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Review

Optimizing Autologous Stem Cell Mobilization Strategies to Improve Patient Outcomes: Consensus Guidelines and Recommendations

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A B S T R A C T

Autologous hematopoietic stem cell transplantation (aHSCT) is a well-established treatment for malignancies such as multiple myeloma (MM) and lymphomas. Various changes in the field over the past decade, including the frequent use of tandem aHSCT in MM, the advent of novel therapies for the treatment of MM and lymphoma, and the addition of new stem cell mobilization techniques, have led to the need to reassess current stem cell mobilization strategies. Mobilization failures with traditional strategies are common and result in delays in treatment and increased cost and resource utilization. Recently, plerixafor-containing strategies have been shown to significantly reduce mobilization failure rates, but the ideal method to maximize stem cell yields and minimize costs associated with collection has not yet been determined. A panel of experts convened to discuss the currently available data on autologous hematopoietic stem cell mobilization and transplantation and to devise guidelines to optimize mobilization strategies. Herein is a summary of their discussion and consensus.

INTRODUCTION

Autologous hematopoietic stem cell transplantation (aHSCT) is used routinely in the treatment of multiple myeloma (MM) [1-8], non-Hodgkin lymphoma (NHL), and Hodgkin lymphoma [9-11]. For patients with MM and relapsed chemosensitive NHL, aHSCT leads to improved progression-free survival and overall survival. Patients with MM achieve higher rates of complete remission with aHSCT than with chemotherapy alone.

Nearly 10,000 aHSCTs are performed in the United States annually, virtually all of them supported by peripheral blood stem cells (PBSCs) [12]. There are 2 general approaches to stem cell collection: cytokine mobilization using cytokines such as filgrastim (granulocyte-colony stimulating factor [G-CSF]), pegfilgrastim, or sargramostim (granulocyte macrophage-colony stimulating factor [GM-CSF]) alone or in combination, and chemomobilization (CM) using chemotherapy followed by cytokine administration. The published literature on these mobilization approaches is vast, but the relative efficacy, safety, and costs of each remain unclear owing to the paucity of high-quality randomized controlled trials comparing various mobilization strategies [13].

Historical Approaches to Stem Cell Mobilization

Following the observation that chemotherapy administration resulted in a temporary increase in circulation of stem cells during hematopoietic recovery, early stem cell mobilization techniques relied on chemotherapy alone

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[14,15]. The discovery and manufacture of hematopoietic cytokines further improved our ability to mobilize and collect PBSCs [16,17]. Currently, both steady-state and chemotherapy-based mobilization rely on the use of myeloid growth factors for the release of stem cells into the peripheral blood (PB). G-CSF, the most potent of the commercially available myeloid growth factors [18], works by inducing the release of various proteases into the marrow, which then cleave adhesion molecules such as SDF-1, releasing hematopoietic stem cells into the PB [19]. The use of chemotherapy before administration of high-dose myeloid growth factors generally produces higher stem cell yields [20-25], and in theory may reduce tumor contamination of the stem cell product, although data to confirm this are lacking.

Mobilization Beyond Myeloid Growth Factors

The biology of hematopoietic stem cell mobilization with agents other than G-CSF has been reviewed recently [26]. The novel stem cell mobilizing agent plerixafor has recently provided another mobilization option for the transplantation community. In 2008, plerixafor was approved for use in the United States in combination with G-CSF for the mobilization of hematopoietic stem cells in patients with NHL and MM undergoing high-dose chemotherapy followed by autologous stem cell rescue. Plerixafor is a reversible CXCR4 antagonist that allows the release of stem cells from the marrow by disrupting the interaction of CXCR4 with SDF-1. Administration of plerixafor in conjunction with G-CSF augments mobilization of $CD34^+$ cells into the PB, with a peak effect occurring 4-9 hours after administration but a much longer sustained effect, allowing for later initiation of apheresis [27].

