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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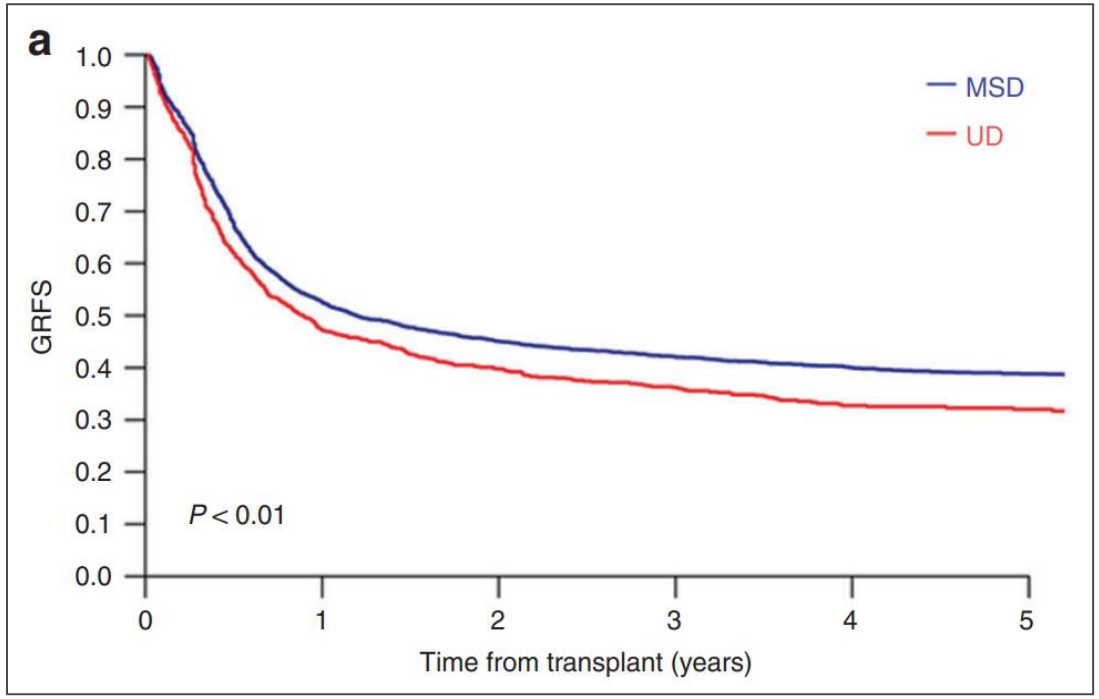
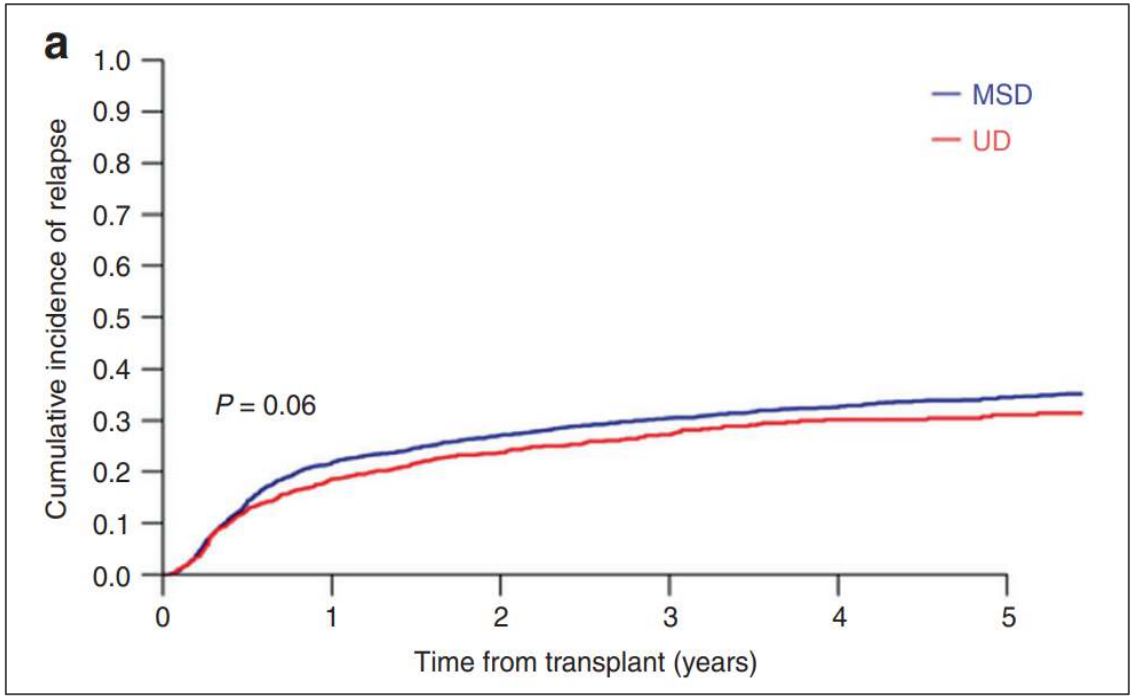
HLA Matched Donor Hematopoietic Stem Cell Transplantation Remains Challenging

GRFS and RFS after AlloHSCT from a Matched Donor

(Adults with AML with intermediate or unfavorable karyotype in first complete remission)





