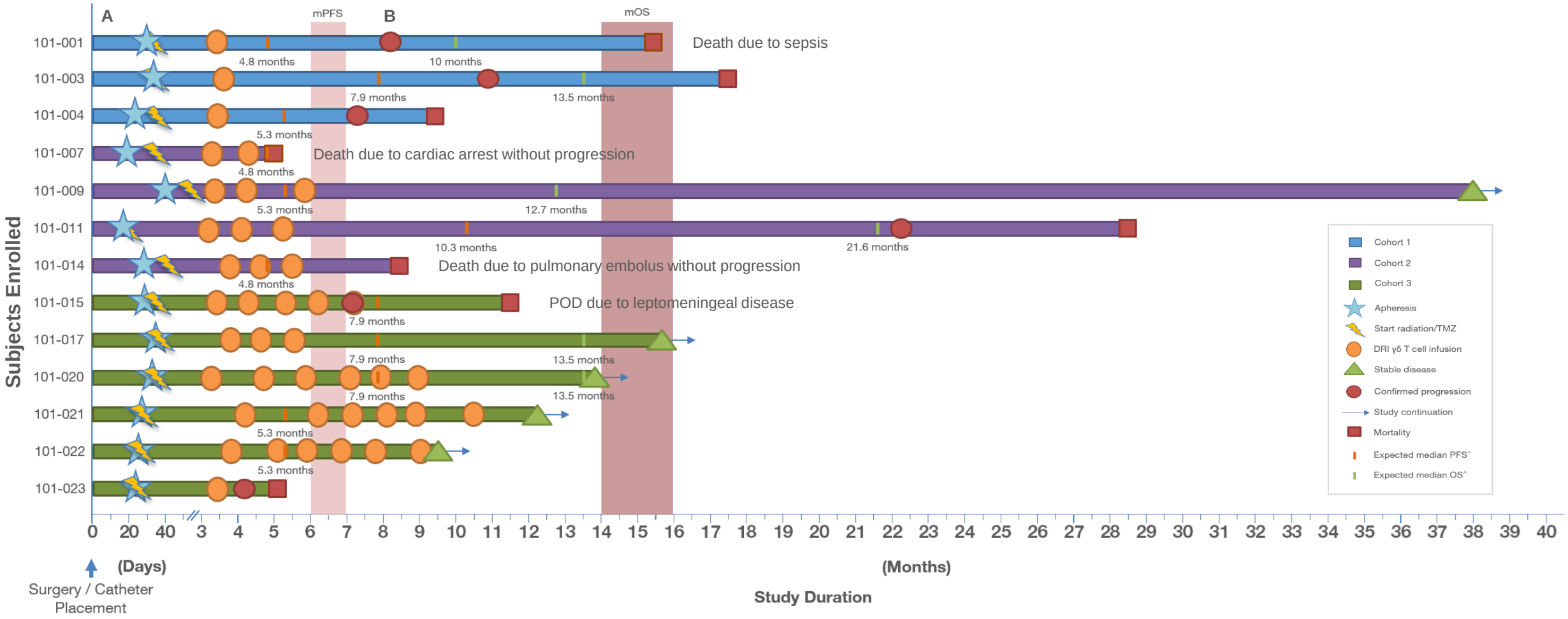
Design: This phase 3, double-blind, randomized, placebo-controlled trial tested the clinical effects of vorasidenib — an oral brain-penetrant inhibitor of mutant IDH1 and IDH2 enzymes — in patients with residual or recurrent grade 2 IDH-mutant glioma who had undergone surgery as their only previous treatment.

Intervention: 331 patients were assigned to receive oral vorasidenib (40 mg once daily) or matched placebo in 28-day cycles. The primary end point was imaging-based progression-free survival.



