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Peripheral blood progenitor cell collections in cancer patients: analysis of factors affecting the yields

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ABSTRACT

***Background and Objective*. Peripheral blood progenitor cells (PBPC) are now widely used to restore hematopoiesis following high dose chemotherapy in patients with malignancies. We sought to identify parameters that could predict the yield of PBPC after mobilization with chemotherapy (CT) with or without granulocyte colony-stimulating factor (G-CSF) in cancer patients.**

***Design and Methods.* One hundred and fifty patients underwent 627 PBPC collections during the recovery phase following CT with (n = 469) or without (n = 142) G-CSF. Hemogram, CFC-assays and $CD34^+$ cell count were performed on peripheral blood and leukaphereses products. After log transformation of the data, differences between groups were assessed with the unpaired t-test or one-way analysis of variance.**

***Results.* Seventeen and two patients required 2 and 3 mobilization cycles respectively to reach our target of 15×10^4 CFU-GM / kg. In patients with lymphoma but not in those with leukemia, the yields of both CFU-GM and $CD34^+$ cells / kg were dramatically increased when G-CSF was added to CT for mobilization. In collections primed with CT and G-CSF, better yields were obtained in patients with breast cancer or small-cell lung carcinoma (SCLC) as opposed to other solid tumors and leukemia. Among potential predictive factors of CT- and G-CSF-primed harvests, we found that the $CD34^+$ cell count in peripheral blood (PB) was strongly correlated with both the CFU-GM and $CD34^+$ cell yields. Except in leukemia patients, more than 1×10^6 $CD34^+$ cells / kg were harvested when the $CD34^+$ cell count in blood was above 20×10^6 / L. Similarly, better results were obtained in collections performed when the percentage of myeloid progenitors in blood on the day of apheresis was above 5 % or when the leukocyte count in blood was above 5×10^9 / L.**

***Interpretation and conclusions.* A diagnosis of breast cancer or SCLC, a leukocyte count in PB of more than 5×10^9 / L, more than 5% myeloid progenitors or more than 20×10^6 $CD34^+$ cells / L in PB were associated with higher yields of PBPC in collections mobilized with CT+G-CSF.**

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Peripheral blood progenitor cells (PBPC) are now widely used to restore hematopoiesis following high dose chemotherapy in patients with malignancies. Compared with autologous bone marrow, PBPC transplants are associated with shorter periods of aplasia, reduced red blood cell and platelet transfusional needs and shorter duration of hospital stay.[1-8] PBPC are usually collected by apheresis during the recovery phase following cytotoxic chemotherapy (CT). Various regimens with granulocyte colony-stimulating factor (G-CSF) have been used successfully but some studies have used granulocyte-monocyte CSF (GM-CSF)[9-11] or no growth factor.[8,12,13] The quantity of progenitor cells to be infused to achieve a prompt recovery post-transplant remains controversial but a minimum of 1-2 and an optimum of 5×10^6 $CD34^+$ cells per kg is usually considered adequate.[14-17] In order to improve the cost effectiveness of apheresis, the number of collections required to achieve this target should be minimized and therefore, analysis of factors affecting the yield is of importance. We have retrospectively analyzed 627 PBPC harvests in cancer patients from a single collection center in order to identify those parameters that are predictive of the yields of both hematopoietic progenitors and $CD34^+$ cells.

Design and Methods

Patients and mobilization

One hundred and fifty patients with either hematologic malignancies or solid tumors who were eligible for high-dose chemotherapy and stem cell rescue underwent PBPC harvests. Patients' details are given in Table 1. Most of the hematologic patients had been heavily pre-treated. PBPC were collected during

Table 1. Patients' characteristics.

	+ G-CSF	– G-CSF
Number of patients*	124	27
Age (median and range)	47 (2-73)	42 (14-61)
Male/Female	65/59	16/11
Diagnosis		
Leukemias	17	10
AML	10	10
ALL	2	–
CML	3	–
MDS	2	–
Lymphomas	30	15
NHL	25	14
HD	5	1
Multiple myeloma	12	–
Breast cancer	23	–
SCLC	24	–
Other solid tumors	18	2
Neuroblastoma	3	–
Ovarian cancer	2	–
Germ cell tumor	3	2
Miscellaneous	10	–

