Orca-Q Demonstrates Favorable GvHD-and-Relapse-Free Survival in Haploidentical Transplants without Post-Transplant Cyclophosphamide

Samer A Srour, MD, MS[1], Amandeep Salhotra, MD[2], Rasmus T Hoeg, MD[3], Ayman Saad, MB/BCH[4], Everett H Meyer, MD, PhD[5], Anna Pavlova, MD, PhD[6], Edmund K. Waller, MD, PhD[7], Mwe Mwe Chao, MD[8], J Scott McClellan, MD, PhD[8], Nathaniel B Fernhoff, PhD[8], Robert Lowsky, MD[5] and Mehrdad Abedi, MD[3]

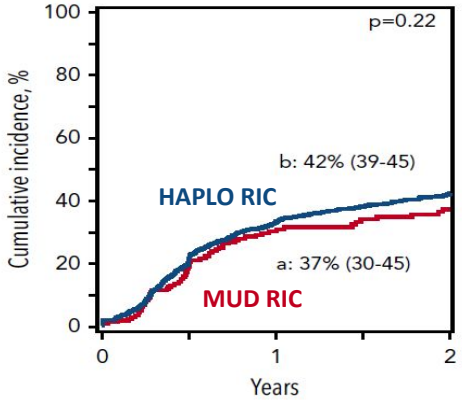
[1]Stem Cell Transplantation and Cellular Therapy, MD Anderson Cancer Center, Houston, TX; [2]Department of Hematology and HCT, Beckman Research Institute, City of Hope National Medical Center, Duarte, CA; [3]Davis Comprehensive Cancer Center, University of California, Sacramento, CA; [4]Comprehensive Cancer Center, The Ohio State University, Columbus, OH; [5]Division of Blood and Marrow Transplantation and Cellular Therapy, Department of Medicine, Stanford University School of Medicine, Stanford, CA; [6]Stanford University, Stanford, CA; [7]Winship Cancer Institute, Emory University, Atlanta, GA; [8]Orca Bio, Menlo Park, CA

^Srour, Salhotra, Lowsky, and Abedi contributed equally

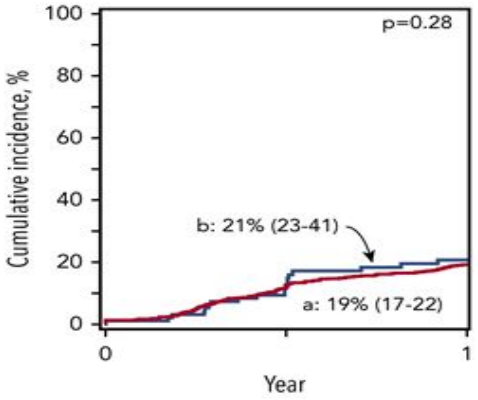
Background

- Allogeneic stem cell transplantation (allo SCT) is curative for several high-risk hematologic malignancies
- Post-transplant cyclophosphamide (PTCy) has enabled larger number of patients to receive allo SCT using alternative Haploidentical donors
- However, 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)

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GvHD, graft-versus-host disease; HLA, human leukocyte antigen; MAC, myeloablative conditioning; MUD, HLA-matched unrelated donor; RIC, reduced intensity conditioning.

Gooptu, M, et al. HLA-haploidentical vs matched unrelated donor transplants with posttransplant cyclophosphamide-based prophylaxis. Blood. 2021; 138 (3): 273–282.

Can We Improve Haplo SCT Outcomes by Optimizing Allograft?

