orcabio

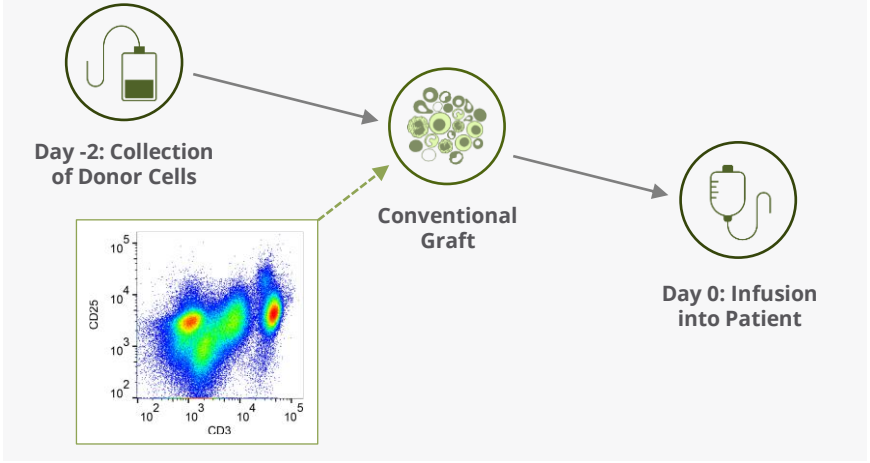
December Data Update*

Orca-T results in high GvHD-Free and Relapse-Free Survival following myeloablative conditioning for hematological malignancies: results of a single center phase 2 and a multicenter phase 1b study

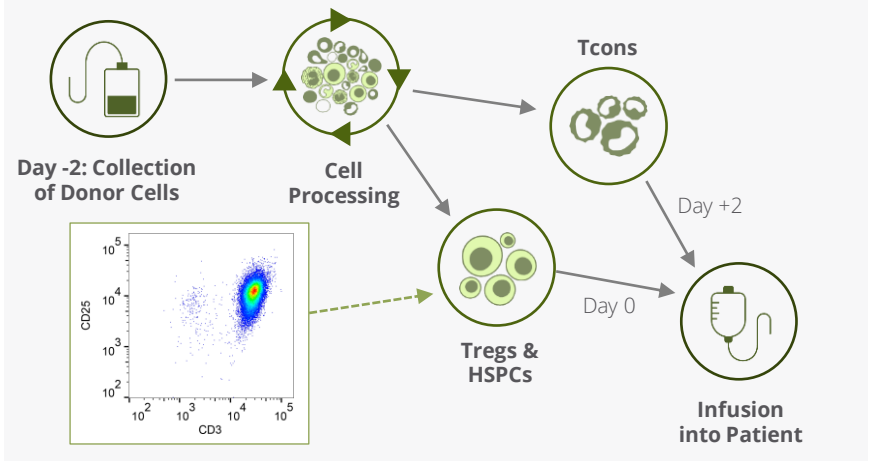
*Data update presented at the 2021 ASH Annual Meeting

Orca-T is a cell therapy product designed to fit into traditional transplant center treatment protocols

Conventional Transplant

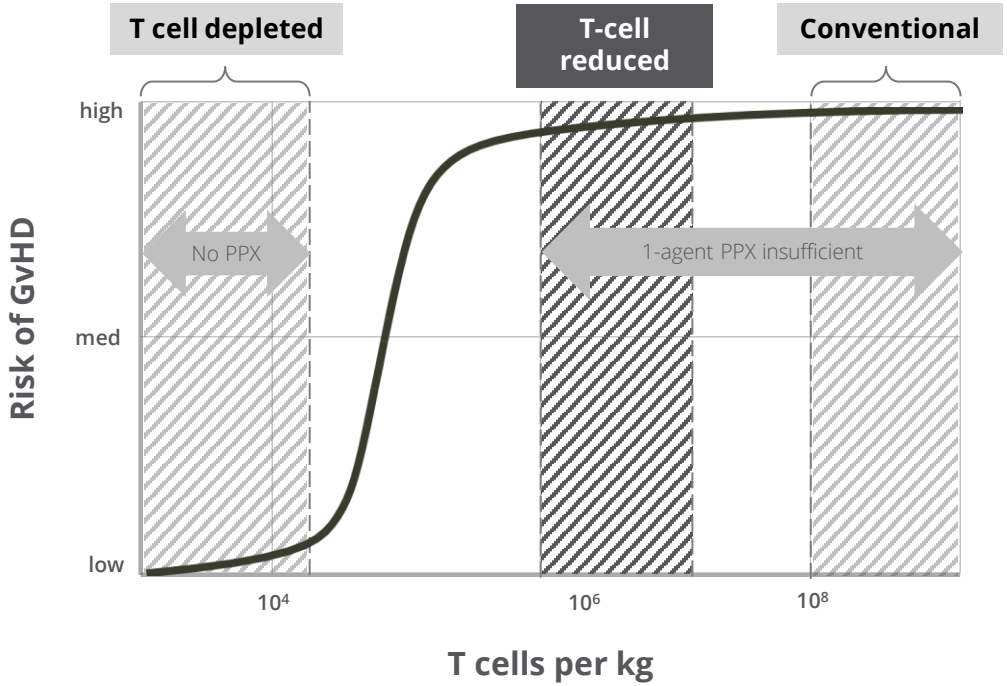


High-Precision Orca-T



Eddinger et al. Nature Medicine 2003 Sep;9(9):1144-50. | Trzonkowski et al. Clin Immunol. 2009 Oct;133(1):22-6. Di Ianni M, et al. Blood. 2011;117(14):3921–3928. | Brunstein, et al. Blood 2016 Feb 127 (8):1044-51. | Kellner H, et al. Oncotarget 2018 Nov 2;9(86):35611-35622.

