



Orca-T, a Precision Treg-Engineered Donor Product, Prevents Acute GvHD with Less Immunosuppression in an Early Multicenter Experience with Myeloablative HLA-Matched Transplants.

Everett H Meyer, MD, PhD¹, Rasmus Hoeg, MD², Anna Moroz, MD, PhD¹, Bryan Xei, BS¹, Hsin-Hsu Wu, MD¹, Rahul Pawar¹, Kartoosh Heydari, MD¹, David B. Miklos, MD, PhD¹, Parveen Shiraz, MD¹, Lori S. Muffly, MD, MS¹, Sally Arai, MD, MS¹, Laura J. Johnston, MD¹, Robert Lowsky, MD, FRCP¹, Andrew R. Rezvani, MD¹, Judith A Shizuru, MD, PhD¹, Wen-Kai Weng, MD, PhD¹, Nathaniel Fernhoff, PhD⁶, Gerhard Bauer², Arpita Gandhi, MD, MS³, Amy Putnam⁶, J. Scott McClellan, MD, PhD⁶, Bronwen E. Shaw, PhD, MRCP, FRCPath⁴, Joseph P. McGuirk, DO⁵, Mehrdad Abedi, MD² and Robert S. Negrin, MD¹

¹Division of Blood and Marrow Transplantation, Stanford University, Stanford, CA | ²Institute For Regenerative Cures (IRC), University of California Davis, Sacramento, CA | ³Oregon Health Sciences University, Portland, OR | ⁴CIBMTR (Center for International Blood and Marrow Transplant Research), Department of Medicine, Medical College of Wisconsin, Milwaukee, WI | ⁵Department of Blood and Bone Marrow Transplant, The University of Kansas Medical Center, Kansas City, KS | ⁶Orca Bio, Menlo Park, CA

Conflicts of interest | Everett Meyer, MD, PhD



Co-founder, scientific advisor



Co-founder, scientific advisor



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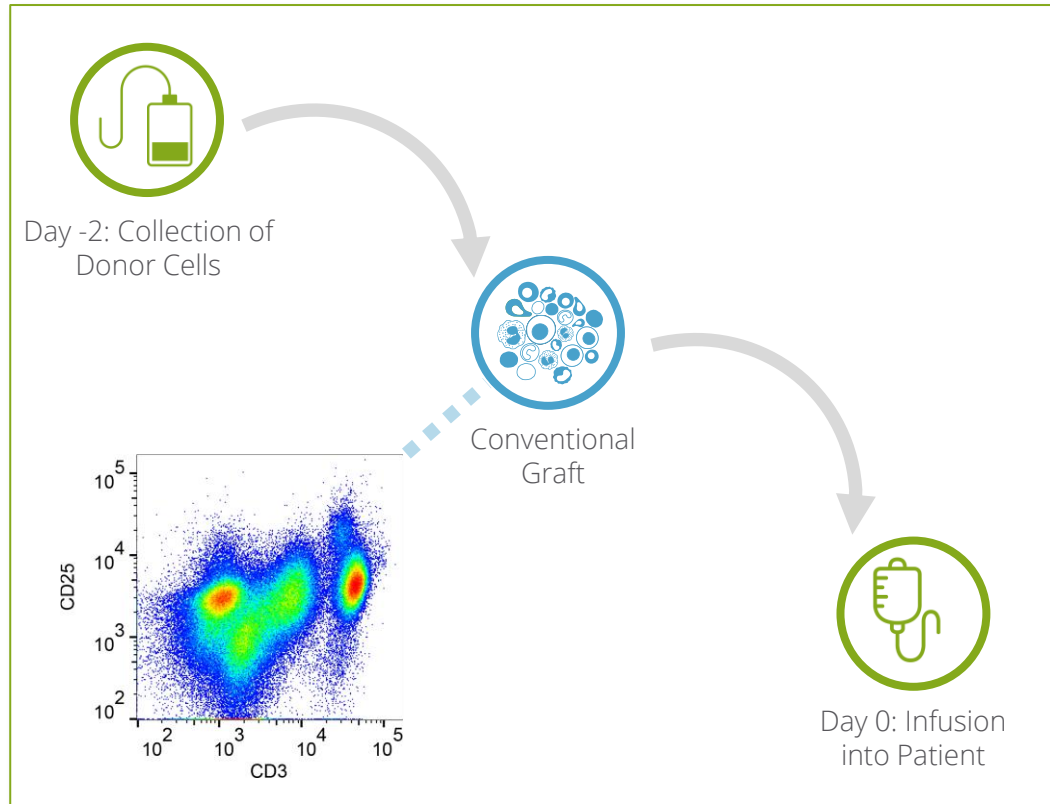


