

Plerixafor Plus Granulocyte Colony-Stimulating Factor Improves the Mobilization of Hematopoietic Stem Cells in Patients with Non-Hodgkin Lymphoma and Low Circulating Peripheral Blood CD34⁺ Cells

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Article history:

Received 8 July 2011

Accepted 11 January 2013

Key Words:

Plerixafor
Non-Hodgkin lymphoma
Peripheral blood stem cell mobilization

A B S T R A C T

Many institutions have adopted algorithms based on preapheresis circulating CD34⁺ cell counts to optimize the use of plerixafor. However, a circulating peripheral blood CD34⁺ cell threshold that predicts mobilization failure has not been defined. The superiority of plerixafor + granulocyte colony-stimulating factor (G-CSF) over placebo + G-CSF for hematopoietic stem cell mobilization and collection was shown for patients with non-Hodgkin lymphoma in a phase III, prospective, randomized, controlled study. The question remains as to which patients may benefit most from the use of plerixafor. In this post hoc retrospective analysis, mobilization outcomes were compared between the 2 treatment arms in patients stratified by peripheral blood CD34⁺ cell count (<5, 5 to 9, 10 to 14, 15 to 19, or ≥20 cells/μL) obtained before study treatment and apheresis. Compared with placebo plus G-CSF, plerixafor plus G-CSF significantly increased the peripheral blood CD34⁺ cells/μL over prior day levels in all 5 stratified groups. The probability of subsequent transplantation without a rescue mobilization was far greater in the plerixafor-treated patients for the lowest initial (day 4) peripheral blood CD34⁺ cells/μL groups (<5, 5 to 9, or 10 to 14). Engraftment and durability were the same for the 2 treatment groups for all strata, but the effect in the lower strata could be altered by the addition of cells from rescue mobilizations. These findings may provide insight into the optimal use of plerixafor in all patients undergoing stem cell mobilization.

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INTRODUCTION

High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) can elicit long-term remission in patients with chemotherapy-sensitive, relapsed, aggressive non-Hodgkin lymphoma (NHL) [1]. A key requirement for successful ASCT is the successful collection and cryopreservation of hematopoietic stem cells (HSCs) with a well-accepted minimum target number of 2×10^6 CD34⁺ cells/kg. Retrospective analyses have reported rates of mobilization failure in patients with NHL from approximately 20% to 30% with cytokines, either alone or in combination with chemotherapy [2–4]. Patients who are unable to collect this minimum number of HSCs often cannot proceed to ASCT [5].

One assay used to screen for poor mobilizers is flow cytometric peripheral blood CD34⁺ enumeration. The number of circulating CD34⁺ cells measured before

apheresis has been shown by some to correlate positively with stem cell yields in patients with hematologic malignancies. In published clinical studies, patients with preapheresis CD34⁺ cell counts above a threshold level, ranging from 5 to 34 CD34⁺ cells/μL, had significantly greater stem cell yields than those patients with lower preapheresis cell counts [6–8]. To date, however, the optimal preapheresis CD34⁺ cell count to predict mobilization success has not been determined, and there is no consensus on the preapheresis CD34⁺ threshold level that should be used to identify patients at risk for failed collection [6–8].

Plerixafor is a first-in-class agent currently approved in the United States, in combination with granulocyte colony-stimulating factor (G-CSF), to mobilize HSCs in patients with NHL or multiple myeloma [9–11]. Plerixafor is an inhibitor of the CXCR4 chemokine receptor that blocks receptor binding of the stromal cell–derived factor-1 α [12]. Disruption of the stromal cell–derived factor-1 α –CXCR4 interaction contributes to the release and trafficking of stem cells from the bone marrow into the peripheral blood and results in elevated levels of circulating HSCs both in humans and in animal models [13,14].

The efficacy and safety of plerixafor + G-CSF in mobilizing stem cells in patients with NHL has been established in a phase III study (study 3101) [10]. Plerixafor + G-CSF was shown to significantly increase the proportion of patients

Financial disclosure: See Acknowledgments on page 674.

