Orca-Q Demonstrates Favorable GvHD-and-Relapse-Free Survival in Haploidentical Transplants without Post-Transplant Cyclophosphamide

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Background

- Allogeneic stem cell transplantation (allo SCT) is curative for several high-risk hematologic malignancies.

- Post-transplant cyclophosphamide (PTCy) has enabled larger number of patients to receive allo SCT using alternative Haploidentical donors.

- However, GvHD-and-relapse-free survival rates (GRFS) in this population remain low.

Myeloablative regimen

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day-28 neutrophil recovery</td>
<td>94 (92-95)</td>
</tr>
<tr>
<td>Day-100 platelet recovery</td>
<td>87 (85-89)</td>
</tr>
<tr>
<td>1-y graft failure</td>
<td>4 (3-6)</td>
</tr>
<tr>
<td>Day-100 grades 2 to 4 acute GvHD</td>
<td>33 (30-37)</td>
</tr>
<tr>
<td>Day-100 grades 3 and 4 acute GvHD</td>
<td>10 (8-12)</td>
</tr>
<tr>
<td>1-y chronic GvHD</td>
<td>33 (30-36)</td>
</tr>
</tbody>
</table>
Can We Improve Haplo SCT Outcomes by Optimizing Allograft?

Conventional Transplants
Uncontrolled mix of over 50 cell types

Orca-Q Precision-Engineered Cell Therapy
Fully Defined Stem and Immune Cells

**Cell Type** | **Intended Use**
--- | ---
High purity HSPCs | Reconstitute blood system
 | Long term reconstitution of immune system
High purity Tregs | GvHD control
High purity iNKT cells | Enhance Treg function
High purity CD4+/CD8+ Tcell subsets | Graft vs. infection
 | Graft vs. leukemia

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

Mix of specific donor cells
Study Hypothesis and Objectives

<table>
<thead>
<tr>
<th>Haplo SCT</th>
<th>RIC</th>
<th>MAC</th>
<th>MA Orca-Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>GVHD Control</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Disease Control</td>
<td>+</td>
<td>++(+)</td>
<td>++(+)</td>
</tr>
<tr>
<td>Rapid Engraftment</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Infection Control</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Pharmacological</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>PTCy + Tacrolimus + MMF</td>
<td>PTCy + Tacrolimus + MMF</td>
<td>(Tacrolimus)</td>
</tr>
</tbody>
</table>

Orca-Q is an investigational, precision-engineered cell therapy comprises of stem cells and propriety mix of immune cells that is hypothesized to reduce GvHD, relapse, and serious infections.

This study explores the role of Orca-Q in patients receiving haplo SCT using MAC and with single agent Tacrolimus GvHD prophylaxis.

GvHD, graft-versus-host disease; PTCy, post-transplant cyclophosphamide.
Study Design and Key Eligibility for Orca-Q

- Phase 1, multi-center, dose expansion (NCT03802695)
- Haplo SCT with negative DSA
  - Haploidentical (≥ 4/8 but < 7/8 matched related donor at HLA-A, -B, -C, and -DRB1)

- Adult patients (18 to 65 years) with high-risk hematologic malignancies
  - Acute leukemia (AML, ALL)
  - Myelodysplastic syndrome (very high- or high-risk)
  - Myelofibrosis

- Eligible for MAC
  - HCT-CI ≤ 4
  - KPS ≥ 70
  - Adequate organ function

Orca-Q Treatment Schedule Using MAC and Single Agent GvHD Prophylaxis with Tacrolimus

**SOC**

**MA Conditioning**
Day-10 to Day-2: MA Conditioning

**Orca-Q**
Myeloablative conditioning
Day-10 to Day-2: MA Conditioning

**Post-Transplant**

Day 0: Infusion of BM or Apheresis Product

- Days +3, +4: Cyclophosphamide
- Day +5: Tacrolimus/MMF

Day 0: Fresh Orca-Q Infusion

- Derived from G-CSF mobilized peripheral blood apheresis
- Manufactured centrally at cGMP Manufacturing Facility in Sacramento, CA
- No manufacturing/distribution failures > Fresh > Vein-to-vein times of <72 hours across the continental USA

