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Original Article

Efficacy of chemotherapy with G-CSF versus plerixafor with G-CSF in autologous stem cell mobilization for lymphoma patients

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Abstract: Aims: To compare the efficacy, safety, hematological recovery, immune reconstitution, infection rates, and quality of life (QoL) between two stem cell mobilization regimens - granulocyte colony-stimulating factor (G-CSF) plus chemotherapy versus G-CSF plus plerixafor - in patients with lymphoma undergoing autologous stem cell transplantation (ASCT). Methods: A retrospective cohort study was conducted in 174 lymphoma patients who underwent stem cell transplantation at Shanxi Province Cancer Hospital from 2010 to 2024. Patients were divided into two cohorts: G-CSF plus chemotherapy (n=129) and G-CSF plus plerixafor (n=45). Baseline demographics, CD34+ cell yield and collection efficiency, time to hematopoietic recovery, transfusion requirements, incidence of fever and infections, hematologic abnormalities, immune reconstitution, and patient-reported QoL at 6 months were collected from de-identified medical records and analyzed. Results: Baseline characteristics were comparable between groups. The G-CSF plus plerixafor group demonstrated significantly higher CD34+ cell counts at the first apheresis, higher total CD34+ cell yields, and a larger proportion of patients achieving $\geq 2 \times 10^6$ and $\geq 5 \times 10^6$ CD34+ cells/kg within 4 days compared with the G-CSF plus chemotherapy group. Hematological recovery (platelet and neutrophil engraftment) was faster in the plerixafor group. The plerixafor group also had shorter hospital stays, fewer febrile episodes during neutropenia, reduced antibiotic use, and higher lymphocyte counts at day 28 post-transplantion. The incidences of leukopenia, lymphopenia, anemia, and gastrointestinal adverse effects were lower in this group. Immune reconstitution, particularly CD4+ and CD8+ T cell recovery at 30 days, was improved post-transplant, and QoL scores at 6 months post-discharge were higher across physical, emotional, and social domains. Conclusion: Mobilization with G-CSF plus plerixafor is associated with higher CD34+ cell yields, faster hematologic and immune recovery, lower complication rates, and better QoL outcomes compared with G-CSF plus chemotherapy in lymphoma patients undergoing ASCT.

Keywords: Lymphoma, stem cell transplantation, mobilization, plerixafor, granulocyte colony-stimulating factor, hematologic recovery

Introduction

Autologous stem cell transplantation (ASCT) remains a cornerstone of therapy for patients with relapsed or refractory lymphoma, offering the potential for durable remission and improved overall survival [1]. The success of ASCT relies heavily on the efficient mobilization and collection of adequate numbers of hematopoietic stem and progenitor cells (HSPCs), particularly CD34+ cells, from peripheral blood [2]. Mobilization failure, defined as the inability to collect the minimum threshold of CD34+ cells required for transplantation, presents a major obstacle to this potentially curative therapy and is associated with increased morbidity, prolonged hospitalization, and heightened healthcare costs [2].

Granulocyte colony-stimulating factor (G-CSF), alone or in combination with chemotherapy, has traditionally been employed for stem cell

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mobilization [3]. Chemotherapy-based regimens, such as those utilizing high-dose etoposide (VP-16), rely on the rebound phenomenon following myelosuppression to stimulate stem cell release [4]. However, their efficacy can be hindered by prior cytotoxic treatments, compromised marrow reserves, and substantial interpatient variability [5]. Additionally, chemotherapy-related toxicities, including cytopenias, heightened infection risk, and gastrointestinal complications, can delay transplantation and adversely affect patient outcomes [6].

Over the past decade, the C-X-C motif chemokine receptor 4 (CXCR4) antagonist plerixafor has emerged as a potent adjunct to conventional mobilization strategies [7]. By specifically disrupting the interaction between CXCR4 on HSPCs and its ligand stromal cell-derived factor-1 in the bone marrow microenvironment, plerixafor induces rapid and robust egress of CD34+ cells into the peripheral blood, thereby enhancing the efficacy of G-CSF-based mobilization [8]. Clinical evidence from both randomized controlled trials and real-world studies has demonstrated that G-CSF combined with plerixafor increases overall CD34+ cell yields, especially in poor mobilizers and heavily pretreated patients [9].

Despite these advances, the optimal mobilization regimen for lymphoma remain uncertain, particularly with regard to efficacy, safety, and post-transplant outcomes [10]. Comparative studies of chemotherapy plus G-CSF versus G-CSF with plerixafor remain limited, and few have directly examined patient-centered outcomes such as hematopoietic recovery, immune reconstitution, adverse reaction profiles, and quality of life (QoL) [10]. Furthermore, logistical and economic considerations, such as the costs of plerixafor, need to be balanced against its clinical benefits and potential gains in healthcare efficiency [11].

Given these knowledge gaps, the present retrospective cohort study was conducted to evaluate the efficacy and safety of chemotherapy combined with G-CSF versus G-CSF plus plerixafor for peripheral blood stem cell mobilization in lymphoma patients at a large tertiary medical center. The study aims to comprehensively compare the two mobilization regimens with respect to stem cell yields, hematopoietic and immune recovery, complication rates, and QOL outcomes. By elucidating the relative effectiveness and patient impact of these approaches, our findings may guide the selection of optimal mobilization strategies and improve the overall success of ASCT in lymphoma patients.

Materials and methods

Grouping criteria

This retrospective cohort study analyzed 174 lymphoma patients who underwent ASCT at Shanxi Province Cancer Hospital between 2010 and 2024. The sample size was determined by the total number of eligible patients during this period. Initially, among these patients, 147 were mobilized using G-CSF in combination with chemotherapy, while 45 patients were mobilized using G-CSF in combination with plerixafor. To minimize selection bias and ensure comparability between groups, propensity score matching (PSM) was performed. After matching, the G-CSF + Chemotherapy group included 129 patients, and the G-CSF + Plerixafor group included 45 patients.

This study was approved by the Institutional Review Board (IRB) and Ethics Committee of Shanxi Province Cancer Hospital. As a retrospective study, it utilizes de-identified medical record data, ensuring that no individual patient could be identified from the data. The study involved no interventions that could potentially influence treatment or prognosis of patients. Given the retrospective design and use of anonymized data, the IRB and Ethics Committee waived the requirement for informed consent.

Treatment strategies

In the G-CSF + Chemotherapy group, stem cell mobilization involved high-dose VP-16 combined with G-CSF. On day 1, patients received high-dose VP-16 (1.6 g/m^2) infused intravenously over 10 hours. G-CSF (filgrastim) was initiated once the absolute neutrophil count (ANC) dropped to 1×10^9/L and was administered subcutaneously at 10 μg/kg body weight once daily. Treatment continued until the peripheral CD34+ cell count reached the predetermined threshold of ≥ 10 cells/μL.

