Predictors for Successful Mobilization of Peripheral Blood Progenitor Cells with ESHAP + G-CSF in Patients with Pretreated Non-Hodgkin's Lymphoma

Jin-Hwang Liu[1]*, Chih-Cheng Chen[1,2], Li-Yen Bai[1,3], Shu-Chauo Chao[1], Mu-Shin Chang[1], Jeong-Shi Lin[4]

Divisions of [1]Hematology/Oncology and [4]Transfusion Medicine, Taipei Veterans General Hospital, National Yang-Ming University School of Medicine, Taipei, [2]Graduate Institute of Clinical Medical Sciences, Chang Gung University, Taoyuan, and [3]Division of Hematology and Oncology, China Medical University Hospital, China Medical University, Taichung, Taiwan, R.O.C.

Background: ESHAP (etoposide/methylprednisolone/cytarabine/cisplatin) plus granulocyte-colony stimulating factor (G-CSF) is an effective regimen of therapy for advanced non-Hodgkin's lymphoma (NHL) and peripheral blood progenitor cell (PBPC) mobilization. However, the timing of PBPC harvest following immobilization and factors to predict optimal PBPC yield remain to be explored. We herein analyzed the factors potentially correlated to optimal PBPC mobilization.

Methods: Twenty patients with pretreated advanced NHL were recruited and mobilized with ESHAP + G-CSF followed by 2 leukapheresis, which were initiated once the white blood cell count (WBC) in peripheral blood exceeded 10×10^9/L.

Results: Total $CD34^+$ cells collected by 2 leukapheresis were $> 2 \times 10^6$/kg body weight in 16 patients; between 1.0 and 2.0×10^6/kg in another 3, and $< 1 \times 10^6$/kg in the remaining 1 patient. The pre-leukapheresis peripheral blood $CD34^+$ cell counts, available for 28 leukapheresis, correlated linearly with the $CD34^+$ cell yields ($r^2 = 0.870$, $p < 0.001$). The $CD34^+$ cell yield with pre-leukapheresis peripheral blood $CD34^+$ cell count $\geq 50 \times 10^6$/L was higher than that with $< 50 \times 10^6$/L (5.60 ± 4.32 *vs.* $0.96 \pm 0.56 \times 10^6$/kg/leukapheresis; $p = 0.004$). Other factors predictive of favorable PBPC yield included preceding chemotherapy cycles < 6 and peripheral blood WBC $> 3{,}500/\mu L$ on the day of mobilization chemotherapy ($p = 0.032$ and 0.013, respectively).

Conclusion: The pre-leukapheresis peripheral blood $CD34^+$ cell count correlates well with PBPC yields. Less than 6 chemotherapy cycles before mobilization and adequate peripheral blood WBC before mobilization chemotherapy also predict a favorable PBPC yield. [*J Chin Med Assoc* 2008;71(6):279–285]

Key Words: autologous transplantation, CD34, leukapheresis, non-Hodgkin's lymphoma, peripheral blood progenitor cell, stem cell mobilization

Jin-Hwang Liu and Chih-Cheng Chen contributed equally to this work.

Introduction

High-dose chemotherapy followed by autologous hematopoietic progenitor cell transplantation (AHPCT) has become an established modality of treatment for patients with refractory or high-risk non-Hodgkin's lymphoma (NHL) as well as a wide variety of hematologic malignancies.[1–3] With the advantages of a relatively easy collection procedure and short duration to engraftment, peripheral blood progenitor cells (PBPCs) or peripheral blood stem cells (PBSCs) are now preferred over bone marrow progenitor cells as a source of

*Correspondence to: Dr Jin-Hwang Liu, Division of Hematology/Oncology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: jhwang.liu@msa.hinet.net • Received: August 30, 2007 • Accepted: February 19, 2008

AHPCT.[4] However, successful engraftment in AHPCT relies much on the cell dose of PBPCs.[5] Clinical trials have shown that engraftment can be accelerated by infusion of large dose of progenitor cells.[6] With respect to a safe cell dose, a number of studies have demonstrated that a $CD34^+$ cell dose of 2×10^6/kg or higher in AHPCT is associated with excellent hematopoietic recovery.[6–8]

