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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INTRODUCTION

- Allogeneic hematopoietic stem cell transplantation (alloSCT) is curative for several high-risk hematologic malignancies
- Despite improvements in donor matching and supportive care, these transplants are associated with significant toxicity and reduced quality of life
- Strategies to maintain or enhance the graft-vs-tumor and graft-vs-infection effects while eliminating GvHD have long been a key goal in the field

AIM

- Orca-T is a high-precision, cellular therapy biologic that includes stem and immune cells, derived from allogeneic donors, that leverages highly purified, polyclonal donor regulatory T cells to control alloreactive immune responses
- This study determined the efficacy, safety and feasibility of Orca-T administered with single-agent tacrolimus as GvHD prophylaxis in patients eligible to myeloablative alloSCT with HLA-matched donors (related or unrelated)

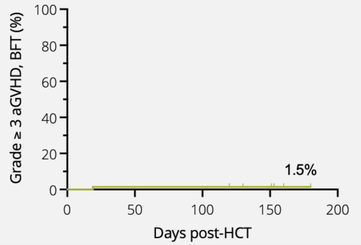
METHODS

- Phase 1b/2, multicenter, study (NCT04013685 / NCT01660607)
- 8/8 matched related or unrelated donor
- Adult patients (18–65 y or 18–72) with high-risk hematologic malignancies with adequate organ function
- Orca-T infusions at Day 0 and Day +2
  - Patients received investigator's choice of myeloablative conditioning regimens
  - For comparison purposes, an independent CIBMTR-based cohort was identified which consisted of patients with AML, ALL, or MDS who received myeloablative alloSCT with a peripheral blood stem cell source between 2016-2018 followed by tacrolimus/methotrexate prophylaxis

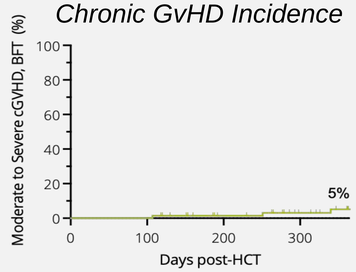
RESULTS

- *As of 25 Oct 2022, 151 patients had received Orca-T and had ≥100 days of follow-up*
  - *GvHD-and-relapse-free survival rates (GRFS) at 1 year were 70% for Orca-T and 21% for CIBMTR controls (n=375)*
  - *Corresponding rates at 1 year for non-relapse mortality (4% vs 10%) and overall survival (88% vs 68%) were encouraging*
  - *Orca-T outcomes were enhanced with busulfan, fludarabine, and thiotepa (BFT) conditioning regimen*
- *For Orca-T + BFT cohort (n=71), median age 53 years; median follow-up 14 months, 55% male, and 59% AML*
  - *Median of 13 and 19 days to neutrophil and platelet engraftment, respectively*
  - *Low incidences of aGvHD (1.5%), and cGvHD (5%) (**Figures**)*
  - *Encouraging GRFS (81%) and relapse-free survival (87%) results were observed at 1 year (**Figures**)*
  - *Positive rates non-relapse mortality (0%), grade 3+ MOP infections (9%)*

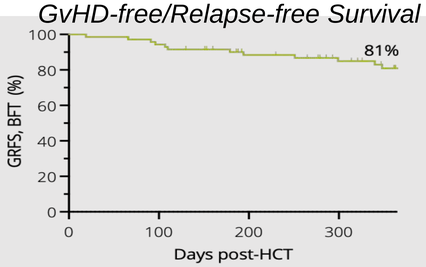
Acute GvHD Incidence



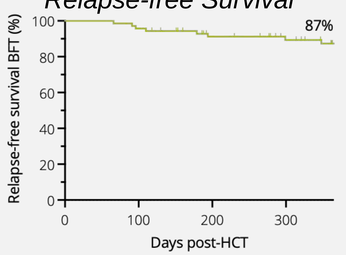
Chronic GvHD Incidence



GvHD-free/Relapse-free Survival



Relapse-free Survival



CONCLUSIONS

- In patients with acute leukemia and high-risk MDS, >1-year outcomes with Orca-T showed:
  - Robust graft-vs-leukemia and graft-vs-infection effects
  - Very low incidence of GvHD
  - Markedly reduced treatment-related mortality despite MAC
- These outcomes were accomplished with consistent and reliable cell manufacturing and distribution of Orca-T at a national scale
- The Phase 3 Orca Precision-T study, utilizing BFT- or TBI-based conditioning, is currently enrolling (NCT05316701)

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CONTACT INFORMATION

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