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J.G. GRIBBEN

*Bartholomew's Hospital, Barts  
and The London School of  
Medicine, London, UK*

## Transplantation for low-grade lymphoma

The low grade lymphomas remains incurable and notwithstanding the excellent remission rates now achieved with combination chemotherapy with monoclonal antibodies, the vast majority of patients are destined to relapse after primary treatment. The management of relapsed patients is then dependent upon a number of factors, most importantly age, performance status, previous therapy administered, the response and duration of response to such therapy, and time from last therapy. Although prior therapy and response to such therapy are important factors in determining next therapy, it is often difficult to determine their importance from published studies. Furthermore, the goal of therapy, whether palliative or aggressive, must also be weighed into the decision when deciding on the next line of treatment. With many potential treatments available, the sequence of treatments and the timing of procedures such as stem cell transplantation remain controversial and have been the focus of previous and ongoing clinical trials.

In follicular lymphoma, high dose therapy followed by autologous stem cell transplantation (SCT) is associated with very high response rates, but may also not be curative in the majority of cases, as these initial remissions are followed by a seemingly relentless pattern of relapse. In a number of phase II studies, five year progression free and overall survival are in the order of 40–60% and 50–80% respectively.<sup>1–3</sup> with good outcome in patients treated by SCT following sequential high dose therapy.<sup>4</sup> These findings suggest that high dose therapy and autologous stem cell transplant may improve outcome compared to conventional chemotherapies, a finding supported by the findings of the CUP study.<sup>5</sup> There have been concerns about the late toxicities associated with high dose therapy, particularly with the use of total body irradiation containing regimens, with therapy related MDS/AML causing specific concern with rates 5 years post autograft ris-

ing to 12%.<sup>1,6</sup> Several studies have retrospectively compared outcome following allogeneic versus autologous transplantation in patients with indolent lymphoma.<sup>7–9</sup> In these studies patients undergoing allogeneic SCT were more likely to have high risk features prior to transplant compared those undergoing autologous transplantation. As would be expected treatment related mortality following allogeneic SCT was significantly higher compared with autologous SCT however a reduced relapse rate resulted in no significant difference in overall survival despite the poor risk characteristics of the patients undergoing allogeneic transplantation.

Although the median age at presentation of CLL patients is 65 years, 40% are younger than age 60, and 12% are younger than age 50 at presentation. In addition, a number of clinical and biological features can be used to identify high-risk patients before they become refractory to chemotherapy. Younger patients with poor risk CLL are being offered therapies such as SCT to attempt to prolong survival and potentially cure their disease. High-dose therapy and autologous hematopoietic SCT are feasible in the many younger patients with poor-risk CLL, but the utility of this approach remains unproven, since no studies to date have compared the role of standard chemotherapy with SCT in CLL. In a study comparing the outcome of autologous versus allogeneic SCT, there was no difference in survival between these two modalities.<sup>10</sup>

Given the older age group of the majority of patients with low grade lymphoma, it seems most reasonable to consider non-meloablative conditioning regimen transplants for patients in whom allogeneic SCT is being considered. This approach appears capable of harnessing the graft versus lymphoma effect whilst keeping transplant related mortality low. A number of studies have demonstrated the graft versus lymphoma effect following reduced intensity conditioning regimens.<sup>11–14</sup>

A planned study will examine the role of autologous versus reduced intensity conditioning allogeneic SCT, to assess the impact of this treatment on outcome in these patients

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