



# Orca-T, a Precision Treg-Engineered Donor Product, in Myeloablative HLA-Matched Transplantation Prevents Acute and Chronic GVHD with Less Immunosuppression in an Early Multicenter Experience

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# Conflicts of interest

Everett Meyer, MD, PhD



Co-founder, scientific advisor



Co-founder, scientific advisor



Scientific Advisory Board



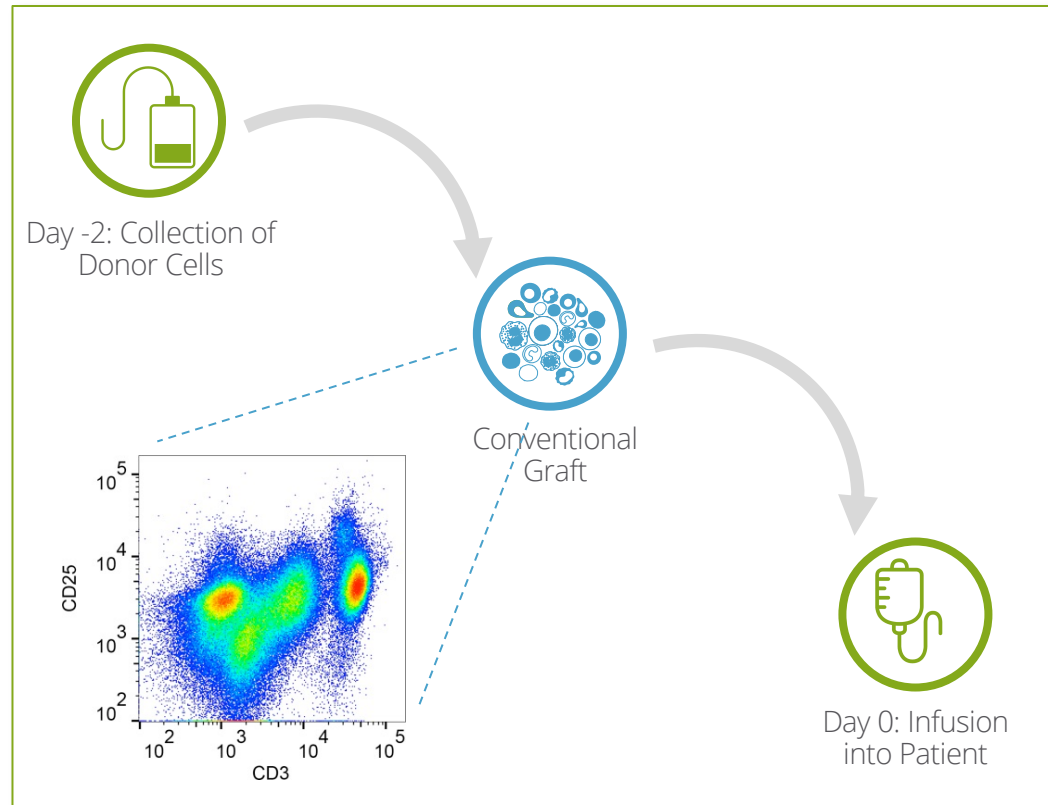
Scientific Advisory Board



Sponsored Research Support