A variety of regimens have been used successfully in NHL patients for PBPC mobilization, including hematopoietic growth factors with or without cyclophosphamide and combinations of granulocyte-colony stimulating factor (G-CSF) and chemotherapy used to treat NHL.[9–12] Nonetheless, the optimal timing for PBPC harvest following mobilizing therapy remains undetermined. Also, since the infused $CD34^+$ cell dose influences the outcome of engraftment,[6–8] how to maximize $CD34^+$ cell yield has continued to be studied. Efforts have been devoted to use peripheral blood $CD34^+$ cell count, total white blood cell count (WBC) or both as surrogate markers to start leukapheresis for maximizing $CD34^+$ cell collection.[13,14] The $CD34^+$ cell count seems to reflect more directly the resultant $CD34^+$ cell yield.[13,14] Other factors such as age, interval between treatment and harvest, preceding chemotherapy and radiotherapy, dose of chemotherapy used for PBPC mobilization, and PB platelet count on the first day of PBPC collection have also been reported to influence PBPC yield.[13,15–17] However, some of the reported results are inconsistent, especially among studies using different mobilizing regimens.

ESHAP (etoposide/methylprednisolone/cytarabine/cisplatin) plus G-CSF has been shown to be effective for mobilizing PBPCs in NHL patients.[11,18] Notwithstanding, factors impacting on maximizing PBPC collection remain to be explored. We conducted an analysis on 20 consecutive advanced NHL patients for whom PBPCs were harvested following ESHAP chemotherapy and G-CSF. The correlation of the pre-apheresis peripheral blood $CD34^+$ cell count on the collection day to the apheresed $CD34^+$ cell yield was analyzed. The predictability of factors for $CD34^+$ cell yield along with the feasibility of this mobilizing regimen are discussed.

Methods

Patients

The patients' characteristics are listed in Table 1. Twenty NHL patients were recruited between March 2003 and September 2006, underwent ESHAP chemotherapy plus G-CSF to mobilize PBPCs and were analyzed for factors potentially correlated to the PBPC yields. There were 10 males and 10 females, with a median age of 48 years (range, 19–72 years). All patients had high-risk diseases that warranted high-dose chemotherapy rescued by AHPCT. Before PBPC mobilization, all patients had received chemotherapy of 4 or more cycles (range, 4–7 cycles) of CHOP (cyclophosphamide, adriamycin, vincristine, prednisolone), but still had residual tumor. One patient had received 6 additional cycles of high-dose methotrexate for brain lymphoma and 2 other patients had received 1–3 additional cycles of ESHAP chemotherapy in addition to the mobilizing ESHAP chemotherapy.

Table 1. Characteristics of the 20 patients

Sex (*n*)	
Male	10
Female	10
Age (yr)	
Median	48
Range	19–72
WHO NHL classification (*n*)	
Diffuse large B cell	17
Primary mediastinal B cell	3
Stage at harvest (*n*)	
II bulky	3
III	11
IV	6*
Number of previous CT cycles	
Mean	5
Range	4–10
Previous RT (*n*)	
Yes	0
No	20
Interval between last CT to mobilization CT (d)	
Mean	29.8
Range	18–43

**Including 2 patients with bone marrow involvement and 1 with extensive hepatic involvement. WHO = World Health Organization; NHL = non-Hodgkin's lymphoma; CT = chemotherapy; RT = radiotherapy.*

All the patients were treated in Taipei Veterans General Hospital. The study was conducted in accordance with the institutional regulations and informed consent was obtained from each patient before enrolment in the study.

Mobilization, leukapheresis and storage

The mobilizing method and timing of leukapheresis have been described previously.[18] Intravenous ESHAP (methylprednisolone 500 mg/day on days 1–4, etoposide 40 mg/m^2/day on days 1–4, cisplatin 25 mg/m^2/day continuous infusion on days 1–4, and cytosine

arabinoside 2 g/m^2 on day 5) was administered and followed by 5 μg/kg/day subcutaneous injection of G-CSF from day 7 until the day when PBPC harvest was completed.

All 20 patients underwent daily blood cell count examination starting from day 6, with day 1 referring to the day when ESHAP chemotherapy was initiated. Two consecutive daily leukaphereses were started once peripheral blood WBC exceeded 10×10^9/L after a nadir. Leukapheresis was conducted using the COBE Spectra Version 6.1 cell separator (COBE BCT, Lakewood, CO, USA). Anticoagulant citrate dextrose solution was used to prevent clotting. Ten liters of blood were processed for each leukapheresis. The product obtained was mixed with DMSO (Merck, Darmstad, Germany) in autologous plasma to a final concentration of 10%. By programmed freezing, the cells were subsequently cryopreserved in liquid nitrogen.

