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

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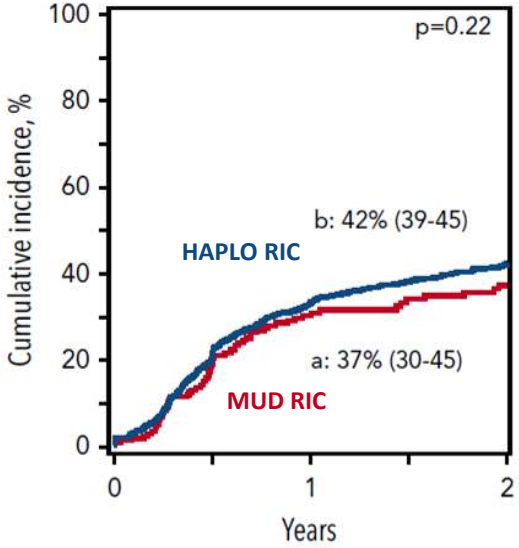
Background

- Allogeneic hematopoietic stem cell transplantation (alloHSCT) has traditionally been limited to patients with HLA-matched donors
- Post-transplant cyclophosphamide (PTCy) has recently enabled patients with haploidentical (HAPLO) donors to receive alloHSCT. However, GvHD-and-relapse-free survival rates (GRFS) in this population remain low



Relapse following RIC regimens

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)

GvHD following MAC regimens

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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.

Study Objective

Orca-Q is an investigational, precision-engineered cell therapy comprised of stem and immune cells isolated from a suitable donor, that is hypothesized to reduce GvHD, relapse, and serious infections

Here, we investigate Orca-Q as a therapy that can be administered with single agent GvHD prophylaxis and does not require PTCy

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

Study Design

Adult patients (18 to 65 years) with high-risk hematologic malignancies eligible for MAC alloHSCT were enrolled between January 2019 to July 2022 in a dose expansion haplo donor arm of a multicenter phase 1 study of Orca-Q (NCT03802695)

Orca-Q (NCT03802695)
• Acute leukemia (AML, ALL) • Myelodysplastic syndrome (very high- or high-risk) • Myelofibrosis
Haploidentical (≥ 4/8 but < 7/8 matched related donor at HLA-A, -B, -C, and -DRB1)
HCT-CI ≤ 4
KPS ≥ 70
Adequate organ function

Primary objectives
Safety, tolerability, efficacy
Secondary objectives
Engraftment

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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.

Baseline Characteristics

Parameter		n = 26
Disease	ALL	9
	AML	15
	CML - bc	2
Disease Status (*All in CR/CRi)*	MRD negative	22
	MRD positive	3
	Unknown	1
Median age (range), years		43 (21-63)
Median follow-up (range), days		211 (32-1125); 9 patients with > 1 year f/u
Disease risk index	Very high	2
	High	4
	Intermediate	17
	Low	3
Male:Female		18:8
Race/Ethnicity	Hispanic/Latino	10
	White	7
	African American	4
	Asian	5

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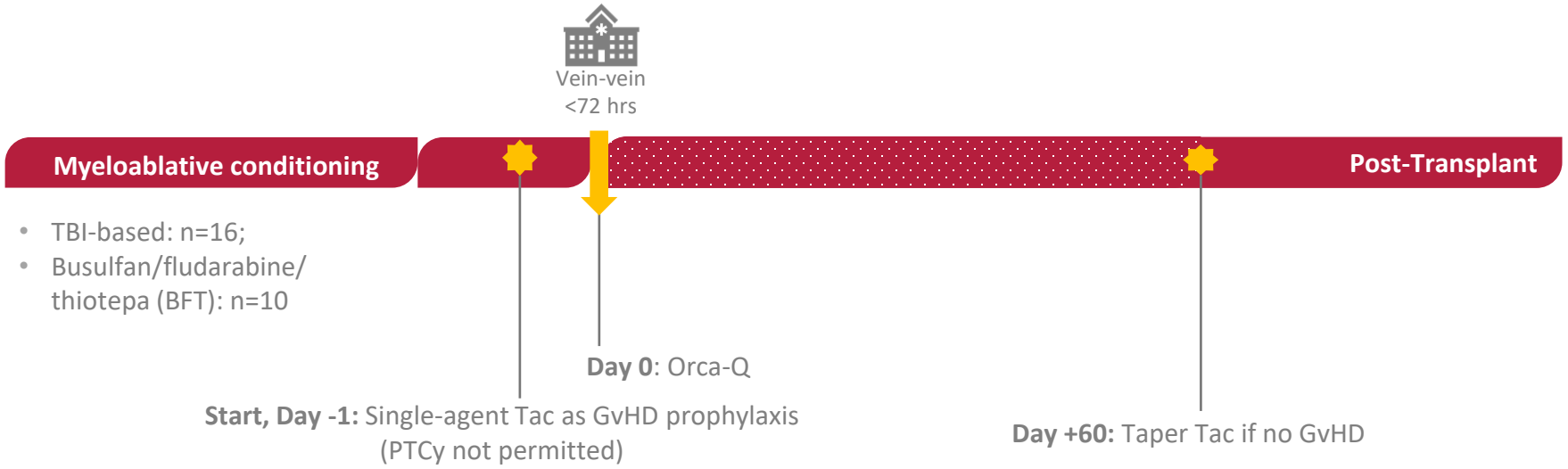
ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML - bc, chronic myelogenous leukemia in primary blast crisis; CR, complete response; CRi, complete remission with incomplete count recovery; f/u, follow-up; MRD, minimum residual disease.