The stem cell population mobilized by the combination of plerixafor and G-CSF differs from that mobilized by G-CSF alone. Plerixafor-mobilized PBSCs and/or apheresis products have higher proportions of cells in growth phase [28], primitive $CD34^+CD38^-$ progenitor cells [29], B and T lymphocytes [30-32], dendritic cells [33], and natural killer cells [30,32]. Stem cells mobilized by plerixafor also have increased expression of VLA-4 and CXCR4 [28], as well as of genes that promote cell adhesion, cell motility, the cell cycle, and antiapoptosis [34]. These characteristics suggest that plerixafor-mobilized cell products may have greater capacity to repopulate the marrow and reconstitute the immune system compared with grafts mobilized by G-CSF alone. These properties have been confirmed in mouse and primate models [35,36].

Shortly after the December 15, 2008, approval of plerixafor in the United States, guidelines and recommendations were published on the current status of stem cell collection and the role of plerixafor in patients with MM [37,38]. The consensus in these publications was that plerixafor, along with novel agents for treating MM, would change the standards of practice for aHSCT over the coming decade. Although the use of plerixafor for stem cell mobilization has become increasingly common since those first publications, the transplantation community at large has yet to determine its optimal role in mobilization not only in patients with MM and NHL, but also in patients with Hodgkin lymphoma and solid tumors. In October 2011, a panel of experts in stem cell mobilization and aHSCT was convened to review recently published mobilization and collection data and update the guidelines for maximizing mobilization outcomes.

Recommendations for Stem Cell Collection

Minimum and Target Cell Doses for aHSCT

The correlation between the number of stem cells infused for aHSCT and engraftment kinetics is well established. Administration of $CD34^+$ cell doses $<1.5\text{-}2.5 \times 10^6$/kg leads to delayed neutrophil recovery [39-43], and administration of doses $<1 \times 10^6$/kg has been associated with increased RBC transfusion requirements and even permanent loss of engraftment [42]. Significant delays in platelet recovery also have been seen with infusion of $<1.5\text{-}2.5 \times 10^6$ $CD34^+$ cells/kg [24,41-44], whereas infusion of $>3\text{-}5 \times 10^6$ cells/kg is associated with earlier neutrophil and platelet engraftment [39,41,45].

A recent post hoc analysis of the utility and added benefit of higher stem cell doses in patients undergoing aHSCT demonstrated that $CD34^+$ cell doses $>6 \times 10^6$/kg were associated with improved long-term platelet recovery and reduced blood transfusion requirements, although there was no significant difference in time to platelet recovery to 20×10^9/L [46]. $CD34^+$ cell doses $>10 \times 10^6$/kg have been associated with earlier neutrophil engraftment by 1 to 2 days and earlier platelet engraftment by 2 to 4 days compared with mid-range cell doses ($\sim 3\text{-}10 \times 10^6$/kg) [40,44]. One study found that $CD34^+$ cell doses $>15 \times 10^6$/kg eliminated the need for platelet transfusion support and significantly reduced the duration of thrombocytopenia $<50 \times 10^9$/L [47]. The data supporting the use of higher cell doses are not well controlled, however, and the higher collections attained for these transplants may be a surrogate for less heavily pretreated, lower-risk patients. More research is needed to determine the impact of higher cell doses on engraftment kinetics and to evaluate whether time to collection and stem cell quality, not simply quantity, may play an important role as well.

