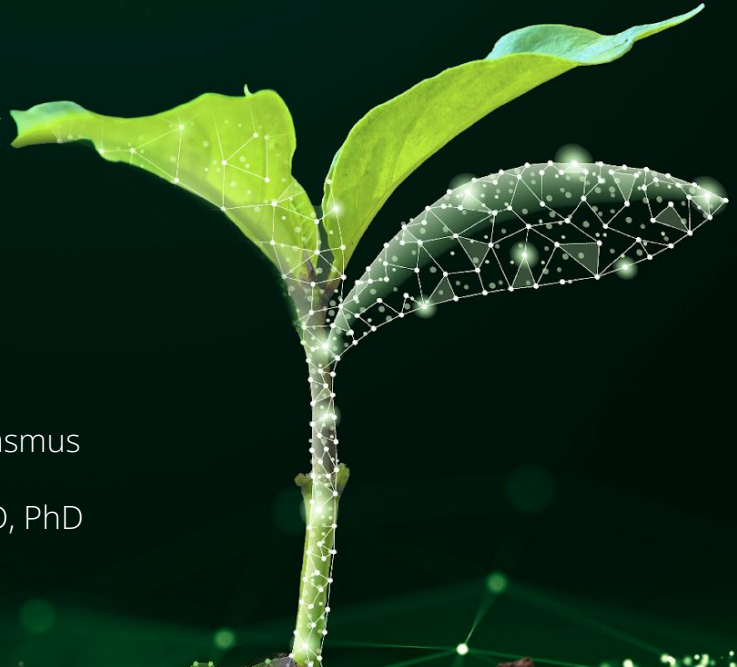


Safety and Efficacy of Orca-Q with Haploidentical Donors for the Treatment of Advanced Hematologic Malignancies without the Use of Post-Transplant Cyclophosphamide

Samer A. Srour, MD, Amandeep Salhotra, MD, Robert Lowsky, MD, Rasmus T. Hoeg, MD, Edmund K. Waller, MD, Anna Pavlova, MD, PhD, J. Scott McClellan, MD, PhD, Nathaniel B. Fernhoff, PhD, Everett H. Meyer, MD, PhD and Mehrdad Abedi, MD



Background

- Standard alloSCT can be curative for several high-risk hematologic malignancies
 - Access was previously limited to patients with a fully-matched donor
- The introduction of PTCy for GvHD prophylaxis has increased the use of haploidentical (haplo) donors
- PTCy-based “conventional” transplants remain challenging:
 - AE profile (CRS, delayed engraftment & T-cell reconstitution, mucositis, infections, cardiac toxicity, and increased NRM)
 - Increased relapse rates

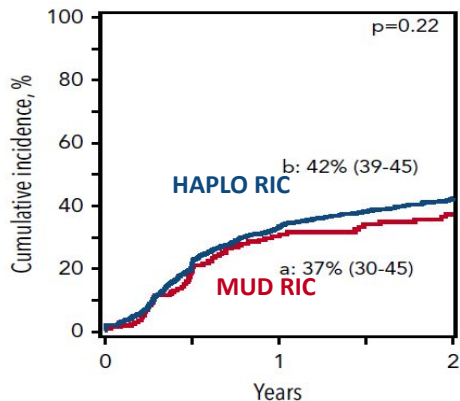
References: Abboud R, et al. *Bone Marrow Transplant*. 2021;56(11):2763–2770; Bolaños-Meade GM, et al. *N Engl J Med*. 2023; 388(25):2338–2348. Duléry R, et al. *JACC CardioOncol*. 2021; 3(2):250–259; Hoover A, et al. *Blood*. 2022; 140 (Supplement 1):282–283; Nagler A, Tsirigotis P. *Bone Marrow Transplant* 2022; 57(11):1640–1641.

