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ORIGINAL ARTICLE

# Efficient mobilization of PBSC with vinorelbine/G-CSF in patients with malignant lymphoma

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**High-dose chemotherapy (HDT) and hematopoietic SCT are effective in patients with relapsing or refractory malignant lymphoma. Collection of sufficient numbers of stem cells is a prerequisite for such a therapy. In a pilot trial, we evaluated the feasibility of stem cell mobilization with vinorelbine/G-CSF in patients with lymphoma, a regimen allowing precise timing and harvesting of sufficient stem cells in myeloma patients. Forty-five patients with lymphoma received vinorelbine 35 mg/m$^2$ i.v. on day 1 and G-CSF 10 μg/kg/day s.c., divided in two daily doses from day 4 until collection. Stem cell collection was successfully performed in 43 patients (96%) with a median of 3.6 × 10$^6$ CD34$^+$ cells/kg (range: 1.4–16) in the collected product. In 28 patients (62%), the first stem cell apheresis was performed on day 8, and for 28 patients a sufficient stem cell yield was reached with one apheresis only. All 43 patients underwent high-dose chemotherapy with BEAM and auto-SCT with hematological recovery on time and without unexpected toxicity. In conclusion, vinorelbine/G-CSF allows accurate timing and safe harvesting of sufficient stem cells in patients with malignant lymphoma.**

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## Introduction

High-dose chemotherapy (HDT) followed by autologous hematopoietic SCT (auto-SCT) is an established treatment for refractory or relapsed non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD).[1,2] High-dose CY (4–7 g/m$^2$) and G-CSF is commonly used to mobilize hematopoietic stem cells when mobilization and collection could not be performed after a previous polychemotherapy cycle.[3] To ensure the safe use of CY in higher doses, nonhematological toxicity may be prevented by hyperhydration and the selective urinary tract protectant mesna. This regimen, however, usually requires hospitalization. In addition, up to 30% of patients following CY and G-CSF have to be admitted to the hospital owing to neutropenic fever.[4] CD34$^+$ stem cells in blood peak 2–3 weeks after mobilization with CY/G-CSF, or with polychemotherapy and G-CSF.[5] The peak values of CD34$^+$ cells over time vary considerably, demanding close monitoring of WBC and CD34$^+$ cell counts over several days to ensure optimal collection.[6]

We reported earlier on the safety and feasibility of collection of PBSC after the administration of vinorelbine/G-CSF in patients with multiple myeloma, with accurate timing of stem cell collection at day 8 after the start of mobilization.[7] Others have shown the potential of ifosfamide/vinorelbine-based chemotherapy with G-CSF for stem cell mobilization in patients with malignant lymphoma,[8] as well as the activity of vinorelbine in pretreated HD and NHL.[9–11]

In this single center phase I/II trial, we assessed the feasibility of stem cell mobilization with vinorelbine/G-CSF in lymphoma patients. We compared the data of these groups of patients with malignant lymphoma mobilized with CY/G-CSF or G-CSF after polychemotherapy. As vinorelbine can be administered in an outpatient setting, we also analyzed the costs of this mobilizing scheme in comparison to the mobilization with CY/G-CSF.

## Patients and methods

### *Study design*

This phase I/II trial was performed at a single, rather small transplantation center. The aim of the study was to assess the efficacy, safety and cost effectiveness of vinorelbine in combination with G-CSF for the mobilization of PBSC for subsequent auto-SCT in patients with malignant lymphoma.

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The trial was carried out in accordance with Good Clinical Practice and the stipulations of the declaration of Helsinki (1996). The study protocol was approved by the local ethics committee and written informed consent was obtained.

*Patients*
From September 1999 to November 2007, all patients with either HD or NHL, who were candidates for auto-SCT and had given written informed consent, were mobilized with vinorelbine/G-CSF. Patients who were mobilized from November 1994 to November 2007 after polychemotherapy or CY, owing to other study protocols, served as control group. We registered patient characteristics before mobilization (that is, age at mobilization, sex, histology, stage at diagnosis, indication for transplantation, number of chemotherapy lines before mobilization, months from diagnosis to mobilization and remission status before mobilization), mobilization data (that is, mobilization regimen, complications of mobilization, days of G-CSF application, days to apheresis, WBC count, CD34% and $CD34^+$ cells $\times 10^6$/l measured in the blood on all days of apheresis, number of aphereses needed, $CD34^+$ cells $\times 10^6$/kg body weight) as well as transplantation data (i.e., days of hospitalization, days with fever $>38\,^{\circ}C$, time until neutrophil (ANC) recovery $>0.5\times10^9$/l, time to platelet recovery $>20\times10^9$/l, number of red cell and platelet units transfused, TRM and remission status at day 100 after transplantation).

