

Ifosfamide, Cisplatin or Carboplatin, and Etoposide (ICE)-based Chemotherapy for Mobilization of Autologous Peripheral Blood Stem Cells in Patients with Lymphomas

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Abstract

Background: High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) is a promising approach for lymphomas. This study aimed to evaluate the effect of ifosfamide, cisplatin or carboplatin, and etoposide (ICE)-based regimen as a mobilization regimen on relapsed, refractory, or high-risk aggressive lymphoma.

Methods: From June 2001 to May 2013, patients with lymphomas who mobilized by ICE-based regimen for ASCT were analyzed in this retrospective study. The results of the autologous peripheral blood stem cells collection, toxicity, engraftment after ICE-based mobilization regimen were analyzed in this study. Furthermore, risk factors for overall survival (OS) and progression free survival (PFS) were evaluated by univariate analysis.

Results: The stem cells were mobilized using ICE-based regimen plus rituximab or ICE-based regimen alone in 12 patients and 54 patients, respectively. The results of stem cell mobilization were excellent. Ninety-seven percentages of the patients had the stem cell collection of at least 2.0×10^6 CD34⁺ cells/kg and 68% had at least 5×10^6 CD34⁺ cells/kg. Fifty-eight percentage of the patients experienced Grade 4 neutropenia, 20% developed febrile neutropenia, and only 12% had Grade 4 thrombocytopenia. At a median follow-up of 63.8 months, the 5-year PFS and OS were 64.4% and 75.3%, respectively.

Conclusion: ICE is a powerful regimen for stem cell mobilization in patients with lymphomas.

Key words: ICE; Mobilization; Rituximab; Stem Cell Transplantation

INTRODUCTION

High-dose chemotherapy (HDC) followed by autologous stem cell transplantation (ASCT) is considered standard treatment for chemosensitive patients with relapsed or refractory aggressive lymphoma, particularly the disease responding to the salvage second-line chemotherapy.^[1] Stem cells for ASCT are almost invariably collected from peripheral blood after mobilization therapy.^[2] A variety of salvage regimens have been investigated, which have a miscellaneous efficacy, toxicity, and mobilization potential for the collection of autologous peripheral blood stem cells (APBSCs),^[3-5] but there is no consensus as to the optimal regimen for the relapsed lymphoma. As reported, combination chemotherapy with ifosfamide, cisplatin or carboplatin, and etoposide (ICE) has the capacity to mobilize and collect a sufficient number of APBSC with

limited nonhematological toxicity, which may complicate consolidative HDCT.^[4,6] However, there are rare data about ICE chemotherapy in the mobilization of APBSC in a Chinese population. Therefore, efforts to identify the optimal mobilization regimen represent are challenging and urgent issues for Chinese patients.

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Received: 31-01-2015 **Edited by:** Li-Min Chen

How to cite this article: Zhou P, Liu P, Zhou SY, He XH, Han XH, Qin Y, Yang S, Zhang CG, Gui L, Yao JR, Zhao LY, Zhang SX, Sun Y, Shi YK. Ifosfamide, Cisplatin or Carboplatin, and Etoposide (ICE)-based Chemotherapy for Mobilization of Autologous Peripheral Blood Stem Cells in Patients with Lymphomas. *Chin Med J* 2015;128:2498-504.

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.164936

Herein, we have retrospectively analyzed the ICE-based chemotherapy in 66 Chinese patients with relapsed, refractory or high-risk lymphomas with regard to the ability to mobilize and collect APBSC, toxicity, response, and long-term progression free survival (PFS) and overall survival (OS).