In the G-CSF + Plerixafor group, Plerixafor, a CXCR4 antagonist, was used to augment G-CSF-induced mobilization. G-CSF (Filgrastim) was administered subcutaneously at 10 μg/kg body weight once daily for four consecutive

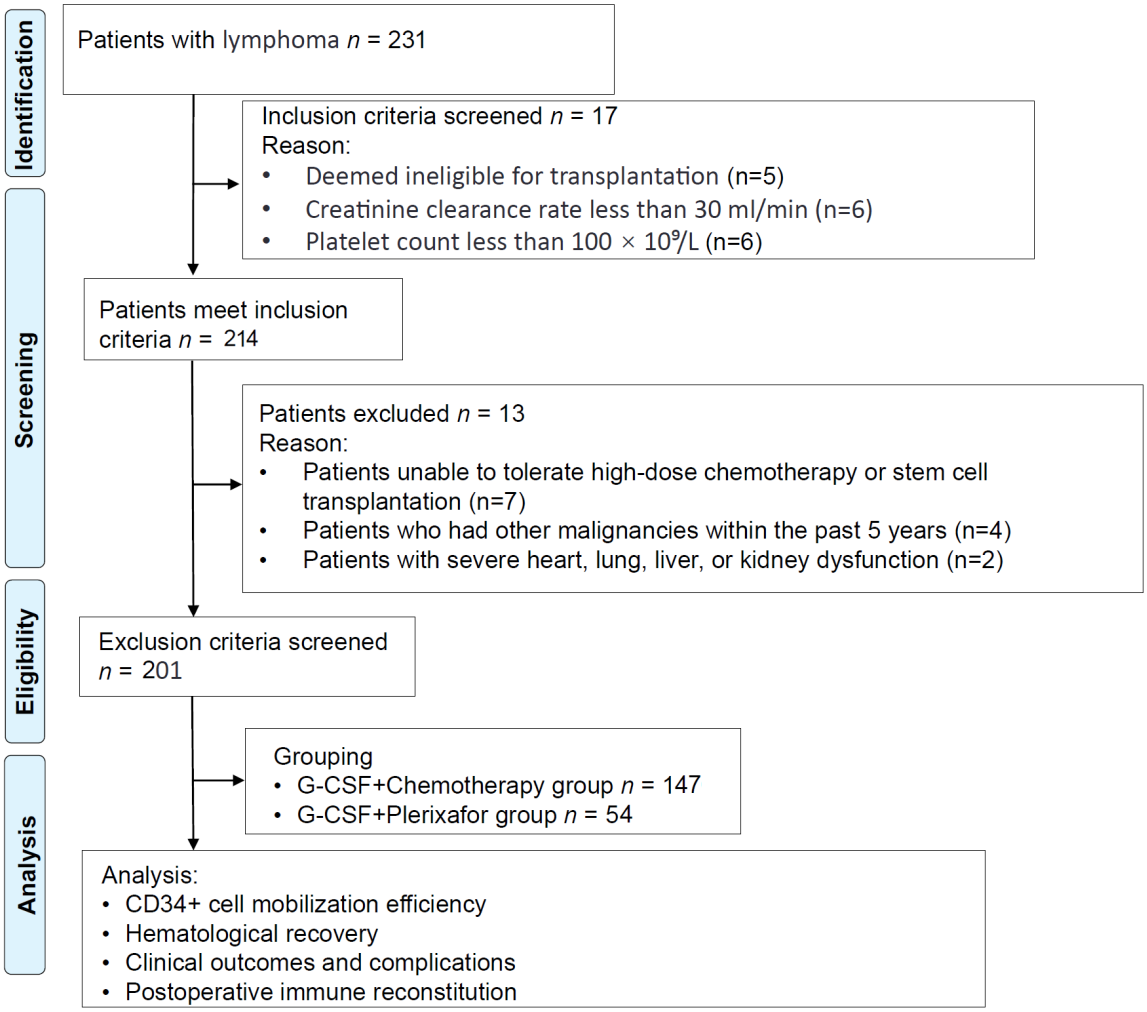

Figure 1. Flowchart of patient selection and study design. G-CSF: granulocyte colony-stimulating factor.

days. Plerixafor was given at a dose of 240 μg/kg subcutaneously on the evening of day 4 following the initiation of G-CSF.

Inclusion and exclusion criteria

Inclusion criteria: patients diagnosed with lymphoma [12] who were deemed eligible for transplantation; age ≥ 18 years; creatinine clearance > 30 ml/min; an ANC > 1500 × 10^6/L; platelet count > 100 × 10^9/L; and availability of complete medical records.

Exclusion criteria: presence of other malignancies within the past 5 years; severe cardiac, pulmonary, hepatic, or renal dysfunction; inability to tolerate high-dose chemotherapy or stem cell transplantation; pregnancy or lactation; or absence of essential clinical or laboratory data.

The patient selection process is summarized in **Figure 1**. A total of 231 patients were initially screened at our hospital. Seventeen patients were excluded during the first review: 5 were ineligible for transplantation, 6 had a creatinine clearance rate < 30 ml/min, and 6 had platelet counts < 100 × 10^9/L, leaving 214 patients. Further screening excluded an additional 13 patients: 7 were unable to tolerate high-dose chemotherapy or stem cell transplantation, 4 had other malignancies within the past 5 years, and 2 had severe dysfunction of the heart, lungs, liver, or kidneys. Ultimately, 201 patients met all eligibility requirement and were enrolled. These eligible patients were then divided into two groups according to the mobilization protocol: the G-CSF + Chemotherapy group (n=147) and the G-CSF + Plerixafor group (n=54).

Data sources and detection methods of indicators

Baseline data: Baseline data were obtained from the medical record system at the time of initial diagnosis. Demographic characteristics, including age and sex, were documented during the first visit. The Ann Arbor stage was determined based on imaging findings, such as computed tomography (CT) scans and positron emission tomography-computed tomography (PET-CT) along with clinical assessment, following the internationally recognized Ann Arbor staging system (stages I-IV) [13]. Risk classification for lymphoma was performed using the International Prognostic Index (IPI), classifying patients into low-risk and high-risk groups [14]. Histopathological subtypes were identified from biopsy samples of lymph nodes or other affected tissues, processed by fixation, staining, and microscopic examination, and confirmed by pathologists as B-cell lymphoma, T-cell lymphoma, or Hodgkin lymphoma. Lymphoma status at mobilization was assessed based on treatment response and categorized as complete response I (CR I), complete response II (CR II), or partial response (PR) [15]. Blood samples were collected via venipuncture into anticoagulant tubes; the CD34+ cell counts were measured by flow cytometry, and lactate dehydrogenase (LDH) levels were measured through biochemical analysis using an automated biochemistry analyzer (e.g., Sysmex XE-5000, Sysmex Corporation, Japan).

