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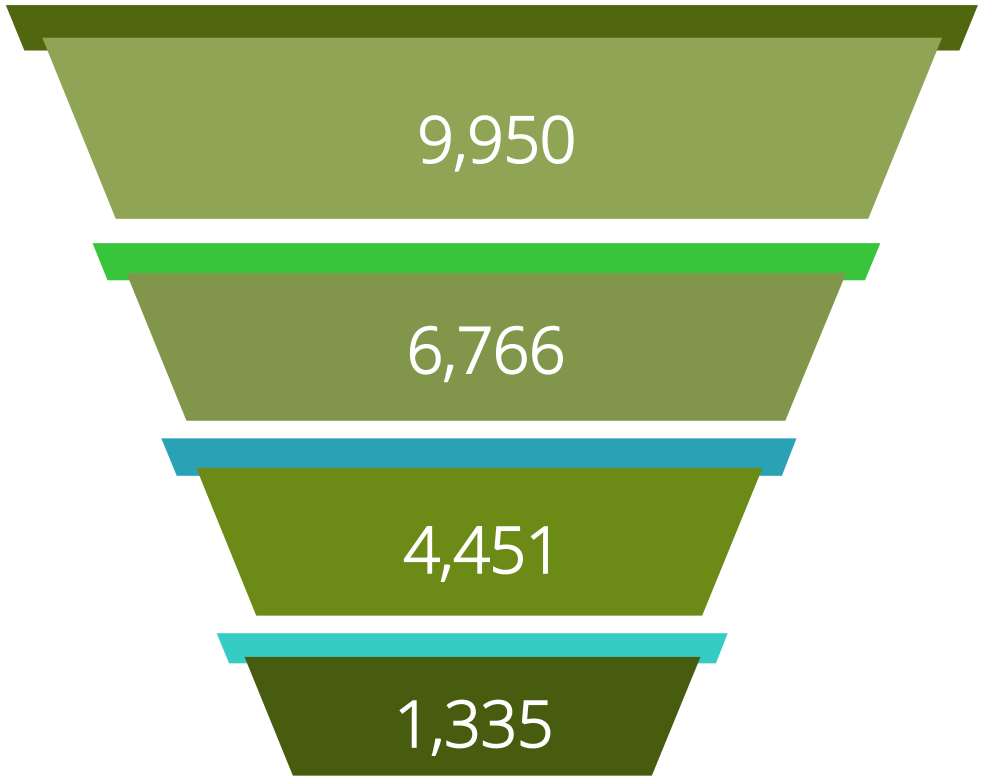
Administration of Orca-T

Centers for Medicare and Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting
March 19, 2024

The population eligible for Orca-T represents a clearly defined and focused subset of patients undergoing standard allograft



Key layers and inputs[1]

Total number of SOC* projected in 2020 for the US based on CIBMTR Registry

Total number of SOC utilized among AML, ALL and MDS** (68%)

Total number receiving myeloablative regimens (67%)