**One NHL patient underwent 2 cycles of mobilization, one with CT+G-CSF and one with CT only. He is, therefore, included in both groups so that the total number of patients appears to be 151 but is really 150.*

the recovery phase following disease-oriented CT either with (469 leukaphereses from 133 cycles of mobilization) or without (142 leukaphereses from 32 cycles) G-CSF (Neupogen™, Amgen, Thousand Oaks, CA, USA). Most lymphoma and myeloma patients were mobilized with cyclophosphamide 4500 mg/m^2 and etoposide 450 mg/m^2, most breast cancer patients with an intensified FEC regimen, most SCLC patients with epirubicin 90 mg/m^2 and ifosfamide 12 g/m^2 and most leukemias with a combination of an anthracycline and Ara-C. Sixteen collections from 6 mobilization cycles were primed with G-CSF alone. All patients gave informed consent according to local regulations. Chemotherapy regimens were chosen for both their efficacy against the patients' disease and their ability to induce a white blood cell (WBC) rebound following aplasia. G-CSF was administered subcutaneously at a dose of 5 µg/kg daily commencing 24 h after the CT ended and continuing until the day before the last leukapheresis.

Leukapheresis and cryopreservation

PBPC were collected using blood cell separators CS3000+ (Baxter-Fenwal Laboratories, Deerfield, IL, USA) or Spectra (Cobe BCT, Lakewood, CO, USA). The first collection was undertaken when the WBC count reached 1×10^9/L or after 4 days of G-CSF administration if no CT was used. A median of 3 (range 1-7) consecutive daily (including during weekends) leukaphereses were performed. Usually 12 liters of blood were processed per apheresis.

Cells in 10% dimethylsulfoxide (DMSO) were frozen to –90ºC by means of a KRYO II Series controlled rate freezer (Planer, Sunbury-on-Thames, England) at a rate of 1°C/min and then stored in the liquid phase of nitrogen.

Blood and leukapheresis characterization

Cell counting

WBC count, differential, platelet count, hemoglobin and hematocrit levels in peripheral blood (PB) and in leukaphereses products were determined for each procedure using a Technicon H1 counter (Bayer, Tarrytown, NJ, USA). A WBC count for identification of myeloid precursors (blasts, promyelocytes, myelocytes and metamyelocytes) was also performed manually.

CFC-assays

Hematopoietic progenitors were grown in 0.9% methylcellulose in a commercially available medium (H4433, Terry Fox Laboratory, Vancouver, BC, Canada). Cultures were incubated at 37°C in a humidified 5% CO_2 atmosphere. Formation of colony-forming unit-granulocyte-macrophage (CFU-GM), burst-forming unit-erythroid (BFU-E) and colonies of multiple lineages (CFU-Mix) were scored on day 14.

Flow cytometry

Aliquots of the leukapheresis products or PB were incubated with phycoerythrin-conjugated monoclonal anti-CD34 (HPCA2, Becton Dickinson, Palo Alto, CA, USA) for 20 minutes at 20°C, washed and fixed with 1 % formaldehyde. A total of 1×10^5 cells was analyzed (FACScan analyzer, Becton Dickinson). The percentage of CD34$^+$ cells in the isotype control was subtracted from the percentage of CD34$^+$ cells to give the final percentage of CD34$^+$ cells. Data acquisition was performed with software (Cellquest, Becton Dickinson).

Data analysis

For data analysis, patients with Hodgkin's disease or non-Hodgkin's lymphoma (NHL) were considered together as lymphomas. Similarly, those with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), acute phase of chronic myelogenous leukemia (CML) or myelodysplastic syndrome (MDS) were grouped under the label *leukemia*. Patients with solid tumors were separated into those with small-cell lung carcinoma (SCLC), those with breast cancer and those with other solid tumors. Patients with myeloma were also analyzed separately. Finally, G-CSF primed collections refers to all leukaphereses mobilized with G-CSF, with (n = 469) or without (n = 16) CT.

Because of the skewed distribution of the data, log transformations were performed. Unpaired t-tests or one-way analysis of variance followed by Tukey's multiple comparison tests were used to compare differ-

Table 2. Yields according to the recruitment protocol.