Abbreviations: alloSCT, allogeneic hematopoietic stem cell transplants; CRS, cytokine release syndrome; GvHD, graft vs. host disease; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide; RIC, reduced intensity conditioning

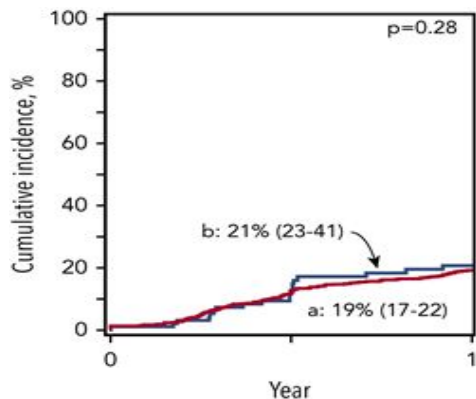
Background

- GvHD-and-relapse-free survival rates (GRFS) in this population remain low

Relapse following RIC regimens

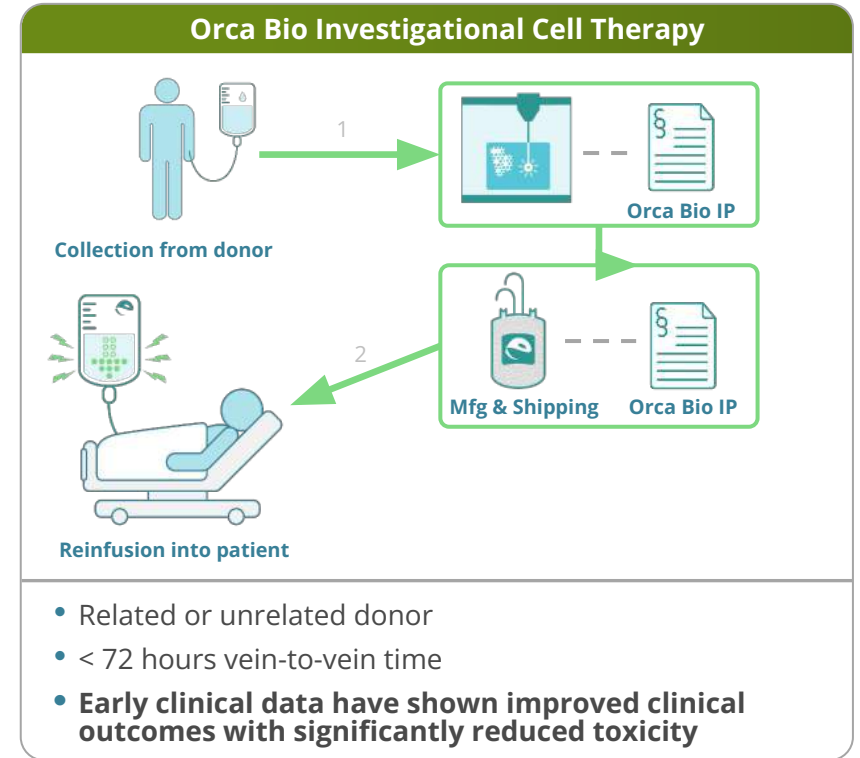
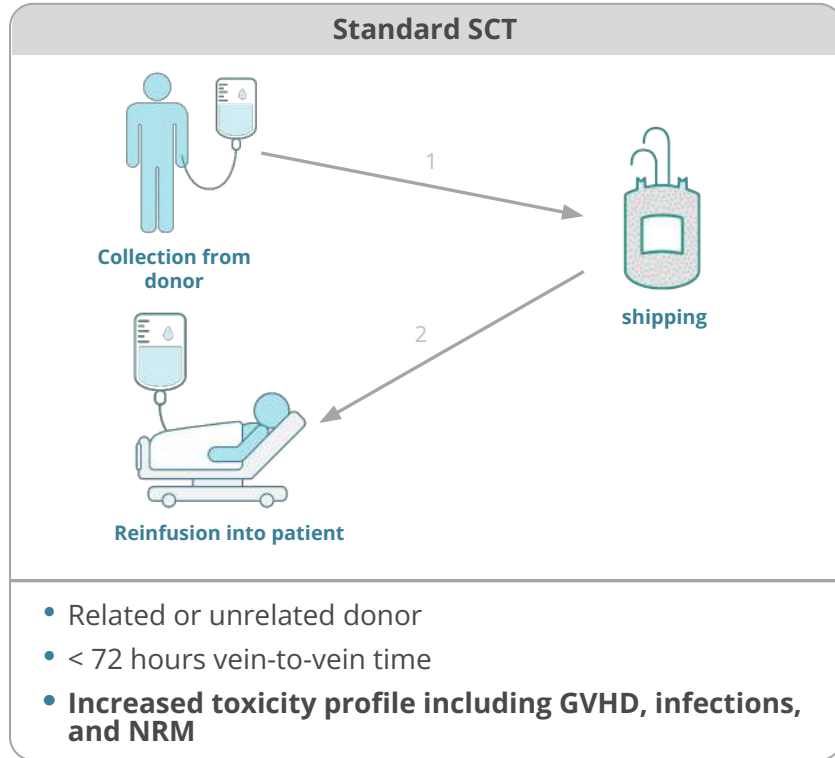