Recommendations for stem cell targets and doses

- The minimum recommended stem cell dose is 2×10^6 $CD34^+$ cells/kg.
- The decision to accept a collection yield of $1\text{-}2 \times 10^6$ $CD34^+$ cells/kg for aHSCT should be individualized to each patient's clinical parameters and circumstances; in some cases, the benefit of aHSCT may be sufficiently compelling to use doses in this range if absolutely necessary.
- Although minimum numbers are clear, the ideal target numbers are less clear. In general, higher target doses may result in faster engraftment times, but consideration should be given to the balance between targets and the number of apheresis sessions required to attain the target collection. The recommended stem cell collection target is $3\text{-}5 \times 10^6$ $CD34^+$ cells/kg, but in some cases it may be reasonable to accept a yield of 2.5×10^6 $CD34^+$ cells/kg in a single apheresis session rather than prolong the mobilization by several days to reach a target of 5×10^6 $CD34^+$ cells/kg.
- $CD34^+$ cell doses of 5×10^6 cells/kg may lead to improved platelet recovery and less resource utilization compared with doses of $\leq 3 \times 10^6$ cells/kg, provided that the higher target can be collected in a few apheresis sessions.
- Higher targets are necessary if multiple transplantations are planned. The collection target in this setting should be double the target used at the individual center for a single transplantation, to allow optimal cell doses for each transplantation [37].

Apheresis Techniques

Various apheresis devices have Food and Drug Administration approval for PBSC collection. A review of the advantages and disadvantages of each machine is beyond the scope of this discussion [48-50]. Patients should have vascular access evaluated before the start of any apheresis procedure to determine whether peripheral access is acceptable or if central venous access is necessary [51]. Stem cell apheresis can be performed as a standard lower-volume procedure, with a typical processing volume of 10-15 L, based on 2 to 3 times the patient's blood volume, as determined by a blood volume calculation of 70 mL/kg of body weight (ie, a 70-kg person would have an estimated blood volume of 4900 mL). Larger-volume leukapheresis (LVL) involves processing 15-30 L (3 to 6 blood volumes). LVL may be preferred, because it often results in a net increase in $CD34^+$ cell yield per apheresis session [52-63], owing to continued mobilization of stem cells from the marrow during the prolonged apheresis session. Poor mobilizers in particular may have improved collection with the use of LVL [55,64,65], with some authors reporting 40%-100% higher stem cell yields in patients with a preapheresis PB $CD34^+$ count <20 cells/μL [55,65]. In fact, the high failure rates reported with the control arms of the Phase III plerixafor trials may be related in part to the relatively low-volume apheresis mandated by the study design (3 times blood volume ± 10%) [66,67].

It should be noted, however, that the processing of large blood volumes may be associated with increased risks. This includes exposure to increased amounts of anticoagulant (sodium citrate in the form of anticoagulant citrate dextrose solution formula A) which may result in decreases in divalent cations, calcium and magnesium. This in turn may result in hypocalemic/hypomagnesemic tetany without appropriate replacement therapy. In addition, LVL can produce coagulopathy and possible thrombocytopenia, owing to increased loss of platelets in the collection bag [61,65,68-70]. Although numerous studies have been published on the safety, feasibility, and effectiveness of LVL, data from these studies cannot be compared owing to the lack of uniform mobilization and apheresis practice among centers, including mobilization regimens, machine efficiency, run variables, blood volumes processed, duration of the apheresis procedure, and patient-associated variables, such as initial patient platelet count. All of these variables will affect the final stem cell collection.

Recommendations for apheresis techniques

- The data regarding apheresis techniques are not standardized and thus are insufficient for defining a rigid, universal optimal apheresis strategy.
- Larger processing volumes should be considered in patients who have mobilized poorly (defined as a PB $CD34^+$ count <10 to 20 cells/μL) and are reasonable even with higher PB $CD34^+$ cell counts, because toxicities are generally mild to moderate.
- Rigorous monitoring of electrolyte and coagulation parameters should be implemented in patients undergoing LVL. RBC and platelet transfusions should be administered as needed to treat anemia or thrombocytopenia before or after the apheresis procedure; transfusions should not be administered during the procedure, which may interfere with the collection interface.
- Regardless of volumes used, extending apheresis beyond 4 days is rarely successful, and remobilization strategies should be considered in patients who have not met targets by day 4 of collection.

