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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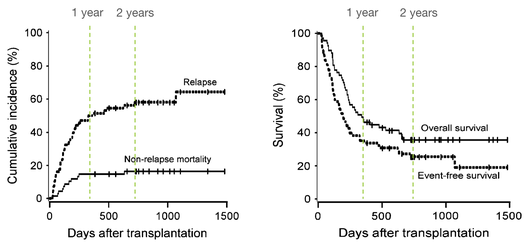
Introduction

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 up to 50% incidence of relapse post-transplant. Infusion of donor derived allogeneic ex vivo activated γδ T cells (EAGD) in older patients post haploidentical stem cell transplantation with reduced intensity conditioning (RIC) regimens 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

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 ← Recommended Phase 2 Dose (RP2D)
3. N = 3 (up to 6) patients, single dose of 1 x 10^7 cells/kg

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
- RP2D of DeltEx™ Allo gamma-delta T cell infusion
- Dose limiting toxicity (DLT)

Secondary Endpoints

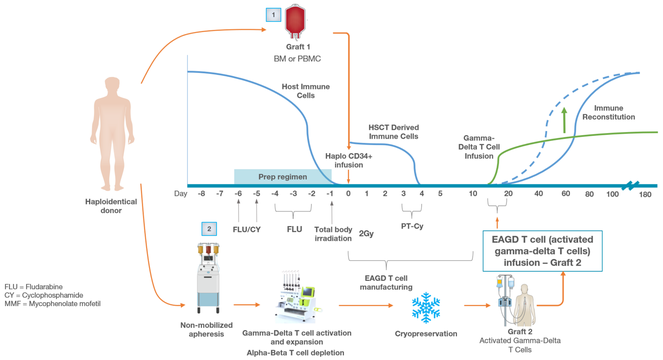
- Incidence of acute and chronic graft versus host disease (aGVHD), relapse, and overall survival

Site

The University of Kansas Cancer Center — Currently on-boarding additional centers

Potential to Provide Protection During a Vulnerable Period

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



Patient Demographics and Summary (N=16)

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 GvHD Chronic limited GvHD	57.2+	Alive
003	1	44 / female	7+3	High-risk AML, trisomy 8+ and del7, IDH2	Acute G2 GvHD	42.4** LTFU	Alive
006	1	66 / male	7+3 IDAC	High-risk relapsed AML	Acute G2 GvHD Chronic extensive GvHD	43.1+	Alive
007	1	71 / male	Ven/Aza+Pembrolizumab	AML	Acute G2 GvHD Chronic limited GvHD	15.5	15.5 died due to IPS
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 GvHD	14.7	20.2
010	2	63 / female	7 cycles Venetoclax/Aza	AML	Acute G2b GvHD	26.5+	Alive
011	2	68 / male	Hydrea/Peg-IFN	ET with MDS/MPN overlap; TP53 mutated		12.4	18.3
012	2	69 / male	2 cycles Venetoclax/Aza	AML		20.1+	Alive
013	2	71 / female	1 cycle Ven/aza/gilteritinib 2 cycles Venetoclax/Aza	AML, FLT3		19.8+	Alive
014	2	71 / male	Venetoclax/Dacogen	AML, del20, -Y		19.4+	Alive
015	2	69 / female	Aza	MDS, Complex cyto, FISH -17p, -7, -5. NGS VUS: NSD1	Acute G1 GvHD Chronic limited GvHD	11.4	Alive @ 12.2+
017	2	69 / male	Revlimid, Azacitidine+CD70 (SGN70 trial), Decitabine +Venetoclax	MDS,5q deletion		8.5+	Alive
018	2	64 / male	Ven/Aza	MDS high-risk, asxl1, kras, srsf2, and tet2 variants	Acute G1 GvHD	8.1+	Alive
019	2	45 / female	Daunorubin /Vesticrine, Cytarabine /Methotrexate, Cyclophosphamide/Methotrexate	B-ALL		5.4+	Alive
020	2	61 / female	Ven/Aza	AML -expression of dim CD45, CD33, CD38, CD117 and myeloperoxidase	Acute G1 GvHD	4.7+	Alive
021	2	71 / female	3 cycles Decitabine/Cedazuridine, Investigational drug	MDS, del 5q and del 7q		1.0+	Alive
023	2	68 / male	Ven/Aza	AML – intermediate risk			

As of January 17, 2025; Early trial results are not indicative of future results, including the outcome of this trial.

