A RANDOMIZED PHASE 3 TRIAL IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES DEMONSTRATES IMPROVED SURVIVAL FREE OF CHRONIC GVHD WITH ORCA-T® COMPARED TO CONVENTIONAL ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT

RAWAN FARAMAND[1], AMANDEEP SALHOTRA[2], ARPITA GANDHI[3], JEREMY PANTIN[4], SAGAR PATEL[5], RASMUS HOEG[6], ALEXANDRA GOMEZ-ARTEAGA[7], RONI TAMARI[7], SATYAJIT KOSURI[8], ANTONIO JIMENEZ[9], JENNIFER HOLTER-CHAKRABARTY[10], BHAGIRATHBHAI DHOLARIA[11], YI-BIN CHEN[12], BETTY HAMILTON[13], JOHN MAGENAU[14], ALIREZA EGHTEDAR[15], ANNA PAVLOVA[16], NATHANIEL FERNHOFF[16], JAMES SCOTT MCCLELLAN[16], CASPIAN OLIAI[17], ROBERT NEGRIN[18], EVERETT MEYER[18]

[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA. [2]Gehr Family Center for Leukemia Research, City of Hope, Duarte, CA, USA. [3]Center for Hematologic Malignancies - Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA. [4]Sarah Cannon Transplant and Cellular Therapy Program at TriStar Centennial Medical Center, Nashville, TN, USA. [5]University of Utah, Huntsman Cancer Institute, Salt Lake City, UT, USA. [6]University of California, Davis, CA, USA. [7]Memorial Sloan Kettering Cancer Center, New York, NY, USA. [8]Hematology/Oncology, University of Chicago Medicine, Chicago, IL, USA. [9]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA. [10]OU Health Stephenson Cancer Center, Oklahoma City, OK, USA. [11]Vanderbilt University Medical Center, Nashville, TN, USA. [12]Hematopoietic Cell Transplant and Cell Therapy Program, Massachusetts General Hospital, Boston, MA, USA. [13]Cleveland Clinic, Cleveland, OH, USA. [14]Rogel Cancer Center, University of Michigan, Ann Arbor, MI, USA. [15]Colorado Blood Cancer Institute, Denver, CO, USA. [16]Orca Biosystems Inc., Menlo Park, CA, USA. [17]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA. [18]Stanford University School of Medicine, Stanford, CA, USA

Introduction

Despite multi-agent prophylaxis, graft-versus-host disease (GVHD) is a leading treatment-related complication after allogeneic HSCT.[1] Orca-T, an investigational allogeneic T-cell immunotherapy, leverages high-purity regulatory T cells to prevent GVHD.[2] We report results from the randomized, phase 3 component of the Precision-T study comparing Orca-T with Tacrolimus to a conventional allograft with Tacrolimus/Methotrexate (Tac/MTX).

Aim and Objectives

Compare moderate-to-severe chronic GVHD-free survival (cGFS) in patients who received either Orca-T or standard GVHD prophylaxis with tacrolimus/methotrexate (Tac/MTX). Secondary endpoints included cumulative incidence of chronic GVHD, GVHD-free, relapse-free survival (GRFS), and overall survival (OS) (NCT05316701).

Methods

Table 1. Study eligibility criteria and endpoints

Study Population	• Basket trial of patients with AML, MDS, ALL, or MPAL who would otherwise have undergone standard allo-HSCT • Patients 18 – 65 years in CR/CRi
Primary Endpoint	• Rate of survival free of moderate-to-severe chronic GvHD ("cGFS")
Secondary Endpoints	• Overall Survival (OS) • GvHD-free, relapse-free survival (GRFS) • Incidence of moderate-to-severe cGvHD

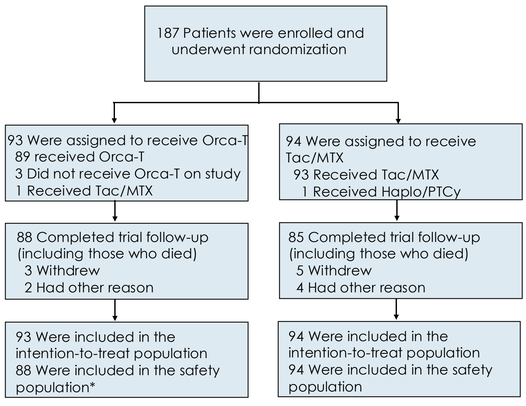


Figure 1. Study eligibility criteria and endpoints

* There were no manufacturing failures for the 5 patients not included in the Orca-T safety population