CD34+ cell parameters and total yield at first apheresis: At the first apheresis, peripheral blood samples were collected via venipuncture into EDTA anticoagulant tubes. White blood cell counts were determined using an automated hematology analyzer (Sysmex XN-2000, Sysmex Corporation, Japan).

Simultaneously, blood samples were labeled with a fluorescently conjugated monoclonal antibody (CD34-PE, Beckman Coulter, Inc., USA) and processed using a flow cytometer (Navios, Beckman Coulter, Inc., USA) according to standard operating procedures. The CD34+ cell count at the first apheresis and daily during mobilization was recorded. Peak CD34+ cell counts were identified from these measurements.

The CD34+ cell yield (cells/kg) at the first apheresis was calculated as:

$$\text{CD34 + cell yield} = \frac{\text{Total number of CD34 + cells harvested}}{\text{Patient's weight (kg)}}$$

After each apheresis session, the collected product was labeled and analyzed using flow cytometry to determine the total number of CD34+ cells. The cumulative total of harvested CD34+ cells was used to calculate the overall yield per kilogram:

$$\text{Total yield CD34 + cells harvested} = \frac{\text{Cumulative total number of CD34 + cells harvested}}{\text{Patient's weight (kg)}}$$

Proportion of patients achieving minimum target within four days post-apheresis: By day 4 after apheresis, the proportion of patients achieving the minimum targets of $\geq 2 \times 10^6$ CD34+ cells/kg and 5×10^6 CD34+ cells/kg was determined based on collected data. According to clinical guidelines, $\geq 2 \times 10^6$ CD34+ cells/kg is the minimum standard for successful engraftment, while $\geq 5 \times 10^6$ CD34+ cells/kg is associated with higher transplantation success rates.

Hematological recovery and related clinical laboratory data post-autologous stem cell transplantation (days to recovery): After ASCT, peripheral blood samples were collected via venipuncture into EDTA anticoagulant tubes. Hematological recovery was assessed using an automated hematology analyzer (Sysmex XE-5000, Sysmex Corporation, Japan). For each patient, the interval from transplantation to hematological recovery criteria was recorded.

Outcomes: Post-transplantation outcomes were extracted from patients' medical records. Variables included CD34+ cell dose ($\times 10^6$/kg), length of hospital stay, duration of antibiotic use, number of platelet and red blood cell transfusions units. During neutropenia, body temperature of patients was measured twice daily, and fever was defined as a temperature $\geq$ 38°C. On day 28 post-transplantation, venous blood samples were collected into an EDTA anticoagulant tube and analyzed with an automated hematology analyzer (Sysmex XE-5000, Sysmex Corporation, Japan) to obtain a complete blood count, including the absolute lymphocyte count.

Infections and adverse reactions: During hospitalization, patients' body temperatures were measured twice daily, fever was defined as ≥ 38°C. Healthcare providers assessed for signs of infection such as redness, swelling, tenderness, or discharge during consultations. If infection was suspected, laboratory tests, including a complete blood count (CBC), were performed. Patients were also interviewed regarding symptoms like diarrhea, constipation, nausea, vomiting, pain, and fatigue, which were documented in their medical records.

Hematological results: Peripheral blood counts were obtained using an automated hematology analyzer, focusing on white blood cells (WBC), neutrophils, lymphocytes, hemoglobin, and platelets. Leukopenia was defined as a WBC count < 4.0×10^9/L, and neutropenia as an absolute neutrophil count < 1.5×10^9/L. Lymphocytopenia was defined as an absolute lymphocyte count < 1.0×10^9/L, and anemia was diagnosed when the hemoglobin levels were < 12 g/dL in men or < 11 g/dL in women, while thrombocytopenia was defined as a platelet count < 100×10^9/L.

Postoperative immune reconstitution: Thirty days after ASCT, peripheral blood samples were collected via venipuncture into EDTA anticoagulant tubes. Fluorescently labeled antibodies were used to identify immune cell subsets: CD3+ T cells with anti-human CD3 antibody (CD3-FITC, Beckman Coulter, Inc., USA), CD4+ T cells with anti-human CD4 antibody (CD4-RD1, Beckman Coulter, Inc., USA), CD8+ T cells with anti-human CD8 antibody (CD8-ECD, Beckman Coulter, Inc., USA), CD19+ B cells with anti-human CD19 antibody (CD19-PC5, Beckman Coulter, Inc., USA), and CD56+ NK cells with anti-human CD56 antibody (CD16+56-PE, Beckman Coulter, Inc., USA). The labeled samples were analyzed using a flow cytometer (Navios, Beckman Coulter, Inc., USA), and data acquisition was performed with the instrument's built-in software (Kalios Software, Beckman Coulter, Inc., USA). Absolute counts of each immune cell subset were calculated from the acquired data.

Quality of life: At a follow-up visit six months after discharge, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [16] was administered to assess patients' QoL across five functional domains: physical functioning (5 items), role functioning (2 items), emotional functioning (4 items), cognitive functioning (2 items), and social functioning (2 items). The questionnaire contains 15 items, each scored on a 1-4 scale. Raw scores for each domain were converted to standardized scores using the following formula:

$$\text{Conversion score} = \frac{\sum \text{Raw score} - n}{n \times (4 - 1)} \times 100,$$

where *n* is the number of items in the domain.

Data analysis

Data were analyzed using SPSS software (version 29.0; IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages [n (%)] and compared between groups using the Chi-square test. Continuous variables were first assessed for normality using the Shapiro-Wilk test. Variables with a normal distribution were presented as mean ± standard deviation (SD) and compared between groups using the independent samples t-test. A two-sided $P < 0.05$ was considered statistically significant.

Additionally, multivariate regression analysis was performed to identify factors associated with successful mobilization (achievement of ≥ 2×10^6 CD34+ cells/kg). Candidate variables were selected based on clinical relevance and potential influence on mobilization outcomes, including treatment regimen, age, sex, disease stage, risk category (high vs. low), and baseline CD34+ count. Before conducting multivariate regression analysis, we first performed univariate analysis to initially identify factors potentially associated with successful mobilization. Based on the results of the univariate analysis, we further selected treatment regimen, age, disease stage, and baseline CD34+ count as variables for multivariate regression analysis. This approach aimed to adjust potential confounders and ensure that the observed effects of the treatment regimen were independent of other influencing factors.

