CT-931

Preliminary Safety and Efficacy of Myeloablative Orca-Q in Patients with Haploidentical Donors

A. SALHOTRA, MD[1], S. SROUR, MB ChB, MS[2], M. ABEDI, MD[3], E. WALLER, MD, PhD[4], H. CHOE, MD[5], A. PAVLOVA, MD, PhD[6], T. ZHARKEVICH, MD, PhD[6], S. KILLIAN, PhD[6], J.S. McCLELLAN, MD, PhD[6], N. FERNHOFF, PhD[6], and R. LOWSKY, MD[7]

1. Department of Hematology/HCT, City of Hope National Medical Center, Duarte, CA
2. Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX
3. Comprehensive Cancer Center, University of California, Davis, Sacramento, CA
4. Bone Marrow and Stem Cell Transplant Center, Emory University Winship Cancer Institute, Atlanta, GA
5. James Cancer Hospital, The Ohio State University, Columbus, OH
6. Orca Bio, Menlo Park, CA
7. Division of Blood and Marrow Transplantation & Cellular Therapy, Stanford University School of Medicine, Stanford, CA

INTRODUCTION

Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is an option for patients without matched donors. Despite advances, outcomes remain limited by immunological barriers, leading to higher risks of graft-versus-host disease (GVHD), delayed immune recovery, and variable relapse rates[1-3]. Orca-Q is a precision-engineered, cellular immunotherapy designed to facilitate immune recovery and maintain GVL while reducing GVHD with less immunosuppression. This study reports interim results from an ongoing study (NCT03802695).

AIM

To explore the safety, tolerability, and efficacy of Orca-Q product, and how these differ in patients with different donor types undergoing HSCT after myeloablative conditioning (MAC) or non-myeloablative/reduced intensity conditioning (NMA/RIC).

METHODS

- Adult patients with high-risk hematologic malignancies and eligible for MAC haplo-HSCT were enrolled in a dose expansion study using tacrolimus for GVHD prevention.
- 44 patients in total were treated, with data reported for 39 patients age <65 with AML, ALL, or MDS.
- Orca-Q was centrally manufactured at an Orca Bio GMP facility (Sacramento, CA) from GCSF-mobilized peripheral blood apheresis products.
- Patients were followed for GVHD and relapse for one year and for overall survival (OS) thereafter.
- GVHD-free, relapse-free survival (GRFS) was defined as time from transplant to the first occurrence of grade 3-4 acute GVHD (aGVHD), moderate to severe chronic GVHD (cGVHD), relapse or death.

CONCLUSIONS

- The study demonstrated high engraftment rates, encouraging OS and RFS, and low incidences of severe aGVHD and cGVHD.
- Outcomes appeared favorable in the TFT subgroup, with improved survival, GRFS, and lower relapse incidence compared to other regimens.
- These findings support the safety and efficacy of Orca-Q in reducing GVHD and achieving durable remissions.
- The Phase 1 study continues to enroll patients to confirm these results.

RESULTS

Manufacturing and Feasibility
- Orca-Q was successfully manufactured and administered for all patients
- Vein-to-vein time of less than 72 hours for 100% of products

Patient Characteristics
- 39 patients were treated
- Median age 44 years (range 21-64)
- 77% male
- Median follow-up was 937 days (range 19-1825)

Conditioning Regimens
- All patients received MAC and one of the following:
  - Bu/Flu/Thio-based
  - TBI/Flu/Thio
  - TBI/Flu
- TFT outcomes are presented separately in Table 1

Engraftment and Tolerability
- Orca-Q was well tolerated
- All patients achieved neutrophil engraftment by day +19 (median 11 days)
- Two patients with busulfan-based conditioning experienced secondary graft failure

Clinical Outcomes
- Mean cumulative serious adverse events (SAEs) at 1 year:
  - 0.43 for patients with TFT regimen
  - 1.08 for patients with other regimens

	All Patients N=39	Patients with TFT Regimen N=14
Median follow-up, days	937	1244
OS at 1, 2, 3 years	80%, 77%, 77%	85%, 85%, 85%
RFS at 1 year	77%	85%
GRFS at 1 year	72%	85%
NRM at 1 year	5.8%	7.7%
Relapse incidence at 1 year	18.2%	8.4%
aGVHD gr 3-4 at D+180	8.1%	0%
Mod-to-severe cGVHD at 1 year	0%	0%
BMT CTN Grade 3+ infections at 1 year	5.3%	7.1%

Table 1. Clinical outcomes in all patients and the TBI/Flu/Thio subgroup.

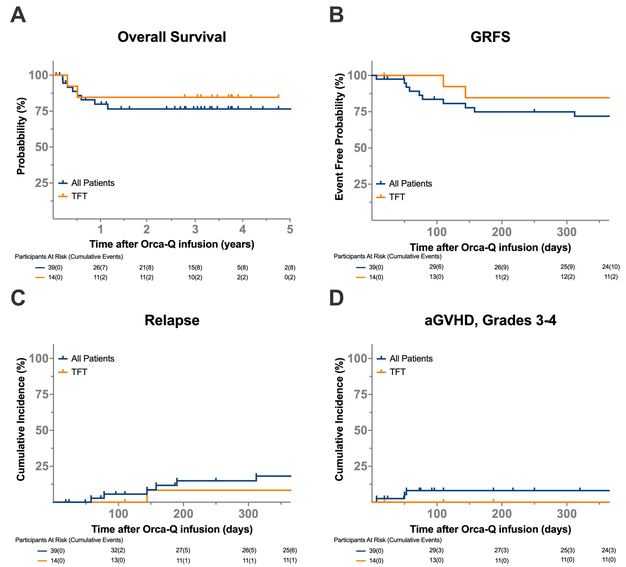

Figure 1. Clinical outcomes following Orca-Q transplantation. (A) OS; (B) GRFS; (C) Relapse; (D) aGVHD. Time-to-event outcomes were estimated using the Kaplan–Meier method for GRFS and OS and cumulative incidence methods for aGVHD and relapse.

DISCLOSURES

Orca Bio sponsored the Phase 1 Orca-Q clinical trials.

REFERENCES

1. **Astigarraga CC et al.** Haploidentical transplantation: An optimal platform for graft manipulation and cellular therapies. *Blood Rev.* 2025;72:101286.
2. **Bertaina A et al.** Unrelated donor vs HLA-haploidentical α/β T-cell- and B-cell-depleted HSCT in children with acute leukemia. *Blood.* 2018;132(24):2594-2607.
3. **Fuchs EJ.** Haploidentical transplantation for hematologic malignancies: where do we stand? *Hematology Am Soc Hematol Educ Program.* 2012;2012:230-236.