Improved Clinical Outcomes with Omidubicel versus Standard Myeloablative Umbilical Cord Blood Transplantation: Results of a Phase III Randomized, Multicenter Study

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Gamida Cell
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Disclosures

• Gamida Cell- institutional research funding
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• Kadmon- advisory board participation
• CareDx- advisory board participation
Umbilical Cord Blood Stem Cell Grafts

• Advantages
  • Readily available stem cells source
  • Tolerance across HLA barriers
  • Nearly 30 year of experience
  • Less chronic GvHD vs. Matched Unrelated donor
    • Eapen M et al Lancet 2010
  • Potent anti-tumor activity
    • Milano F et al NEJM 2016

• Disadvantages
  • Low stem cell dose
    • Delayed hematopoietic recovery
    • Delayed immunologic recovery
  • Increased transplant-related morbidity and mortality
  • Increased resource utilization

Potential Solution

Ex-vivo Expansion Cord Blood Stem Cells
Nicotinamide Alters Metabolic Pathways Mimicking Bone Marrow Endosteum

Importance of Nicotinamide

- Plays a key role in metabolic reprogramming of cells
- Is a master regulator of NAD-related signaling pathways
- Directly involved in control of redox-sensitive enzymes
- Preserves cellular functionality and phenotype during expansion
Phase 3 Registration Study of Omidubicel

Primary Endpoint
Time to neutrophil engraftment

Secondary Endpoints
Platelet engraftment
Infections
Hospitalization

• Cord blood units selected prior to randomization
• Randomization stratified by:
  – Treatment center
  – Disease risk index
  – Age
  – Intent to perform single vs double cord transplant in the control arm
• Minimization algorithm was used to balance prognostic factors in the treatment groups.

• Age 12-65
• High-risk hematologic malignancies
• Eligible for allogeneic bone marrow transplantation
• No matched donor

Enrollment Completed: 12/2019
Day 180 Follow Up Completed: 9/2020
ITT: Intent to Treat; AT: As Treated population: received transplantation with omidubicel or standard cord per protocol.

Patient Disposition

Randomized (n=125)

- Randomized to Omidubicel (n=62)
- Randomized to Standard Cord (n=63)

ITT (N=125)
- Transplanted with Omidubicel (n=52)
- Transplanted with Standard Cord (n=56)

AT (N=108)
## Demographics | Intent-to-Treat (ITT) Population

<table>
<thead>
<tr>
<th></th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>30 (48%)</td>
<td>23 (37%)</td>
</tr>
<tr>
<td>Male</td>
<td>32 (52%)</td>
<td>40 (63%)</td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>40 (13-62)</td>
<td>43 (13-65)</td>
</tr>
<tr>
<td>12-17</td>
<td>8 (13%)</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>18-39</td>
<td>23 (37%)</td>
<td>23 (36%)</td>
</tr>
<tr>
<td>40-59</td>
<td>27 (44%)</td>
<td>31 (49%)</td>
</tr>
<tr>
<td>60-65</td>
<td>4 (7%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>78.6 (43-134)</td>
<td>77.4 (46-133)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>35 (57%)</td>
<td>37 (59%)</td>
</tr>
<tr>
<td>Black</td>
<td>11 (18%)</td>
<td>9 (14%)</td>
</tr>
<tr>
<td>Asian</td>
<td>7 (11%)</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>9 (15%)</td>
<td>7 (11%)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latino</td>
<td>10 (16%)</td>
<td>6 (10%)</td>
</tr>
</tbody>
</table>
## Patient and Transplant Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML</td>
<td>27 (44%)</td>
<td>33 (52%)</td>
</tr>
<tr>
<td>ALL</td>
<td>20 (32%)</td>
<td>21 (33%)</td>
</tr>
<tr>
<td>MDS</td>
<td>6 (10%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>CML</td>
<td>4 (7%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>3 (5%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Rare Leukemia</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td><strong>Myeloablative Conditioning Regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBI 1350cGy, Fludarabine, Thiotepa</td>
<td>7(11%)</td>
<td>9(14%)</td>
</tr>
<tr>
<td>TBI 1320cGy, Fludarabine, Cyclophosphamide</td>
<td>24(39%)</td>
<td>21(33%)</td>
</tr>
<tr>
<td>Thiotepa, Busulfan, Fludarabine</td>
<td>27(44%)</td>
<td>28(44%)</td>
</tr>
<tr>
<td>Transplanted off-study</td>
<td>4(6%)</td>
<td>5(8%)</td>
</tr>
<tr>
<td><strong>HLA match (CBU #1)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/6</td>
<td>46 (74%)</td>
<td>46 (73%)</td>
</tr>
<tr>
<td>5/6</td>
<td>15 (24%)</td>
<td>16 (25%)</td>
</tr>
<tr>
<td>6/6</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>Intended CBU transplant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>20 (32%)</td>
<td>21 (33%)</td>
</tr>
<tr>
<td>Double</td>
<td>42 (68%)</td>
<td>42 (67%)</td>
</tr>
</tbody>
</table>
Primary Endpoint
Time to Neutrophil Engraftment (ITT)