GvHD Risk with reduced T-cell grafts remains significant

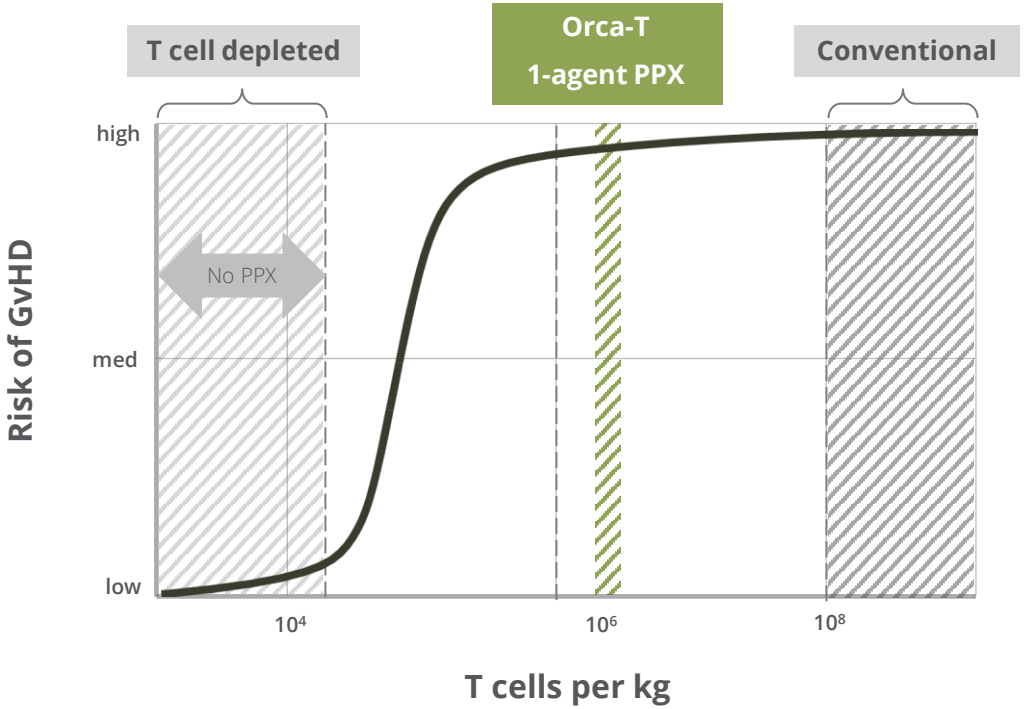


T cell reduced grafts

- Previous studies employing T cell reduction of allografts alone still show significant acute and chronic GVHD with single-agent cyclosporin prophylaxis*

*Montero et al. BBMT 12:1318-1325 (2006)
Nakamura et al. BJH 115:95-104 (2001)
Barrett et al. BMT 21: 543-551 (1998)

Evaluation of high-precision Orca-T to control GvHD

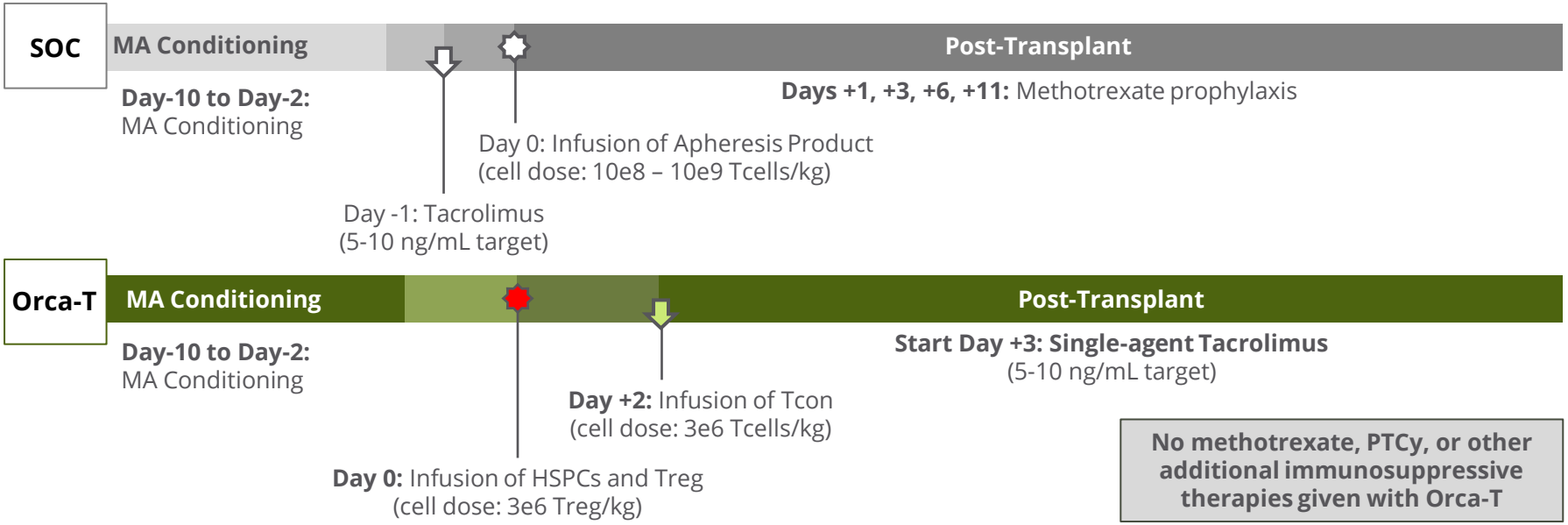


Orca-T + 1-agent PPX

- Yield of Treg from apheresis: 2-3 million Treg/kg
- Target ratio of T-cell to Treg: 1:1
- Conventional T-cell dose: 3 million/kg
- CD34 dose: >2 million/kg