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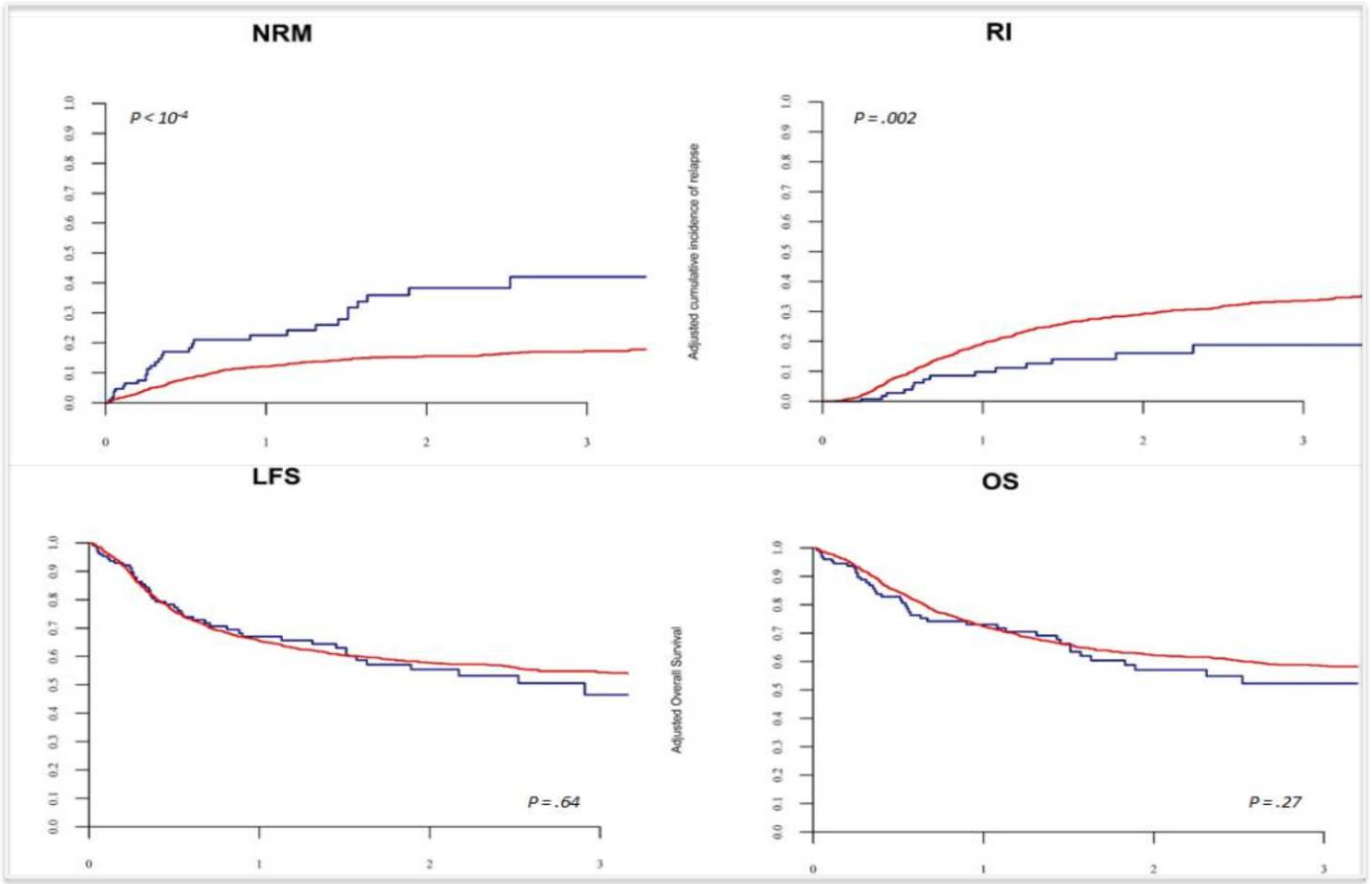
AlloHSCT, allogeneic hematopoietic stem cell transplant; AML, acute myeloid leukemia; TRM, treatment-related mortality.

Battipaglia G, Ruggeri A, Labopin M, et al. Refined graft-versus-host disease/relapse-free survival in transplant from HLA-identical related or unrelated donors in acute myeloid leukemia. *Bone Marrow Transplant*.2018; 53, 1295–1303.

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

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Bu/Flu/Thio (BFT), Bulsulfan, fludarabine, thiotepa; Bu/Flu (BF), Bulsulfan, fludarabine; MRD, minimum residual disease; NRM, non-relapse mortality; OS, overall survival; RFS, relapse-free survival; URD, unresectable disease.
Oncotarget. 2018 Jan 9; 9(3): 3379–3393

Opportunity to Improve Clinical Outcomes from AlloHSCT with Precision Engineering