Relapse & GvHD following MAC



Myeloablative regimen	
Day-28 neutrophil recovery	94 (92-95)
Day-100 platelet recovery	87 (85-89)
1-y graft failure	4 (3-6)
Day-100 grades 2 to 4 acute GvHD	33 (30-37)
Day-100 grades 3 and 4 acute GvHD	10 (8-12)
1-y chronic GvHD	33 (30-36)

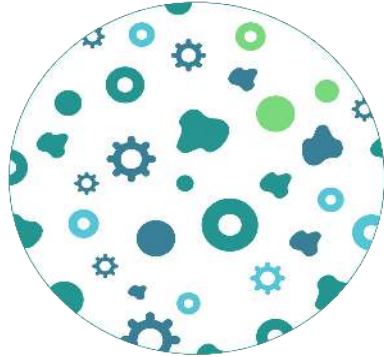
High-Precision Cell Therapies as Alternative to Standard SCT



Orca-Q: Improves Haplo SCT Outcomes Via Allograft Optimization

Conventional Transplants

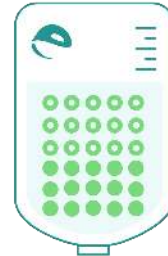
Uncontrolled mix of over 50 cell types



Hematopoietic stem cells
Progenitor cells
Conventional T cells
T regulatory cells
Memory cells
NK cells
Invariant NKT cells
Dendritic cells
Myeloid derived suppressor cells