METHODS

Patient selection

Between June 2001 and May 2013, a total of 66 patients with relapsed, refractory or high-risk non-Hodgkin's lymphoma (NHL) or Hodgkin's lymphoma (HL) were included in this study. Patients were identified from a database of prospective observational research on HDC/ASCT in malignant lymphoma. The analysis was approved by the Institutional Review Board of the Cancer Hospital, Chinese Academy of Medical Science & Peking Union Medical College (CAMS & PUMC). All of the patients were histologically confirmed at the Department of Pathology, Cancer Hospital, CAMS & PUMC using the 2008 World Health Organization (WHO) classification of lymphoma.^[7] According to the requirements, all patients were younger than 65 years old and had adequate organ function including a bone marrow reserve. Patients were excluded if they had a human immunodeficiency virus or central nervous system disease, active hepatitis B or C, or Grade ≥ 2 peripheral neuropathy. Patients were staged according to Ann Arbor System before mobilization. Staging procedures included physical examination, reporting of B-symptoms, computed tomography (CT) scans, or positron emission tomography (PET)-CT and bone marrow biopsy. Because this was a retrospective review of patients treated in clinical practice, over time there was variability in the use of PET-CT to aid in the assessment of response. The median age of patients was 28.5 years (range, 11–47 years). Summary of patient characteristics is provided in Table 1.

Treatment before autologous peripheral blood stem cell mobilization

For patients with NHL, induction chemotherapy included cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP); cyclophosphamide, doxorubicin, vincristine, prednisone, and etoposide (CHOEP); bleomycin, epirubicin, cyclophosphamide, vincristine, and prednisone (BACOP); and prednisone, doxorubicin, cyclophosphamide, and etoposide, followed by cytarabine, bleomycin, vincristine, and methotrexate with leucovorin, rescue (proMACE-CytaBOM). For patients with HL, epirubicin, bleomycin, vinblastine, and dacarbazine (ABVD) was the induction regimen. Patients with relapsed or refractory disease were rescued with the ICE-based regimen as the second-line chemotherapy, and 2–4 cycles of ICE-based regimens were conducted for the salvage therapy and APBSC mobilization.

Mobilization and collection of autologous peripheral blood stem cell

Of all patients in our study, APBSC were mobilized with the chemotherapy of ICE-based regimen, combined with

Table 1: Patient characteristics (n = 66)

Characteristics	Number	Percentage (%)
Sex		
Male	35	53.0
Female	31	47.0
Histology*		
HL	10	15.2
B cell origin		
DLBCL	20	30.3
Non-DLBCL	7	10.6
T cell origin		
PTCL-NOS	7	10.6
ALCL	9	13.6
Others	8	12.1
Ann Arbor Stage		
I/II	17	25.8
III/IV	49	74.2
ECOG		
<2	62	93.9
≥ 2	4	6.1
Elevated LDH	28	42.4
B-symptom	26	39.4
Bulky disease(≥ 10 cm)	25	37.9
Extranodal site >1	35	53.0
aaIPI (NHL)		
0–1	33	58.9
2–3	23	41.1
Disease status		
CR or PR to first-line therapy	28	42.4
CR or PR to second-line therapy	27	40.9
Primary refractory	11	16.7
Prior radiation therapy	18	27.3

*The cell origin of five NHL patients was unknown. HL: Hodgkin's lymphoma; NHL: Non-Hodgkin's lymphoma; aaIPI: Age-adjusted international prognostic index; ECOG: Eastern cooperative oncology group; LDH: Lactate dehydrogenase; CR: Complete response; PR: Partial response.

recombinant human granulocyte colony-stimulating factor (rhG-CSF). Fifty-three patients were mobilized with DICE \pm rituximab and the others were mobilized with ICE \pm rituximab. DICE was administrated as follows: Oral dexamethasone, 10 mg/m², from day 1 to day 4; ifosfamide, 1000 mg/m², from day 1 to day 4; cisplatin, 25 mg/m², from day 1 to day 4; etoposide, 60 mg/m², from day 1 to day 4. ICE consisted of etoposide 100 mg/m², from days 1 to 3, ifosfamide 5000 mg/m², day 2 and carboplatin at an area under the curve (AUC) of 5 (maximum dose, 800 mg) based on 12-hour measured creatinine clearance on day 2. Twelve patients received rituximab, 375 mg·m⁻²·d⁻¹, for 4 days, in details, the day before mobilization, day 7 after mobilization, the day before APBSC reinfusion and day 8 after reinfusion.