*PBSC mobilization with vinorelbine*
Vinorelbine was administered at a dose of $35\,mg/m^2$ i.v. over 5–10 min on day 1 in the outpatient clinic. Hydration and antiemetic drugs were not used. G-CSF 10 μg/kg/day s.c. divided into a morning and an evening dose was started on day 4 and continued daily until aphereses led to a sufficient number of $CD34^+$ cells in the product.

*PBSC mobilization in control patients*
Data from two control groups were compared to the data of the vinorelbine group. The first group was treated with 2–6 cycles of combination chemotherapy, and then mobilized with high-dose CY ($4\,g/m^2$) and G-CSF 10 μg/kg per day s.c., divided into two daily doses, starting on day 4 and continued until completion of harvesting, according to a protocol, formerly used as standard, at our institute. Two days of hospitalization were required for hyperhydration, administration of CY, mesna and antiemetic therapy with ondansetrone.

In the second control group, patients were mobilized with G-CSF 10 μg/kg per day s.c. starting on day 6 of the first to the third cycles of chemotherapy with (R)-DHAP, (R)-ICE, ESHAP or (R)-EPOCH, and continued until the last apheresis.

*$CD34^+$ PBSC enumeration*
Absolute numbers of $CD34^+$ cells in peripheral blood and apheresis samples were enumerated by flow cytometry using an FACSCalibur (BD Biosciences, San Jose, CA, USA). Initially, a dual-platform assay was employed according to the Milan protocol, that is, the percentage of $CD34^+$ cells was determined as a fraction of all leukocytes on the basis of light scatter characteristics, and was combined with the absolute WBC count from a hematology cell analyzer (Sysmex XE-2100, Sysmex Digitana, Horgen, Switzerland). From 2001, absolute counts of viable $CD34^+$ cells were directly derived from the flow cytometer by using fluorescent counting beads (Trucount, BD Biosciences) following the sequential gating strategy of the ISHAGE protocol exactly as described earlier.[12]

*Collection and cryopreservation of PBSCs*
To determine the optimal time point of PBSC harvesting, circulating WBC and $CD34^+$ cells were monitored daily in the peripheral blood, starting on day 8 after the administration of vinorelbine or CY, and from day 10 following polychemotherapy regimens. Leukapheresis was performed when the peripheral $CD34^+$ cell count was $\geqslant20\times10^6$/l, using a COBE Spectra separator (COBE, Lakewood, CO, USA) or an Amicus cell separator (Baxter Healthcare, Deerfield, IL, USA), processing 15 l of blood through an inguinal central venous access device with continuous flow. If the first apheresis yielded $<2.5\times10^6$ $CD34^+$ cells/kg, an additional apheresis was performed on the next day, whereas G-CSF application was pursued. Apheresis products were frozen in an Icecube controlled rate freezer (Sylab, Neupurkersdorf, Austria) with the cryoprotectant DMSO at a final concentration of 7.5%, and stored in the vapor phase of liquid nitrogen until transplantation.

*Pre-transplantation conditioning regimen*
All patients were administered HDT according to the BEAM-regimen (BCNU $300\,mg/m^2$ i.v. on day −6, etoposide $200\,mg/m^2$ i.v. per day on days −6 to −3, cytarabine $200\,mg/m^2$ i.v. twice daily on days −6 to −3 and melphalan $140\,mg/m^2$ i.v. on day −2) followed by auto-SCT on day 0. Filgrastim 5 μg/kg per day s.c. was given from day 5 onwards until neutrophil granulocytes reached $0.5\times10^9$/l on two consecutive days.

*Cost analysis*
Costs for mobilization with vinorelbine/G-CSF were compared with the control group mobilized with CY/G-CSF. Taken into account were costs of hospitalization for the application of CY and mesna and of antiemetics, G-CSF, WBC and CD34 measurements before harvesting. All other procedures were not considered, as they do not differ between the two mobilization schemes.

*Statistical analysis*
The SPSS version 10.0 (SPSS Schweiz AG, Zürich, Switzerland) was used to calculate *P*-values with the Mann–Whitney and Wilcoxon *U*-tests.