*Montero et al. BBMT 12:1318-1325 (2006)
Nakamura et al. BJH 115:95-104 (2001)
Barrett et al. BMT 21: 543-551 (1998)

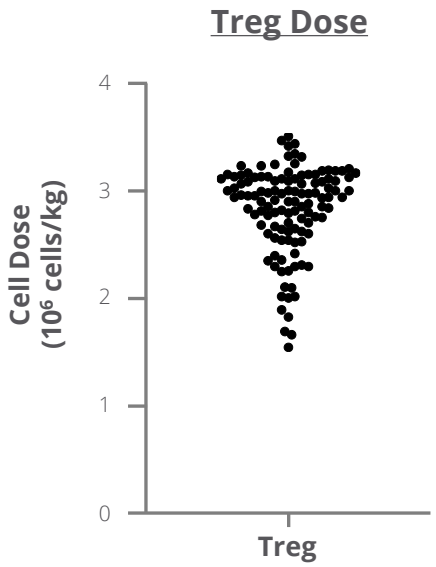
Orca-T treatment consisted of MAC with single agent post-treatment tacrolimus and no methotrexate

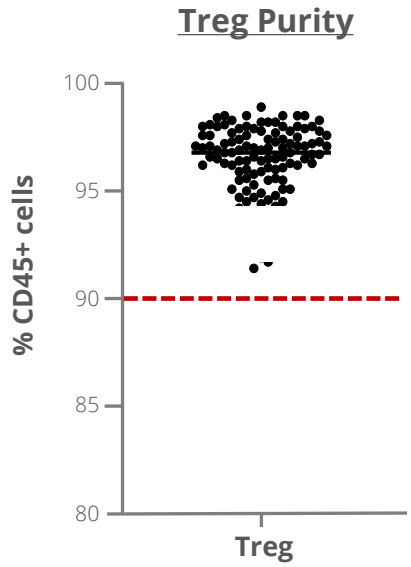


Meyer, E. H., Laport, G., et al. JCI INSIGHT. 2019; 4 (10)

Orca manufacturing has reliably manufactured to deliver consistent Treg dose and purity

High purity Orca-T products have been delivered to >130 patients to date

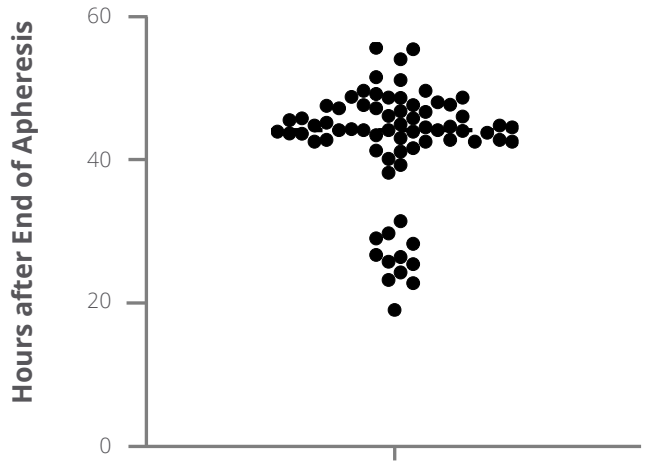




Orca manufacturing has reliably manufactured and delivered Orca-T at transplant centers across the US

Vein-to-vein times of <72 hours consistently achieved

Time from End of Apheresis to Delivery at Transplant Center (Hours)



Orca-T is being evaluated in a single-institutional phase 2 study and a multicenter phase 1b study

Key Eligibility Criteria

Stanford Single Center Phase 2 Trial (NCT04013685)	Orca Multicenter Phase 1b Trial (NCT01660607)
• Acute leukemia (AML, ALL, mixed phenotype), including patients with active disease at time of transplant • Myelodysplastic syndrome • Myelofibrosis • Non-Hodgkin Lymphoma • CML in accelerated phase or blast crisis	• Acute leukemia (AML, ALL, mixed phenotype), including patients with active disease at time of transplant (≤ 10% BM blast burden) • Myelodysplastic syndrome • Myelofibrosis • BPDCN • CML in accelerated phase or blast crisis
8/8 matched related or unrelated donor	8/8 matched related or unrelated donor
HCT-CI ≤ 4	HCT-CI ≤ 4
KPS≥70	KPS≥70
Age 18-72	Age 18-65
Adequate organ function	Adequate organ function