Enumeration of CD34+ cells

The circulating CD34+ cell count was determined in peripheral blood sampled in the early morning of each leukapheresis day. Mononuclear cells were stained with phycoerythin (PE)-conjugated anti-CD34 (anti-HPCA-2) mouse monoclonal antibody and counterstained with fluorescein isothiocyanate (FITC)-conjugated anti-CD45 mouse monoclonal antibodies (Becton Dickinson, San Jose, CA, USA). Simultest™ control γ1/γ2a (Becton Dickinson) was used as a negative control to quantify the non-antigen-specific antibody binding. More than 60,000 cells were detected using a FACS flow cytometer and analyzed with Cellquest software (Becton Dickinson).

Statistical analysis

SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Pearson's correlation analysis was applied for evaluating the relevance of pre-leukapheresis peripheral blood CD34+ cell count and CD34+ cell yield per leukapheresis. The Mann-Whitney test was used to test the significance of difference between CD34+ cell yields of cohorts with peripheral blood CD34+ cell count $\geq 50 \times 10^6$/L and $< 50 \times 10^6$/L. The cut-off value of peripheral blood CD34+ cell count was set at 50×10^6/L. The mean CD34+ yield of 2 leukaphereses in the cohort with less than the cut-off value in pre-leukspheresis peripheral blood CD34+ cells was 1.80×10^6/kg, a value that is less than the safe CD34+ cell dose (2.0×10^6/kg) for PBPC autografting.[6–8] To evaluate other factors affecting the CD34+ cell yield per leukapheresis, a 2×2 crosstable with χ^2 test was used. Statistical significance was considered for all tests when $p < 0.05$.

Results

Leukapheresis and yield

For the 20 patients, the first day when leukapheresis started ranged from day 12 to day 18 (median, day 15), with day 1 referring to the day when ESHAP chemotherapy was initiated. Two leukaphereses were performed for each patient. The mean ± standard error of the total mononuclear cells and the total CD34+ cells harvested for the 20 patients were $6.48 \pm 3.52 \times 10^8$/kg and $14.4 \pm 16.7 \times 10^6$/kg, respectively. Fourteen (70%) patients had their CD34+ cell yield on the first leukapheresis day exceeding 2×10^6 cells/kg. Sixteen patients (80%) had CD34+ cell yield of 2 leukaphereses above 2×10^6/kg body weight; another 3 (15%) between 1–2×10^6/kg and the remaining 1 (5%) below 1×10^6/kg.

Correlation of pre-leukapheresis peripheral blood CD34+ cell count to PBPC yield

The pre-leukapheresis peripheral blood CD34+ cell counts on the PBPC collection days were available among 28 of the 40 leukaphereses. The mean CD34+ cells collected per leukapheresis was $6.70 \pm 7.46 \times 10^6$/kg. A significant correlation between the pre-leukapheresis peripheral blood CD34+ cell count and the CD34+ cell yield of each leukapheresis was shown by a linear regression analysis ($r^2 = 0.870$, $p < 0.0001$; Figure 1A). The mean ± standard error of CD34+ cell yield of patients with pre-leukapheresis peripheral blood CD34+ cell count $\geq 50 \times 10^6$/L was $5.60 \pm 4.32 \times 10^6$/kg/leukapheresis, while that of patients with pre-leukapheresis peripheral blood CD34+ cell count $< 50 \times 10^6$/L was $0.96 \pm 0.56 \times 10^6$/kg/leukapheresis (median, 0.56×10^6/kg/leukapheresis). The CD34+ yield in the group with pre-leukapheresis peripheral blood CD34+ cell count $\geq 50 \times 10^6$/L had a significantly higher total CD34+ cell yield ($p < 0.001$; Figure 1B).

