



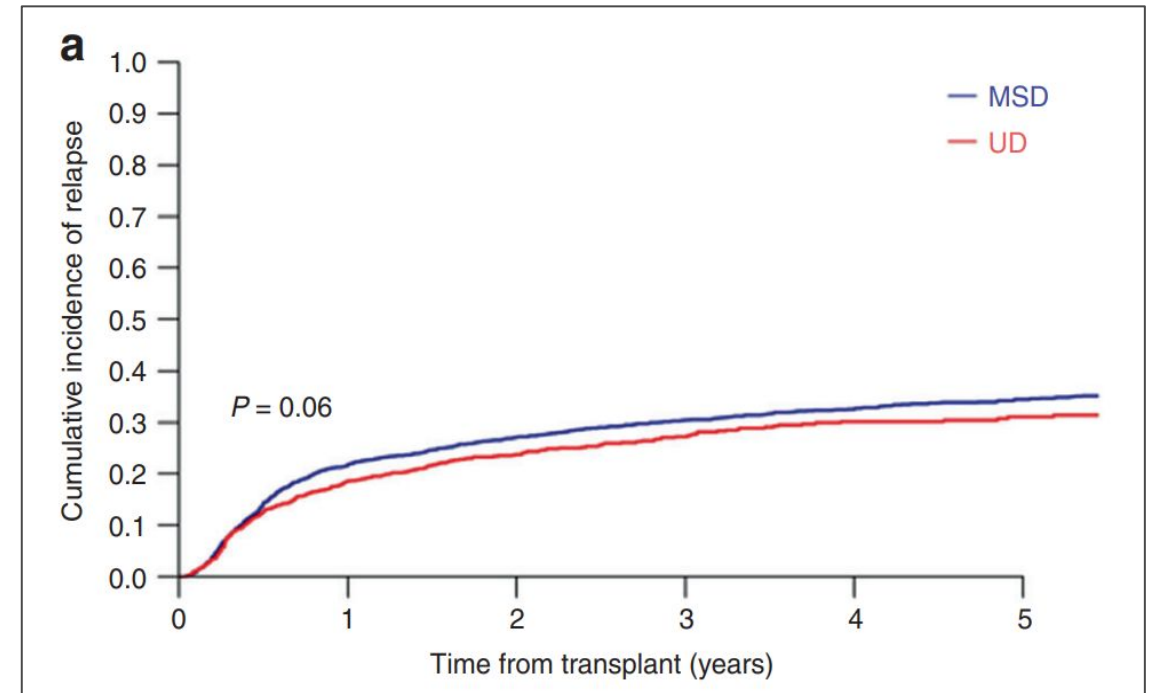
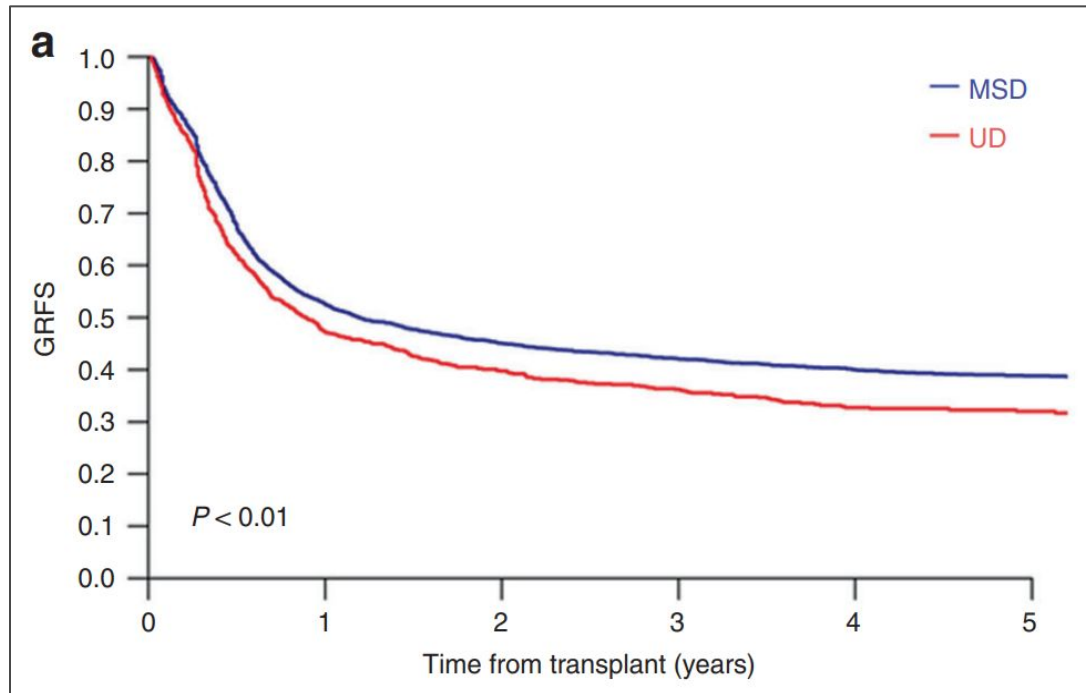
# Precision-Engineered Cell Therapy Orca-T Demonstrates High Relapse-Free Survival at 1 Year While Reducing Graft-Versus-Host Disease and Toxicity