# Regulatory T cells (Tregs) in hematopoietic stem cell transplantation

## Conventional Transplant



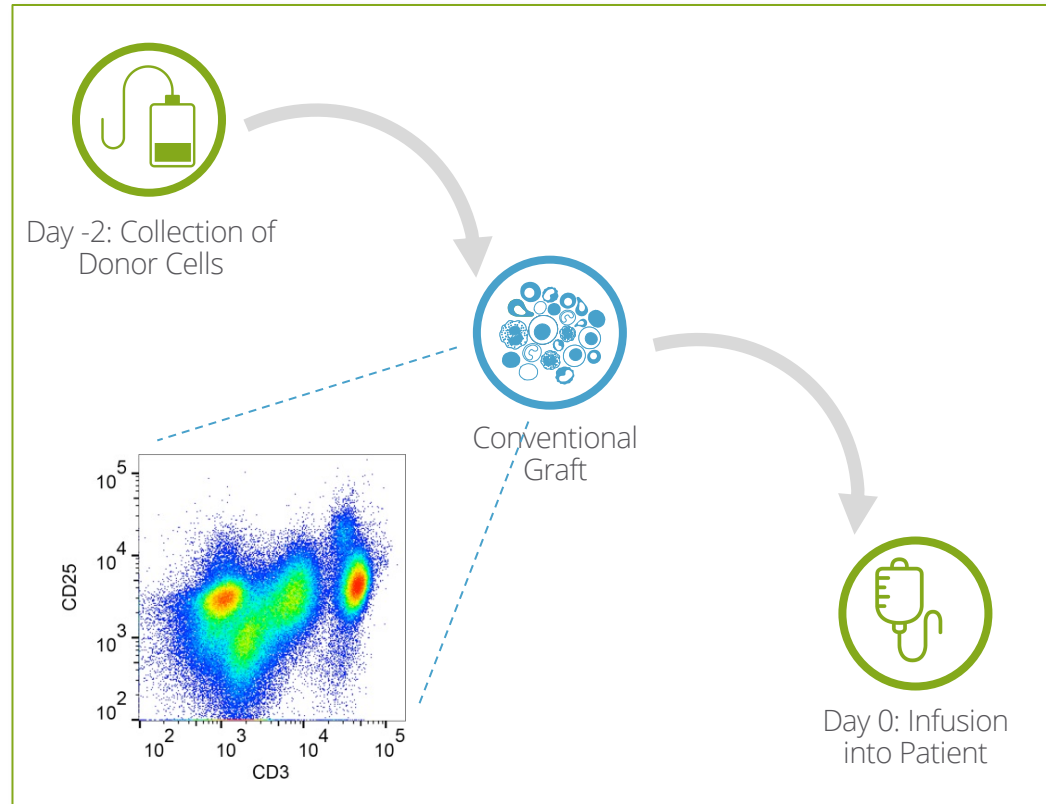
T Regulatory Cell

CD4<sup>+</sup>CD25<sup>+</sup>CD127<sup>lo</sup>FoxP3<sup>+</sup>

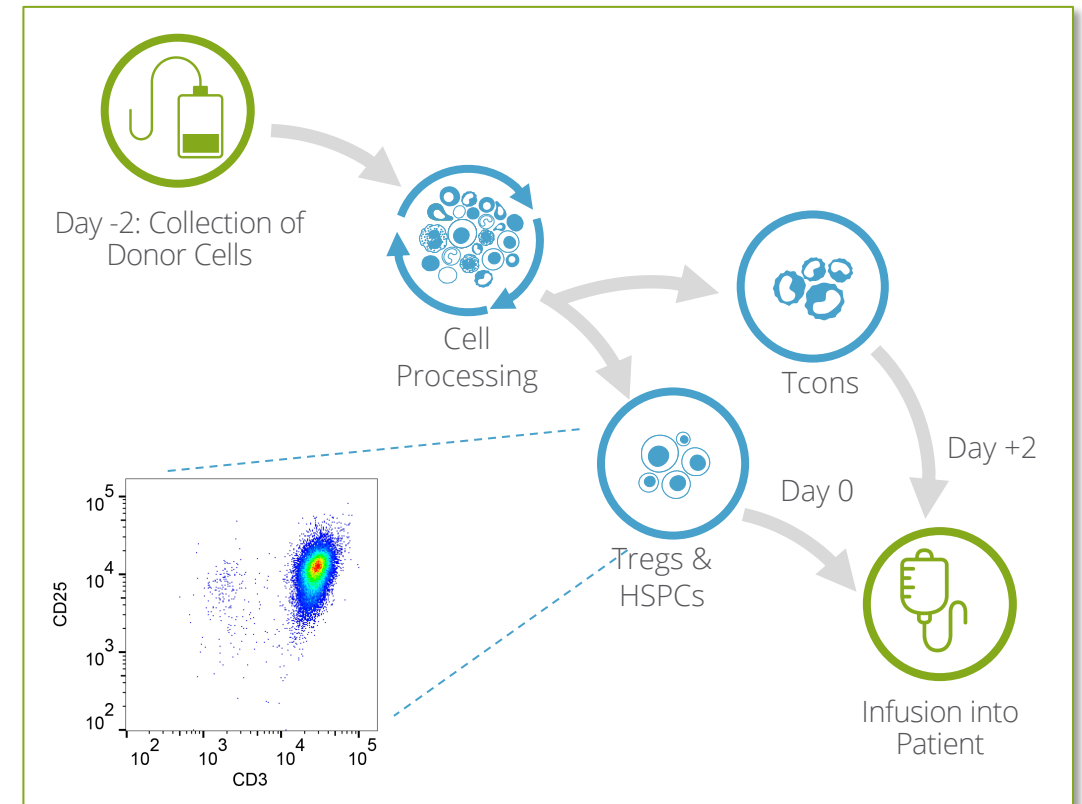
Eddinger et al. Nature Medicine 2003 Sep;9(9):1144-50. | Trzonkowski et al. Clin Immunol. 2009 Oct;133(1):22-6.  
Di Ianni M, et al. Blood. 2011;117(14):3921-3928. | Brunstein, et al. Blood 2016 Feb 127 (8):1044-51. | Kellner H, et al.  
Oncotarget 2018 Nov 2;9(86):35611-35622.