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Sponsored Research Support

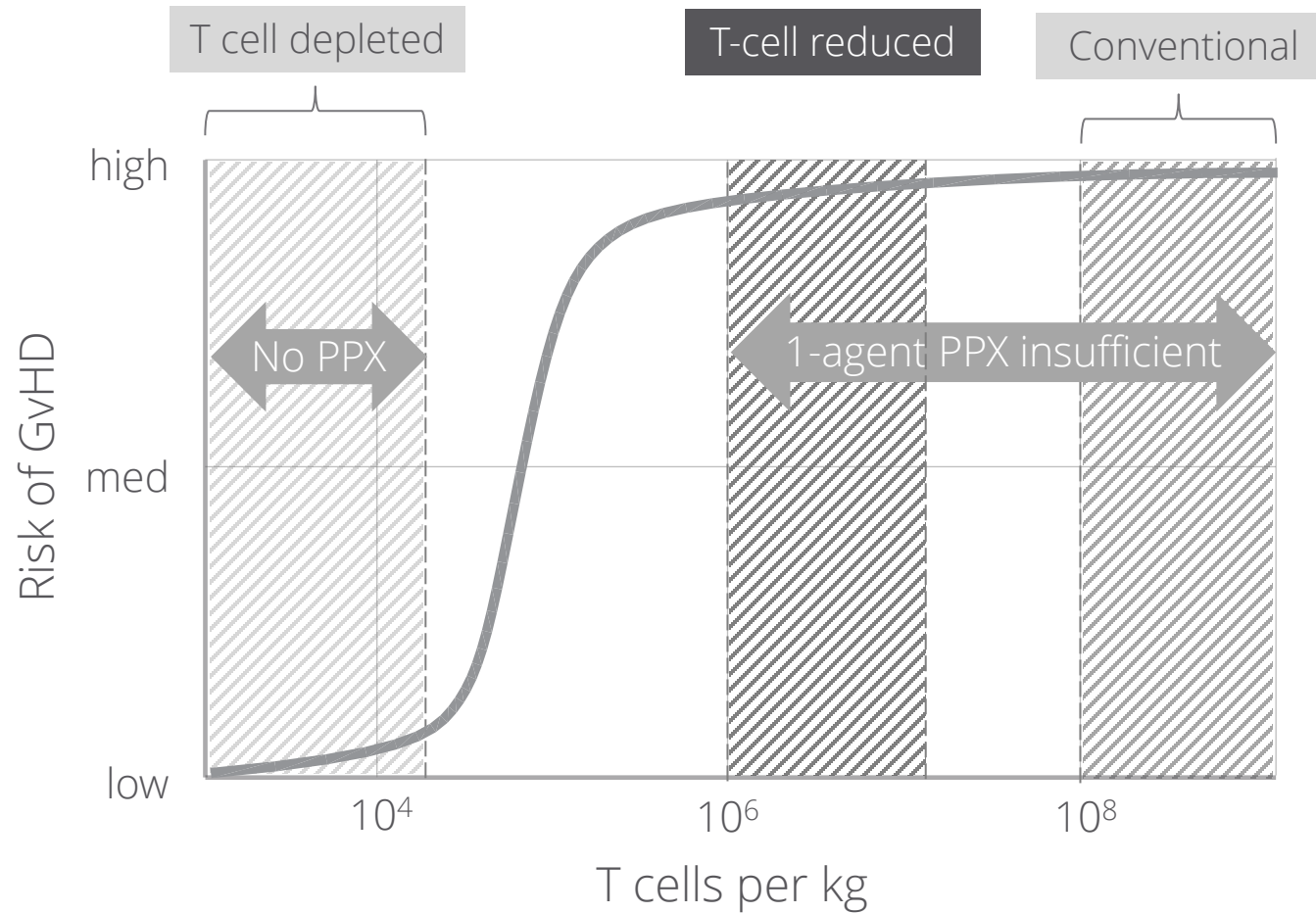
Graft versus Host Disease (GvHD) remains a major problem in hematopoietic stem cell transplantation (HSCT)



GvHD in HSCTs

- Donor T-cells drive GvHD pathophysiology
- 40 years of clinical research to control GvHD by controlling donor T cell

GvHD risk with reduced T-cell grafts remains significant



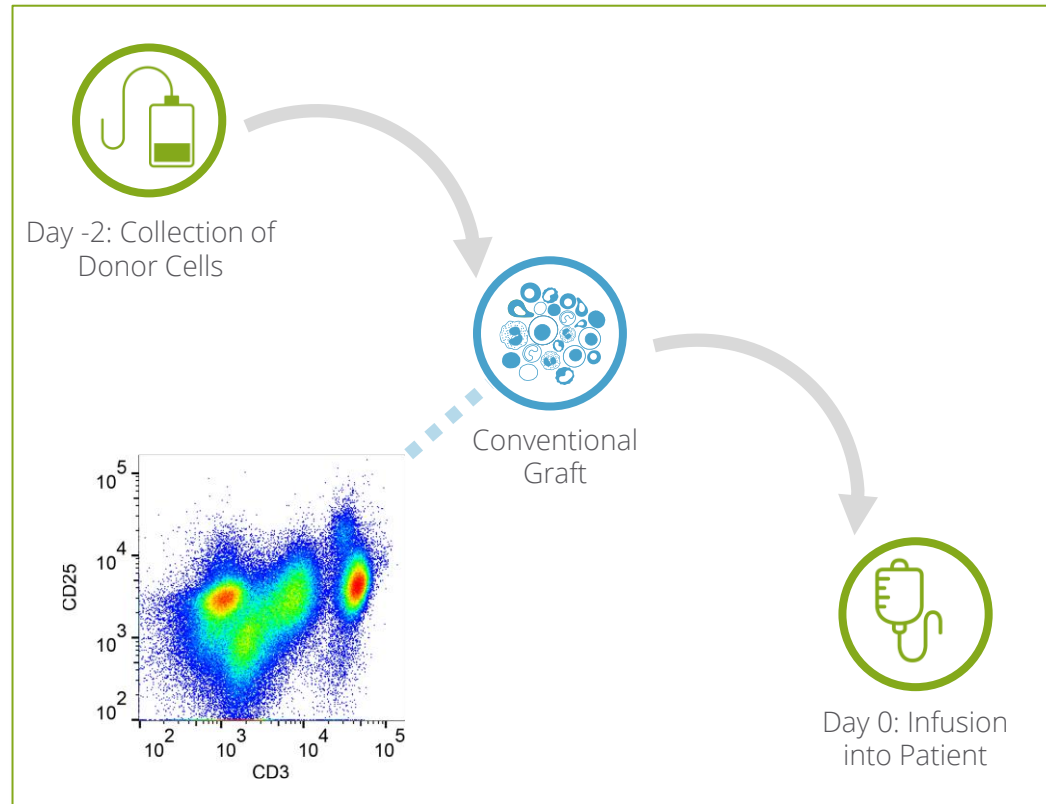
*Montero et al. BBMT 12:1318-1325 (2006)
Nakamura et al. BJH 115:95-104 (2001)
Barrett et al. BMT 21: 543-551 (1998)