Orca-Q Manufacturing and Transplant

- Manufactured centrally at Orca Bio's cGMP Manufacturing Facility in Sacramento, CA
- Derived from G-CSF mobilized peripheral blood apheresis



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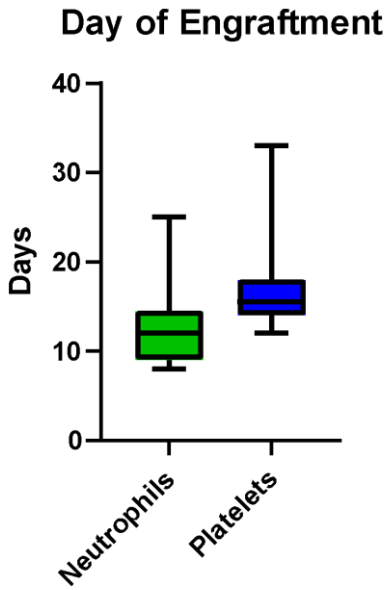
cGMP, current Good Manufacturing Practice; G-CSF, granulocyte colony-stimulating factor; GvHD, graft-versus-host disease; HLA, human leukocyte antigen; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide; Tac, tacrolimus; TBI, total body irradiation.

Rapid Engraftment Observed in Orca-Q Patients



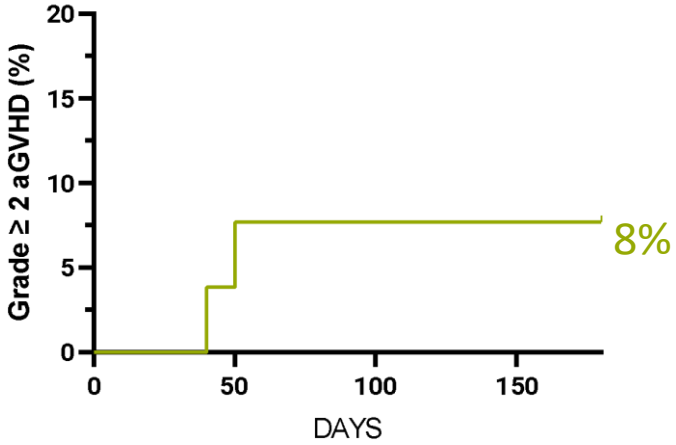
- Engraftment was rapid with median engraftment of neutrophils and platelets at 12 and 16 days, respectively
  - The elimination of post-transplant cyclophosphamide may promote more rapid engraftment
- Two patients experienced secondary graft failure
- No Grade > 1 CRS was observed

CRS, cytokine release syndrome.

