INB-100: Pilot Study of Donor Derived, Ex-Vivo Expanded/Activated Gamma-Delta T Cell Infusion Following Haploidentical Hematopoietic Stem-Cell Transplantation and Post-Transplant Cyclophosphamide

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EHA EUROPEAN HEMATOLOGY ASSOCIATION
Abstract: P1460

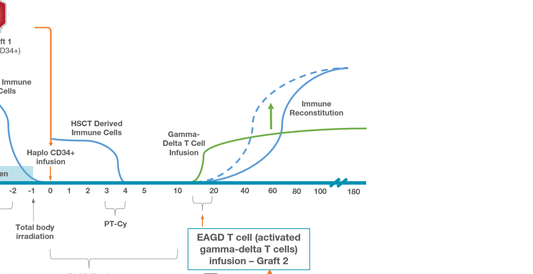
Introduction

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. γδ T cells recognize and lyse malignant cells via innate sensing of stress-associated antigens. These MHC unrestricted cells do not initiate graft-versus-host disease (GvHD), are directly anti-leukemic and may address the 50% incidence of relapse post-transplant. Infusion of donor derived allogeneic ex vivo activated γδ T cells (EAGD) post haplo-identical stem cell transplantation may decrease relapse without severe GvHD. We present updated clinical and correlative data from the Phase 1 study.

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 up to ~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



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

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	49.6+	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	35.5+	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 19.1+
010	2	63 / female	7 cycles Venetoclax/Aza	AML	Acute G2b rash - GvHD	18.9+	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 16.0+
012	2	69 / male	2 cycles Venetoclax/Aza	AML		12.5+	Alive
013	2	71 / female	1 cycle Ven/aza/gilteritinib 2 cycles Venetoclax/Aza	AML, **FLT3**	Acute G1 diarrhea - not GvHD Oral sensitivity- not GvHD	12.2+	Alive
014	2	71 / male	Venetoclax/Dacogen	AML, del20, -Y	Acute G1 diarrhea - not GvHD Acute G1 rash - not GvHD	11.8+	Alive

Note: As of May 31, 2024; Early trial results are not indicative of future results, including the outcome of this trial.

Median 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

Treatment Emergent AE's in ≥ 20% of Patients (n=10)

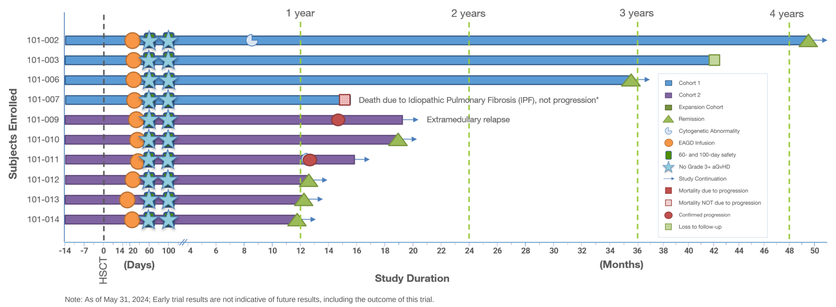
Adverse Events	Total (%)	Grade 1/2 (%)	Grade 3 (%)	Grade 4 (%)
Platelet count decreased	100	40	60	
WBC decreased	90	50	30	10
ANC decreased	80	40	10	30
ALC decreased	60		40	20
Anemia	90	50	40	
Hypomagnesemia	60	60		
Creatinine increased	50	50		
Hyperglycemia	20	10	10	
Hypokalemia	40	40		
Hyponatremia	40	40		
Hypertension	30	30		
Hypotension	20	20		
Nausea	20	10	10	
Vomiting	20	20		
Diarrhea	20	20		
Dry Mouth	40	40		
Decreased appetite	20		20	
Peripheral edema	20	20		
Peripheral sensory neuropathy	20	20		
Dyspnea	30	30		
Insomnia	20	20		
Pollakiuria	20	20		
Rash maculopapular	60	50	10	

Note: As of May 15, 2024 2024 with no new safety signals noted since May 15th DCO; Early trial results are not indicative of future results, including the outcome of this trial.

