High dose therapy (HDT) and Heamopoietic Stem Cell Transplantation (HSCT) in advanced Waldenström's Macroglobulinemia patients.

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Conventional therapies for symptomatic Waldenström's Macroglobulinemia (WM) achieve response rates up to 80% but complete response is infrequent and currently the disease is incurable. Due to the indolent nature of this disease and the advanced age of the patients, the use of high dose therapy and stem cell transplantation as a therapeutic option has not been widely tested. In this EBMT retrospective analysis, 106 patients received Allo-SCT. The median age at transplant was 49 years (21 - 65) and the median time from diagnosis to allo-SCT 34 months (5 - 310). Median number of treatment lines prior to allo-SCT was 3 (1 - 10) and 19 patients had previously failed an ASCT. 70% of the patients were transplanted with chemosensitive and 30% with chemorefractory disease. 44 patients had a conventional myeloablative and 62 a reduced intensity conditioning allo-SCT. With a median follow up of 31 months (3 - 169), 59 patients are alive and free of disease. 48 patients developed acute graft versus host disease (aGVHD), 16 developed limited and 11 extensive chronic GVHD. 17 patients relapsed, 35 patients died, 5 from disease progression and 30 from treatment related toxicity. At 3 years, NRM was 33%, and relapse rate 18%. PFS was 48% and OS 63% at 5 years. Chemosensitive disease ($p<0.03$) and TBI conditioning ($p<0.02$) were significantly associated with a lower RR.

For the Autologous SCT group of patients the median age at transplantation was 53 years (22-73) and median time from diagnosis to transplant was 20 months (3 - 239). 86% had chemosensitive and 14% chemorefractory disease at transplant. With a median follow-up of 32 months (5 - 163), 49% are alive and free of disease, 18% of the patients relapsed and 33% died. Overall survival (OS) was 61%, relapse rate (RR) 55% and progression free survival (PFS) 39% at 5 years. Chemosensitive disease at ASCT and ≥3 line therapies prior to the ASCT were the most important prognostic factors for NRM ($p<0.001$), RR ($p<0.01$), PFS ($p<0.001$) and OS ($p<0.001$). When compared the long term outcome in patients that underwent an ASCT or Allo-SCT as first transplant, patients treated with an Allo-SCT had poorer prognostic features before transplant than those treated with ASCT. Allo-SCT was associated with significantly higher NRM but lower relapse rate while ASCT had acceptable toxicity but higher relapse rate. In summary, both transplant procedures are feasible in patients with WM and should be considered as therapeutic options in selected patients. The role of these two procedures requires evaluation in prospective clinical trials.