Results

Propensity score matching

Baseline characteristics were compared between the G-CSF + Chemotherapy group and the G-CSF + Plerixafor group (**Table 1**). No sig-

Table 1. Baseline data before propensity score matching

Parameter	G-CSF + Chemotherapy group (n=147)	G-CSF + Plerixafor group (n=54)	t/χ^2	P
Age	55.89±7.86	55.25±7.74	0.517	0.606
Gender			0.273	0.601
Female	62 (42.18%)	25 (46.3%)		
Male	85 (57.82%)	29 (53.7%)		
BMI	23.08±3.01	23.74±3.11	1.354	0.177
Education level			0.127	0.938
Junior high school and below	39 (26.53%)	15 (27.78%)		
High school	69 (46.94%)	26 (48.15%)		
College and above	39 (26.53%)	13 (24.07%)		
Stage, Ann Arbor			8.026	0.045
I	12 (8.16%)	12 (22.22%)		
II	32 (21.77%)	12 (22.22%)		
III	36 (24.49%)	12 (22.22%)		
IV	67 (45.58%)	18 (33.33%)		
Lymphoma stage at diagnosis			0.006	0.936
Low risk	40 (27.21%)	15 (27.78%)		
High risk	107 (72.79%)	39 (72.22%)		
Histopathological Subtypes			6.268	0.044
B-cell lymphoma	79 (53.74%)	23 (42.59%)		
T-cell lymphoma	43 (29.25%)	13 (24.07%)		
Hodgkin Lymphoma	25 (17.01%)	18 (33.33%)		
Lymphoma disease status at mobilisation			0.754	0.686
CR I	67 (45.58%)	23 (42.59%)		
CR II	60 (40.82%)	21 (38.89%)		
PR	20 (13.61%)	10 (18.52%)		
Steady-state CD34			1.840	0.175
> 10/ul	91 (61.90%)	39 (72.22%)		
< 10/ul	56 (38.10%)	15 (27.78%)		
LDH > normal at diagnosis	105 (71.43%)	39 (72.22%)	0.012	0.912
Prior radiotherapy, n (%)	52 (35.37%)	18 (33.33%)	0.072	0.788
Mobilization History			3.759	0.053
Primary mobilization	116 (78.91%)	49 (90.74%)		
Re-mobilization	31 (21.09%)	5 (9.26%)		
Mobilization types			0.269	0.874
Primary steady-state mobilizations	73 (49.66%)	25 (46.30%)		
Preemptive mobilizations	33 (22.45%)	12 (22.22%)		
Salvage mobilizations	41 (27.89%)	17 (31.48%)		
Number of prior chemotherapy lines			3.103	0.212
1 line	30 (20.41%)	17 (31.48%)		
2 line	82 (55.78%)	28 (51.85%)		
≥ 3 line	35 (23.81%)	9 (16.67%)		

G-CSF: granulocyte colony-stimulating factor; BMI: body mass index; CR: Complete Response; PR: Partial Response; LDH: Lactate Dehydrogenase.

nificant differences were observed in age, sex distribution, BMI, lymphoma stage at diagnosis, LDH levels at diagnosis, prior radiotherapy, mobilization types, or the number of prior che-

motherapy lines. However, significant differences were noted in Ann Arbor stage and histopathological subtypes. The G-CSF + Chemotherapy group showed a higher proportion of patients in Stage IV compared to the G-CSF + Plerixafor group, while the latter had a higher proportion of patients in Stage I. Regarding histopathological subtypes, the G-CSF + Chemotherapy group had a greater proportion of B-cell lymphoma cases but fewer Hodgkin Lymphoma cases compared to the G-CSF + Plerixafor group.

Summary characteristics at baseline

A total of 174 lymphoma patients were enrolled, including 129 in the G-CSF plus chemotherapy group and 45 in the G-CSF plus plerixafor group. Baseline demographic and clinical characteristics were well balanced between groups (**Table 2**). The mean age, sex distribution, and BMI were comparable. No significant differences found in education level, Ann Arbor stage, lymphoma risk stratification, or disease status at mobilization; the majority of patients in both groups were classified as high risk at diagnosis. Steady-state CD34+ counts before mobilization and the proportion of patients with elevated LDH at diagnosis were also comparable between groups. Thus, the two groups were well matched at baseline, supporting the comparability of subsequent efficacy analyses.

Mobilization efficiency and CD34+ cell collection during first apheresis

At the first apheresis, the mean CD34+ cell concentration was significantly higher in the G-CSF + plerixafor group compared with the G-CSF + chemotherapy group (**Tables 3**, **4**). The peak CD34+ cell count during mobilization was also greater in the plerixafor group. Both the CD34+ cell yield at first apheresis and the total yield of harvested CD34+ cells were significantly higher in the plerixafor group. Although the mean WBC count was similar between groups, a larger proportion of patients in the plerixafor group achieved the minimum CD34+ cell threshold within four days after apheresis, both at the $\geq 2 \times 10^6$/kg target and the $\geq 5 \times 10^6$/kg. These findings demonstrate that mobilization using G-CSF combined with plerixafor resulted in higher CD34+ cell counts and superior collection efficiency compared with the G-CSF plus chemotherapy regimen.

Hematological recovery and related clinical laboratory data

Following ASCT, hematological recovery was generally faster in the G-CSF + plerixafor group compared with the G-CSF + chemotherapy group (**Figure 2**). Specifically, the plerixafor group achieved platelet counts > 20×10^9/L and > 50×10^9/L significantly earlier. Median time to neutrophil recovery was also shorter in the plerixafor group, both for neutrophils exceeding 0.5×10^9/L and 1.0×10^9/L. Leukocyte recovery was similarly more rapid in the plerixafor group. No significant differences were observed between groups in the time to achieve a platelet count > 100×10^9/L or leukocyte count > 0.5×10^9/L. Overall, G-CSF combined with plerixafor was associated with accelerated hematopoietic recovery compared to the chemotherapy-based regimen.

Post-transplantation outcomes and clinical benefits of G-CSF plus plerixafor mobilization

The G-CSF + plerixafor group demonstrated a significantly higher mean infused CD34+ cell dose and a shorter median hospital stay compared to the G-CSF + chemotherapy group (**Table 5**). Patients in the plerixafor group also experienced fewer febrile episodes during the neutropenic period, fewer days of antibiotic treatment, and had higher lymphocyte counts on day 28 post-transplantation. There were no significant differences in the incidence or volume of platelet and red blood cell transfusions between groups. These findings suggest that mobilization with G-CSF and plerixafor was associated with improved early post-transplantation outcomes compared to G-CSF plus chemotherapy in lymphoma patients.