Median patient age ~68 y/o

Majority have AML

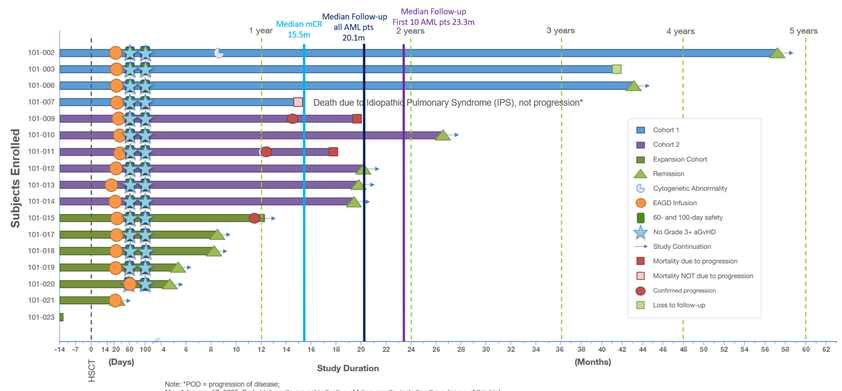
Received up to 7 prior therapies

23 enrolled, n=16 dosed and evaluable for safety
- 1 patient expired prior to dosing
- 2 patients received an out of specification product; 1 under EAP
- 1 manufacturing failure
- 2 screen failures, 1 relapse prior to treatment and 1 donor issue
- 1 patient waiting to be dosed

- **Median follow-up = 18.8m**
- **Median follow-up of AML patients = 20.1m, 23.3m ex-expansion cohort**

100% Patients Remained in CR ≥ 12 Months

Three patients with high-risk disease remain relapse free for >3 years with median follow-up of all patients of 18.8 months; No AML patients have relapsed to date with median follow up of 20.1 months (23.3 months, ex-expansion cohort)



Note: *POD = progression of disease;
*As of January 17, 2025; Early trial results are not indicative of future results, including the outcome of this trial.

Chimerism Demonstrates Durable Remissions in AML

	Dose Level 1				Dose Level 2 - RP2D										
	101-002 AML	101-003 AML	101-006 AML	101-007 AML	101-009 ALL	101-010 AML	101-011 MDS/MPN	101-012 AML	101-013 AML	101-014 AML	101-015 MDS	101-017 MDS	101-018 MDS	101-019 B-ALL	101-020 AML
Infusion	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Day 30	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Day 60	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Day 100	✓	✓	na	✓	✓	na	✓	✓	na	✓	✓	✓	✓	✓	
Day 180	⬢	na	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Day 365	✓	na	✓	✓	✓	✓	⬢	✓	na	✓	⬢				
Morphologic CR @ 1yr	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	●				

Dose Level 1
Dose Level 2
EAGD Infusion
Cytogenetic CR
Complete Remission
Mixed chimerism requiring clinical intervention
Relapse

- Chimerism measured by next generation sequencing (NGS) predicts risk of relapse
- AML and MDS patients appear different following HSCT and treatment with γδ T cells

As of January 17, 2025; Early trial results are not indicative of future results, including the outcome of this trial.

INB-100 treated patients have improved 1-year PFS and OS

	IN8bio INB-100 all haplo (N=11)	IN8bio INB-100 AML, (N=8)	KUCC All haplo, (N=98)*	KUCC AML, (N=54)*	CIBMTR AML, (N=684)^
Age (median)	68 (44-72)	68 (44-72)	64.3 (21-74)	64.1 (21-74)	65.6 (19.2-80.8)
Sex, female %	45.5% (5)	50% (4)	31.6% (31)	33.3% (18)	45.9% (314)
Karnofsky performance Status ≥ 90%	18.2% (2)	12.5% (1)	22.4% (22)	14.5% (8)	40.9% (280)
HCT-specific comorbidity index ≥3, n (%)	54.6% (6)	75% (6)	57.1% (56)	63% (34)	58.9% (403)
Female donor %	27.3% (3)	25% (2)	45.9% (45)	42.6% (23)	39.7% (271)
Day-100 acute graft-vs-host disease (GVHD), n (%)	72.7% (8)	62.5% (5)	61.2% (60)	64.8% (35)	NA
Non-relapse mortality (NRM), % (N)	9.1% (1)	12.5% (1)	30.6% (30)	25.9% (14)	NA
Outcomes at 1 year					
Progression Free Survival (PFS)	90.9% (10)	100% (8)#	59.2% (58)	57.4% (31)#	67.8% (679)
Overall Survival (OS)	100% (11)	100% (8)	69.4% (68)	66.7% (36)	74.7% (684)