# Regulatory T cells (Tregs) in hematopoietic stem cell transplantation

## Conventional Transplant



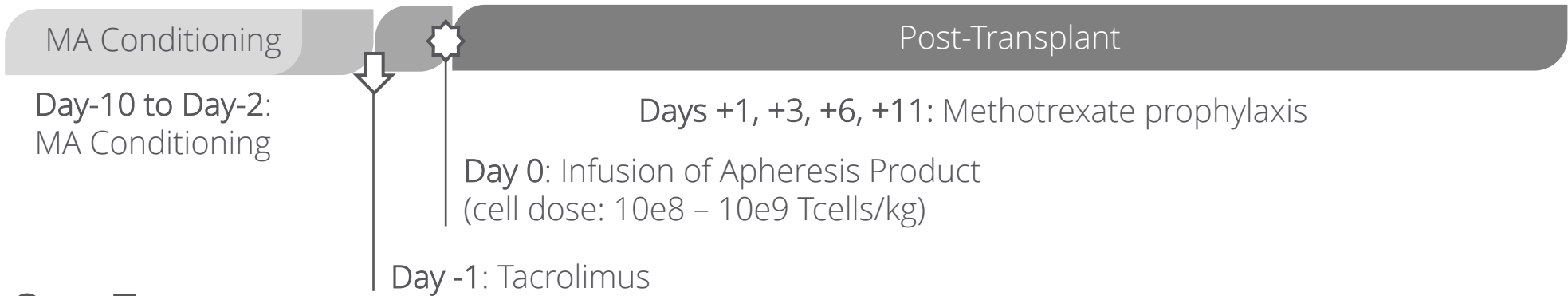
## High-prec. Orca-T



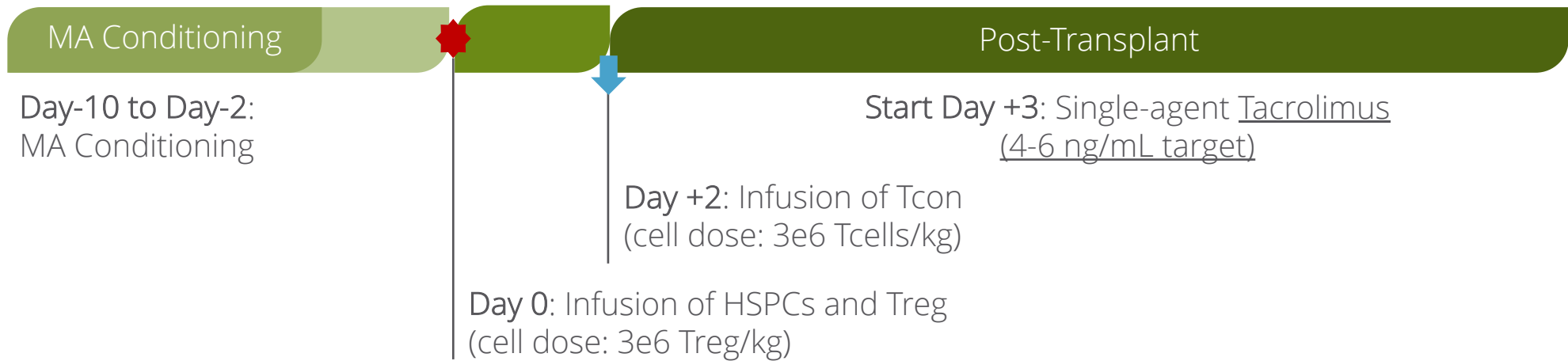
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# Clinical protocol Orca-T

## SOC



## Orca-T



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

# Clinical protocol Orca-T

## Eligible Patients

High risk, MRD+, active disease

Leukemia, lymphoma, MDS, MPN

Myelodysplastic syndrome

KPS >70

Age <65

Matched related or unrelated donor

NCT01660607	Stanford Single Center Phase 2 Trial
NCT04013685	Orca Multicenter Phase 1b Trial

# Patient demographics Orca-T and SOC control cohort

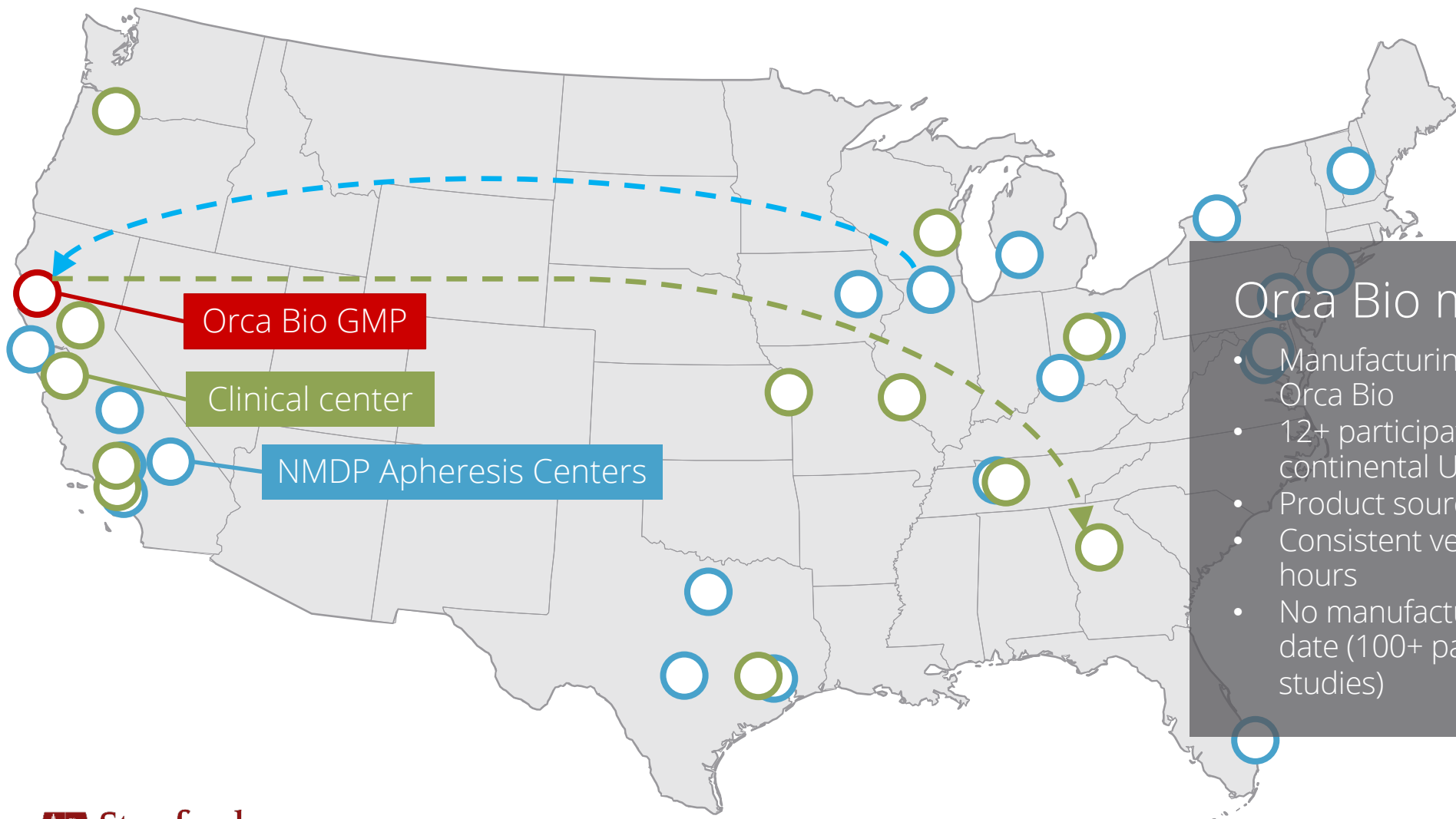
	Orca-T*	SOC Control Cohort
Cohort size	50	144
Median age (range)	47 (20-65)	48 (20-64)
% Male	52%	49%
Race		
White	60%	44%
African American	2%	2%
Asian	14%	19%
Unspecified	26%	30%
Primary Disease %		
AML	42%	39% #
ALL	28%	26%
CML	4%	6% #
B-cell lymphoma	2%	8% #
MDS/MF	16%	19% #
Other (E.g. mixed phenotype acute leukemia)	8%	2%
Graft source HLA-matched siblings/URD	62%/38%	56%/44%
% with active leukemia at time of transplant	23%	21%
Median f/u (days)	223 days (30 – 1561 days)	886 days (55-1783)