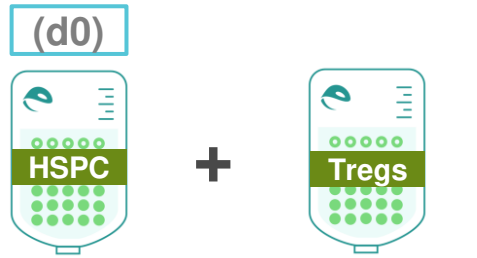
Current Transplants

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



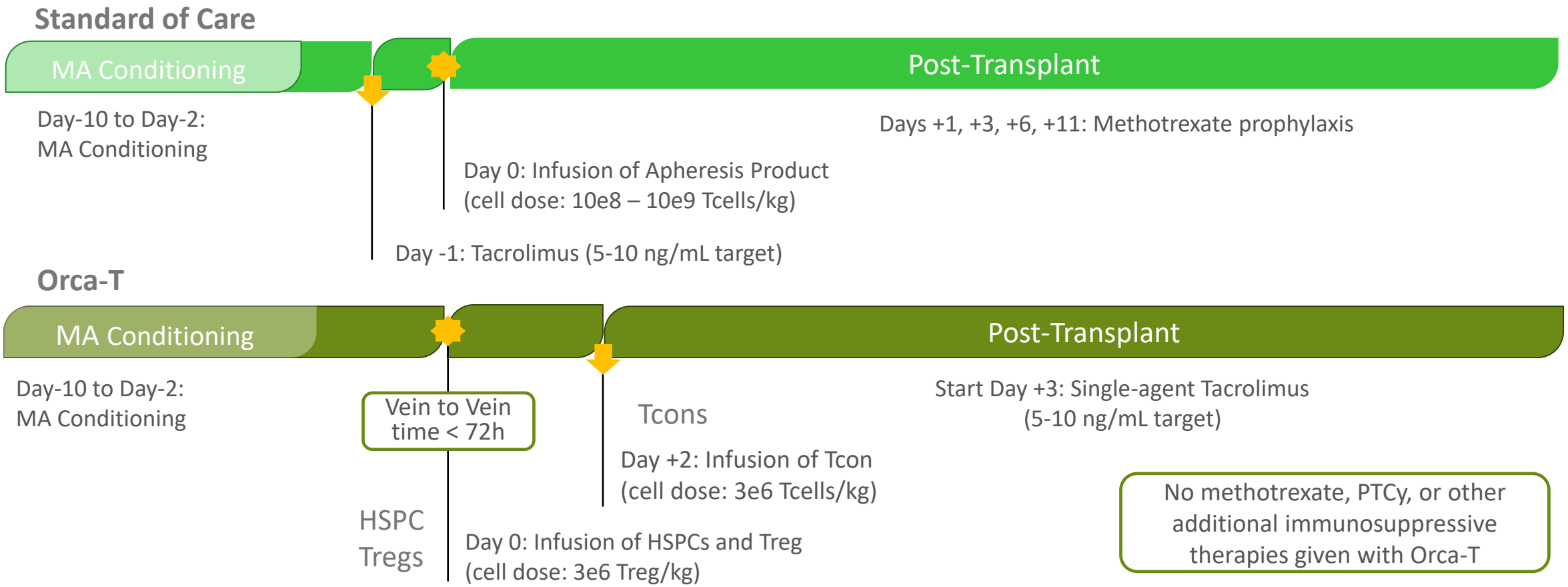
Long term blood and immune reconstitution

High purity to Prevent GvHD

Bridge immune reconstitution
Disease control
Infection control

HSPC, hematopoietic stem and progenitor cells; NK, natural killer;

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



Meyer, E. H., Laport, G., et al. Transplantation of donor grafts with defined ratio of conventional and regulatory T cells in HLA-matched recipients. *JCI INSIGHT*. 2019; 4 (10)

Study Key Eligibility Criteria

Single Center Phase 2 Trial (NCT01660607)* Multicenter Phase 1b Trial (NCT04013685)
• Acute leukemia (AML, ALL, mixed phenotype), in CR • Acute leukemia (AML, ALL, mixed phenotype), with active disease at time of transplant (≤ 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 ≤ 4
KPS ≥ 70
Age 18-65 (or 18 –72)*
Adequate organ function

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ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; BPDCN, Blastic plasmacytoid dendritic cell neoplasm; CML, chronic myeloid leukemia; CR, complete remission; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; HLA, human leukocyte antigen; KPS, Karnofsky performance Score.

Baseline Characteristics

Single Center Phase 2 (NCT01660607, n=34) Multicenter Phase 1b (NCT04013685, n=117)		CIBMTR Control (n = 375)	Orca-T (n = 151)
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 ALL MDS Other	47% 20% 33% n/a	44% 31% 15% 9%
Male		57%	57%
Donor (HLA matched)	Related Unrelated	45% 55%	52% 48%
Cond. Regimen	Busulfan-based TBI-based	77% 20%	77% 23%

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

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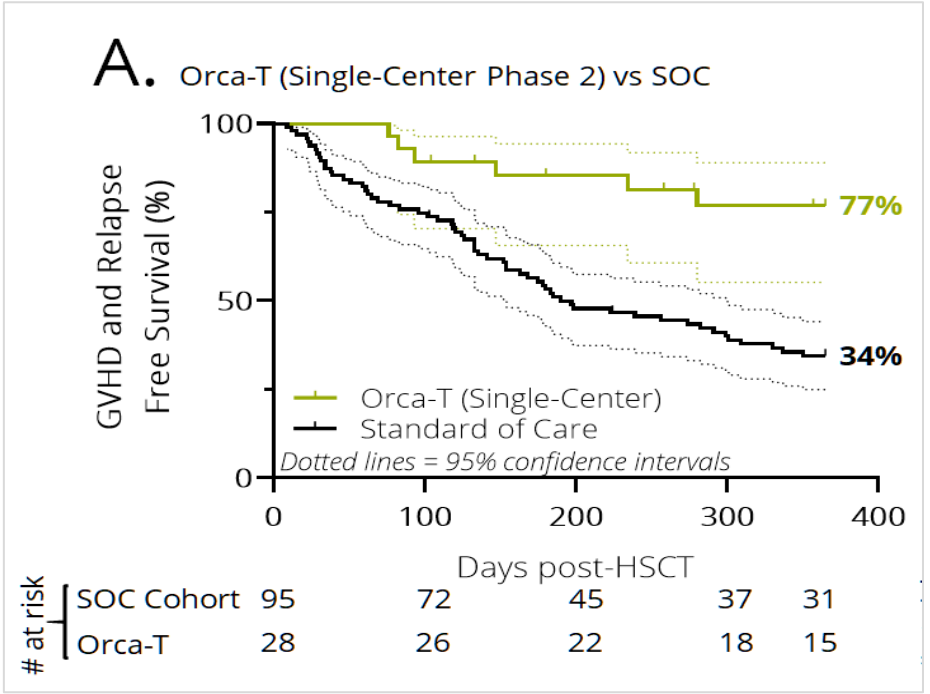
ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete response; HLA, human leukocyte antigen; MDS, myelodysplastic syndrome; TBI, total body irradiation.