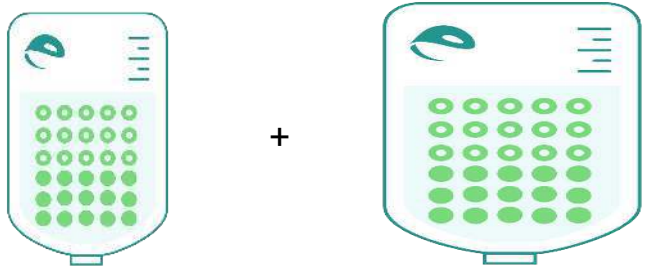
Conventional Transplants

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 Precision-Engineered Cell Therapy

Fully Defined Stem and Immune Cells



HSPC + **Mix of specific donor cells**

Cell Type	Intended Use
High purity HSPCs	Reconstitute blood system Long term reconstitution of immune system
High purity Tregs	GvHD control
High purity iNKT cells	Enhance Treg function
High purity CD4+/CD8+ Tcell subsets	Graft vs. infection
	Graft vs. leukemia

Study Hypothesis and Objectives

Haplo SCT	RIC	MAC	MA Orca-Q
GVHD Control	++	+	+++
Disease Control	+	++(+)	++(+)
Rapid Engraftment	++	++	+++
Infection Control	++	++	++
Pharmacological Prophylaxis	PTCy + Tacrolimus + MMF	PTCy + Tacrolimus + MMF	(Tacrolimus)

Orca-Q is an investigational, precision-engineered cell therapy comprises of stem cells and propriety mix of immune cells that is hypothesized to reduce GvHD, relapse, and serious infections

This study explores the role of Orca-Q in patients receiving haplo SCT using MAC and with single agent Tacrolimus GvHD prophylaxis

GvHD, graft-versus-host disease; PTCy, post-transplant cyclophosphamide.

Study Design and Key Eligibility for Orca-Q

- Phase 1, multi-center, dose expansion (NCT03802695)
- Haplo SCT with negative DSA
  - ✔ Haploidentical (≥ 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

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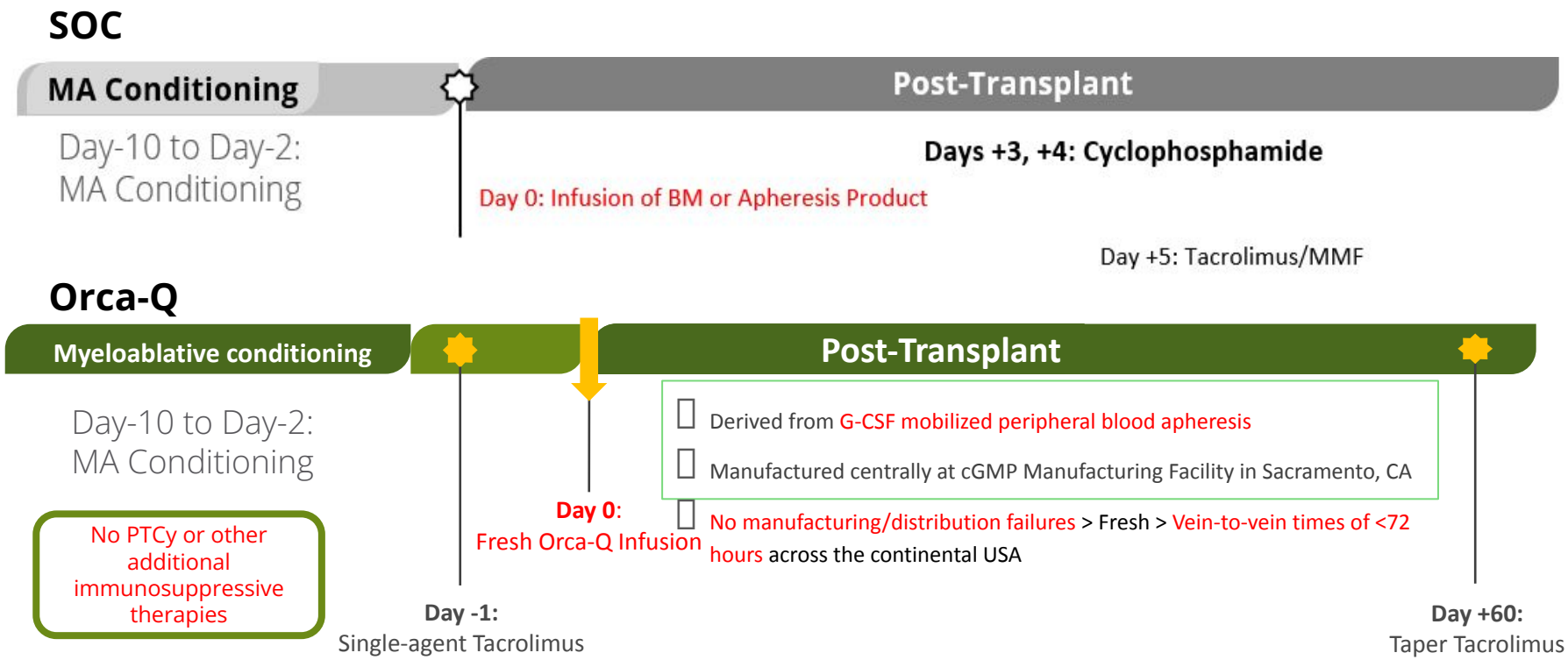
ALL, acute lymphocytic leukemia; AlloHSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myelogenous leukemia; HLA, human leukocyte antigen; HCT-CI, Hematopoietic Cell Transplantation-Comorbidity Index; KPS, Karnofsky Performance Scale; MAC, myeloablative conditioning.