Yields	*+ G-CSF*	*– G-CSF*	*p*
MNC ($\times 10^8$/kg)	1.00 [0.01-12.39]	0.68 [0.08-4.80]	< 0.0001
CFU-GM ($\times 10^4$/kg)	9.94 [0-695.5]	2.08 [0-48.7]	< 0.0001
BFU-E ($\times 10^4$/kg)	25.13 [0-1832]	5.67 [0-75.50]	<0.0001
CFU-Mix ($\times 10^4$/kg)	1.56 [0-239.5]	0.07 [0-6.82]	<0.0001
CD34$^+$ ($\times 10^6$/kg)	1.27 [0-249.8]	0.88 [0-9.5]	< 0.0001

(median [range]).

ences between groups and Pearson's correlations were used to examine the relationship between various parameters and the yields of leukapheresis.

Results

Overall leukapheresis yields

We performed 627 leukaphereses after 171 mobilization cycles in 150 patients with the aim of collecting a minimum of 1×10^6 CD34$^+$ cells/kg or 5×10^4 CFU-GM/kg and if possible 5×10^6 CD34$^+$ cells/kg. Seventeen patients required 2 mobilization cycles and 2 patients required 3 such cycles in order to achieve this target. Per leukapheresis, the yields (median [range]) were 0.88 [0.01-12.39] $\times10^8$ MNC/kg, 6.24 [0-695.53] $\times10^4$ CFU-GM/kg, 14.47 [0-1831.69] $\times10^4$ BFU- E/kg, 0.84 [0-239.51] $\times10^4$ CFU-Mix/kg and 1.17 [0-249.76] $\times10^6$ CD34$^+$ cells/kg irrespective of the method of mobilization.

Role of G-CSF

Collections primed with G-CSF were associated with significantly higher yields of hematopoietic progenitors and CD34$^+$ cells compared with those primed with CT alone (Table 2). This effect of G-CSF was observed in the lymphoma group (median [range] for CFU-GM: 7.78 [0-327.2] vs 1.85 [0.07-28.10] $\times10^4$/kg and for CD34$^+$ cells: 1.26 [0.02-32.18] vs 0.64 [0-7.65] $\times10^6$/kg) but was not found in the leukemia group either for the yield of CFU-GM (median 4.31 [range 0-213.8] vs 2.86 [0-48.7] $\times10^4$/kg, NS) or for that of CD34$^+$ cells (median 0.76 [range 0.01-249.8] vs 1.19 [0.06-9.05] $\times10^6$/kg, NS). Only G-CSF primed collections were therefore considered for further analysis. We found strong correlations between the numbers of CFU-GM/kg and MNC/kg ($r = 0.63$, $p < 0.0001$) or CD34$^+$ cells/kg ($r = 0.74$, $p < 0.0001$) as well as between CD34$^+$ cells/kg and MNC/kg ($r = 0.62$, $p < 0.0001$) collected. We also found strong correlations between CFU-GM/kg and BFU-E/kg ($r = 0.88$, $p < 0.0001$) or CFU-Mix/kg ($r = 0.86$, $p < 0.0001$).

Table 3. Influence of diagnosis on the yields in G-CSF primed collections.

Diagnosis	*MNC/kg ($\times10^8$)*	*CFU-GM/kg ($\times10^4$)*	*BFU-E/kg ($\times10^4$)*	*CFU-Mix/kg ($\times10^4$)*	*CD34/kg ($\times10^6$)*
Breast cancer	1.35 [0.16-11.7]	27.8 [0.10-373]	36.06 [0.24-461.70]	5.16 [0-161.30]	2.48 [0.05-38.02]
SCLC	1.52 [0.27-6.45]	18.73 [0.28-97.5]	44.41 [6.65-455.30]	3.26 [0-40.60]	2.22 [0.19-17.00]
Lymphoma	0.85 [0.02-11.52]	7.78 [0-327.2]	24.09 [0-1832.00]	1.34 [0-239.50]	1.26 [0.02-32.18]
Myeloma	0.74 [0.10-3.45]	5.79 [0-695.5]	19.08 [0.03-892.30]	0.61 [0-179.60]	0.78 [0.02-61.53]
Leukemia	0.89 [0.01-9.01]	4.31 [0-213.8]	4.82 [0-390.40]	0.65 [0-78.70]	0.76 [0.01-249.8]
Other solid tumors	0.82 [0.12-12.39]	3.37 [0-293.9]	7.03 [0-436.80]	0.11 [0-85.64]	0.84 [0-13.06]

(median [range]).