Overall Orca-T Study Population Outperforms Standard of Care AlloHSCT

Single Center Phase 2 Trial (NCT01660607)* Multicenter Phase 1b Trial (NCT04013685)	CIBMTR Control (n = 375)		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%

Phase 2 trial has reached endpoint of improved GVHD-free relapse-free survival with Orca-T



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

AlloHSCT, allogeneic hematopoietic stem cell transplant; CIBMTR, Center for International Blood and Marrow Transplant Research

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Baseline Characteristics

Single Center Phase 2 Trial (NCT01660607, n=34) Multicenter Phase 1b Trial (NCT04013685, n=117)	Orca-T (Total n=151)	Orca-T + Bu/Flu/Thiotepa (n=71)
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 Unrelated	 52% 48%	 51% 49%
Conditioning regimen (%) Busulfan-based TBI-based	 77% 23%	 100% 0%

TBI, total-body irradiation.

Baseline Characteristics: Indication for Transplant

Single Center Phase 2 Trial (NCT01660607, n=34) Multicenter Phase 1b Trial (NCT04013685, n=117)	Orca-T (Total n=151)	Orca-T + Bu/Flu/Thiotepa (n=71)
DISEASE		
AML	44%	59%
ALL	31%	11%
Mixed phenotype acute leukemia	3%	1%
MDS	15%	23%
CML	5%	6%
NHL	1%	0%
MRD STATUS (LEUKEMIA ONLY)		
MRD+	19%	27%
MRD-	54%	42%
Unknown MRD status	27%	31%
Active disease	3%	5%

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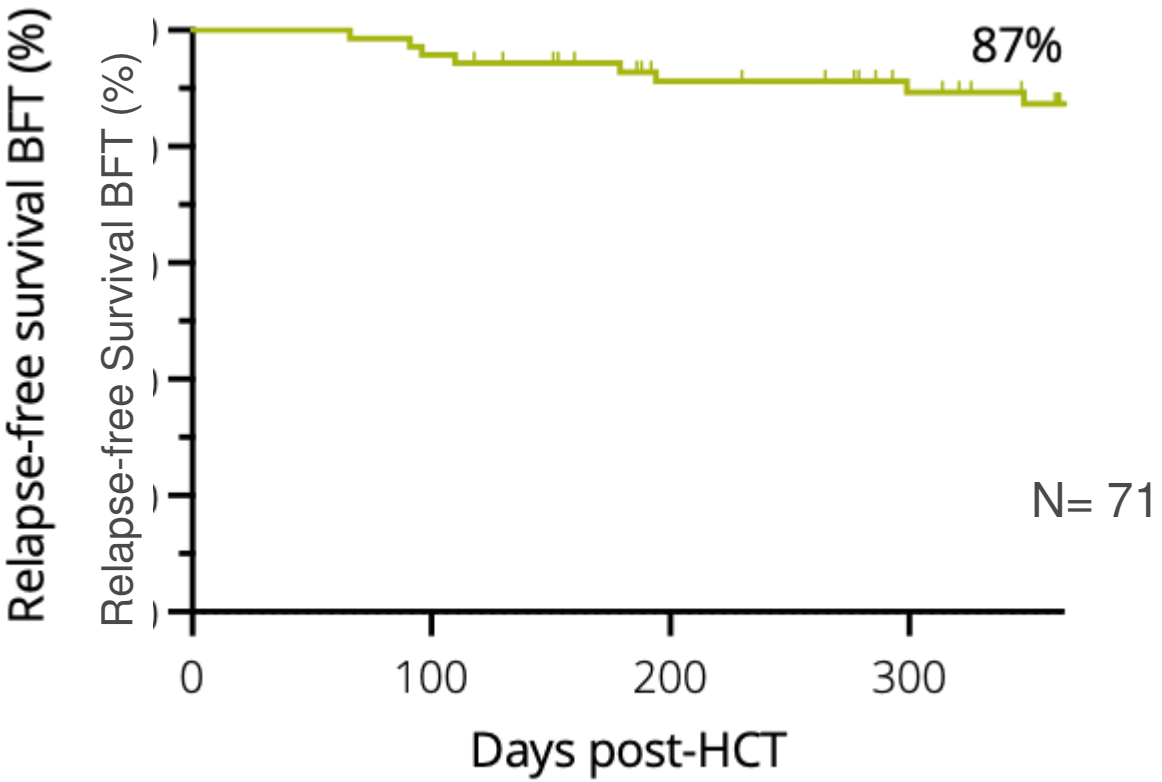
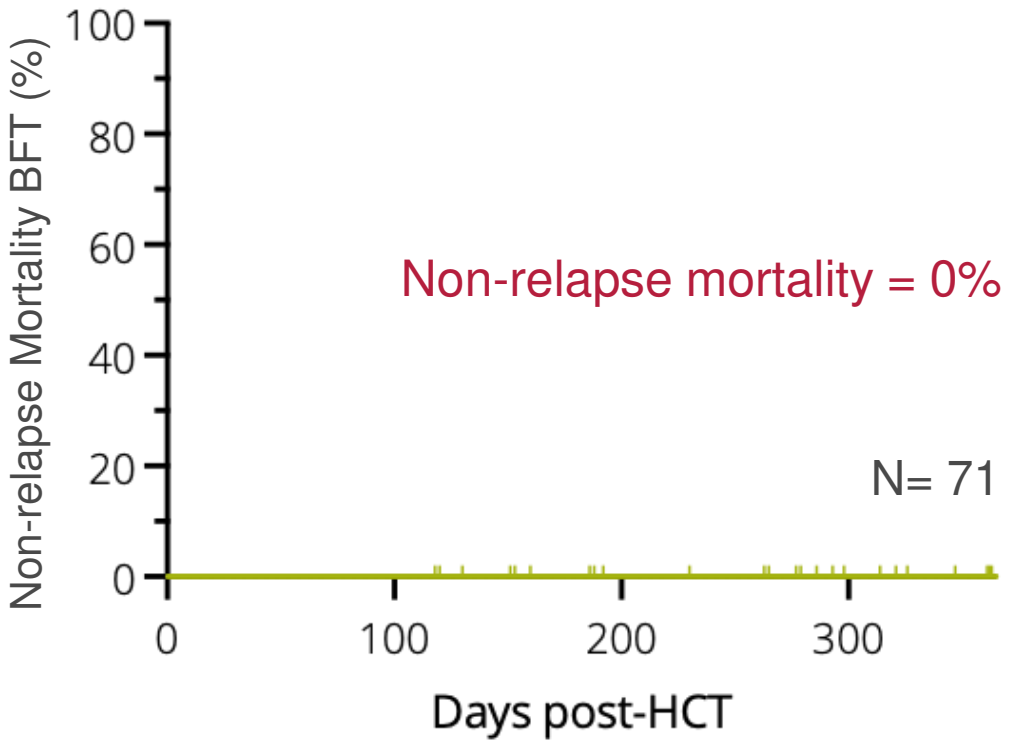
ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML, chronic myelogenous leukemia; CR, complete response; DRI, disease risk index; HLA, human leukocyte antigen; MDS, myelodysplastic syndrome; MRD, minimum residual disease; NHL, Non-Hodgkin's Lymphoma.