A daily blood routine test was conducted during the mobilization period. rhG-CSF was subcutaneously administrated from the day when the white blood cell (WBC) counts first rose from the nadir after chemotherapy to the day prior to the last apheresis, which was firstly administrated at a fixed dose of 300 μ g/d (150 μ g/d for patients whose

weight was <45 kg). APBSC were collected as previously described when WBC counts, mononuclear cells (MNCs) counts, and the percentage of CD34⁺ cells in peripheral blood exceeded $10 \times 10^9/L$, $2 \times 10^9/L$, and 1%, respectively. Continuous APBSC collection was conducted daily (with a CS-3000 Plus Blood Cell Separator, Baxter Healthcare Corp., Deerfield, IL, USA) until a target collection of at least 2×10^6 CD34⁺ cells/kg or 4×10^8 MNCs/kg was achieved. The blood volume processed by each single apheresis was 110–150 ml/kg at a speed of 40–70 ml/min. Venous access was obtained by a double lumen catheter (Arrow International Inc., PA, USA) placed in a femoral vein.^[8–10] Successful mobilization was defined as a collection of at least of 2×10^6 CD34⁺ cells/kg body weight in a single mobilization. Optimal mobilization was defined as a collection of 5×10^6 CD34⁺ cells/kg body weight collection in a single mobilization.^[11] Failed mobilization was defined as failure to collect a minimum of 2×10^6 CD34⁺ cells/kg body weight in the initial aphaeresis. Conditioning regimens of transplantation ASCT was not proceeded in 6 (9%) patients, since APBSC mobilization (CD34⁺ cell count: $0.3 \times 10^6/kg$) failed in one patient, relapse affected two soon after mobilization but before ASCT, and three refused transplantation due to personal reasons. Conditioning regimens for the remaining 60 patients included carmustine, etoposide, cytarabine, and melphalan (BEAM); carmustine, etoposide, cytarabine, and cyclophosphamide (BEAC); and cyclophosphamide, carmustine and etoposide (CBV).

Evaluation of toxicity and engraftment

Toxicity was evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events. Engraftment after transplantation was defined, if absolute neutrophil counts (ANC) and platelets (PLT) counts recovered to more than $0.5 \times 10^9/L$ and more than $50 \times 10^9/L$ for 2 consecutive days without transfusion support, respectively.^[9,10] rhG-CSF (300 µg/d) was administrated on day 6 after APBSC infusion, and the administration continued until the neutrophil counts recovered.

Response and survival

Response to mobilization regimen was evaluated according to WHO criteria.^[12] Response to therapy was initially assessed at month 3 after transplantation. Thereafter, routine follow-up by imaging analysis was performed every 3 months for the first 2 years, every 6 months for the next 3 years, and then annually or whenever clinically indicated.^[13] OS was measured from the first date of mobilization to the date of a patient's death for any reasons or the last follow-up. PFS was measured from the first date of mobilization to progress or death, whereas patients with stable disease or remission were censored.

Statistical methods

All calculations and statistical analyses were conducted using SPSS software (version 19.0, SPSS Inc., Chicago, IL, USA). Quantitative variables were described in medians, ranges, and proportions by descriptive statistics and

frequency analysis. Categorical variables between groups were compared by the Chi-square test or Fisher's exact tests and continuous variables between two groups were compared by Mann–Whitney *U*-test. Survival data were analyzed using the Kaplan–Meier method, and survival curves were compared using the log-rank test. Two-sided values of $P < 0.05$ were considered statistically significant.

RESULTS

Patients

A total of 66 consecutive transplant-eligible patients with relapsed, refractory, or high-risk lymphoma who received ICE-based mobilization regimen were analyzed. The median age of the patients was 28.5 years, ranging from 11 to 47 years. Among them, 36.3% were histologically confirmed as T cell lymphoma, 40.9% were B cell lymphoma, and 15.2% were HL, with cell origin of the others unclear. A median number of prior chemotherapy cycles was 6 ranging from 2 to 22. The baseline characteristics of the patients are listed in Table 1.

