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Single-dose pegfilgrastim is comparable to daily filgrastim in mobilizing peripheral blood stem cells: a case-matched study in patients with lymphoproliferative malignancies

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Abstract Pegfilgrastim (PEGFIL) has been found to be comparable to daily filgrastim (FIL) in managing chemotherapy-induced neutropenia. In the present study, we evaluated the ability of PEGFIL to mobilize stem cells in 38 consecutive patients with lymphoproliferative diseases (multiple myeloma, $n=18$; lymphomas, $n=15$; chronic lymphocytic leukemia, $n=5$). Patients were mobilized using PEGFIL (6–18 mg as a single dose) during 2005–2006; 32 then received high-dose chemotherapy followed by autologous stem cell transplantation. PEGFIL-mobilized patients were matched by age, disease, and treatment line at a ratio of 1:2 to historical FIL-mobilized controls. The primary study endpoint was the blood $CD34^+$ concentration at onset of leukapheresis. Leukapheresis began a median of 10 days from the beginning of mobilization chemotherapy in both groups. At the onset of leukapheresis, median blood $CD34^+$ cell counts did not differ significantly in the FIL group compared with the PEGFIL group ($79 \times 10^6/L$ vs $64 \times 10^6/L$, respectively; $p=0.44$). In the different disease categories, the respective $CD34^+$ cell counts after FIL and PEGFIL mobilization were $72 \times 10^6/L$ vs $123 \times 10^6/L$ ($p=0.08$) in myeloma, $51 \times 10^6/L$ vs $62 \times 10^6/L$ ($p=0.6$) in lymphomas, and $27 \times 10^6/L$ vs $30 \times 10^6/L$ ($p=0.62$) in CLL, respectively.

The target $CD34^+$ cell yield was harvested with one leukapheresis in 53% of PEGFIL-mobilized patients. Engraftment after autografting did not differ significantly in the two groups. Stem cell mobilization with a single dose of PEGFIL was, therefore, comparable to that achieved using daily FIL in patients with lymphoproliferative diseases. PEGFIL is a more practical way to mobilize stem cells than daily FIL.

Keywords Autologous stem cell transplant · Filgrastim · Pegfilgrastim · Mobilization · Lymphoproliferative disease

Introduction

High-dose chemotherapy supported by autologous stem cell transplantation (ASCT) is currently a widely used treatment modality in various hematological and oncological malignancies. A prerequisite for ASCT is sufficient mobilization of stem cells so that adequate yields can be obtained using leukapheresis. A combination of cytostatic chemotherapy with granulocyte or granulocyte-macrophage colony-stimulating factor (G-CSF or GM-CSF) has been shown to be the most efficient regimen for achieving sufficient mobilization of stem cells [1–3]. Filgrastim (FIL) is a recombinant G-CSF used in cancer patients for the prevention of chemotherapy-induced neutropenia and for the mobilization of stem cells into peripheral blood. Because FIL has a half-life of 3–4 h, daily subcutaneous administration is required. Pegfilgrastim (PEGFIL) is a pegylated form of FIL. It has a prolonged terminal elimination half-life of 33 h and self-regulating serum levels as a result of neutrophil-mediated clearance [4, 5]. A single dose of PEGFIL has been shown to be as effective as multiple doses of daily FIL in the management of chemotherapy-induced

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neutropenia [6–8]. There are also some reports on the use of PEGFIL for the mobilization of stem cells into peripheral blood [9–13]. The aim of this study was to compare stem cell mobilization using a single dose of PEGFIL with that achieved using daily FIL, both as adjuncts to chemotherapy, in patients with lymphoproliferative malignancies.

