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Mobilization and Hematopoietic Stem Cell Collection in Poor Mobilizing Patients with Lymphoma: Final Results of the German OPTIMOB Study

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Abstract
Introduction: Successful mobilization and collection of peripheral hematopoietic stem cells (HSCs) are necessary for lymphoma patients eligible for myeloablative chemotherapy with subsequent autologous stem cell transplantation (ASCT). Albeit G-CSF alone or combined with chemotherapy is well-established methods for HSC mobilization, up to 40% of the patients fail to mobilize (poor mobilizer, PM). Plerixafor (PLX) is commonly used in PM patients resulting in increased migration of HSCs into peripheral blood and thus improves the collection outcome. ***Methods:*** The prospective, multicenter, open-label, non-interventional OPTIMOB study assessed mobilization and collection parameter of patients with lymphoma or multiple myeloma to get deep insights in the treatment of those patients in clinical routine focusing on PM patients. PM was defined as follows: (1) no achievement of ≥20 $CD34^+$ progenitor cells/μL before first apheresis, (2) PLX administration at any time point during the observational period, (3) reduction of the initially planned $CD34^+$ progenitor cell yield as necessity due to failed mobilization or HSC collection, and (4) no performance of apheresis due to low $CD34^+$ progenitor level. Primary objective of the study was to assess mobilization success by the proportion of PM patients achieving $>2 \times 10^6$ $CD34^+$ progenitor cells/kg body weight on the first day of apheresis. Here, the data of the lymphoma cohort are presented. ***Results:*** Out of 238 patients with lymphoma documented in the study, 32% were classified as PM. 87% of them received PLX. Demographic data revealed no obvious differences between PM and good mobilizing (GM) patients. All patients were treated highly individualized prior to mobilization. Majority of all PM patients were able to undergo apheresis (95%) and reached their individual requested $CD34^+$ progenitor cell target (72%). 57% of the PM patients achieved $>2.0 \times 10^6$ $CD34^+$ progenitor cells/kg body weight on day 1 of apheresis and nearby 70% of them underwent ASCT. Median time to engraftment was similar in PM and GM patients of the lymphoma cohort. ***Conclusions:*** Majority of PM patients with lymphoma were successfully mobilized and underwent ASCT. Most of them received PLX during the study.

Introduction

Hematological malignancies such as lymphoma account for ~6.5% of all cancers worldwide [1]. Based on the biological heterogeneity which leads to a very diverse group of diseases, clinical presentation of patients with lymphoma is complex and individualized treatment is needed [2–4]. Immunochemotherapy represents the first-line treatment for lymphoma, but in some patients, complete remission of the disease is not possible. High-dose chemotherapy (HDT) followed by autologous stem cell transplantation (ASCT) might be therefore indicated in refractory or relapsed lymphoma [2, 5, 6] as it can improve response and progression-free survival [7–10]. In addition, according to current clinical guidelines HDCT/ASCT is recommended as consolidation therapy during first-line treatment and in case of chemosensitivity upon relapse in patients with peripheral T-cell lymphoma [11]. Thus, successful mobilization and collection of hematopoietic stem cells (HSCs) are necessary for patients eligible for ASCT. Albeit most of the patients can achieve enough $CD34^+$ progenitor cells, estimated 15–40% of patients experienced unsuccessful mobilization [6, 12] and therefore, are so-called poor mobilizer (PM). The European Society for Blood and Marrow Transplantation (EBMT) consensus defines PM as those with a $CD34^+$ progenitor cell count <10 cells/μL on day 4 of mobilization or failure to obtain half of the number of $CD34^+$ progenitor cells required for ASCT [13]. Mobilization failure often results in a prolonged treatment including thus the risk of disease progression, increases treatment burden for affected patients, and leads to significant costs for healthcare systems. Therefore, it is of large interest to characterize poor mobilizing patients in more detail and to identify possible factors for a poorer mobilization ability to be able to adapt the treatment accordingly.

Current standard regimens for HSC mobilization comprise chemotherapy or granulocyte colony-stimulating factor (G-CSF) or a combination of both, G-CSF and chemotherapy [14–17]. During the last decades, plerixafor (PLX) was frequently used, especially in PM patients, to improve mobilization success and collection outcome [17–20]. The pivotal phase III trials in patients with multiple myeloma and lymphoma had demonstrated that PLX effectively mobilized HSCs [21, 22]. In the pivotal trial including patients with non-Hodgkin lymphoma, 59.3% of the patients treated with PLX were able to achieve $\geq 5 \times 10^6$ $CD34^+$ progenitor cells/kg body weight within ≤4 days [22]. In the pivotal trial on patients with multiple myeloma, 75.7% of those patients supported by PLX achieved $\geq 6 \times 10^6$ $CD34^+$ progenitor cells/kg body weight within a number of ≤4 days [19]. This outcome was confirmed in several other studies [20, 23–25]. In addition to its positive effects on HSC mobilization, PLX is known to be safe and well tolerated by the patients [21, 22, 25, 26].

Up to now, detailed information on PM patients with lymphoma regarding distribution, treatment and

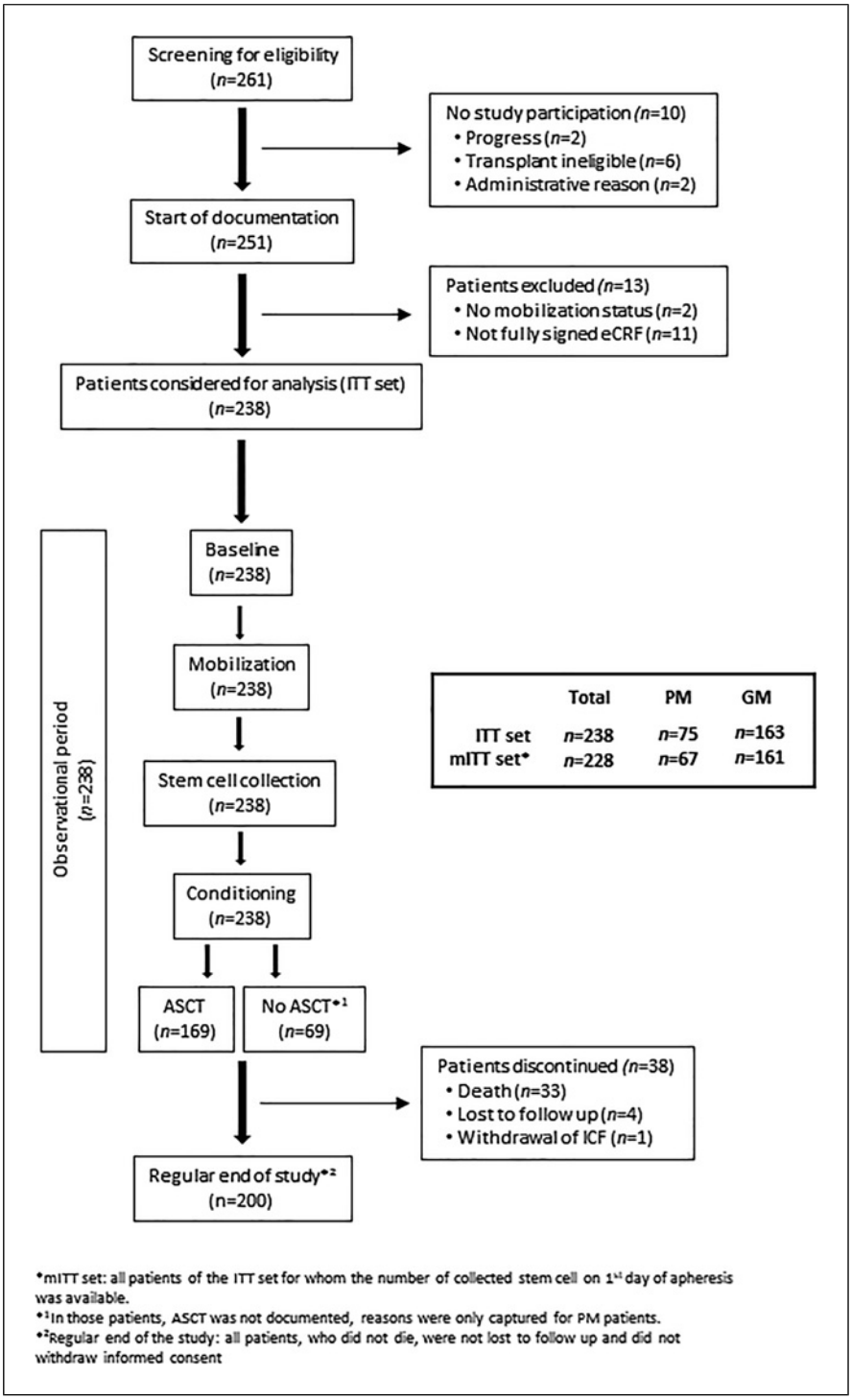


Fig. 1. Study flow diagram of the lymphoma cohort of the OPTIMOB study (consort flow chart). ASCT, autologous stem cell collection; ICF, informed consent form; *n*, number of patients.