^CIBMTR CM24-35, "Retrospective analysis of RFS and OS in AML patients undergoing haploidentical transplant with 62% (N=424) receiving reduced intensity conditioning (RIC) regimen."
*Patient and transplant-related characteristics after Flu/Cy/TBI non-myeloablative RIC haploidentical HCT with PT-Cy-based GVHD prophylaxis in AML patients 2016-2024 (KUCC)

- Relapse in leukemia patients who have undergone haplo-HSCT are significant and often leads to death
- INB-100 patients have an **increased rate of Progression Free Survival (PFS) and Overall Survival (OS) at 1-year** compared to retrospective control data sets
- **100% AML patients remaining in remission to-date**, with median follow-up of 20.1 months and 23.3 months excluding patients in the expansion cohort

Treatment Emergent AE's in ≥ 20% of Patients (n=17)

Adverse Events	Total (%)	Grade 1/2	Grade 3	Grade 4
Platelet count decreased	82.4	11.8	17.6	52.9
WBC decreased	58.8	54.5	17.6	23.5
Anemia	88.2	17.6	70.6	0
ANC decreased	58.8	17.6	5.9	35.3
Hypomagnesemia	70.6	70.6	0	0
ALC decreased	35.3	0	23.5	11.8
Creatinine increased	52.9	52.9	0	0
Rash maculopapular	41.2	35.3	5.9	0
Vomiting	29.4	29.4	0	0
Hypokalemia	47.1	47.1	0	0
Diarrhea	41.2	41.2	0	0
Nausea	35.3	29.4	5.9	0
Hypertension	29.4	29.4	0	0
Hyponatremia, Pollakiuria, Dyspnea, Peripheral edema, Fatigue, Insomnia, Tremor	23.5	23.5	0	0

- **No treatment related deaths**
- **No DLT's to date**
- **No SUSAR's or unexpected safety events**
- **No change in AE profile from DL1 to DL2**

Conclusions & Next Steps

- In this Phase 1 trial, allogeneic **INB-100 γδ T cells are demonstrating a well tolerated safety profile** with no cytokine release syndrome (CRS), neurotoxicity (ICANS) or treatment related deaths with limited incidence of infections and in-line rate of acute GvHD
- **100% of INB-100 treated AML patients remain alive and in complete remission (CR) with median CR of 20.1 months, a notable improvement over real-world and retrospective control AML patients with a 1-year PFS of 67.8% and OS 74.7% (CIBMTR) and PFS 57.4% and OS 66.7% (KUCC)**
- **Across all patients, INB-100 is demonstrating an overall 1-year PFS of 90.9%** (1 MDS patient relapsed at day 348) and **OS of 100% compared to a 1-year PFS of 59.2% and OS of 69.4% at KUCC**
- CIBMTR's 2024 Transplant Center-Specific Survival Report demonstrates that KUCC is among the top large transplant programs in the U.S., ranked highly for predicted versus actual 1-year survival outcomes post-HSCT; It is a tertiary referral center and treats many patients with complex high-risk disease
- This is the **first trial to demonstrate in vivo expansion and persistence of γδ T cells** for 1-year post-HSCT indicating elevated γδ T cells and continued immune surveillance could be driving the prolonged PFS
- The INB-100 therapy is **promising for the treatment of older patients with high-risk AML** who typically have limited treatment options, a challenge that is compounded by high mortality rates post relapse following haploidentical transplant. A 15-patient expansion cohort at DL2 continues to enroll and treat patients with a potential future randomized controlled trial in AML
- **We thank all the patients and caregivers for their participation in this study**