T-cell reduced grafts

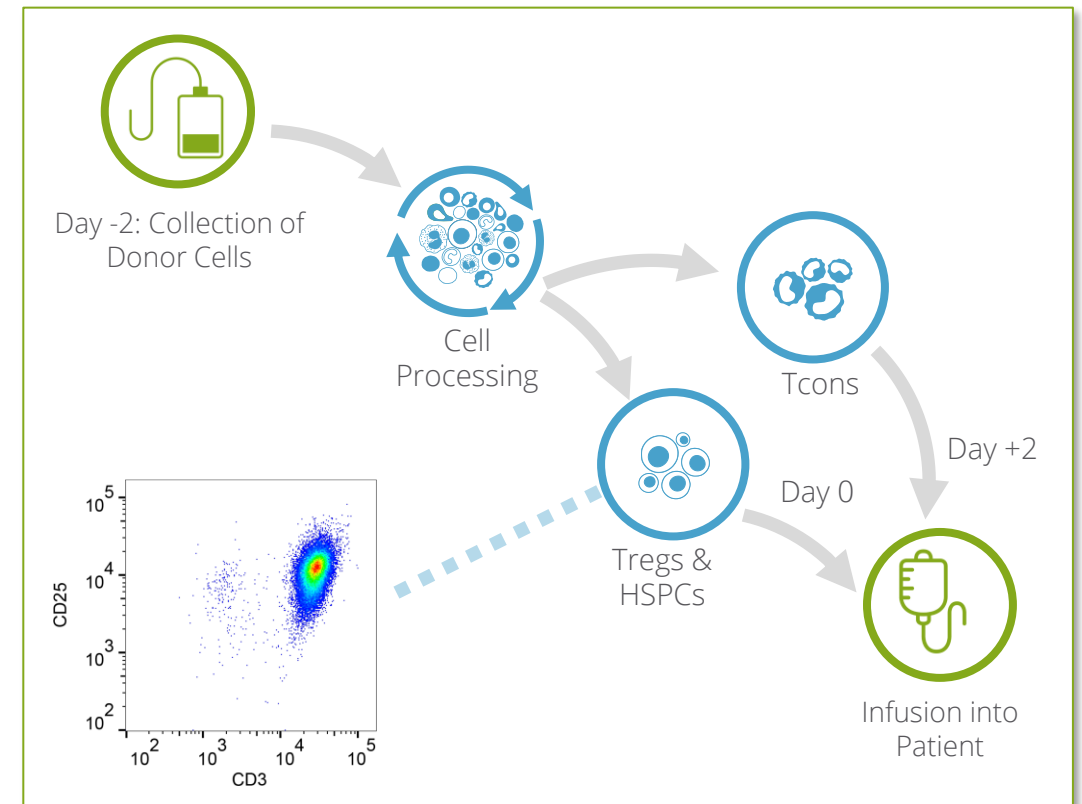
- Previous studies employing T cell reduction of allografts alone still show significant acute and chronic GVHD with single-agent cyclosporin prophylaxis*

Tregs in hematopoietic stem cell transplantation

Conventional Transplant

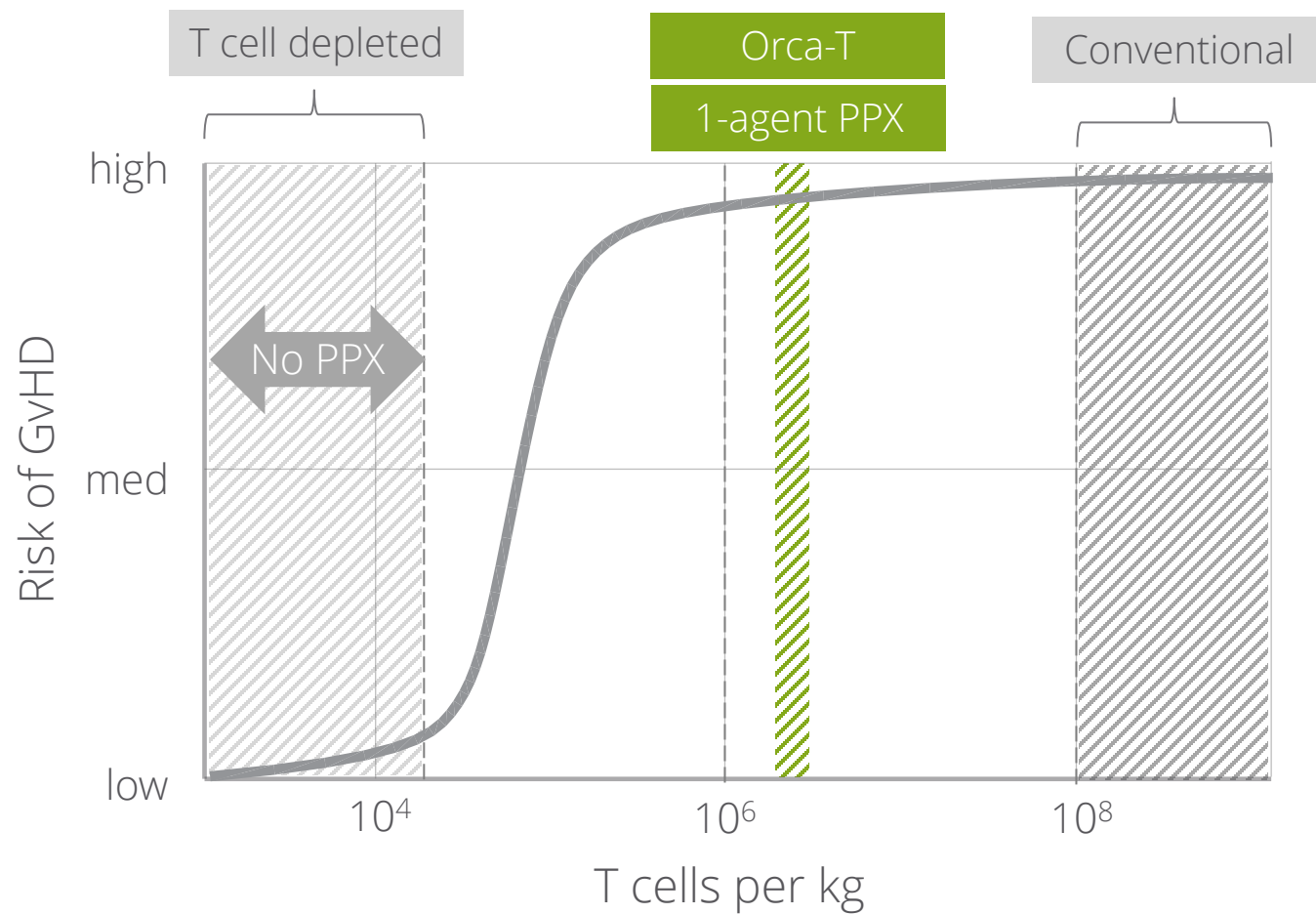


High-Precision Orca-T



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.