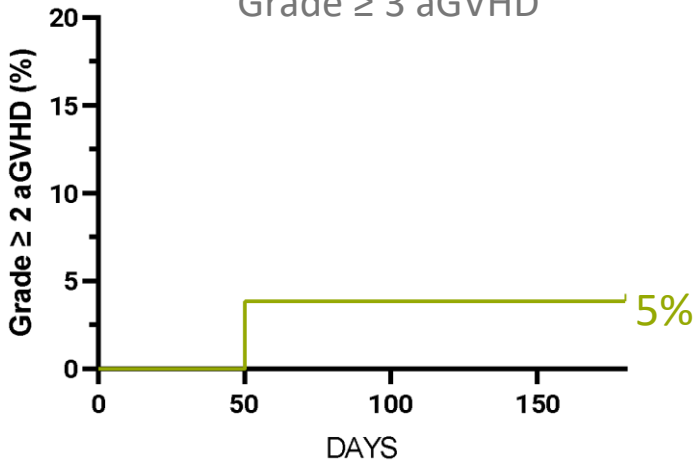
Acute Graft-vs-Host Disease was Rare

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

Grade ≥ 2 aGVHD

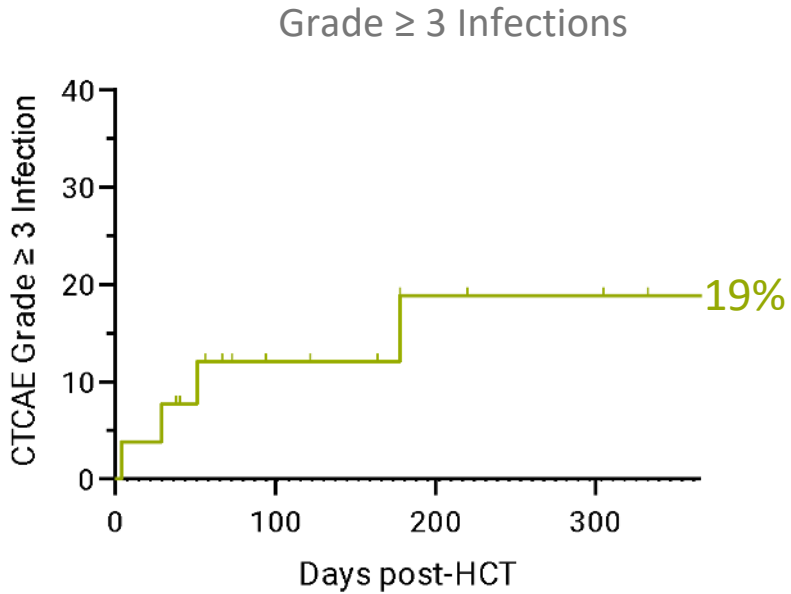


Grade ≥ 3 aGVHD



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

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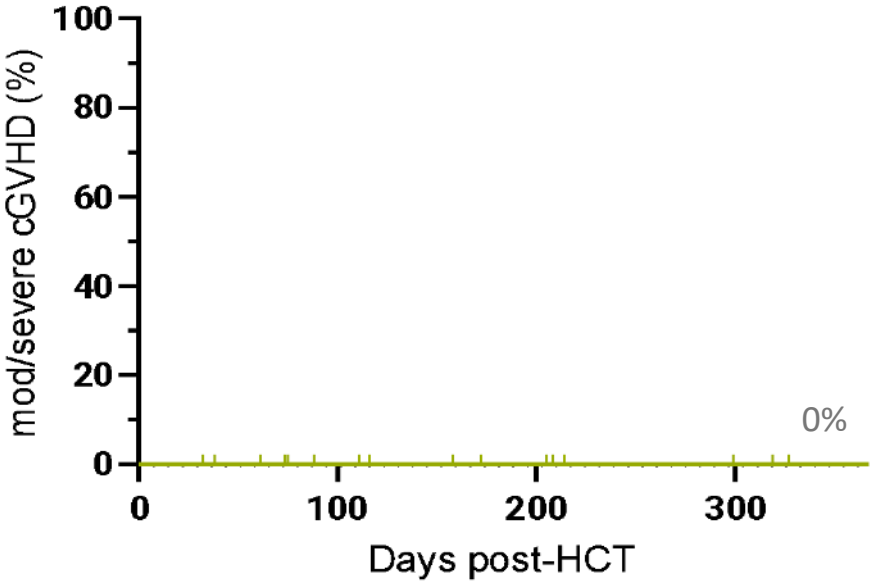
CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; CTCAE, common terminology criteria for adverse events; EBV, Epstein-Barr Virus; PLTD, post-transplantation lymphoproliferative disorder.