RECOMMENDATIONS FOR STEM CELL MOBILIZATION

Initial Mobilization Strategies

The primary goal of mobilization is to collect sufficient stem cells to allow the patient to proceed to aHSCT. Optimal mobilization not only requires the collection of the targeted stem cell dose, but also should incorporate strategies to minimize the number of apheresis sessions required, reduce costs, and avoid mobilization-related complications, such as hospitalization for febrile neutropenia. Prevention of mobilization failure should be a top priority, given that failure rates with traditional strategies are high as 40% [20,71-77] (Table 1). Risk factors for failure include advanced age [78-80], diagnosis of NHL [80], previous radiation therapy or extensive chemotherapy [78,79,81], previous treatment with lenalidomide or a purine analog [39,74,77,82-87], previous mobilization failure, and low preapheresis circulating PB $CD34^+$ cell counts (Table 2). Recent data suggest that both diabetes and smoking may play a role in mobilization failure [88-90].

Can we predict poor mobilizers?

Unfortunately, predicting mobilization failure based on baseline patient characteristics is highly inaccurate [91], because even within high-risk groups there will be a subset of patients who will mobilize sufficiently with standard approaches, and there are patients with no high-risk characteristics who either mobilize poorly or do not mobilize. Thus, although tailoring mobilization regimens based on upfront predictive models will identify many of those destined to fail, it is not uniformly predictive, and alternative strategies are needed.

One strategy for predicting and preventing mobilization failure is commonly referred to as the "preemptive" (or "just in time") approach, which identifies poor mobilizers before collection based on circulating PB $CD34^+$ counts, based on the well-established correlation between preapheresis PB $CD34^+$ cell count and collection yield [92,93]. A recent study demonstrated a direct linear correlation between PB $CD34^+$ cell count and overall collection, such that a doubling of the preapheresis PB $CD34^+$ count doubles the number of $CD34^+$ cells collected during apheresis [94]. Thus, identification of patients with suboptimal preapheresis PB $CD34^+$ counts may allow for the salvage of initial mobilization attempts with novel agents, thereby reducing the high failure rates seen with traditional strategies. Many centers have developed algorithms to guide mobilization strategies based on PB $CD34^+$ cell counts, and this approach has been shown to improve initial mobilization success rates while efficiently managing resources [95-99].

Steady-state mobilization with growth factors

G-CSF alone as first-line mobilization is an attractive option owing to predictable mobilization kinetics, which in turn allows for predictable apheresis scheduling and staffing while decreasing costs of growth factors and the collection procedure compared with CM. Reported mobilization failure rates with standard-dose G-CSF (5-16 μg/kg/day) are as high as 38%, however [20,21,23,39,100-103]. Single-agent G-CSF has shown some improvement in stem cell yield at higher doses. up to 40 μg/kg/day [104,105], but with increased