Evaluation of high-precision Orca-T to control GvHD

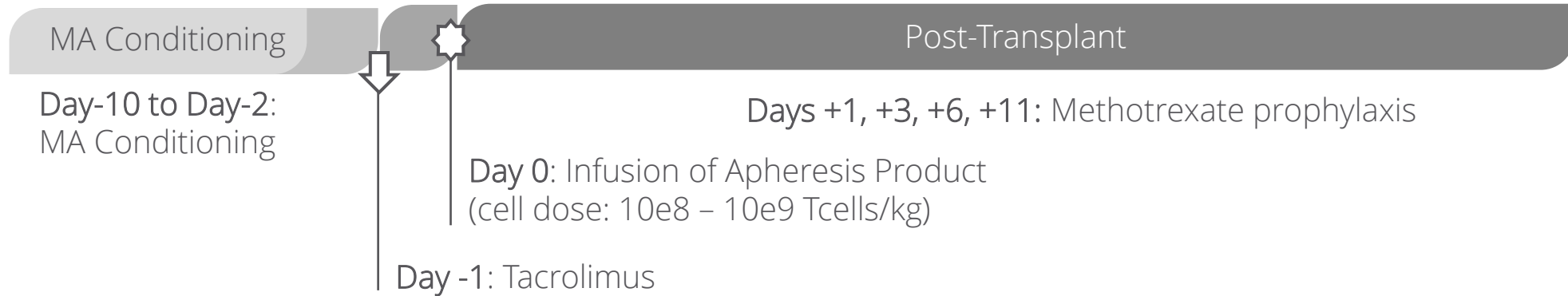


Orca-T + 1-agent PPX

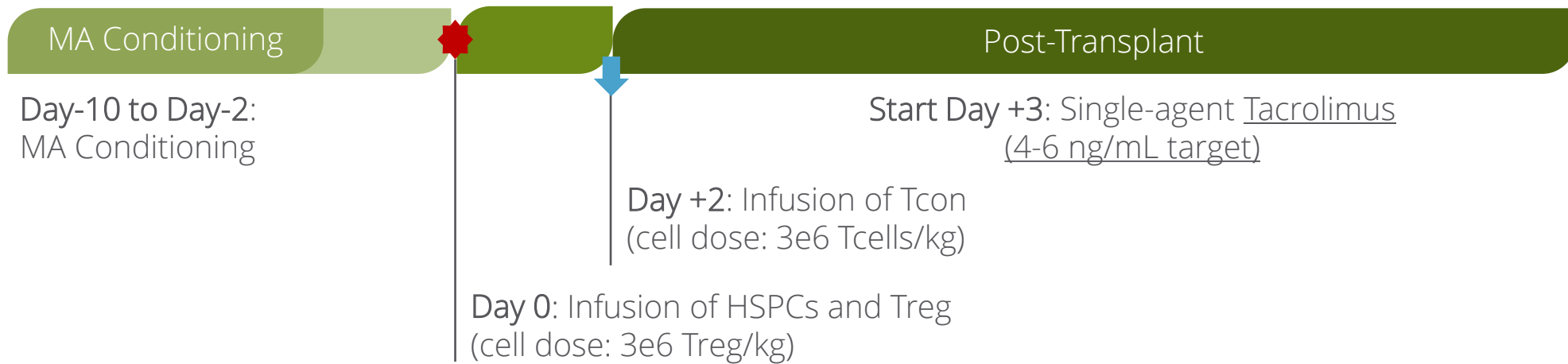
- Yield of Treg from apheresis: 2-3 million Treg/kg
- Target ratio of T-cell to Treg: 1:1
- Conventional T-cell dose: 3 million/kg
- CD34 dose: >2 million/kg