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1083-8791/\$ – see front matter © 2013 American Society for Blood and Marrow Transplantation.

<http://dx.doi.org/10.1016/j.bbmt.2013.01.005>

achieving optimal ($\geq 5 \times 10^6$) CD34+ stem cell yields for ASCT in fewer apheresis days, compared with placebo + G-CSF [10]. Additionally, plerixafor + G-CSF in compassionate-use protocols was shown to effectively salvage patients with NHL who failed to mobilize peripheral blood stem cells after cytokines + chemotherapy [4,5,15,16]. Similarly, other published studies of plerixafor in combination with chemotherapy + G-CSF in patients with NHL or multiple myeloma have shown the tolerability and preliminary efficacy of such a regimen in augmenting peripheral blood CD34+ cell count and subsequent HSC collection [17–19].

Current guidelines acknowledge the potential impact of plerixafor on stem cell collection strategies, but debate over its optimal use remains, as outlined in a position paper on multiple myeloma [20]. The relatively large database from the plerixafor licensure study [10] provides information to assess any benefit for NHL patients with various levels of peripheral blood CD34+ cells/ μL (<5, 5 to 9, 10 to 14, 15 to 19, or ≥ 20 cells/ μL) after 4 days of G-CSF. The post hoc analyses presented here were conducted to assess the change in peripheral blood CD34+ cells/ μL after addition of plerixafor or placebo on day 4 for apheresis start on day 5 and the subsequent effect on the total number of cells collected during apheresis and the ability of patients to proceed to transplantation. The potential limitation of data is that the study peripheral blood CD34+ cells/ μL value was from a central laboratory, whereas the values used for decisions at the site were those of a local study site laboratory. Even so, these data may provide information about which patients benefit the most from plerixafor when G-CSF mobilization is used for NHL patients.

METHODS

Study Design

Post hoc analyses of patients enrolled in a phase III, randomized, double-blind, placebo-controlled study were performed to evaluate the safety and efficacy of plerixafor (.24 mg/kg s.c.) + G-CSF (10 $\mu\text{g}/\text{kg}/\text{day}$ s.c.) versus placebo + G-CSF in mobilizing CD34+ cells in patients with NHL [10]. Patients were stratified by threshold levels of peripheral blood CD34+ cells: <5, 5 to 9, 10 to 14, 15 to 19, or ≥ 20 CD34+ cells/ μL , as measured on the morning of day 4, before the first plerixafor/placebo dose. The increase in peripheral blood CD34+ cells on day 5, the apheresis yields, the number of patients proceeding to transplantation, time to engraftment, and graft durability were compared between the plerixafor and placebo groups for patients with different thresholds of peripheral blood CD34+ cells/ μL .

Patient Eligibility

Patient eligibility followed guidelines of the previously published 3101 study [10]. Key inclusion criteria were as follows: first or second complete or partial response to prior therapy, last cycle of chemotherapy completed ≥ 4 weeks before enrollment, Eastern Cooperative Oncology Group performance score of 0 or 1, white blood cell count $>2.5 \times 10^9$ cells/L, absolute neutrophil count $>1.5 \times 10^9$ cells/L, platelet count $>100 \times 10^9$ cells/L, serum creatinine ≤ 2.2 mg/dL, and liver function tests $<2.5 \times$ upper limit of normal. Patients were not eligible if they had failed previous stem cell collection attempts, had prior stem cell transplantation, had received G-CSF within 14 days of the first dose of G-CSF on study, had $>20\%$ bone marrow involvement, or had received prior radioimmunotherapy. Patients who had their peripheral blood CD34+ cell counts measured on day 4, before apheresis, were included in these post hoc analyses [10].

