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

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Background and methods

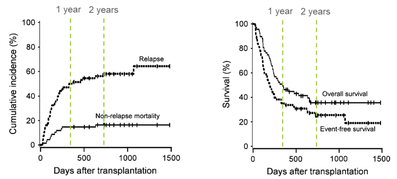
Background: Gamma-delta (γδ) T cells are MHC unrestricted lymphocytes that recognize and lyse malignant cells in allogeneic settings. Although haploidentical transplant with PTCy has reduced the risk of graft-versus-host disease (GvHD); the incidence of relapse remains up to 50% at year 1. Early post-transplant infusion of haploidentical expanded and activated γδ T cells (EAGD) may decrease relapse risk through a graft-versus-leukemia (GvL) effect without severe GvHD. We present updated clinical and correlative data from our Phase I trial using our recommended phase 2 dose (RP2D).

Methods: Adults with newly diagnosed or relapsed ALL, CML, AML undergoing first haploidentical transplant with reduced-intensity flu/cy/TBI conditioning received EAGD intravenously within 7 days of neutrophil engraftment. Peripheral blood was collected at EAGD infusion and monthly through day 90, with additional collections every 6 months through 1 year. Primary endpoints include dose-limiting toxicities (DLT), grade (G) 3-4 adverse events including GvHD with secondary endpoints of relapse and overall survival. Biologic parameters included multiparameter flow cytometric immunophenotyping and additional serum cytokine analysis using the Olink® 48 target panel.

Haploidentical stem cell transplantation (HSCT)

Relapse is the biggest HSCT problem

- Haploidentical transplants have expanded access to stem cell transplantation
- However, 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



An allogeneic therapy to reduce leukemic relapse

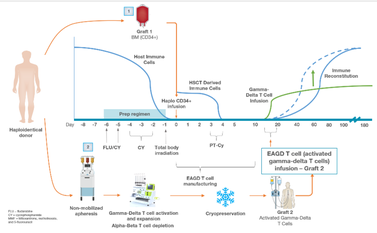
INB-100: Single-center, dose-escalation trial of DeltEx Allo γδ T cells post-haploidentical HSCT

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



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

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

Site

THE UNIVERSITY OF KANSAS CANCER CENTER

Key eligibility criteria

- Adult patients with a haploidentical donor identified
- KPS ≥70
- Acute myeloid leukemia (AML) in morphologic complete remission (mCR) with intermediate/high-risk features or relapsed disease
- Chronic myelogenous leukemia (CML) in any chronic phase
- Myelodysplastic syndromes (MDS) with intermediate/high risk features
- Acute lymphocytic leukemia (ALL) in mCR with high-risk features or relapsed disease

Patient demographics and summary

Patient	Dose Level	Age / Sex	Prior Therapies	Disease	Acute / Chronic GvHD	mCR Duration (mos)
002	1	63 / female	Idasanutlin + 7+3	**High-risk AML trisomy 8+ and del7**	Acute G2 skin GvHD Chronic limited mild skin GvHD	**42.7+**
003	1	44 / female	7+3	**High-risk AML trisomy 8+ and del7**	Acute G2 GI, Acute G2 rash GvHD	**40.3+**
006	1	66 / male	7+3 IDAC	**Relapsed AML**	Acute G2 rash GvHD Chronic extensive GvHD	**28.6+**
007	1	71 / male	Ven/Aza+Pembrolizumab	AML	Acute G2 rash GvHD Chronic limited mod GvHD	**14.3+**
009	2	68 / male	R-CHOP Blinatumomab Inotuzumab Flu/Mel/TBI Vincristine/steroids Flu/cy/brentuximab **CAR-T with Tecartus**	**Relapsed Ph- ALL; p53 mutated** by FISH and NGS	Acute G2c rash GvHD	**12.2+**
010	2	63 / female	7 cycles Venetoclax/Aza	AML	Acute G2b rash - GvHD	**12.0+**
011	2	68 / male	Hydrea/Peg-IFN	ET with MDS/MPN overlap	Acute G1 rash - not GvHD Acute G1 diarrhea - not GvHD	**9.0+**
012	2	69 / male	2 cycles Venetoclax/Aza	AML		**5.6+**
013	2	71 / female	1 cycle Ven/aza/gliteritinib 2 cycles Venetoclax/Aza	AML, FLT3	Acute G1 diarrhea - not GvHD	**5.3+**
014	2	71 / male	Venetoclax/Dacogen	AML	Acute G1 diarrhea - not GvHD Acute G1 rash - not GvHD	**4.9+**

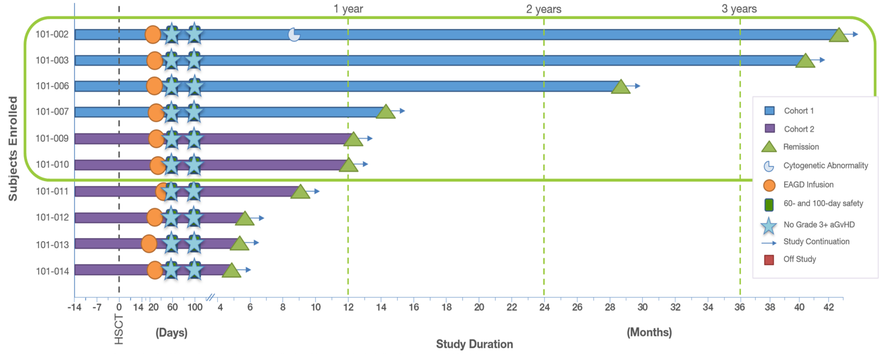
Note: *As of November 3, 2023; Early trial results are not indicative of future results, including the outcome of this trial.