Materials and methods

Patients

Between May 2005 and October 2006, 38 consecutive adult patients with lymphoproliferative diseases requiring stem cell mobilization prior to ASCT and who were successfully mobilized using PEGFIL were included in this study. Each PEGFIL patient was matched by age (± 5 years), disease type, and treatment line with two historical patients who had been successfully mobilized with daily FIL between January 1996 and April 2005. The 76 historical control patients were searched consecutively backwards from April 2005 and those who met the three selection criteria were chosen as case-matched controls. They were matched from a total number of 251 patients with lymphoproliferative diseases including multiple myeloma (MM), chronic lymphocytic leukemia (CLL), and lymphomas who were mobilized with FIL and transplanted during years 1996–2005.

Oral and written consents from the patients were obtained, and the study was conducted according to Good Clinical Practice and the declaration of Helsinki. The analysis was included in the quality management part of our stem cell transplantation program accredited by the JACIE/EBMT in 2006 and approved also by the Finnish administratives responsible for complying with the EU directive 2004/23/EY on the use of human tissues and cells.

Mobilization therapy

All patients received mobilizing cytostatic chemotherapy according to standard practice. PEGFIL was given on day 2 to the majority of patients, 1 day after the end of 1-day cytotoxic therapy. If the chemotherapy course was longer, PEGFIL was administered 1 day after the last dose. Most patients ($n=31$) were administered PEGFIL 12 mg; however, the first patient included in the study (with lymphoma) was treated with PEGFIL 18 mg, while the last eight patients (five with MM, two with CLL, and one with lymphoma) received the dose of 6 mg. FIL was administered at a dose of 5 $\mu\text{g/kg}$ on day 2 or 1 day after the end of cytotoxic therapy and was continued each day until the end of leukapheresis. A successful mobilization in this study is defined as a sufficient mobilization of CD34^+ cells into blood so that a sufficient number of CD34^+ cells could be

harvested. Accordingly, the primary study endpoint is the blood CD34^+ concentration at onset of leukapheresis.

Stem cell collection

Following mobilization with chemotherapy plus G-CSF, daily measurements of blood CD34^+ cells were initiated on days 9–10 when the blood leukocyte count had recovered from its nadir to a level of $1.0 \times 10^9/\text{L}$. Apheresis was initiated when the blood CD34^+ count reached $\geq 15 \times 10^6$ cells/L with three exceptions (two patients with lymphoma and one with CLL) in the FIL group where apheresis was started though blood CD34^+ count was between $10 \times 10^6/\text{L}$ and $15 \times 10^6/\text{L}$. The target yield for single transplantation was 4×10^6 CD34^+ cells/kg, but a minimum of 1.5×10^6 CD34^+ cells/kg was accepted for transplantation. For patients with MM aged less than 60 years, the aim was to collect sufficient stem cells for double transplantation ($\geq 6 \times 10^6$ CD34^+ cells/kg). Prior to February 2000 ($n=13$), apheresis was performed using a Fenwall CS-3000 Plus (Baxter Healthcare, Deerfield, IL, USA). After this date, apheresis was performed using the COM.TEC Blood Cell Separator (Fresenius Hemo Care, Bad Homburg, Germany) with a reduced volume program. Whole blood flow rates were 50–70 mL/min. Until year 2004, a total of approximately 10 L of blood was processed for each collection. Since the beginning of year 2004, the apheresis collection volume was increased to a mean of 12 L (range 6.6–17.4 L). The mean collection volume for the PEGFIL patients was 13.5 L (median 13 L; range 6.6–17.4 L) and for FIL patients 11.2 L (median 11 L; range 6.8–16.5 L). The final product containing 10% dimethyl sulfoxide was frozen using a computer-controlled device (Kryo 10, Planer, Sunbury-on-Thames, UK) and stored at -196°C in liquid nitrogen.

Laboratory methods

Blood and apheresis CD34^+ cell enumeration was performed using flow cytometry. Until mid-1999, a two-platform method was used, as described previously [14]; this procedure was later modified according to Nordic recommendations [15]. Since then, a single-platform assay in TrueCount™ tubes using Procount™ reagents and software have been used (Becton-Dickinson, San Jose, CA, USA), using a FacsScan flow cytometer (Becton-Dickinson) until late 1999, and a FacsCalibur (Becton-Dickinson) flow cytometer thereafter.