mobilization strategies are rarely described in the literature. The German non-interventional OPTIMOB study addressed this lack of knowledge by analyzing mobilization and collection parameters in adult, transplant eligible, good and poor mobilizing patients with lymphoma or multiple myeloma who were treated with or without PLX. In the current manuscript, the lymphoma cohort of the OPTIMOB study is presented.

Materials and Methods

Study Design, Study Participants, and Data Collection

The OPTIMOB study was a prospective, multicenter, open-label, non-interventional study (NIS) in German patients with lymphoma or multiple myeloma who were eligible for ASCT. The aim of the study was the comprehensive evaluation of HSC mobilization and collection in these patients to get a better understanding of mobilization procedures as well as planning and implementation of transplants in a real-world setting with the aim to improve treatment strategies, especially in poor mobilizing patients.

Adult patients (≥18 years) with lymphoma or multiple myeloma confirmed by World Health Organization criteria eligible for ASCT who gave their signed informed consent prior to documentation start were allowed to be documented in the OPTIMOB study. Patients who had another disease indicating the need for ASCT, patients who were no longer a candidate for ASCT according to general documentation criteria and medical recommendations/internal clinic standards at the time of the $CD34^+$ progenitor cell count in the peripheral blood (PB) on the day before apheresis, and/or patients with another hematological or solid tumors were excluded from documentation. Baseline was defined as start of documentation prior to the first mobilization attempt within the OPTIMOB study.

A total of 28 in stem cell transplantation experienced German sites participated in the study. Patients were classified as good mobilizer (GM) or PM in accordance with following criteria for poor mobilization capability: (1) no achievement of ≥20 $CD34^+$ progenitor cells/μL before first apheresis, (2) PLX administration at any time point during the observational period, (3) reduction of the initially planned $CD34^+$ progenitor cell yield as necessity due to failed mobilization or HSC collection, and (4) none performance of apheresis due to low $CD34^+$ progenitor level. As there are different approaches to PM patients in the literature, a complex definition of PM patients had to be formulated for this study to consider all eventualities regarding the heterogeneity and complexity of the participating centers. The chosen definition allowed to include as many PM as possible. Physicians had to decide which kind of definition (1–4) fits most or occurred first, nevertheless, patients could belong to more than one of the predefined groups.

Data collection was done during the observational period (shown in Fig. 1) and included a detailed assessment of mobilization, apheresis, and ASCT parameters in those patients characterized as PM. In GM patients, data were collected in an abbreviated form. The observational period ended regularly up to 30 days after ASCT with a follow-up visit.

Study Objectives

The primary objective of the OPTIMOB study was the assessment of successful HSC collection in PM patients defined as the proportion of patients achieving $>2.0 \times 10^6$ $CD34^+$ progenitor cells/kg body weight on the first day of apheresis. Secondary objectives were the explorative evaluation of mobilization efficacy represented by an increase of $CD34^+$ progenitor cell count between the day before and the first day of apheresis, the rate of PM patients in relation to the total number of documented patients, exploratory evaluation of the total $CD34^+$ progenitor collection result and the achievement of the requested individual $CD34^+$ progenitor cell target, the rate of PM patients reaching a total collection result of $>2.0 \times 10^6$ $CD34^+$ progenitor cells/kg body weight, the rate of patients with mobilization failure defined as non-performance or discontinuation of apheresis, and finally, the explorative evaluation of the time to engraftment after ASCT.

Statistical Analysis

Statistical analyses were performed using SAS version 9.4. All screened patients fulfilling the documentation criteria and providing their informed consent, were considered for analysis (intention-to-treat set, ITT set, shown in Fig. 1). All patients of the ITT set having a documentation of the number of collected stem cells on day 1 of apheresis were included in the modified ITT set (mITT set, shown in Fig. 1). Due to the non-interventional

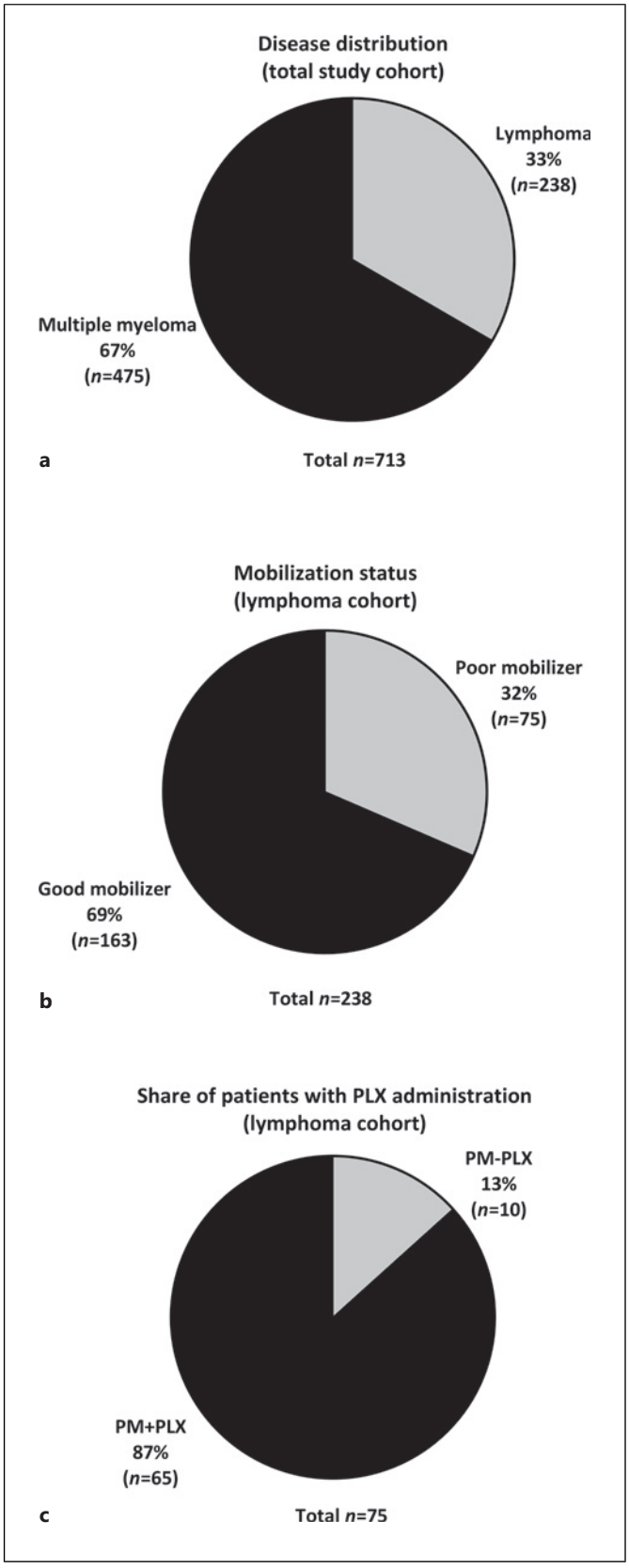


Fig. 2. Share of patients with lymphoma (**a**), their mobilization status (**b**), and plerixafor (PLX). Administration among PM patients (**c**) in the lymphoma cohort of the OPTIMOB study. PM, poor mobilizer; +PLX, patients with plerixafor administration; -PLX, patients without plerixafor administration; *n*, number of patients.