## Results

*Patient characteristics*

Forty-five patients with either HD or NHL, who were candidates for auto-SCT, were mobilized with vinorelbine and G-CSF according to the protocol. Data from 23 patients, who were mobilized after polychemotherapy or CY, were collected and served as control group. The main characteristics of patients are presented in Table 1. There was no statistically significant difference between the groups.

*Mobilization data*

Out of 45 patients mobilized after vinorelbine, 39 (87%) reached $CD34^+$ cell counts $\geqslant 20 \times 10^6$/l in the peripheral blood compared to 6 out of 9 patients (66%; not significant (NS)) after CY, and 13 out of 14 patients (93%; *NS*) in the polychemotherapy group, as an indicator to start collection. The time point of collection was significantly more accurately predictive after mobilization with vinorelbine than in the other two groups, as shown in Figure 1. The time to first apheresis in patients mobilized with vinorelbine/G-CSF was significantly shorter compared with those patients mobilized with CY/G-CSF ($P = 0.007$) and those mobilized with G-CSF after polychemotherapy ($P = 0.001$). There was no difference between the latter two groups. Therefore, the number of days of G-CSF varied significantly between the vinorelbine group and the CY ($P = 0.011$) and polychemotherapy groups ($P = 0.001$). The mobilization data are summarized in Table 2. There was no statistically significant difference in the other parameters. Of the 45 patients mobilized with vinorelbine/G-CSF, 38 (84%) patients accomplished a stem cell collection of $\geqslant 2.5 \times 10^6$ $CD34^+$ cells/kg compared to 8 out of 9 (89%, *NS*) after CY, and all 14 patients (100%, NS) in the polychemotherapy group. However, less second apheresis were needed in the vinorelbine group, as shown in Figure 2. In the vinorelbine group, another five patients reached $1.0–2.4 \times 10^6$ $CD34^+$ cells/kg, and in the CY group, one patient reached $1.8 \times 10^6$ $CD34^+$ cells/kg in the apheresis product. All six patients went on to auto-SCT with hematological recovery on time.

In one patient, stem cell collection was not initiated in the vinorelbine group because of low levels of $CD34^+$ cells in the blood ($\leqslant 2 \times 10^6$/l). In another patient, stem cell collection was not initiated due to progression of lymphoma during mobilization period, in spite of $27 \times 10^6$ $CD34^+$ cells in the peripheral blood.

ANC and platelet counts did not decrease during the mobilization period after vinorelbine. Serious adverse events were not observed and transfusions of red cells and platelet units were not required. In contrast, three and one patients were admitted to the hospital owing to neutropenic fever following mobilization with CY and polychemotherapy, respectively.

*Transplantation data*

All 43 patients after successful stem cell collection with vinorelbine/G-CSF, all 9 patients in the CY group and 13 of the 14 patients in the group of mobilization with G-CSF after polychemotherapy (one patient died owing to rapid lymphoma progression after mobilization before HDT) underwent conditioning chemotherapy with BEAM followed by auto-SCT. The main transplantation data are presented in Table 3.

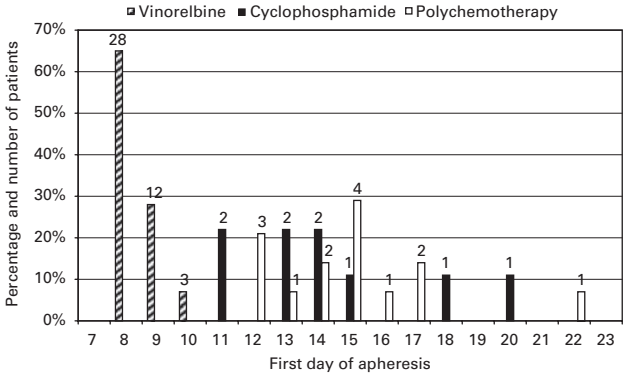


**Figure 1** First day of apheresis (*x* axis) vs percentage (*y* axis) and number (at top of the bars) of patients after mobilization with vinorelbine/G-CSF (diagonal dashed bar), CY/G-CSF (solid bar) and G-CSF after a polychemotherapy regimen (others) (open bar).