Factors affecting CD34+ cell yield

Data were analyzed to determine possible factors affecting the CD34+ cell yield (Table 2). Patients who experienced 6 or more courses of preceding chemotherapy had lower CD34+ cell yield ($p = 0.032$). In addition, patients with > 3,500/μL of peripheral blood WBC before mobilizing chemotherapy had better CD34+ cell yield than those with < 3,500/μL. On the other hand, sex, age or whether bone marrow was involved at the initial diagnosis did not significantly affect PBPC yield. Peripheral blood hemoglobin and platelet count on day 1 of mobilization, chemotherapy, severity of neutropenia and thrombocytopenia after ESHAP, along with the time required for white cells

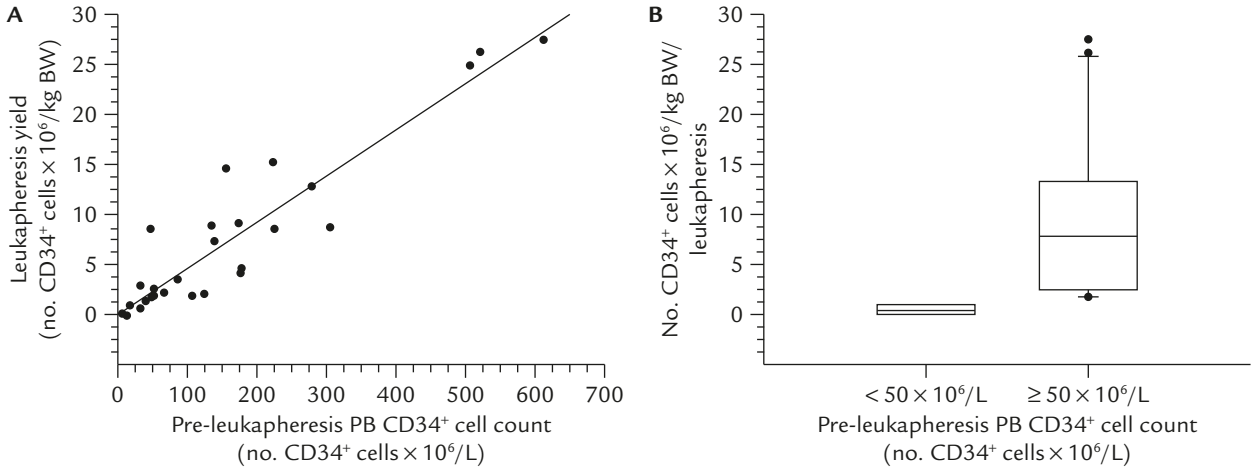

Figure 1. The correlation between same-day pre-leukapheresis peripheral blood (PB) $CD34^+$ cell count and $CD34^+$ cell yield. (A) Linear regression made by plotting $CD34^+$ cell yield against pre-leukapheresis peripheral blood $CD34^+$ cell count, with $r^2 = 0.870$ and $p < 0.001$ calculated by variance analysis. (B) $CD34^+$ cell yields per leukapheresis illustrated graphically in box plots with pre-leukapheresis peripheral blood $CD34^+$ count $< 50 \times 10^6$/L and $\geq 50 \times 10^6$/L. Dots mark outliers, capped bars indicate 5th and 95th percentiles, extent of boxes indicates 25th and 75th percentiles, and lines inside boxes indicate means. ($5.60 \pm 4.32 \times 10^6$/kg/leukapheresis *vs.* $0.96 \pm 0.56 \times 10^6$/kg body weight/leukapheresis; $p < 0.001$, Mann-Whitney test.)

to recover from nadir to number above 10×10^9/L, all of which possibly represent marrow-reserving capacity, did not affect PBPC yield either.

Engraftment after high-dose therapy in NHL patients

Sixteen of the 20 NHL patients later proceeded to high-dose chemotherapy and AHPCT. Four patients did not proceed to AHPCT due to disease progression shortly after PBPC harvesting (in 1 patient) or complete remission achieved after chemotherapy (in 2 patients) or inadequate PBPC ($< 1.0 \times 10^6$/kg) harvested (in 1 patient). Among the 16 patients undergoing PBPC autografting, 14 had $CD34^+$ cell dose $\geq 2.0 \times 10^6$/kg and the other 2 had $CD34^+$ cell doses of 1.26 and 1.60×10^6/kg, respectively. The median time to myeloid engraftment (defined as absolute neutrophil count $\geq 0.5 \times 10^9$/L for 3 consecutive days) was 10 days (range, 9–11 days), while engraftment of platelets (defined as platelet count $\geq 20 \times 10^9$/L for 7 consecutive days without transfusional support) was seen at a median of 15 days (range, 12–18 days).