Table 1. Patient demographics and medical characteristics at baseline

	Poor mobilizer + PLX, *n* (%)	Poor mobilizer – PLX, *n* (%)	Good mobilizer, *n* (%)
Number of patients	65 (100)	10 (100)	163 (100)
Age, median (range), years	60 (29–79)	57 (32–70)	61 (22–78)
Age (categorical) ≥70 years	15 (23)	1 (10)	18 (11)
Weight (range), kg	75 (47–124)	85 (58–116)	79 (44–143)
Sex, *n* (%)			
Male	43 (66)	9 (90)	111 (68)
Female	22 (34)	1 (10)	52 (32)
ECOG/Karnofsky performance status			
0 (= Karnofsky 90–100%)	24 (37)	0 (0)	78 (48)
≥1 (= Karnofsky <90%)	21 (32)	8 (80)	48 (29)
Missing	20 (31)	2 (20)	37 (23)
Disease status			
Recently diagnosed (no relapse/in remission without disease progression)	29 (45)	6 (60)	92 (56)
≥1st relapse	36 (55)	4 (40)	70 (43)
Not evaluated	0 (0)	0 (0)	1 (1)
Mobilization status			
1st mobilization attempt	57 (88)	10 (100)	160 (98)
Remobilization*	3 (5)	0 (0)	0 (0)
2nd mobilization attempt*[1]	3 (5)	0 (0)	0 (0)
Missing/unknown	2 (3)	0 (0)	3 (2)
Subtype lymphoma classification			
B-cell lymphoma	52 (80)	8 (80)	111 (68)
T-cell lymphoma	6 (9)	0 (0)	27 (17)
Hodgkin lymphoma	7 (11)	2 (20)	22 (14)
Other*[2]	0 (0)	0 (0)	3 (2)
Thrombocytopenia (yes)	22 (34)	5 (50)	46 (28)*[3]
Leukopenia (yes)	13 (20)	3 (30)	21 (13)*[3]
Relevant comorbidities (yes)*[4]	53 (82)	7 (70)*[3]	116 (71)*[3]
Previous or concomitant medication (yes)	54 (83)	8 (80)	97 (60)

+PLX, patients with PLX administration; −PLX, patients without PLX administration; PLX, plerixafor; ECOG, Eastern Cooperative Oncology Score. *Remobilization was defined as mobilization after failed mobilization and/or sampling failure. *[1]Second mobilization attempt was defined as mobilization for 2nd stem cell transplantation. *[2]Including primary CNS lymphoma and transplant-associated lymphoproliferative disease with cerebral involvement. *[3]For 1 patient, data were missing or unknown. *[4]Relevant comorbidities were diabetes type 1 and type 2, cardiovascular diseases, joint disorders (arthritis), hyperlipidemia, arteriosclerosis, infections, coagulation disorders (thrombosis).

character of the current study, descriptive statistics (number and percentage for categorical parameters; median and range for continuous variables) were primarily used. Patients were stratified by their mobilization status (GM, PM with PLX administration [PM + PLX], PM without PLX administration [PM – PLX]) for analysis. The primary endpoint was calculated for the PM patients of the mITT set, for secondary endpoint analyses, the ITT set was used. The time to recovery of the hematopoietic system was calculated as days until reaching $>0.5 \times 10^9$ neutrophils/L and $> 50 \times 10^9$ platelets (PLT)/L after ASCT. Adverse events (AEs) and serious AEs were documented in the OPTIMOB study without grading.

Ethical Statement

The study was approved by the responsible Central Ethic Committee (Ethikkommission der Ärztekammer Hamburg, Hamburg, Germany, approval number: PV5559) as well as by all other Ethics Committees of state chambers of the participating physician and conducted in accordance with local regulatory requirements. Written informed consent was obtained from all patients prior to documentation start.

Results

Patient Disposition

A total of 713 patients were documented in the OPTIMOB study between July 02, 2018, and November 03, 2021 (provided in Fig. 2). Thereof, 33% of the patients (n = 238) had lymphoma, 67% (n = 475) had multiple myeloma (shown in Fig. 2a). All 238 patients with lymphoma had a baseline assessment and were documented at the time of mobilization, apheresis, and conditioning, for 169 patients, ASCT data were available (shown in Fig. 1). 38 patients discontinued the study due to death (n = 33), lost to follow-up (n = 4), or withdrawal of informed consent form (n = 1, shown in Fig. 1). Regarding mobilization capability, 32% of the lymphoma patients (n = 75) were classified as PM (provided in Fig. 2b). 87% of them received PLX within the OPTIMOB study (n = 65, shown in Fig. 2c). In most of the

Table 2. Therapy regimens prior to mobilization – overview*

	Poor mobilizer + PLX, *n* (%)	Poor mobilizer – PLX, *n* (%)	Good mobilizer, *n* (%)
Number of patients	65 (100)	10 (100)	163 (100)
BEACOPP (+/– other)	0 (0)	0 (0)	3 (2)
CHOEP (+/– other)	4 (6)	0 (0)	14 (9)
R-CHOP (+/– other)	11 (16)	2 (20)	29 (18)
DHAP (+/– other)	5 (8)	1 (10)	10 (6)
R-DHAP	13 (20)	2 (20)	33 (20)
R-DHAP-R-CHOP (+/– other)	1 (2)	0 (0)	5 (3)
Other	23 (35)	1 (20)	47 (29)
Missing	8 (12)	4 (40)	22 (14)
Number of patients receiving rituximab in the last treatment prior to mobilization	38 (59)	5 (50)	90 (55)
Share of patients, whose last treatment was part of another clinical trial	1 (2)	1 (10)	10* (6)

BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, prednisone, etoposide; R-CHOEP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, etoposide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; DHAP, dexamethasone, cytarabine, cisplatin; R-DHAP, rituximab, dexamethasone, cytarabine, cisplatin; R-DHAP-R-CHOP, rituximab, dexamethasone, cytarabine, cisplatin-rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone. *For 3 patients, no details were documented about the last treatment prior to mobilization.

patients, physicians selected definition 2 (requirement of PLX) as most fitting or firstly occurring criterion for PM classification (online supplementary Table 1; for all online suppl. material, see https://doi.org/10.1159/000531936). Table 1 gives an overview on patient demographics and disease characteristics at baseline. The lymphoma cohort had a wide age range from 22 to 79 years (median age: 61 years). In the PM +PLX group, the share of patients ≥70 years was slightly greater as in the PM – PLX group and in the GM group (23% vs. 10% vs. 11%). In all 3 patient groups, more males were affected by lymphoma (PM + PLX: 66%, PM – PLX: 90%, GM: 68%). Most patients had B-cell lymphoma (total n = 171, 68–80% of patients in each group). Diffuse large B-cell lymphoma without further classification (72 of 171 patients, 42%) and mantle cell lymphoma (45 of 171 patients, 26%) were the most frequently documented B-cell lymphoma types. 17.2% of the lymphoma cohort had a bone marrow infiltration (n = 41). Newly diagnosed/in remission without disease progression was 45–60% of the patients, in PM + PLX patients more than half of the patients had ≥1st relapse at baseline. However, the majority of the patients underwent first mobilization attempt within the OPTIMOB study independent of their mobilization status. More than 70% of the patients in the lymphoma cohort had comorbidities and more than 80% of the PM patients received a previous or concomitant medication, nevertheless, physical performance/activity was mostly good as shown by the Eastern Cooperative Oncology Score (ECOG)/Karnofsky performance status.

Previous Treatment

Table 2 provides an overview on the most often documented last therapies prior to documentation. Rituximab in various treatment regimens was frequently used in the lymphoma cohort (from 50% to 59% of the patients in the respective group). Treatment in lymphoma patients was very individualized due to a variety of B- and T-non-Hodgkin lymphoma sub-entities with a common documentation of R-CHOP and R-DHAP-based treatments (between 16% and 20% in the respective group). The number of patients whose last treatment prior to mobilization within the OPTIMOB study was part of another clinical trial was low with 1 patient each in both PM groups and 10 patients in the GM group (6%).