92%* Exceeding Stupp Regimen Median PFS of 7 months

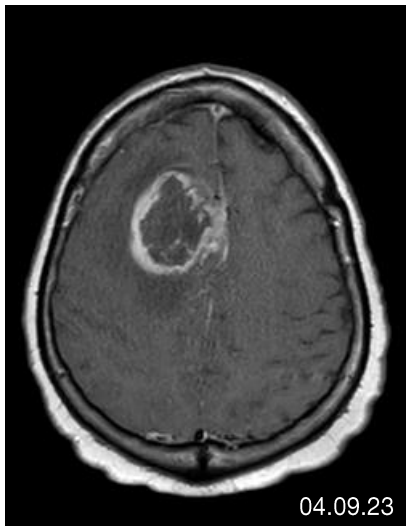
Median Follow-up: 12.3 months

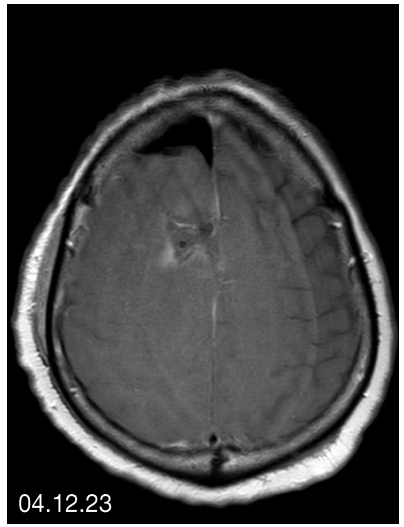


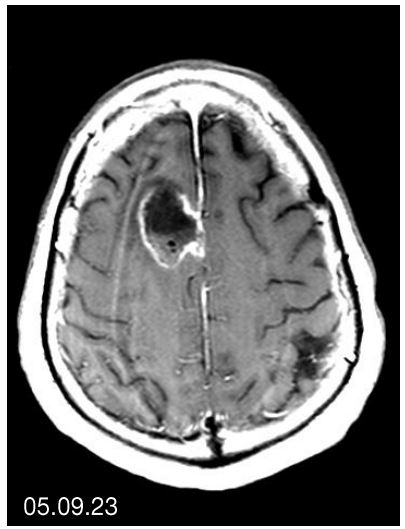
Note: ***Of Evaluable Subjects; POD = progression of disease***; As of August 1, 2024; Source: ^NEJM 2005; 352:987-996 & 352:997-1003 DOI: 10.1056/NEJMoa043330, DOI: 10.1056/NEJMoa043331; NEJM 2017; 376:1027-1037 DOI: 10.1056/NEJMoa1611977; ˣ Not yet treated; Early trial results are not indicative of future results, including the outcome of this trial.

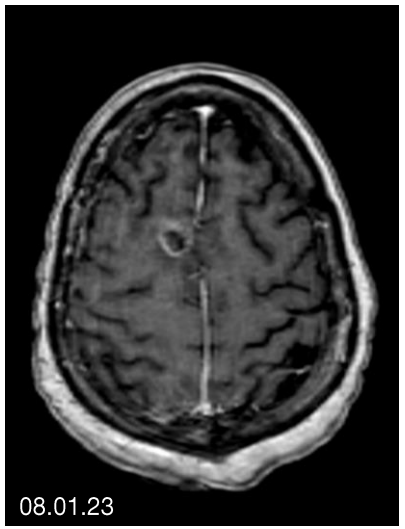
Patient 017 – Female 77y, IDH-wt, MGMT-methylated

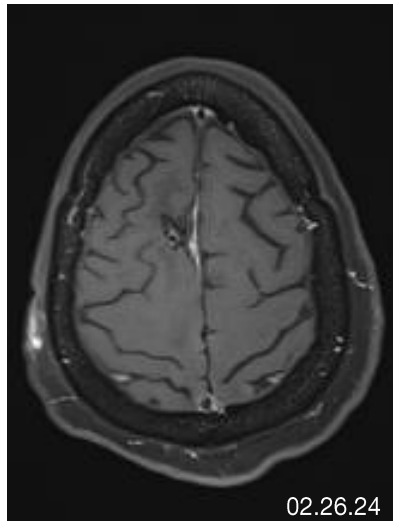
Remains alive and relapse-free at 12.7+ months; “Demonstrated continued slight decrease in size of heterogenous enhancing lesions and decrease in size of nodular enhancing component”