1. https://precisiontstudy.com/. Accessed 24Oct2022. 2. https://clinicaltrials.gov/ct2/show/NCT05316701. Accessed 24Oct2022.

Orca-Q Treatment Schedule Using MAC and Single Agent GvHD Prophylaxis with Tacrolimus



GvHD, graft-versus-host disease; HLA, human leukocyte antigen; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide

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Baseline Characteristics

26 patients enrolled between January 2019 – July 2022

Parameter		n = 26
Median age (range), years		43 (21-63)
Gender		
	Male	18 (69%)
	Female	8 (31%)
Race/Ethnicity		
	Hispanic/Latino	10 (39%)
	White	7 (27%)
	African American	4 (15%)
	Asian	5 (19%)
Disease subtype		
	AML	15 (58%)
	ALL	9 (34%)
	CML (blast phase)	2 (8%)
Disease risk index		
	High/Very-high	6 (23%)
	Intermediate	17 (65%)
	Low	3 (12%)
Donor median age (range), years		36 (18-58)
Donor gender		
	Female	12
	Male	14
Donor CMV status		
	Positive	17
	Negative	9
Myeloablative regimen		
	TBI-based	16 (62%)
	BFT	10 (38%)

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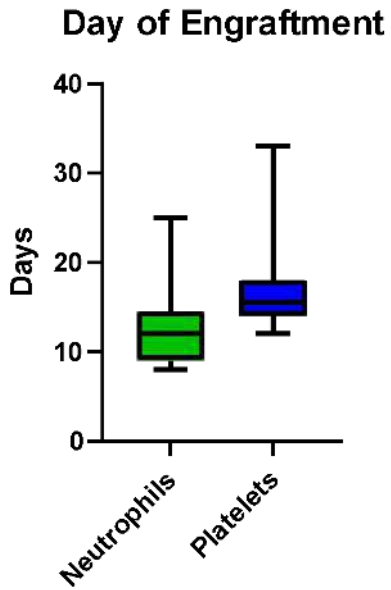
ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML - chronic myelogenous leukemia; BFT, Busulfan/fludarabine/thiotepa