Mobilization and Apheresis

Detailed information on mobilization was provided for both PM patient groups. 68% of the patients in the PM + PLX group were mobilized with "standard therapy" defined as chemo-mobilization as part of therapeutic chemotherapy (n = 39 out of 57 patients undergoing their first mobilization attempt within the OPTIMOB study, shown in Fig. 3a). Separate chemo-mobilization was applied in 25% of the patients (n = 14, shown in Fig. 3a). Steady state mobilization with G-CSF only received 7% of the patients undergoing first mobilization attempt (n = 4, shown in Fig. 3a). In the PM patients without PLX support, 80% of the patients (n = 8) were mobilized with chemo-mobilization + G-CSF, mainly with "standard therapy" (n = 7, shown in Fig. 3a). Most of the PM patients received G-CSF 6–10 times during the mobilization process (58%, n = 39). Filgrastim was used

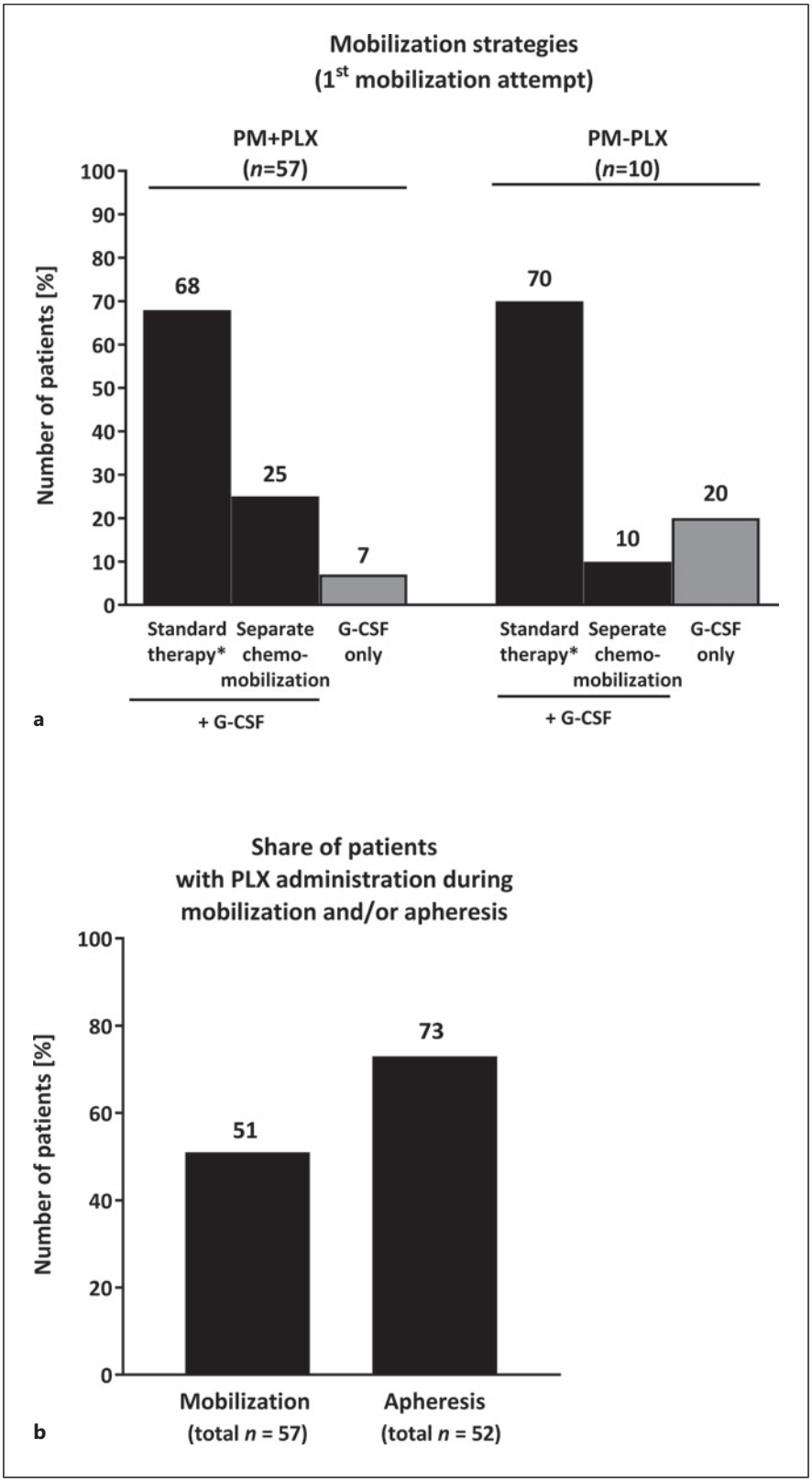


Fig. 3. Mobilization strategies (**a**) and share of patients receiving PLX during mobilization and/or apheresis* (**b**) within the 1st mobilization attempt performed in the OPTIMOB study. PM, poor mobilizer; +PLX, patients with plerixafor administration; −PLX, patients without plerixafor administration; *n*, number of patients. *Defined as chemo-mobilization as part of therapeutic chemotherapy.

in 87% of the patients (n = 58) during 1st mobilization attempt, followed by lenograstim (12%, n = 8), 1 patient received pegfilgrastim. The median dose of filgrastim per patient was 10.00 μg/kg body weight during 1st mobilization attempt (range: 5.00–10.00) resulting in a median total dosage of 480 μg per patient (range: 352.50–960.00). During 1st mobilization attempt, PLX was administered to 51% of the PM patients during mobilization procedure (n = 29) and

Table 3. Chemotherapy regimen used for mobilization in PM patients of the lymphoma cohort within the OPTIMOB study

Chemotherapy for mobilization	Poor mobilizer + PLX, *n* (%)	Poor mobilizer- PLX, *n* (%)
Patients, *n*	53 (100)	8 (100)
AraC-based regimen	6 (11)	1 (13)
CHOP	2 (4)	0 (0)
CY based (≥1 g)	3 (6)	0 (0)
Dexa-BEAM	0 (0)	3 (38)
DHAP	8 (15)	0 (0)
ICE	4 (8)	4 (50)
Other	30 (57)	1 (13)

AraC, cytarabine; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CY, cyclophosphamide; Dexa-BEAM, dexamethasone, carmustine, etoposide, cytarabine, melphalan; DHAP, dexamethasone, cytarabine, cisplatin; ICE, ifosfamide, carboplatin, etoposide (±rituximab). Patients who received DHAP were not included in AraC-based regimen.

to 73% of them during apheresis (n = 38, multiple answers possible, shown in Fig. 3b). PLX dosage was 0.24 mg/kg body weight per day per patient documented in 17 patients during 1st mobilization attempt. For 12 patients, PLX was documented to be given as fixed dose of 20 mg. During apheresis, 26 patients received PLX as fixed dose, 12 patients were supported with a median dosage of 0.24 mg/kg body weight per day per patient. Table 3 provides an overview on chemotherapy regimens used for mobilization in the PM patient groups showing a high variability in the applied regimens.

Mobilization Success and Collection Results

In total, 95% of the patients receiving PLX (n = 62) and 90% of the PM patients without PLX support (n = 9) were able to undergo apheresis in the OPTIMOB study. Mobilization success defined by a collection result of >2.0 × 10^6 $CD34^+$ progenitor cells/kg body weight on day 1 of apheresis was achieved by 57% of the mITT set (38 out of 67 evaluable patients, shown in Table 4). The share of patients with successful mobilization was slightly greater in PM patients without than in patients with PLX support (67% vs. 55%). However, in both PM groups, for majority of patients, mobilization result was stated as good (PM + PLX: 67%, n = 39, PM − PLX: 89%, n = 8, mITT set) and most of the PM patients reached their individual requested $CD34^+$ progenitor collection target (PM + PLX: 68%, n = 39, PM − PLX: 90%, n = 9, ITT set, shown in Table 4). The rate of patients with mobilization failure was ≤10.0% in both PM patient groups as shown in Table 4.