**Table 1** Patient characteristics

| | *Vinorelbine* n = *45* *median (range or %)* | *CY* n = *9* *median (range or %)* | *Polychemotherapy (R)-DHAP* n = *4 (R)-ICE* n = *4 others* n = *6 median (range or %)* |
|---|---|---|---|
| Age at mobilization (years) | 53 (19–69) | 49 (29–62) | 55 (30–64) |
| Weight (kg) | 72 (49–119) | 73 (60–98) | 70 (49–93) |
| Female/male | 22/23 | 1/8 | 4/10 |
| Aggressive NHL *n* (%) | 28 (62) | 7 (78) | 11 (79) |
| Indolent NHL *n* (%) | 12 (27) | 1 (11) | 0 |
| Hodgkin's disease | 5 (11) | 1 (11) | 3 (21) |
| Stage I/II | 14 (31) | 4 (44) | 4 (29) |
| Stage III/IV | 31 (69) | 5 (56) | 10 (71) |
| Front line | 6 (13) | 2 (22) | 0 |
| Refractory/relapse | 39 (87) | 7 (78) | 14 (100) |
| Months from diagnosis to mobilization. | 16 (3–202) | 16 (1.5–130) | 11 (2–133) |

*P*-values were calculated for age, weight and time from diagnosis to mobilization with Mann–Whitney and Wilcoxon *U*-tests to compare the vinorelbine group with the CY group and the group with polychemotherapy regimens, respectively. There was no statistically significant difference between the groups.

**Table 2** Mobilization data

| | *Vinorelbine* n = *45* *median (range or %)* | *CY* n = *9* *median (range or %)* | *Polychemotherapy* *(R)-DHAP* n = *4 (R)-ICE* n = *4 others* n = *6 median (range or %)* |
|---|---|---|---|
| Interval (days) from day 1 of chemotherapy to the first day of apheresis | 8 (8–10) | 14 (11–20) | 15 (12–22) |
| | | $P = 0.007$ | $P = 0.001$ |
| Days of G-CSF | 5 (5–8) | 11 (9–18) | 11 (7–17) |
| | | $P = 0.011$ | $P = 0.001$ |
| Patients needing two aphereses | 15 (33) | 5 (56) | 4 (28) |
| *Peripheral blood (on first day of apheresis)* | | | |
| WBC $\times 10^9$/l | 24.1 (4.2–66.9) | 11.9 (1.0–49.0) | 22.5 (3.1–66.2) |
| CD34+ cells/μl | 32 (13–286) | 58.5 (12–610) | 34 (17–429) |
| *Apheresis product (final product)* | | | |
| CD34+ cells $\times 10^6$/kg body weight | 3.6 (1.4–16.0) | 5.2 (2.4–30.8) | 3.82 (2.5–15.9) |

*P*-values were calculated for all parameters with Mann–Whitney and Wilcoxon *U*-tests to compare the vinorelbine group with the CY group and with the group of polychemotherapy regimens, respectively. Interval between chemotherapy and start of apheresis and the number of days of G-CSF varied significantly. There was no statistically significant difference in the other parameters.

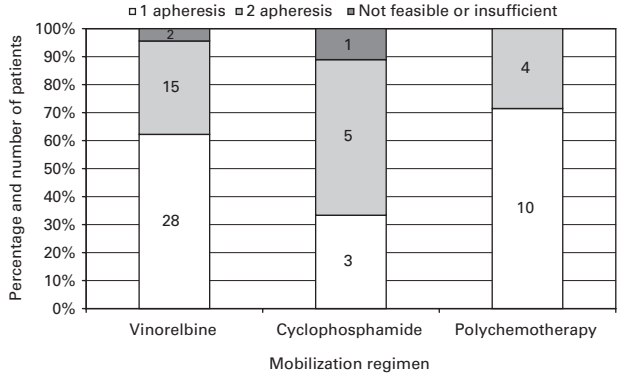


**Figure 2** Number (in the bar) and percentage (*y* axis) of patients requiring one (white boxes) or two (gray boxes) aphereses to collect sufficient stem cells after mobilization with vinorelbine/G-CSF ($n = 45$), CY/G-CSF ($n = 9$) or G-CSF after a polychemotherapy regimen (others, $n = 14$) in patients with malignant lymphoma. Number of patients failing stem cell collection (dark boxes).

### *Costs analysis*

Drug costs were compared between the group mobilized with vinorelbine/G-CSF and the group mobilized with CY/G-CSF. Both mobilization schemes were analyzed for a standardized patient with a body surface area of 1.7 $m^2$. Costs of CY 4 g/$m^2$ and 60% mesna were equal to those of vinorelbine. A large proportion of the price difference amounted from the additional 6 days of G-CSF application following CY until sufficient $CD34^+$ cells in the blood, which resulted in supplementary costs of about 2000 € per standardized patient. Two days of hospitalization for the application of CY and mesna accounted for a difference in costs of 1100 €. In total, mobilization with vinorelbine and G-CSF reduced costs by approximately 3100 € per patient in comparison to mobilization with CY.