Mobilization efficacies

Sixty-four patients (97%) received a successful mobilization defined as total CD34⁺ cells $> 2 \times 10^6/kg$ and 45 patients (68%) achieved an optimal mobilization defined as a total CD34⁺ cells $> 5 \times 10^6/kg$. The median collection for the first apheresis was $4.99 \times 10^6/kg$ (range, 0.30–21.35). The median total CD34⁺ yield was $6.31 \times 10^6/kg$ (range, 0.30–32.7). The median days from the initial mobilization to first apheresis were 17 days (range, 13–23 days). There was no significant difference observed in patients mobilized with rituximab or not. Among the 54 patients mobilized without rituximab which had a median CD34⁺ cells count of $6.30 \times 10^6/kg$ (range, 0.30–27.94), 52 patients of them received a successful mobilization and 37 patients received an optimal mobilization. For all the patients, 35 patients reached a complete response (CR) after mobilized by ICE-based regimen and overall response rate was 86.3%. Among the 11 primary refractory patients, 6 patients reached a CR, 2 patients reached a partial response (PR) after mobilized by ICE-based mobilization regimen. The detailed data are shown in Table 2.

Toxicity

Mobilization-induced neutrophil nadir developed on a median of 10 days after ICE-based chemotherapy was provided, which was significantly delayed in the R-(D) ICE group (12.5 days, $P = 0.021$), the same as the day of WBC and PLT nadir ($P = 0.008$, $P = 0.001$, respectively). However, the counts of WBC, neutrophil and PLT at nadir were similar. During the collection phase, there was a relatively low incidence of treatment-related adverse events [Table 3]. The most common toxicity was hematologic toxicity. Fifty-eight percentage of the patients experienced Grade 4 neutropenia, 20% developed febrile neutropenia, and only 12% had Grade 4 thrombocytopenia. There were no significant differences between two groups about the adverse events [Table 3]. One patient in the (D)ICE group

died of multiorgan failure during the transplant and was not considered to be related to mobilization chemotherapy.

Conditioning regimens and engraftment

In terms of conditioning regimens for the 60 patients proceeding to ASCT, 22 (37%) patients received BEAM, 30 (50%) patients received BEAC, and 8 (13%) patients received CBV. The median number of CD34⁺ cells and MNCs reinfused was $4.76 \times 10^6/\text{kg}$ (1.24–16.87) and $3.04 \times 10^6/\text{kg}$ (1.03–6.90), respectively. Furthermore, the recovery of WBC, PLT, neutrophil was not affected by rituximab addition [Table 4].

Survival data

At a median follow-up of 63.8 months, the 5-year PFS rate and OS rate among the patients, after mobilized by ICE-based regimen in our study, were 64.4% and 75.3%,

respectively [Figure 1]. Of the 35 patients who achieved a CR to the ICE-based regimen, 12 (34.3%) experienced a relapse during the follow-up time, and median survival duration was 25.6 months.

Univariate analysis was employed to evaluate the possible factors related to successful outcomes following ASCT. There was no significant difference in PFS rate or OS rate depending upon patient age, tumor origin, stage, disease status or a number of prior chemotherapy regimens. Of the 54 patients without rituximab, 5-year OS rate and 5-year PFS rate were 72.7% and 64.2%, respectively. Of the 12 patients received rituximab 5-year OS rate and 5-year PFS rate were 75.4% and 64.0%, respectively. However, the differences were not statistically significant [Table 5]. In the analysis of survival, the few patients who progressed after mobilization

