To the Editor:

Nademanee et al have recently published preliminary results of autologous bone marrow transplantation (ABMT) in poor-risk aggressive lymphomas during first complete remission (CR).¹ In this series, 84% of patients were alive and disease-free after a median follow-up of 3 years, suggesting that ABMT may improve the outcome of such patients. These results emphasize the importance to identify patients not likely to be cured with conventional chemotherapy in whom intensive consolidation therapy could be appropriate. There are several prognostic classifications for aggressive lymphomas, including the G.E.L.A. index² used by the referred investigators,¹ and the recently proposed International Prognosis Index.² Main variables considered in these classifications to separate different risk groups of patients are performance status (PS), Ann Arbor stage, bulky disease, extranodal involvement, and serum LDH. However, most studies do not take into consideration that prognostic factors may change once a CR is achieved. Therefore, to select patients in CR candidate to receive further therapy, including ABMT, specific analysis of prognostic factors in CR patients are necessary.⁴

We analyzed prognostic factors for survival by multivariate study in a series of 133 patients (median age, 53 years; range, 17 to 82) with large cell lymphomas, treated with doxorubicin-containing regimens. Variables considered were age; sex; histologic subtype (immunoblastic v no immunoblastic); immunologic phenotype (B or T); PS; presence of B symptoms; number of nodal and extranodal involved sites; Ann Arbor stage; bulky disease; BM involvement; hemoglobin, white blood cell, lymphocyte, and platelet counts; serum albumin and LDH; and treatment used (CHOP v no CHOP). Four different groups were considered: (1) all patients; (2) patients in stages II through IV; (3) patients who achieved CR; (4) patients who achieved CR and were younger than 60 years. Results are summarized in Table I.

As shown, in this analysis only initial serum LDH (incidentally, a variable present in all patients transplanted by Nademanee et al)¹ retained its predictive value in CR patients, even in the group ≤60 years. This study points out the need for a careful selection of patients to be included in experimental treatment approaches.

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REFERENCES


Table 1. Large Cell Lymphoma. Prognostic Factors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients (N = 133)</th>
<th>Stage II-IV (N = 111)</th>
<th>CR Patients (N = 91)</th>
<th>CR Patients ≤60 yrs (N = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ann Arbor stage</td>
<td>&lt;.001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Immunoblastic type</td>
<td>.021</td>
<td>.021</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Performance status</td>
<td>.018</td>
<td>.001</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Bulky disease</td>
<td>.004</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Bone marrow (+)</td>
<td>NS</td>
<td>.009</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>LDH</td>
<td>NS</td>
<td>&lt;.001</td>
<td>.008</td>
<td>.016</td>
</tr>
</tbody>
</table>

Abbreviation: NS, not significant.
We appreciate Dr. Lopez-Guillermo's comments about the poor prognostic features for patients with aggressive large cell lymphoma. We agree that most studies do not consider the fact that prognostic factors may change once a complete remission is achieved. We are very pleased to learn that the initial serum lactic dehydrogenase (LDH) level retains its predictive value even in patients who achieve a complete remission. All patients in our study had elevated LDH levels at the time of diagnosis. Taken together, these studies show that disease-free survival (DFS) can be improved with high-dose therapy and autologous bone marrow transplantation (ABMT) when performed during first complete remission.

We appreciate that Sierra et al. shared the results from the Spanish cooperative group, GEL/TAMO, which support our data that high-dose therapy and ABMT in first complete remission can produce long-term DFS in patients with poor prognostic features at presentation. However, there are two differences between the two studies. First, it is unclear which prognostic models were used in their study to select the patients for transplantation. In our study, an elevated LDH level was one of the criteria for inclusion. Secondly, there is a difference in the incidence of toxic death, occurring 14% in their series versus 0% in our series. We have now expanded our experience to include 40 patients with intermediate/high-grade and low-grade lymphoma who were transplanted in first complete remission and, so far, have not encountered any toxic deaths in this group. The explanation for these differences is unclear. Perhaps supportive care and patient selection might be the reason.

Due to the small sample size of our study, a multivariate analysis of the prognostic factors for DFS after transplantation has not been performed. Although all the patients in our study had elevated LDH at presentation, only three of them had relapsed after transplantation. Further analysis will be performed to identify the risk factors for relapse after transplantation once the sample size is larger.

These reports indicate that poor risk factors can be identified using several prognostic models and the most recent international index. These results showed that there are patients with aggressive large cell lymphoma who had poor prognostic features at presentation whose survival is poor despite attaining complete remission. The results from Sierra et al. and our studies show that high-dose therapy and ABMT can improve their DFS. Careful patient selection based on a well-described international index as well as further randomized studies are necessary to determine the role of high-dose therapy and ABMT during first remission in this selected group of patients.

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Selection of patients with aggressive lymphoma in remission candidates to autologous bone marrow transplantation [letter; comment]

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