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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

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: Gamma-delta (gd) 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 EAGD cells 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.

Results: 14 subjects were enrolled with 4 treated at Dose Level (DL) 1 of 1 x 10^6 EAGD/kg and 6 subjects treated at the RP2D of DL2 (3 x 10^6 EAGD/kg). Untreated subjects included: One screen failure, a manufacturing failure, one subject who died prior to dosing, and one subject who received an out of study specification product. Treated subjects were 60% male, median age of 68, and primarily AML subjects in CR1. RP2D was defined by an acceptable toxicity profile, no DLT's, prolonged RFS and elevated gd levels. Peripheral lymphodepletion persisted through the first 100 days post-BMT followed by T cell recovery from a CD45+CD27-effector phenotype to central and effector memory phenotype. Notably, DL2 showed significant increases in gd T cell count recovery at days 60, 100 and 180 post-BMT vs. DL1 and historically untreated Haplo/PTCy patients, p = <0.05. NK cells remained within the low normal range and <3% of circulating T cells were Tregs. Preliminary serum cytokine analysis revealed elevated IL-6 and IL-15 in serum post- transplant prior to EAGD infusion, but dropped to normal median levels at day 60, 20-30 days after EAGD infusion.

One subject received intermittent hypomethylating therapy for emergence of recipient chimerism. Treatment emergent AE's included transient WBC and ANC decreases (100% each), platelet count decrease and anemia (88.9% each) and maculopapular rash, hypomagnesemia and blood creatine increased (55.6% each). EAGD related toxicities were primarily G1-2, included G1-2 skin acute GvHD and gastrointestinal GvHD, and one case of G3 platelet count decrease. Treatment related serious AE's of G3 nausea and G2 rash were reported. No DLTs, neurotoxicity, cytokine release syndrome or treatment related deaths were reported.

Conclusions: Post-BMT infusion of donor-derived, EAGD cells has demonstrated manageable safety with no infusional toxicity or ≥G3 acute GvHD or extensive chronic GvHD. Durable relapse free survival at a maximum of >3 years in subjects with poor risk cytogenetics and adverse clinical risk factors combined with ongoing homeostatic reconstitution of increasing gd T cell effectors post-BMT suggests this therapy may be an effective measure in mitigating relapse after HaploBMT. NCT03533816

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Subject	DL	Age/Sex	Disease	Acute/chronic GvHD	Morphologic CR (mos)
002	1	54/F	AML trisomy8, del7, Flt3 TKD	Acute G2 skin Chronic mild skin GvHD	39.0+
003	1	45/F	AML trisomy8, del7	Acute G2 GI Acute G2 rash	36.6+
006	1	66/M	AML	Acute G2 rash	25.0+
007	1	71/M	AML	Acute G2 rash	10.6+
009	2	68/M	Ph-ALL, p53 mut	Acute G2c rash	8.6+
010	2	62/F	AML	Acute G2b rash	8.3+
011	2	68/M	ET with MDS/MPN	Acute G1 rash Acute G1 diarrhea	5.4+
012	2	69/M	AML		1.9+
013	2	71/F	AML	Acute G1 diarrhea	1.6+
014	2	70/M	AML	Acute G1 diarrhea Acute G1 rash	1.2+

Figure 1

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