Stem cell transplantation

Patients achieving the acceptable yield of CD34^+ cells underwent high-dose chemotherapy followed by ASCT. High-dose chemotherapy was selected according to patients' disease, mainly melphalan 200 mg/m^2 for myelo-

ma and BEAM, etoposide, ara-C, and melphalan for lymphoma. After stem cell infusion, G-CSF was administered until neutrophil recovery $>1.0 \times 10^9/\text{L}$.

Statistical analyses

Clinical and laboratory data were analyzed using the statistical program package SPSS for Windows 11.5. Because most of the variables were not normally distributed, medians and ranges are used to describe the distribution of continuous data. Continuous and ordinal data were tested using the Mann–Whitney *U* test and nominal data using the chi-square or Fisher's exact test where appropriate. All tests were two-sided at the 5% significance level.

Results

Patient demographics and disease characteristics

Thirty-eight patients were included in the study and mobilized with PEGFIL. The diagnoses were MM ($n=18$),

lymphomas ($n=15$), and CLL ($n=5$). Patient characteristics are given in Table 1 and there are no significant differences between the PEGFIL and case-matched FIL groups. Details of the mobilization chemotherapy used in these patients are also given in Table 1. The most frequently used mobilization chemotherapy was high-dose cyclophosphamide, at a dose of 1.5–2 g/m² for patients with myeloma and 2–4 g/m² for lymphomas if used as a single agent.

Mobilization efficiency and leukapheresis

There was no difference in median time to apheresis onset between the PEGFIL and FIL groups (10 days in each group; Table 2). On the day of the first apheresis, median blood CD34⁺ cell count, leukocyte count, and platelet count seemed to be higher in the FIL group than in the PEGFIL group, but differences did not reach statistical significance (Table 2). Mobilization and apheresis data in the subgroups of patients with MM, lymphoma, and CLL are also shown in Table 2. There were no significant differences in the median CD34⁺ cell counts at onset of apheresis between the different disease entities. However, the CD34⁺ cell count in

Table 1 Patient characteristics and mobilization chemotherapy

	Pegfilgrastim	Filgrastim	<i>p</i> value
Number of patients	38	76	
Disease, <i>n</i> (%)			1.00
Multiple myeloma	18 (47)	36 (47)	
Lymphoma	15 (39)	30 (39)	
Chronic lymphocytic leukemia	5 (13)	10 (13)	
Median age (range), years	57 (24–73)	54 (23–71)	0.87
Sex (female/male), <i>n</i> (%)	12 (32)/26 (68)	30 (39)/46 (61)	0.41
Number of cytotoxic regimens, <i>n</i> (%)			0.74
1	27 (71)	54 (71)	
≥2	11 (29)	22 (29)	
Response to treatment at mobilization, <i>n</i> (%)			0.91
Complete response	6 (16)	13 (17)	
Partial response	28 (74)	53 (70)	
Stable disease	4 (11)	10 (13)	
Mobilization chemotherapy, <i>n</i> (%)			0.157
Cyclophosphamide-containing regimens			
High-dose cyclophosphamide (median 2 g/m ² ; range 2–4 g/m ²)	24 (63)	58 (76)	
CHOP, CHOEP, COAP (cyclophosphamide 750 mg/m ²)	6 (16)	5 (6.6)	
M-BACOD (cyclophosphamide 600 mg/m ²)	0	2 (3)	
Other regimens			
IMVP-16	5 (13)	8 (11)	
Cytarabine	3 (8)	1 (1)	
DexaBEAM	0	1 (1)	
Magrath regimen	0	1 (1)	
Median time from onset of treatment to mobilization (range), months	5 (3–125)	5 (2–124)	0.59
Sepsis at mobilization, <i>n</i> (%)	3 (8)	4 (5)	0.68