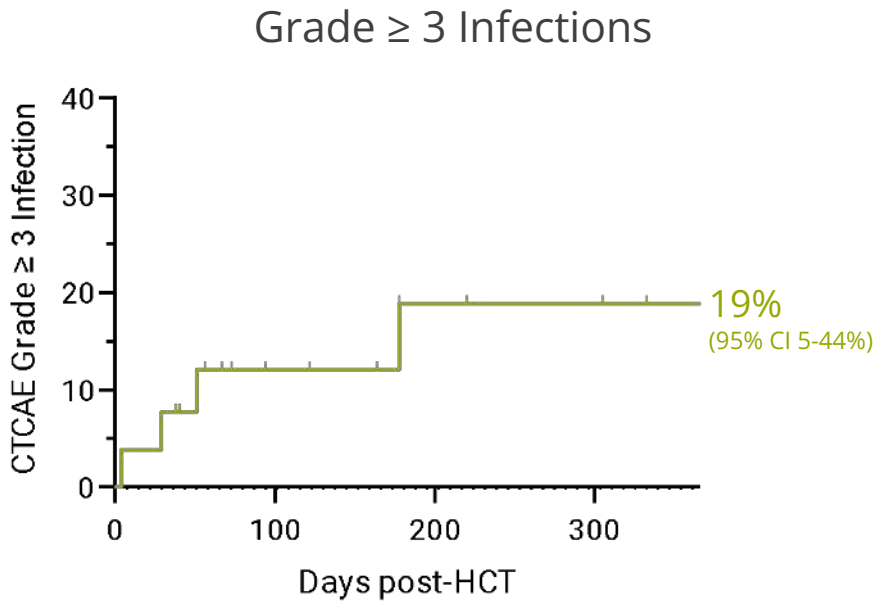
Rapid Engraftment Observed in Orca-Q Patients



- None of the patients had primary graft failure
- Median time to neutrophil and platelet engraftments were 12 and 16 days, respectively
- Two patients experienced secondary graft failure
- No Grade > 1 CRS was observed; Two patients had Grade 1 CRS

CRS, cytokine release syndrome

Severe Infections were Uncommon in Orca-Q Recipients



- CMV viremia was reported in 4 patients (15%); no CMV-related end-organ damage noted
- EBV viremia reported in 1 patient; no PTLD observed
- 2 patients died of infectious causes
  - COVID-19 pneumonia (n=1)
  - Pulmonary aspergillosis (n=1)

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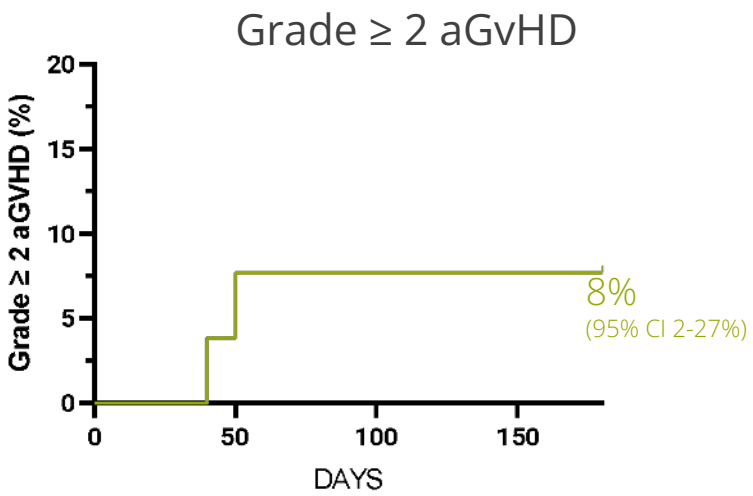
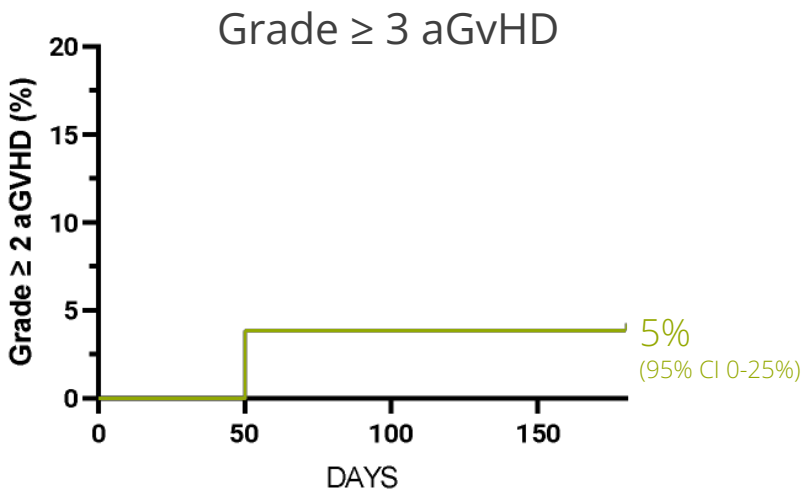
CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; CTCAE, common terminology criteria for adverse events; EBV, Epstein-Barr Virus; PLTD, post-transplantation lymphoproliferative disorder.