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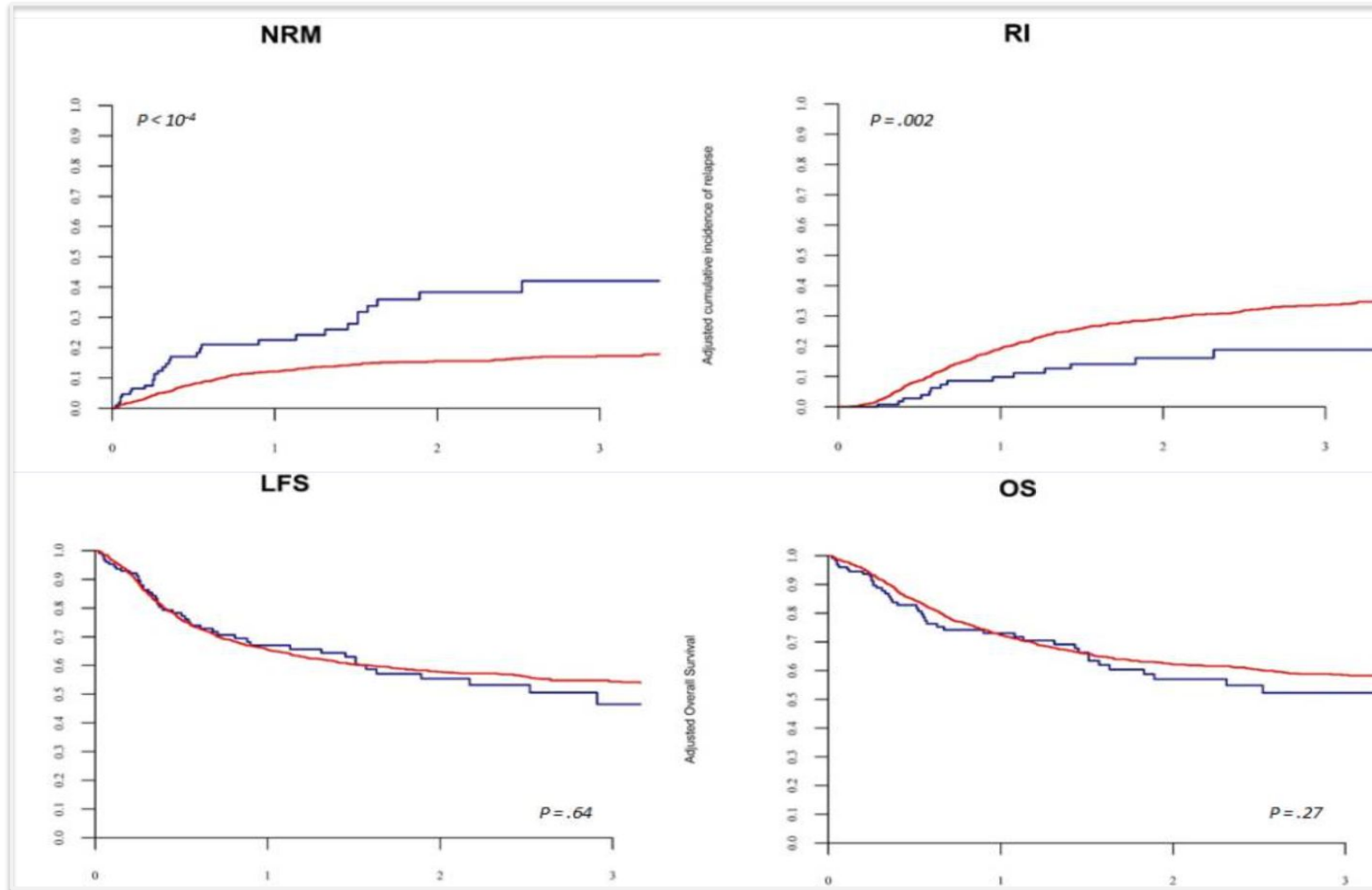


# HLA Matched Donor Hematopoietic Stem Cell Transplantation Remains Challenging

GRFS and RFS after AlloHSCT from a Matched Donor  
(Adults with AML with intermediate or unfavorable karyotype in first complete remission)



# Enabling Higher Intensity Conditioning to Reduce Relapse and Improve Survival Would Be Ideal



BFT compared to BF for MRD/URD transplant in acute myeloid leukemia in first remission

— Bu/Flu/Thio (BFT)  
— Bu/Flu (BF)

- Better Disease Control
- Worse NRM
- Equivalent RFS/OS

# Opportunity to Improve Clinical Outcomes from AlloHSCT with Precision Engineering

## Current Transplants

Uncontrolled mix of over 50 cell types  
10e8 – 10e9 cells/kg



- Hematopoietic stem cells
- Progenitor cells
- Conventional T cells
- T regulatory cells
- NK cells
- Invariant NKT cells
- Dendritic cells
- Myeloid derived suppressor cells