- **No DLT's, CRS or ICANs to date**
- **2 patients with CMV reactivation**
- **Treatment-related SAE's:**
  - G2 Rash maculopapular
  - G3 Nausea (aGvHD 2B GI)
- **Other non-treatment related SAE's include:**
  - G3 Acute Kidney Injury
  - G3 Anemia
  - G3 CMV reactivation
  - G3 Fall
  - G3 Decreased appetite
- **Low rates of infection**
- **No treatment-related deaths**
- **No SUSAR's or unexpected safety events**
- **No change in AE profile from DL1 to DL2**

100% Patients Remained in CR ≥ 12 Months

- Median follow-up of 17.4 months
- Three patients with high-risk disease remain relapse free for >35 months



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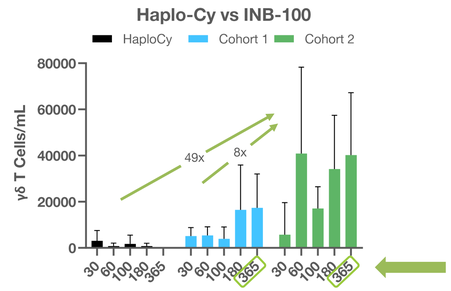
Chimerism Data Confirms 1-year RFS for 10/10 Patients

	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 May 31, 2024; Early trial results are not indicative of future results, including the outcome of this trial.

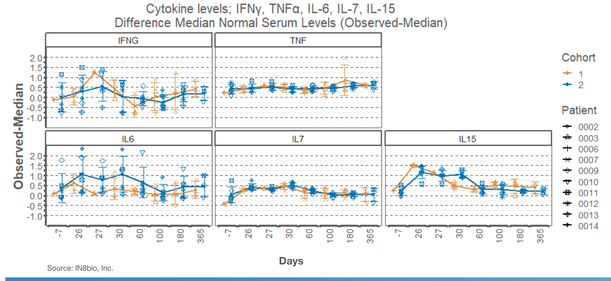
One-Year *In Vivo* Persistence and Expansion of γδ T Cells



Source: IN8bio, Inc. and UAB *previously unpublished data from laboratory of Dr. Lawrence Lamb; as of May 31, 2024

- 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

Serum Cytokines Consistent with Absence of Cytokine Induced Toxicity



Source: IN8bio, Inc.

- Following infusion of the γδ T cells, there is a decrease in IL-6, and IL-7, which increases post-BMT, indicating a positive impact of γδ T cells on immune function and a reduction in inflammatory cytokines.
- IFN-γ levels increase following γδ T cell infusion, suggesting immune activation and activity

Conclusions & Next Steps

- **100% of subjects treated with gamma-delta T cell infusion have maintained CR ≥12 months at an updated DCO of May 31, 2024, despite previously reported relapse rates of up to 51% at 1-year post-haploidentical transplantation**
- At a median follow-up of **17.4 months,** chimerism data confirms the 1-yr relapse free survival incidence
- Manageable consistent safety profile across dose cohorts with no new safety signals noted since May 15th DCO
- No greater than grade 2 acute GvHD and 30% incidence of chronic GVHD reported
  - One subject with chronic extensive and two with chronic limited GVHD
- No cytokine release syndrome (CRS), neurotoxicity (ICANS) or treatment related deaths with limited incidence of infections
- This is the first trial to demonstrate **in vivo expansion and persistence of γδ T cells for up to 1-year post-transplantation** suggesting continued γδ T cell surveillance against leukemic relapse
- Immune reconstitution post-γδ infusion is consistent with post-transplant immune reconstitution
- Given favorable risk:benefit ratio and prolonged relapse free survival (RFS), 10 patient expansion at DL2 is underway and the design of a confirmatory study will be announced soon
- We thank all the patients and caregivers for their participation in this study