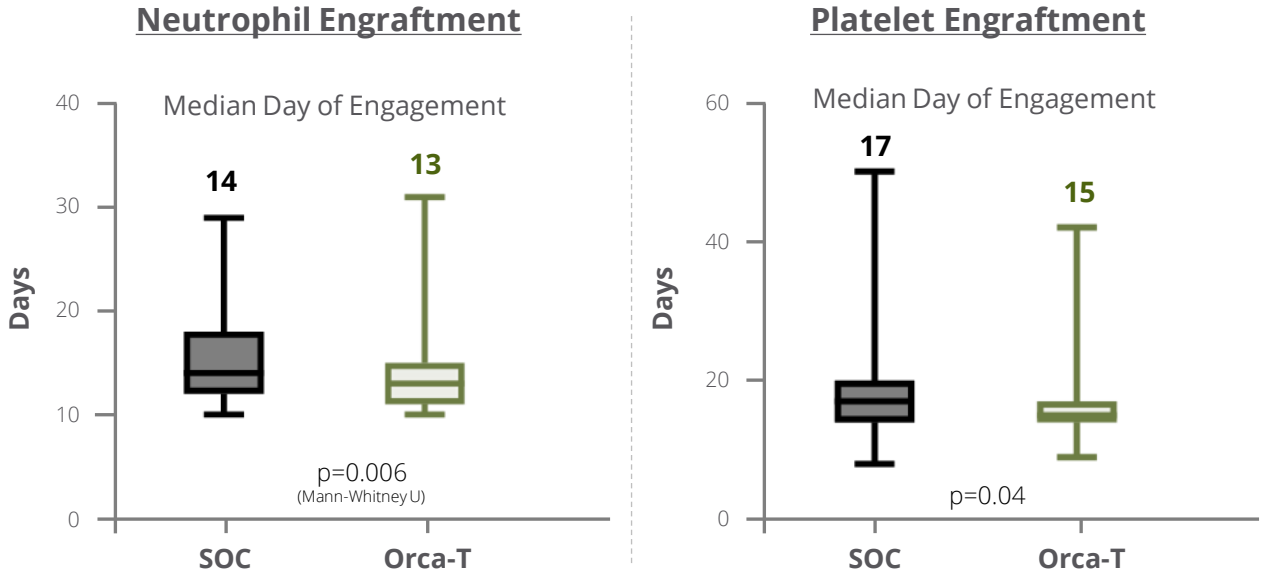
Patient demographics: Orca-T and SOC control cohort

For comparison purposes, a standard-of-care comparator cohort was identified using patients treated contemporaneously at Stanford University Hospital: n=95 consecutive patients who received a PBSC-derived graft and Tac/MTX GVHD prophylaxis

		Orca-T: Stanford Phase 2*	Orca-T: Multicenter Phase 1b*	SOC Control Cohort
Cohort size		**29**	**80**	**95**
Median age (range)		42 (19-71)	49 (22-65)	48 (20-64)
% Male		72%	51%	49%
Race	White (Non-Hispanic and Hispanic)	52%	67%	44%
	African American	1%	1%	2%
	Asian	17%	13%	19%
	Unspecified	28%	16%	30%
Primary Disease %	AML	39%	45%	39%
	ALL	26%	34%	26%
	MDS/myelofibrosis	13%	19%	19%
	CML	8%	1%	6%
	Non-Hodgkin Lymphoma	8%	0%	8%
	Other (e.g. mixed phenotype acute leukemia)	5%	1%	2%
% with active leukemia at time of transplant		28%	19%	21%
Graft source: HLA-matched sibling/ HLA-matched unrelated donor		72%/28%	53%/47%	56%/44%
Median f/u in days (range)		617 days (148-1809)	209 days (27-704)	886 days (55-1783)

*All subjects reported have ≥ 90 days follow-up (or death prior to Day +90). Data from NCT04013685 and NCT01660607

Rapid engraftment was observed with Orca-T

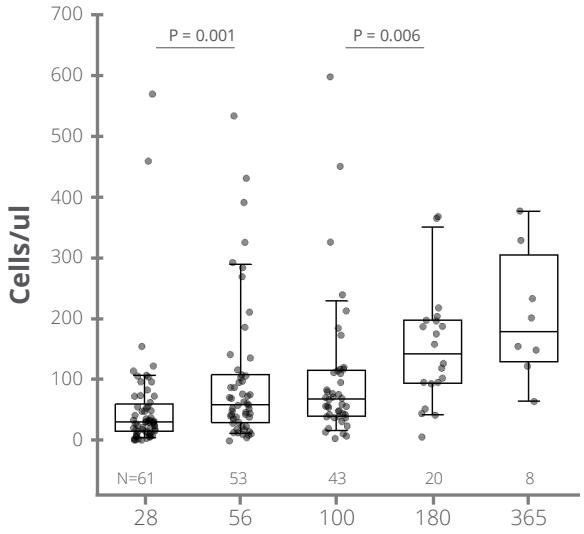


Only 1 of 109 patients experienced graft failure with Orca-T

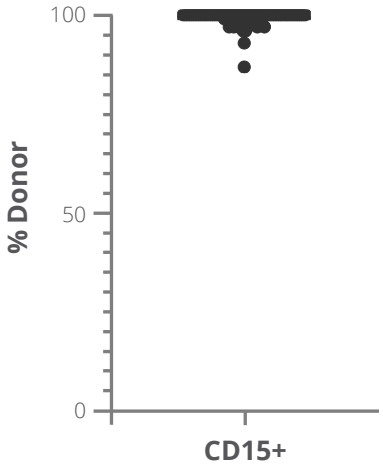
- A Ph+ ALL patient who experienced apparent graft rejection followed by rapid autologous recovery within weeks of TBI/Cy conditioning
- One additional Orca-T patient experienced "poor graft function" requiring a CD34 boost
- Patient remains disease-free >400 days post-transplant