## Orca Bio's Precision-Engineered Cell Therapy

Defined Cell Population of Tregs and Tcons

(d0)



+



Long term blood and immune reconstitution

High purity to Prevent GvHD

(d+2)



Bridge immune reconstitution  
Disease control  
Infection control

# Orca-T Treatment Consists of MAC with Single-Agent Tacrolimus

## Standard of Care

### MA Conditioning

Day-10 to Day-2:  
MA Conditioning

### Post-Transplant

Days +1, +3, +6, +11: Methotrexate prophylaxis

Day 0: Infusion of Apheresis Product  
(cell dose:  $10e8 - 10e9$  Tcells/kg)

Day -1: Tacrolimus (5-10 ng/mL target)

## Orca-T

### MA Conditioning

Day-10 to Day-2:  
MA Conditioning

### Post-Transplant

Start Day +3: Single-agent Tacrolimus  
(5-10 ng/mL target)

Vein to Vein  
time < 72h

### Tcons

Day +2: Infusion of Tcon  
(cell dose:  $3e6$  Tcells/kg)

HSPC  
Tregs

Day 0: Infusion of HSPCs and Treg  
(cell dose:  $3e6$  Treg/kg)

No methotrexate, PTCy, or other  
additional immunosuppressive  
therapies given with Orca-T

# Study Key Eligibility Criteria

## Phase 1b/2 Trial

- Acute leukemia (AML, ALL, mixed phenotype), in CR
- Acute leukemia (AML, ALL, mixed phenotype), with active disease at time of transplant ( $\leq 10\%$  BM blast burden)
- Myelodysplastic syndrome
- Myelofibrosis
- BPDCN
- CML in accelerated phase or blast crisis
- Non-Hodgkin Lymphoma\*

8/8 matched related or unrelated donor

HCT-CI  $\leq 4$

KPS  $\geq 70$

Age 18-65 (or 18 -72)\*

Adequate organ function

# Baseline Characteristics

		<b>CIBMTR Control (n = 375)</b>	<b>Phase 1b/2 Orca-T (n = 151)</b>
Median age (range), years		52 (18 – 65)	48 (19-71)
Median follow-up in months (range)		30 (4 – 50)	15 (3-43)
Primary Disease	AML	47%	44%
	ALL	20%	31%
	MDS	33%	15%
	Other	n/a	9%
Male		57%	57%
Donor (HLA matched)	Related	45%	52%
	Unrelated	55%	48%
Cond. Regimen	Busulfan-based	77%	77%
	TBI-based	20%	23%

As of 25 Oct 2022, 151 patients had received Orca-T and had ≥100 days of follow-up

# Overall Orca-T Study Population Outperforms Standard of Care AlloHSCT

	CIBMTR Control (n = 375)		Phase 1b/2 Orca-T (n = 151)	
	1 year	18 months	1 year	18 months
GvHD and Relapse-Free Survival	21%	19%	70%	65%
Non-relapse mortality	10%	10%	4%	4%
Overall survival	68%	64%	88%	84%

Outcomes with Orca-T appeared to be enhanced further with conditioning regimen consisting of busulfan, fludarabine, and thiotepa (BFT)