\* subjects with ≥ 30 days f/u. Data from NCT04013685 and NCT01660607

# these numbers have been edited post TCT

# Orca-T manufacturing and supply

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



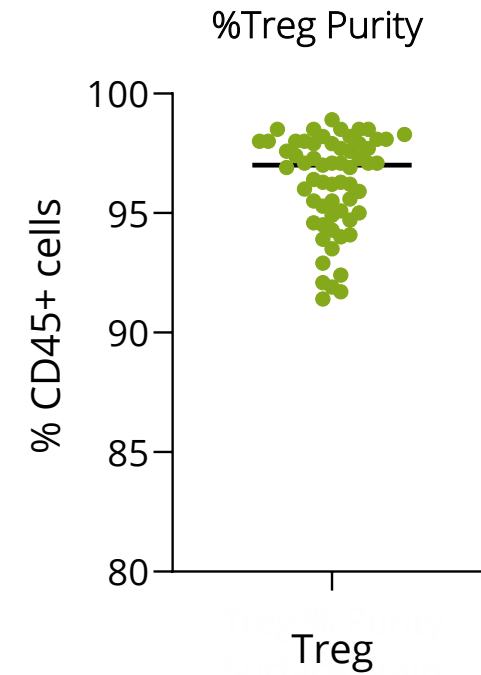
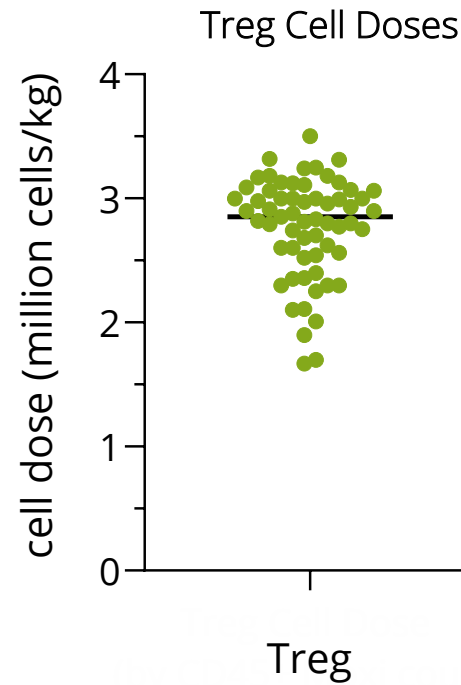
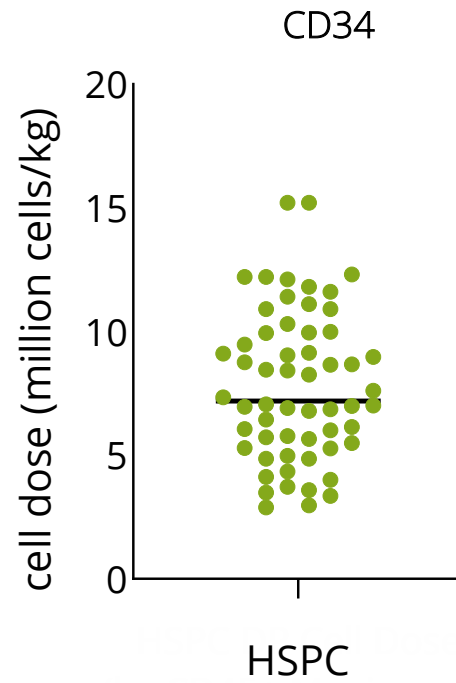
## Orca Bio mfg platform

- Manufacturing and logistics carried out by Orca Bio
- 12+ participating clinical sites in the continental US across 3 studies
- Product sourced from MRD and MUDs
- Consistent vein-to-vein time of less than 72 hours
- No manufacturing nor logistic failures to date (100+ patients treated across all studies)