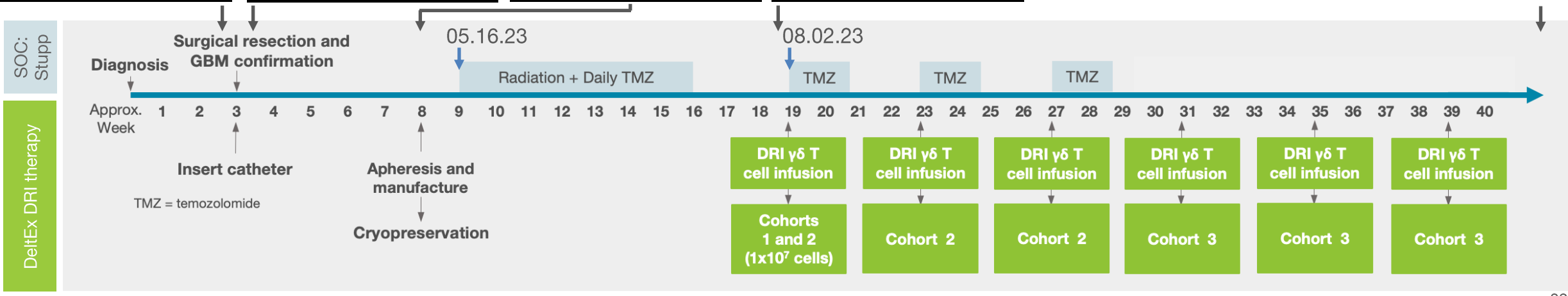










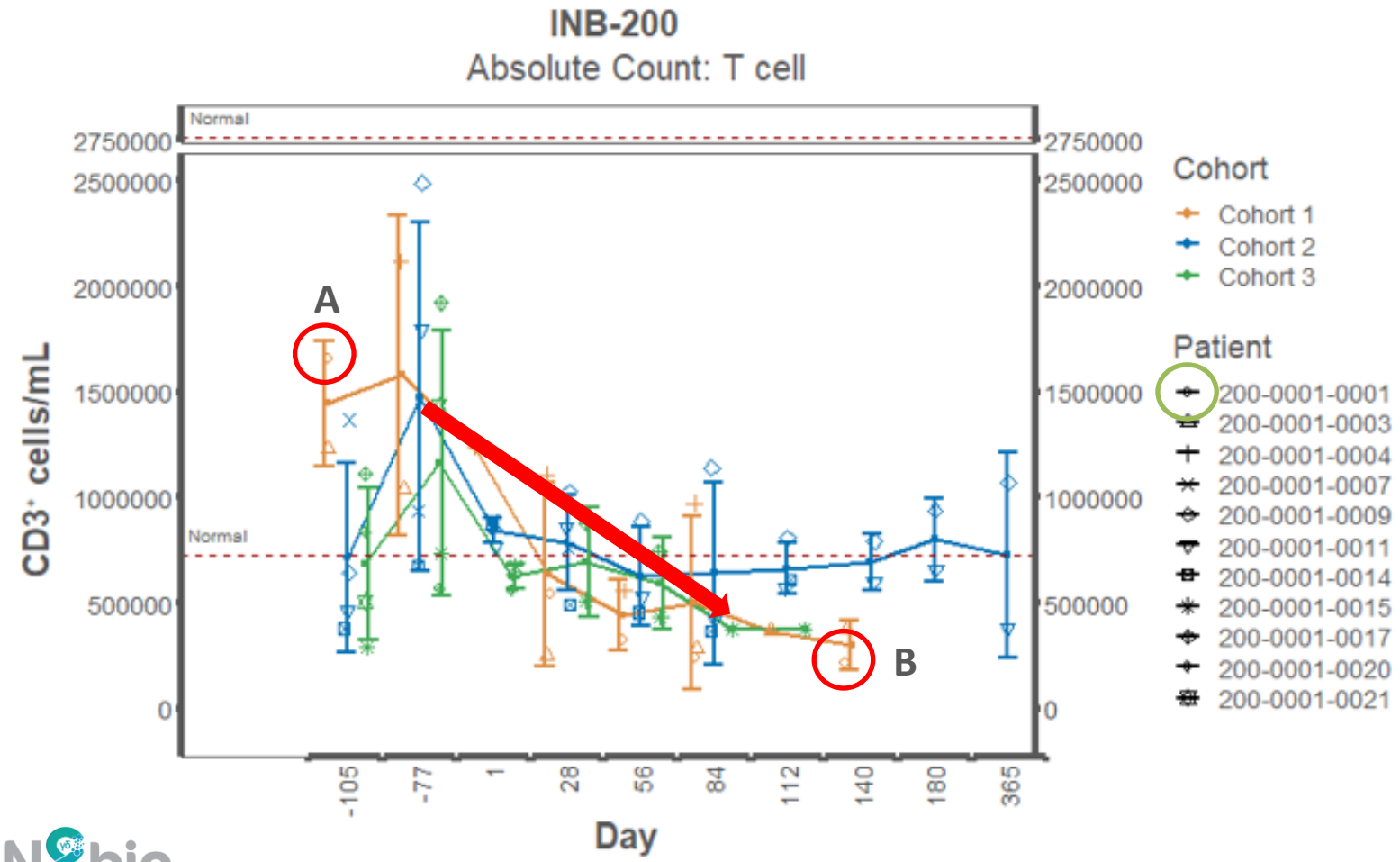


Results from one patient are not indicative of future results including the outcome of this trial