Infection rates and adverse reactions following mobilization

The incidence of fever was significantly lower in the G-CSF + plerixafor group compared with the G-CSF + chemotherapy group, as was the proportion of patients with identified pathogens (**Figure 3**). Nausea and vomiting were also less frequent in the plerixafor group. Rate of other infections, including bacterial, viral, and fungal infections, and gastrointestinal adverse events such as diarrhea, constipation, pain, and fatigue were similar between groups. These findings indicate that mobilization with G-CSF

Table 2. Demographic and clinical characteristics of patients

Parameter	G-CSF + Chemotherapy group (n=129)	G-CSF + Plerixafor group (n=45)	t/χ^2	P
Age	55.12±7.33	54.86±7.67	0.205	0.838
Gender			0.052	0.819
Female	57 (44.19%)	19 (42.22%)		
Male	72 (55.81%)	26 (57.78%)		
BMI	23.17±2.98	23.88±3.04	1.362	0.175
Education level			0.079	0.961
Junior high school and below	34 (26.36%)	12 (26.67%)		
High school	63 (48.84%)	21 (46.67%)		
College and above	32 (24.81%)	12 (26.67%)		
Stage, Ann Arbor			0.299	0.960
I	11 (8.53%)	5 (11.11%)		
II	31 (24.03%)	10 (22.22%)		
III	34 (26.36%)	12 (26.67%)		
IV	53 (41.09%)	18 (40.00%)		
Lymphoma stage at diagnosis			0.067	0.796
Low risk	37 (28.68%)	12 (26.67%)		
High risk	92 (71.32%)	33 (73.33%)		
Histopathological Subtypes			0.224	0.894
B-cell lymphoma	63 (48.84%)	22 (48.89%)		
T-cell lymphoma	41 (31.78%)	13 (28.89%)		
Hodgkin Lymphoma	25 (19.38%)	10 (22.22%)		
Lymphoma disease status at mobilisation			0.057	0.972
CR I	59 (45.74%)	21 (46.67%)		
CR II	54 (41.86%)	18 (40.00%)		
PR	16 (12.40%)	6 (13.33%)		
Steady-state CD34			0.131	0.718
> 10/ul	88 (68.22%)	32 (71.11%)		
< 10/ul	41 (31.78%)	13 (28.89%)		
LDH > normal at diagnosis	95 (73.64%)	33 (73.33%)	0.002	0.968
Prior radiotherapy, n (%)	42 (32.56%)	13 (28.89%)	0.208	0.649
Mobilization History			0.053	0.817
Primary mobilization	116 (89.92%)	41 (91.11%)		
Re-mobilization	13 (10.08%)	4 (8.89%)		
Mobilization types			0.081	0.960
Primary steady-state mobilizations	69 (53.49%)	23 (51.11%)		
Preemptive mobilizations	24 (18.60%)	9 (20.00%)		
Salvage mobilizations	36 (27.91%)	13 (28.89%)		
Number of prior chemotherapy lines			1.620	0.445
1 line	28 (21.71%)	14 (31.11%)		
2 line	79 (61.24%)	24 (53.33%)		
≥ 3 line	22 (17.05%)	7 (15.56%)		

plus plerixafor was associated with a reduced risk of fever, fewer identified pathogens, and less nausea and vomiting, while most infection types and other adverse reactions did not differ significantly between groups.

Hematological abnormalities

The incidence of hematological abnormalities following ASCT differed between groups (**Figure 4**). The G-CSF + plerixafor group had a signifi-

Table 3. Comparison of CD34+ cell parameters at first apheresis and total harvest yield between the two groups

Parameter	G-CSF + Chemotherapy group (n=129)	G-CSF + Plerixafor group (n=45)	t/χ^2	P
WBCs × 10^9/L	11.69±1.51	12.16±1.19	1.901	0.059
CD34+ cells × 10^6/L	18.45±1.92	19.01±1.33	2.137	0.035
Peak CD34+ cell count × 10^6/L	35.41±4.53	37.32±4.08	2.499	0.013
CD34+ cell yield × 10^6/kg	3.76±1.09	4.17±0.83	2.637	0.010
Total yield CD34+ cells harvested × 10^6/kg	8.27±1.65	9.38±1.46	4.010	< 0.001

WBCs: White Blood Cells.

Table 4. Comparison of proportion of patients achieving the minimum target within 4 days after apheresis between the two groups

Parameter	G-CSF + Chemotherapy group (n=129)	G-CSF + Plerixafor group (n=45)	t/χ^2	P
Proportions of patients reaching the minimum target of ≥ 5 × 10^6 CD34+ cells/kg			3.904	0.048
Reached target CD34+ cell collection	70 (54.26%)	32 (71.11%)		
Failure to reach target CD34+ cell collection	59 (45.74%)	13 (28.89%)		
Proportions of patients reaching the minimum target of ≥ 2 × 10^6 CD34+ cells/kg			3.870	0.049
Reached target CD34+ cell collection	93 (72.09%)	39 (86.67%)		
Failure to reach target CD34+ cell collection	36 (27.91%)	6 (13.33%)		