Discussion

As infused $CD34^+$ cell dose correlates well with hematopoietic recovery and transplant outcome in PBPC transplantation, adequate PBPC collection has become a prerequisite for successful autograft. Hematopoietic progenitor cells can be mobilized into the circulation by G-CSF, chemotherapy or both. To maximize efficient PBPC yield, the timing for PBPC collection after these mobilizations is critical. Some criteria have been utilized to determine when to initiate collection. Among them, circulating peripheral blood $CD34^+$ cell count has been a predictor of PBPC yield mobilized with regimens other than the ESHAP + G-CSF used in this study.[13,14,19] Using ESHAP + G-CSF, we hereby proved that circulating peripheral blood $CD34^+$ cell count remains a predictor of $CD34^+$ cell yield.

Choosing mobilizing modality has been a field of controversy for years. The jury on the Second International Consensus Conference on High-Dose Therapy with Hematopoietic Stem Cell Transplantation in Aggressive NHL recommended that chemotherapy plus cytokines, rather than either alone, should be used to mobilize hematopoietic stem cells.[20] Based on that recommendation, high-dose cyclophosphamide followed by G-CSF has been traditionally used as a mobilization regimen.[20] Additionally, combinations of NHL treatment regimen and growth factors, which benefit patients with both tumor-killing and PBPC mobilization, were employed in increasing frequency and demonstrated to be effective mobilization regimens.[9,11,12,18] Some of them, including ESHAP + G-CSF, appeared to be superior in PBPC yield.[9,11,12]

In this study, using ESHAP + G-CSF for NHL patients as a PBPC-mobilizing regimen, the mean $CD34^+$ cells collected per leukapheresis was $7.2 \pm 8.3 \times 10^6$/kg.

Table 2. Patient characteristics affecting CD34+ cell yield in patients with non-Hodgkin's lymphoma

	Total CD34+ cell yield		*p**
	$< 2 \times 10^6$/kg BW	$\geq 2 \times 10^6$/kg BW	
Sex			1.00
Male	2	8	
Female	2	8	
Age			0.675
> 50 yr	1	5	
≤ 50 yr	3	11	
Number of previous CT cycles			0.032
< 6	1	14	
≥ 6	3	2	
WBC before mobilizing CT			0.013
≤ 3,500/μL	3	1	
> 3,500/μL	1	15	
Hb before mobilizing CT			0.549
≤ 11.0 g/dL	2	4	
> 11.0 g/dL	2	12	
Platelet before mobilizing CT			0.509
≤ 150,000/μL	1	2	
> 150,000/μL	3	14	
BM involvement at initial diagnosis			1.00
Yes	1	0	
No	3	15	
Nadir of ANC after ESHAP			0.509
≤ 1,000/μL	1	2	
> 1,000/μL	3	14	
Nadir of platelet after ESHAP			0.285
≤ 70,000/μL	1	10	
> 70,000/μL	3	6	

χ^2 test. BW = body weight; CT = chemotherapy; WBC = white blood cell; Hb = hemoglobin; BM = bone marrow; ANC = absolute neutrophil count.

The result is comparable with those in other reports.[11,12,18] Among them, Lee et al reported that a mean of 6.0×10^6 CD34+ cells/kg/leukapheresis was mobilized with ESHAP + G-CSF with a mean of 6 cycles of previous chemotherapy in patients with relapsed or refractory lymphoma.[11] A better CD34+ cell yield was found in patients treated with ESHAP + G-CSF than in those who underwent high-dose cyclophosphamide + G-CSF.[11] We confirmed that ESHAP + G-CSF is not only an active alternative therapy for advanced NHL but is also effective in progenitor cell mobilization.[11,21]

To mobilize PBPCs with ESHAP + G-CSF in NHL patients, one of the significant findings of this study is that the pre-leukapheresis peripheral blood CD34+ cell count on the day of PBPC collection reliably predicted CD34+ cell yield. The pre-leukapheresis peripheral blood CD34+ cell count of 50×10^6/L on the day of PBPC collection could be regarded as a distinctly safe threshold guaranteeing successful PBPC harvesting.