Total number patients 60+

1 CIBMTR Summary Slides

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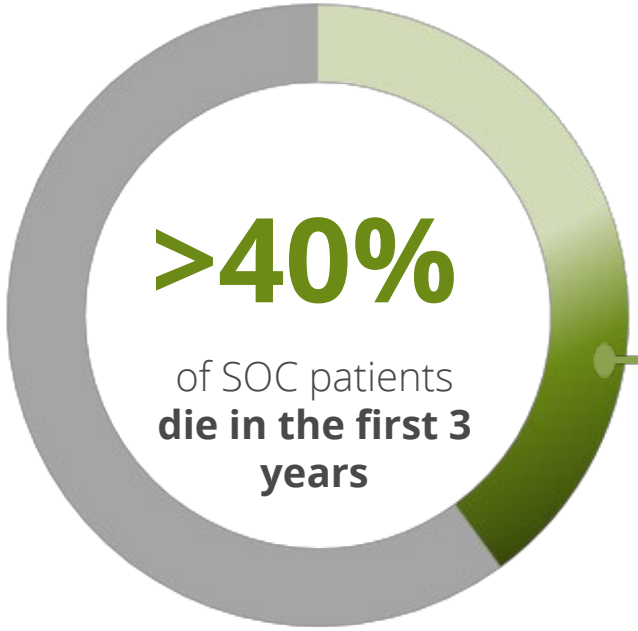
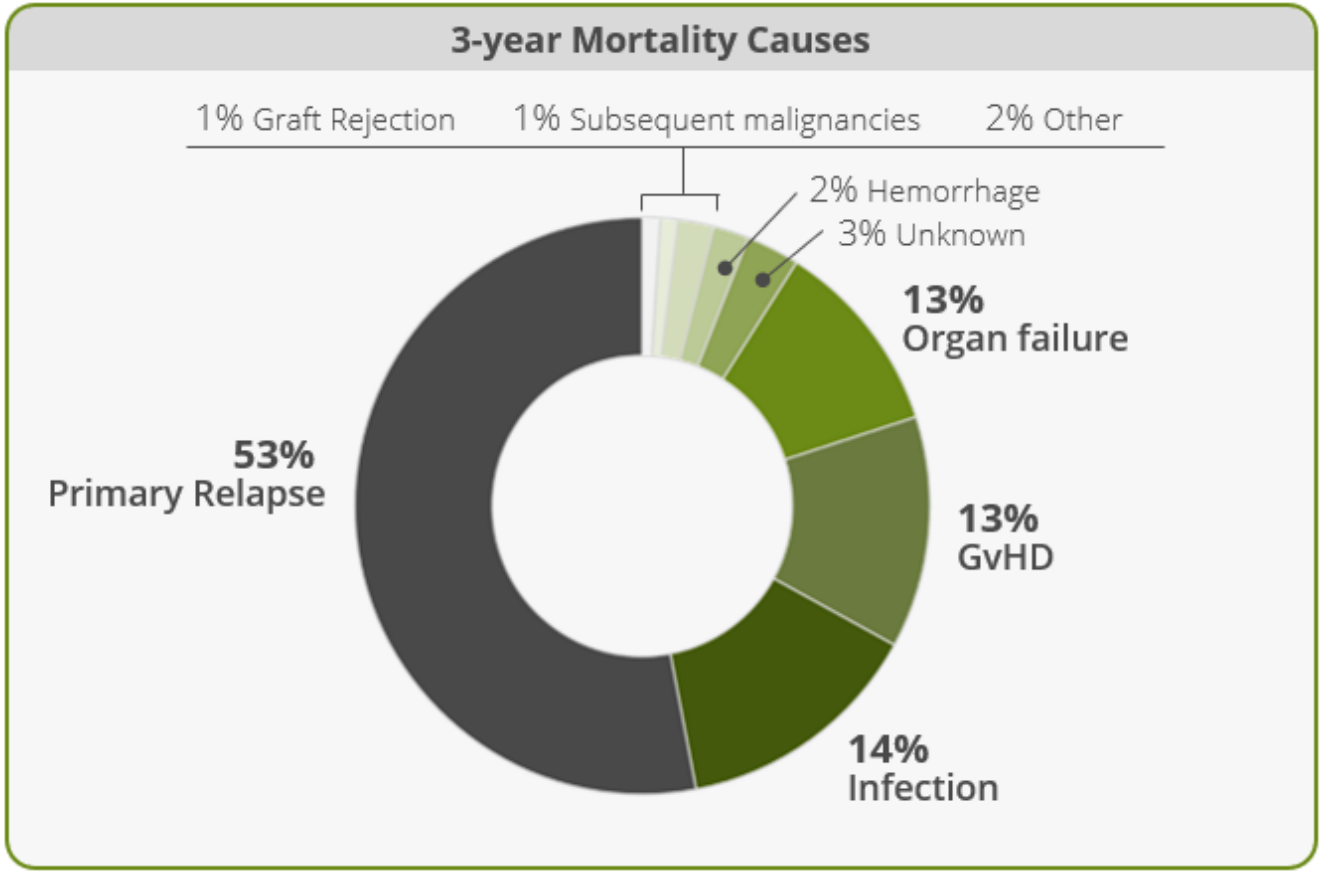
*Standard of Care - conventional allograft; transplant
**acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS)