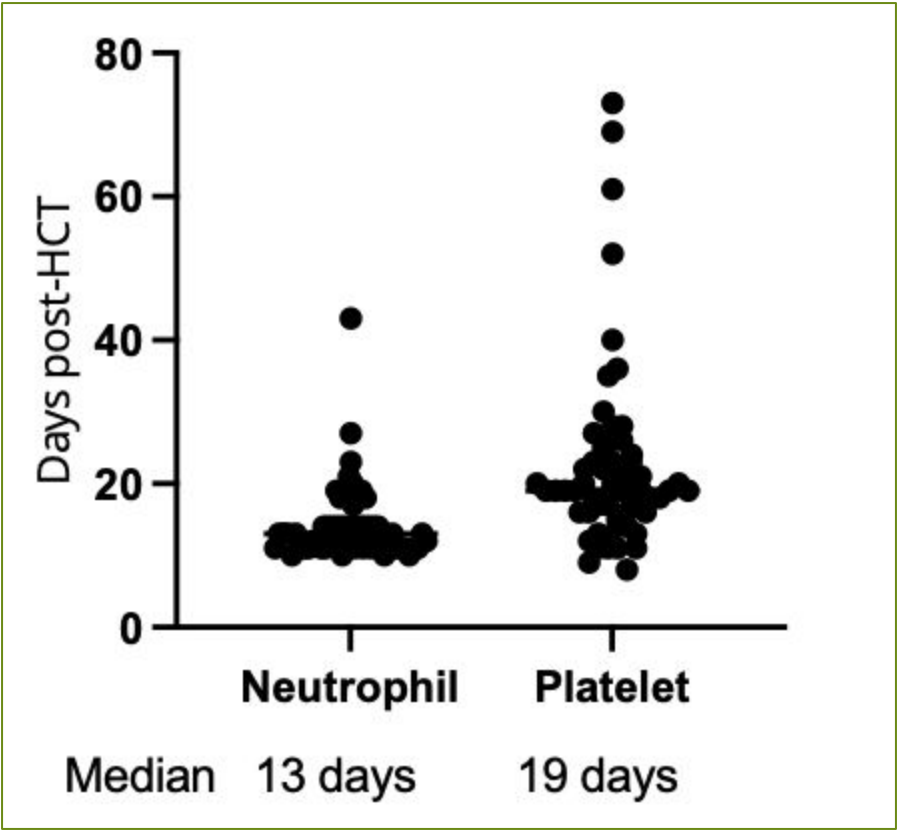
# Baseline Characteristics

	<b>Orca-T (Total n=151)</b>	<b>Orca-T + Bu/Flu/Thiotepa (n=71)</b>
Median age (range), years	48 (19-71)	53 (19-71)
Median follow-up in months (range)	15 (3-43)	14 (4-35)
Male, %	57%	55%
Donor (HLA-matched) (%)		
Related	52%	51%
Unrelated	48%	49%
Conditioning regimen (%)		
Busulfan-based	77%	100%
TBI-based	23%	0%

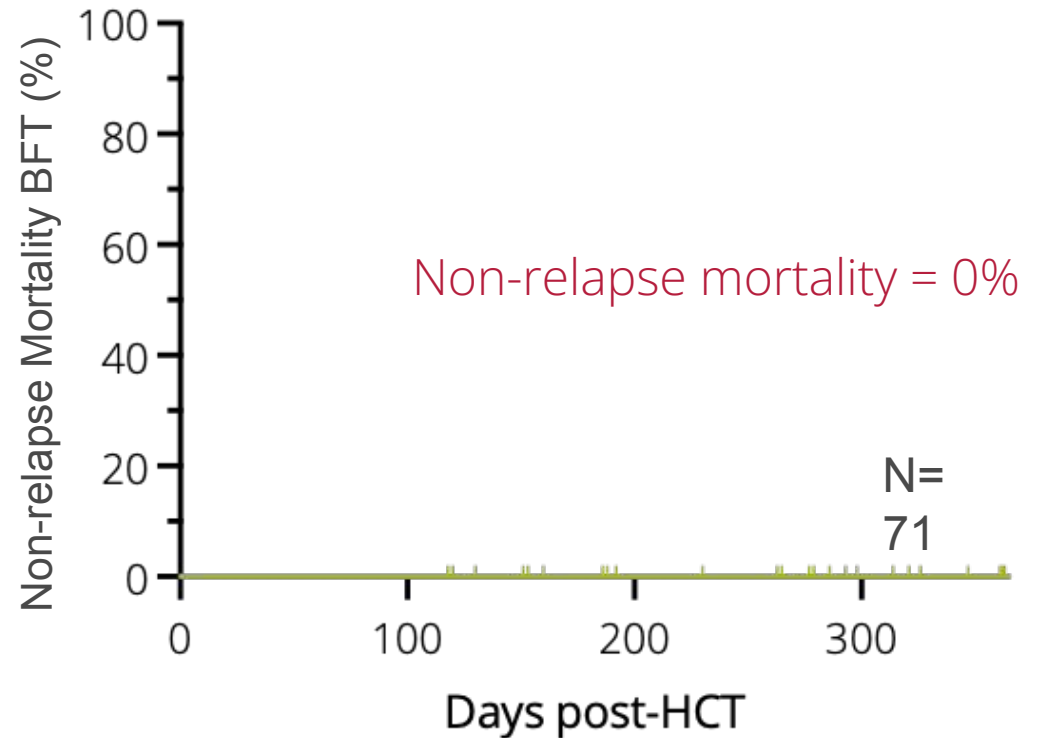
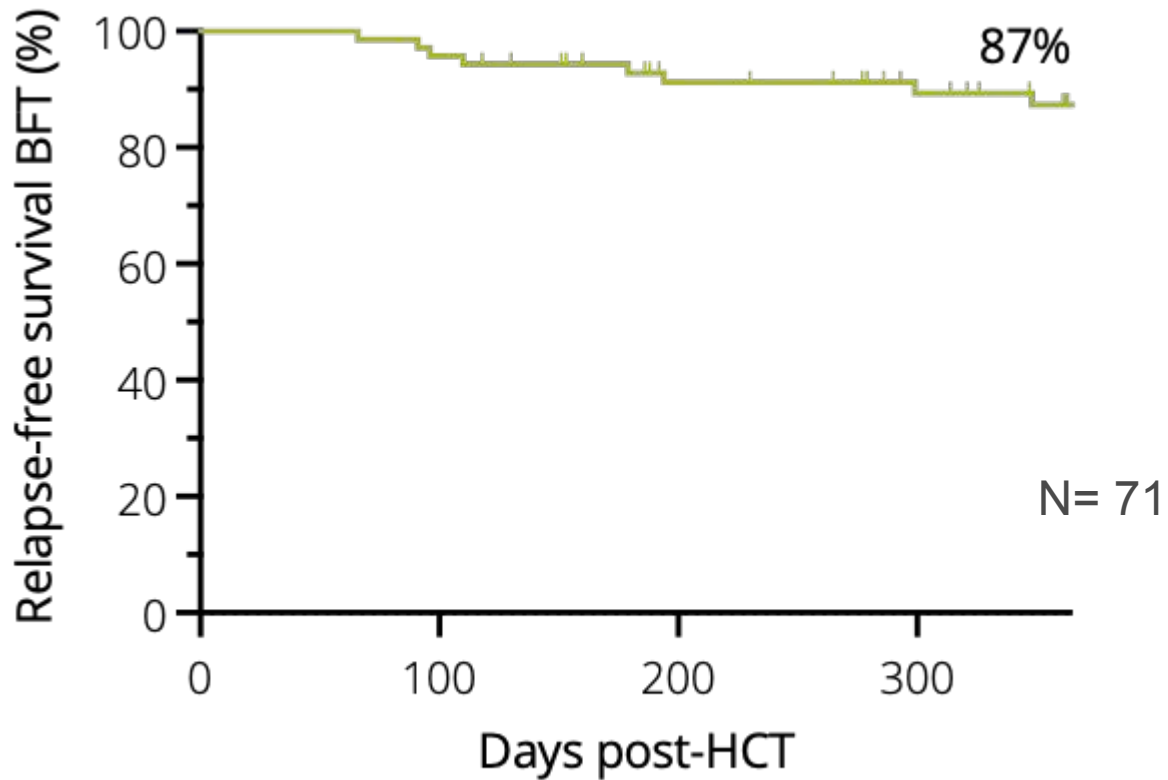
# Baseline Characteristics: Indication for Transplant