Orca-Q Cell Therapy

Fully Defined Stem and Immune Cells



HSPC

+



Mix of specific donor cells

High Purity Cell Type

HSPCs

Regulatory T cells

iNK T cells

CD4+/CD8+ T cell subsets

Intended Use

Reconstitute blood system
Long term reconstitution of immune system

GvHD control

Enhance regulatory T cell function

Graft vs. infection

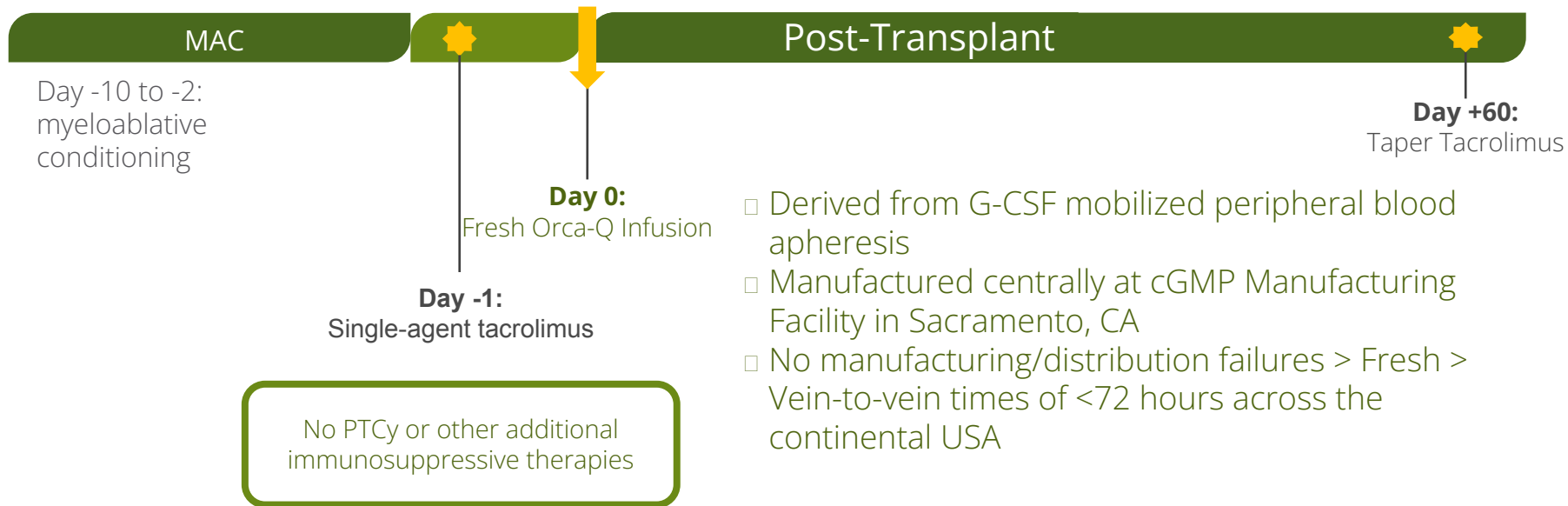
Graft vs. leukemia

Orca-Q: Study Design, Key Eligibility and Outcomes

- Phase 1, multi-center, dose expansion (NCT03802695)
- Haplo SCT with negative DSA
 - ✓ Haploidentical ($\geq 4/8$ but $< 7/8$ matched related donor at HLA-A, -B, -C, and -DRB1)
- Adult patients (18 to 65 years) with high-risk hematologic malignancies
 - ✓ Acute leukemia (AML, ALL)
 - ✓ Myelodysplastic syndrome (very high- or high-risk)
 - ✓ Myelofibrosis
- Eligible for MAC
 - ✓ HCT-CI ≤ 4
 - ✓ KPS ≥ 70
 - ✓ Adequate organ function
- Primary Endpoints
 - ✓ Dose-limiting toxicities
 - ✓ Primary graft failure

Abbreviations: ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CRS, cytokine release syndrome; DSA, donor-specific antibodies; HLA, human leukocyte antigen; transplantation; MAC, myeloablative conditioning; SCT, stem cell

Orca-Q Treatment Regimen



Abbreviations: G-CSF, granulocyte colony stimulating factor; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide

Orca-Q Baseline Characteristics

Patients N = 33	
Median age, years [range]	43 [21–63]
Female sex, n (%)	9 (27)
Hispanic or Latino Ethnicity, n (%)	10 (30.3)
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	10 (30.3)
Acute myeloid leukemia	21 (63.3)
Chronic myelogenous leukemia	2 (6.1)
Disease Risk Index, n (%)	
High/Very High	6 (18)
Intermediate	26 (79)
N/A	1 (3)