CHOP cyclophosphamide, doxorubicin, vincristine, and prednisone, *CHOEP* cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone, *COAP* cyclophosphamide, vincristine, cytarabine, and prednisone, *dexaBEAM* dexamethasone, BCNU (carmustine), etoposide, cytarabine, and melphalan, *IMVP-16* ifosfamide, methotrexate, and etoposide, *M-BACOD* cyclophosphamide, methotrexate, bleomycin, doxorubicin, vincristine, and dexamethasone

Table 2 Stem cell mobilization data in all patients and in different diseases (myeloma, lymphoma, and CLL)

	All patients			Multiple myeloma			Lymphoma			CLL		
	Pegfilgrastim	Filgrastim	<i>p</i> value	Pegfilgrastim	Filgrastim	<i>p</i> value	Pegfilgrastim	Filgrastim	<i>p</i> value	Pegfilgrastim	Filgrastim	<i>p</i> value
<i>N</i>	38	76		18	36		15	30		5	10	
Median (range) onset of apheresis, days	10 (10–18)	10 (10–18)	0.75	10 (10–11)	10 (10–12)	0.75	12 (10–16)	12 (10–18)	0.16	12 (10–18)	12 (11–18)	0.06
Number of apheresis cycles (1/2/3/4)	20/14/4/0	27/36/10/3	0.39	9/7/2/0	13/21/2/0	0.52	9/5/1/0	12/12/5/1	0.15	2/2/1/0	2/3/3/2	0.23
Median (range) blood CD34 ⁺ at onset of apheresis; $\times 10^6/L$	64 (17–805)	79 (10–390)	0.44	123 (25–377)	72 (19–390)	0.08	62 (17–805)	51 (13–365)	0.60	30 (19–110)	27 (10–86)	0.62
Median (range) leukocyte count at onset of apheresis; $\times 10^9/L$	10.6 (1.3–63)	14.5 (2.6–88)	0.07	9.5 (1.3–36)	18.8 (2.6–88)	0.007	16.8 (3–62)	12 (2.6–87)	0.69	7.5 (4.7–16)	13 (3.2–40)	0.39
Median (range) platelet count at onset of apheresis; $\times 10^9/L$	93 (23–339)	120 (22–301)	0.30	93 (23–224)	128 (58–298)	0.18	78 (24–339)	92 (22–301)	0.78	108 (45–191)	102 (46–171)	0.90
Median (range) CD34 ⁺ apheresis yield; $\times 10^6/kg$	4.9 (1.6–27)	8.5 (1.5–33.1)	0.002	5.1 (2.5–17.9) ^a	9.6 (3–28.1) ^a	0.002	4.9 (1.6–27)	6.8 (1.5–33)	0.12	4.8 (2.6–10.7)	4.9 (2.7–13.6)	0.90
Patients with target CD34 ⁺ cell yield ($\geq 4 \times 10^6/kg$ for single, $> 6 \times 10^6/kg$ for double transplants), %	79	86		78	92		77	90		80	80	

^a Leukapheresis was attempted for two transplantations in nine patients in the pegfilgrastim group and in 16 patients in the filgrastim group

patients with MM tended to be higher after PEGFIL mobilization compared to FIL mobilization: $123 \times 10^6/L$ vs $72 \times 10^6/L$ ($p=0.08$), respectively.

In the PEGFIL group, a median apheresis yield of 4.9×10^6 CD34⁺ cells/kg was collected following a median (range) of 1 (1–3) apheresis cycle. In the FIL group, the respective figure was 8.5×10^6 CD34⁺ cells/kg collected following a median (range) of 2 (1–4) apheresis cycles. The target yield of CD34⁺ cells was obtained in all patients because only successful mobilizations were included in the analyses.