Factors influencing progenitor cell yield have been extensively studied in numerous trials.[7,13,17,22] However, it is still difficult to draw a definite conclusion regarding these factors from these studies owing to the heterogeneity in the patient population in terms of their different disease characteristics. Nonetheless, there still exists the general consensus that drugs with stem cell-toxic properties, such as melphalan, cyclophosphamide, carmustine, lomustine and mechlorethamine, are associated with inferior stem cell yield.[7,16,23] In our patients, the only 2 factors with a favorable impact on the harvest were less than 6 preceding chemotherapy cycles and more than 3,500/μL for pre-mobilization WBC, which might reflect bone marrow reserve. Since the CHOP regimen has always been the frontline treatment for our patients in this study, it is unknown

whether the aggregate effect of all the chemotherapeutic agents or the cumulative dose of cyclophosphamide played the major role in impairing the $CD34^+$ cell yield.

In conclusion, with PBPC mobilization using ESHAP + G-CSF, pre-leukapheresis peripheral blood $CD34^+$ cell count $\geq 50 \times 10^6$/L on the day of collection was a good indicator for initiating stem cell harvesting. We confirmed that ESHAP + G-CSF is an efficient mobilization regimen for NHL patients. High-dose chemotherapy followed by AHPCT has been proven to be superior to conventional chemotherapy in patients with chemosensitive relapse of aggressive NHL.[24] Also patients with NHL may benefit from high-dose chemotherapy followed by AHPCT as part of first-line therapy.[2] It is possible to decide before 6 cycles of frontline chemotherapy whether patients with NHL will undergo AHPCT and have PBPC harvested. From our data, ESHAP + G-CSF is recommended for PBPC harvesting before 6 cycles of chemotherapy with CHOP or equivalent regimen once high-dose chemotherapy followed by AHPCT is contemplated. However, PBPC mobilization after 6 cycles of frontline chemotherapy may still possibly have suboptimal quantity of $CD34^+$ cells adequate for autograft.

Acknowledgments

This work was supported by grant V96-C1-142 from Taipei Veterans General Hospital, Taiwan.