	Orca-T (Total n=151)	Orca-T + Bu/Flu/Thiotepa (n=71)
<b>DISEASE</b>		
AML	44%	59%
ALL	31%	11%
Mixed phenotype acute leukemia	3%	1%
MDS	15%	23%
CML	5%	6%
NHL	1%	0%
<b>MRD STATUS (LEUKEMIA ONLY)</b>		
MRD+	19%	27%
MRD-	54%	42%
Unknown MRD status	27%	31%
Active disease	3%	5%

# Neutrophil and Platelet Engraftment



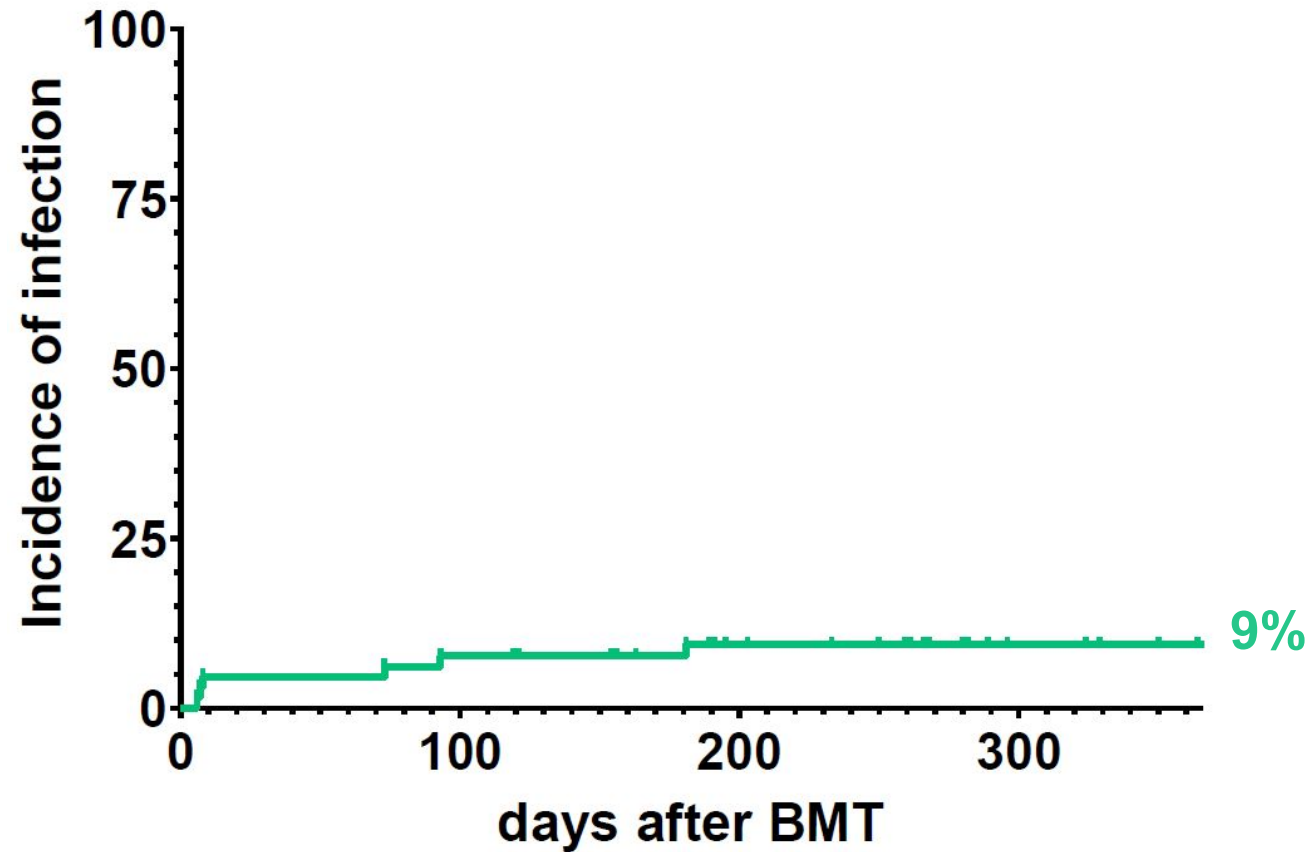
# Relapse Free Survival, Orca-T & BFT Cohort at 1 Year