Table 2: Results of APBSC collection

Parameters	All	R+(D)ICE (n = 12)	(D)ICE (n = 54)	P
Days of rhG-CSF treatment (range)	6 (3–12)	6 (3–8)	6 (4–12)	0.765
Days to first apheresis (range)	17 (13–23)	17.5 (14–23)	16 (13–21)	0.091
Number of apheresis procedures (range)	1 (1–3)	2 (1–3)	1 (1–3)	0.129
CD34 ⁺ cell percentage in PB for the first apheresis (%) (range)	2.87 (0.17–17.27)	3.67 (0.66–17.27)	2.3 (0.17–12.2)	0.306
CD34 ⁺ CD38 ⁻ cell percentage in PB for the first apheresis (%) (range)	0.30 (0–4.43)	0.25 (0.07–4.43)	0.32 (0–2.64)	0.721
CD34 ⁺ cells collected for the first apheresis, $\times 10^6/\text{kg}$ (range)	4.99 (0.30–21.35)	4.88 (0.91–15.19)	4.99 (0.3–21.35)	0.803
CD34 ⁺ cells collected in total, $\times 10^6/\text{kg}$ (range)	6.31 (0.3–32.70)	6.45 (2.36–32.7)	6.30 (0.3–27.94)	0.678
Optimal mobilization rate of CD34 ⁺ cells collection in total (%)	45 (68.2)	8 (66.7)	37 (68.5)	0.901
Successful mobilization rate of CD34 ⁺ cells collection in total (%)	64 (97.0)	12 (100)	52 (96.3)	0.498
CR rate after ICE-based regimen (%)*	35 (53.0)	10 (83.3)	25 (46.3)	0.026

*The status after ICE-based regimen was evaluated in 62 patients (93.9%). PB: Peripheral blood; rhG-CSF: Recombinant human granulocyte colony-stimulating factor; CR: Complete response; APBSC: Autologous peripheral blood stem cells.

Table 3: Toxicities of two groups

Parameters	All	R+(D)ICE (n = 12)	(D)ICE (n = 54)	P
Days of WBC nadir (range)	11 (8–17)	12.5 (9–16)	11 (8–17)	0.008
WBC count at nadir (range)	1 (0.27–3.63)	0.95 (0.50–3.63)	1 (0.27–2.30)	0.511
Days of neutrophil nadir (range)	11 (8–24)	12.5 (9–17)	11 (8–24)	0.021
ANC at nadir (range)	0.22 (0–1.79)	0 (0–1.79)	0.28 (0–1.60)	0.720
Days of PLT nadir (range)	15 (9–22)	16.5 (13–22)	14 (9–20)	0.001
PLT count at nadir (range)	55.5 (12–173)	58.5 (32–160)	54.5 (12–173)	0.690
Number of patients with PLT transfusions (%)	30 (45.5)	6 (50)	24 (44.4)	0.758
Number of patients with RBC transfusions (%)	4 (6.1)	1 (8.3)	3 (5.6)	0.561
Neutropenic fever (%)	13 (19.7)	4 (33.3)	9 (16.7)	0.194

WBC: White blood cell; ANC: Absolute neutrophil count; PLT: Platelet; RBC: Red blood cell.

Table 4: Engraftment of two groups

Parameters	ALL	R+(D)ICE (n = 12)	(D) ICE(n = 54)	P
Number of patients without ASCT (%)	6 (9.1)	0	6	0.582
Median number of CD34 ⁺ cells infused, $\times 10^6/\text{kg}$ * (range)	4.76 (1.24–16.87)	4.18 (1.73–12.27)	4.83 (1.24–16.87)	0.966
Median number of MNC cells infused, $\times 10^9/\text{kg}$ * (range)	3.04 (1.03–6.90)	2.49 (1.70–5.05)	3.3 (1.03–6.90)	0.492
Median days to WBC recovery (range)	11 (8–17)	11 (1–14)	11 (8–17)	0.754
Median days to PLT recovery (range)	12 (7–26)	11 (9–26)	12 (7–20)	0.844
Median days to neutrophil recovery (range)	10 (8–17)	10.5 (10–13)	10 (8–17)	0.902

*The data of CD34⁺ and MNC cells infused was missed in 24 patients (36.4%). ASCT: Autologous stem cell transplantation; MNC: Mononuclear cells; WBC: White blood cell; PLT: Platelet; CR: Complete response; PFS: Progression free survival; OS: Overall survival.