Low Incidence of Acute Graft-vs-Host Disease

- Despite using only single-agent tacrolimus as GvHD prophylaxis in the haploidentical transplant setting, aGvHD was rare

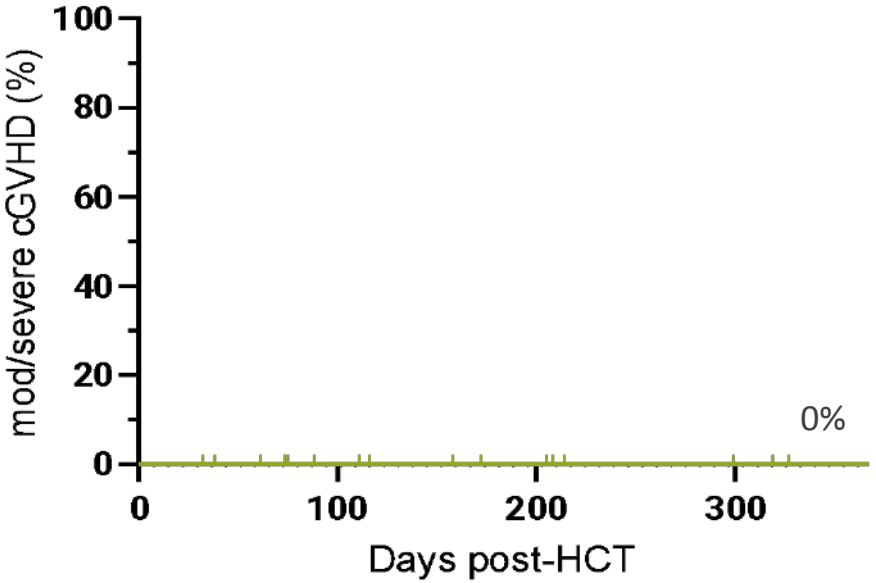




aGvHD, acute graft-versus-host disease; GvHD, graft-versus-host disease.

No Moderate-to-Severe cGvHD has Occurred

- Median follow-up 211 (32-1125) days
- Nine patients > 1 year
- Of the 16 patients with > 3 months follow-up, only 1 developed mild cGvHD
- No Orca-Q patients have developed moderate-to-severe cGvHD
- This compares favorably to the 24% - 33% rate of chronic GvHD post haplo-HCT in various historical cohorts



cGvHD, chronic graft-versus-host disease; GvHD, graft-versus-host disease; haplo-HCT, haploidentical hematopoietic cell transplantation; HCT, hematopoietic cell transplantation.

1. Gooptu, M, et al. HLA-haploidentical vs matched unrelated donor transplants with posttransplant cyclophosphamide-based prophylaxis. Blood. 2021; 138 (3): 273–282. https://doi.org/10.1182/blood.2021011281. 2. Sanz, J, et al. Post-transplant cyclophosphamide after matched sibling, unrelated and haploidentical donor transplants in patients with acute myeloid leukemia: a comparative study of the ALWP EBMT. J Hematol Oncol. 2020; 13:46. https://doi.org/10.1186/s13045-020-00882-6. 3. Baker, M, et al. Comparative Outcomes after Haploidentical or Unrelated Donor Bone Marrow or Blood Stem Cell Transplantation in Adult Patients with Hematological Malignancies. Biol Blood Marrow Transplant. 2016; 22; 2047-2055. http://dx.doi.org/10.1016/j.bbmt.2016.08.0031083-8791.