Influence of diagnosis

In univariate analysis, the diagnosis group was an important parameter determining the yields of MNC/kg ($p < 0.0001$), CFU-GM/kg ($p = 0.0001$), BFU-E ($p < 0.0001$), CFU-Mix ($p = 0.0213$) as well as CD34$^+$ cells/kg ($p = 0.0033$) collected with G-CSF (Table 3). Higher yields were achieved in patients with breast cancer or SCLC (all p values < 0.05) than in patients with other solid tumors, lymphoma, myeloma or leukemia .

Influence of WBC count in blood

Yields of CFU-GM ($r = 0.58$, $p < 0.0001$) or CD34$^+$ cells ($r = 0.52$, $p < 0.0001$) were strongly correlated with the PB WBC count. Collections performed when the WBC count was below 2×10^9/L yielded significantly lower amounts of CFU-GM compared with those realized when the WBC count was between 2 and 5 or above 5×10^9/L (all $p < 0.0001$) (Table 4). The amounts of CD34$^+$ cells or CFU-Mix collected per kg were significantly higher only when the PB WBC count was above 5×10^9/L ($p < 0.0001$). There was a 70% probability of collecting > 1×10^6 CD34$^+$ cells/kg when the PB WBC count was > 5×10^9/L. In leukemia patients the optimal threshold for the PB WBC count was 5×10^9/L (2.13×10^6 [range 0.56-249.80] vs 0.22 [0.01-2.78] CD34$^+$ cells/kg, $p < 0.0001$). In the group of patients with breast cancer, this threshold was 10 $\times10^9$/L with a median of 3.60×10^6 CD34$^+$ cells/kg collected versus 0.89×10^6 CD34$^+$ cells/kg ($p < 0.0001$). Similar data were obtained in the lymphoma, myeloma and SCLC groups with a threshold of 10×10^9/L, 10×10^9/L and 5×10^9/L, respectively.

Table 4. Yields in G-CSF primed collections according to the number of WBC in the peripheral blood.

WBC in blood (x 10^9/L)	*≤ 2*	*2–5*	*> 5*
MNC/kg ($\times 10^8$)	0.30 [0.01-1.43]	0.61 [0.05-12.39]	1.50 [0.02-11.70]
CFU-GM/kg ($\times 10^4$)	0.29 [0-43.97]	3.38 [0-102.80]	20.08 [0-695.50]
BFU-E ($\times 10^4$)	1.64 [0-115.70]	8.48 [0-379.30]	41.16 [0-1832]
CFU-Mix ($\times 10^4$)	0 [0-14.41]	0.57 [0-51.14]	3.40 [0-239.50]
CD34/kg ($\times 10^6$)	0.44 [0-6.36]	0.47 [0-14.84]	2.29 [0-249.80]

(median [range]).

Table 5. Yields in G-CSF primed collections according to the percentage of myeloid precursors in the peripheral blood.

Myeloid precursor in blood (%)	*≤ 5*	*> 5*
MNC/kg ($\times 10^8$)	0.83 [0.01-12.39]	1.69 [0.03-11.70]
CFU-GM/kg ($\times 10^4$)	4.68 [0-695.50]	38.42 [0.11-612.70]
BFU-E ($\times 10^4$)	10.34 [0-892.30]	99.48 [0.85-1832.00]
CFU-Mix ($\times 10^4$)	0.65 [0-179.6]	9.40 [0-239.50]
CD34/kg ($\times 10^6$)	0.80 [0-61.53]	4.54 [0.02-249.80]

(median [range]).

Influence of the speed of WBC recovery during collection

ΔWBC, a measure of the rapidity of WBC recovery, was defined as the difference in the PB WBC count between the third and the first collections divided by the WBC count on the day of the first collection. There was only a weak but significant correlation between ΔWBC and the yields of CFU-GM/kg ($r = 0.24$, $p < 0.0001$) and $CD34^+$ cells/kg ($r = 0.24$, $p < 0.0001$). These correlations were found only in breast cancer, lymphoma and leukemia but not in SCLC, myeloma or solid tumors. G-CSF primed collections when the ΔWBC was above 1.5 were associated with increased yields of CFU-GM ($p = 0.0003$) and $CD34^+$ cells ($p < 0.0001$). This was true in breast cancer for both CFU-GM and $CD34^+$ cells (both $p < 0.0001$), in leukemia only for CFU-GM ($p = 0.04$) whilst it did not reach statistical significance in lymphoma.