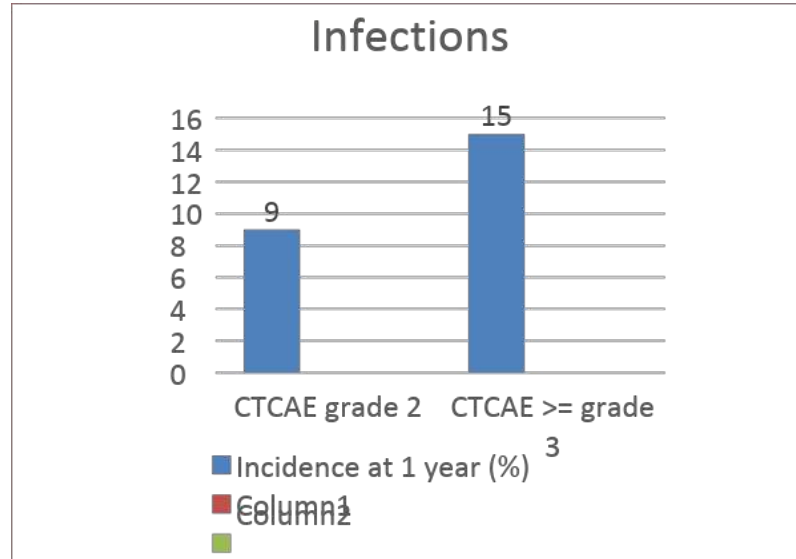
Disease status at transplantation	24
CR1	8
CR2	1
CML accel phase	
Conditioning regimen, n (%)	
TBI-based	17 (51.5)
Busulfan-based	16 (48.5)
Donor	
Sex, n	
Female	9
Male	24
CMV status, n (%)	
Positive	10 (30.3)
Negative/Not detected	12 (36.3)
N/A	11 (33.3)

Abbreviations: CMV, Cytomegalovirus; CR1, first complete remission; CR2, second complete remission; CR3, third or subsequent complete remission; IPSS-R, Revised International Prognostic Scoring System; NA, not applicable; Q1, first quartile; Q3, third quartile; SD, standard deviation; TBI, total body irradiation.

Rapid Engraftment Observed in Orca-Q Patients

- None of the patients had primary graft failure
- All patients engrafted with median time:
 - Neutrophils - 12.0 days (range: 8 – 25)
 - Platelets – 15.5 days (range: 8 – 79)
- Two patients had secondary graft failure
- Grade 1-2 CRS: 3 patients (9%)
 - Grade 1: 2 patients
 - Grade 2: 1 patient

Low Incidence of Severe Infections



Abbreviations: CTCAE, common terminology criteria for adverse events (v5); GvHD, graft vs. host disease; MAGIC, Mt. Sinai Acute GvHD International Consortium

Low Incidence of Acute GvHD

Acute Grade 2-4 GvHD*:

- 5 events (15%)

Grade 3-4 acute GvHD*:

- Grade 3 - 1 event
- Grade 4 - 0 events

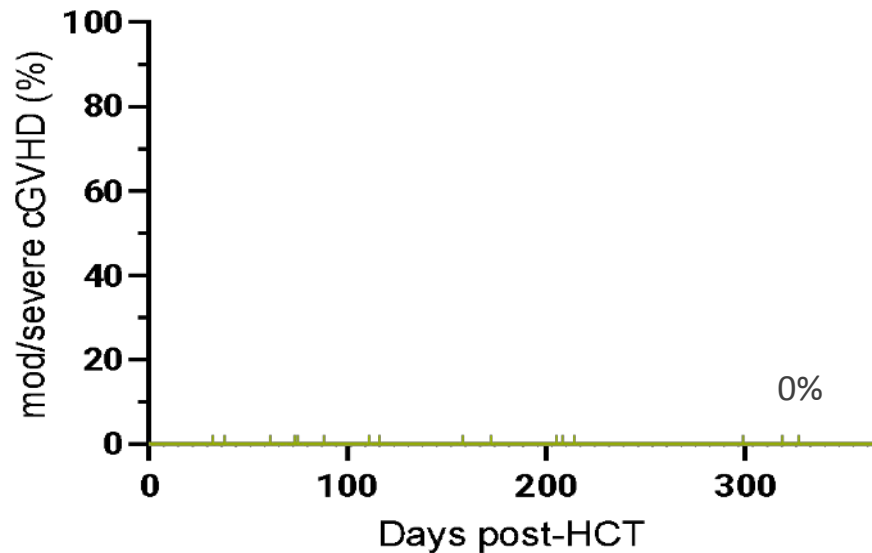
*assessed via MAGIC criteria

Abbreviations: CTCAE, common terminology criteria for adverse events (v5); GvHD, graft vs. host disease; MAGIC, Mt. Sinai Acute GvHD International Consortium