14 enrolled, n=10 dosed and evaluable for safety

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

100% patients remain in mCR with six ≥ 12 months

Three patients with high-risk disease remain relapse free for >28 months



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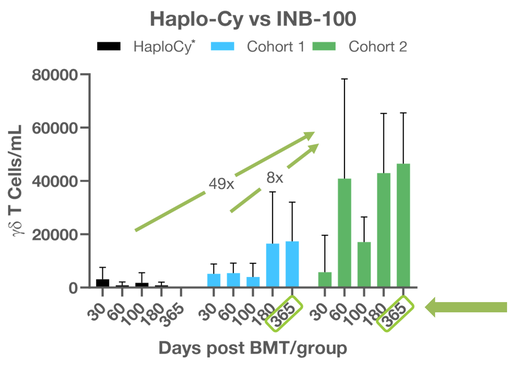
One–year in vivo persistence and expansion of γδ T cells



- 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
- Cohort 2 patients receive 3x the γδ T cell dose as Cohort 1
- Dose dependent increase of circulating γδ T cells at Days +60, +100, +180 and +365 for INB-100 treated patients
- At 1 year Cohort 2 γδ T cells are 2.7x greater than Cohort 1

Source: IN8bio, Inc. and UAB *previously unpublished data from laboratory of Dr. Lawrence Lamb, as of April 21, 2023

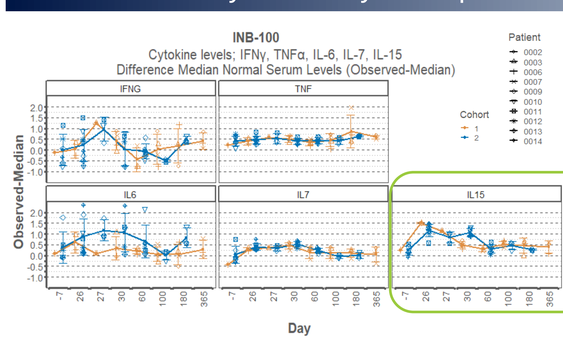
Treatment emergent AE's in ≥ 20% of patients (n=10)

Adverse Events	Total (%)	Grade 1/2	Grade 3	Grade 4
Platelet count decreased	100	36.3	45.5	18.2
WBC decreased	90.9	45.4	27.3	18.2
Anemia	90.9	36.4	54.5	
ANC decreased	90.9	36.3	18.2	36.4
ALC decreased	54.5		36.4	18.2
Hypomagnesemia	54.5	54.5		
Creatinine increased	54.5	54.5		
Rash maculopapular	54.5	54.5		
Vomiting	36.4	36.4		
Hypokalemia	36.4	36.4		
Hyponatremia	36.4	36.4		
Dyspnea	27.3	27.3		
Peripheral edema	27.3	27.3		
Hypertension	27.3	27.3		
Pollakiuria	27.3	27.3		
Diarrhea	18.2	18.2		
Decreased appetite	18.2		18.2	

Note: *As of November 3, 2023; Early trial results are not indicative of future results, including the outcome of this trial.

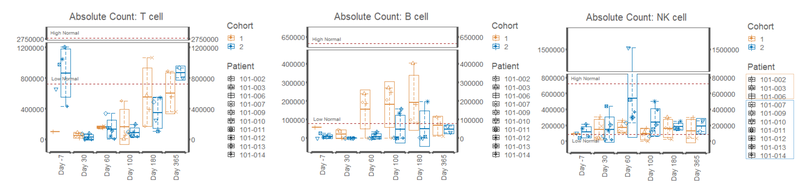
- **No DLT's to date**
- **Treatment Related SAE's:**
  - G2 Rash maculopapular (18.2%)
  - G3 Nausea (aGvHD 2B GI)
  - G3 Anemia
- **Other non-treatment related SAEs include:**
  - G3 Acute Kidney Injury
  - G3 CMV reactivation
  - G3 Fall
  - G3 Decreased appetite
- **No treatment related deaths**
- **No SUSAR's or unexpected safety events**
- **No change in AE profile from DL1 to DL2**

Immune recovery: serum cytokine profile



- IL-6 concentration is higher in the second cohort but insufficient to initiate clinical manifestations of CRS. This is also evidenced by decreases of inflammatory cytokines TNF-α, IFN-γ, and IL-7 following transplant and infusion. These data are consistent with a favorable clinical safety profile.
- Initial higher concentrations of serum IL-15 are favorable for homeostatic reconstitution, expansion, and durability of the infused γδ T cell population consistent with the observed intermediate and longer-term efficacy.

T cell, B cell and NK cell recovery



- T cells recover slowly to low normal values from day 180
- B cell recover slowly, where interestingly patient 012's B cells recovered after viral infection at day 59 and remained at normal levels
- NK cells recover to low normal to normal levels from day 60 post transplant, with one outlier

Conclusions & Next Steps

- **100%** of patients achieved and remain in **CR**
  - **70%** of patients with **CR ≥ 6 months** with **60%** of patients remaining in **CR ≥12 months**
  - Two patients with high-risk cytogenetic AML remaining in mCR for 3+ years and another patient with relapsed AML for 2+ years
  - Median follow-up of **12.1 months**
- Safety profile remains manageable and consistent across dose cohorts with primarily grade 2 acute GvHD with no cytokine release syndrome (CRS), neurotoxicity (ICANS) or ≥ grade 3 acute GvHD reported
- This is the first trial to demonstrate **in vivo expansion and persistence of γδ T cells for up to 1-year post-HSCT** suggesting continued γδ T cell surveillance against leukemic relapse
- Given favorable risk-benefit ratio and prolonged event free survival (EFS), a Phase 1b expansion of 10 patients at DL2 is underway to further validate this signal