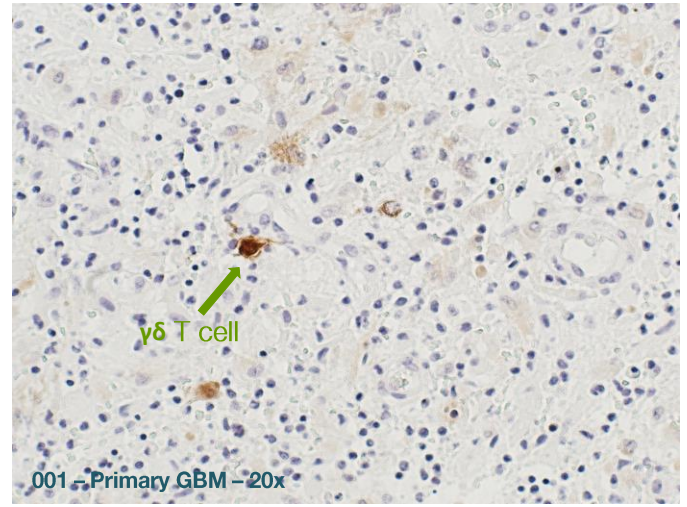
Source: IN8bio and UAB

γδ T Cells are Infiltrating and Persisting in Tumor Tissue

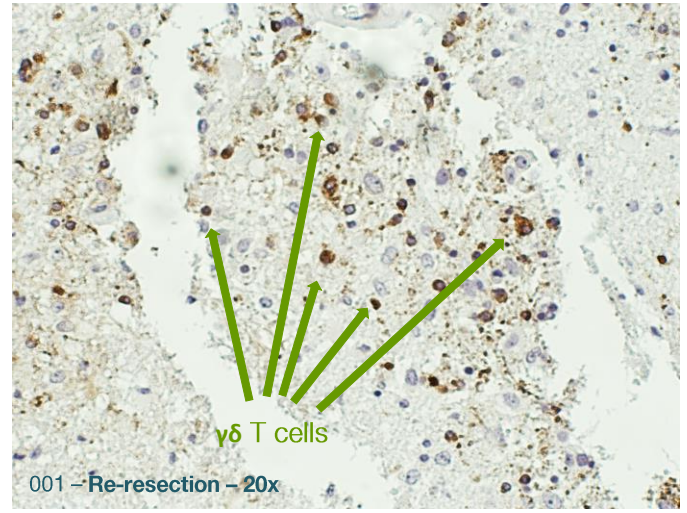
Preserved γδ cells in relapsed tumor 148 days post-DRI infusion despite significant peripheral lymphodepletion in patient 001