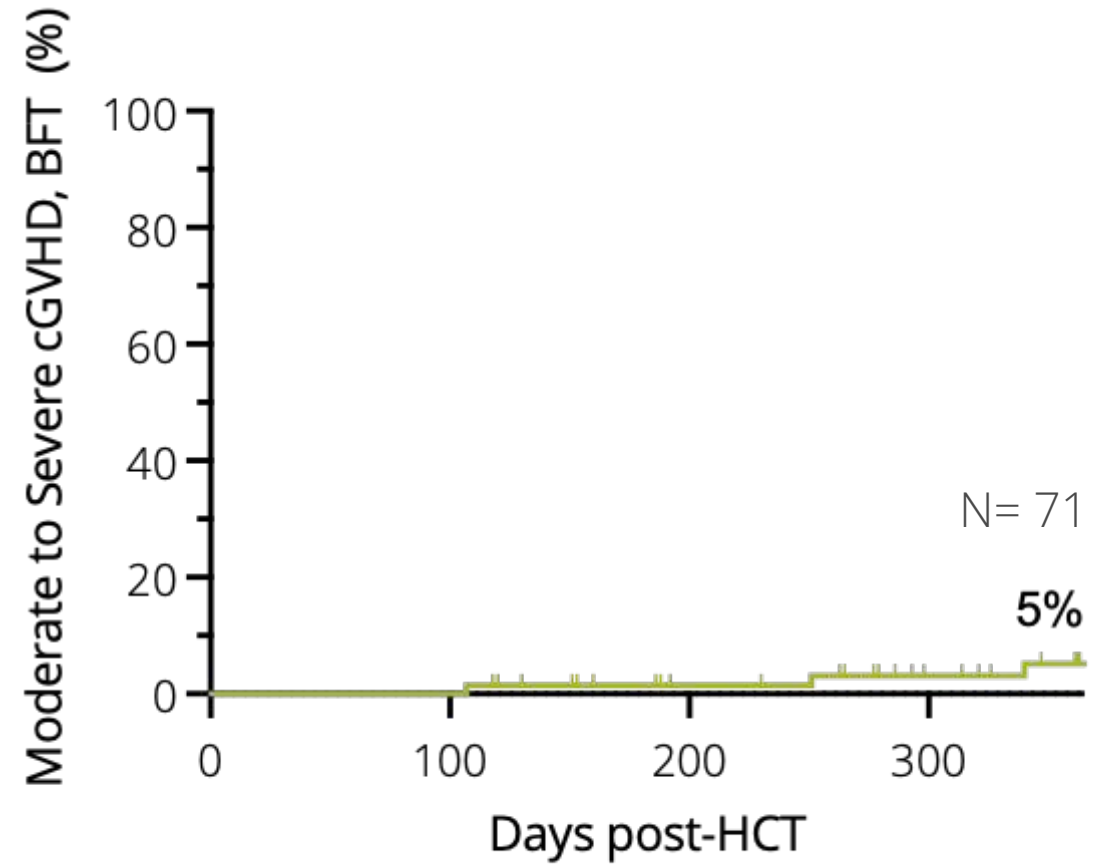
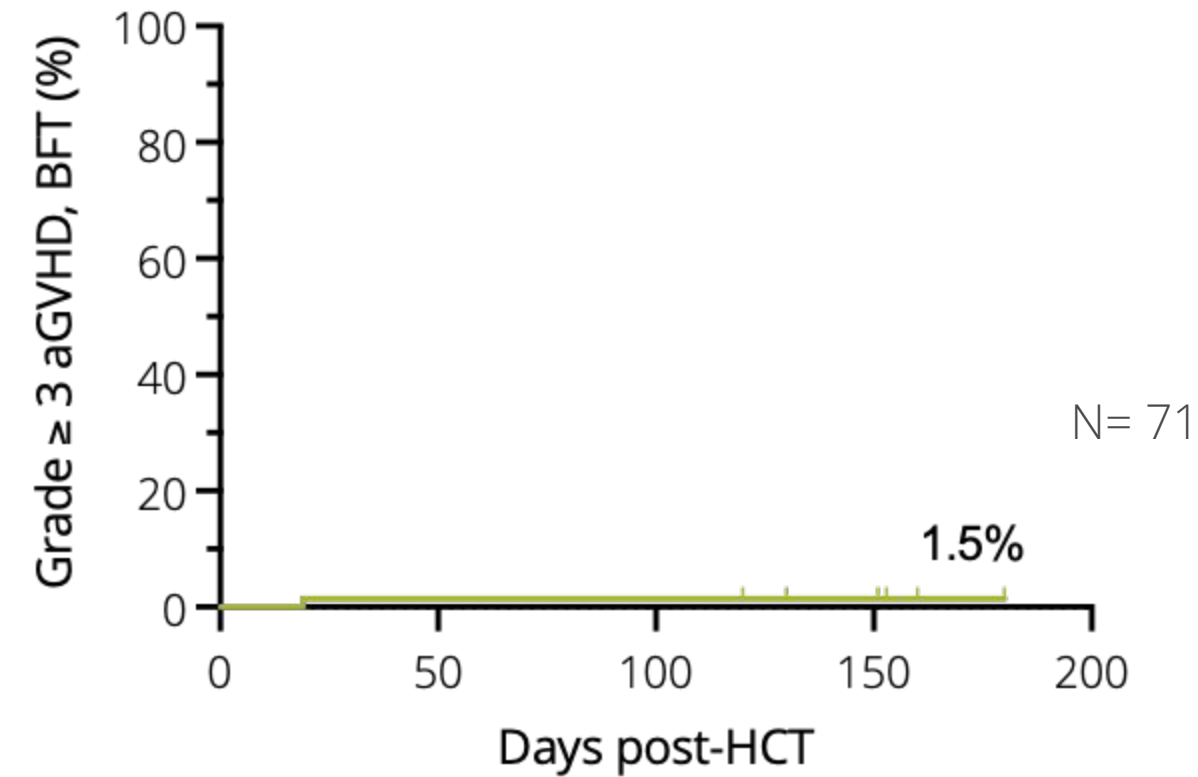
Median follow-up 413 days