Table 5: Univariate analysis for PFS and OS for all 66 patients

Characteristics	n	5-year PFS (%)	P	5-year OS (%)	P
Disease status at transplantation*					
CR	35	64.1	0.002	73.8	<0.001
PR	22	70.2		83.3	
PD/SD	5	20.0		20.0	
Number of prior regimens					
1 or 2	49	66.4	0.284	74.7	0.853
3 or more	17	58.8		76.0	
Receipt of rituximab					
Yes	54	64.0	0.628	75.4	0.662
No	12	64.2		72.7	
Chemotherapy failure before mobilization					
Yes	38	61.7	0.379	68.8	0.362
No	28	67.9		83.9	
Time to relapse					
<12 months	31	56.7	0.184	62.7	0.098
≥12 months	7	85.7		–	

*The data of disease status at transplantation was missed in 4 patients (6.1%). CR: Complete response; PR: Partial response; SD: Stable disease; PD: Progressive disease; PFS: Progression free survival; OS: Overall survival.

had a significantly poor prognosis ($P < 0.001$, Figure 2), with a median survival of 5.1 months. There were 28 patients who did not have chemotherapy failure before mobilization, and the 5-year OS rate was 83.9%, without significant difference compared with other patients ($P = 0.362$, Figure 3). When time to first relapse was compared, 5-year OS rate and 5-year PFS rate for patients who relapsed <12 months before mobilization were 62.7% and 56.7% respectively, while 5-year survival for patients who relapsed ≥12 months before mobilization was not reached. As shown in Figure 4, there was a slight trend toward improved 5-year OS rate and 5-year PFS rate in patients who relapsed >12 months, but it was not statistically significant possibly due to the smaller number ($P = 0.098$, $P = 0.184$).

DISCUSSION

The ideal mobilization regimen for patients who are eligible for ASCT is respected to have a high APBSC mobilization capacity, high response rate, and limited toxicity.^[14] The benefit of ASCT in relapsed or refractory aggressive lymphoma is largely restricted to patients with chemosensitive disease, and patients who undergo transplantation in CR have better outcomes than those patients who undergo transplantation in PR as previously reported.^[15,16] Therefore, the way of improving outcome is to potentiate the effects of chemotherapy regimen and increase the CR rate.

This study analyzed the efficacy of ICE-based salvage regimen in mobilizing patients with high-risk or relapsed/refractory NHL or HL, who were treated within a single center. The ICE-based regimen was proved to be highly effective on mobilizing a sufficient number of CD34⁺

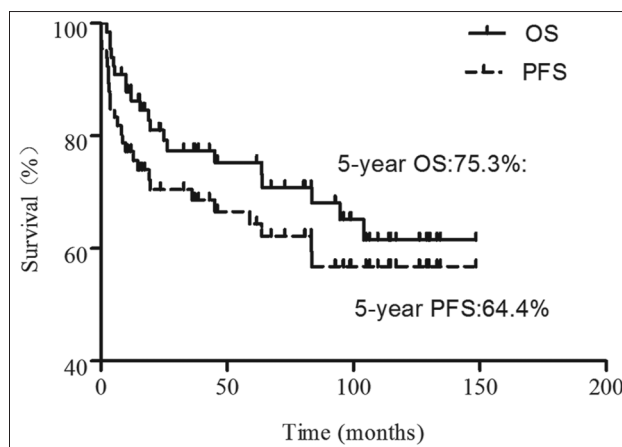


Figure 1: Overall survival (OS) and progression-free survival (PFS) of all the patients ($n = 66$).

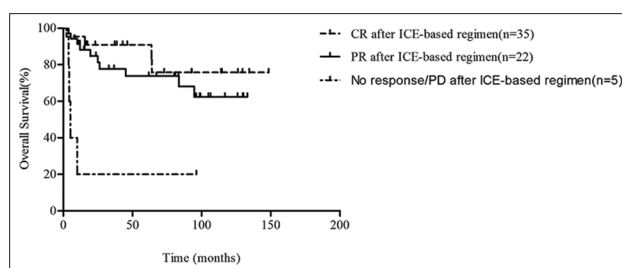


Figure 2: Overall survival (OS) according to disease status at ICE-based regimen for assessable patients ($n = 62$).

