High dose chemotherapy with stem cell transplantation for Waldenstrom's Macroglobulinemia (WM)

Nikhil C. Munshi and Bart Barlogie, Dana Farber Cancer Institute and University of Arkansas for Medical Sciences.

Despite effectiveness of standard chemotherapy regimens, complete responses are infrequent in WM and there are no cures. Since WM shares certain biological and clinical features with myeloma, including responsiveness to alkylating agents, evaluation of high-dose therapy with transplant, which is effective in myeloma, is an obvious next step in an effort to achieve high response rates and improve survival. Due to the indolent nature of the disease and older patients (pts) with co-morbidity, such evaluations have been infrequent in the past. We have evaluated the safety and efficacy of high-dose melphalan with peripheral blood stem cell support in 8 patients between ages 45-69 with WM. Adequate numbers of stem cells were collected in 6 patients; however, two patients with more extensive prior fludarabine therapy failed to collect adequate cells and required a second attempt at stem cell collection. Seven pts were treated with melphalan 200 mg/m2, including 2 pts who received tandem transplants and 1 pt who received melphalan 140 mg/m2 with total body irradiation. There was no treatment-related mortality and toxicities were manageable. Recovery of bone marrow after transplant was prompt except in 1 pt with extensive prior use of fludarabine. All the eight pts achieved at least partial response (PR), including one complete response (CR). Five pts are alive and with out relapse (77+ to 6+ months post transplant). Other investigators have reported similar experience suggesting safety and efficacy of high-dose therapy in WM. However, therapy with purine analogues leads to stem cell damage with decreased ability to collect adequate number of stem cells. This suggests that the peripheral blood stem cells should preferably be procured prior to extensive use of purine analogues. A formal large co-operative group trial is underway to evaluate role of melphalan at 200 mg/m^2 in WM.

Based on the existence of graft versus myeloma effect, evaluation of feasibility and safety of allogeneic transplantation is also warranted in WM. Future strategies in WM will include a plan to evaluate the role of high-dose therapy along with biological agents, role of purging using Rituxan, and evaluation of non-myeloablative regimen containing Fludarabine to achieve higher response rates and improve survival.