Unmet need for eligible patients undergoing a standard allograft

Nearly half of all SOC patients die in 3 years due to relapse, graft versus host disease (GvHD), infection, or organ failure





*Data reflects 3-year mortality

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Source: CIBMTR 2020 Annual Report
SOC- Conventional allograft transplant

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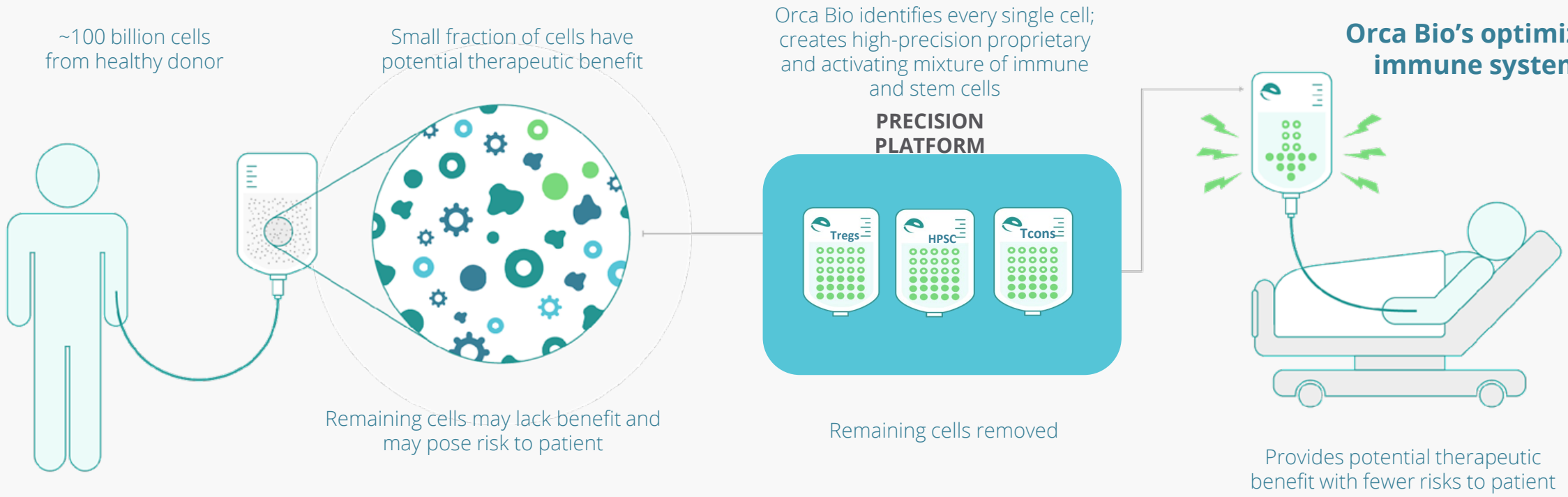
Orca-T product overview

Our proprietary high-precision manufacturing approach allows us to replace standard allograft with precisely defined “donor derived” cell therapies that are designed to improve safety and efficacy