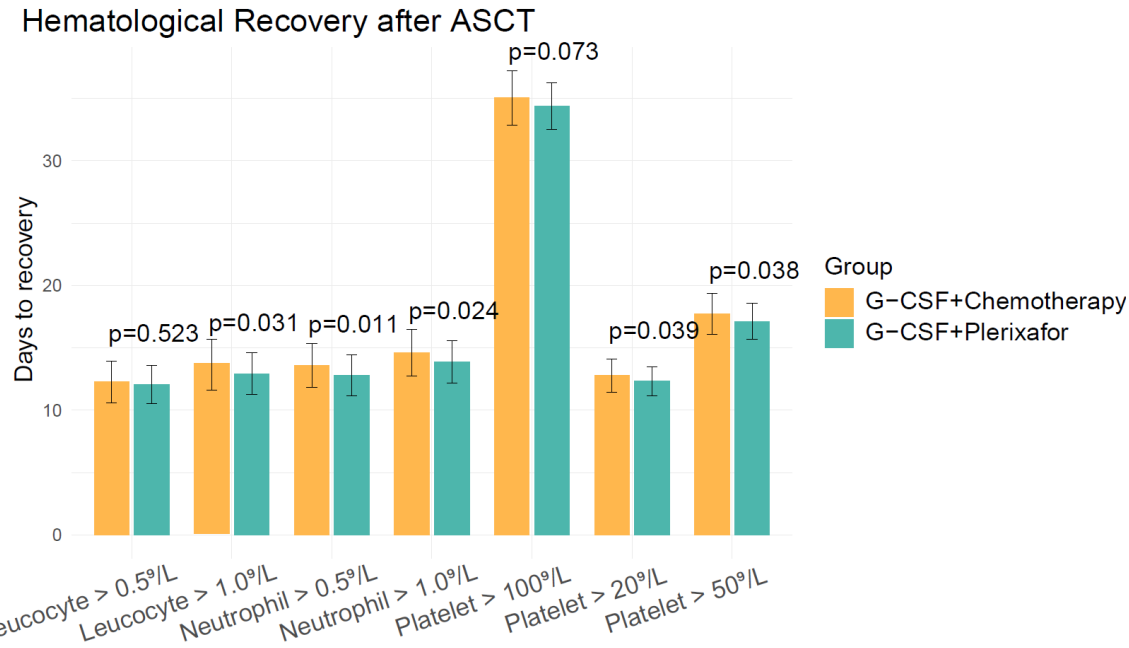

Figure 2. Comparison of hematological recovery and related laboratory data between the two groups after ASCT. ASCT: Autologous stem cell transplantation.

cantly lower incidence of leukopenia, lymphopenia, and anemia compared to the G-CSF + chemotherapy group. No significant differences were observed between groups in the rates of neutropenia or thrombocytopenia. These results indicate that mobilization with G-CSF and plerixafor was associated with a lower frequency of certain hematological abnormalities compared with the chemotherapy-based regimen.

Table 5. Comparison of key clinical outcomes and hematologic parameters between the two groups

Parameter	G-CSF + Chemotherapy group (n=129)	G-CSF + Plerixafor group (n=45)	t/χ^2	P
CD34+ × 10^6/kg dose	4.84±1.59	5.36±1.15	2.356	0.020
Hospital Stay (days)	20.23±2.31	19.33±1.92	2.368	0.019
Patients afebrile throughout the whole neutropenic period (%)	36 (27.91%)	6 (13.33%)	3.870	0.049
Days on antibiotics	9.17±2.14	8.42±1.87	2.088	0.038
Platelet transfusion	107 (82.95%)	35 (77.78%)	0.594	0.441
Units of platelets transfused per patient	2.25±1.14	2.14±0.92	0.578	0.564
Red blood cell transfusion	45 (34.88%)	14 (31.11%)	0.212	0.645
Units of red blood cell transfused per patient	1.42±0.73	1.34±0.64	0.634	0.527
Actual lymphocyte count (10^9/L) day 28	1.54±0.29	1.64±0.24	2.164	0.032

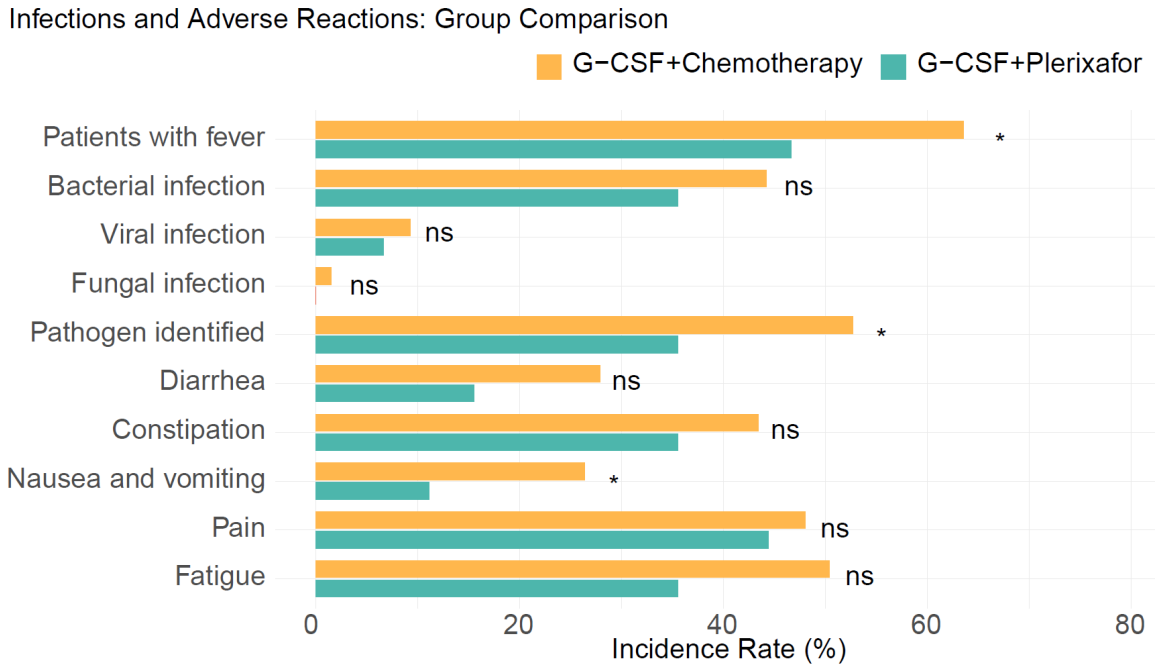

Figure 3. Comparison of infections and adverse reactions between the two groups. Ns: no significant; *: P < 0.05.

Immune reconstitution

At 30 days post-transplantation, patients in the G-CSF + plerixafor group exhibited significantly higher CD4+ T cell counts and CD8+ T cell counts compared with those in the G-CSF + chemotherapy group (**Table 6**). No significant differences were observed between groups in CD3+ T cells, CD19+ B cells, or CD56+ NK cells. These results suggest that immune reconstitution, particularly of T cell subsets, was more robust in the plerixafor group at 30 days following transplantation.