<table>
<thead>
<tr>
<th>Intent-to-treat</th>
<th>Median Time to Neutrophil Engraftment (Days)*</th>
<th>95% CI</th>
<th>p&lt;0.001**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omidubicel (N = 62)</td>
<td>12.0</td>
<td>(10.0, 15.0)</td>
<td></td>
</tr>
<tr>
<td>Control (N = 63)</td>
<td>22.0</td>
<td>(19.0, 25.0)</td>
<td></td>
</tr>
</tbody>
</table>

*Patients not transplanted or who do not engraft on/before Day 42 post transplant were assigned to Day 43
**Mann-Whitney test
Day 42 Neutrophil Engraftment  
(As-Treated Population N=108)

Median Time to Neutrophil Engraftment  
(Days)  

<table>
<thead>
<tr>
<th>Treatment Received</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omidubicel (N=52)</td>
<td>10.0 (95% CI: 8, 13)</td>
</tr>
<tr>
<td>Control (N=56)</td>
<td>20.5 (95% CI: 18, 24)</td>
</tr>
</tbody>
</table>
## Secondary Endpoint: Platelet Engraftment by Day 42 (ITT Population)

<table>
<thead>
<tr>
<th>Intent-to-treat</th>
<th>Day 42 Cumulative Incidence</th>
<th>Difference in Cumulative Incidence</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omidubicel (N = 62)</td>
<td>0.55</td>
<td>0.20</td>
<td>(0.03, 0.35)</td>
<td>0.028</td>
</tr>
<tr>
<td>Control (N = 63)</td>
<td>0.35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Day 100 Platelet Engraftment
As-treated population

Cumulative Incidence of Platelet Engraftment

Treatment Received
- Omidubicel (N=52)
- Control (N=56)

Median Time to Platelet Engraftment (Days)  P value
- Omidubicel: 37 (95% CI: 33, 42)  p<0.023
- Control: 50 (95% CI: 42, 58)

Days post Transplant

N at risk
- NiCord: 52  52  52  36  22  12  7  5  3  3  2
- UCB: 56  56  56  51  35  23  11  7  7  6  4

83%  73%
Secondary Endpoint: Grade 2-3 Bacterial or Invasive Fungal Infection by 100 Days (ITT Population)

P=0.027

Omidubicel (N=62)
Control (N=63)

57%
37%
Fewer Viral Infections in Recipients of Omidubicel

Incidence of First Grade 3 Viral Infection

- Omidubicel (N=62)
- Control (N=63)

Days Post-Transplant

26% for Omidubicel
10% for Control

No. of Infections

- HUMAN HERPESVIRUS 6
- CYTOMEGALOVIRUS
- BK POLYOMAVIRUS
- HUMAN PARAINFLUENZA VIRUS
- RHINOVIRUS
- ADENOVIRIDAE
- HUMAN RESPIRATORY SYNCYTIAL VIRUS
Secondary Endpoint: Days Alive and Out of the Hospital in the First 100 Days Post-Transplant (ITT Population)

Omidubicel: Median 60.5 days
Control: Median 48.0 days
p = 0.005
Acute GvHD

Grade II-IV Acute GVHD Day 100

- Omidubicel (N=59)
- Control (N=58)

P=0.18

Grade III-IV Acute GVHD Day 100

- Omidubicel (N=59)
- Control (N=58)

P=0.33
Chronic GvHD

All Grades Chronic GVHD 1 Year

Omidubicel (N=59)

Control (N=58)

P=0.57
Non-relapse Mortality and Relapse Incidence (ITT Population)

Non-relapse Mortality

<table>
<thead>
<tr>
<th>Days post-Randomization</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

Relapse

<table>
<thead>
<tr>
<th>Days post-Randomization</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

p = 0.09

p = 0.32
Disease-free and Overall Survival (ITT population)

**Disease-free Survival**

- Probability of Disease-free Survival
  - Days post-Randomization:
    - Omidubicel (N=62)
    - Control (N=63)
  - 
P=0.68

**Overall Survival**

- Probability of Survival
  - Days post-Randomization:
    - Omidubicel (N=62)
    - Control (N=63)
  - 
P=0.16

- Disease-free Survival: 73%
- Overall Survival: 62%
Summary and Conclusion

• Myeloablative transplantation with omidubicel results in
  • Faster hematopoietic recovery
  • Fewer early infections
  • Fewer days in the hospital
• No excessive toxicity associated with omidubicel compared to standard umbilical cord blood transplantation
  • Durable engraftment >10yrs (earlier studies)
• Omidubicel should be considered a new standard of care for patients eligible for umbilical cord blood transplantation
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