Table 6. Yields in collections primed with G-CSF according to the concentration of $CD34^+$ cells in blood.

$CD34^+$ cells in blood ($\times 10^6$/L)	*≤ 20*	*20-60*	*> 60*
MNC/kg ($\times 10^8$)	0.59 [0.01-3.54]	1.17 [0.02-11.70]	1.77 [0.03-11.52]
CFU-GM/kg ($\times 10^4$)	2.22 [0-95.52]	11.31 [0-373]	38.91 [0.11-695.5]
BFU-E ($\times 10^4$)	4.63 [0-180.20]	25.40 [0-461.70]	97.51 [1.20-1832.00]
CFU-Mix ($\times 10^4$)	0.23 [0-27.49]	1.74 [0-48.01]	9.52 [0-239.50]
CD34/kg ($\times 10^6$)	0.31 [0-3.94]	1.18 [0.01-38.02]	4.06 [0.02-61.53]

(median [range]).

Influence of the percentage of myeloid precursors in blood

The percentage of myeloid precursors in the blood was correlated with the quantities of CFU-GM ($r = 0.46$, $p < 0.0001$) and $CD34^+$ cells ($r = 0.49$, $p < 0.0001$) harvested. Collections performed when the percentage of myeloid precursors in the blood was higher than 5% were significantly better ($p < 0.0001$) in terms of yields (Table 5). This threshold was not affected by diagnosis (data not shown).

Influence of the $CD34^+$ cell count in blood

The number of $CD34^+$ cells in PB measured before collection was strongly correlated with the yields of CFU-GM ($r = 0.62$, $p < 0.0001$) and $CD34^+$ cells ($r = 0.74$, $p < 0.0001$) (Figure 1) in the related harvest. This relation was observed in each diagnostic group and was particularly strong in leukemia. When there were less than 20×10^6 $CD34^+$ cells/L in the blood, both CFU-GM/kg and $CD34^+$ cells/kg were significantly lower than when there were between 20 and 60 or above 60, ($p < 0.0001$) (Table 6). In each diagnostic group except leukemia, more than 1×10^6 $CD34^+$ cells/kg (median) were harvested when the PB $CD34^+$ cell count was above 20×10^6/L. However, in leukemia patients the $CD34^+$ cell count ($\times10^6$/kg) in the harvest was only significantly higher when the corresponding PB cell count was above 60×10^6/L (3.90 [1.05-17.69] vs 0.35 [0.06- 2.78] if $CD34^+$ cells in blood were $< 20\times10^6$/L, $p < 0.0001$, and vs 0.75 [0.25-2.34] if between 20 and 60×10^6/L, $p = 0.0054$). A value of 20×10^6/L $CD34^+$ cells in PB was associated with a 73% probability of obtaining 1 and a 25% probability of obtaining 5×10^6 $CD34^+$ cells/kg, while a value of 60 was associated with a 90% probability of obtaining 1 and a 40% probability of obtaining 5×10^6 $CD34^+$ cells/kg.