The majority of the patients ($n=29$) were treated with the PEGFIL dose of 12 mg. Due to the small number of patients with other doses (eight patients received 6 mg, one patient received 18 mg), no meaningful comparison between the different dose levels can be obtained. However, we observed a higher CD34⁺ cell count at onset of leukapheresis in the PEGFIL 12-mg group when compared to the PEGFIL 6-mg group (median 74, range 24.5–804.5 and median 29, range 20–79, respectively; $p=0.015$).

The patients with mobilization failure, defined as a blood CD34⁺ cell count less than 15×10^6 cells/L and/or unsuccessful harvesting, were not included in this analysis. During the study period, there were two patients with mobilization failure (5.3%) receiving PEGFIL (details given in Table 3). Between January 1996 and April 2005, there were a total of 251 patients who had been successfully mobilized with daily FIL and 18 patients (7%) who had a failed mobilization.

The target yield of CD34⁺ cells was obtained following one leukapheresis cycle in 20 of 38 (53%) patients in the PEGFIL group and in 27 of 76 (36%) patients in the FIL group. Sufficient CD34⁺ cells for double transplantation were obtained in nine (53%) and 16 (57%) MM patients in the PEGFIL and FIL groups, respectively.

High-dose therapy and autografting

As of December 2006, 32 of the 38 patients in PEGFIL group and all 76 patients in the FIL group had received high-dose therapy followed by ASCT. There were no significant difference in the infused CD34⁺ cell dose in the two groups (Table 4). Engraftment was comparable in both patient groups following transplantation with no significant differences in the recovery of blood counts (Table 4). The median time to discharge from hospital after transplantation was 17 days in the PEGFIL group and 14 days in the FIL group.

Discussion

The main finding of the present case-matched study was that a single dose of PEGFIL (6–12 mg) as an adjunct to cytotoxic chemotherapy was capable of mobilizing a

Table 3 Patient characteristics for the two patients with mobilization failure after PEGFIL mobilization

Disease	Age	Cytotoxic regimens	No. of cytotoxic cycles	Response to treatment	Mob. regimen	Max blood CD34 ⁺ count ($\times 10^6/L$)	Number of apheresis cycles	CD34 ⁺ cells collected ($\times 10^6/kg$)
Lymphoma	35	CHOP	8	Partial	CY 1 g/m ² +PEGFIL 12 mg	20.4	1	0.43
CLL	53	FC	4	Complete	CY 2 g/m ² +PEGFIL 12 mg	5.4	0	–

CHOP cyclophosphamide, doxorubicin, vincristine, and prednisone, FC fludarabine and cyclophosphamide

sufficient number of CD34⁺ cells for successful autografting in patients with different lymphoproliferative malignancies, and its mobilization capacity was comparable to that of FIL. Moreover, the stem cell collection could be begun on day +10 in both groups. No significant differences in engraftment following autografting were observed between the PEGFIL and FIL groups. Accordingly, compared with daily FIL, mobilization with a single dose of PEGFIL offers a practical and more convenient method for mobilizing stem cells.

There are a couple of important issues in the study design that are worth discussing. First, the time period was different for mobilization with PEGFIL (2005–2006) and FIL (1995–2006) and basically might have an impact on the results. This may, however, not be the case because the

mobilization protocols have remained essentially the same during all these years for the majority of our patients. Most variation in both groups has occurred in the choice of mobilization chemotherapy for patients with lymphoma where different disease-specific chemotherapies have been in use during many years (Table 1). Second, as described in the “Materials and methods” section, there have been significant changes in apheresis device and collection procedures (collection volume, target of harvested cell numbers) during the study years. This is a major limitation for making reliable comparisons of harvesting outcomes between PEGFIL and FIL groups, but does not influence our main endpoint of the study, enumeration of blood CD34⁺ cells after mobilization at the onset of apheresis. The harvesting outcomes, however, are also given (Table 2)