Mobilization and Transplantation

Patients received G-CSF (10 $\mu\text{g}/\text{kg}$) s.c. daily for up to 8 days, given in the morning following the protocol-directed timing of administration. Starting on the evening of day 4 and continuing daily for up to 4 days, patients received either plerixafor (.24 mg/kg) or placebo s.c. Starting on day 5, patients began daily apheresis (3.0 blood volume $\pm 10\%$) for up to 4 days or until sufficient CD34+ cells were collected ($\geq 5 \times 10^6$ cells/kg). Within 5 weeks of last apheresis, patients received high-dose chemotherapy and underwent transplantation using collected CD34+ cells

according to local practice guidelines. Patients who failed to collect either $\geq 8 \times 10^6$ CD34+ cells/kg after 2 days of apheresis or $\geq 2 \times 10^6$ CD34+ cells/kg after 4 days of apheresis were eligible to enter an open-label rescue protocol as described previously and are included in the analysis [10].

Determination of Hematologic Parameters for Endpoint Analysis

Peripheral blood CD34+ cell count was measured within 30 minutes before G-CSF administration on the morning of day 4 (before plerixafor/placebo treatment) and 10 to 11 hours after study drug treatment on the morning of day 5. Enumeration of CD34+ cells in peripheral blood and apheresis products was done by fluorescent activated cell sorter analysis at a local laboratory and a central laboratory (Esoterix, Inc., Austin, TX). The local laboratory values were used for all clinical decisions. Efficacy endpoints were calculated using the percentage of CD34+ cells determined by the central laboratory applied to the white blood cell count from the local laboratory. Neutrophil engraftment was defined as neutrophil count $\geq 5 \times 10^9/\text{L}$ for 3 days or $\geq 1.0 \times 10^9/\text{L}$ for 1 day. Platelet engraftment was defined as platelet count $\geq 20 \times 10^9/\text{L}$ without a transfusion for the preceding 7 days.

Statistical Analysis

For continuous outcomes, *P* values were calculated using Wilcoxon rank sum test. For dichotomous outcomes, *P* values were calculated using chi-square test. *P* < .05 was considered statistically significant, and all analyses were performed using SAS version 8.2 or above (SAS Institute., Cary, NC).

RESULTS

Patients

A total of 298 patients were enrolled in the 3101 study and randomized to receive either plerixafor + G-CSF (*n* = 150) or placebo + G-CSF (*n* = 148) [10]. Day 4 peripheral blood CD34+ cell counts were available for 132 patients (88.0%) in the plerixafor group and for 124 patients (83.8%) in the placebo group. Patients were stratified by threshold levels of peripheral blood CD34+ cells: <5, 5 to 9, 10 to 14, 15 to 19, or ≥ 20 CD34+ cells/ μL . Baseline characteristics and patient demographics, by threshold group, are presented in Table 1, including age, median time from diagnosis to progression, median time from most recent progression to randomization, and prior radiotherapy, and were not statistically different.

Efficacy

Peripheral blood CD34+ cells

Comparing plerixafor + G-CSF-treated patients with placebo + G-CSF-treated patients, the median absolute peripheral blood CD34+ cells/ μL on day 4 were not significantly different between the 2 treatment arms for any of the 5 peripheral blood threshold groups (Table 2). On day 5, however, the median absolute number of circulating peripheral blood CD34+ cells/ μL in the plerixafor-treated group were significantly greater compared with the placebo-treated patients for all threshold groups (<5 cells/ μL group: 14.3 versus 3.6 cells/ μL ; 5 to 9 cells/ μL group: 36.6 versus 11.2 cells/ μL ; 10 to 14 cells/ μL group: 57.8 versus 18.5 cells/ μL ; 15 to 19 cells/ μL group: 80.3 versus 23 cells/ μL ; ≥ 20 cells/ μL group: 113.4 versus 42 cells/ μL ; *P* < .001 for all plerixafor versus placebo comparisons in all threshold groups) (Table 2).

