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ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Safety and Efficacy of Orca-Q with Haploidentical Donors for the Treatment of Advanced Hematologic Malignancies without the Use of Post-Transplant Cyclophosphamide

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BACKGROUND
Allogeneic stem cell transplantation (SCT) can be curative for several high-risk hematologic malignancies, but access was previously limited to patients with a fully matched donor. The introduction of post-transplant cyclophosphamide (PTCy) GvHD prophylaxis has increased the use of haploidentical donors (haplo) for patients who lack an HLA-matched donor. However, clinical outcomes associated with PTCy-based regimens remain challenging due to increased relapse rates (particularly in the setting of reduced intensity conditioning) and the adverse event profile including higher incidence of mucositis, cytokine release syndrome (CRS), delayed engraftment & T cell reconstitution, infections, early cardiotoxicity events and death from organ failure (Dulery 2021, Abboud 2021, Nagler 2022, Hoover 2022, Bolaños-Meade 2023). Additionally, the incidence of chronic GvHD after haplo SCT with PTCy is 24 - 33% at 1 year in various historical cohorts.
Orca-Q -an investigational precision engineered cell therapy biologic- represents an alternative strategy which may be administered with single agent prophylaxis and does not require PTCy. The cellular composition of Orca-Q includes enriched CD34+ stem cells, combined with specific T-cell subsets, and is intended to reconstitute the blood and immune systems.
METHODS
Adult patients with high-risk hematologic malignancies eligible for MAC SCT were enrolled on the haplo donor dose expansion arm of a multicenter phase1 study of Orca-Q (NCT03802695). Haplo was defined as ≥ 4/8 but < 7/8 matched related donor at HLA-A, -B, -C, and -DRB1 typed using DNA-based high-resolution. Patients received MAC conditioning and single agent GVHD prophylaxis with tacrolimus (starting on day -1 and taper day +60). Orca-Q was manufactured centrally at Orca Bio Manufacturing Site in Sacramento, CA from G-CSF mobilized peripheral blood apheresis.
RESULTS
Orca-Q was successfully manufactured and delivered to all subjects with a vein-to-vein time (time between end of donor apheresis to start of recipient's Orca-T infusion) of < 72 hours. A total of 33 patients (21 AML, 10 ALL, 2 CML) were included. Median age was 43 (range, 21 - 63) years, 73% were male. Median follow-up was 375 (range, 73 - 1384) days. Sixteen patients received TBI-based MAC; 17 received busulfan-based MAC (Table). All patients engrafted with median time of 12.0 (range, 8 - 25) and 15.5 (range, 8 - 79) days for neutrophil and platelet engraftment, respectively. Two patients had secondary graft failure. Two patients had Grade 1 CRS; 1 patient had Grade 2 CRS. Grade 2+ aGvHD through Day 180+ occurred in 15% of patients. Grade 3-4 acute GvHD (aGvHD) was rare with only 1 event of grade 3 aGvHD and no grade 4 aGvHD. No patients had moderate-to-severe cGvHD. Estimated incidence of CTCAE grade 2 and > grade 3 infections were 9% and 15% at 1 year,

respectively. 5 patients died (2 from relapsed disease) during the study period. NRM was 9% at 1 year. The 1-year relapse-free survival, GvHD-and-relapse free survival (Figure), and overall survival at 1 year was 82%.

CONCLUSIONS

Our findings reveal promising safety and efficacy outcomes using Orca-Q cell therapy for haplo-SCT despite the use of MAC with only single-agent tacrolimus, and without PTCy. With median follow-up of approximately 1 year, no patients experienced moderate or severe cGvHD, the low AE profile in the haplo setting remains favorable, and 1 year GvHD-free, relapse-free survival of 83% is very encouraging. This phase 1 study continues to enroll patients across the US.

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Table. Baseline characteristics Orca Q*

Baseline Characteristics (n = 33)	
Age (years)	
median	43
min, max	21, 63
Sex, n (%)	
female	9 (27.2)
male	24 (72.7)
Ethnicity, n (%)	
Hispanic or Latino	10 (30.3)
Not Hispanic or Latino	23 (69.7)
Race, n (%)	
Asian	5 (15.2)
Black or African American	7 (21.2)
White	14 (42.4)
Other	7 (21.2)
Primary disease, n (%)	
Acute lymphoid leukemia (ALL)	10 (30.3)
Acute myeloid leukemia (AML)	21 (63.6)
Chronic myelogenous leukemia (CML)	2 (6.1)
Disease status at transplantation: ALL, n | AML, n	
CR1	6 | 17
CR2	3 | 4
CR3	0 | 0
Not available	0 | 1
Conditioning regimen, n (%)	
TBI-based	16 (48.5)
Busulfan-based	17 (51.5)
Donor CMV status, n (%)	
Positive	10 (30.3)
Negative/Not Detected	12 (36.3)
Not Applicable	1 (3.0)
Unknown	0
Not Done	7 (21.2)
Missing	3 (9.1)

*haploidentical-related donors; single-agent GVHD prophylaxis

Abbreviations: CMV, Cytomegalovirus; CR1, first complete remission; CR2, second complete remission; CR3, third or subsequent complete remission; Q1, first quartile; Q3, third quartile; SD, standard deviation; TBI, total body irradiation.

Figure. GVHD-free and relapse-free survival at 1 year.

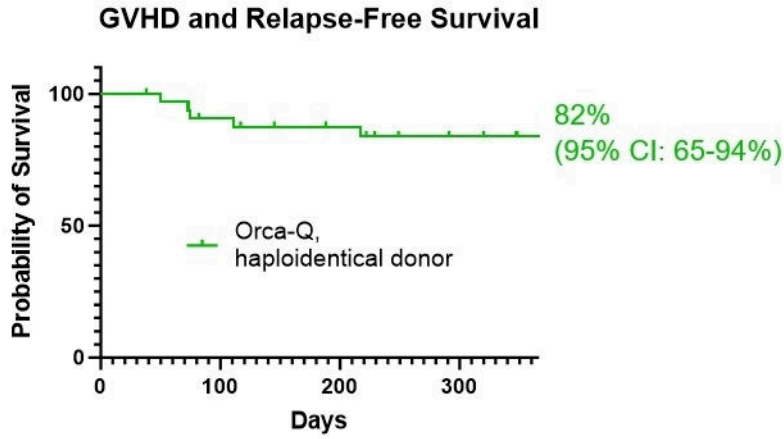

Figure 1

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