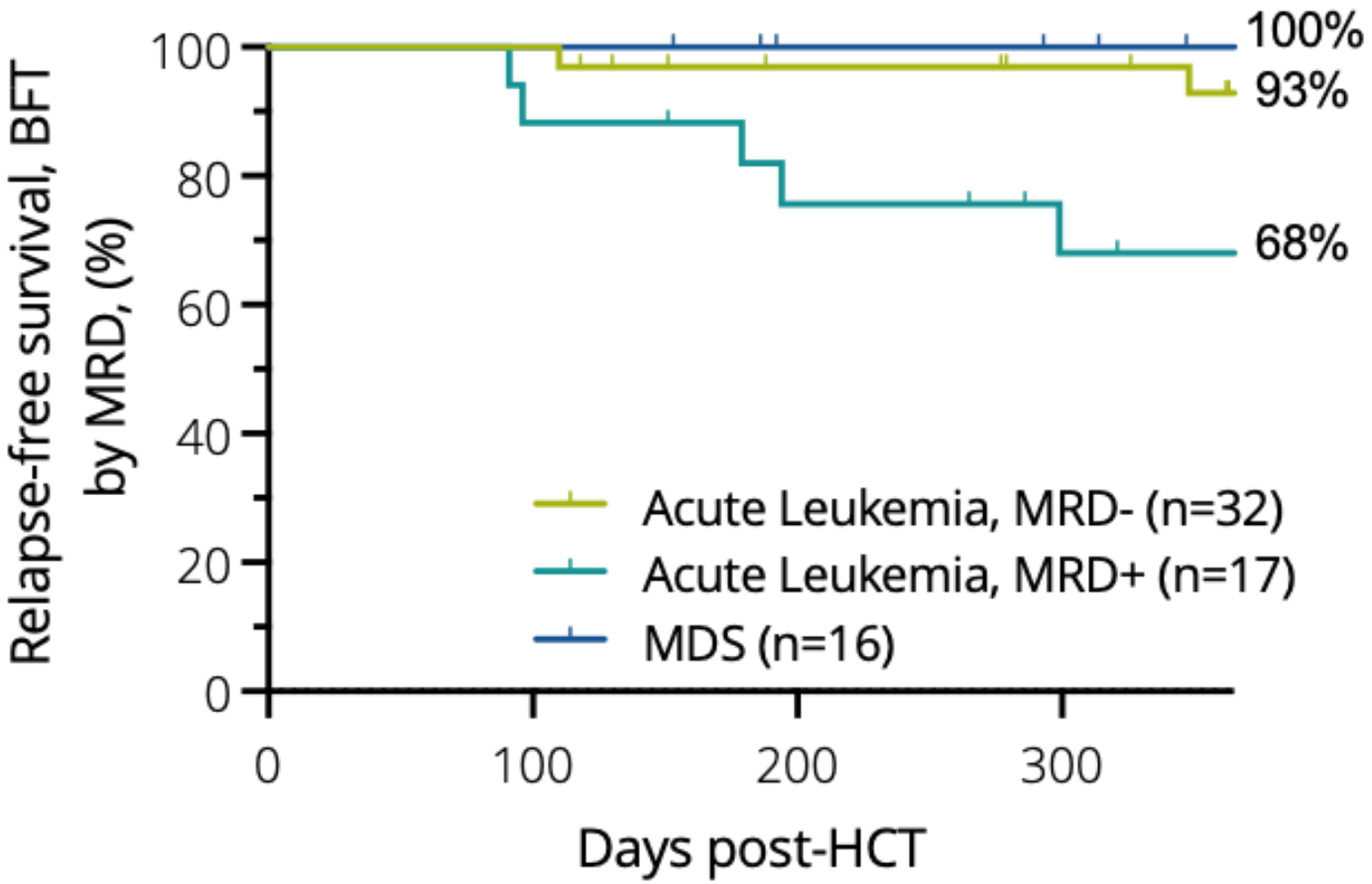
Relapse Free Survival, Orca-T & BFT Cohort @ 1 Year