Immune reconstitution has been robust with Orca-T

Peripheral Blood CD4+ T Cells



Myeloid Donor Chimerism, Day +28

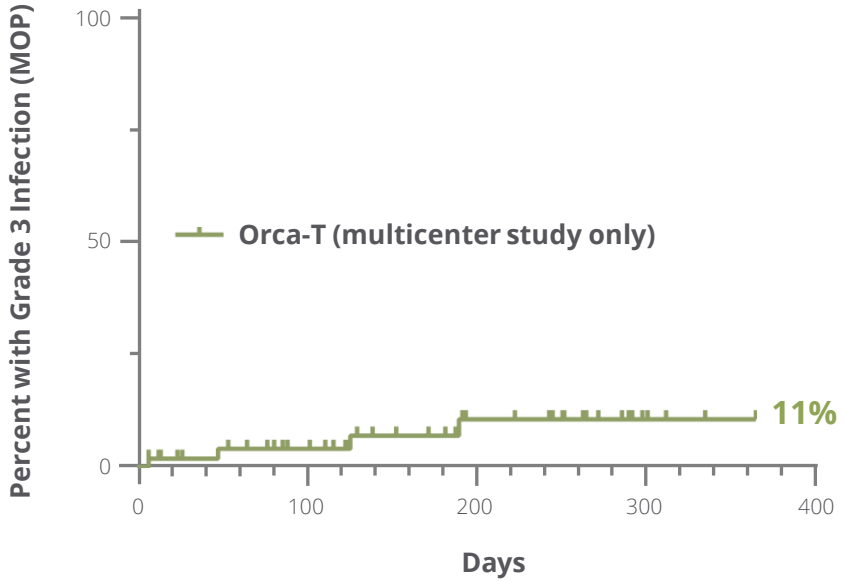


T cell, B cell, and NK cell donor chimerism, Day +100:

Lineage Marker	% of patients with >90% donor chimerism at Day+100
CD3+ T cells	80%
CD19+ B cells	100%
CD56+ NK Cells	98%

Data from Multicenter Phase 1b Trial

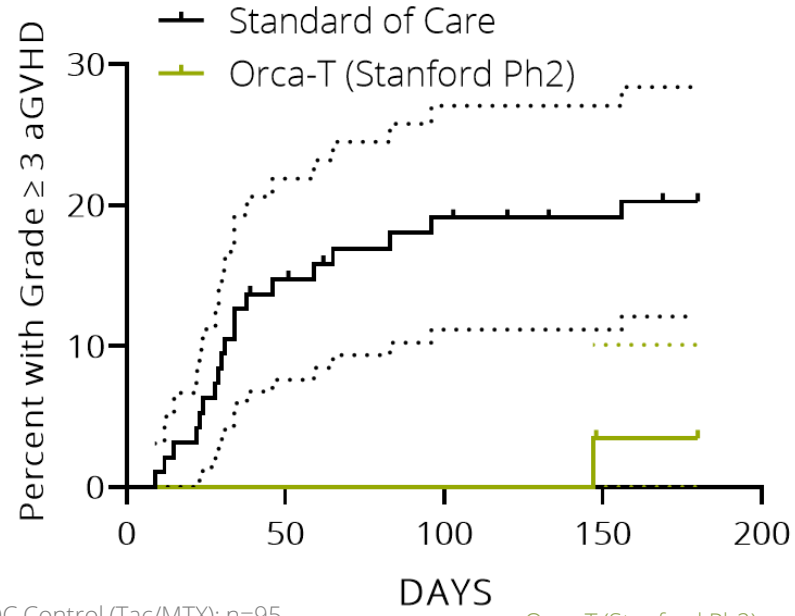
Low infectious disease complications have been seen with Orca-T



- Data available for the first 52 patients treated on the multicenter study
- Infections graded per the BMT CTN Manual of Procedures; independently assessed by external pathologist

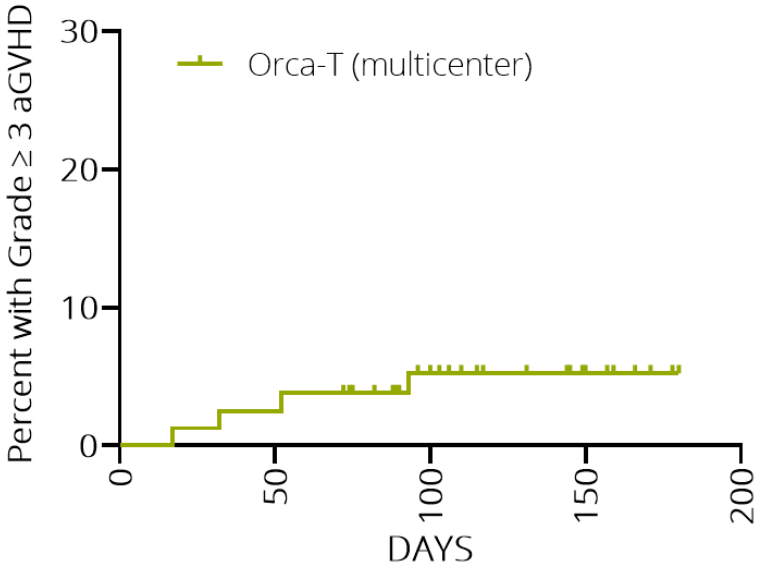
Acute GVHD is reduced with Orca-T

Grade ≥3 Acute GvHD



SOC Control (Tac/MTX): n=95
(rate at 1 year and 95% confidence intervals shown)

