# 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 $10 \times 10^9$/L.

**Results:** Total $CD34^+$ cells collected by 2 leukapheresis were $> 2 \times 10^6$/kg body weight in 16 patients; between 1.0 and $2.0 \times 10^6$/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 ($5.60 \pm 4.32$ *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 $2 \times 10^6$/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