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

NCT04013685

Stanford Single Center Phase 2 Trial

NCT01660607

Orca Bio Multicenter Phase 1b Trial

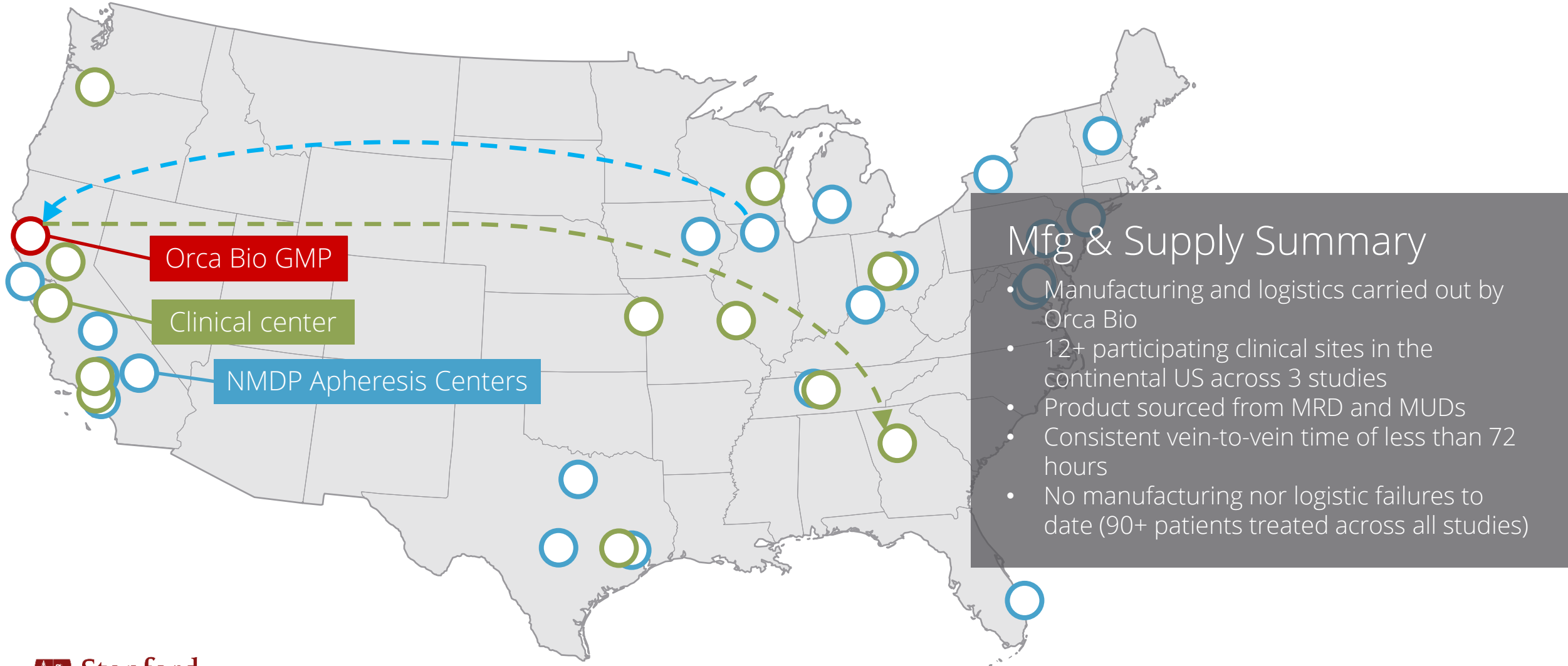
Patient demographics Orca-T and SOC control cohort

	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%	53%
ALL	28%	26%
CML	4%	7%
B-cell lymphoma	2%	6%
MDS/MF	16%	22%
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 days)