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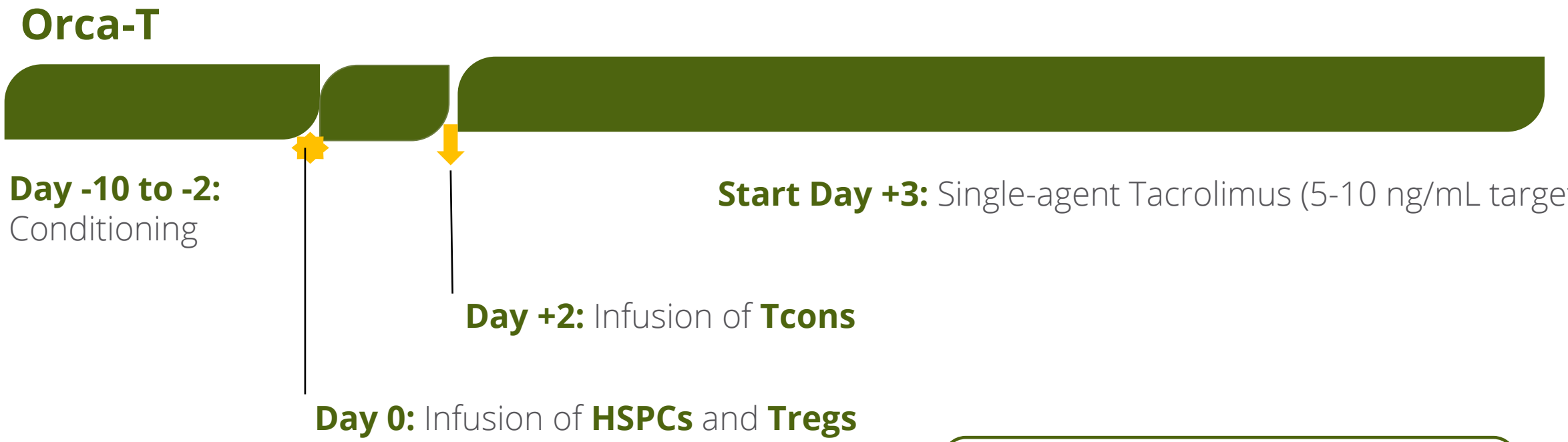
Orca-T product overview (continued)

Orca's precision-engineered allogeneic stem cell and T-cell immunotherapy biologic is being regulated under Section 351 of the Public Health Service Act (42 U.S.C. § 262)



Vein to Vein time < 72h

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

Precision-T: Orca-T's pivotal Phase 3 study is underway

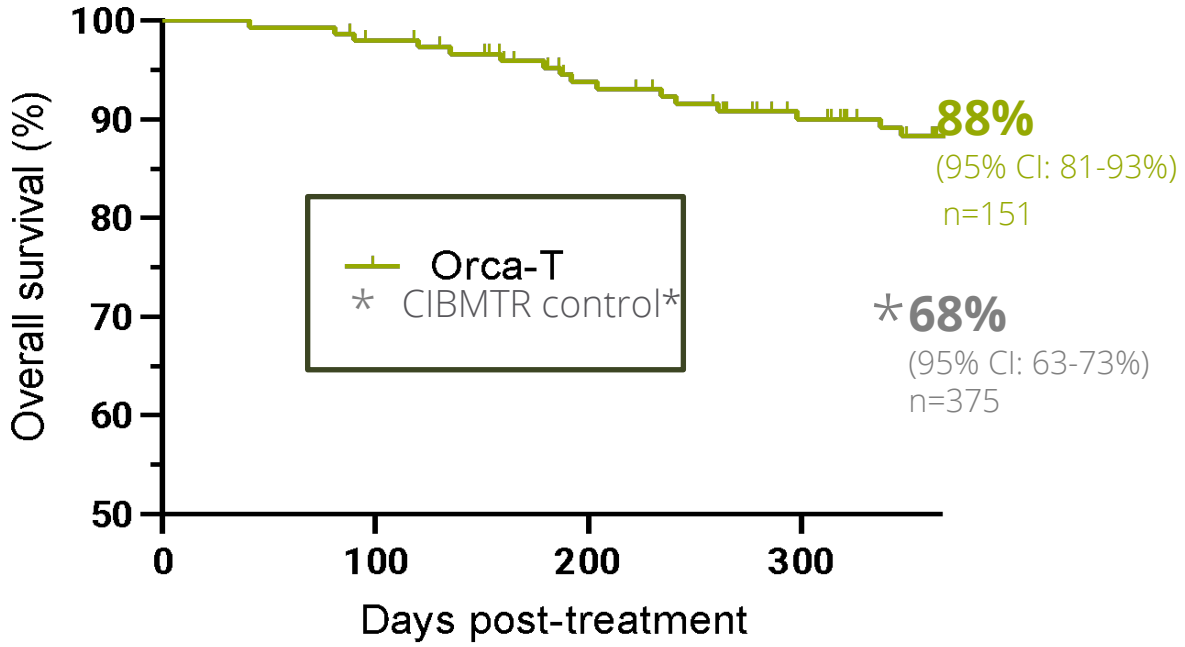
Type of Trial	• Randomized, multicenter study, blinded to Orca Bio • Trial completed when 56 events have occurred, where an event is defined as moderate-to-severe chronic GvHD or death
Primary Endpoint	• Rate of survival free of moderate-to-severe chronic GvHD ("cGFS")
Secondary Endpoint	• Relapse-free survival ("RFS")
Trial Size	• 174 patients in total; 87 patients per arm
Duration	• Duration is not fixed and is based on reaching a pre-specified number of events • Biostats estimate for statistically significant data is between Q1 and Q3 of 2024 depending on rate of enrollment and events
Design	• Patients with AML, ALL, or MDS in CR/CRi • **Randomized 1:1 -- Orca-T/tacrolimus vs SOC allograft plus Tac/MTX** • Myeloablative conditioning with Bu/Flu/Thiotepa, TBI/Cy, or TBI/etoposide

