High-dose Therapy and Stem Cell Transplantation (SCT) in Waldenstrom's Macroglobulinemia (WM)

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The role of high dose therapy and haemopoietic stem cell transplantation (SCT) has not been well established in patients with Waldenstrom's Macroglobulinemia (WM). Several reasons can account for that; the high median presentation age of patients, the high variability in overall survival between different subgroup of patients, and the increasing number of new conventional therapeutic options. Conventional chemotherapeutic regimens have improved response rates and depth of response and achieved prolonged survivals for symptomatic disease. Few studies with limited numbers of patients support the concept of a dose-response effect in WM and confirm that high dose therapy may induce long-term responses even in heavily pre-treated patients.

In this retrospective EBMT analysis**,** we present the long-term outcome of a group of 244 WM patients reported to the EBMT registry between January 1991 and December 2005 and treated with an Autologous SCT (ASCT; n=158) or Allogeneic SCT (n=86). The aims of this study were to analyze outcomes and determine the prognostic factors that have a significant impact on outcome. For patients treated with ASCT the median time from diagnosis to ASCT was 1.7 years (range, 0.3 to 20.3 years), 32% of the patients experienced treatment failure with at least three lines of therapy, and 93% had sensitive disease at the time of ASCT. Conditioning regimen was chemotherapy based for 72% of the patients. Median follow-up for surviving patients was 4.2 years (range, 0.5 to 14.8 years). Non-relapse mortality was 3.8% at 1 year and relapse rate was 52.1% at 5 years. Progression-free (PFS) and overall survival (OS) were of 39.7% and 68.5% at 5 years, and significantly influenced by the number of previous line therapies and chemorefractoriness disease status at ASCT. The achievement of a negative immunofixation after ASCT had a positive impact on PFS after ASCT. Ten patients developed a secondary malignancy (SM), with a cumulative incidence of 8.4% at 5 years. When used as consolidation at first response, ASCT provided a PFS of 51.5% and OS of 77% at 5 years.

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A total of 86 patients received allograft by using either myeloablative (MAC;n= 37) or reduced-intensity conditioning (RIC; n= 49) regimens. The median age was 49 years (range, 23 to 64 years); 47 patients had received three or more previous lines of therapy, and eight patients had experienced failure on a prior ASCT. A total of 59 patients (68.6%) had chemotherapy-sensitive disease at the time of allo-SCT. Median follow-up of the surviving patients was 50 months (7 to 142 months). For the group of patients who underwent Allo-SCT, non-relapse mortality (NRM) at 3 years was 33% for MAC and 23% for RIC. The overall response rate was 75.6%. The relapse rates (RRs) at 3 years were 11% for MAC and 25% for RIC. Fourteen patients received donor lymphocyte infusions (DLIs) for disease relapse. PFS and OS at 5 years were 56% and 62% for MAC and 49% and 64% for RIC, respectively. The occurrence of chronic graft-versus-host disease (cGVHD) was associated with a higher NRM and a lower RR, leading to an improvement in PFS.

Conclusion

ASCT is a feasible procedure in young patients with high risk WM. ASCT should not be offered to patients with chemoresistant disease and to those who received more than 3 therapy lines**.** Allogeneic SCT can induce durable remissions in a selected population of young and heavily pre-treated or relapsed refractory patients with WM. The low RR, the achievement of additional disease responses after DLIs, and the lower RR in patients developing cGVHD suggest the existence of a clinically relevant graft-versus-WM effect. International prospective trial is required to further define the role of high dose therapy for the management of WM.