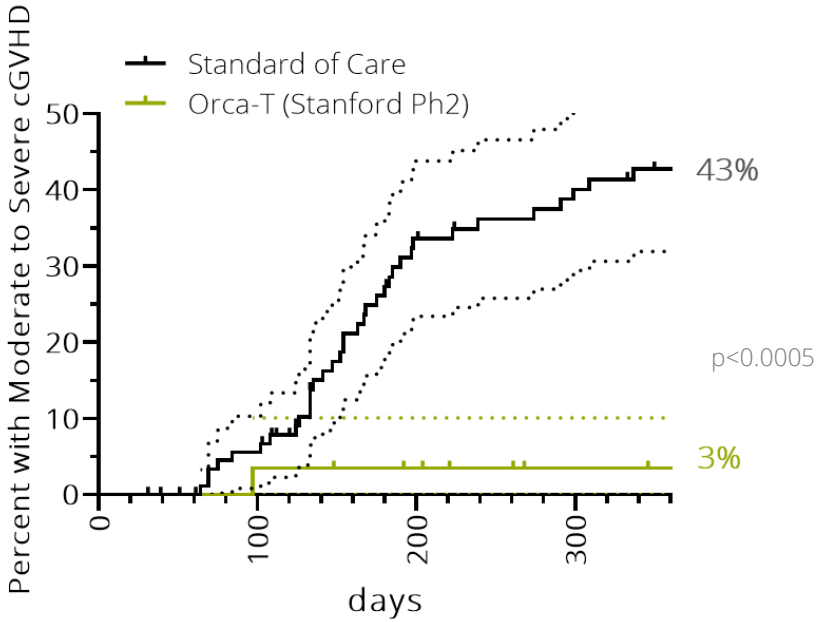
Orca-T (Stanford Ph2): n=29



Orca-T (Multicenter): n=80

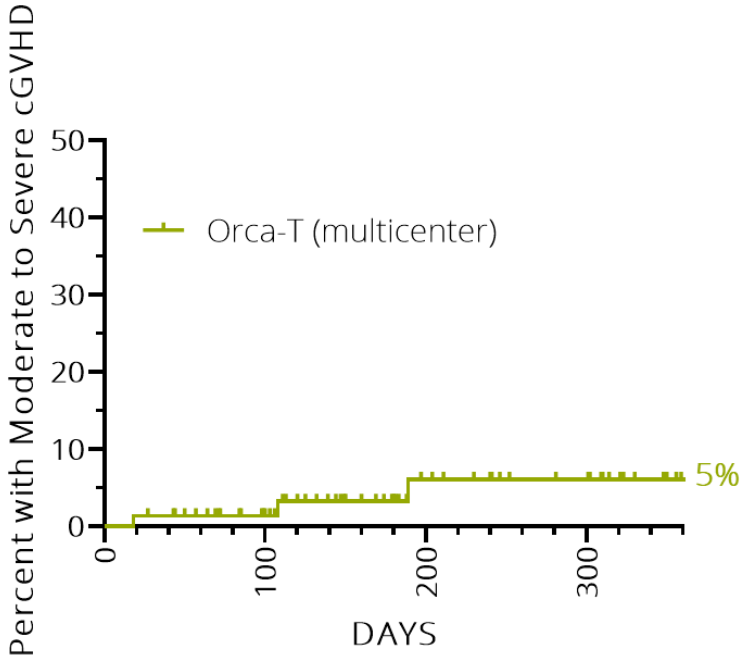
Chronic GVHD is profoundly reduced with Orca-T

Moderate to Severe Chronic GvHD



SOC Control (Tac/MTX): n=95
(rate at 1 year and 95% confidence intervals shown)

Orca-T (Stanford Ph2): n=29

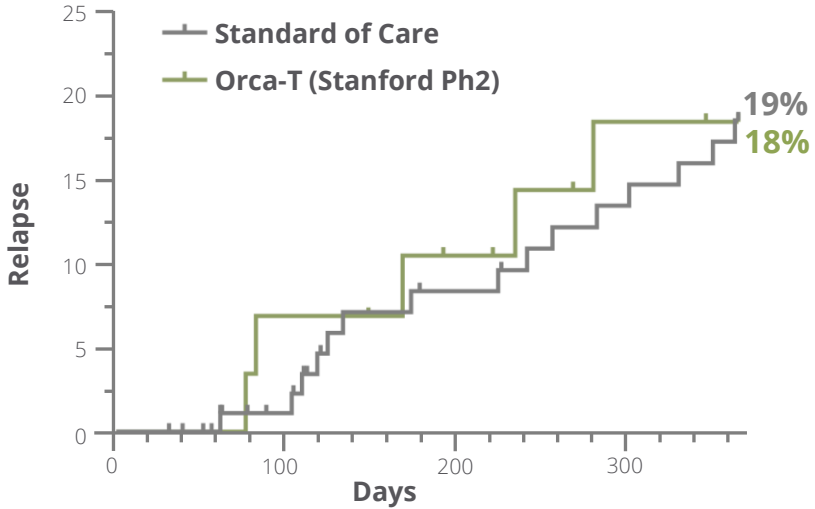


Orca-T (Multicenter): n=80

Relapse does not appear to be increased with Orca-T

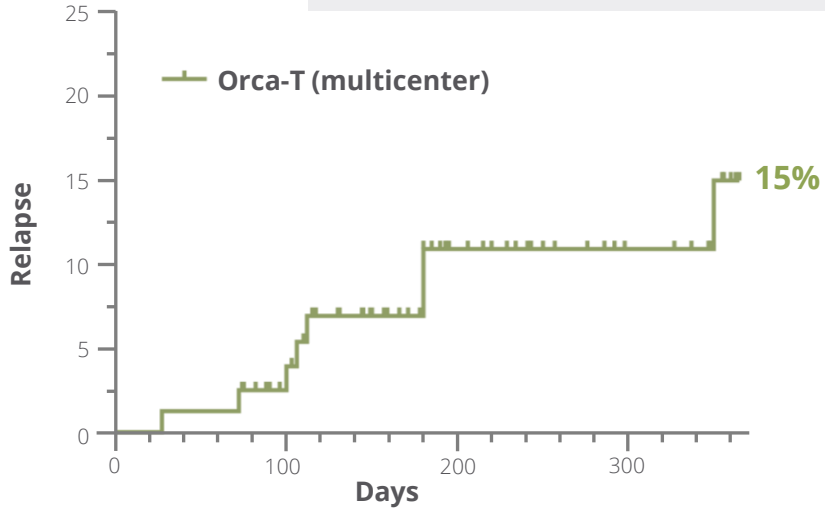
Relapse rate (%)

