Outcomes of Older Patients Undergoing 2-Step Approach to Haploidentical and Matched Related Peripheral Blood Hematopoietic Stem Cell Transplantation (HSCT): A Single Institutional Experience

Sameh Gaballa, MD  
Thomas Jefferson University Hospital

Seyfettin Onder Alpdogan, MD  
Thomas Jefferson University Hospital

Matthew Carabasi, MD  
Thomas Jefferson University Hospital

Joanne Filicko-O'Hara, MD  
Thomas Jefferson University

Margaret Kasner, MD  
Thomas Jefferson University

See next page for additional authors

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Authors
Sameh Gaballa, MD; Seyfettin Onder Alpdogan, MD; Matthew Carabasi, MD; Joanne Filicko-O’Hara, MD; Margaret Kasner, MD; Benjamin E Leiby, PhD; Ubaldo E. Martinez-Outshoorn, MD; Edward C Pequignot, MD; Sarah Rosado; Shannon Rudolph, MS; John L Wagner, MD; Mark Weiss, MD; Neal Flomenberg, MD; and Dolores Grosso, DNP

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Introduction

HSCT is a curative option for many patients (pts) with hematological malignancies. Significant advances in supportive care and conditioning regimens over the past decade have allowed the extension of this therapy to older individuals. Information regarding the outcomes of this older subset of pts undergoing HSCT is limited, especially those undergoing haploidentical (HI) HSCT.

Objectives

I. To describe the outcomes of patients 60 years of age or older undergoing haploidentical and matched related (MR) HSCT using the 2-step approach.

Methods

We did a retrospective chart review of outcomes in pts 60 years of age or older undergoing the 2-step approach1,2,3 or matched related HSCT trials. Details of the 2-step approach are shown in figure 1.

Results

• Multivariate statistics using cox regression analysis identified the following factors affecting:

I. Overall survival:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPS 60-80 vs 90/100</td>
<td>6.2</td>
<td>2.74</td>
<td>14.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age 60 – 78 years</td>
<td>1.12</td>
<td>1.01</td>
<td>1.23</td>
<td>0.033</td>
</tr>
</tbody>
</table>

HCT-CI (0 vs >0) and presence of active disease at the time of transplant had a strong trend with decreased OS on univariate statistics (p = 0.07 and p = 0.08 respectively).

II. Non-Relapse Mortality:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPS 60-80 vs 90/100</td>
<td>7.37</td>
<td>2.48</td>
<td>21.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age 60 – 78 years</td>
<td>1.37</td>
<td>1.11</td>
<td>1.68</td>
<td>0.003</td>
</tr>
<tr>
<td>Conditioning MA vs RIC</td>
<td>6.6</td>
<td>1.15</td>
<td>37.87</td>
<td>0.034</td>
</tr>
<tr>
<td>CD34 Dose (x 10^5/kg)</td>
<td>1.4 – 10.6</td>
<td>0.67</td>
<td>0.46</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Recipient gender M vs F 4.82 1.3 17.87 0.019

- After a median follow-up of 8 months (range 1-74), 54% of pts were alive.
- Relapse related mortality was 18% while non-relapse related mortality was 26%.
- No rejections or engraftment failures were observed.
- GVHD was controlled in all cases with steroids and/or photopheresis.

The 2 Step Approach

Figure 1

Step 1

Donor Conditioning* Lymphocytes → 2 Days Rest → CY x 2 → Stem Cells (2x10^7 CD34+/kg)

* Myeloablative (MA) = 12 Gy TBI over 4 days
* Reduced Intensity (RIC) = 4 days of Fludarabine 30mg/m² + Cytarabine 2g/m² or Thiopeta 5mg/kg

Step 2

Tacrolimus + MMF

Donor CD 34

Results

Patient Characteristics:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Myeloablative</th>
<th>Reduced Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>Median Recipient Age (range)</td>
<td>63 (60-68)</td>
<td>68 (60-78)</td>
</tr>
<tr>
<td>Median Donor age (range)</td>
<td>36 (19-70)</td>
<td>44 (24-68)</td>
</tr>
<tr>
<td>Age &gt;/= 65 (%)</td>
<td>8 (28)</td>
<td>26 (77)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>19/9</td>
<td>21/13</td>
</tr>
<tr>
<td>Median CD34 cells (x 10^5/kg)</td>
<td>4.41 (2-10)</td>
<td>4.44 (1.4-10.6)</td>
</tr>
<tr>
<td>CD 3 cell dose (x 10^5/kg)</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Donor Source

Haploidentical (%) 23 (82) 33 (97)

Matched Related (%) 5 (18) 1 (3)

Disease

AML/MDS 23 (82) 20 (59)

ALL 1 (4) 1 (3)

NHL 4 (14) 11 (32)

Other 0 2 (6)

Active disease at time of HSCT (%) 19 (68) 25 (74)

AML/MDS 15 (54) 14 (41)

NHL 4 (14) 9 (26)

Others 0 2 (6)

KPS

60 % 1(4) 0

70-80% 5 (18) 12 (35)

90-100% 22 (79) 22 (65)

HCT-CI

0 3 (11) 6 (18)

1-2 10 (36) 8 (24)

3 15 (54) 19 (56)

Outcomes:

Median ANC recovery (days) 11 11

Median Platelet recovery (days) 16 20

aGVHD III-IV (%) 9 (32) 12 (35)

aGVHD III-IV (%) 0 3 (9)

cGVHD (%) 3 (10) 0

Cause of Death

Relapse 4 (14) 7 (21)

Non-Relapse Mortality (%) 7 (25) 9 (27)

Infection 2 (7) 3 (9)

Toxicity 4 (14) 4 (12)

GVHD 1 (4) 2 (6)

Conclusions

- Factors associated with decreased overall survival in patients above the age of 60 undergoing HSCT using the 2 step approach included older age (>66) and lower KPS (70/80%) in a multivariate analysis.
- Factors associated with higher non-relapse mortality were older age (>66), lower KPS (70/80%), use of myeloablative conditioning, male gender and a lower CD34 dose.
- Haploidentical or matched related HSCT utilizing the 2 step approach are associated with acceptable outcomes in older pts.
- Age and lack of a MR donor should not be barriers to HSCT if patients are fit.
- Patients with lymphoma and controlled myeloid malignancies fared better in this older population.

References