Quality of life

Six months after transplantation, patients in the G-CSF + plerixafor group reported significantly higher scores in physical functioning, emotional functioning, and social functioning compared with those in the G-CSF + chemotherapy group (**Table 7**). No significant differences were observed in role or cognitive functioning scores between the groups. These findings indicate that QOL, particularly in the domains of physical, emotional, and social functioning, was more favorable following

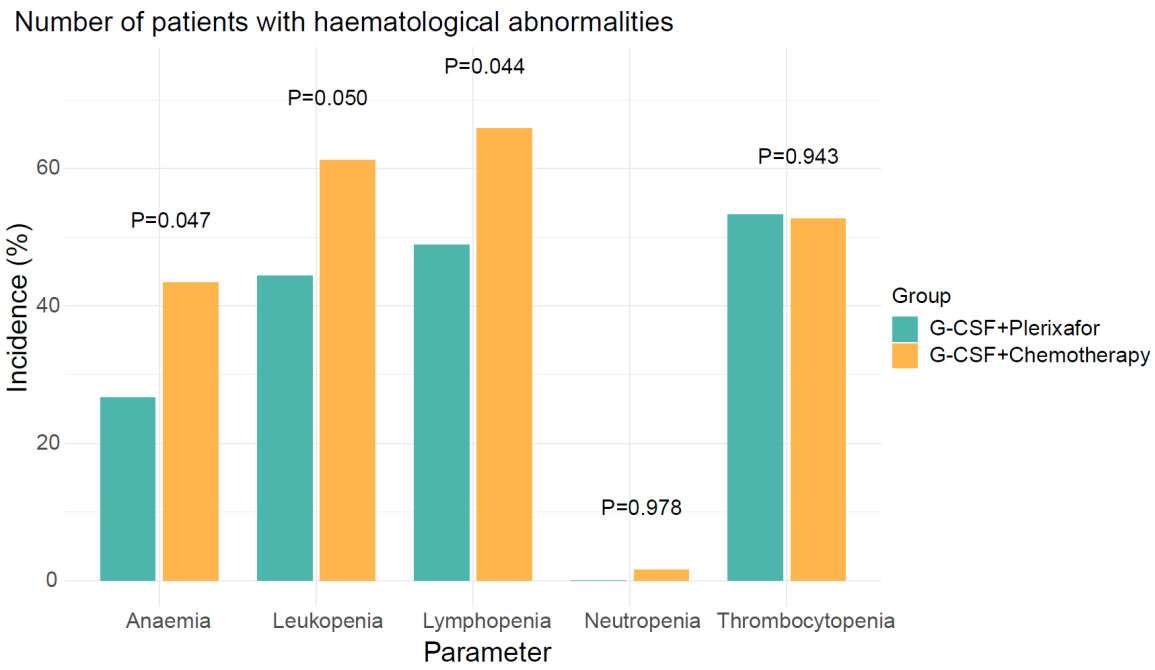

Figure 4. Comparison of the incidence of hematological abnormalities between the two groups.

Table 6. Comparison of immune reconstitution 30 days post-transplantation between the two groups

Parameter	G-CSF + Chemotherapy group (n=129)	G-CSF + Plerixafor group (n=45)	t/χ^2	P
CD3+ T Cells (cells/μL)	718.84±130.93	735.11±138.53	0.707	0.480
CD4+ T Cells (cells/μL)	386.60±72.12	411.62±66.28	2.044	0.042
CD8+ T Cells (cells/μL)	259.49±64.54	282.31±69.95	1.998	0.047
CD19+ B Cells (cells/μL)	69.95±7.17	72.13±6.34	1.807	0.073
CD56+ NK Cells (cells/μL)	356.71±82.29	363.60±84.76	0.480	0.632

Table 7. Comparison of quality of life parameters 6 months post-transplantation between the two groups

Parameter	G-CSF + Chemotherapy group (n=129)	G-CSF + Plerixafor group (n=45)	t/χ^2	P
Physical Functioning	68.82±5.58	71.06±4.72	2.403	0.017
Role Functioning	80.95±5.19	81.74±4.67	0.904	0.367
Emotional Functioning	78.45±5.87	80.59±5.14	2.165	0.032
Cognitive Functioning	85.32±6.13	86.30±5.38	0.950	0.344
Social Functioning	86.35±6.47	88.51±5.23	2.028	0.044

stem cell mobilization with G-CSF and plerixafor.

Multivariate regression analysis of factors affecting total CD34+ yield

Multivariate analysis of factors affecting mobilization efficiency identified G-CSF + Plerixafor was associated with significantly higher odds ratio (OR) of successful mobilization compared to G-CSF + chemotherapy ($P < 0.001$) (**Table 8**). A baseline CD34+ cell count > 10/μL also significantly increased the likelihood of success ($P < 0.001$). Prior radiotherapy was negatively associated with mobilization success ($P = 0.002$). High-risk patients had lower odds com-

Table 8. Multivariate regression analysis of factors affecting total CD34+ yield

Parameter	OR	95% CI	P
G-CSF + Plerixafor vs. G-CSF + Chemotherapy	5.303	2.129, 16.142	< 0.001
Age (per 1-year increase)	0.426	0.206, 0.589	0.154
Male vs. female	0.645	0.281, 0.849	0.382
Number of Chemotherapy Lines (I/II vs. III/IV)	1.163	1.054, 1.374	0.061
Prior Radiotherapy (Yes vs. No)	0.337	0.169, 0.667	0.002
Stage III/IV vs. stage I/II	0.312	0.062, 0.684	0.102
High risk vs. low risk	4.173	1.758, 11.596	0.003
Baseline CD34+ > 10/μL	7.273	3.573, 15.296	< 0.001

pared to low-risk patients (P=0.003). Age, sex, number of chemotherapy lines, and disease stage did not significantly affect mobilization efficiency (all P > 0.05).

Discussion

By comparing mobilization with G-CSF plus chemotherapy and G-CSF combined with plerixafor, our results confirm the clinical advantages of plerixafor-based regimens.

Plerixafor, a selective antagonist of the CXCR4 chemokine receptor, disrupts the interaction between CXCR4 expressed on hematopoietic stem/progenitor cells and stromal derived factor-1 (SDF-1) expressed by bone marrow stromal cells [11, 17]. This interaction is crucial for anchoring stem cells within the bone marrow microenvironment [18]. Relevant studies indicate that by blocking the CXCR4-SDF-1 axis, plerixafor effectively dislodges stem cells, driving their egress into the peripheral circulation, where they can be collected via apheresis [19]. This action is synergistic with G-CSF, which mobilizes stem cell niche through neutrophil-mediated protease release and suppression of C-X-C motif chemokine ligand 12 (CXCL12), albeit through a slower mechanism [20]. Clinically, in patients requiring rapid engraftment, such as those with aggressive lymphomas, plerixafor accelerates recovery of critical hematopoietic lineages, shortens hospital stays, and improves overall outcomes.