# Severe Infection Was Uncommon with Orca-T

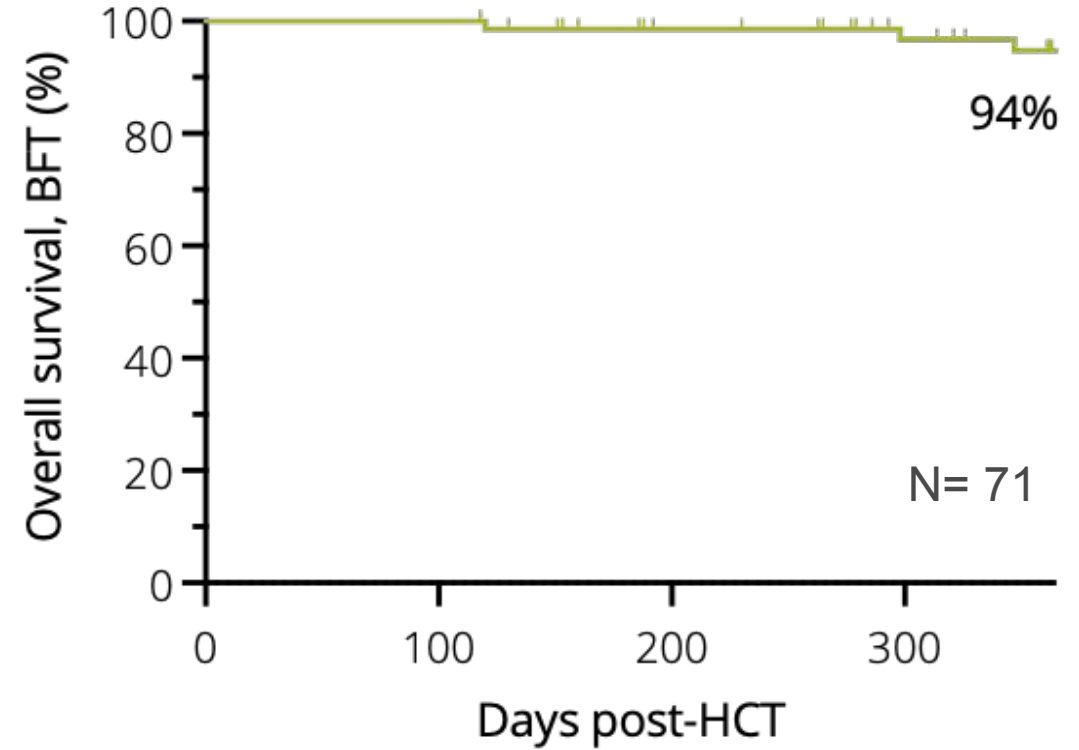
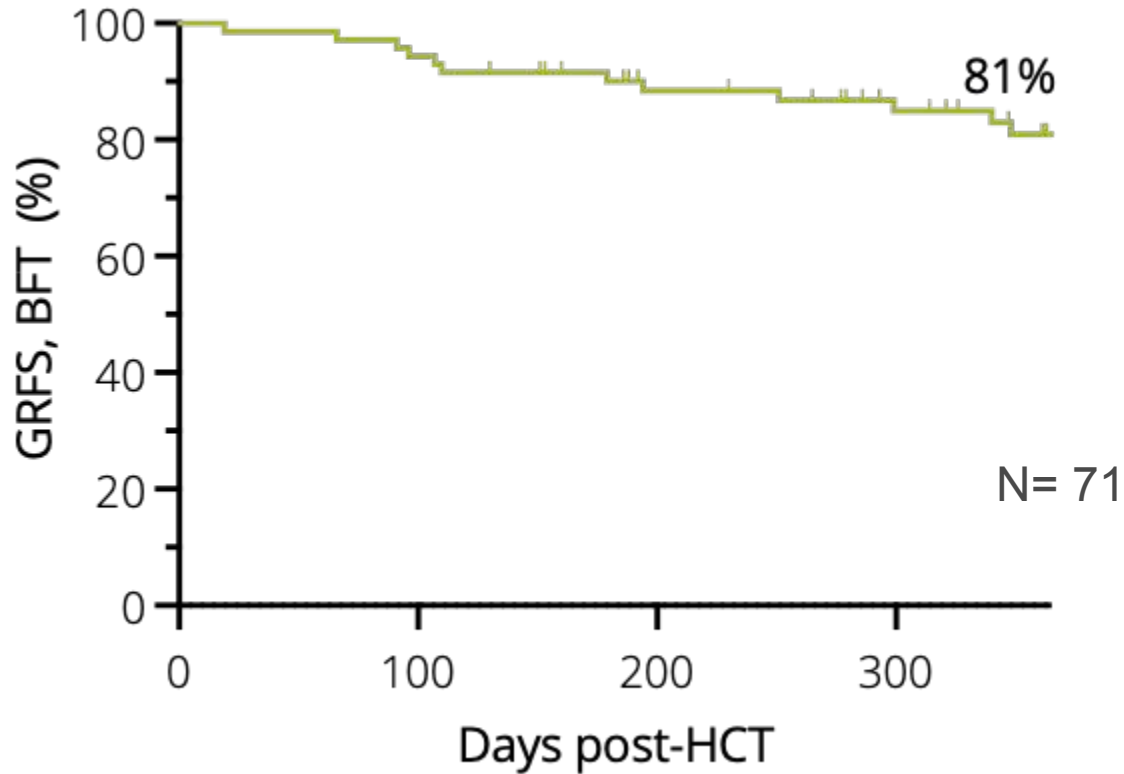
## Gr 3+ MOP infections (BFT patients)