Table 4 ASCT and engraftment

	Pegfilgrastim group	Filgrastim group	<i>p</i> value
Transplanted patients	32	76	
Multiple myeloma	17	36	
Lymphoma	10	30	
CLL	5	10	
Transplanted CD34 ⁺ cells, $\times 10^6/kg$, median (range)			
Multiple myeloma	4.7 (2.5–8.9)	4.7 (3–8.5)	0.45
Lymphoma	5.0 (4.9–13.7)	5.9 (1.8–16.8)	0.73
CLL	4.4 (2.6–6.6)	3.5 (1.9–9.6)	0.22
Neutrophil recovery to $\geq 1 \times 10^9/L$; days, median (range)			
Multiple myeloma	11 (10–14)	11 (10–16)	0.09
Lymphoma	11 (10–12)	11 (9–20)	0.52
CLL	16 (11–16)	12 (10–13)	0.42
Platelet recovery to $\geq 20 \times 10^9/L$; days, median (range)			
Multiple myeloma	14 (11–27)	13 (11–33)	0.89
Lymphoma	19 (12–27)	13 (11–27)	0.18
CLL	18 (15–19)	13 (9–23)	0.55
Platelet recovery to $\geq 100 \times 10^9/L$; days, median (range)			
Multiple myeloma	28 (14–94)	25 (14–54)	0.65
Lymphoma	33 (16–50)	26 (12–52)	0.33
CLL	25 (19–38)	32 (13–125)	0.46
Discharge from hospital; days, median (range)			
Multiple myeloma	17 (13–24)	17 (12–41)	0.52
Lymphoma	16 (12–24)	14 (11–37)	0.55
CLL	20 (12–21)	16 (12–24)	0.39

CLL chronic lymphocytic leukemia

because we wanted to have this data for practical reasons. When comparable numbers of CD34⁺ cells were collected, regardless of the collection techniques, the engraftment data can well be compared between the two mobilization groups.

The optimal dose of PEGFIL for mobilization is still unknown. A study in eight healthy volunteers demonstrated that the neutrophil and progenitor cell response to PEGFIL administration was dose- and time-dependent [9]. In another study, in the allogeneic setting, PEGFIL at a dose of 12 mg was successfully used to mobilize and collect blood stem cells from 25 healthy family and unrelated donors [16]. In patients with chemotherapy-induced neutropenia, however, a single PEGFIL dose of 6 mg once per cycle has been shown to be as effective as multiple daily doses of FIL 5 µg/kg [8, 17]. Similarly, when used after high-dose chemotherapy and ASCT, a single 6-mg dose of PEGFIL given up to 5 days after autografting has been shown to be at least as effective as daily FIL for promoting engraftment [18, 19].

In the autograft setting, there are few single-arm studies that demonstrate the feasibility and efficacy of single-dose PEGFIL in stem cell mobilization. In patients with lymphomas, a single 6-mg dose of PEGFIL resulted in adequate mobilization of stem cells and sufficient yield after only one apheresis cycle in the majority of patients, including previously treated patients who were possibly poor mobilizers [11, 12, 20]. In patients with myeloma, PEGFIL at doses of 6–12 mg [10, 13, 21, 22] has been used successfully for stem cell mobilization. The 6-mg dose was shown to be as efficient as the 12-mg dose [13], and mobilization efficacy and harvesting outcomes were comparable between the single-dose PEGFIL and daily FIL groups [10, 13, 22]. In some studies, there has been a tendency toward lower peak CD34⁺ cell counts in blood after PEGFIL mobilization when compared to FIL mobilization [10, 22], but this is not the case in all studies [13]. After mobilization with PEGFIL, the onset of leukapheresis has been possible 2 to 3 days earlier than with FIL [13, 22]. When preparing this paper, no randomized studies had been published in the setting of autologous stem cell mobilization. In one study, a historical case-matched control group receiving FIL had been used for comparison with PEGFIL 12 mg [22]. To date, there are no published data of stem cell mobilization with PEGFIL in patients with CLL.