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

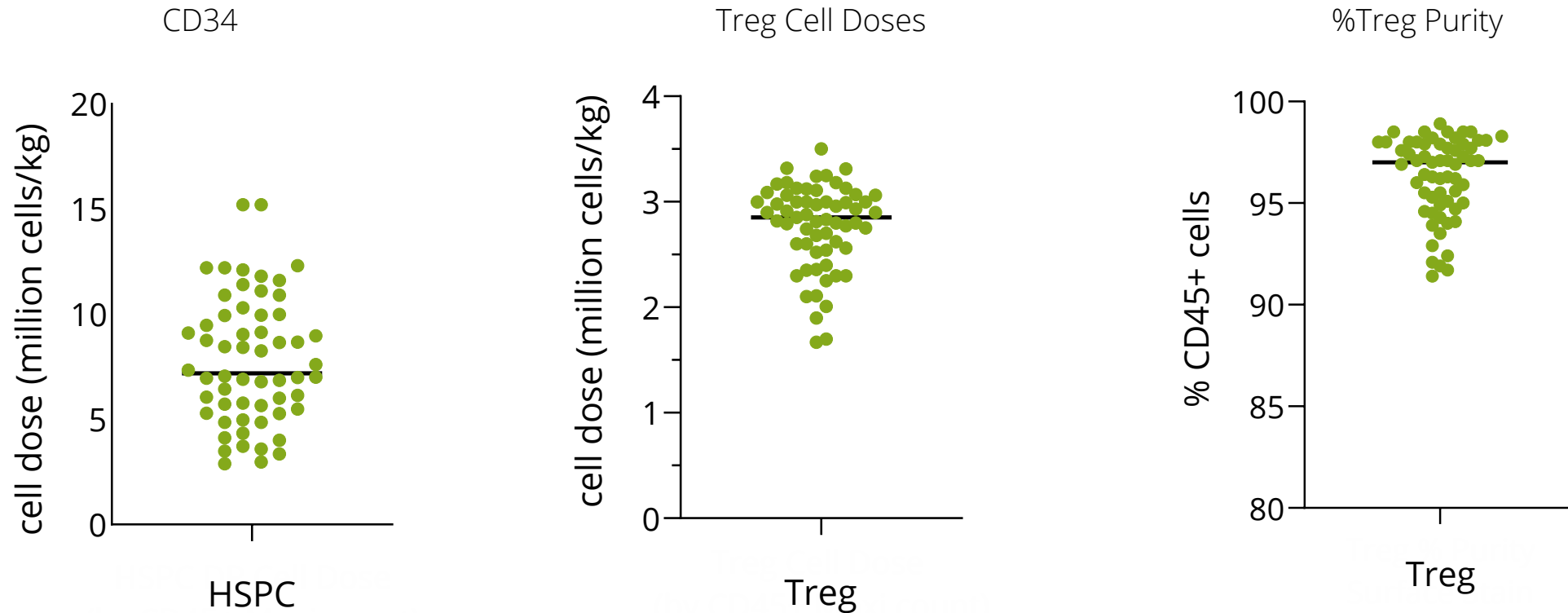
Orca-T manufacturing and supply

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



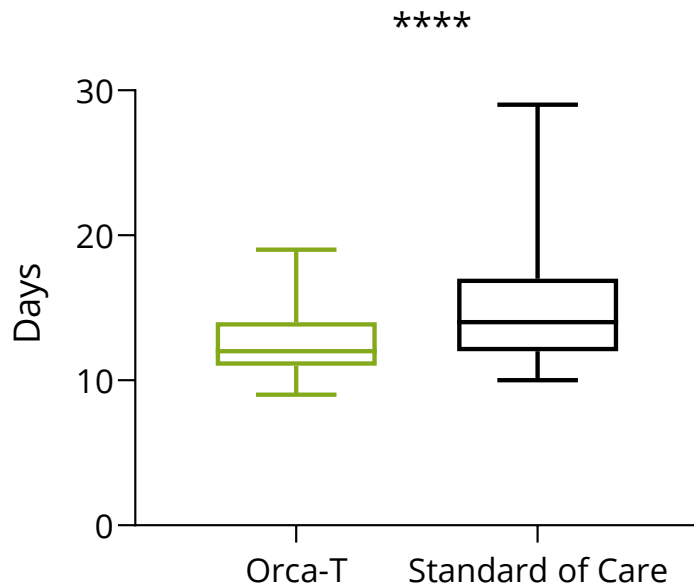
Orca-T manufacturing and supply

Central manufacturing with consistent quality and performance to date



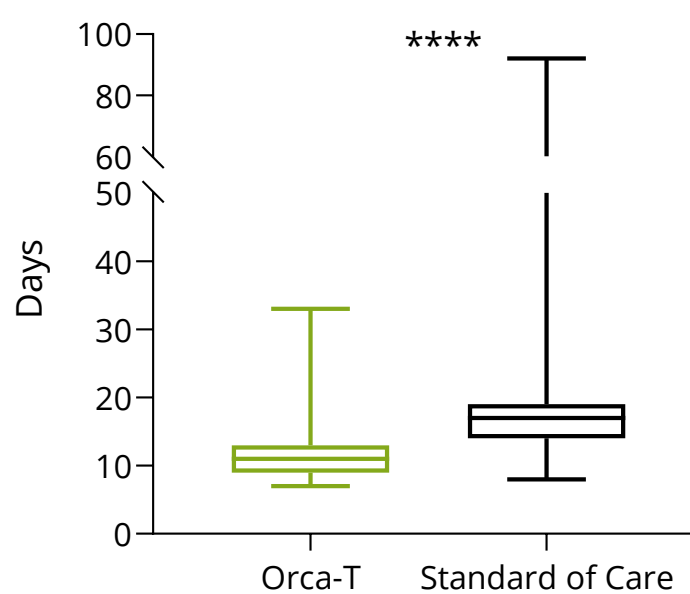
More rapid engraftment & hospital discharge with Orca-T

Time to Neutrophil Engraftment (Days)



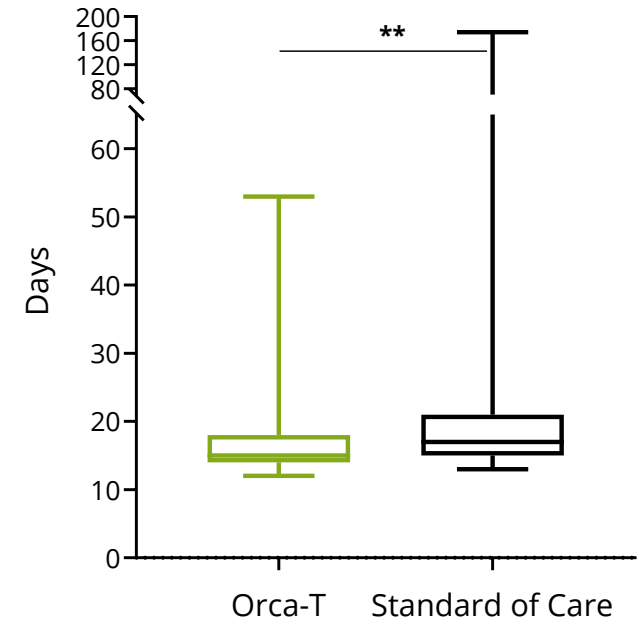
Median 12 vs 14 days; $p < 0.0001$

Time to Platelet Engraftment (Days)



