[haematologica reports]
2006;2(7):72

High-dose therapy. Experience of the non-Hodgkin's lymphoma Co-operative Study Group (NHLCSG)

G. SANTINI
FOR THE NHLCSG

Department of Haematology, San Martino Hospital, Genoa, Italy

In aggressive, advanced stage non-Hodgkin's lymphoma (NHL), 2nd and 3rd generation regimens gave results similar to those observed with CHOP therapy with a CR of approximately 50%, a 3-year survival probability of approximately 50% and a PFS of 35-40%.

In order to improve outcome of these patients we started the 1st our study on the use of high-dose therapy as front-line therapy. The aim of this multi-center randomised study was to compare conventional therapy with conventional plus high-dose therapy (HDT) and autologous bone marrow transplantation (ABMT) for advanced-stage, intermediate- and high-grade NHL. Between October 1991 and June 1995, one hundred and twenty-four patients, age 15-60 years, with diffuse intermediate to high-grade NHL (Working Formulation groups F, G, H and K), stages II bulky (≥10 cm), III or IV were enrolled. Sixty-one patients were randomised to VACOP-B for 12 weeks and DHAP as salvage regimen (Arm A), and 63 patients to VACOP-B for 12 weeks plus HDT and ABMT (Arm B). There was no significant difference in terms of complete remissions (CR) in the two groups of patients: 75% for Arm A and 73% for Arm B. With a median follow-up observation time of 42 months there was no difference in overall survival (65% and 65%), disease-free survival (DFS) (60% and 80% for Arm A and B, respectively) and progression-free survival (PFS) (48% and 60% for Arm A and B, respectively). A statistical improvement in terms of DFS (p=0.008) and a favourable trend in terms of PFS (p=0.08) for intermediate/high- plus high-risk group patients receiving HDT and ABMT was observed. In this study, conventional chemotherapy followed by HDT and ABMT as front-line therapy seemed to be no more successful than conventional treatment in terms of overall results (*JCO 16: 2796, 1998*).

In 1997, the Milan Group suggested a statistical improvement in the outcome of pts treated with High-Dose Sequential Therapy (HDS) in comparison with those pts treated with conventional chemotherapy (CT). Only B-cell type, G and H/WF, and BM negative pts were included. CR rate was 96% vs 70%, overall survival 81% vs 55%, and PFS 84% vs 49% in the two arms respectively.

We therefore started a 2nd study in which 223 pts with aggressive, advanced stage NHL were randomised to receive VACOP-B for 12 weeks (plus HDS/HDT in case of persistent disease) (Arm A), or VACOP-B for 8 weeks plus upfront HDS/HDT (Arm B). According to the intention-to-treat analysis, the CR rate was 75% for Arm A and 72.6% for Arm B. With a median follow-up of 62 months there was no difference in 7-year probability of survival (60% and 57.8%; p=0.5), DFS (62% and 71%; p=0.2) and PFS (44.9% and 40.9%; p=0.7) between the two arms. Subgroup analyses confirmed that the best results in terms of survival, DFS and PFS were achieved by patients with large B-cell NHL without BM involvement, independently of the treatment arm. Results were poorer in other categories of patients and poorest in patients with BM involvement. There was no difference in using HDS after CT in all cases or only in case of persistent disease and aggressive NHL did not benefit from upfront HDS/HDT (*Ann Oncol 16:1941, 2005*).

Following the stimulating results reported with the use of Rituximab plus CT for aggressive NHL, from 2002 to 2005 we performed our 3rd study. The study included 1st CR patients (after conventional CT or, when resistant, after CT plus HDS) randomized to 4 administrations of Rituximab or observation. First interim analysis on 98 1st CR patients showed a positive trend in favour of patients receiving Rituximab. Now the final analysis is ongoing.