References

1. Barlogie B, Shaughnessy J, Tricot G, Jacobson J, Zangari M, Anaissie E, Walker R, et al. Treatment of multiple myeloma. *Blood* 2004;103:20–32.
2. Schmitz N, Buske C, Gisselbrecht C. Autologous stem cell transplantation in lymphoma. *Semin Hematol* 2007;44:234–45.
3. Majhail NS, Weisdorf DJ, Defor TE, Miller JS, McGlave PB, Slungaard A, Arora M, et al. Long-term results of autologous stem cell transplantation for primary refractory or relapsed Hodgkin's lymphoma. *Biol Blood Marrow Transplant* 2006; 12:1065–72.
4. Gratwohl A, Passweg J, Baldomero H, Urbano-Ispizua A. European Group for Blood and Marrow Transplantation. Hematopoietic stem cell transplantation activity in Europe 1999. *Bone Marrow Transplant* 2001;27:899–916.
5. Ergene U, Cagirgan S, Pehlivan M, Yilmaz M, Tombuloğlu M. Factors influencing engraftment in autologous peripheral hematopoetic stem cell transplantation (PBSCT). *Transfus Apher Sci* 2007;36:23–9.
6. Ketterer N, Salles G, Raba M, Espinouse D, Sonet A, Tremisi P, Dumontet C, et al. High $CD34^+$ cell counts decrease hematological toxicity of autologous peripheral blood progenitor cell transplantation. *Blood* 1998;91:3148–55.
7. Haas R, Mohle R, Fruhauf S, Goldschmidt H, Witt B, Flentje M, Wannenmacher M, et al. Patient characteristics associated with successful mobilizing and autografting of peripheral blood progenitor cells in malignant lymphoma. *Blood* 1994;83: 3787–94.
8. Kiss JE, Rybka WB, Winkelstein A, deMagalhaes-Silverman M, Lister J, D'Andrea P, Ball ED. Relationship of $CD34^+$ cell dose to early and late hematopoiesis following autologous peripheral blood stem cell transplantation. *Bone Marrow Transplant* 1997;19:303–10.
9. Assouline S, Sylvestre MP, Carriere P, Shustik C, Laneuville P. Comparison of peripheral blood progenitor cell yield from standard chemotherapy used in the treatment of lymphoid malignancies and high-dose cyclophosphamide: a retrospective review of 141 patients. *Transfusion* 2006;46:174–9.
10. Pavone V, Gaudio F, Guarini A, Perrone T, Zonno A, Curci P, Liso V. Mobilization of peripheral blood stem cells with high-dose cyclophosphamide or the DHAP regimen plus G-CSF in non-Hodgkin's lymphoma. *Bone Marrow Transplant* 2002;29: 285–90.
11. Lee JL, Kim S, Kim SW, Kim EK, Kim SB, Kang YK, Lee J, et al. ESHAP plus G-CSF as an effective peripheral blood progenitor cell mobilization regimen in pretreated non-Hodgkin's lymphoma: comparison with high-dose cyclophosphamide plus G-CSF. *Bone Marrow Transplant* 2005;35:449–54.
12. Watts MJ, Ings SJ, Leverett D, MacMillan A, Devereux S, Goldstone AH, Linch DC. ESHAP and G-CSF is a superior blood stem cell mobilizing regimen compared to cyclophosphamide 1.5 g/m^2 and G-CSF for pre-treated lymphoma patients: a matched pairs analysis of 78 patients. *Br J Cancer* 2000;82:278–82.
13. Ikeda K, Kozuka T, Harada M. Factors for PBPC collection efficiency and collection predictors. *Transfus Apher Sci* 2004; 31:245–59.
14. Chapple P, Prince HM, Quinn M, Bertoncello I, Juneja S, Wolf M, Januszewicz H, et al. Peripheral blood $CD34^+$ cell count reliably predicts autograft yield. *Bone Marrow Transplant* 1998;22:125–30.
15. Ketterer N, Salles G, Moullet I, Dumontet C, ElJaafari-Corbin A, Tremisi P, Thieblemont C, et al. Factors associated with successful mobilization of peripheral blood progenitor cells in 200 patients with lymphoid malignancies. *Br J Haematol* 1998;103: 235–42.
16. Moskowitz CH, Glassman JR, Wuest D, Maslak P, Reich L, Gucciardo A, Coady-Lyons N, et al. Factors affecting mobilization of peripheral blood progenitor cells in patients with lymphoma. *Clin Cancer Res* 1998;4:311–6.
17. Zimmerman TM, Michelson GC, Mick R, Grinblatt DL, Williams SF. Timing of platelet recovery is associated with adequacy of leukapheresis product yield after cyclophosphamide and G-CSF in patients with lymphoma. *J Clin Apheresis* 1999; 14:31–4.
18. Petit J, Boque C, Cancelas JA, Sarrà J, Muñoz J, Garcia J, Grañena A. Feasibility of ESHAP + G-CSF as peripheral blood hematopoietic progenitor cell mobilisation regimen in resistant and relapsed lymphoma: a single-center study of 22 patients. *Leukemia Lymphoma* 1999;34:119–27.
19. Elliott C, Samson DM, Armitage S, Lyttelton MP, McGuigan D, Hargreaves R, Giles C, et al. When to harvest peripheral-blood stem cells after mobilization therapy: prediction of $CD34^+$ cell yield by preceding day $CD34^+$ concentration in peripheral blood. *J Clin Oncol* 1996;4:970–3.
20. Shipp MA, Abeloff MD, Antman KH, Carroll G, Hagenbeek A, Loeffler M, Montserrat E, et al. International Consensus Conference on High-Dose Therapy with Hematopoietic Stem Cell

Transplantation in Aggressive Non-Hodgkin's Lymphomas: report of the jury. *J Clin Oncol* 1999;17:423–9.
21. Velasquez WS, McLaughlin P, Tucker S, Hagemeister FB, Swan F, Rodriguez MA, Romaguera J, et al. ESHAP—an effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study. *J Clin Oncol* 1994;12: 1169–76.
22. Koumakis G, Vassilomanolakis M, Hatzichristou H, Barbounis V, Filis J, Papanastasiou K, Moraki M, et al. Predictive factors affecting mobilization and peripheral blood stem cell collection using single apheresis for rescuing patients after high-dose chemotherapy in various malignancies. *Bone Marrow Transplant* 1996;18:1065–72.
23. Drake M, Ranaghan L, Morris TC, Nolan L, Desai ZR, Irvine AE, Jordan A, et al. Analysis of the effect of prior therapy on progenitor cell yield: use of a chemotherapy scoring system. *Br J Haematol* 1997;98:745–9.
24. Strehl J, Mey U, Glasmacher A, Djulbegovic B, Mayr C, Gorschlüter M, Ziske C, et al. High-dose chemotherapy followed by autologous stem cell transplantation as first-line therapy in aggressive non-Hodgkin's lymphoma: a meta-analysis. *Haematologica* 2003;88:1304–15.