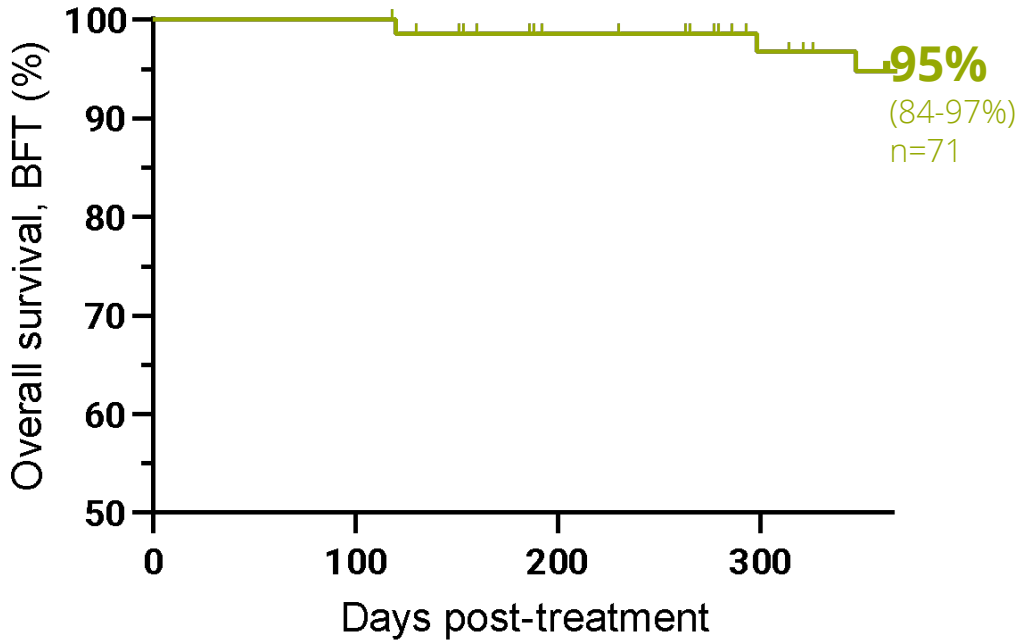
This table is a summary of the trial design as agreed with the FDA

Orca-T may lead to overall improved survival without compromising QOL

Includes the total pooled patients from our Phase 1b/2 studies.[1]

Subset of patients who were given the preferred conditioning regimen being used in our Phase 3 study.