In our study, the dose of PEG was 12 mg in the majority of the patients (76%), but was 18 mg for one patient and 6 mg for eight patients. Our data on different dosages must be interpreted with caution due to the small patient numbers, and no meaningful comparisons between them can be done. However, in agreement with earlier reports, we found a difference in mobilization efficiency between the 6 and 12 mg doses of PEG in favour of the higher dose.

In the study of Bruns et al. [13], no dose dependence was observed between PEG doses of 6 and 12 mg in patients with MM. Accordingly, we currently mainly use the 6-mg dose as an adjunct to chemotherapy for mobilizing stem cells in patients with lymphoproliferative diseases.

In a number of previous studies of stem cell mobilization, a faster leukocyte recovery and an earlier occurrence of blood CD34⁺ peak has been found in PEGFIL-treated patients compared with patients receiving FIL [10, 13, 22]. This difference was not apparent in our study. In accordance with other previous studies [10], the median blood CD34⁺ cell count 10 days following mobilization chemotherapy and the observed CD34⁺ cell peak count tended to be lower in the PEGFIL group compared with the FIL group, but this difference was not statistically significant, either. We did not, however, study stem cell kinetics; for practical reasons, the stem cells were collected and the patients were discharged from hospital as quickly as possible. Thus, we may have missed the real peak value of blood CD34⁺ cells in many patients. Leukapheresis was started a little earlier in our patients than has been reported in other studies. In our paper, the onset of leukapheresis was a median of 10 days after chemotherapy for patients with MM, compared with 12–15 days reported by Bruns et al. [13]. In patients with lymphoma, median onset was after 12 days by us, compared to 11–14 days reported by others [11, 12]. These small differences in the onset of stem cell collection can most apparently be explained by the differences in timing the onset of growth factor administration, which has varied between days 1 and 6 from the onset of chemotherapy in the other studies [10–13, 22]. We could begin the leukapheresis on the same day +10 in both the PEGFIL and FIL groups, whereas a delay of 2 to 3 days at the onset after FIL has been observed by others [13, 22]. We also did not record for how long blood CD34⁺ cell levels persisted above the collection threshold. In some earlier trials with PEGFIL, the impression has been that high levels of blood CD34⁺ cells are maintained over a period of several days [11, 12], which allows a longer time window for stem cell collection.

In addition to the 38 successful harvestings following chemotherapy plus PEGFIL mobilization, we have had two mobilization failures, a failure rate of 5%. The corresponding historical failure rate with FIL mobilization was 7%. However, it is not possible to draw any conclusions about the possible differences in failure rates because our study was not a prospective, randomized comparison.

With regard to the harvest yields in our study, no significant comparisons can be made between PEGFIL and FIL mobilization because of the changes in harvesting device and procedures as already discussed. We also aimed to collect only the target yield and no more. In practice, the most important determinant for the CD34⁺ cell yield with harvesting is the blood CD34⁺ cell concentration at

leukapheresis [14], which emphasizes the significance of blood CD34⁺ cell count as a valid marker of mobilization efficiency. From a practical point of view, an important observation was that the target yield of CD34⁺ cells could be harvested using only a single apheresis in 53% of patients receiving PEGFIL. The respective figure in the historical controls was 36% of patients undergoing FIL mobilization. This difference was not statistically significant but confirms the feasibility and practicality of PEGFIL treatment.

PEGFIL has been reported to be well-tolerated with an adverse event profile similar to that of FIL [16, 23, 24]: bone pain and headache are the main side effects. We advised patients to take oral paracetamol if they experienced pain; however, no patient reported significant pain (or other side effects).

In summary, PEGFIL was comparable to FIL as an adjunct to chemotherapy in mobilizing stem cells in patients with lymphoproliferative diseases. Stem cell mobilization into blood, engraftment postautografting, and tolerability did not differ between the PEGFIL and FIL groups. Compared with a daily application of FIL, a single dose of PEGFIL is more practical, facilitates treatment compliance, and increases patient convenience.

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