[Abstract 47]

NOVEL APPROACHES TO TRANSPLANT THERAPY FOR INDOLENT LYMPHOMAS

David G. Maloney, MD PhD, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.

The use of high dose conditioning and autologous hematopoietic stem cell transplantation (HCT) is a recognized standard treatment for patients with chemosensitive relapsed aggressive NHL. More controversial is the use of this approach in patients with follicular NHL. Early application in first remission has been associated with prolonged relapse free survival, however late relapses are common and toxicity of the treatment including the late development of secondary myelodysplasia or leukemia temper this approach. Patients with relapsed disease probably do benefit from this approach compared with standard chemotherapy, although continued risk of relapse has been observed.

The use of high dose conditioning and allogeneic HCT may provide a curative option for patients with low grade NHL, although the approach has been limited to young patients without comorbidities. The high early treatment related mortality (TRM) (10-30% by day 100) and the long-term risk of mortality due to graft-vs-host-disease (GVHD) and infection generally restrict the application of this to relapsed, young patients with matched related donors. However, the graft vs tumor activity provides additional therapy that appears to decrease the risk of relapse. Most long-term follow-up of allogeneic HCT for low grade NHL has been associated with a very low risk of relapse after 2-3 years.

The recent observation that allogeneic HCT can be accomplished following nonmyeloablative conditioning has allowed treatment of older patients or patients with comorbidities. This approach relies on graft-vs-tumor responses to eradicate the underlying malignancy presumably through recognition of minor antigen polymorphisms that differ between patient and donor. Particularly encouraging results have been reported in the treatment of patients with low-grade NHL, which appear very sensitive to graft vs tumor effects. The Seattle group has utilized low dose TBI (200 cGy) +/- fludarabine while the MD Anderson group has used fludarabine with cyclophosphamide for conditioning and use both matched related or matched unrelated donors. Both treatments rely on the generation of graft-vs-tumor responses that are often associated with clinical GVHD. Long-term toxicity (2 year) still includes 20-25% mortality associated with GVHD and infections. Patients with follicular NHL and other low-grade B cell malignancies including those with Waldenström's macroglobulinemia have had a high rate of clinical complete remissions. Longer follow up is required to determine if this approach will ultimately result in cure of the disease, however this approach allows a new treatment option even for older patients (60-70 years) with refractory disease.