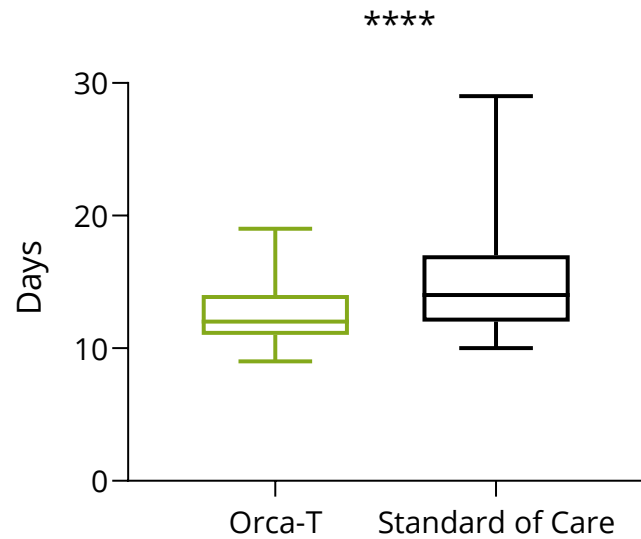


# Orca-T manufacturing and supply

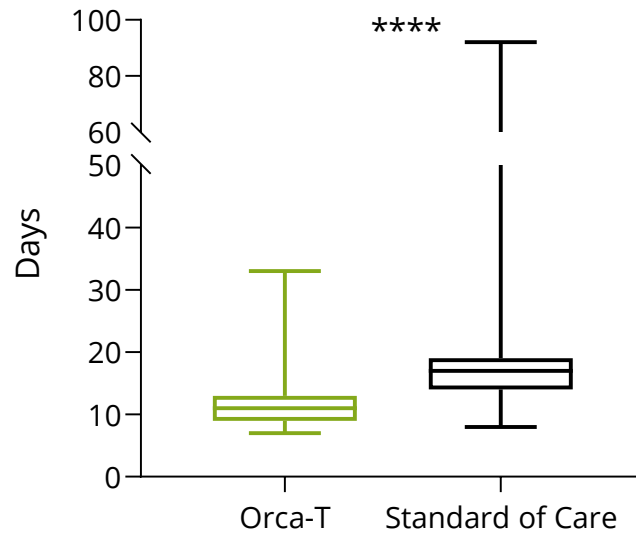
Central manufacturing with consistent quality and performance to date



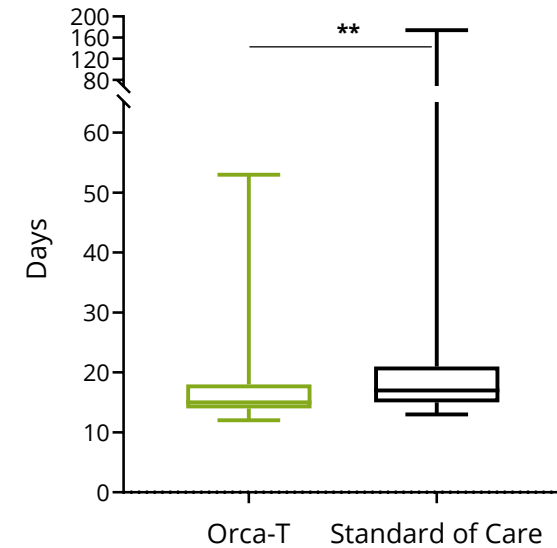
# More rapid engraftment and hospital discharge with Orca-T