Biopsy A: at diagnosis



Biopsy B: at relapse, 148 days after single dose



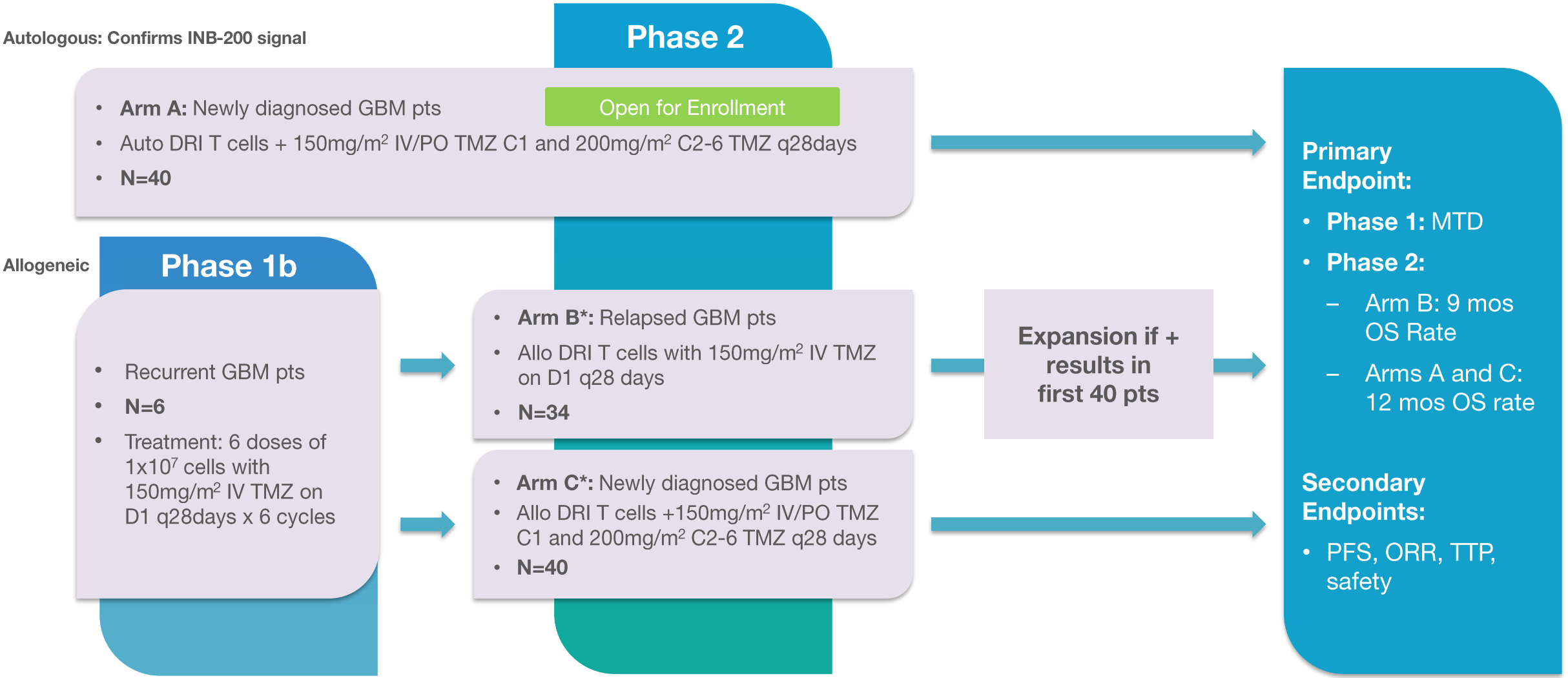
Source: IN8bio and UAB

INB-400

DeltEx DRI for GBM

Phase 2 – “Arm A” Enrolling Newly Diagnosed GBM Patients

INB-400: Study Design and Treatment Schema



*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)

Corporate

Historical & Anticipated Milestones Across Pipeline^

Balance Sheet

(as of June 30, 2024)

- Cash of ~$10.2M
  - Provides runway into 1Q25
  - Potential for up to ~$33M in additional capital at increasing valuations from convertible securities issued in 4Q23
  - $0 debt
- $108.2M accumulated deficit on $122.0M raised

- Ticker: **INAB**
- 46.8 million common shares outstanding as of August 1, 2024

2023 2H

INB-100	100% of Patients in Phase 1 leukemia trial in mCR (ASH Dec. 11, 2023)
INB-200	Additional Phase 1 data (cohorts 2 & 3) in GBM (SNO Nov. 17, 2023)
INB-300	Positive preclinical data demonstrated proof-of-concept of nsCAR CD33 platform @ R&D Day
INB-400	Initiation of enrollment of first patient in 2H23
INB-500	iPSC development update (SITC Nov. 4, 2023)

2024

INB-100	Enroll patients in expansion cohort at DL 2
	Report long-term follow-up results at multiple medical meetings in 2024
	Potentially submit IND for registrational RCT trial in AML
INB-200	Completion of Phase 1 enrollment
	Long-term follow-up results at multiple medical meetings in 2024
INB-300	Updated proof-of-concept data on nsCAR platform targeting AML at American Association for Cancer Research (AACR) 2024
INB-400	Dose first patient in 1H24
	Potentially submit IND for Allo Phase 1b in relapsed GBM in 2025

^Timing of next anticipated milestones are estimates based on the successful raise of additional capital to fund our programs and subject to change

Harnessing the Power of γδ T Cells

- Utilizing innovative approaches to efficiently advance our programs
- Demonstrating the ability to execute and to build our business methodically and intentionally
- Pursuing rigorous science to achieve better patient outcomes
- Completed enrollment in INB-100 and INB-200 Phase 1 trials
- Actively enrolling patients in INB-400 Phase 2 trial
- Near-term value creating milestones with presentations and clinical data updates at medical meetings throughout 2024 and 2025

Join Us on Our Mission to Achieve…

Cancer Zero™

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