Please see Abstract# 1819, Gandhi et al., for results of Orca-T in patients with myelofibrosis (Saturday Evening Poster Session)



SOC Control (Tac/MTX): n=95

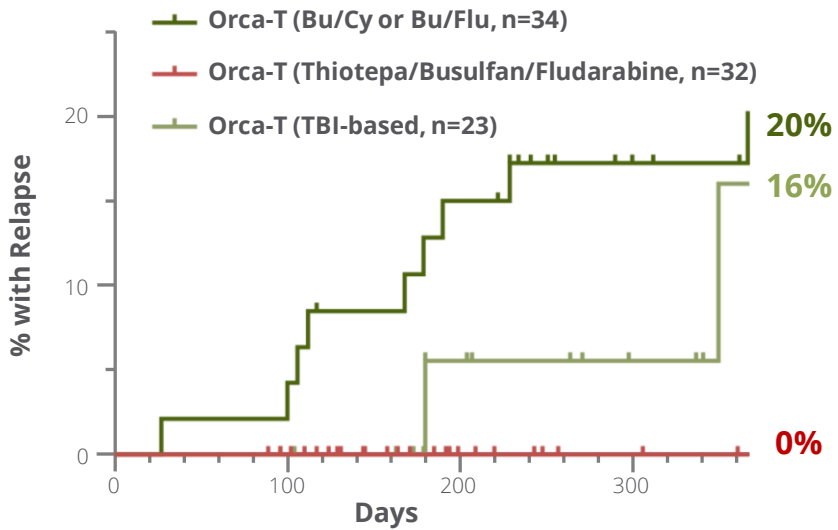
Orca-T (Stanford Ph2): n=29



Orca-T (Multicenter): n=80

Disease control with Orca-T may be further optimized by conditioning regimen choice

Relapse through 1-year post-transplant
(data from Stanford Ph2 and multicenter combined)

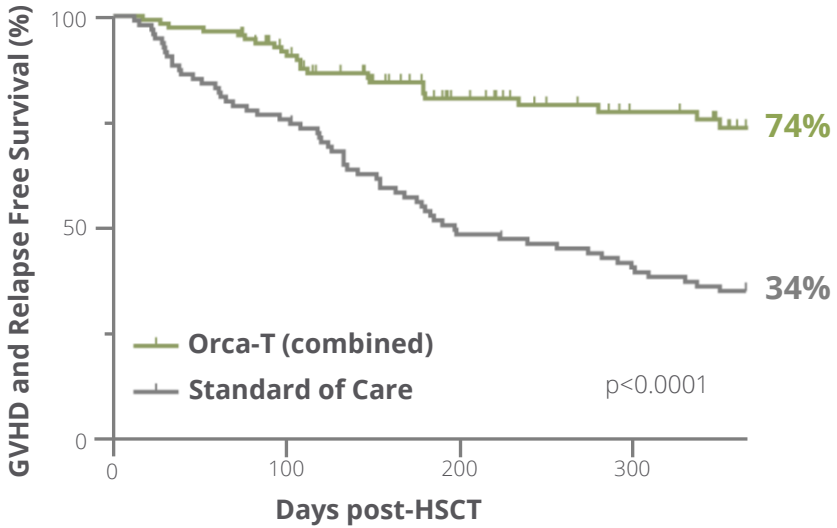


Other regimens, n=20, data not shown

- Bu/Flu/Thiotepa (BFT), n=32, median f/u 172 days with 7 patients having > 1 year f/u
- TBF regimen well tolerated with Orca-T; no NRM to date

Both the Stanford Phase 2 and multicenter data suggests that Orca-T can achieve a markedly improved 1-year GRFS

GVHD and Relapse-Free Survival
(Combined Ph2 and Multicenter)

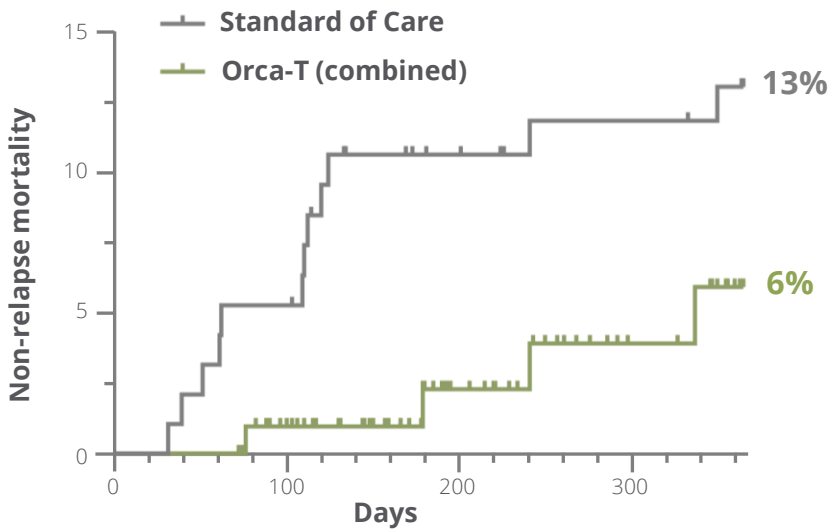


SOC Control (Tac/MTX): n=95 (shown for illustrative purposes only)