The collection result on the first day of apheresis is provided in Figure 4c. PM patients had a lower median number of $CD34^+$ progenitor cells × 10^6/kg body weight than GM patients, but the individual result varied widely in the PM group (range: 0.2 to 77.0 $CD34^+$ progenitor cells × 10^6/kg body weight). Regarding the total collection result, no obvious differences were observed between PM patients with and without PLX support (shown in Fig. 4d). Additionally, the $CD34^+$ progenitor cells/μL in PB on the day before and the day of apheresis did not differ considerably between PM + PLX and PM − PLX patients (shown in Fig. 4b). Nevertheless, the median number of $CD34^+$ progenitor cells/μL in PB increased from 11 cells/μL to 34 cells/μL after PLX administration in those patients receiving PLX in the OPTIMOB study (shown in Fig. 4a). ASCT was performed in 68% of the PM + PLX (n = 44) and in 70% of the PM − PLX patients (n = 7).

Engraftment of the Hematopoietic System

Successful engraftment was documented in 46% of the PM + PLX (n = 30) and in 30% of the PM − PLX patients (n = 3). For the time until PLT engraftment, no obvious differences were observable between PM + PLX (in median 21 days) and GM patients (in median 20 days). Neutrophil engraftment was reached in median after 10 days in PM − PLX and GM patients, PM + PLX patient needed in median 10.5 days. Details on the recovery of the hematopoietic system are provided in online supplementary Table 2 and Figure 5a and b. In general, the number of patients with available data concerning engraftment was rather low which must be considered for interpretation.

Safety Aspects

Online supplementary Table 3 provides an overview on safety data of the lymphoma cohort during the observational phase. Four patients experienced at least one AE with potential causal relationship to PLX (abdominal pain, nausea, body temperature increased, bone pain, and drug ineffective, each AE was experienced by 1 patient as shown in online suppl. Table 3). Reported AEs with potential causal relationship to PLX were in line with the known safety profile of PLX [19–21].

Discussion

The OPTIMOB study evaluated the mobilization and collection of HSCs in PM patients with lymphoma and multiple myeloma in detail. The goal was to gain a better understanding of the current situation of these patients in German clinical practice and to possibly identify options for improvement of mobilization and collection procedures. In the here presented lymphoma cohort, the high proportion of PM patients (32%) underlines the importance of establishing adequate HSC mobilization and collection strategies to enable successful ASCT outcomes. In the literature, the proportion of PM patients varies depending on the applied definition of poor mobilization ability. In the OPTIMOB study, the definition for classifying a patient as PM included no achievement of ≥20 $CD34^+$ progenitor

Table 4. Efficacy of mobilization and mobilization failure in poor mobilizing patients with lymphoma

	Poor mobilizer + PLX, *n* (%)	Poor mobilizer – PLX, *n* (%)	Poor mobilizer total, *n* (%)
Number of patients from the mITT set with available data	58 (100)	9 (100)	67 (100)
Number of patients with a collection result of >2.0 × 10^6 $CD34^+$ cells/kg body weight on day 1 of apheresis	32 (55)	6 (67)	38 (57)
Mobilization result			
Good	39 (67)	8 (89)	47 (70)
Insufficient	19 (33)	1 (11)	20 (30)
Number of patients from the ITT set undergoing 1st mobilization attempt	57 (100)	10 (100)	67 (100)
Number of patients who reached their requested individual $CD34^+$ cell count			
Yes	39 (68)	9 (90)	48 (72)
No	13 (23)	0 (0)	13 (19)
Number of patients with mobilization failure*	5 (9)	1 (10)	6 (9)

HDT, high-dose chemotherapy; mITT set, modified intention-to-treat set, all patients of the ITT set for whom the number of collected stem cells on day 1 of apheresis was available; ITT set, intention-to-treat set, all enrolled patients who gave their informed consent and participation was possible. *Mobilization failure, i.e., collection was not started, or apheresis was discontinued.

cells/μL before 1st apheresis, PLX administration at any time point during the observational period, a reduction of the initially planned $CD34^+$ progenitor cell yield as necessity due to failed mobilization or HSC collection, and no performance of apheresis due to low $CD34^+$ progenitor level. To be classified as PM, the patient had to meet at least one of these four options. The EBMT consensus defines PM much more strictly [13], so that the generous PM definition in the OPTIMOB study may have contributed to the high number of PM patients in the lymphoma cohort. However, it must be considered that other studies also defined PM differently from the EBMT consensus leading to an elevated proportion of PM patients there as well. In addition to that, transplant-eligible lymphoma patients usually receive ASCT when they have relapsed and/or refractory lymphoma and do not qualify for chimeric antigen receptor T-cell therapy [6–8], so these patients are already pretreated including radiotherapy in some of them, and thus, the ability to mobilize enough HSCs might be limited [25, 27]. In the OPTIMOB study, the last treatment prior to mobilization was highly individualized which might be associated with the various diseases covered by the term "lymphoma" that require a correspondingly adapted therapy. This makes it difficult to conclude that certain pretreatments might have impaired the mobilization process. 57% of the PM patients were pretreated with a regimen including rituximab. However, rituximab is not considered to negatively impact mobilization capability [28–30].

Mobilization was mainly performed within standard therapy in PM patients of the lymphoma cohort with additional administration of G-CSF. Mobilization was quite good in the PM patients which might be associated with the PLX usage in the majority of the PM patients (87%). In the OPTIMOB study, the administration of PLX led to an obvious increase of $CD34^+$ progenitor cells in PB as mentioned in previous studies [31–34], suggesting sufficient mobilization results in those treated with PLX so that planned HSC collection could have been performed even PM patients. This suggestion was confirmed since 95% of the patients receiving PLX were able to undergo apheresis and 68% of them reached their individual requested $CD34^+$ progenitor cell collection target. However, only 55% of the PM + PLX patients of the mITT set achieved a collection result of >2.0 × 10^6 $CD34^+$ progenitor cells/kg body weight on the 1st day of apheresis and in 33% of the PM + PLX patients from the mITT set, mobilization result was stated as insufficient. In a study from Worel et al. [34], 97% of the patients achieved at least >2.0 × 10^6 $CD34^+$ progenitor cells/kg body weight, which seems to be a markedly higher proportion of patients than in the OPTIMOB study. However, Worel et al. [34] included patients with MM and lymphoma in their analysis which might have an impact on the achievement of >2.0 × 10^6 $CD34^+$ progenitor cells/kg body weight. In the pivotal trial on non-Hodgkin lymphoma patients, 59% of the PM patients given PLX collected ≥5 × 10^6 $CD34^+$ progenitor cells/kg body weight [20] which is considered as sufficient collection result for ASCT. In the OPTIMOB study, in most of the patients with insufficient mobilization, this statement based on the fact that the individual requested $CD34^+$ progenitor target was not achieved which was not a "real" mobilization failure (23%). Looking at the rate of patients with mobilization failure which meant (by definition) that the collection was either not started or aborted, solely 9% of the patients receiving