CD34+ cell yields

During the first mobilization period, the peripheral blood stem cell collection yield was more than doubled for the plerixafor groups in all cases when the peripheral blood CD34+ cells/ μL value was ≤ 15 (Table 2). The yield was higher for all 5 plerixafor groups. In the 3 combined groups with ≤ 15 peripheral blood CD34 cells/ μL on day 4, only 12 of 93

Table 1
Patient Characteristics, Demographics, and Relevant Cancer History at Baseline by Peripheral Blood Threshold Group

	Threshold Peripheral Blood CD34+ Cells/ μ L on Day 4									
	<5		5-9		10-14		15-19		≥ 20	
	Placebo + G-CSF (n = 45)	Plerixafor + G-CSF (n = 48)	Placebo + G-CSF (n = 28)	Plerixafor + G-CSF (n = 29)	Placebo + G-CSF (n = 20)	Plerixafor + G-CSF (n = 12)	Placebo + G-CSF (n = 9)	Plerixafor + G-CSF (n = 15)	Placebo + G-CSF (n = 22)	Plerixafor + G-CSF (n = 28)
Median age (range), yr	62 (22-75)	61 (29-74)	60 (41-71)	57 (30-71)	63 (34-74)	54 (34-74)	55 (27-73)	52 (30-70)	57 (35-71)	52 (31-65)
Median time from diagnosis to randomization (range), mo	13 (4-95)	24 (4-136)	15 (4-115)	16 (4-120)	10 (4-60)	7 (4-60)	16 (5-87)	11 (4-83)	14 (3-151)	7 (4-59)
Median time from most recent progression/relapse to randomization (range), mo	5 (2-16)	4 (3-14)	3 (0-25)	4 (2-19)	4 (2-6)	4 (3-5)	3 (2-6)	4 (2-18)	4 (2-11)	4 (2-7)
Prior radiotherapy, n (%)										
Yes	10 (22.2)	14 (29.2)	7 (25.0)	4 (13.8)	4 (21.0)	2 (16.7)	3 (33.3)	2 (13.3)	1 (4.6)	2 (7.1)
No	35 (77.8)	34 (70.8)	21 (75.0)	25 (86.2)	15 (79.0)	10 (83.3)	6 (66.7)	13 (86.7)	21 (95.4)	26 (92.9)

patients (13%) achieved a yield of 2×10^6 CD34+ cells/kg in 1 day in the placebo group, whereas 34 of 89 (38.2%) did so in the plerixafor group [21] (data not shown). No patient in a placebo group achieved $\geq 5 \times 10^6$ CD34+ cells/kg on day 1 except in the ≥ 20 group, where 6 of 22 patients (27%) reached this level (compared with 10/28 [36%]) in the corresponding plerixafor group [21] (data not shown).

In the plerixafor groups with < 20 CD34+ cells, 19 of 104 reached 5×10^6 CD34+ cells/kg in 1 day. At the lowest value of peripheral blood CD34+ cell/ μ L (< 5), few patients in the placebo group collected 2×10^6 CD34+ cells/kg, whereas most of the plerixafor group did. When evaluating the group with < 5 CD34+ cells/ μ L for the effect of plerixafor on the number of apheresis required to collect cells, the effect was very different from the placebo group. By day of apheresis the median collection (CD34+ cells $\times 10^6$ /kg) for plerixafor versus placebo was day 1: 1.00 versus .40, $P < .001$; day 2: 2.17 versus .70, $P < .001$; and day 4: 3.31 versus .78, $P < .001$. When the CD34+ cells/ μ L value was at least 15 by day 4 of G-CSF, all patients in both groups could collect 2×10^6 CD34+ cells/kg.

Table 3 shows the apheresis yields for the placebo group and the plerixafor group separated into the 5 categories of peripheral blood CD34+ cells/ μ L on day 4 (before either placebo or plerixafor dose). The collection of < 1 , 1 to < 2 , 2 to < 5 , and $\geq 5 \times 10^6$ cells/kg is shown for the total apheresis period which could be 1 to 4 days (see Methods). These data show that (per the central reference laboratory) at least a peripheral blood count of 15 CD34+ cells/ μ L was needed so that almost all patients collect 2×10^6 CD34+ cells/kg. The likelihood of collecting 5×10^6 CD34+ cells/kg is enhanced with at least a peripheral blood count of 20 CD34+ cells/ μ L.