Day -1:
Single-agent Tacrolimus

Day +60:
Taper Tacrolimus

GvHD, graft-versus-host disease; HLA, human leukocyte antigen; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n = 26</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age (range), years</strong></td>
<td>43 (21-63)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (69%)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (31%)</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>10 (39%)</td>
</tr>
<tr>
<td>White</td>
<td>7 (27%)</td>
</tr>
<tr>
<td>African American</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Asian</td>
<td>5 (19%)</td>
</tr>
<tr>
<td><strong>Disease subtype</strong></td>
<td></td>
</tr>
<tr>
<td>AML</td>
<td>15 (58%)</td>
</tr>
<tr>
<td>ALL</td>
<td>9 (34%)</td>
</tr>
<tr>
<td>CML (blast phase)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td><strong>Disease risk index</strong></td>
<td></td>
</tr>
<tr>
<td>High/Very-high</td>
<td>6 (23%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>17 (65%)</td>
</tr>
<tr>
<td>Low</td>
<td>3 (12%)</td>
</tr>
<tr>
<td><strong>Donor median age (range), years</strong></td>
<td>36 (18-58)</td>
</tr>
<tr>
<td><strong>Donor gender</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
</tr>
<tr>
<td><strong>Donor CMV status</strong></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>17</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
</tr>
<tr>
<td><strong>Myeloablative regimen</strong></td>
<td></td>
</tr>
<tr>
<td>TBI-based</td>
<td>16 (62%)</td>
</tr>
<tr>
<td>BFT</td>
<td>10 (38%)</td>
</tr>
</tbody>
</table>

26 patients enrolled between January 2019 – July 2022
Rapid Engraftment Observed in Orca-Q Patients

- None of the patients had primary graft failure
- Median time to neutrophil and platelet engraftments were 12 and 16 days, respectively
- Two patients experienced secondary graft failure
- No Grade > 1 CRS was observed; Two patients had Grade 1 CRS
Severe Infections were Uncommon in Orca-Q Recipients

- CMV viremia was reported in 4 patients (15%); no CMV-related end-organ damage noted
- EBV viremia reported in 1 patient; no PTLD observed
- 2 patients died of infectious causes
  - COVID-19 pneumonia (n=1)
  - Pulmonary aspergillosis (n=1)

CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; CTCAE, common terminology criteria for adverse events; EBV, Epstein-Barr Virus; PLTD, post-transplantation lymphoproliferative disorder.
Low Incidence of Acute Graft-vs-Host Disease

- Despite using only single-agent tacrolimus as GvHD prophylaxis in the haploidentical transplant setting, aGvHD was rare.
No Moderate-to-Severe cGvHD has Occurred

- Median follow-up 211 (32-1125) days
- Nine patients > 1 year
- Of the 16 patients with > 3 months follow-up, only 1 developed mild cGvHD
- No Orca-Q patients have developed moderate-to-severe cGvHD
- This compares favorably to the 24% - 33% rate of chronic GvHD post haplo-HCT in various historical cohorts

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Encouraging GvHD-and-Relapse Free and Overall Survival

GRFS was 75% at 1-year with Orca-Q, which compares favorably to a GRFS of 46% previously reported in the context of MAC haplo alloHSCT with PTCy. 

Conclusions

- Our findings demonstrate very encouraging outcomes with Orca-Q in the Haplo SCT setting using myeloablative conditioning and only single agent tacrolimus
  - Low rates of overall and severe aGvHD and cGvHD
  - Low adverse event profile
  - Improved GRFS

- The phase 1 study continues to enroll patients across the U.S.
Acknowledgements

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MD Anderson Cancer Center

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