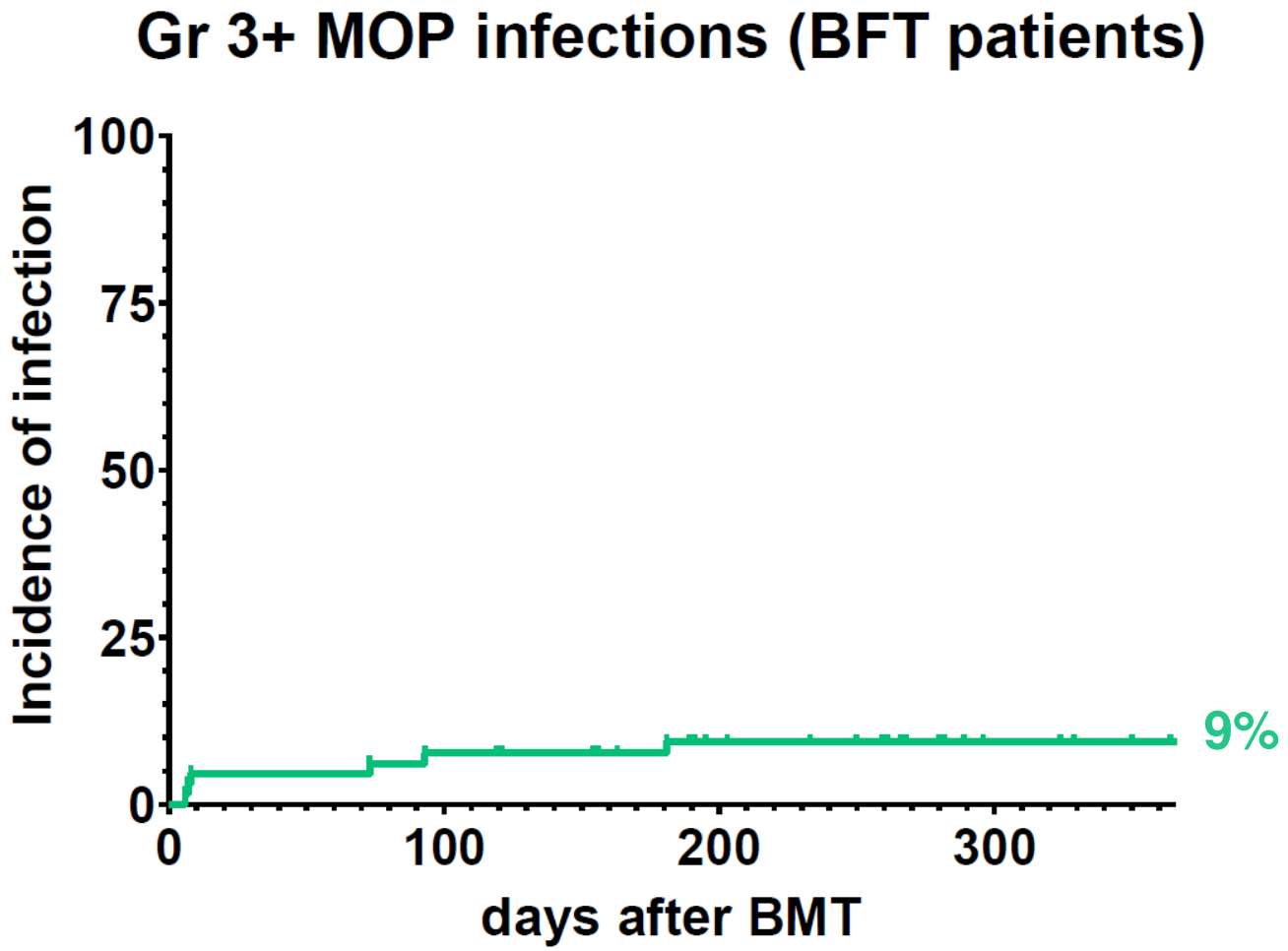


Median follow-up 413 days

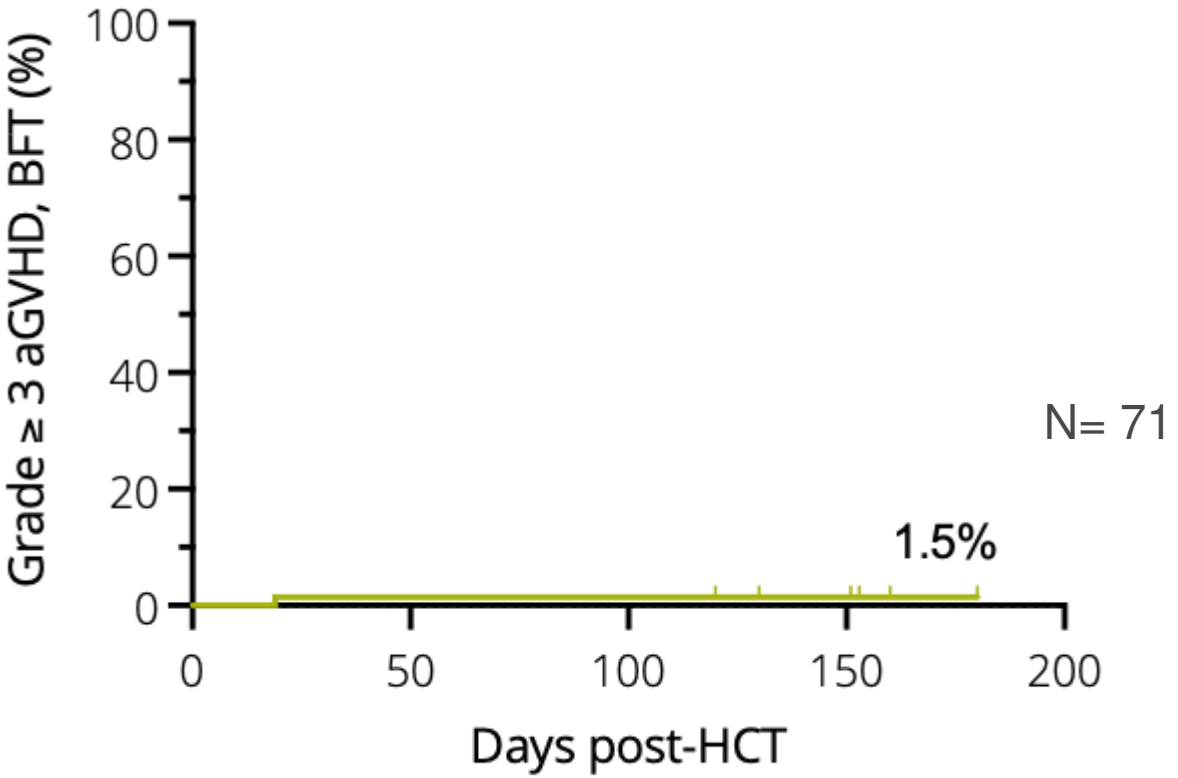
Relapse Free Survival by MRD Status @1 Year