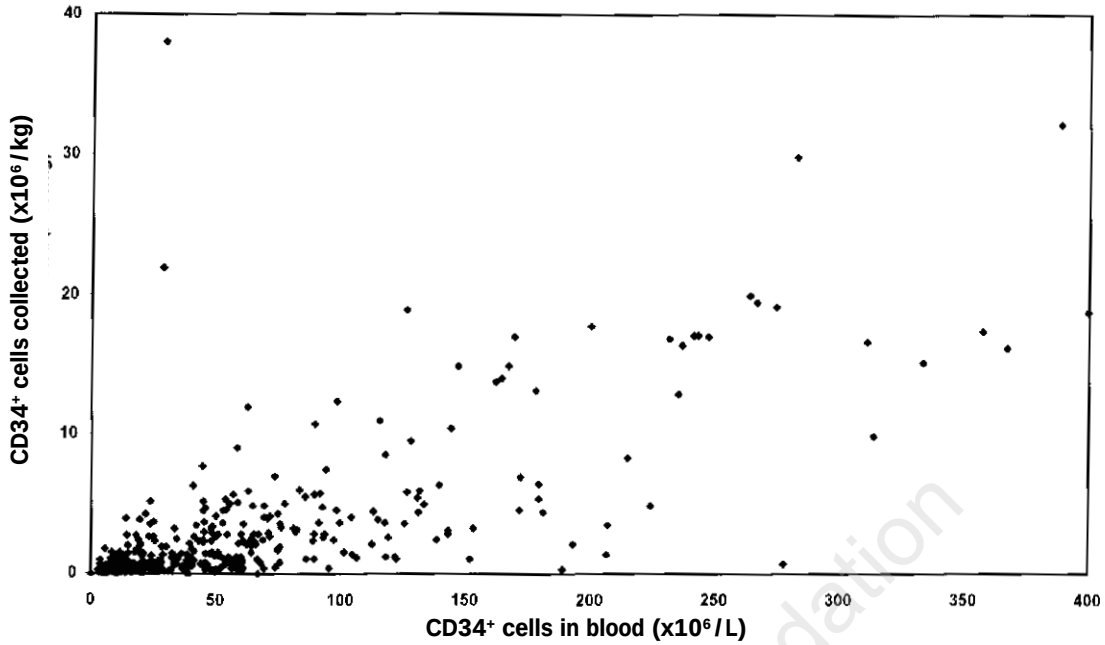

Figure 1. CD34⁺ cells collected per kg according to the CD34⁺ cell count in the peripheral blood after mobilization with CT + G-CSF (r = 0.74, p < 0.0001).

Discussion

We analyzed 627 PBPC collections and tried to define some predictive factors in order to rationalize our leukapheresis scheme. We show that CFU-Mix and BFU-E correlate extremely well with CFU-GM and therefore their determination does not add much to that of CFU-GM alone. The present study also demonstrates a strong correlation between CFU-GM and CD34⁺ cells collected per leukapheresis after mobilization with CT and G-CSF. Such relationships have been reported previously by most authors.[11,18-25] In agreement with previous studies,[26] we report a strong correlation between MNC and both CFU-GM or CD34⁺ cells collected. These findings suggest that the quality of a leukapheresis product may be judged from its CD34⁺ cell content alone and that cultures of hematopoietic progenitors might be abandoned altogether.

The influence of diagnosis on the yields is highlighted by our finding of higher numbers of harvested PBPC in patients with breast cancer or SCLC. The role of previous stem cell damage from cytotoxic drugs is the likely explanation[6,14,20,27] as these patients had been less heavily pretreated than those with leukemia or lymphoma. However, this observation could also support a previous finding concerning the favorable impact of a diagnosis of breast cancer rather than NHL.[28] Such differences in the yield of CFU-GM were not observed among patients with NHL, myeloma or solid tumors mobilized with cyclophosphamide.[12] We did not find any correlation between the age of the patients and the yields achieved. This is consistent with results in most papers[6,12,29] although inverse correlations between age and progenitor cell yields have been found by some researchers.[14,30] Age, diagnosis and previous therapies are, however, seldom controlled for at time of PBPC mobilization and such prognostic factors are almost irrelevant in practice.

Collections primed with G-CSF in addition to disease-oriented CT yielded significantly higher numbers of CFU-GM and CD34⁺ cells than those mobilized with CT alone.[10,31,32] While an improvement in the yields of progenitor cells was seen in the lymphoma group treated with G-CSF, such a favorable effect was not really observed in leukemia patients. In a study including 22 patients mainly with AML, Teshima *et al.*[32] reported higher yields of MNC, CFU-GM and BFU-E when G-CSF and CT were used to recruit PBPC as compared to CT alone. This discrepancy with our results may be linked to differences in the clinical status of the patients or in the CT regimens used.

Like many investigators, we have chosen to start leukaphereses when the PB WBC count reaches 1×10^9/L. However, collections performed while the WBC count was above 5×10^9/L were associated with higher numbers of CD34⁺ cells and CFU-GM collected. In breast cancer and lymphoma patients, more than 3.6×10^6 CD34⁺ cells/kg (median) were collected when the WBC count was > 10×10^9/L. These data suggest that starting leukaphereses when the WBC count is between 1 and 2×10^9/L will produce lower yields in the first collections with subsequent improve-

ment as the WBC count increases. This is supported by the previous observation that the maximum mobilization of CFU-GM and $CD34^+$ cells started 2 days after the WBC count rose to 2×10^9/L and was then maintained over 4 to 5 days.[11] It has, however, been demonstrated that the peak number of LTC-IC coincides with the early rise of WBC and not necessarily with the peak of $CD34^+$ cells or CFU-GM.[31] Furthermore, early PBPC collections contain more cytotoxic effector cells and could therefore theoretically be associated with better antitumor effects.[33] Finally, contamination with tumor cells may be considerably increased in the later collections.[34,35] Great care should clearly be taken to avoid improving the yields of $CD34^+$ cells or CFU-GM at the expense of excluding more primitive hematopoietic cells or decreasing the purity or anti-tumor effect of the product.