Transplantation and engraftment

In Table 2, the number of cells infused for transplantation is given for each group of patients listed by initial peripheral blood CD34+ cells/ μ L value at day 4. However, the total is either that obtained during the first mobilization period only or a combination of cells from the first mobilization period plus the trial mandated rescue mobilization period. Those patients undergoing rescue are listed in the last horizontal row in the Table 2. Therefore, in the predicted worst patients to mobilize (< 5 CD34+ cells/ μ L on day 4), some of the plerixafor-treated patients (14/48; 29%) were not mobilized during the first mobilization period, whereas most of the placebo-treated patients (36/45; 80%) failed. When those failing to mobilize during the first mobilization period were then mobilized with G-CSF + plerixafor and the combined yields were used for transplantation, the majority of both groups were transplanted. The 2 groups with peripheral blood CD34+ cells/ μ L values of < 5 and 5 to 9 were mobilized at day 4, and there were fewer requiring rescue: in the plerixafor group (6/77; 8%) and in the placebo group (32/73; 44%). When the peripheral blood CD34+ cell/ μ L value was 10 to 14 in the placebo group, 25% (5/20) still needed rescue.

Engraftment

Postautologous HSCT, the median engraftment for every group for platelets was between 19 and 21 days and for neutrophils was 10 or 11 days (data not shown). All patients in both groups had durable grafts at 1 year, with the exception of 2 patients in the plerixafor arm (1 with < 5 cells/ μ L and 1 with ≥ 20 cells/ μ L); as previously reported, 1 patient had myelodysplastic syndrome and the other remained clinically stable at the 18-month follow-up [10].

Table 2
Comparison of CD34+ Progenitor Yield and Transplant Outcomes Between Study Groups

	Threshold Peripheral Blood CD34+ Cells/ μ L on Day 4									
	<5		5-9		10-14		15-19		≥ 20	
	Placebo + G-CSF (n = 45)	Plerixafor + G-CSF (n = 48)	Placebo + G-CSF (n = 28)	Plerixafor + G-CSF (n = 29)	Placebo + G-CSF (n = 20)	Plerixafor + G-CSF (n = 12)	Placebo + G-CSF (n = 9)	Plerixafor + G-CSF (n = 15)	Placebo + G-CSF (n = 22)	Plerixafor + G-CSF (n = 28)
Median absolute peripheral blood CD34+ cells/ μ L (range)										
Day 4	2.0 (0-4.8)	2.1 (0-4.9)	7.2 (5.0-9.4)	7.0 (5.0-9.7)	12.0 (10.0-14.0)	11.6 (10.0-14.0)	17.2 (15.2-19.2)	18.6 (15.0-18.5)	25.0 (20.0-154.4)	28.6 (20.0-60.5)
Day 5	3.6 (0-20.0)	14.3 (5-58.7)	11.2 (4.3-28.0)	36.6 (4.9-126.4)	18.5 (0-38.0)	57.8 (11.6-110.4)	23.0 (13.0-34.0)	80.3 (42.5-206.0)	42.0 (5.1-165.0)	113.4 (24.3-196.0)
Median cells collected in first mobilization $\times 10^6$ /kg (range)	.8 (1-10.6)	3.3 (0-9.4)	2.5 (3-8.0)	5.4 (4-29.2)	3.1 (8-9.7)	7.0 (4.9-15.7)	4.5 (2.6-6.8)	6.7 (3.2-23.8)	5.8 (5-15.0)	8.9 (2.3-21.9)
Median infused CD34+ cell dose $\times 10^6$ /kg (range) for nonrescue transplant	2.7 (2.0-4.7)	3.7 (2.0-6.7)	3.5 (2.2-6.5)	5.2 (2.3-16.6)	3.9 (2.0-7.4)	6.5 (3.1-8.9)	4.4 (2.5-6.7)	7.2 (4.5-16.6)	5.5 (3.6-8.7)	7.0 (2.8-17.6)
Total patients proceeding to transplant (%)	38 (84.4)	43 (89.6)	25 (89.3)	28 (96.6)	20 (100)	12 (100)	8 (88.8)	15 (100)	22 (100)	28 (100)
Patients transplanted via remobilization in the rescue protocol (%)	25 (56.6)	4 (8.3)	7 (25.0)	2 (6.9)	5 (25.0)	0	0	0	3 (13.6)	0