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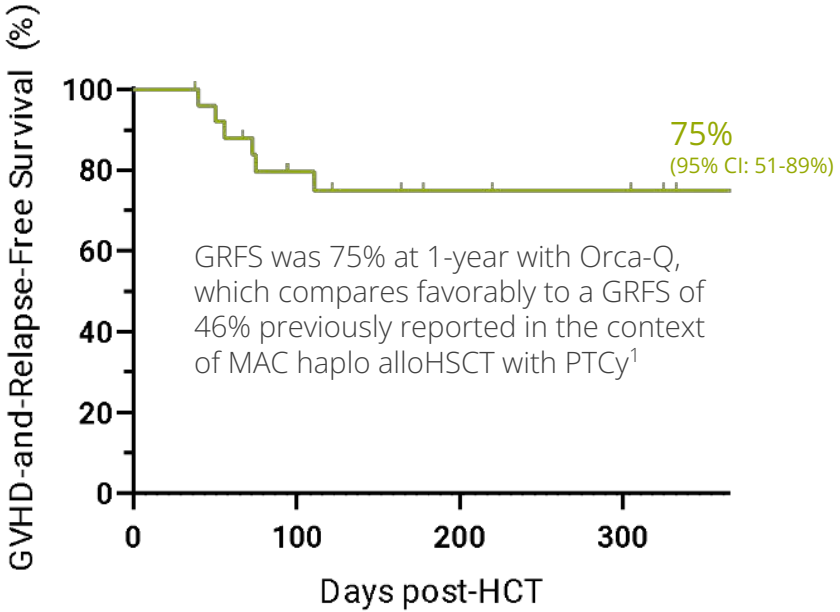
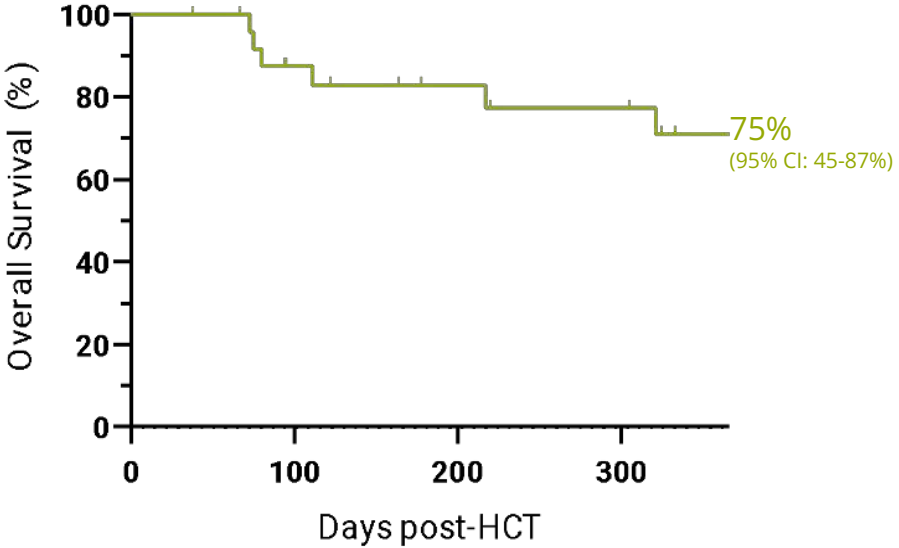
Encouraging GvHD-and-Relapse Free and Overall Survival



GRFS was 75% at 1-year with Orca-Q, which compares favorably to a GRFS of 46% previously reported in the context of MAC haplo alloHSCT with PTCy[1]



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.

1. Sanz, J, et al. Post-transplant cyclophosphamide after matched sibling, unrelated and haploidentical donor transplants in patients with acute myeloid leukemia: a comparative study of the ALWP EBMT. *J Hematol Oncol*. 2020; 13:46. https://doi.org/10.1186/s13045-020-00882-6

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Conclusions

- Our findings demonstrate very encouraging outcomes with Orca-Q in the Haplo SCT setting using myeloablative conditioning and only single agent tacrolimus
  - Low rates of overall and severe aGvHD and cGvHD
  - Low adverse event profile
  - Improved GRFS

- The phase 1 study continues to enroll patients across the U.S.

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