Time to Neutrophil Engraftment (Days)  
Median 12 vs 14 days;  $p < 0.0001$

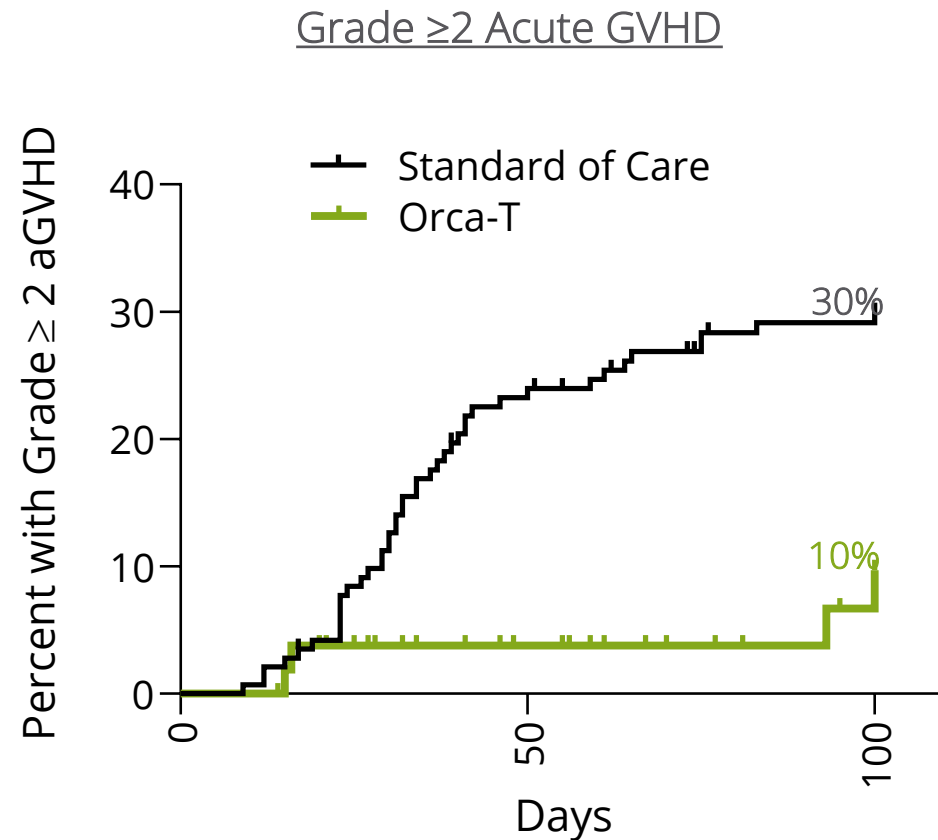


Time to Platelet Engraftment (Days)  
Median 11 vs 17 days;  $p < 0.0001$



Time from Day 0 to Hospital Discharge (Days)  
Median 15 vs 17 days;  $p = 0.01$

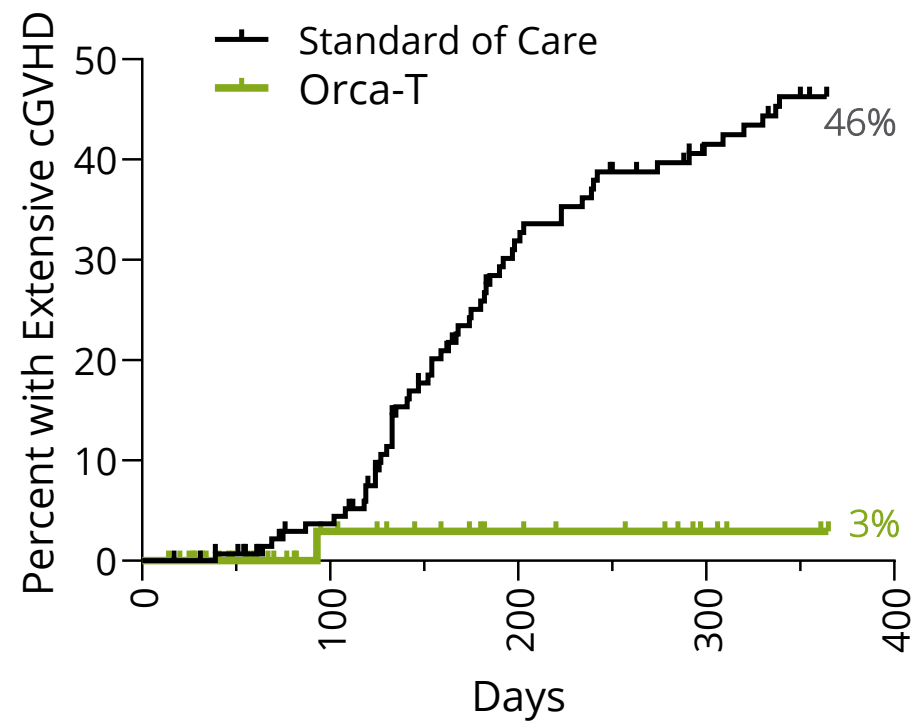
# Reduction of acute GVHD with Orca-T



Organ	Stage	Grade (MAGIC)	Steroid response	Secondary response
GI tract	3	3	Responsive	n/a
GI tract	3	3	Unresponsive	Resp. to ruxolitinib
Liver	1	2	Responsive	n/a
GI tract	1	2	Responsive	n/a

# Reduction of Chronic GVHD with Orca-T

Chronic GVHD



Organ	Severity (NIH Consensus)	Steroid response
Skin and soft tissue	Moderate	Responsive

# Orca-T plus single-agent GVHD PPX is well-tolerated

## Infectious Complications seen with Orca-T plus single agent PPX (n=50)

### CMV

No reactivation	n=36 (72%)
Low level viremia	n=8 (16%)
Required treatment	n=6 (12%)

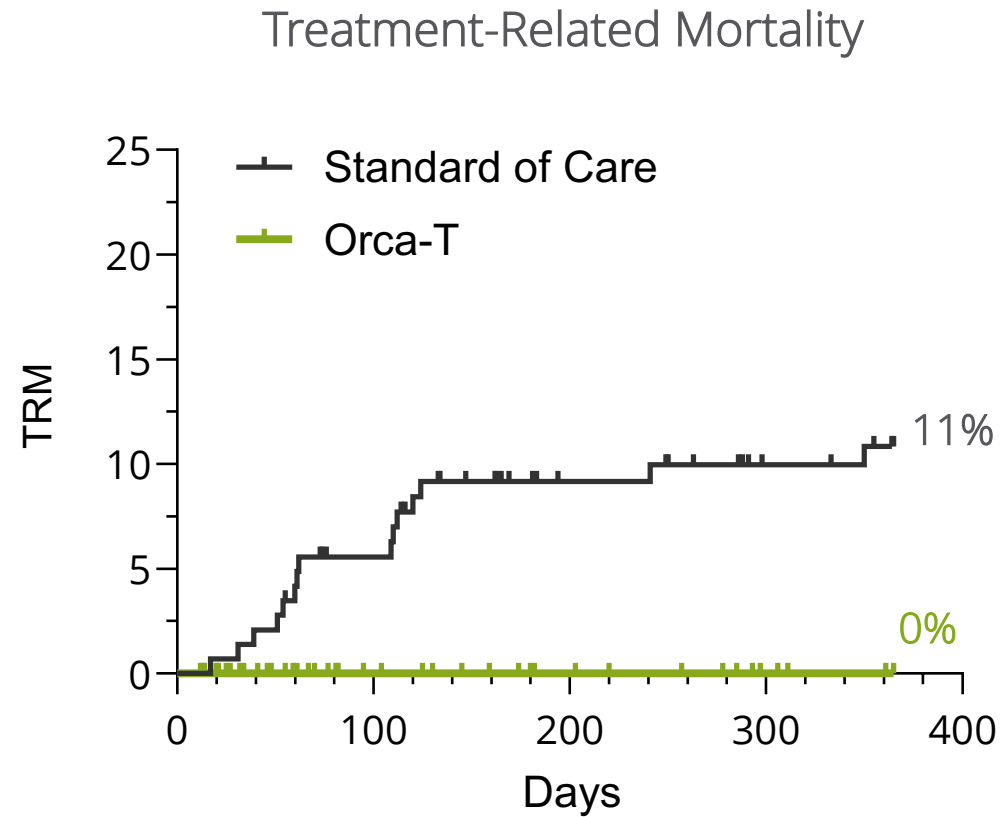
### Other infections

• EBV reactivation	n=8 (1 requiring therapy)	• URI (Adenovirus)	n=3
• BK viruria/viremia	n=4	• HHV-6	n=2
• Rhinovirus	n=1	• COVID-19	-
• C. Difficile	n=4	• Fungal infections	-
• Bacteriemia	n=7	• Pneumonia	-
• Norovirus	n=1		