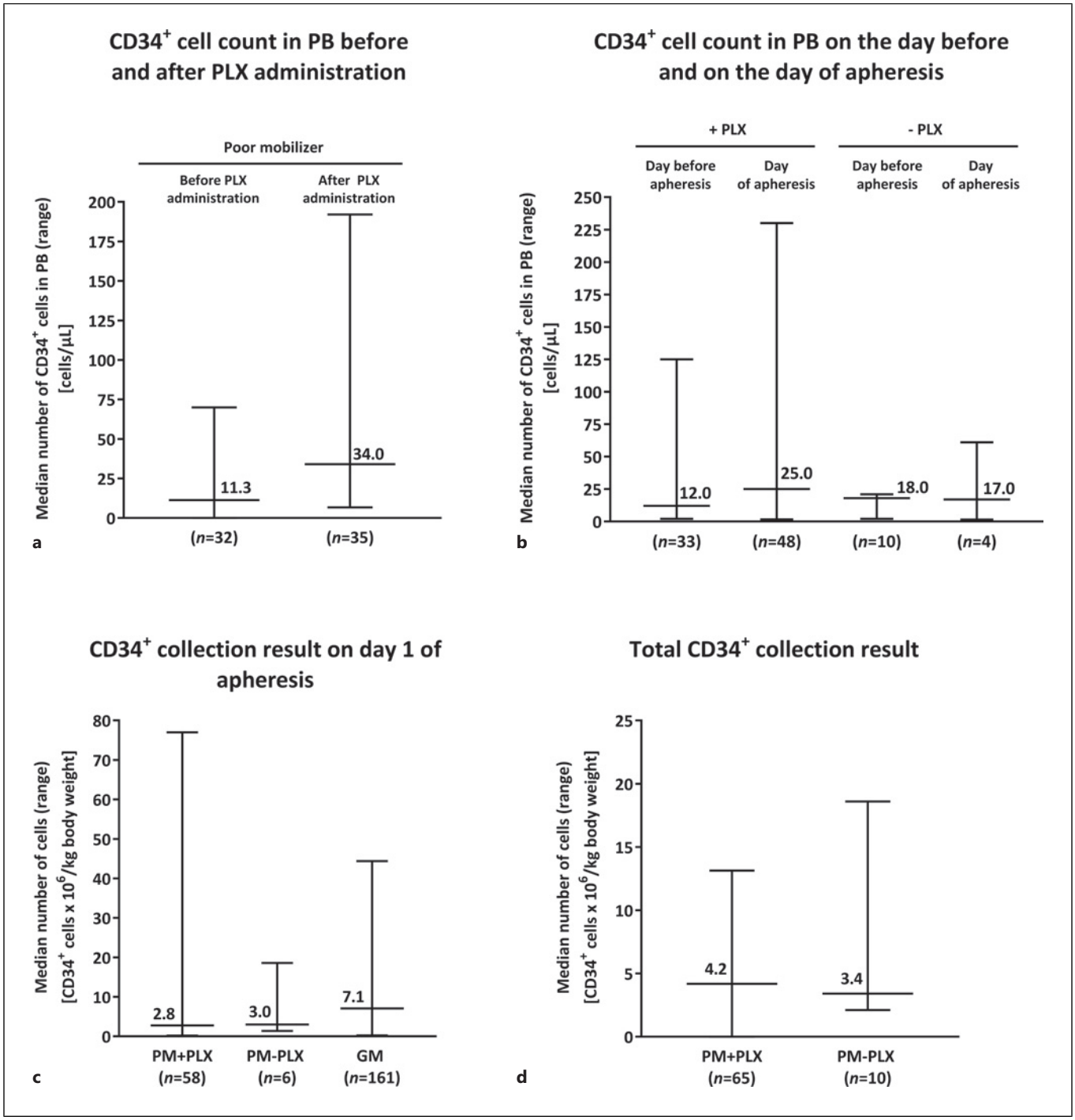
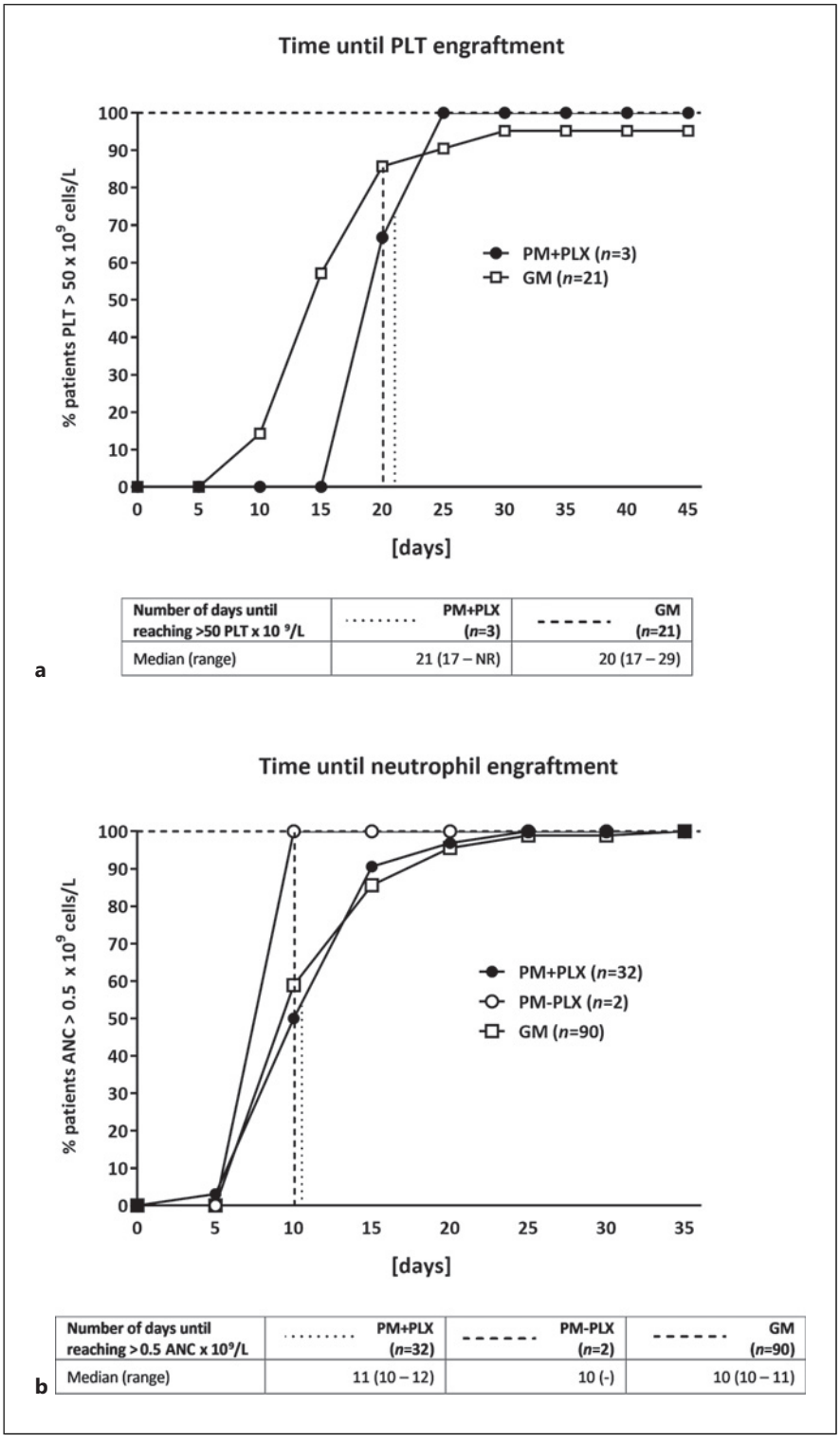


Fig. 4. CD34$^+$ progenitor cell count in PB before and after PLX administration (**a**), CD34$^+$ progenitor cell count in PB on the day before and the day of apheresis (**b**), collection result on day 1 (**c**), and total collection result* (**d**) of the lymphoma cohort of the OPTIMOB study. *Total collection result was only assessed in PM patients. ASCT, autologous stem cell transplantation; GM, good mobilizer; PM, poor mobilizer; +PLX, patients with plerixafor administration; −PLX, patients without plerixafor administration; *n*, number of patients.

PLX failed to mobilize successfully during the 1st mobilization attempt confirming the result from another study, where PLX was administered to adult patients predicted as PM leading to a low failure rate of 4% in the patients [17]. One may have expected a better collection result in the PM + PLX group but nevertheless, it was sufficient for a large proportion of patients, as 68% were still able to undergo ASCT, and presumably might have a better prognosis [7–10]. The share of patients undergoing ASCT was markedly lower than in the pivotal trial on patients with



a

Number of days until reaching >50 PLT x 10 ^{9}/L	PM+PLX (*n*=3)	GM (*n*=21)
Median (range)	21 (17 – NR)	20 (17 – 29)

b

Number of days until reaching > 0.5 ANC x 10^9/L	PM+PLX (*n*=32)	PM-PLX (*n*=2)	GM (*n*=90)
Median (range)	11 (10 – 12)	10 (-)	10 (10 – 11)

Fig. 5. Engraftment of platelets (PLT) (**a**)* and absolute neutrophils (ANC) (**b**) in lymphoma patients stratified by mobilization status. ANC, absolute neutrophil count; GM, good mobilizer; NR, not reached; PLT, platelets; PM + PLX, poor mobilizer with plerixafor administration; PM – PLX, poor mobilizer without plerixafor administration; *n*, number of patients. *PLT count >50 cells × 10^9/L was not documented for any of the PM – PLX patients in the OPTIMOB study.

non-Hodgkin lymphoma (90%) but in the OPTIMOB study even in GM patients, solely 72% proceeded to subsequent ASCT.

