Haploidentical Stem Cell Transplantation with Post-Transplantation Cyclophosphamide for High Risk Acute Pediatric Leukemia. Promising Results Using a Protocol with Peripheral Blood and a Medium Intensity Conditioning.

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Introduction

T cell replete haploidentical stem cell transplantation with post-transplantation cyclophosphamide has shown encouraging results for the treatment of hematologic malignancies, its main advantage is that almost every patient will have a donor in a timely manner. However this technique has been explored mainly in adults and using bone marrow as a cellular source. Here we present our experience using T cell replete haploidentical peripheral blood stem cell transplantation (TCR-Haplo-PBSCT) with post-transplantation cyclophosphamide in 21 pediatric patients with high-risk acute leukemia.

Methods and Patients

The preparative regimen consisted of fludarabine plus busulfan or melphalan and TBI 200-400 cGy (see conditioning). All patients were given cyclophosphamide 50 mg/kg/day on day+3 and +4, followed by ciclosporin and mycophenolate starting on day + 5. In all cases filgrastim was administered after transplant beginning on day + 6. After a signed informed consent, 21 patients who needed an urgent transplant, were allografted; median age was 11 years (range 1-16), the diagnosis were: acute lymphoblastic leukemia 11 patients, acute myeloid leukemia 9, and blastic phase of chronic myeloid leukemia one. 19% were in first remission (CR1), 43% in second (CR2), and 39% in third or with refractory disease(CR3).

Results I

All the donors shared 4 out of 8 alleles with the recipient; in 62% of the cases the donor was the mother in 19% the father and in the other 19% was one sibling. 17 patients were given Flu Bu TBI while 4 received Flu Mel TBI combination

A median of 16 million of PBSC CD34+ cells/kg were infused. The engraftment rate was 100%, median time to achieve 500 neutrophil or more was 15 days (range 14-20), 1 patient out of 21 died without platelet recovery, the remaining had a self- sustained platelet count of 20,000 or more at a median of 14 days (range 10-21). Chimerism at day + 100 was available in 19 cases; all of them had full donor hematopoiesis.

Results II

The median follow-up is 11 months (range 3-28), the cumulative incidence of graft versus host disease (GVHD) acute grade II-IV and chronic moderate to severe was 23.8% and 25% respectively. Six patients have died, the causes were; pneumonia (n:1) and relapse of leukemia(n:5).

Table 1 overall survival (OS) and event free survival (EFS) for the whole group and discriminated according remission

<table>
<thead>
<tr>
<th>Remission</th>
<th>OS 12 months</th>
<th>±</th>
<th>EFS 12 months</th>
<th>±</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR1</td>
<td>77.4%</td>
<td>±10</td>
<td>71.5%</td>
<td>±10.9</td>
</tr>
<tr>
<td>CR2</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>CR3</td>
<td>47.3%</td>
<td>±18.8</td>
<td>43.8%</td>
<td>±18.8</td>
</tr>
</tbody>
</table>

Conditioning

The use of TCR-Haplo-PBSCT with post transplantation cyclophosphamide and a medium intensity conditioning for treating pediatric high risk acute leukemia is promising; it is associated with very good engraftment rate, low transplantation related mortality and an acceptable incidence of GVHD despite the use of peripheral blood. This protocol produces a remarkable leukemia free survival rate, especially in patients in CR1 and CR2. This approach could be a good alternative for children with high-risk leukemia and without suitable matched donors. It deserves further studies.

Conclusion

There are not relevant conflicts of interest to disclose

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