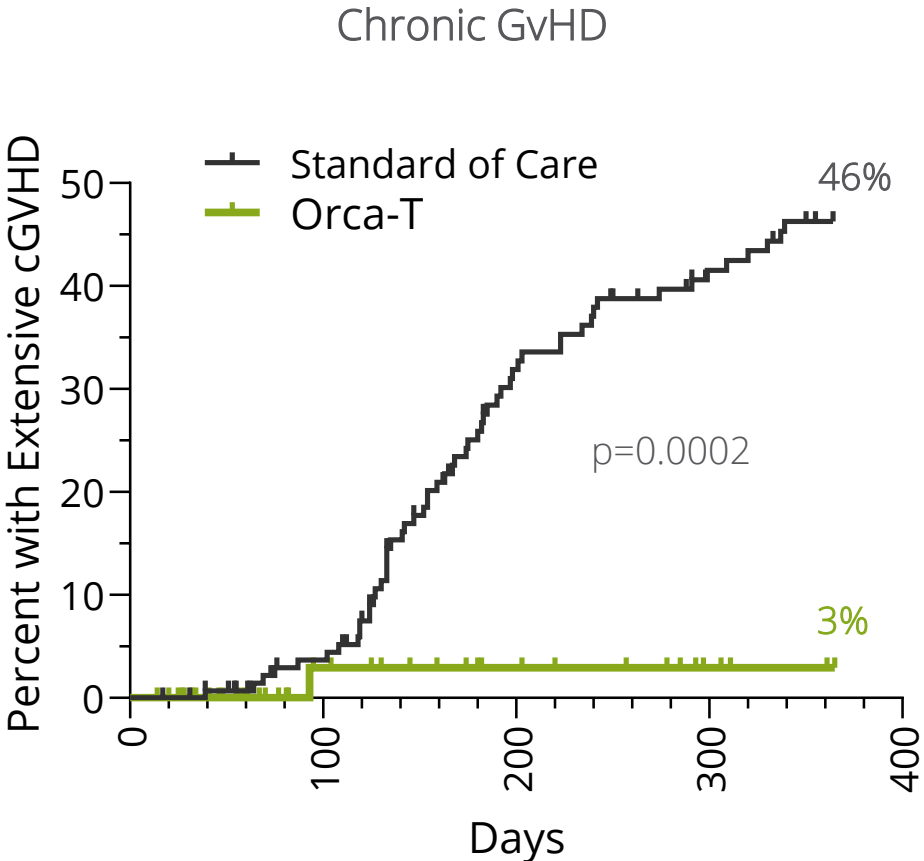
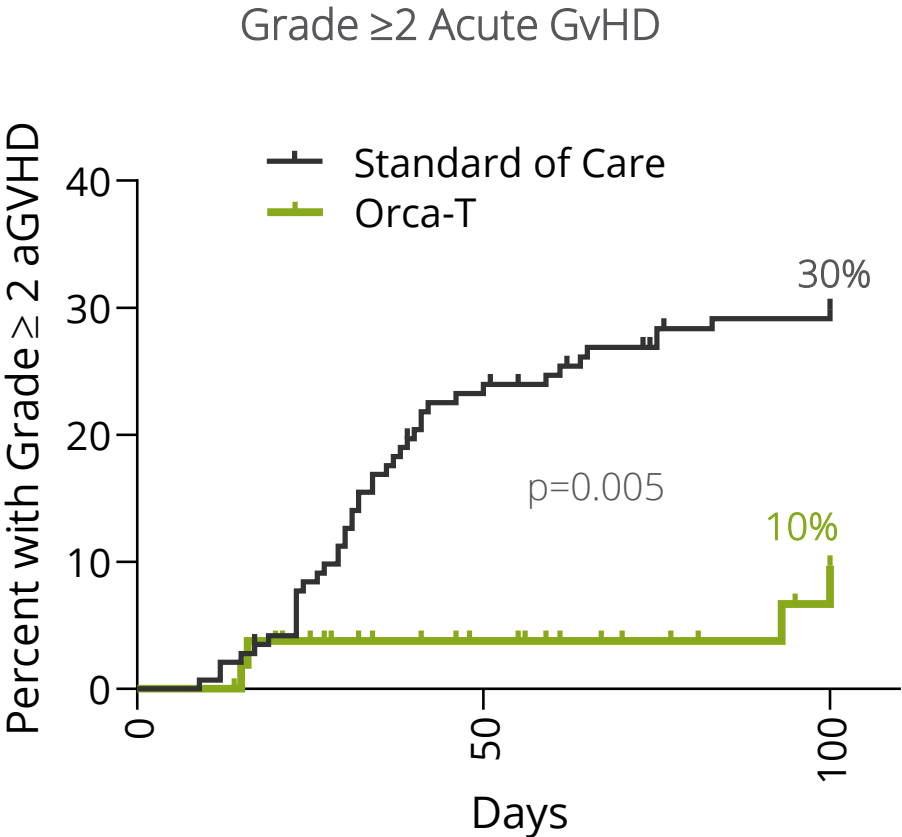
Median 11 vs 17 days; $p < 0.0001$

Time from Day 0 Hospital Discharge (Days)