## Discussion

The easy-to-administer outpatient regimen of vinorelbine 35 mg/$m^2$ i.v. and G-CSF, allows an accurately timed, reliable, safe and cost-effective PBSC mobilization in patients with malignant lymphoma. Mobilization with vinorelbine/G-CSF resulted in $CD34^+$ cell counts in the peripheral blood and the apheresis product comparable to the cell counts collected after mobilization with CY/G-CSF or G-CSF after polychemotherapy. However, significantly less days of G-CSF application were needed to achieve a sufficient yield after vinorelbine mobilization. The date of first apheresis after mobilization with vinorelbine/G-CSF could be planned more accurately, as two-thirds of patients achieved sufficient $CD34^+$ cells in peripheral blood on day 8, the first day of $CD34^+$ cell count, to initiate stem cell collection. This allows a better planning of the collection procedure and processing in the laboratory. In addition, vinorelbine has a low toxic potential. Although having a myelosuppressive effect, none of the patients in the vinorelbine group had to be admitted to the hospital during the mobilization period because of neutropenic fever, and no toxicities ⩾grade 3 were recorded.

The interval from the start of mobilization until transplantation was reduced after mobilization with vinorelbine *vs* CY. A delayed time point of collection of about 1 week after CY and a higher rate of febrile neutropenia after mobilization were responsible for the longer interval to transplantation. Moskowitz *et al.*[13] reported that relatively poor mobilization of PBSCs is generally observed in heavily pretreated patients. We found that successful PBPC collection with vinorelbine/G-CSF could also be obtained in patients with multiple previous chemotherapy lines (range: 1–6). The rapid onset of neutrophil engraftment after a median of 10 days and of transfusion-independent platelet levels of $\geqslant 20 \times 10^9$/l after a median of 16 days indicate no alteration of stem cells or diminished proliferation capacity owing to mobilization with vinorelbine. In addition, the overall response rate of 73% (48% complete remission) after transplantation in this heterogeneous patient group also indicates no negative influence of mobilization with vinorelbine on the results of HDT with the BEAM protocol.[14]

Mobilization with vinorelbine/G-CSF allows the reduction of costs of about 3000 €. Many of the additional costs

**Table 3** Transplantation data

| | *Vinorelbine* n = *43 median (range or %)* | *CY* n = *9 median (range or %)* | *Polychemotherapy (R)-DHAP* n = *4 (R)-ICE* n = *3 others* n = *6* |
|---|---|---|---|
| Interval from the first day of apheresis to stem cell reinfusion (days) | 20 (7–93) | 31 (15–63)<br>$P = 0.002$ | 24 (19–63)<br>*NS* |
| Days to recovery of ANC $\geqslant 0.5 \times 10^9$/l after stem cell reinfusion | 10 (8–17) | 11 (10–15) | 10 (9–11) |
| Days to transfusion-independent platelet levels $\geqslant 20 \times 10^9$/l after reinfusion | 16 (9–49) | 15 (8–47) | 13 (9–28) |
| Hospitalization days, including chemotherapy | 23 (16–55) | 29 (25–40) | 22 (16–31) |
| Days with fever $>38\,^{\circ}C$ | 4 (1–14) | 6 (3–25) | 6 (2–22) |
| RBC units | 8 (0–18) | 12 (5–22) | 8 (0–23) |
| Platelet units | 4 (1–23) | 9 (1–18) | 4 (4–13) |
| Deaths until day 100 (any reason) | 3 | 1 | 3 |
| CR at day 100 | 21 (48) | 8 | 7 |
| Partial remission at day 100 | 11 (25) | | 3 |

Except for deaths until day 100 and the remission rates, *P*-values were calculated with Mann–Whitney and Wilcoxon *U*-tests to compare the vinorelbine group with the CY group and the group with polychemotherapy regimen, respectively. There was no statistically significant difference between each group except the delay from the first day of apheresis to reinfusion varied significantly.

of the mobilization and collection procedure cannot be calculated precisely. The fact that all stem cell collections were carried out between day 8 and 10 after vinorelbine enables us to plan all procedures during working days. Weekend apheresis can be avoided with vinorelbine mobilization. Moreover, if the patient suffers from febrile neutropenia, costs increase considerably because of hospitalization and the use of i.v. antibiotics.

