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

Disclosures

• **Consulting or advisory role**: AbbVie, Amgen, Boehringer-Ingelheim, Celgene/BMS, Helsinn Healthcare, Janssen, Novartis, Roche, Takeda.

• **Speakers’ Bureau**: Takeda.

• **Honoraria**: Celgene/BMS

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• **Travel, accommodations, expenses**: Celgene/BMS, Gilead, Roche, Takeda.
Umbilical cord blood stem cell grafts

Advantages
- Readily available stem cells source
- Tolerance across HLA barriers
- Less chronic GvHD vs. Matched Unrelated donor
- Potent anti-tumor activity

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

Potential solution
Ex-vivo expansion of cord blood stem cells
Omidubicel

Cellular product consisting of two cryopreserved fractions derived from a single entire cord blood unit (CBU) and thawed at the transplant center immediately before infusion

• Cells obtained after CD133+ selection *ex vivo* expanded for 21 days in the presence of nicotinamide*

• Non-cultured CD133- cells, including T cells

*Nicotinamide* increases stem and progenitors cells, inhibits differentiation and increases migration, BM homing, and engraftment efficiency while preserving cellular functionality & phenotype
Omidubicel: phase I/II trial (N=36)

Patients: 36 patients with high-risk hematologic malignancies (78% with intermediate/high DRI) undergoing myeloablative conditioning

UCB grafts:
- CD34+ cells infused (median): 6.3 x 10^6/kg

Results
- Very fast hematopoietic engraftment
  - Median time to neutrophil engraftment, days: 11.5*
  - Median time to platelet engraftment, days: 34*
  - Median days alive & out of hospital before day +100: 73*
- Durable long-term hematopoietic engraftment (>10 years)

* P < .001 as compared to 146 similar patients reported to the CIBMTR

Phase 3 trial of omidubicel

Primary Endpoint
Time to neutrophil engraftment

Secondary Endpoints
Time to 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

- Age 12-65
- High-risk hematologic malignancies: AML, ALL, MDS, CML, lymphoma
- Eligible for allogeneic stem cell transplantation
- No matched donor

* Grade 2/3 bacterial or invasive fungal infections by 100 days post transplant
** Days alive and out of the hospital in the first 100 days post transplant
**CBU selection criteria**

- **Randomization**
  - Omidubicel
  - Standard Cord

- **Production**
  - Omidubicel
    - CF + NF

- **Omidubicel**
  - CBU #1

- **Standard Cord**
  - CBU #1

- **CBU #1**
  - 4-6/6 HLA Match
  - TNC count $\geq 1.8 \times 10^9$ cells
  - TNC dose $\geq 1.5 \times 10^7$ cells/kg
  - CD34$^+$ count $\geq 8 \times 10^6$ cells
  - Red cell and plasma reduced
  - At least 1 allele match at DRB1

- **OR**
  - (per EBMT 2006 CBU selection guidelines)*

- **CBU #1 + CBU #2**

* 5 – 6/6 HLA match: TNC dose $< 2.5 \times 10^7$ cells/kg OR CD34$^+$ dose $< 1.2 \times 10^5$ cells/kg

4 – 6/6 HLA match: TNC dose $< 3.5 \times 10^7$ cells/kg OR CD34$^+$ dose $< 1.7 \times 10^5$ cells/kg
Patient disposition

Randomized (n=125)

(33 centers [US, Europe, South America & Asia])

Randomized to Omidubicel (n=62)

Randomized to Standard Cord (n=63)

Transplanted with Omidubicel (n=52)

Transplanted with Standard Cord (n=56)

ITT (N=125)

AT (N=108)

ITT: Intent to treat; AT: As treated population (received transplantation with omidubicel or standard cord per protocol)
### Demographics

<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>Disease</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<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>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease Risk Index</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>15 (24%)</td>
<td>15 (24%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>27 (44%)</td>
<td>25 (40%)</td>
</tr>
<tr>
<td>High/Very High</td>
<td>20 (32%)</td>
<td>23 (37%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Myeloablative Conditioning Regimen</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBI, Fludarabine, Cyclophosphamide or Thiotepa</td>
<td>31 (50%)</td>
<td>30 (47%)</td>
</tr>
<tr>
<td>Thiotepa, Busulfan, Fludarabine</td>
<td>27 (44%)</td>
<td>28 (44%)</td>
</tr>
</tbody>
</table>
## Graft characteristics: HLA match & intended number of CBUs to be transplanted