Interestingly, in the PM – PLX group mobilization and collection results were also quite good. 90% of patients without PLX support performed apheresis, 89% had a good mobilization result (mITT set), 67% achieved >2.0 × 10^6 $CD34^+$ progenitor cells/kg body weight on day 1 of apheresis (mITT set), and all of them reached their individual prespecified collection target (ITT set). However, the number of PM – PLX patients was rather small which must be considered for interpretation. In the MM cohort (data are presented in a separate companion manuscript in this special issue), the number of patients without PLX

support was also rather low, indicating that PLX is frequently used in patients who might have mobilization failure. Additionally, since it was not asked in the case report form why some of the PM patients did not receive PLX, it can only be speculated why the treating physician decided not to administer PLX. A closer look at the PM – PLX patients did not reveal any obvious differences in terms of pretreatment, including the mean number of therapy lines and cycles, as well as the regimens used, demographics, and mobilization procedures, which might have been a possible reason to refrain PLX administration specifically in these patients. ASCT was also possible in majority of PM – PLX patients which is a thoroughly pleasing result, as it shows, that even poor mobilizing lymphoma patients were able to mobilize enough HSCs for subsequent ASCT.

Another important parameter in the treatment of lymphoma patients with HDT-ASCT represents the reconstitution of the hematopoietic system. Cell doses of $\geq 5 \times 10^6$ $CD34^+$ progenitor cells/kg body weight are considered to improve PLT recovery resulting in a less frequent need of blood transfusion [17]. In the OPTIMOB study, it was not assessed how many patients achieved a result of $\geq 5 \times 10^6$ $CD34^+$ progenitor cells/kg body weight but in median patients supported by PLX achieved a total collection result of 4.2×10^6 $CD34^+$ progenitor cells/kg body weight, a good prerequisite for successful recovery of the hematopoietic system. In the OPTIMOB study, engraftment was documented as successful in most of the PM patients. However, for a considerable number of patients, the documentation was missing resulting in a small number of evaluable patients. Despite the small number of patients with documented data, the number of days until PLT and neutrophil engraftment up to 30 days after ASCT was in the expected range [22, 35]. Regarding PLT engraftment, it must be noticed that for none of the patients without PLX support, achievement of $>50 \times 10^9$ cells/L was documented but due to the small number of patients without PLX support, conclusions must be drawn carefully. However, in the literature, it was shown that PLX administration positively impacts engraftment [34, 35]. In the OPTIMOB study, no differences were observed between PM + PLX and GM patients regarding PLT and neutrophil recovery.

In the lymphoma cohort of the OPTIMOB study, PLX was well tolerated, and no new safety issues were identified during the study, confirming results of previous studies on PLX safety [21–23, 34]. The OPTIMOB study provides detailed real-world evidence of treatment and mobilization procedures in patients with lymphoma (and multiple myeloma) in Germany. In contrast to randomized clinical trials, patients were documented in a real-world setting without restrictions on age, disease status, and/or previous treatments. Therefore, the patient population was heterogenous regarding age, underlying disease type, and prior treatments. This diversity of the study population might be a reason why a considerable number of patients with lymphoma were classified as PM. Additionally, the treatment decision was not predefined in the OPTIMOB study but was in the hands of the treating physician leading to various mobilization regimens. In some PM patients, no PLX support was used; nevertheless, majority of these patients also achieved a good mobilization and collection result. This shows that there is still a great need to characterize PM patients to optimize their treatment options even more specifically. In around 70% of the PM patients, ASCT was performed, potentially improving their treatment outcome, progression-free time, and survival. PLX was frequently administered in PM patients of the lymphoma cohort to support mobilization resulting in sufficient collection results, good recovery of the hematopoietic system, and low rates of mobilization failure. Nevertheless, further real-world studies for treatment optimization in lymphoma patients are required to reduce patients' disease and treatment burden and to improve progression-free survival.

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Statement of Ethics

This study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study was approved by the responsible Central Ethic Committee (Ethikkommission der Ärztekammer Hamburg, Hamburg, Germany, approval number: PV5559, approval date: 22 SEP 2017) and written informed consent was obtained from all participants.

Conflict of Interest Statement

K.K. received research funding from Bristol Myers Squibb and Sanofi-Aventis Deutschland GmbH. M.B. received honoraria for advisory board and consultancy activities from Bristol Myers Squibb, Sanofi-Aventis Deutschland GmbH, Glaxo Smith Kline GmbH & Co. KG, research funding from Bristol Myers Squibb (Celgene), Otsuka Pharmaceuticals, Sanofi, Chugai Pharma, Abbvie, AMGEN, and Janssen, and owns shares from Abbvie. S.S. received honoraria and research funding from Sanofi-Aventis Deutschland GmbH, Bristol Meyers Squibb, Amgen, and Janssen. C.T.-S. received honoraria from Sanofi. M.G. (Matthias Grube) received honoraria from Sanofi, Janssen, and Bayer. V.V. received honoraria from Sanofi, Bristol Myers Squibb, Novartis, Amgen, and Janssen.

D.W. received honoraria for advisory board activities and travel support from Sanofi.

A.B. received honoraria from Incyte and AOP Orphan and scientific support from AOP Orphan.

M.S.-H. received honoraria for consultancy activities from Celgene GmbH, Amgen GmbH, Kite/Pharma Gilead, Sanofi-Aventis Deutschland GmbH, Glaxo Smith Kline GmbH & Co. KG, Bristol Myers Squibb GmbH & Co. KG, Shionogi GmbH, Stemline Therapeutics (no individual payment) and financial support of educational meetings from Janssen-Cilag GmbH, Takeda Pharma Vertrieb GmbH & Co. KG, Novartis Pharma GmbH, Pfizer Pharma GmbH, Roche Pharma AG, Vifor Pharma Deutschland GmbH, and Celgene GmbH (no individual payment). Additionally, M.S.-H. participated in different clinical trials supported by the industry (including the OPTIMOB study).

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C.K. (Christian Kunz) received honoraria for advisory board activities from Abbvie, Sanofi, Bristol Meyer Squibb, and Amgen as well as financial support for congress participation from Abbvie, Amgen, and Bristol Meyer Squibb.

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Author Contributions

All authors were involved in data collection, analysis, and interpretation of the data. Nicolaus Kröger, Max Bittrich, Katharina Kriegsmann, and Franziska Brand were involved in drafting of the manuscript and revising it critically for intellectual content. All authors approved the final version of this manuscript and agreed to be accountable for all aspects of the work.

Data Availability Statement

All data supporting the findings of this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