No Moderate-to-Severe cGvHD at ~ 1 Year Median Follow-up

- Median follow-up 375 days (range: 73 – 1384)
- No Orca-Q patients have developed moderate-to-severe chronic GvHD (cGvHD)*
- Historical cohorts: incidence of chronic GvHD after haplo SCT w/PTCy is 24-33% at 1 year

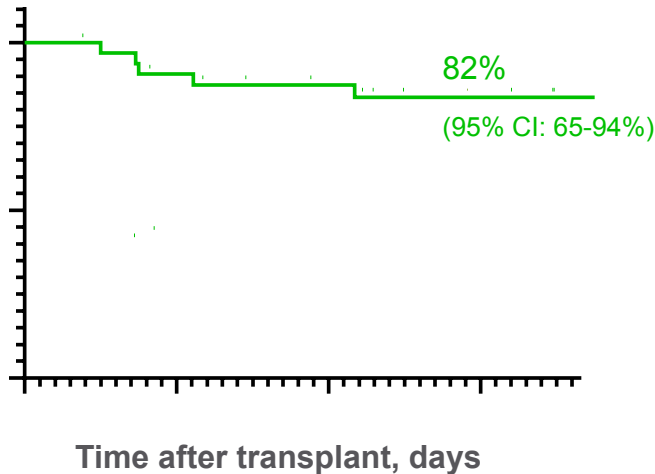
* per NIH consensus criteria (2015)



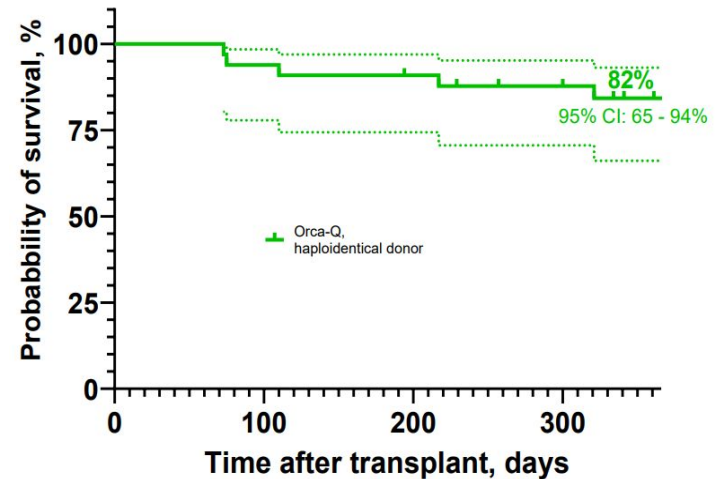
Jagasia et al., *Biol Blood Marrow Transplant* 2015; 21:389-401.

GRFS & Overall Survival Remain Encouraging

GVHD and Relapse-Free Survival



Overall survival



Modified GRFS: Grade3-4 aGvHD, moderate/severe cGvHD, disease relapse, or death from any cause

Abbreviations: GRFS, GvHD-free/relapse-free survival; GvHD, graft-versus-host disease; haplo alloHSCT, haploidentical hematopoietic stem cell transplantation; HCT, hematopoietic cell transplantation; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide.
Reference: Sanz, J, et al. *J Hematol Oncol.* 2020; 13:46. <https://doi.org/10.1186/s13045-020-00882-6>

Conclusions

- Our findings reveal promising safety and efficacy outcomes using Orca-Q cell therapy for haplo-SCT
 - Despite the use of MAC without PTCy and only single-agent tacrolimus
 - Low incidence of severe acute and chronic GVHD
- No new safety signals in this haplo setting were identified
- Very encouraging 1-year GvHD-free, relapse-free survival of 82%
- This phase 1 study (NCT03802695) continues to enroll patients across the US