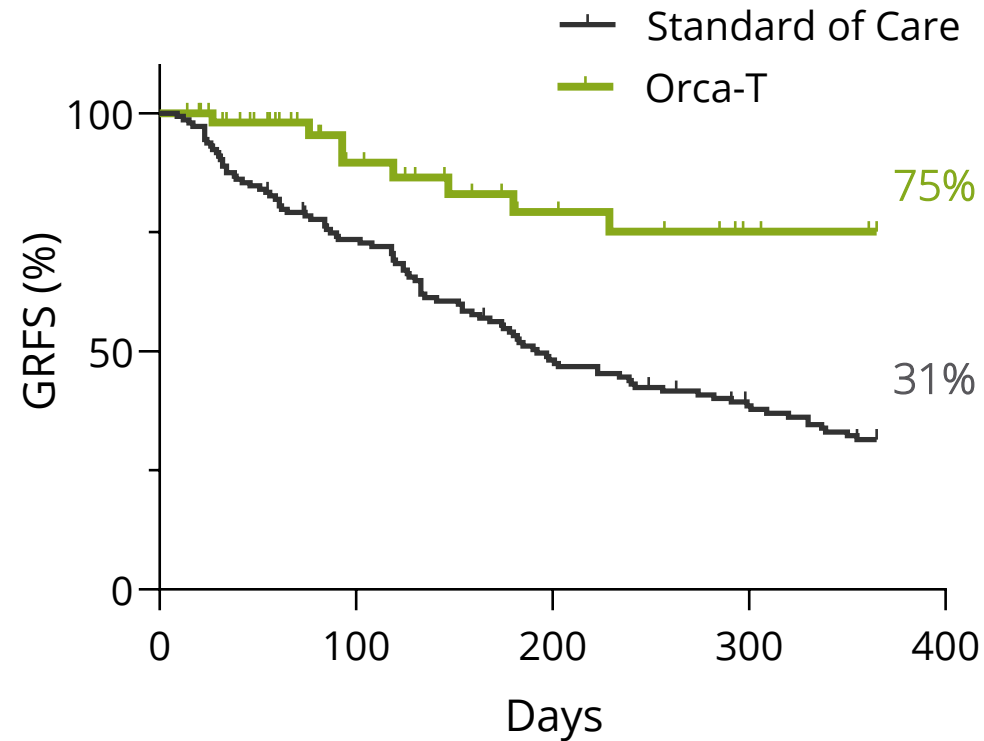
### Only minimal complications with Orca-T

- 18% (n=9) of patients have experienced serious adverse events
- 10% of patients with SOS/VOD
- No deaths due to infection to date