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[1] 64th American Society of Hematology (ASH) Annual Meeting, oral presentation
BFT- busulfan/fludarabine/thiotepa
*NON-randomized contextual control

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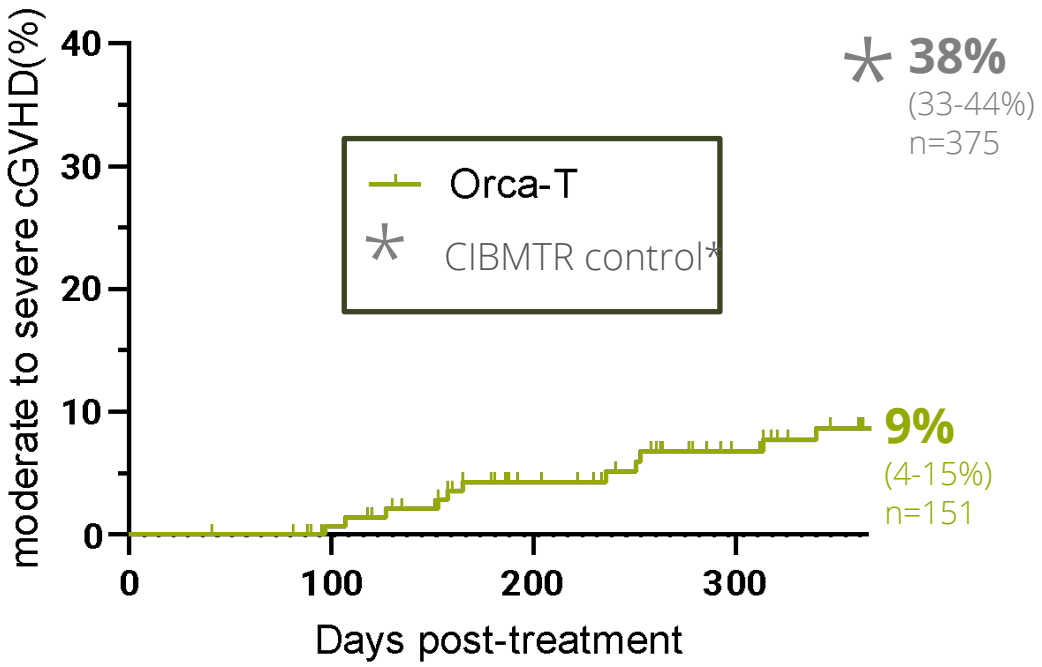
Chronic GvHD at 1 year was substantially reduced with Orca-T

Includes the total pooled patients from Orca Bio's Phase 1b/2 studies.



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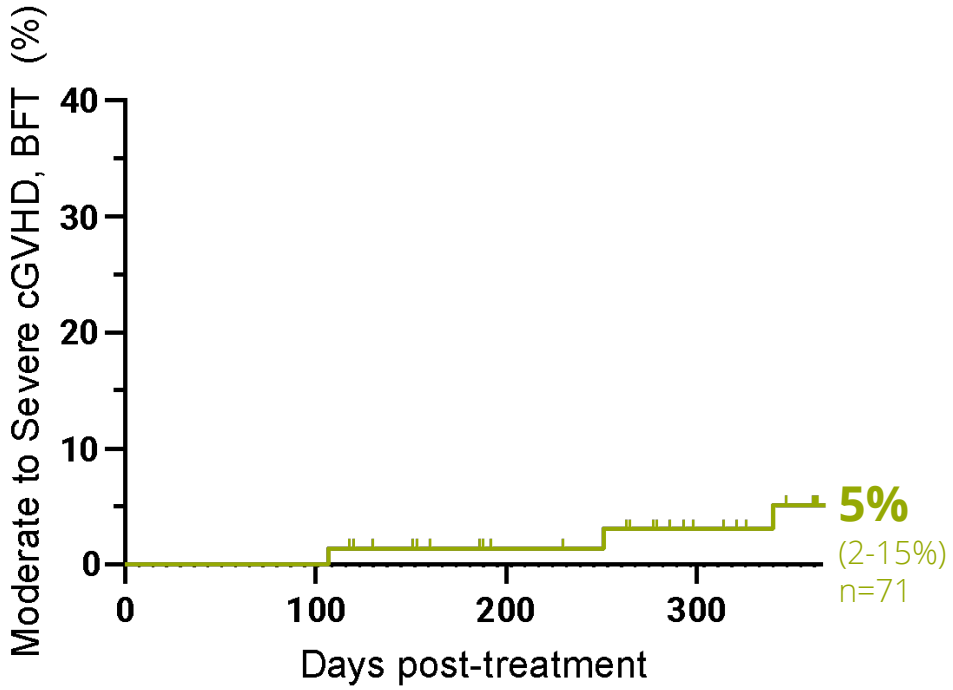

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[2] NON-randomized contextual control

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Summary of experience with Orca-T to date

GRFS[1]

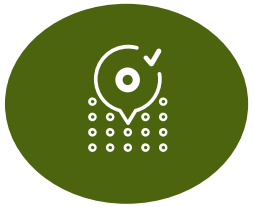
With Orca-T, 1-yr GRFS more than doubled with Orca-T compared to SOC.