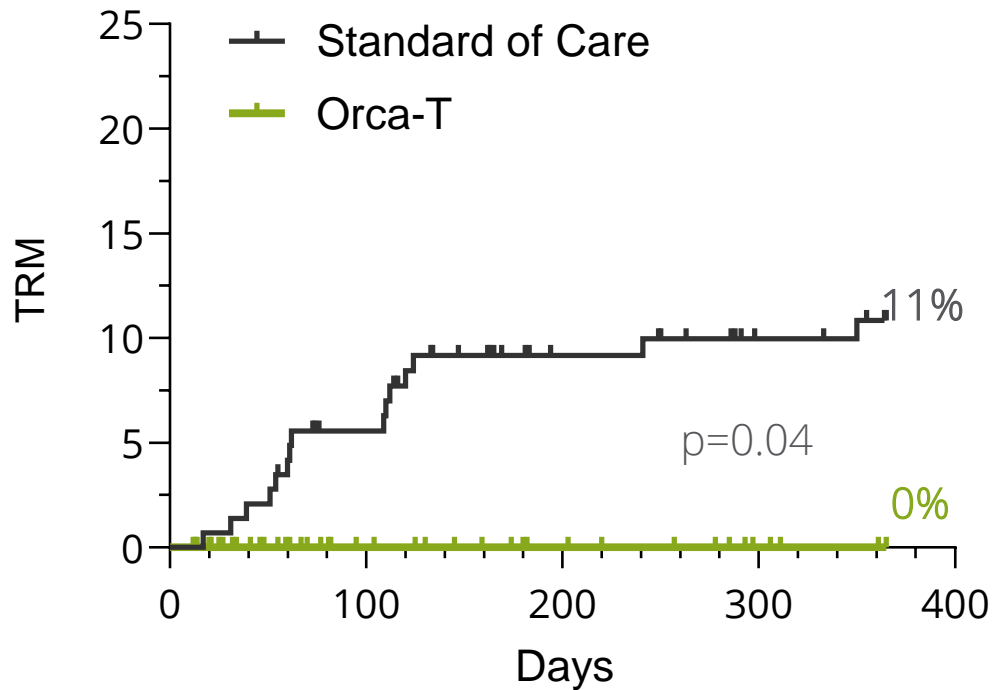
Median 15 vs 17 days; $p = 0.01$

Profound reduction of GVHD with Orca-T

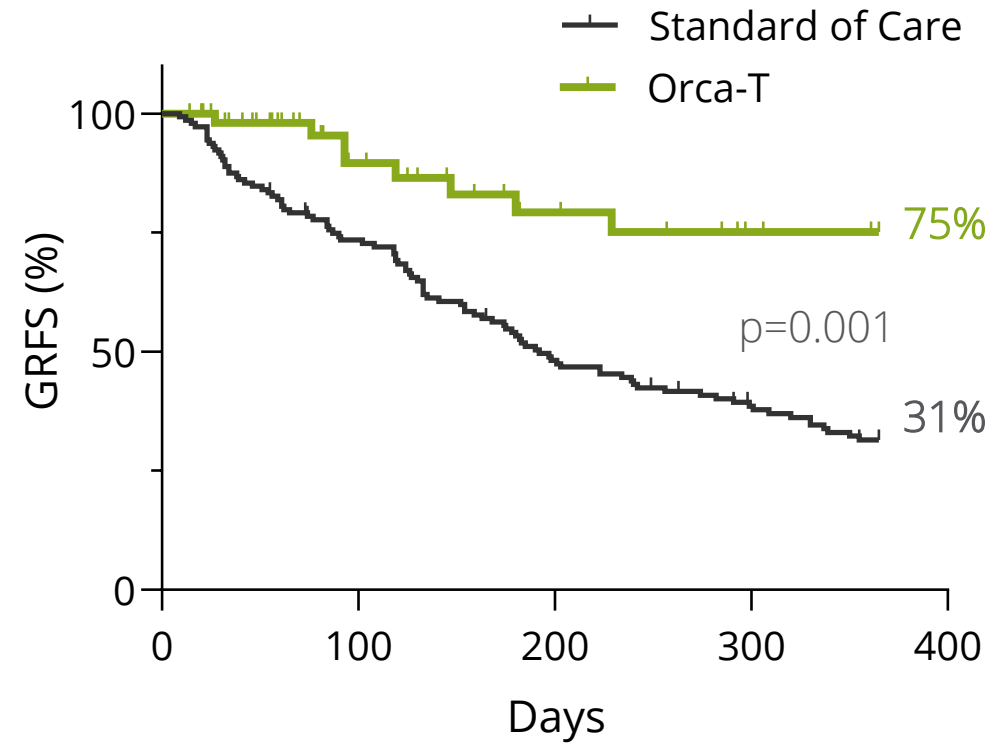


Significant improvement in GVHD-free relapse-free survival with Orca-T

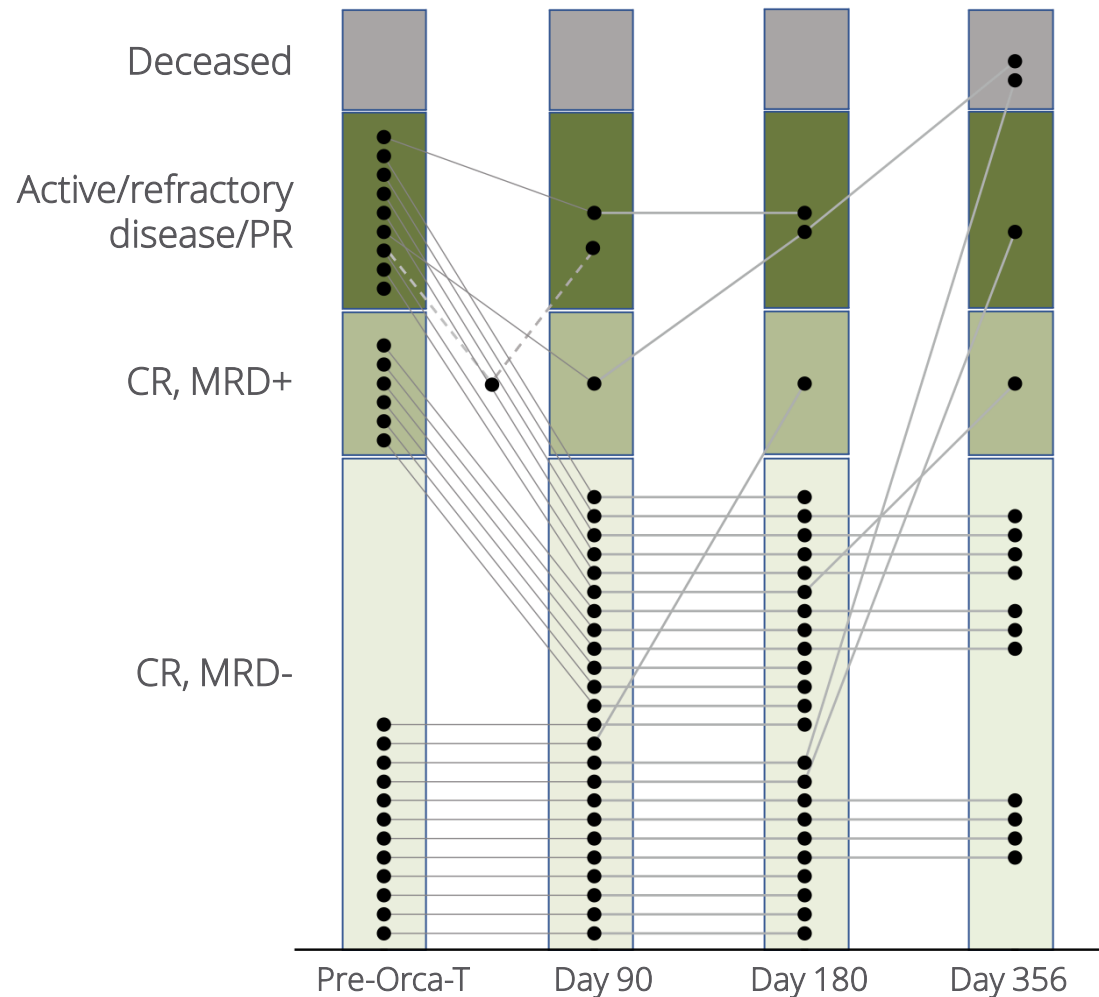
Treatment-Related Mortality



GVHD (\geq grade 3) and Relapse-Free Survival











Durable disease control demonstrated with Orca-T



Orca 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.

Orca-T presentation summary

-  1-yr GVHD relapse-free survival (GRFS) more than doubled compared to SOC.
-  Dramatically reduced acute and chronic GvHD compared to SOC despite reduced use of immunosuppressive meds.
-  No Transplant Related Mortalities observed to date.
-  Improved time-to-engraftment compared to SOC.
-  Disease control demonstrated in several patients with active disease at time of Tx
-  Central GMP laboratory production with no manufacturing/distribution failures
-  Vein-to-vein times of less than 72 hours across the continental United States
-  Orca-T has been granted Regenerative medicine advanced therapy (RMAT) by the FDA

Acknowledgments

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Questions