# Acute and Chronic GvHD Incidence



# GvHD and Relapse Free Survival and Overall Survival at 1 Year



# Phase 3 Randomized Precision-T Study is Currently Enrolling

<b>Orca Precision-T (NCT05316701)</b>
<ul style="list-style-type: none"> <li>• AML, ALL, MPAL, undifferentiated, in CR or CRI</li> <li>• Myelodysplastic syndrome (high-risk, therapy-related), including patients with active disease at time of transplant (<math>\leq 10\%</math> BM blast burden)</li> </ul>
<p>Planned to undergo MA-alloHSCT including one of the following myeloablative conditioning regimens:</p> <ul style="list-style-type: none"> <li>• BFT</li> <li>• TBI/Etoposide</li> <li>• TBI/Cy</li> </ul>
8/8 matched related or unrelated donor
HCT-CI $\leq 4$
KPS $\geq 70$
Age 18-65
Adequate organ function

<b>Study arms</b>
<b>Experimental (n = 87)</b>
Orca-T + single-agent Tac PPX
<b>Active comparator (n = 87)</b>
SOC (unmanipulated allograft) + dual-agent Tac/Mtx prophylaxis
<b>Endpoints</b>
<b>Primary Endpoint</b>
Chronic GvHD-free survival
<b>Secondary Endpoint</b>
RFS, GRFS, moderate-severe cGvHD



# Summary

- In patients with acute leukemia and high risk MDS, >1-year outcomes with Orca-T, a high-precision cell-therapy, demonstrated:
  - Robust graft-vs-leukemia and graft-vs-infection effects
  - Very low incidence of GvHD
  - Markedly reduced treatment related mortality despite myeloablative conditioning
- These outcomes were accomplished with consistent and reliable cell manufacturing and distribution of Orca-T at a national scale
- A multi-center randomized controlled phase 3 trial comparing Orca-T to SOC, utilizing BFT or TBI-based conditioning, is currently enrolling across the U.S. (NCT05316701)

# Participating Centers & Acknowledgements

MANY THANKS TO THE PATIENTS, THEIR FAMILIES AND CAREGIVERS, AND STUDY STAFF

**Stanford Hospital and Clinics**

**University of California Davis**

**MD Anderson Cancer Center**

**UCLA Medical Center**

**City of Hope**

**Methodist Hospital**

**University of Kansas**

**Emory University**

**Vanderbilt University**

**University of Utah Health**

**Oregon Health Sciences  
University**

**Medical College of Wisconsin**

**TriStar Centennial Medical  
Center**

**Be The Match Biotherapies**