Our pilot study makes the mobilization regimen with vinorelbine/G-CSF an interesting alternative to CY/G-CSF in patients with malignant lymphoma. Our feasibility and cost analysis support the use of vinorelbine, as it can be administered in an outpatient, cost-effective setting calling for fewer days of G-CSF application, is associated with minimal risk of febrile neutropenia and, furthermore, allows the reliable prediction of the time point of successful apheresis in two-thirds of patients.

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## References

1 Milpied N, Deconinck E, Gaillard F, Delwail V, Foussard C, Berthou C *et al*. Initial treatment of aggressive lymphoma with high-dose chemotherapy and autologous stem-cell support. *N Engl J Med* 2004; **350**: 1287–1295.
2 Philip T, Guglielmi C, Hagenbeek A, Somers R, Van Der Lelie H, Bron D *et al*. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. *N Engl J Med* 1995; **333**: 1540–1545.
3 Goldschmidt H, Hegenbart U, Haas R, Hunstein W. Mobilization of peripheral blood progenitor cells with high-dose cyclophosphamide (4 or 7 g/m2) and granulocyte colony-stimulating factor in patients with multiple myeloma. *Bone Marrow Transplant* 1996; **17**: 691–697.
4 Haas R, Mohle R, Fruhauf S, Goldschmidt H, Witt B, Flentje M *et al*. Patient characteristics associated with successful mobilizing and autografting of peripheral blood progenitor cells in malignant lymphoma. *Blood* 1994; **83**: 3787–3794.
5 Koc ON, Gerson SL, Cooper BW, Laughlin M, Meyerson H, Kutteh L *et al*. Randomized cross-over trial of progenitor-cell mobilization: high-dose cyclophosphamide plus granulocyte colony-stimulating factor (G-CSF) versus granulocyte-macrophage colony-stimulating factor plus G-CSF. *J Clin Oncol* 2000; **18**: 1824–1830.
6 Desikan KR, Barlogie B, Jagannath S, Vesole DH, Siegel D, Fassas A *et al*. Comparable engraftment kinetics following peripheral-blood stem-cell infusion mobilized with granulocyte colony-stimulating factor with or without cyclophosphamide in multiple myeloma. *J Clin Oncol* 1998; **16**: 1547–1553.
7 Bargetzi MJ, Passweg J, Baertschi E, Schoenenberger A, Gwerder C, Tichelli A *et al*. Mobilization of peripheral blood progenitor cells with vinorelbine and granulocyte colony-stimulating factor in multiple myeloma patients is reliable and cost effective. *Bone Marrow Transplant* 2003; **31**: 99–103.
8 Magagnoli M, Sarina B, Balzarotti M, Castagna L, Timofeeva I, Nozza A *et al*. Mobilizing potential of ifosfamide/vinorelbine-based chemotherapy in pretreated malignant lymphoma. *Bone Marrow Transplant* 2001; **28**: 923–927.
9 Devizzi L, Santoro A, Bonfante V, Viviani S, Bonadonna G. Vinorelbine: a new promising drug in Hodgkin's disease. *Leuk Lymphoma* 1996; **22**: 409–414.
10 Rule S, Tighe M, Davies S, Johnson S. Vinorelbine in the treatment of lymphoma. *Hematol Oncol* 1998; **16**: 101–105.
11 Aapro MS, Harper P, Johnson SA, Vermorken JB. Developments in cytotoxic chemotherapy: advances in treatment utilising vinorelbine. *Crit Rev Oncol Hematol* 2001; **40**: 251–263.
12 Gatama JW, Keeney M, Sutherland DR. Enumeration of CD34+ hematopoietic and progenitor cells. *Curr Prot Cytometry* 1999; **6**: 1–22.
13 Moskowitz CH, Glassman JR, Wuest D, Maslak P, Reich L, Gucciardo A *et al*. Factors affecting mobilization of peripheral blood progenitor cells in patients with lymphoma. *Clin Cancer Res* 1998; **4**: 311–316.
14 Seyfarth B, Josting A, Dreyling M, Schmitz N. Relapse in common lymphoma subtypes: salvage treatment options for follicular lymphoma, diffuse large cell lymphoma and Hodgkin disease. *Br J Haematol* 2006; **133**: 3–18.