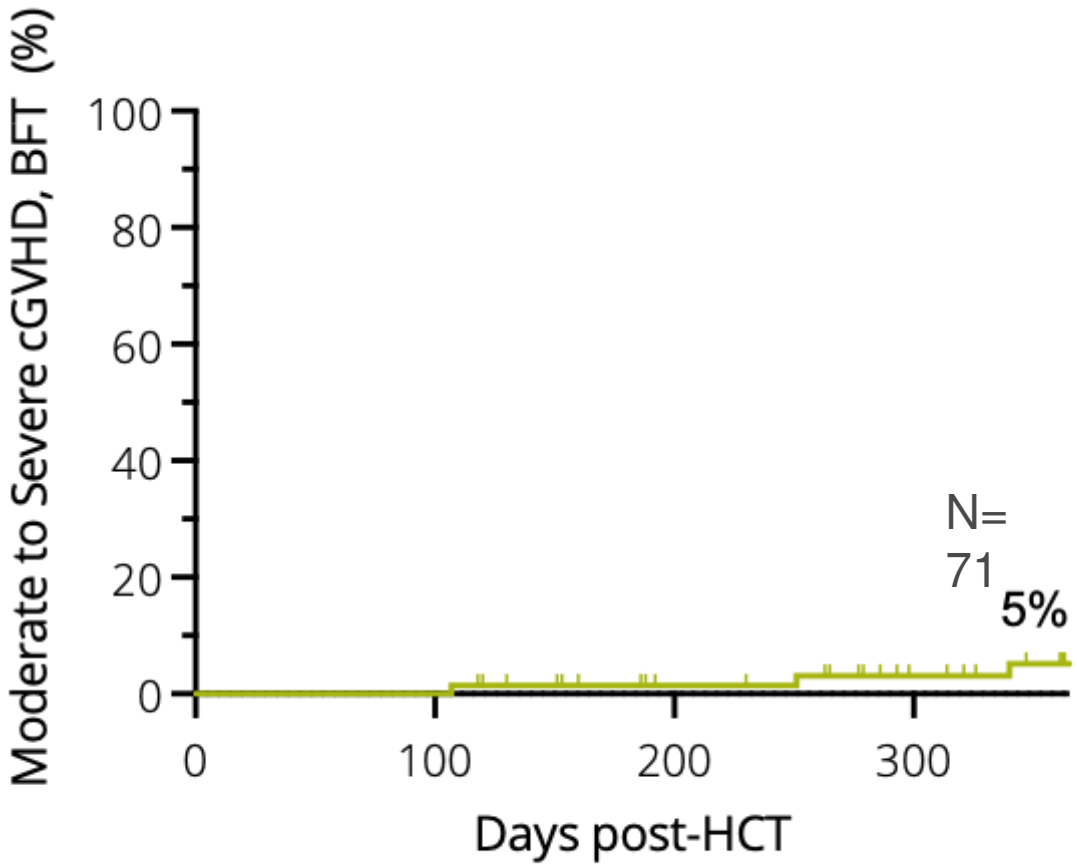


Severe Infection Was Uncommon with Orca-T

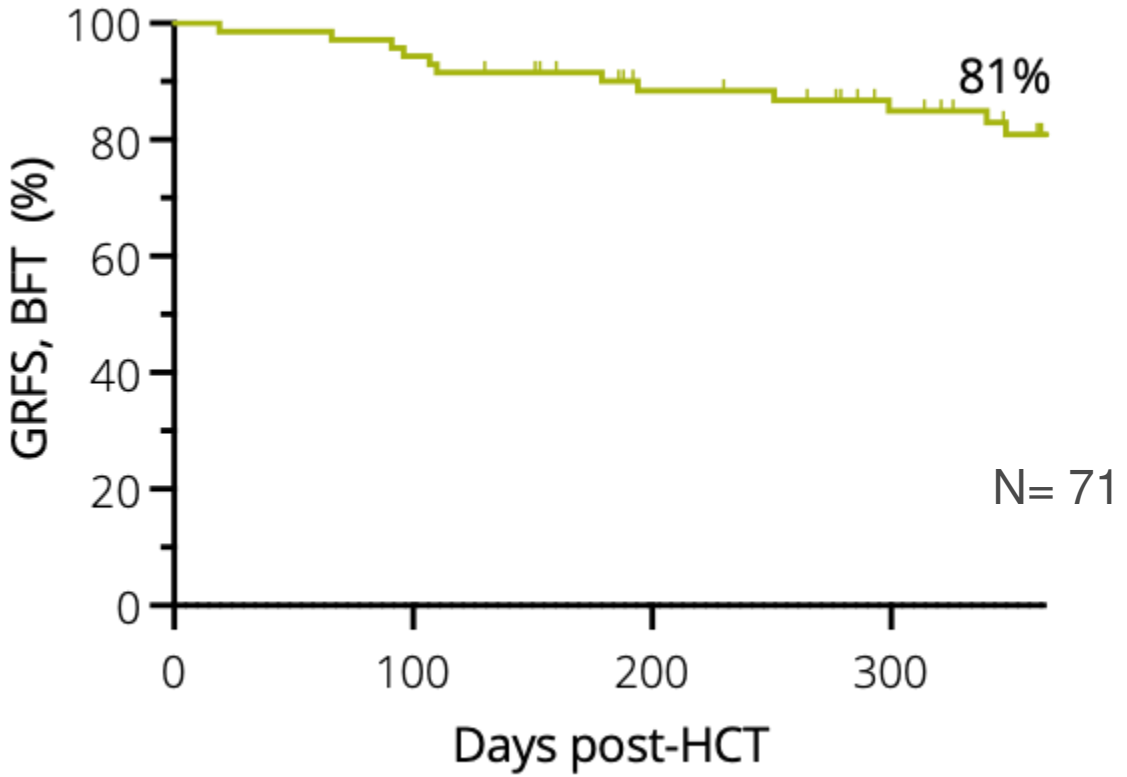


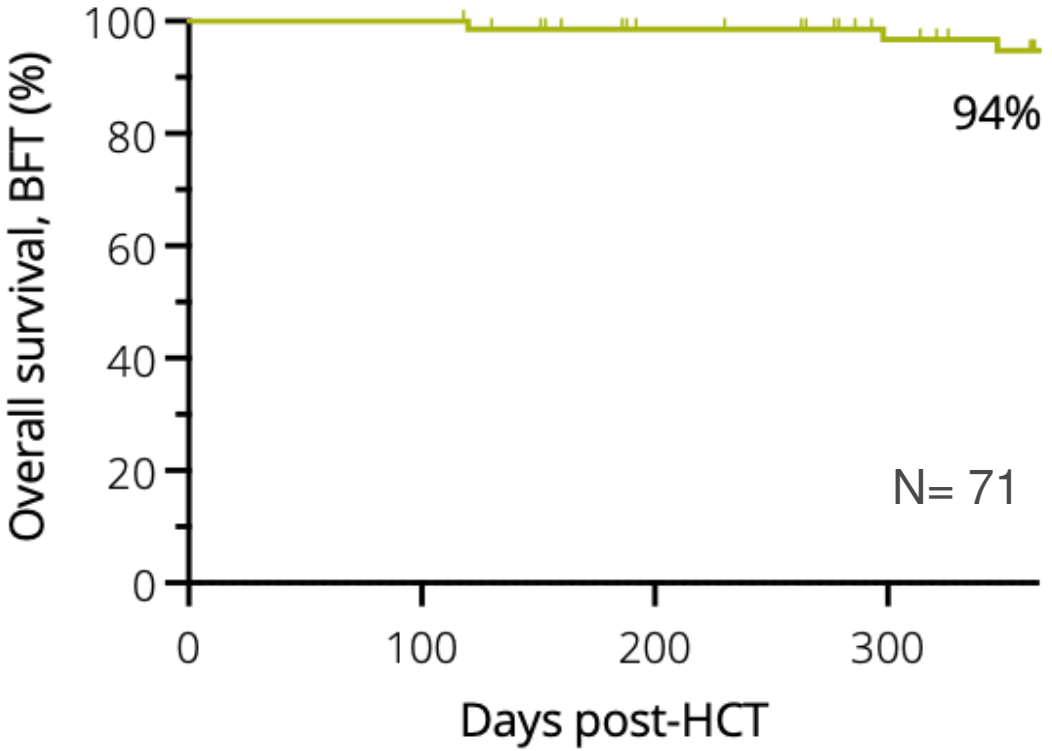
Acute and Chronic GVHD Incidence





GVHD and Relapse Free Survival and Overall Survival @1 Year





Phase 3 Randomized Precision-T Study is Currently Enrolling

Orca Precision-T (NCT05316701)
• AML, ALL, MPAL, undifferentiated, in CR or CRi • Myelodysplastic syndrome (high-risk, therapy-related), including patients with active disease at time of transplant (≤ 10% BM blast burden)
Planned to undergo MA-alloHSCT including one of the following myeloablative conditioning regimens: • BFT • TBI/Etoposide • TBI/Cy
8/8 matched related or unrelated donor
HCT-CI ≤ 4
KPS ≥ 70
Age 18-65
Adequate organ function

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

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ALL, Acute lymphocytic leukemia, AML, acute myeloid leukemia; BFT, busulfan, fludarabine, and thiotepa; BM, bone marrow; cGVHD, chronic graft-versus-host disease; CR, complete remission; CRi, complete remission with incomplete count recovery; Cy, cyclophosphamide; GRFS, graft-versus-host and relapse-free survival; HCT-CI, hematopoietic cell transplantation comorbidity index; KPS, Karnofsky Performance Score; MPAL, mixed phenotype acute leukemia; Mtx, methotrexate; RFS, relapse-free survival; Tac, tacrolimus, TBI, total-body irradiation.

1. https://precisiontstudy.com/. Accessed 24Oct2022. 2. https://clinicaltrials.gov/ct2/show/NCT05316701. Accessed 24Oct2022.

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)

BFT, busulfan, fludarabine, and thiotepa; MAC, myeloablative conditioning; NRM, non-relapse mortality; SOC, standard of care; TBI total body irradiation.

Participating Centers & Acknowledgements

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

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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

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