Table 1
Initial Mobilization Failure Rates with Traditional Approaches

Author	Patient Population	Regimen	$CD34^+$ Yield, $\times 10^6$/kg	FD	Failure Rate, %
Bensinger et al. [39]	MM, lymphoma, BC, other	n = 124 CM + G-CSF/GM-CSF	10.75	O	7
		n = 119 G-CSF	5.21		5
Pusic et al. [20]	MM, lymphoma	n = 976 G-CSF	3.36	M	18.6
		n = 64 CM + G-CSF	5.43		18.75
Gertz et al. [73]	MM, lymphoma	n = 1775 G-CSF ± Cy	NR	O	47
Pavone et al. [72]	Lymphoma	n = 97 Cy + G-CSF	28.8 (median for all cohorts)	O	17.9
		n = 87 DHAP + G-CSF			
		n = 83 MAD + G-CSF			
Roberts et al. [75]	MM, lymphoma	n = 97 CM + G-CSF	NR	O	29.9
		n = 155 G-CSF	NR		38.1
Alegre et al. [21]	MM	n = 18 Cy + GM-CSF	6.8	NA	NR
		n = 22 G-CSF	4.9		NR
Narayanasami et al. [100]	Lymphoma	n = 22 G-CSF	2.5	M	4.5
		n = 24 Cy + G-CSF	7.2		4.2
Desikan et al. [23]	MM	n = 22 G-CSF	5.8	O	23
		n = 22 Cy + G-CSF	33.4		18
Dazzi et al. [101]	NHL	n = 12 G-CSF	2.89	NA	NR
		n = 12 Cy + G-CSF	6.41		NR
Schiller [191]	MM	n = 37 Cy + G-CSF	4.65	M	0
Pavone et al. [192]	NHL	n = 38 DHAP + G-CSF	5.9	O	14.7
		n = 34 Cy + G-CSF	7.1		10.5
Zeller et al. [104]	Lymphoma, testicular cancer	n = 33 G-CSF 10 μg/kg/d	11.32	NA	NR
		n = 34 G-CSF 24 μg/kg/d	48.25		NR
Weaver et al. [108]	MM, NHL, BC	n = 49 CM + G-CSF	7.1	M	4
		n = 49 CM + GM-CSF	2		8
		n = 52 CM + G-CSF/GM-CSF	5.5		2
Arora et al. [109]	MM	n = 37 Cy + GM-CSF	12	NA	NR
		n = 34 Cy + G-CSF	16		NR
Demirer et al. [193]	MM, lymphoma, BC, other	n = 25 CM + G-CSF 8 μg/kg/d	2.4	NA	NR
		n = 25 CM + G-CSF 16 μg/kg/d	7.9		NR
Desikan et al. [24]	MM	n = 117 G-CSF	6.2	O	26
Gojo et al. [194]	MM	n = 28 Cy + G-CSF	21.6	M	14
		n = 49 Cy + VP + G-CSF	22.5		4
Lefrere et al. [195]	MM	n = 31 VAD + G-CSF	7.7	M	10
		n = 51 Cy 120 mg/kg + G-CSF	5.9		4
Stiff et al. [107]	Lymphoma (high risk)	n = 54 G-CSF	2.4	M	26
		n = 48 SCF + G-CSF	3.6		16
Glaspy et al. [45]	BC	n = 39 G-CSF	3.2	M	7.6
		n = 129 SCF + G-CSF	7.7 (for SCF doses >10 μg)		1
		n = 4 SCF alone	0.2		75
Chao et al. [22]	MM, lymphoma	n = 143 CM + G-CSF	18.6	M	4.2
		n = 84 G-CSF	7		16.7
Damon et al. [126]	MCL	n = 69 EAR + G-CSF	15.9	M	0
Geisler et al. [127]	MCL	n = 160 DSCM	NR	M	3
Hiwase et al. [122]	MM	n = 61 Cy 1-2 g/m^2 + G-CSF	5.1	M	11
		n = 26 Cy 3-4 g/m^2 + G-CSF	7.7		8
Sizemore et al. [125]	MM	n = 37 Cy 2 g/m^2 + G-CSF	NR	M	13.5
		n = 35 Cy 4 g/m^2 + G-CSF	NR		3
Sizemore et al. [124]	NHL	n = 28 Cy 2 g/m^2 + G-CSF	NR	M	32
		n = 28 Cy 4 g/m^2 + G-CSF	NR		4
Wood et al. [196]	MM	n = 152 VP-16 + G-CSF	12	M	0
Wood et al. [197]	Lymphoma	n = 159 VP-16 + G-CSF	6.2	M	6
Bruns et al. [113]	MM	n = 15 Cy + PEG 6 mg	10	M	0
		n = 15 Cy + PEG 12 mg	7.4		0
		n = 15 Cy + G-CSF	8.6		0
Zappasodi et al. [114]	MM	n = 23 DCEP + PEG	5.7	M	13
Steidl et al. [115]	MM	n = 12 Cy + PEG 12 mg	7.4	M	0
Fruehauf et al. [116]	MM	n = 26 CAD + PEG 12 mg	9.7	O	12
Isidori et al. [117]	Lymphoma	n = 25 IEV + PEG 6 mg	8.7	M	4
Putkonen et al. [118]	MM, lymphoma, CLL	n = 38 CM + PEG 6-18 mg	4.9	O	21
Simona et al. [119]	Lymphoma	n = 38 ESHAP + PEG 6 mg	9.42	O	17
Russell et al. [76]	NHL	n = 29 ICE + PEG 6 mg	4.9	M	31
		n = 29 ICE + PEG 12 mg	4.4		41
		n = 32 ICE + G-CSF	5.1		28
Tricot et al. [120]	MM	n = 140 DTPACE + PEG 6 mg × 2	14.5	O	11
		n = 97 DTPACE + G-CSF	10		29
Cesaro et al. [121]	Pediatric, various diagnoses	n = 36 CM + PEG	8.3 on day 1	Other*	17
		n = 36 CM + G-CSF	8.8 on day 1		8