In contrast, high-dose VP-16 mobilization relies on the cytotoxic effects chemotherapy, inducing transient pancytopenia followed by hematopoietic recovery and a “rebound” release of progenitor cells, particularly when combined with G-CSF [21, 22]. Although effective, its efficacy has been reported to vary with patient’s prior chemotherapy exposure and bone marrow reserve [23]. In patients who underwent extensive pre-treatment or had lower risk profiles, there was a risk of insufficient stem cell mobilization. The cytotoxicity of VP-16, though beneficial for disease debulking, may also impair HSPC function and viability, leading to lower mobilization efficiency compared with the targeted stem cell egress promoted by plerixafor [24]. Biological differences in stem cell trafficking likely underlie the observed disparities in mobilization efficacy. For patients with comorbidities or at higher risk for chemotherapy-induced toxicity, plerixafor might be a better option, as it preserves primitive stem cell subsets and their quiescent state, avoiding the transient bone marrow suppression induced by VP-16, which could compromise the functional integrity of collected progenitor cells.

The accelerated hematopoietic recovery observed in the plerixafor group can be partly explained by the higher number and quality of harvested and infused CD34+ cells [25]. Previous studies [26, 27] have shown a strong correlation between the dose of transplanted CD34+ cells and post-transplant engraftment kinetics, particularly for neutrophil and platelet recovery. Clinicians often consider plerixafor-based mobilization for patients requiring rapid engraftment, such as those with aggressive lymphomas needing prompt immune reconstitution. Additionally, plerixafor is also advantageous for patients with comorbidities or at higher risk of chemotherapy-induced toxicity. Evidence suggests that stem cells mobilized by plerixafor possessed greater engraftment potential, and functional capacity, possibly due to the preservation of primitive stem cell subsets and maintenance of a more quiescent state upon mobilization [28]. In contrast, VP-16

induced transient marrow suppression, which may compromise the functional integrity of collected progenitor cells, resulting in a slower recovery trajectory despite adequate cell yields [29]. Moreover, the lower burden of adverse events such as cytopenias, fever, and gastrointestinal symptoms following plerixafor mobilization minimized additional delays in hematopoietic recovery often seen with chemotherapy-based approaches. This suggests that plerixafor enhances patient comfort and reduces hospital stay, leading to better overall outcomes.

The lower rates of infections, fever, and certain hematological abnormalities observed in the plerixafor group may be explained by the avoidance of intensive chemotherapy during mobilization, which reduces mucosal injury, neutropenic risk, and exposure to infectious complications. Our findings align with those of DiPersio, J. F., whose phase III trial demonstrated that plerixafor-based graft mobilization accelerated neutrophil recovery by 1-2 days [30]. Chemotherapy-induced neutropenia is a well-recognized driver of opportunistic infections in the peri-transplant setting [31]. By minimizing toxic exposure before transplantation, plerixafor preserved host defenses and mucosal integrity, thus decreasing infectious morbidity. Furthermore, the rapid engraftment of neutrophils and platelets enhanced host defenses against pathogens and shortened the period of susceptibility, explaining the reduced fever rates and decreased need for antibiotic interventions observed in this cohort [32].

A compelling aspect of our findings concerns early immune reconstitution. At 30 days after transplantation, patients mobilized with G-CSF plus plerixafor demonstrated significantly higher absolute of CD4+ and CD8+ T cell counts. This accelerated recovery may reflect superior preservation and mobilization of lymphoid progenitors by plerixafor compared to chemotherapy-induced mobilization [33]. Previous experimental studies indicate that mobilization regimens affect not just the quantity but also the phenotypic and functional diversity of mobilized stem cell populations, including their associated immune cell subsets [34, 35]. Plerixafor appears to mobilize a broader spectrum of progenitors, facilitating faster post-transplant immune reconstitution [36]. Efficient immune recovery, particularly of T cell subsets, is critical for reducing infectious complications and may also enhance disease control and long-term outcomes through improved immunosurveillance [37].

The improvements in QoL among recipients of plerixafor-based mobilization were likely multifactorial. Yang et al. also reported better post-treatment QoL scores in patients treated with plerixafor [38]. Lower toxicity during mobilization, shorter aplastic phases, fewer febrile episodes, and less need for transfusions and antibiotic contributed to a more favorable early transplant experience [39]. Additionally, shorter hospital stays and a quicker return to baseline physical and social activities promoted psychosocial recovery [40]. Fewer complications alleviated psychological distress and minimized disruption of patients' normal social and occupational activities during post-transplant convalescence [41]. These observations reinforce recommendations to consider not only traditional endpoints such as engraftment speed and infection rates but also patient-centered outcomes when evaluating and selecting mobilization regimens.

Despite clear advantages, certain limitations and mechanistic considerations regarding plerixafor remain. Plerixafor has demonstrated superiority as a first-line mobilization agent, particularly in "poor mobilizers" or those with prior intensive chemotherapy or radiation exposure. However, its optimal use - whether as a first-line agent for all or as a rescue for at-risk populations - remains under debate. Inter-patient variability in response may be influenced by disease biology, prior therapies, and bone marrow reserve. A notable limitation of our study is the unequal sample size between groups, potentially introducing selection bias and limiting the generalizability of our findings. Additionally, the extended study period from 2010 to 2024 could have introduced potential confounding factors, despite the use of consistent mobilization protocols. Advancements in supportive care and diagnostic criteria could have influenced outcomes, adding variability to our results.

To optimize the application of plerixafor, future research should focus on several areas. Despite controlling for many baseline prognostic

factors in our study, residual confounding inherent to retrospective designs may persist. Prospective, randomized trials are needed to validate these findings and explore the biological impact of different mobilization regimens on short- and long-term outcomes. Identifying biomarkers predictive of responses to plerixafor would enable more personalized mobilization strategies, improving patient outcomes while optimizing resource allocation. Randomized controlled trials should also explore the optimal timing and dosing of plerixafor to maximize efficacy and minimize side effects. Longitudinal studies is warranted to assess the impact of different mobilization regimens on long-term clinical outcomes such as immune reconstitution, relapse rates, and overall survival, providing valuable insights into the broader clinical utility of plerixafor. Additionally, this study did not conduct a cost-effectiveness analysis of plerixafor, which is an important consideration given its substantially higher price compared with traditional chemotherapy regimens. Future research should incorporate economic evaluations to determine whether the improved clinical outcomes associated with plerixafor justify its added cost.

Conclusion

In conclusion, the superior efficacy of G-CSF plus plerixafor mobilization over G-CSF plus chemotherapy for stem cell transplantation in lymphoma is biologically plausible and supported by multiple mechanisms. These include targeted disruption of the stem cell niche, preservation of stem cell and immune progenitor health, reduced toxicity, and accelerated host recovery - each translating into meaningful clinical and quality-of-life benefits. Our findings support the adoption of plerixafor-based mobilization as a preferred strategy for ASCT in lymphoma, warranting continued integration into clinical practice and further mechanistic exploration.

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Disclosure of conflict of interest

None.

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