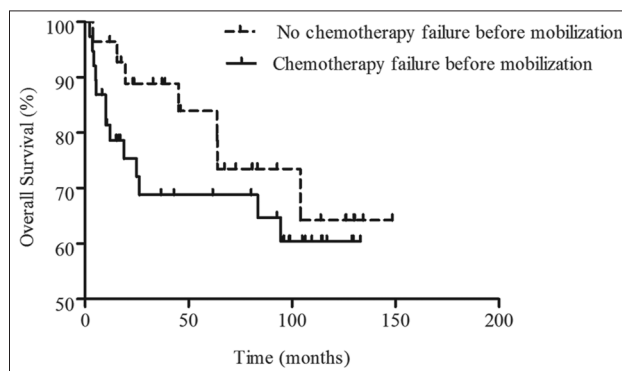


Figure 3: Overall survival (OS) according to chemotherapy failure before mobilization ($n = 66$).

cells. The median number of CD34⁺ cells collected after mobilization was $6.31 \times 10^6/\text{kg}$, and 45 patients (68.2%) achieved an optimal mobilization. The mobilization yield seemed similar to the yield from etoposide in the WA Wood study ($6.23 \times 10^6/\text{kg}$)^[17] but better than that from the rhG-CSF alone ($1.98 \times 10^6/\text{kg}$).^[18] Likewise, it was superior to that associated with the ICE regimens, in which CD34⁺ cell yield was $3.6\text{--}6.3 \times 10^6/\text{kg}$.^[4,6,19] Possibly because of the excellent mobilization, 90.9% of the patients mobilized by ICE-based regimen in our series proceeded to transplantation, as was favorable when compared to the other regimens reported previously.^[20,21] However, the cross-trial comparison is of limited value.

Though direct comparison are unwarranted, as ours was not a randomized study and baseline characteristics among the patient populations may have varied, Table 6 suggests that our results are at least comparable, from an efficacy standpoint to other mobilization strategies. The CD34⁺ stem cell yield with ICE-based chemomobilization ($6.31 \times 10^6/\text{kg}$) appears similar to the yield from the plerixafor arm in the Dipersio study ($5.69 \times 10^6/\text{kg}$) and better than the rhG-CSF alone arm ($1.98 \times 10^6/\text{kg}$).^[18]

The secondary age-adjusted International Prognostic Index score (saaPI), early relapse <12 months after diagnosis, and prior rituximab treatment were reported to be independent factors affecting response rate after salvage therapy.^[20] A nonrandomized study^[19] demonstrated that adding rituximab to ICE in patients with relapsed or primary refractory diffuse large B-cell lymphoma (DLBCL) appeared to achieve double CR rates, from 27% to 53%. When added to CHOP, rituximab significantly increased the CR rate among patients with DLBCL.^[22] In our study, CR rate was somewhat higher than that reported in previous studies investigating mobilization by ICE-based regimens.^[4,6,19] However, this conclusion should be interpreted in cautiously given the limitation in our study. First, the younger age may contribute to the higher CR rate. Second, a potential concern as to the limitation of the current study was that the response assessment of mobilization was not universally performed by integrated PET-CT. Third, patients with the refractory disease were in a minority, who appeared to have a poorer prognosis.^[15,20]

A critical question is whether the improved CR rate will be translated into improved outcomes after ASCT. The 5-year OS rate of patients who were mobilized without rituximab was similar to that with rituximab (72.7% vs.