# No treatment-related mortality noted with Orca-T to date

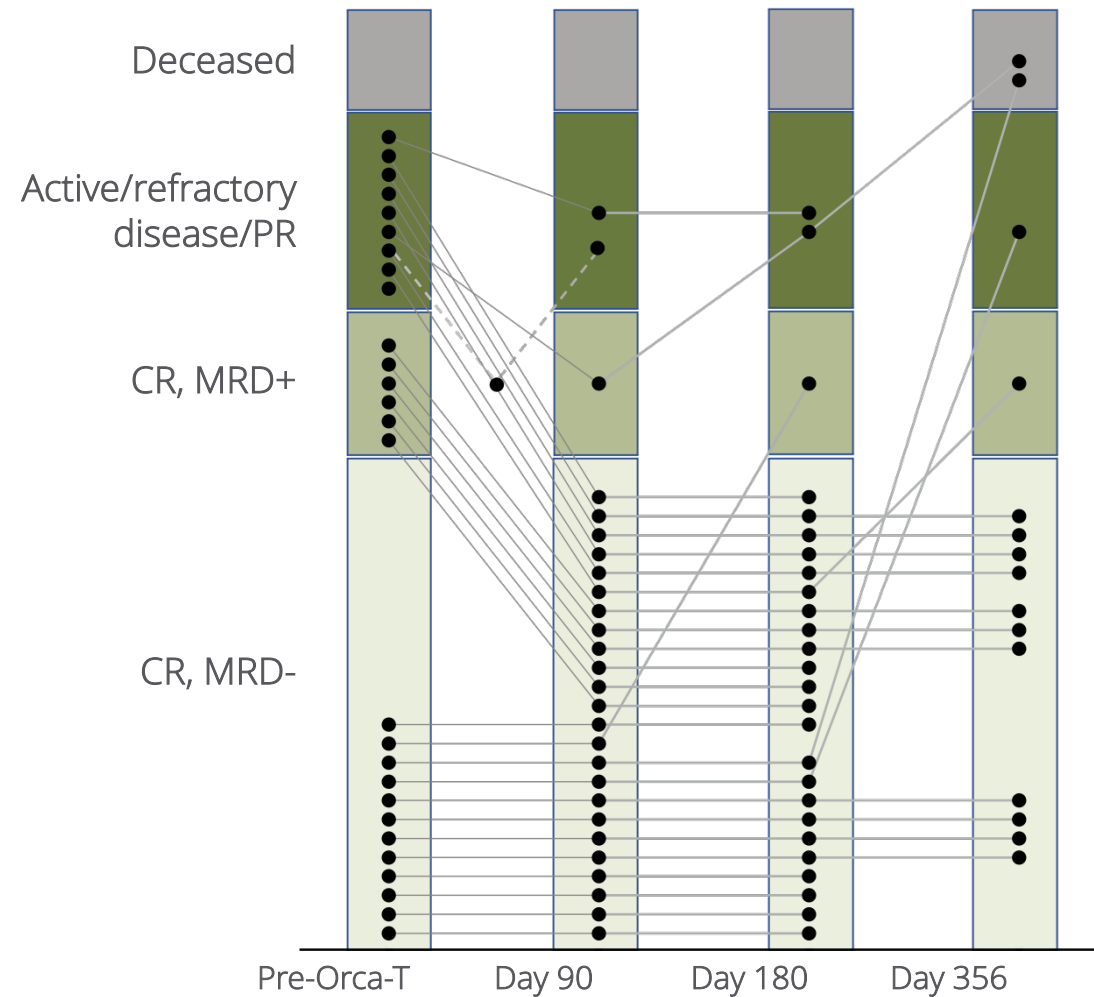


# Profound improvement in GVHD-free relapse-free survival (GRFS) with Orca-T



GVHD event: Grade 3 or greater acute and moderate to severe chronic GVHD

# Disease status pre- and post-transplant in Orca-T patients

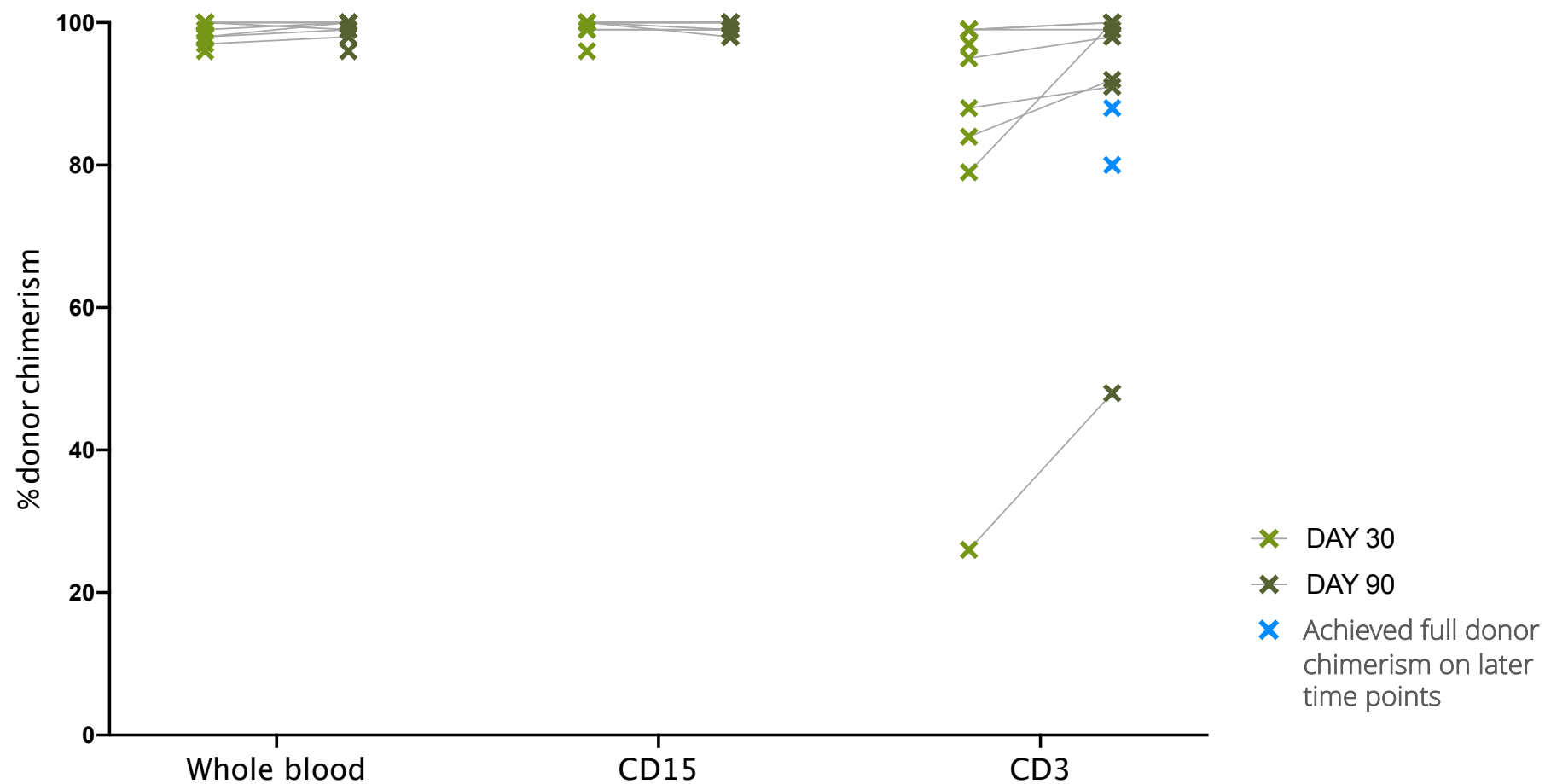


## Orca-T retains GvT effect

- Despite markedly reduced GVHD rates with Orca-T, early data suggests that GvT effect is preserved
- Patients at relapse or with at least 180 days of follow up.



# Donor chimerism at day +30 and day +90



# Orca-T presentation summary

GVHD

## Graft versus Host Disease

Orca-T demonstrates significantly reduced GVHD

TRM

## Treatment Related Mortalities

No TRMs with Orca-T observed to date

GRFS

## GVHD relapse-free survival

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



## Mfg and Logistics Scalability

Orca-T is scaled across the continental US with vein-to-vein times < 72 hours

# Acknowledgments

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RESEARCH PROGRAM**

# Questions