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GRANULOCYTE-COLONY STIMULATING FACTOR AFFECTS CD62L EXPRESSION ON LYMPHOCYTES AND NK CELL SUBPOPULATIONS PRESENT ON PBPC GRAFTS

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Granulocyte-colony stimulating factor (G-CSF) can be used to mobilise peripheral blood progenitor cells (PBPC). It has been shown that G-CSF mobilization leads to a down-modulation of adhesion molecules, namely L- selectin on haematopoietic cells. The aim of this study was to determine if G-CSF affects adhesion properties of lymphocytes and NK cells present in PBPC grafts. Thus, the expression of a L- selectin (CD62L) and an integrin (CD11a) was evaluated on both peripheral blood (PB) prior to mobilization and PBPC grafts from healthy donors (n=27) and patients with haematologic malignancies candidates to autologous transplantation (n=26). For both groups of individuals blood samples were collected prior to the beginning of mobilization and PBPC were collected by apheresis started on the 5th day of mobilization. Lymphocytes and NK cells were identified using four colour fluorescence labelling together with a lyse and wash technique. Based on the expression of CD56, NK cells were sub-divided in two major sub-populations: NK bright cells (CD56++) and NK dim cells (CD56+). All the results are presented as median values of percentage of positive cells. In the present study, both donor and patient PB lymphocytes and NK cells were CD11a+ (median values >95%) and CD62L was expressed on the majority of lymphocytes (60% and 55% for donors and patients respectively) and CD56++NK cells (86% and 93% for donors and patients respectively). Only a small number of CD56+ NK cells from donors (25%) and patients (18%) express CD62L. After G-CSF mobilisation there was a significant increase in PB leukocyte counts, reflected in the number of PBPC collected by apheresis. In PBPC grafts there were no significant changes in CD11a expression in the studied cell types. For both groups there was a significant decrease in the percentage of lymphocytes CD62L+ (6% and 18% for donors and patients respectively) and CD56+ NK cells CD62L+ (12 and 14% for donors and patients respectively), in comparison with the same cells prior to mobilization. Both for donors and patients the majority of CD56++ NK cells from PBPC grafts continue to express CD62L. In summary, the G-CSF mobilization lead to a similar down modulation of CD62L expression on lymphocytes and CD56+NK cells. Furthermore, this mobilization procedure did not have an effect on the expression of CD11a on lymphocytes and NK cells present on PBPC grafts as compared to premobilization PB. However, in this study and independently from the CD62L expression, both NK cell subpopulations migrated to the blood in response to G-CSF stimuli. CD62L might not be down regulated from CD56++NK cells or have a different time response to the G-CSF in comparison with other cells. Thus, G-CSF mobilisation seems to induce selective changes on CD62L expression on lymphocytes and a NK cell subpopulation present on PBPC Integrins and selectins may have a different role in mobilisation and the effect of these changes in engraftment following haematopoietic transplantation deserves further investigations.

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PREVENTION OF NEUTROPENIC FEVER DURING ADMINISTRATION OF HIGH DOSE VP-16 PLUS G-CSF FOR MOBILIZATION OF PBSC-THE EFFICIENCY OF PROPHYLACTIC ANTIBIOTIC TREATMENT

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Neutropenia after high –dose VP-16 plus G-CSF, as mobilization chemotherapy regimen prior autologous setting in patients with hematological malignancies, is common finding, although infectious complications have not been previously described. In the attempt to reduce infective complications and the higher incidence of hospitalization for neutropenic, fever prophylactic antibiotic regimen was administered for patients receiving this regimen. We evaluated 35 patients with lymphoproliferative malignancies (NHL13, HD 6, MM 12, and ALL 4) treated with HDT/ASCT at Department of hematology, Skopje, Macedonia. The patients were mobilized with VP-16 (2 gr/m^2) and G-CSF 10mcg/kg starting from day 5 of chemotherapy regimen. The regimen was effective in the progenitor cell mobilization and almost 84% of analyzed patients reached at least 2x10 (6)/kg CD34+ cells with median 3 (ranges 1-6) apheresis procedures. Only two patients with HD and one AML failed mobilization. The patients were devided in two groups:1) no specific antibiotic prophylaxis (n=7); (2) vancomycin i.v., cefixime p.o, (n=13); (3) amoxicillin/ clavulonic acid and ciprofloxacin p.o. (n= 15). The first group of patients revealed higher incidence of need for hospitalization (67%) due to neutropenic fever, versus second (28%) and third group (15%) of patients respectively ($p<0,001$ between the first and the other two groups). At the end we conclude that VP-16+G-CSF mobilization schedule revealed significant high incidence of neutropenic fever that can be substantially reduced by a vigorous antibimicrobial prophylactic program.

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A PRELIMINARY REPORT OF BORTEZOMIB PLUS DEXAMETHAZONE IN 17 RELAPSED OR REFRACTORY MULTIPLE MYELOMA PATIENTS

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Introduction. Multiple myeloma is an incurable haematological malignancy of B-cell origin. Although patients generally respond to front-line chemotherapy, eventually the majority either relapse or become refractory. Clinical studies suggest that bortezomib, a proteasome inhibitor, is effective in patients with refractory or relapsed multiple myeloma. The addition of dexamethasone may offer some additional response effect and is suggestive of possible synergy. Purpose of this study is to report the preliminary results of clinical evaluation of efficacy and toxicities of bortezomib in combination with dexamethasone in 17 refractory or relapsed multiple myeloma patients. *Patients and* Method. Seventeen patients aged 58-80 years, 10 men and 7 women, who had either refractory or relapsed multiple myeloma after front and second-line chemotherapy, were designed to receive bortezomib 1.3 mg/m^2 intravenous bolus twice weekly for 2 weeks (days 1, 4, 8 and 11) of a 21-d cycle for up to eight cycles, in combination with dexamethasone 20mg daily on days 1,2 of each cycle. Botrezomib was withheld from patients with drug-related grade 3 non-haematological or grade 4 haematological toxicity and then resumed at 1.0mg/m^2 or 0.7 mg/m^2. Evaluation of response was designed to perform between days 11–18 of cycles 2, 4 and 6, and following cycle 8. Responses were assessed using the European Group for Blood and Marrow Transplantation (EBMT) response criteria. Adverse events were assessed at each visit and graded according to the World Health Organization Common Toxicity Criteria. *Results.* After completion of 3-5 cycles of treatment, 1 patient experienced CR, 7 patients experienced PR and 8 patients had evidence of stable