Table 2. Patient baseline characteristics

Characteristics	Orca-T (N = 93) n (%)	Tac/MTX (N = 94) n (%)	Total (N = 187) n (%)
Age			
Mean – years	43.4 yrs	43.8 yrs	43.6 yrs
≥55 yr old- no.(%)	23 (23.7)	27 (28.7)	50 (26.7)
Sex			
Male	53 (57.0)	50 (53.2)	103 (55.1)
Female	40 (43.0)	44 (46.8)	84 (44.9)
Ethnicity / Race			
Hispanic or Latinx	26 (28.0)	24 (25.5)	50 (26.7)
Am. Indian/Native	1 (1.1)	2 (2.1)	3 (1.6)
Asian	10 (10.8)	8 (8.5)	18 (9.6)
Black	1 (1.1)	2 (2.1)	3 (1.6)
Pacific Islander	1 (1.1)	1 (1.1)	2 (1.1)
White	76 (81.7)	63 (67.0)	139 (74.3)
NR/ Unknown	4 (4.3)	18 (19.1)	22 (11.8)
Primary disease			
ALL	30 (32.3)	27 (28.7)	57 (30.5)
AML	49 (52.7)	51 (54.3)	100 (53.5)
High-risk MDS	12 (12.9)	11 (11.7)	23 (12.3)
Baseline HCT-CI Score			
0	18 (19.4)	27 (28.7)	45 (24.1)
1	30 (32.3)	18 (19.1)	48 (25.7)
2	22 (23.7)	20 (21.3)	42 (22.5)
3	11 (11.8)	21 (22.3)	32 (17.1)
4	12 (12.9)	7 (7.4)	19 (10.2)
5	0	1 (1.1)	1 (0.5)
Donor Type, n (%)			
Matched sibling	46 (49.5)	49 (52.1)	95 (50.8)
Matched unrelated	47 (50.5)	45 (47.9)	92 (49.2)
DRI score, n (%)			
High	19 (20.4)	16 (17.0)	35 (18.7)
Intermediate	74 (79.6)	78 (83.0)	152 (81.3)

Results

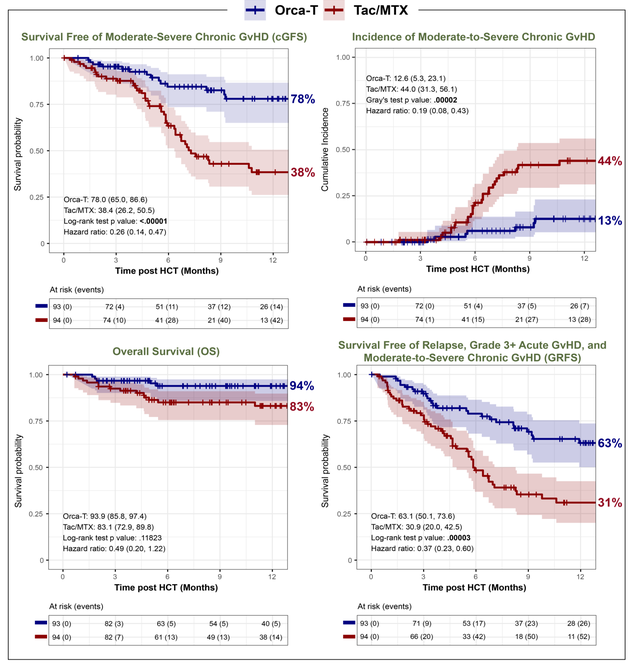


Figure 1. Primary and secondary outcomes: survival probabilities and cumulative incidence of cGVHD

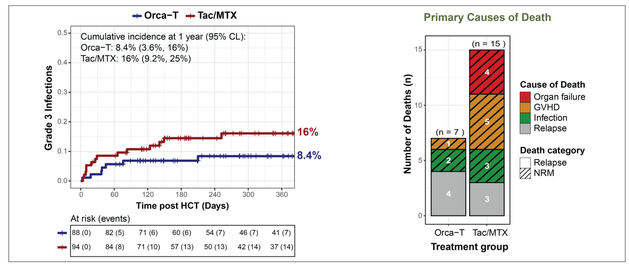


Figure 2. Incidence of serious infections and causes of death

Table 3. Other toxicity and efficacy outcomes

Survival Outcomes	Orca-T Arm	Tac/MTX Arm
1-year non-relapse mortality (NRM)	3.4%	13%
1-year relapse-free survival (RFS)	76%	74%
Major Transplant Toxicities		
No. of participants with a serious TEAE	34 (39%)	53 (56%)
1-year incidence of Grade 2+ aGvHD	22%	30%
1-year incidence of Grade 3+ aGvHD	6.2%	16%
No. of participants with cGvHD (all grades)	15 (17%)	46 (49%)
Engraftment and Hospitalization		
Median timing of neutrophil engraftment	13 days	14 days
Median timing of platelet engraftment	17 days	18 days
Number of participants re-hospitalized due to AE	24 (27%)	43 (46%)
Graft failure (primary)	0 (0.0%)	0 (0.0%)
Graft failure (secondary)	1 (1.1%)	0 (0.0%)

Summary

The trial met its primary endpoint, demonstrating higher cGFS with Orca-T, likely driven by reduced chronic GVHD and a positive trend in OS

Conclusion

- Orca-T significantly improved cGFS compared to conventional allograft + Tac/MTX (P<0.00001)
- Orca-T demonstrated significant improvement in cGvHD (P=0.00002) and GRFS (P=0.00003), and a trend for improved OS (P=0.11823)
- Fewer serious TEAEs, grade2+ GVHD, grade 3 infections and rehospitalizations observed with Orca-T

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References

1. Garnett C et al. *Ther Adv Hematol*. 2013
2. Oliai et al. *Blood*. 2022

clinicaltrials@orcabio.com