<table>
<thead>
<tr>
<th>HLA match (CBU #1)</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<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>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HLA match (CBU #2)</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/6</td>
<td>31 (74%)</td>
<td></td>
</tr>
<tr>
<td>5/6</td>
<td></td>
<td>10 (24%)</td>
</tr>
<tr>
<td>6/6</td>
<td></td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intended CBU transplant</th>
<th>Omidubicel (N=62)</th>
<th>Control (N=63)</th>
</tr>
</thead>
<tbody>
<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>
Graft characteristics: cell dose

Median CD34+ cell expansion:
130-fold (range 32-233)
Primary endpoint
Time to neutrophil engraftment (ITT population)

<table>
<thead>
<tr>
<th>Intent-to-treat</th>
<th>Median Time to Neutrophil Engraftment (Days)*</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omidubicel (N = 62)</td>
<td>12.0</td>
<td>(10.0 – 15.0)</td>
<td>&lt;0.001**</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 did not engraft by Day 42 post transplant were assigned Day 43
**Mann-Whitney test
Neutrophil engraftment (treated population, N = 108)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median Time to Neutrophil Engraftment (Days)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omidubicel:</td>
<td>10.0 (95% CI: 8, 13)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Control:</td>
<td>20.5 (95% CI: 18, 24)</td>
<td></td>
</tr>
</tbody>
</table>
### Secondary endpoint: Time to platelet engraftment (ITT population)

<table>
<thead>
<tr>
<th>Intent-to-treat</th>
<th>Cumulative Day 42 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>
Platelet engraftment
(treated population, N = 108)

Median Time to Platelet Engraftment
(Days)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median Time (Days)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omidubicel (N=52)</td>
<td>37</td>
<td>(33, 42)</td>
<td>0.023</td>
</tr>
<tr>
<td>Control (N=56)</td>
<td>50</td>
<td>(42, 58)</td>
<td></td>
</tr>
</tbody>
</table>

83% vs 73%
Secondary endpoint: Grade 2-3 bacterial or invasive fungal infection by 100 days (ITT Population)

![Graph showing incidence of first grade 2/3 bacterial or invasive fungal infection over days post-transplant. The graph compares Omidubicel (N=62) and Control (N=63) groups. The P-value is 0.027.]

- Omidubicel (N=62) incidence: 37%
- Control (N=63) incidence: 57%
Viral infections (ITT population)

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

P=0.029

Cumulative Incidence of First Grade 3 Viral Infection

Days Post-Transplant
Secondary endpoint: Days alive and out of the hospital in the first 100 days post-transplant (ITT)

- **Omidubicel**: Median 60.5 days
- **Control**: Median 48.0 days
- \( P = 0.005 \)
Acute GvHD

Grade II-IV Acute GVHD Day 100

- Incidence of Acute Grade II-IV GVHD
  - Omidubicel (N=59)
  - Control (N=58)

  \[ P=0.18 \]

Grade III-IV Acute GVHD Day 100

- Incidence of Acute Grade III-IV GVHD
  - Omidubicel (N=59)
  - Control (N=58)

  \[ P=0.33 \]
Chronic GvHD

All Chronic GVHD at One Year

P=0.57
Non-relapse mortality and relapse (ITT)

Non-Relapse Mortality

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

Cumulative Incidence of Non-Relapse Mortality

Days post Randomization

Relapse

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

Incidence of Relapse

Days post Randomization

p=0.09

p=0.32
Disease-free and overall survival (ITT)

Disease-Free Survival

Overall Survival

HR 0.59 (95% CI = 0.29 – 1.12)

p=0.16

p=0.68
Conclusions

• This global phase III randomized study demonstrated that transplantation with omidubicel compared to standard cord blood transplantation results in
  – Faster hematopoietic recovery
  – Fewer infections
  – Fewer days in hospital

• Omidubicel should be considered as the new standard of care for patients eligible for UCBT
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