75.4%), and 5-year PFS rate of the two groups were almost the same (64.2% vs. 64.0%). Therefore, new therapies for relapsed or refractory patients which could improve outcomes in a large proportion of patients are needed. A recent study, using ofatumumab instead of rituximab as the immunotherapy component of the second-line therapy, reported a higher CR rate compared to that in CORAL study, in which the median PFS and OS were 9.5 months and 16.7 months, respectively. However, rituximab plus with chemotherapy appeared to improve outcomes for patients with transformed indolent NHL, compared with those mobilized without rituximab.^[23]

The CORAL study^[20] found that the response to the first-line treatment, saaPI, and early relapse were the powerful predictors of outcomes following the salvage therapy, consistent with the results of the earlier international prospective randomized phase III PARMA trial.^[24] Similarity, in a recent study which employed ofatumumab combined with ICE or DHAP for relapsed or refractory lymphoma, the independent prognostic factors in CORAL retained their prognostic relevance.^[25] Furthermore, it was reported that elevated lactate dehydrogenase, lymphopenia, bulk >10 cm and response to induction regimen were prognostic factors.^[14,15] However, based on this retrospective and small sample study, the number of prior regimens, chemotherapy failure before mobilization and the time to relapse were not prognostic factors.

This study has several limitations. It was uncontrolled, retrospective, single center study, which included the patients treated over many years. However, it was believed that our results to be reliable for selecting an effective chemomobilization regimen because the clinical characteristics that might affect the APBSC mobilization

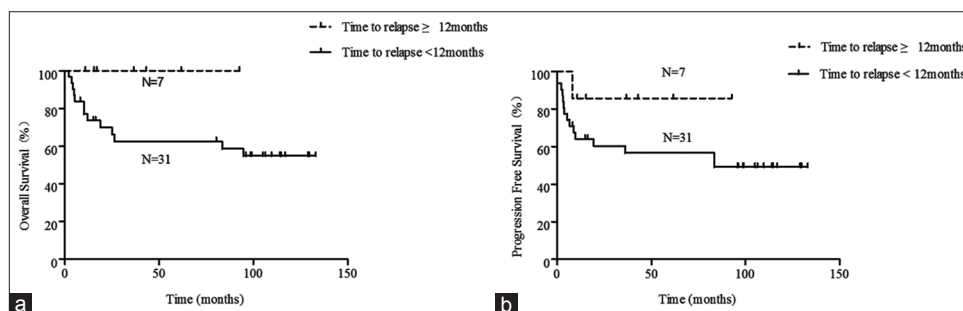


Figure 4: (a) Overall survival according to the time to first relapse before mobilization ($n = 38$); (b) Progression-free survival according to the time to first relapse before mobilization ($n = 38$).

Table 6: Comparison of efficacy of mobilization with published data			
Parameters	(D)ICE±R (current sample) ($n = 66$)	G-CSF alone (published) ($n = 148$)	G-CSF+P (published) ($n = 150$)
CD34 ⁺ cells collected in total, $\times 10^6/\text{kg}$ (range)	6.31 (0.30–32.70)	1.98 (0.06–15.00)	5.69 (0.03–29.22)
Number of patients proceeding to ASCT (%)	60 (90.9)	66 (45.0)	135 (90.0)
Median number of days to PLT recovery (range)	12 (7–26)	20	20
Median number of days to neutrophil recovery (range)	10 (8–17)	10	10

ASCT: Autologous stem cell transplantation; G-CSF: Granulocyte colony-stimulating factor; P: Plerixafor; PLT: Platelet.

yield were comparable and all apheresis procedures were usually performed according to similar guidelines.

In conclusion, taking the limitations of the retrospective nature of analysis and the small size into account, our data suggests that ICE-based regimen is an effective mobilization regimen for patients with relapsed or refractory NHL or HL, which achieved excellent APBSC mobilization and a higher chance of proceeding to ASCT. APBSC mobilization and engraftment were not negatively affected by adding rituximab to ICE.

Financial support and sponsorship

This work was supported in part by grants from National Science-Technology Support Plan Projects (No. 2014BAI09B01), Research Special Fund for Public Welfare Industry of Health (No. 200902002-1), Chinese National Major Project for New Drug Innovation (No. 2008ZX09312, No. 2012ZX09303012), Chinese National High Technology Research and Development Program of China (No. 2011AA02A110), the Ministry of Education Doctor Foundation of China (No. 20010023018, No. 20050023045 and No. 200800230019).

Conflicts of interest

There are no conflicts of interest.

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