DISCUSSION

The goal of these post hoc analyses was to explore the efficacy of plerixafor in augmenting stem cell collection in patients with NHL across varying preapheresis circulating CD34+ cell thresholds. This task was facilitated by availing ourselves of two matched patient cohorts from the phase III randomized 3101 trial [10]. By stratifying patients in these analyses according to preapheresis levels of peripheral blood CD34+ cells, we hoped to understand the impact of plerixafor use on mobilization yields in patients with varying preapheresis CD34+ cell counts.

A positive effect of plerixafor on stem cell collection was observed across all peripheral blood CD34+ threshold groups, including the group with a preapheresis CD34+ cell count <20 cells/ μ L, composed of patients generally considered to be “slow” or “poor” mobilizers. Although there is no consensus on the preapheresis CD34+ threshold level that should be used to identify patients at risk for poor mobilization, previous studies have shown that patients with preapheresis CD34+ cell counts ≥ 20 cells/ μ L were significantly more readily mobilized with G-CSF \pm chemotherapy and able to collect sufficient HSCs for ASCT than were patients with cell counts <20 cells/ μ L [8,22]. If one accepts this level as “standard,” then 80% of the patients included in this analysis of the 3101 study were considered at risk for poor mobilization, recognizing that >50% of patients treated with G-CSF + placebo had CD34+ progenitors of <10/ μ L on day 4 (Table 2). In our analysis, the median cumulative stem cell yield in patients with a preapheresis cell count <20 cells/ μ L treated with placebo + G-CSF did not reach minimum collection targets, even after 4 days of apheresis, requiring that these patients underwent a second mobilization procedure, to pursue ASCT.

Treatment with plerixafor + G-CSF significantly rescued these patients with low cell counts, providing strong support that the upfront use of plerixafor could benefit patients with preapheresis CD34+ cell counts <20 cells/ μ L who do not mobilize sufficiently with G-CSF alone (approximately 40% of cases), particularly in the setting where G-CSF is dosed by U.S. Food and Drug Administration label standards rather than at higher doses, as some single institutional studies have reported [23]. In particular, our analysis carries relevance for patients with preapheresis peripheral blood CD34+ cell counts <5 cells/ μ L who are consistently precluded from apheresis based on their low cell counts. Treatment with plerixafor + G-CSF allowed more than 70% of these patients to reach minimum stem cell collection targets.

The obvious question is what is the “low” peripheral blood CD34+ cells/ μ L value that provides the most benefit of all for the use of plerixafor? Every patient in both groups with a CD34+ cell/ μ L value of ≥ 20 was able to be mobilized for transplantation. The only potential benefit of plerixafor was to use it in fewer apheresis procedures or to mobilize more cells [10]. Other potential reasons to use plerixafor at this level of CD34+ cells/ μ L include presentation of risk factors for poor mobilization (age, prior chemotherapy, prior fludarabine or lenalidomide exposure, etc.) and the need for predictable cell collection. Patients with 15 to 19 CD34+ cells/ μ L likewise all mobilized at $\geq 2 \times 10^6$ CD34+ cells/kg. However, when there were <15 CD34+ cells/ μ L, 25% or more of patients who did not receive plerixafor failed to mobilize and collect enough cells for transplantation. At <5 CD34+ cells/ μ L, G-CSF alone was clearly unacceptable without a subsequent rescue mobilization in these NHL patients. At the same level of CD34+ cells/ μ L, plerixafor + G-CSF was

Table 3
Total Apheresis Yield (CD34+ cells/kg) by Peripheral Blood Threshold Group