Orca-T (combined): n=109
Orca-T (Stanford Ph2): n=29; Orca-T (multicenter): n=80

Orca-T plus single-agent GVHD PPX has been well-tolerated with low NRM

Non-Relapse Mortality



Non-relapse causes of death with Orca-T (n=4 events through 1 year with Orca-T)

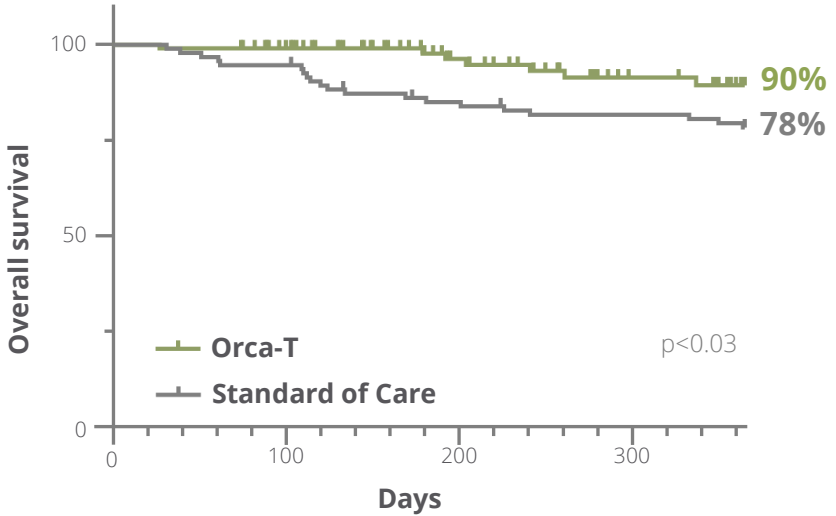
- Mucormycosis
- Congestive heart failure
- Viral pneumonia
- COVID-19 pneumonia

SOC Control (Tac/MTX); Control cohort identified prior to COVID era: n=95

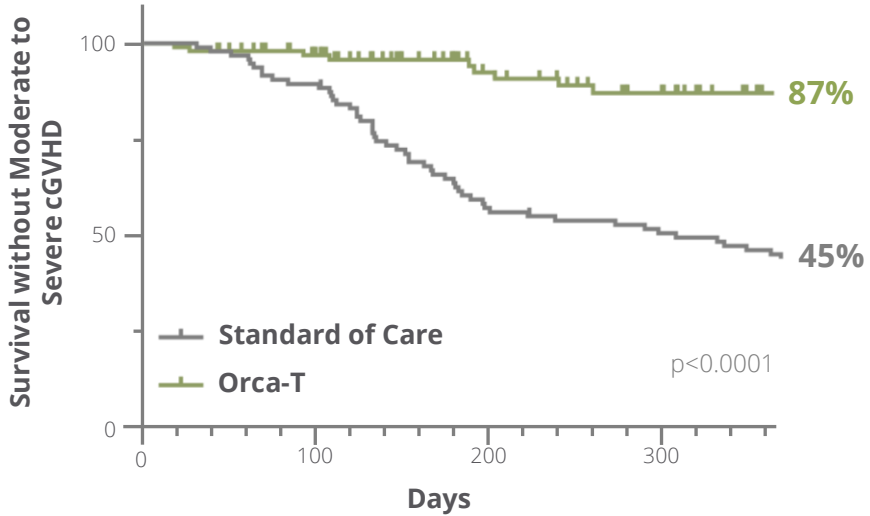
Orca-T (Combined Stanford Ph2 & multicenter): n=109

Orca-T may lead to improved overall survival

Overall Survival



Chronic-GVHD-free survival



SOC Control (Tac/MTX): n=95 Orca-T (combined): n=109

Summary of experience with Orca-T to date

GRFS With Orca-T, 1-yr GRFS more than doubled compared to standard of care

GvHD With Orca-T, significantly reduced acute and chronic GvHD compared to SOC despite reduction of immunosuppressive meds

NRM Orca-T was well-tolerated with reduced non-relapse mortality

Engraft-ment Improved time-to-engraftment compared to SOC

GVI Robust immune reconstitution leading to low rates of severe infections post-transplant

Central GMP laboratory production with no manufacturing/distribution failures

Vein-to-vein times of less than 72 hours across the continental United States

Orca is initiating a Phase III study comparing Orca-T to standard-of-care allograft with first patient treated expected in early 2022

Participating Centers and Acknowledgements

UC Davis Medical Center
- Rasmus Hoeg
- Mehrdad Abedi
- Gerhard Bauer

Oregon Health Sciences University
- Arpita Ghandi

UCLA Medical Center
- Caspian Oliai

MD Anderson Cancer Center
- Rohtesh Mehta
- Samer Srour

University of Kansas
- Joseph McGuirk

Emory University
- Ned Waller

Medical College of Wisconsin
- Bronwen Shaw

Stanford Hospital and Clinics
- Anna Pavlova
- Lori Muffly
- Parveen Shiraz
- Sally Arai
- Laura Johnston
- Robert Lowsky
- Andrew Rezvani
- Wen-Kai Weng
- David Miklos
- Matthew Frank
- John Tamaresis
- Ying Lu
- Vaibhav Agrawal
- Robert Negrin

Orca Bio
- Nate Fernhoff
- J. Scott McClellan
- Amy Putnam

Thank you to the patients who participated in these studies and to their families!

Questions