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Mobilization of peripheral blood progenitor cells with G-CSF alone in lymphoma patients: steady-state circulating progenitor cell count predicts the autograft yield

Nowadays the first choice procedure to collect hematopoietic progenitor cells for autografts is the harvest of peripheral blood progenitor cells (PBPC) mobilized with cytokines, associated or not with chemotherapy. A large amount of data is available on factors affecting mobilization, such as sex, age, number of previous chemotherapy regimens, radiotherapy, and exposure to fludarabine.[1-3] The individual response to mobilization is, however, highly variable from patient to patient and only a few studies have investigated biological parameters that could predict successful mobilization of PBPC for a single patient when a given regimen is employed. Findings of this study show that when G-CSF is used as a single mobilizing agent, the baseline PBPC has a predictive value.

Sir,

We investigated some steady state parameters in 41 patients (21 F, 20 M) affected by non-Hodgkin's (n=31) and Hodgkin's (n=10) lymphoma. The patients had a median age of 40 years (range 15-58) and all patients had been homogeneously treated and mobilized at a median time of 4 months (range 2-19) from the end of a single line of chemotherapy. At the time of the harvest all patients were in partial or complete remission and none had bone marrow involvement. Total nucleated cells (TNC), CD34$^+$ cells and CFU-GM were evaluated in PB and bone marrow (BM) the day before starting a mobilization protocol consisting of a daily G-CSF dose of 16 µg/kg, given as a single subcutaneous injection from day –3. PB CD34$^+$ cells were monitored from day 0 and leukaphereses were performed with PB CD34$^+$ cells ≥ 10/µL and continued until at least 2.5×10^6/kg b.w. CD34$^+$ cells were collected. Steady-state PB and BM characteristics are summarized in Table 1. There were no significant differences between patients with non-Hodgkin's and Hodgkin's lymphoma (data not shown). Baseline BM TNC, CD34$^+$ cell count and CFU-GM/mL did not correlate with the yield of the harvest evaluated as CD34$^+$ cells collected/kg b.w. Otherwise steady-state PB CD34$^+$ cell count and

Table 1. Baseline peripheral blood and bone marrow characteristics.

		Steady-state		
	Peripheral blood		*Bone marrow*	
TNC x10^6/mL	median	5	median	22.9
	range	3-11.8	range	4.7-72.8
CD34+ x10^3/mL	median	1.25	median	83.16
	range	0-16	range	1.1-763
CFU-GM/mL	median	10.6	median	576
	range	0-224	range	69-7000

TNC: total nucleated cells; CFU-GM: colony-forming units granulocyte macrophage.

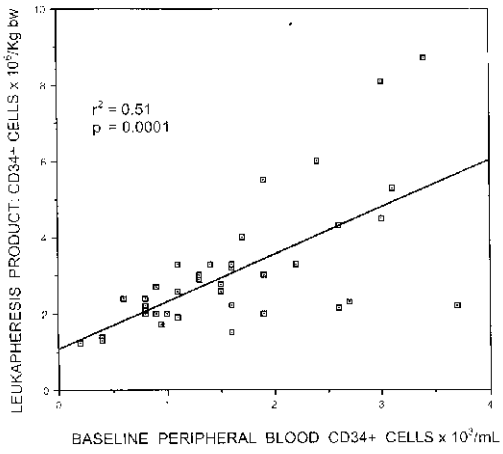

Figure 1. Relationship between steady-state CD34$^+$ peripheral cells and CD34$^+$ cells collected/kg b.w. Enumeration of CD34$^+$ cells was performed incubating 1×10^6 cells with the phycoerythrin conjugated (PE) moAb HPCA-2 (CD34) and the FITC moAb HLE-1 (CD45); after lysis of erythrocytes samples were washed twice and analyzed using a FACScan flow cytometer (Becton Dickinson). Forty-five thousand CD45$^+$ events or at least 100 CD34 positive events were acquired according to the ISHAGE protocol, using a cumulative gating strategy to identify true CD34$^+$ cells and minimize the number of non-specifically stained events (*Sutherland DR et al. J Hematother 1996; 5:213*). Negative controls for each sample were also analyzed (using FITC and PE irrelevant isotypic immunoglobulins).

CFU-GM/mL did have a predictive value on collection (r^2= 0.51, p=0.0001 for PB CD34$^+$ cell count as shown in Figure 1; r^2= 0.57, p=0.0001 for CFU-GM, data not shown).

A large number of studies proved that the quantification of CD34$^+$ cells mobilized in PB is the most reliably factor predicting an adequate harvest.[4,5] Only a few authors investigated baseline parameters able to reflect mobilization capacities in single patients. Fruehauf *et al.*[6] in 1995 found that steady state PBPC counts allow estimation of the yield of mobilization when G-CSF is used in association with chemotherapy; the same authors recently confirmed this finding in a larger group of patients.[7] Paralleling the results of Husson *et al.*[8] and Haug *et al.*[9] our data prove that also when G-CSF is used as a single mobilizing agent the baseline PBPC count has a predictive value.

The amount of steady-state circulating CD34$^+$ cells before mobilization probably reflects the BM reserves which can depend on some individual characteristics and/or of therapy-induced microenvironment damage. The simple and fast flow-cytometric evaluation of circulating PBPC can help to recognize poor mobilizers,[10] identifying patients eligible for second attempts of mobilization or for experimental collection protocols using combinations of growth factors (e.g. G-CSF + stem cell factor) or alternative harvesting procedures (e.g. cytokine-activated BM).

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Key words

Steady state CD34$^+$ cells, G-CSF, mobilization, PBSC transplantation.

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Satellite DNA analysis shows stability of donor hematopoiesis following allogeneic transplantation of peripheral blood stem cells

We assessed the hematologic reconstitution and long term stability of donor hematopoiesis after allogeneic PBSC transplantation in 34 patients with different hematologic disorders. Their blood counts remained stable during the observation period (1-4 years). Donor chimerism, evaluated by satellite DNA, could be predictive of a low risk of relapse.

Sir,

After initial experiments in mice[1] suggesting that circulating stem cells (PBSC) provide marrow repopulation after myeloablation, PBSC have been used in humans to restore hemopoietic function after high dose chemotherapy. Both in autologous and allogeneic settings, it has been demonstrated that PBSC are able to increase the speed of hematologic recovery.[2,3] Recent reports[4-9] suggest that PBSC ensure not only a faster, but also a stabler hematologic recovery following allogeneic transplantation (PBSCT). We present here the analysis of engraftment and chimerism in 34 patients who underwent PBSCT for different hematologic diseases. Donor mobilization, as well as cell characterization were performed following standard guidelines.[10] In all patients the graft consisted of PBSC alone, with a median content of 82.2×10^4/kg CFU-GM, 8.4×10^6/kg CD34$^+$ cells. All patients engrafted but one who died on day +7. The patients recovered > 0.5×10^9/L polymorphonuclear cells at a median of 14