The predictive value of the $CD34^+$ cell count in the blood has previously been reported and attempts have been made to define a threshold at which to start apheresis.[18,23,36] A strong correlation between the preceding day $CD34^+$ concentration in blood and the yield of $CD34^+$ cells has been reported.[37,38] We also found a strong correlation between the blood $CD34^+$ cell count and the $CD34^+$ cell content of the same day leukapheresis product. When the $CD34^+$ cell count was more than 20×10^6/L, PBPC yield reached a median of 1.18×10^6 $CD34^+$ cells/kg (73% probability of obtaining > 1×10^6 $CD34^+$ cells/kg) and a median of 11.31×10^4 CFU-GM/kg. A $CD34^+$ cell count below 20×10^6/L was associated with an 83% probability of failure to reach 1×10^6 $CD34^+$ cells/kg. In leukemia patients the cut-off effect appeared even stronger but set at a higher level with considerably better yields when the $CD34^+$ cell count was above 60×10^6/L. Similarly, investigators in Heidelberg observed that more than 2.5×10^6 $CD34^+$ cells/kg were likely to be collected when the $CD34^+$ cell count in the blood was above 50×10^6/L.[39] Peripheral blood CFU-GM predicted the yields of CFU-GM or $CD34^+$ cells even better, but this is of no clinical use given the time required for progenitor cell cultures.

Potential surrogates for PB $CD34^+$ cell count may be the presence of myeloid precursors in the peripheral blood or the speed of leukocyte recovery. Watanabe *et al.*[40] found a correlation between blood myelocytes and the numbers of CFU-GM collected. Craig *et al.*[41] noticed that the CFU-GM yield was poorer when more than 4 days were needed for WBC to recover from 1 to 5×10^9/L in patients mobilized with CY and G-CSF while Schwartzberg *et al.*[24] found this parameter relevant only after mobilization with CT alone. We found a weak but significant correlation between ΔWBC and progenitor cell yields in patients mobilized with G-CSF but not in those treated with CT alone. We also report a very significant correlation for the presence of myeloid precursors (primarily myelocytes) and found that a median of 4.54×10^6 $CD34^+$ cells /kg were harvested if there were more than 5% myeloid precursors in PB. However, these parameters provided less efficient prediction than the one obtained with the $CD34^+$ cell count which should remain the gold standard.

In conclusion, our analysis has shown that multiple parameters affect the yields of PBPC collections. Better collections are obtained in patients with breast cancer or SCLC probably because of lower exposure to cytotoxic drugs. A leukocyte count above 5×10^9/L, more than 5% myeloid progenitors in the blood or more than 20×10^6 $CD34^+$ cells/L in blood were all associated with higher yields. In lymphoma patients but, surprisingly, not in leukemia patients, the addition of G-CSF to the CT regimen has dramatically improved the yields. Confirming previous observations in this journal,[42,43] the he best predictor appears to be the $CD34^+$ cell count in the blood on the day of the harvest and patients with > 20×10^6 $CD34^+$ cells/L have a 73% probability of obtaining at least 1×10^6 $CD34^+$ cells/kg in the leukapheresis product.

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BS wrote the paper. BS and VF collected and analyzed the data. Leukaphereses were carried out by EB and DS, progenitor cell cultures by J-MP, and CD34 analyses by NS-L. M-FF, J-PH, GF and YB took care of the patients with hematologic malignancies, LB of those with lung cancer, and GJ and VB of those with other solid tumors. YB designed the study and reviewed the manuscript. The order in which the names of the authors appear in this paper is related to the importance of their contribution. YB, as the senior author, is cited last. We greatly appreciated the help of the nursing staff of the Blood Bank at the University Hospital (CHU) of Liège. We are also indebted to Dr. Robert Wynn, Paterson Institute for Cancer Research, Manchester, U.K., for his careful review of the manuscript.

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