We report the treatment outcome of allogeneic bone marrow transplantation in ten patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Six patients are alive and well for 6 to 30 months (median 19 months) after transplantation. Four patients died with transplant-related complications. In view of the poor prognosis associated with this disease, marrow ablation followed by allogeneic or syngeneic marrow grafting may be the preferred treatment modality if a suitable marrow donor is available.

RESULTS

By the end of the first month following BMT, all patients showed signs of engraftment, documented by appropriate genetic marker analysis. One patient (UPN 323) has become a mixed lymphohematopoietic chimera. Five patients showed no signs of acute GVHD, whereas in two patients GVHD was mild (grade 1) and in three patients it was moderate to severe (grades II through IV).

Six patients are currently alive and in continued CR for 6 to 30 months (median 19 months) after BMT. The performance status of the six surviving patients is 80 to 100 (median 100); one of them (UPN 271) has mild chronic GVHD. Four patients died within the first 4 months following marrow grafting: 2 with GVHD and interstitial pneumonia (IP), 1 with polymicrobial infection, and 1 with a combination of veno-occlusive disease (VOD), bleeding, and fungemia. Details of the ten BMT recipients on this study are shown in Table 1.
Table 1. Bone Marrow Transplantation for Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia

<table>
<thead>
<tr>
<th>UPN</th>
<th>Age/Sex</th>
<th>WBC/µl</th>
<th>Initial Immuno-phenotype</th>
<th>DX → CR (wk)</th>
<th>Status at BMT</th>
<th>Blasts in BM (%)</th>
<th>Preparatory Regimen</th>
<th>Graft Versus Host Disease</th>
<th>Acute GVHD</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>264</td>
<td>23/M</td>
<td>8,900</td>
<td>CALLA</td>
<td>4</td>
<td>3</td>
<td>1.CR &lt; 5</td>
<td>FTBI/CY CsA/PSE</td>
<td>Alive in CCR, day + 892</td>
<td></td>
<td></td>
</tr>
<tr>
<td>271</td>
<td>28/M</td>
<td>1,500</td>
<td>Null</td>
<td>4</td>
<td>5</td>
<td>1.CR &lt; 5</td>
<td>FTBI/CY CsA/PSE</td>
<td>Alive in CCR, day + 836</td>
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<td></td>
</tr>
<tr>
<td>323</td>
<td>28/M</td>
<td>7,400</td>
<td>PRE-B</td>
<td>4</td>
<td>2</td>
<td>1.CR &lt; 5</td>
<td>FTBI/CY CsA/PSE</td>
<td>Alive in CCR, day + 523</td>
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<td></td>
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<tr>
<td>397</td>
<td>29/F</td>
<td>2,900</td>
<td>PRE-B</td>
<td>2</td>
<td>2</td>
<td>1.CR &lt; 5</td>
<td>FTBI/VP16 CsA/PSE</td>
<td>Died with polymicrobial infection</td>
<td>Day + 63</td>
<td></td>
</tr>
<tr>
<td>304</td>
<td>36/M</td>
<td>4,600</td>
<td>CALLA</td>
<td>NA</td>
<td>NA</td>
<td>IF</td>
<td>FTBI/VP16 MTX/PSE</td>
<td>Died with GVHD/IP and sepsis</td>
<td>Day + 121</td>
<td></td>
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<tr>
<td>306</td>
<td>25/M</td>
<td>350,000</td>
<td>PRE-B</td>
<td>4</td>
<td>4</td>
<td>1.RIF</td>
<td>FTBI/VP16 MTX/PSE</td>
<td>Alive in CCR on day + 620</td>
<td></td>
<td></td>
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<tr>
<td>309</td>
<td>23/M</td>
<td>315,000</td>
<td>PRE-B</td>
<td>NA</td>
<td>NA</td>
<td>IF</td>
<td>STBI/VP16 CsA/PSE</td>
<td>Died with GVHD/IP on day + 93</td>
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<tr>
<td>353</td>
<td>42/M</td>
<td>400</td>
<td>CALLA</td>
<td>8</td>
<td>14</td>
<td>1.RIF</td>
<td>BU/CY CsA/PSE</td>
<td>Died with VOD, GI bleeding, and fungemia on day + 36</td>
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<td></td>
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<tr>
<td>355</td>
<td>23/M</td>
<td>8,550</td>
<td>PRE-B</td>
<td>4</td>
<td>3</td>
<td>1.REL</td>
<td>FTBI/VP16 CsA/PSE</td>
<td>Alive in CCR on day + 335</td>
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<tr>
<td>392</td>
<td>45/M</td>
<td>20,000</td>
<td>PRE-B</td>
<td>6</td>
<td>22</td>
<td>1.RIF</td>
<td>FTBI/VP16 CsA/PSE</td>
<td>Alive in CCR on day + 171</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Abbreviations: UPN, unique patient number; DX, diagnosis; NA, not applicable (because patient failed to attain CR); IF, induction failure; RIF, reinduction failure; REL, relapse; STBI, single-dose total body irradiation; VP16, etoposide; CCR, continued CR.

DISCUSSION

Six of 10 patients with Phl-positive ALL were transplanted successfully with marrow from histocompatible siblings, whereas four patients died with BMT-related complications. Three of the four patients who had undergone BMT during first CR are surviving; the other three survivors were in more advanced stages of their disease when preparation for BMT was begun.

There are several caveats regarding our study: The patient group under study is relatively small and the observation time is still limited to 6 to 30 months. Neither can we conclude from our data the preparatory regimen to recommend. This issue must be addressed in future studies.

Nevertheless, our data, which require confirmation by other transplant centers, can be viewed as encouraging. Indeed, considering the poor prognosis for patients with this variant of ALL, BMT performed early during the course of this disease may currently be the treatment of choice if a suitable donor is available.

REFERENCES

Bone marrow transplantation for patients with Philadelphia chromosome-positive acute lymphoblastic leukemia

SJ Forman, MR O'Donnell, AP Nademanee, DS Snyder, PJ Bierman, GM Schmidt, JL Fahey, AS Stein, PM Parker and KG Blume