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Abstracts

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A CONCEPT FOR THE TREATMENT OF RELAPSED INTERMEDIATE AND HIGH-GRADE NHL: STEM CELL COLLECTION AFTER IEV CHEMOTHERAPY PLUS G-CSF, IMMUNOMAGNETIC PURGING OF P.B.S.C. USING MOABS AGAINST B-CELL ANTIGENS IN PATIENTS WITH CB/CC NHL AND STEM CELL TRANSPLANTATION AFTER HIGH-DOSE BU/CY.

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Since 6/93 we have treated 13 patients with relapsed intermediate and high-grade NHL with IEV salvage chemotherapy (Ifosfamide 2.500 mg/m^2 day 1-3, Epirubicin 100 mg/m^2 day 1, VP-16 150 mg/m^2 day 1-3) followed by G-CSF (Filgrastim 5 µg/kg/d) at our institution. Leukapheresis was commenced at the time of rapid neutrophil recovery (ANC > 1 x 10^9/l). Using either a Cobe Spectra or a Fresenius AS 104 cell separator, a median of 9.7 l (range 4.8 l - 14.6 l) of blood were processed during a median of 5 (range 2-10) collections. The aim was to collect an optimum number of progenitor cells (50 x 10^4 CFU-GM/kg). This was possible in 9/13 patients. A median of 25,7 x 10^4 CFU-GM/kg (range 0,13 - 367 x 10^4 CFU-GM/kg) was collected per leukapheresis. The results show that IEV plus G-CSF has the potential to very effectively mobilise peripheral blood progenitor cells.

3 patients have been transplanted so far after high-dose Bu/Cy (Busulfan 16 mg/kg, Cyclophosphamide 120 mg/kg). They have received optimum numbers of progenitor cells as autografts. In 1 patient it is too early to analyse the haematopoietic recovery. The other 2 patients showed a fast engraftment and reached ANC > 0.5 x 10^9/l after 9 and 9 days and platelets > 50 x 10^9/l after 12 and 15 days.

Today it has become obvious from several studies employing the PCR technique that there do exist circulating lymphoma cells in the majority of patients with cb/cc NHL, which will contaminate peripheral blood stem cell harvests (P.B.S.C.). As a pilot study, we have started to purge the P.B.S.C. of patients with cb/cc NHL by applying an immunomagnetic technique. The MaxSep^{TM} system (Baxter, München) is being used, which allows for the removal of cells expressing B-cell antigens from the autografts, including the residual lymphoma cells. A panel of 5 different mouse monoclonal antibodies (MoAbs) directed against the antigens CD19, CD20, CD22, CD23 and CD37 is being used in conjunction with magnetic beads which carry sheep anti-mouse IgG. The bead/B-cell complexes are being removed from the autografts with a strong magnet. Our initial experience shows that leukapheresis products can be purged directly without any further processing. We did not observe any cell clumping and the formation of bead/target cell rosettes as well as the results of the FACS analysis suggested that purging was successful. The actual purging efficacy, however, has to be determined by PCR. For this we either use a t(14;18) or a clone-specific PCR approach. The purging efficacy of clinical immunomagnetic purging by negative selection of B-cells is being compared with the purging effect of a positive selection of CD34+ cells. For this, an aliquot of the P.B.S.C. is used for the positive selection of CD34+ cells (Isolex^{TM}50, Baxter, München.