NRM[2]

Orca-T was well-tolerated with reduced non-relapse mortality.

GvHD

Orca-T significantly reduced acute and chronic GvHD compared to SOC despite reduction of immunosuppressive meds.



Reduced the rate of relapse and the number of rehospitalizations compared to SOC.

These outcomes and others will be tracked in the randomized Phase 3 trial.

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1 GRFS- GvHD Free Relapse Free Survival
2 NRM- Non-Relapse Mortality

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Dosage and documentation

- A one-time allogeneic stem cell and T-cell immunotherapy biologic drug infusion and comprises 3 separate single-dose infusion.
  - Each infusion bag will contain a controlled dose of cellular drug product with final specifications pending FDA approval.
  - Comprised of 3 defined cellular drug products: controlled for purity, dose, viability & safety
    - CD34+
    - Tregs
    - Tcons

- Documentation of administration within the medical record would most commonly be found in the Medication Administration Record (MAR), physician orders and progress notes as a Cellular therapy, T-cell immunotherapy and/or a novel cell therapy

Safety

- **Based on current clinical experience with Orca-T, no hypersensitivity reactions or cytokine release syndrome has been observed.**
- Allergic reactions may occur with the infusion of Orca-T. The manufacturing of Orca-T cellular therapy product involves iron dextran, dimethyl sulfoxide, hetastarch and human serum albumin, some of which have been associated with hypersensitivity reactions, including anaphylaxis and/or death.
- Patients with a history of allergic reactions to dimethyl sulfoxide, hetastarch and human serum albumin should be monitored for allergic reactions following Orca-T administration.
- Infusion reactions may begin within minutes of the start of infusion of Orca-T, although symptoms may continue to intensify and not peak for several hours after the completion of the infusion. When a reaction occurs, pause the infusion and institute supportive care as needed. Premedication with antipyretics, histamine antagonists, and corticosteroids may reduce the incidence and intensity of infusion reactions.

Preparation and administration

- Orca-T is a one-time biologic drug infusion comprised of 3 separate single-dose infusion bags for allogeneic use only. Do not use a leukodepleting filter. Orca-T infusions should be performed at room temperature. Blood warmers should NOT be used.
- Orca-T should be administered by a health care professional. Central venous access is recommended for the infusion of Orca-T. Prime the tubing with normal saline prior to infusion.
- Confirm the patient's identity matches the patient identifiers on each of the Orca-T cell therapy infusion bags.
- Infuse the entire contents of Orca-T CD34+ infusion bag, followed by the Treg infusion bag on Day 0 beginning by either gravity or a peristaltic pump at a rate of up to 5 mL/min.
- Infuse the entire contents of the Orca Treg infusion bag on Day 0 as soon as the CD34+ infusion bag has been infused (no waiting time is required between infusions).
- Infuse the entire contents of the Orca-T Tcon infusion bag on Day +2 (48-72 hours) after the start of the CD34+ infusion. Infusion of the Orca-T Tcon infusion bag may be delayed up to Day +5.
- Begin infusion of Orca-T CD34+ and Treg infusion bags before the expiration time printed on the product label.
- Orca-T Tcon infusion bag is thawed and diluted at the clinical site. Gently agitate the infusion bag to prevent cell clumping. Begin infusion of Tcon infusion bag within 1 hour after thaw.
- Following infusion of Orca-T CD34+, Treg and Tcon infusion bags, patients should be monitored per institutional guidelines for patients who have received an allograft with vital signs recorded as described.