We assessed the impact of unpurged autologous stem cell transplantation (ASCT) on long-term outcome of 118 patients with acute myeloid leukemia (AML) in first complete remission (CR1). With a median follow-up of 95 months, the 10-year overall survival, disease-free survival and relapse risk are, respectively, 54%, 50% and 46%. De novo AML, the presence of a favorable karyotype and intensification of treatment prior to ASCT are independently associated with clinical outcome by multivariate analysis. Thus, a remarkable proportion of AML patients in CR1 can be cured with high-dose therapy and ASCT.

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References

Stem Cell Transplantation

Autologous stem cell transplantation for acute myeloid leukemia patients in first complete remission: a 10-year follow-up study of 118 patients

The role of autologous stem cell transplantation (ASCT) in the treatment of patients with acute myeloblastic leukemia (AML) in first complete remission (CR1) remains unsettled. Phase II and III trials showed that ASCT provides lower relapse rates than conventional chemotherapy and improves disease-free survival (DFS) in some but not in all studies.1,2 We studied the long-term outcome of 118 AML patients in CR1 treated in a single institution between January 1990 and December 2001 (Table 1). Karyotype was considered as: (i) favorable [t (8;21) or inv(16)]; (ii) intermediate (diploid, insufficient numbers of metaphases, or a single numerical abnormality other than that defined as unfavorable); (iii) unfavorable (ie trisomy 8, abnormalities of chromosome 5 and/or 7, abnormality of chromosome 11, multiple or complex translocation).3 Induction chemotherapy consisted of the standard 3/7 daunorubicine/cytosine arabinoside regimen (Dauno/Ara-C) [Dauno 45-60 mg/m2/day (days 1-3) and Ara-C 100 mg/m2/day by continuous iv infusion (days 1-7)] from January 1990 to December 1992 (N=42); 2) ICE regimen [idarubicin 10 mg/m2/day (days 1,3,5), Ara-C 100 mg/m2/day by continuous iv infusion (days 1-10) and etoposide 100 mg/m2/day (days 1-5)] from January 1995 until the end of the study (N=76). Three different consolidation regimens were adopted, depending on the study period: 1) two courses of standard 3/7 Dauno/Ara-C from January 1990 to December 1992 (N=42); 2) a single NOVIA consolidation cycle [Ara-C 500 mg/m2/twice a day (days 1-6) and mitoxantrone 12 mg/m2/day (days 4-6)] from January 1993 to June 1996 (N=32); 3) double FLAN consolidation therapy [Dauno 30 mg/m2/day iv (days 1-5), Ara-C 2 mg/m2/day (days 1-5) and mitoxantrone 6 mg/m2/day (days 1-3)] from July 1996 to December 2001 (N=44).
Letters to the Editor

Table 2. Multivariate analysis of factors affecting OS, DFS and relapse.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survival (%)</th>
<th></th>
<th>DFS (%)</th>
<th></th>
<th>Relapse (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR 95%CI RR</td>
<td>p</td>
<td>RR 95%CI RR</td>
<td>p</td>
<td>RR 95%CI RR</td>
<td>p</td>
</tr>
<tr>
<td>Karyotype</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable vs. Intermediate</td>
<td>0.2212</td>
<td>0.02</td>
<td>0.4913</td>
<td>0.01</td>
<td>0.5004</td>
<td>0.02</td>
</tr>
<tr>
<td>Intermediate vs. Unfavorable</td>
<td>0.48</td>
<td>0.04</td>
<td>0.3808</td>
<td>0.04</td>
<td>0.3368</td>
<td>0.03</td>
</tr>
<tr>
<td>Secondary AML, No vs Yes</td>
<td>0.47</td>
<td>0.03</td>
<td>0.4363</td>
<td>0.007</td>
<td>0.5227</td>
<td>0.05</td>
</tr>
<tr>
<td>Number of cycles prior to ASCT 3 vs 2</td>
<td>2.4</td>
<td>0.02</td>
<td>2.438</td>
<td>0.02</td>
<td>2.3799</td>
<td>0.02</td>
</tr>
</tbody>
</table>

In univariate analysis, patients with a favorable karyotype had better survival and lower probability of relapse than did patients with an intermediate or unfavorable karyotype. A significant difference was also observed between the outcome of patients with an intermediate karyotype and that of patients with an unfavorable one. Age was identified as a significant prognostic factor for survival, but not for relapse. The diagnosis of secondary leukemia significantly affected OS, DFS and TTR. The attainment of CR after induction and the number of chemotherapy cycles prior to ASCT (3 vs. 2) were strong predictors of both survival and relapse. Time from diagnosis to ASCT also had a significant impact on OS, DFS and TTR with a better outcome for those patients transplanted seven or more months after diagnosis. Initial hyperleukocytosis, stem cell source, number of CD34+ cells infused and number of total nucleated cells infused did not significantly affect long-term outcome. Multivariate analysis identified karyotype, secondary leukemia and the number of cycles prior to ASCT as important independent predictors for OS, DFS and TTR (Table 2).

We report the longest follow-up study for AML patients post-ASCT. Our results show that patients with favorable and intermediate karyotype may benefit from ASCT. In addition, effective in vivo purging by a double-reinforcement strategy was an independent predictor of a superior DFS and OS in both univariate and multivariate analyses. As reported earlier, PBSC transplantation led to faster hematologic recovery and less time in hospital.² ³

However, we did not observe any difference between PBSC and BM grafts in terms of OS, DFS and, interestingly, TRM. Moreover, the relapse rate of patients who received PBSC and BM was similar. Overall, low TRM translated into a 50% of AML patients surviving at 10 years disease-free. In conclusion, our data demonstrate that a significant proportion of AML patients in CR1 can be cured with high-dose therapy and ASCT. This strategy should still be considered as a valuable option for patients in CR1 without a HLA-matched sibling donor.

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