Total CD34+ Cells/kg Collected	Threshold Peripheral Blood CD34+ Cells/ μ L on Day 4											
	<5		5-9		10-14		15-19		≥ 20			
	Placebo + G-CSF (n = 45)	Plerixafor + G-CSF (n = 48)	Placebo + G-CSF (n = 28)	Plerixafor + G-CSF (n = 29)	Placebo + G-CSF (n = 20)	Plerixafor + G-CSF (n = 12)	Placebo + G-CSF (n = 9)	Plerixafor + G-CSF (n = 15)	Placebo + G-CSF (n = 22)	Plerixafor + G-CSF (n = 28)		
<1.0 $\times 10^6$ cells/kg	28 (62.2)	5 (10.4)	3 (10.7)	2 (6.9)	2 (10.0)	0	0	0	0	2 (9.1)	0	0
1 to <2 $\times 10^6$ cells/kg	8 (17.8)	9 (18.8)	9 (32.1)	1 (3.5)	5 (25.0)	0	0	0	0	2 (9.1)	0	0
2 to <5 $\times 10^6$ cells/kg	5 (11.1)	20 (41.7)	13 (46.4)	9 (31.0)	8 (40.0)	1 (8.3)	6 (66.7)	3 (33.3)	3 (20.0)	5 (22.7)	4 (14.3)	4 (14.3)
$\geq 5 \times 10^6$ cells/kg	4 (8.9)	14 (29.2)	3 (10.7)	17 (58.6)	5 (25.0)	11 (91.7)	3 (33.3)	12 (80.0)	13 (59.1)	24 (85.7)	24 (85.7)	24 (85.7)

successful in 34 of 48 patients (71%). Thus, in the predicted worst patients, G-CSF + plerixafor can be a viable means to mobilize peripheral blood stem cell in NHL patients, especially when chemomobilization may not be appropriate.

Although it is current standard practice for stem cell transplant centers to determine CD34+ cell counts before apheresis, one must recognize the potential variability in these assays. There can be center-to-center variability in the preapheresis cell count threshold used to predict collection failure. Pre-collection CD34+ enumeration is more predictive after G-CSF + chemotherapy mobilization compared with G-CSF alone, because CD34+ cells can be counted more accurately with a lower coefficient of variability in the background of low circulating leukocytes after G-CSF + chemotherapy than in the background of high circulating leukocytes after G-CSF alone [24]. As a result, some centers will dilute the circulating white blood count in this setting to normalize the collection. Furthermore, the variability that arises from differing cell quantification methods effectively precludes cross-study comparisons that may allow clinical validation of a specific cell count threshold as a predictor of mobilization success [25].

We recognize that individual institutions set their own algorithms for utilization of preapheresis CD34+ cell count to guide the apheresis decision; however, given the potential variability, such algorithms need to be prospectively and institutionally validated. Continued clarification of this issue of CD34+ cell count assessment is a necessary hurdle toward the goal of developing standard treatment guidelines outlining the optimal use of plerixafor in patients with NHL and other hematologic malignancies. To this end, our findings provide significant insight into the specific patient population that may derive the greatest benefit from plerixafor treatment, an important step toward defining the optimal use of this drug.

ACKNOWLEDGMENTS

We thank Anna Lau, PhD, and Purdi Mody, PhD, for providing editorial assistance.

Financial disclosure: Supported by Genzyme Corporation, a subsidiary of Sanofi Pharmaceuticals.

Conflict of Interest Statement: R.T.M., A.P.N., P.J.S., and B.J.B. received research funding and an honorarium from Genzyme. A.P.N., I.N.M., P.J.S., and B.J.B. consulted for Genzyme. I.N.M. received research funding from Genzyme. G.C. was but is no longer employed by Genzyme. J.A. is employed by and has ownership interest in Genzyme. J.F.D. received an honorarium from Genzyme.

Authorship Statement: R.T.M., G.C., and B.J.B. designed the study. R.T.M. and G.C. conducted the study. R.T.M., G.C., and J.A. collected, analyzed, and interpreted the study data. J.A. performed statistical analyses. R.T.M., P.M., and A.L. wrote the first a draft of the manuscript, and R.T.M. and G.C. wrote the subsequent drafts. All authors reviewed and approved the manuscript.

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