References

1 Tietsche de Moraes Hungria V, Chiattone C, Pavlovsky M, Abenoza LM, Agreda GP, Armenta J, et al. Epidemiology of hematologic malignancies in real-world settings: findings from the hemato-oncology Latin America observational registry study. J Glob Oncol. 2019 Nov;5:1–19.
2 Matasar MJ, Zelenetz AD. Overview of lymphoma diagnosis and management. Radiol Clin North Am. 2008 Mar;46:175–98.
3 Ansell SM. Hodgkin lymphoma: 2023 update on diagnosis, risk-stratification, and management. Am J Hematol. 2022 Nov;97(11):1478–88.
4 Ansell SM. Non-hodgkin lymphoma: diagnosis and treatment. Mayo Clin Proc. 2015 Aug;90(8):1152–63.
5 Zahid U, Akbar F, Amaraneni A, Husnain M, Chan O, Riaz IB, et al. A review of autologous stem cell transplantation in lymphoma. Curr Hematol Malig Rep. 2017 Jun;12(3):217–26.
6 Carreras E, Dufour C, Mohty M, Kröger N, editors 7th ed. The EBMT handbook: hematopoietic stem cell transplantation and cellular therapies. Cham: Springer; 2019.
7 Philip T, Guglielmi C, Hagenbeek A, Somers R, Van der Lelie H, Bron D, et al. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. N Engl J Med. 1995 Dec;333(23):1540–5.
8 Schmitz N, Pfistner B, Sextro M, Sieber M, Carella AM, Haenel M, et al. Aggressive conventional chemotherapy compared with high-dose chemotherapy with autologous haemopoietic stem-cell transplantation for relapsed chemosensitive Hodgkin's disease: a randomised trial. Lancet. 2002 Jun;359(9323):2065–71.
9 Duong HK, Savani BN, Copelan E, Devine S, Costa LJ, Wingard JR, et al. Peripheral blood progenitor cell mobilization for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American Society for Blood and Marrow Transplantation. Biol Blood Marrow Transpl. 2014 Sep;20(9):1262–73.
10 Beitinjaneh A, Saliba RM, Medeiros LJ, Turturro F, Rondon G, Korbling M, et al. Comparison of survival in patients with T cell lymphoma after autologous and allogeneic stem cell transplantation as a frontline strategy or in relapsed disease. Biol Blood Marrow Transpl. 2015 May;21(5):855–9.
11 Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie e.V. [Internet]. Berlin: Onkopedia Leitlinie: Periphere T-Tell Lymphome, Version Juni 2021 [cited 2023 Feb 21]. Available from: https://www.onkopedia.com/de/onkopedia/guidelines/periphere-t-zell-lymphome/@@guideline/html/index.html.
12 Wuchter P, Ran D, Bruckner T, Schmitt T, Witzens-Harig M, Neben K, et al. Poor mobilization of hematopoietic stem cells-definitions, incidence, risk factors, and impact on outcome of autologous transplantation. Biol Blood Marrow Transpl. 2010 Apr;16(4):490–9.

13 Mohty M, Hübel K, Kröger N, Aljurf M, Apperley J, Basak GW, et al. Autologous haematopoietic stem cell mobilisation in multiple myeloma and lymphoma patients: a position statement from the European Group for Blood and Marrow Transplantation. Bone Marrow Transpl. 2014 Jul;49(7):865–72.
14 Zheng G, He J, Cai Z, He D, Luo Y, Shi J, et al. A retrospective study of autologous stem cell mobilization by G-CSF in combination with chemotherapy in patients with multiple myeloma and lymphoma. Oncol Lett. 2020 Jan;19(1):1051–9.
15 Pusic I, Jiang SY, Landua S, Uy GL, Rettig MP, Cashen AF, et al. Impact of mobilization and remobilization strategies on achieving sufficient stem cell yields for autologous transplantation. Biol Blood Marrow Transpl. 2008 Sep;14(9):1045–56.
16 Gertz MA. Current status of stem cell mobilization. Br J Haematol. 2010 Sep;150(6):647–62.
17 Giralt S, Costa L, Schriber J, Dipersio J, Maziarz R, McCarty J, et al. Optimizing autologous stem cell mobilization strategies to improve patient outcomes: consensus guidelines and recommendations. Biol Blood Marrow Transpl. 2014 Mar;20(3):295–308.
18 Jantunen E, Varmavuo V, Valtola J. Plerixafor injection: a hematopoietic stem cell mobilizer in non-Hodgkin lymphoma and multiple myeloma. Expert Rev Hematol. 2016 Aug;9(8):723–32.
19 Ataca Atilla P, Bakanay Ozturk SM, Demirer T. How to manage poor mobilizers for high dose chemotherapy and autologous stem cell transplantation? Transfus Apher Sci. 2017 Apr;56(2):190–8.
20 Mohty M, Azar N, Chabannon C, Le Gouill S, Karlin L, Farina L, et al. Plerixafor in poor mobilizers with non-Hodgkin's lymphoma: a multi-center time-motion analysis. Bone Marrow Transpl. 2018 Mar;53(3):246–54.
21 DiPersio JF, Stadtmauer EA, Nademanee A, Micallef IN, Stiff PJ, Kaufman JL, et al. Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma. Blood. 2009 Jun;113(23):5720–6.
22 DiPersio JF, Micallef IN, Stiff PJ, Bolwell BJ, Maziarz RT, Jacobsen E, et al. Phase III prospective randomized double- blind placebo-controlled trial of plerixafor plus granulocyte colony-stimulating factor compared with placebo plus granulocyte colony-stimulating factor for autologous stem-cell mobilization and transplantation for patients with non-Hodgkin's lymphoma. J Clin Oncol. 2009;27(28):4767–73.
23 Hübel K, Fresen MM, Salwender H, Basara N, Beier R, Theurich S, et al. Plerixafor with and without chemotherapy in poor mobilizers: results from the German compassionate use program. Bone Marrow Transpl. 2011 Aug;46(8):1045–52.
24 Bilgin YM, de Greef GE. Plerixafor for stem cell mobilization: the current status. Curr Opin Hematol. 2016 Jan;23(1):67–71.
25 Danylesko I, Sareli R, Varda-Bloom N, Yerushalmi R, Shem-Tov N, Shimoni A, et al. Plerixafor (mozobil): a stem cell-mobilizing agent for transplantation in lymphoma patients predicted to Be poor mobilizers: a pilot study. Acta Haematol. 2016;135(1):29–36.
26 Sureda A, Chabannon C, Masszi T, Pohlreich D, Scheid C, Thieblemont C, et al. Analysis of data collected in the European Society for Blood and Marrow Transplantation (EBMT) Registry on a cohort of lymphoma patients receiving plerixafor. Bone Marrow Transpl. 2020 Mar;55(3):613–22.
27 Olivieri A, Marchetti M, Lemoli R, Tarella C, Iacone A, Lanza F, et al. Proposed definition of "poor mobilizer" in lymphoma and multiple myeloma: an analytic hierarchy process by ad hoc working group Gruppo Italiano Trapianto di Midollo Osseo. Bone Marrow Transpl. 2012 Mar;47(3):342–51.
28 Kamezaki K, Kikushige Y, Numata A, Miyamoto T, Takase K, Henzan H, et al. Rituximab does not compromise the mobilization and engraftment of autologous peripheral blood stem cells in diffuse-large B-cell lymphoma. Bone Marrow Transpl. 2007 May;39(9):523–7.
29 Papajik T, Pikalova Z, Raida L, Skoumalova I, Vondrakova J, Faber E, et al. Rituximab does not adversely affect the stem cell mobilization and engraftment after high-dose therapy and autologous transplantation in patients with diffuse large B-cell lymphoma in first complete or partial remission. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2009 Sep;153(3):211–4.
30 Lefrère F, Bastit-Barrau D, Hequet O, Bourin P, Mathieu-Nafissi S, Bohbot A, et al. Impact of rituximab on stem cell mobilization following ACVBP regimen in poor-risk patients with diffuse large B-cell lymphoma: results from a large cohort of patients. Transfusion. 2013 Jan;53(1):115–22.
31 Maziarz RT, Nademanee AP, Micallef IN, Stiff PJ, Calandra G, Angell J, et al. 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$^+$ progenitor cells. Biol Blood Marrow Transpl. 2013;19(4):670–5.
32 Milone G, Martino M, Spadaro A, Leotta S, Di Marco A, Scalzulli P, et al. Plerixafor on-demand combined with chemotherapy and granulocyte colony-stimulating factor: significant improvement in peripheral blood stem cells mobilization and harvest with no increase in costs. Br J Haematol. 2014 Jan;164(1):113–23.
33 Greil C, Kiote-Schmidt C, Fink G, Ihorst G, Hildenbeutel S, Bosse R, et al. Successful peripheral blood stem cell mobilization with a cost-efficient single fixed-dose plerixafor schedule in poor mobilizers. Leuk Lymphoma. 2017 Aug;58(8):1849–58.
34 Worel N, Fritsch G, Agis H, Böhm A, Engelich G, Leitner GC, et al. Plerixafor as preemptive strategy results in high success rates in autologous stem cell mobilization failure. J Clin Apher. 2017 Aug;32(4):224–34.
35 Hübel K, Ostermann H, Glaß B, Noppeney R, Kron F, Kron A, et al. Plerixafor in non-Hodgkin's lymphoma patients: a German analysis of time, effort and costs. Bone Marrow Transpl. 2019 Jan;54(1):123–9.