No Moderate-to-Severe cGvHD has Occurred

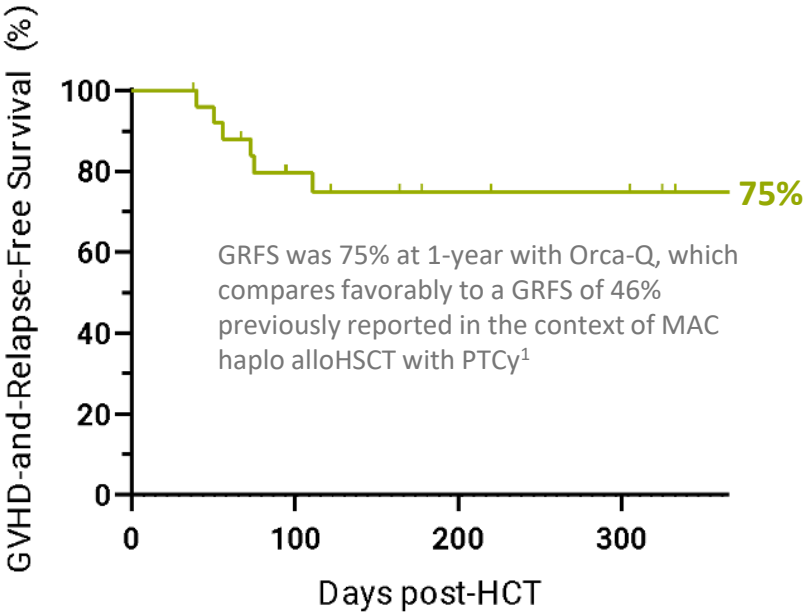
- Of the 16 patients who had > 3 months follow-up, only 1 has developed mild cGvHD
- No Orca-Q patients have developed moderate-to-severe cGvHD
  - (median follow-up 211 days; 9 patients > 1 year)
- 24% - 33% rate of chronic GvHD post haplo-HCT in various historical cohorts

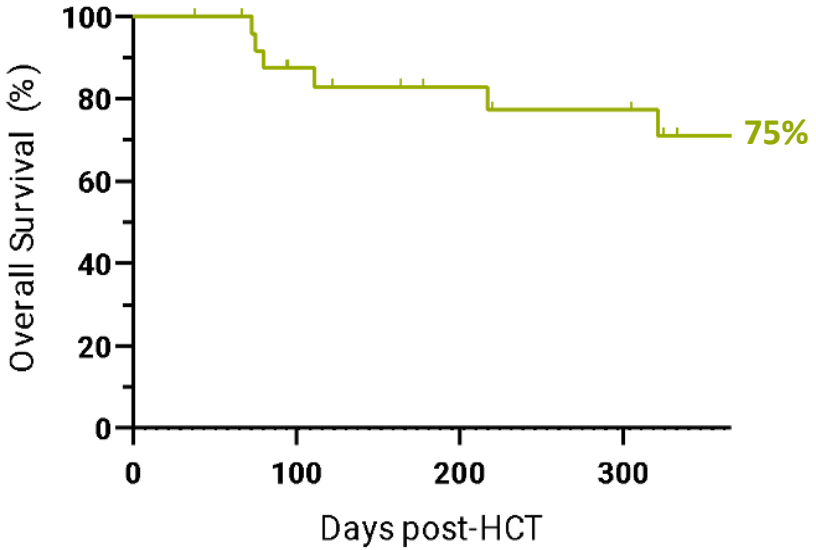


cGvHD, chronic graft-versus-host disease; GvHD, graft-versus-host disease; haplo-HCT, haploidentical hematopoietic cell transplantation; HCT, hematopoietic cell transplantation.

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.

Encouraging GvHD-and-Relapse Free and Overall Survival





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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

Conclusions

Initial Orca-Q data demonstrate promising myeloablative therapy for patients with haploidentical donors using only single agent tacrolimus and no PTCy or MMF

Patients treated with haplo Orca-Q experienced a low adverse event profile, low incidence and severity of aGvHD and cGvHD, and improved GRFS.

This phase 1 study of Orca-Q continues to enroll patients with haplo donors across the U.S.

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aGvHD, acute graft-versus-host disease; cGvHD, chronic graft-versus-host disease; GRFS, **GRFS, GVHD-free/relapse-free survival;** GvHD, graft-versus-host disease; MMF, mycophenolate mofetil; PTCy, post-transplant cyclophosphamide.

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