BC indicates breast cancer; CAD, cyclophosphamide, doxorubicin, and dexamethasone; CLL, chronic lymphocytic leukemia; Cy, cyclophosphamide; DHAP, dexamethasone, cisplatin, and cytarabine; DSCM, mobilization off of disease-specific chemotherapy administered as part of the initial 3-6 cycles; EAR, etoposide, cytarabine, and rituximab; ESHAP, etoposide, cytarabine, cisplatin, and methylprednisolone; FD, failure definition; HCVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; ICE, ifosfamide, carboplatin, and etoposide; IEV, ifosfamide, epirubicin, and etoposide; M, minimal number of $CD34^+$ cells required for transplantation; MAD, mitoxantrone, cytarabine, and dexamethasone; MCL, mantle cell lymphoma; MM, multiple myeloma; NR, not reported; O, optimal number of $CD34^+$ cells required for transplantation; PEG, pegfilgrastim; SCF, stem cell factor; VAD, vincristine, doxorubicin, and dexamethasone; DTPACE, bortezomib, dexamethasone, thalidomide, cisplatin, docorubicin, cyclophosphamide, and etoposide; VP-16, etoposide.

* Inability to attain blood peak of at least 20 × 10^6 $CD34^+$ cells/L before leukapheresis.

Table 2
Risk Factors Associated with Poor Mobilization

Baseline	At Time of Mobilization
Treatment-related	Low steady-state PB
• Numerous cycles of previous chemotherapy	$CD34^+$ cell count
• Previous exposure to melphalan, fludarabine, platinum-containing regimens, alkylating agents, or lenalidomide	Steady-state thrombocytopenia
• Previous radiation therapy to the bone marrow	Low preapheresis PB $CD34^+$ cell count
Patient-related	Low day 1 apheresis yield
• Advanced age	
• Diagnosis of NHL	
• Diabetes	
Bone marrow–related	
• Bone marrow involvement	
• Thrombocytopenia	

toxicity and expense [104,106]. Stem cell factor added to G-CSF may result in higher $CD34^+$ cell yield [45,107], but this combination is not available in the United States.

GM-CSF has been shown to be inferior to G-CSF in terms of number of stem cells collected and in post-transplantation outcomes of hematopoietic recovery, transfusion and antibiotic support, febrile episodes, and hospitalizations [108,109]. It is most often used in remobilization strategies, alone or in combination with other cytokines or chemotherapy.

Data on the use of pegfilgrastim in steady-state mobilization are both limited and mixed. A study of patients with MM mobilized with a single fixed dose of pegfilgrastim 12 mg s.c. demonstrated predictable mobilization kinetics and similar collection yields and apheresis days compared with a separate G-CSF cohort [110]. Unfortunately, that study was limited by its relatively small sample size (19 patients in the pegfilgrastim arm), nonrandomized study design, and previous therapy restricted to thalidomide, dexamethasone, and bortezomib. In an unpublished randomized controlled trial comparing G-CSF 10 μg/kg/day, pegfilgrastim 6 mg single dose, and pegfilgrastim 12 mg single dose, conducted in 2003 and 2004, a total of 38 patients with NHL or Hodgkin lymphoma completed collection, with only 37% of those patients collecting at least 2×10^6 $CD34^+$ cells/kg (54% of the G-CSF group, 31% of the pegfilgrastim 6 mg group, and 27% of the pegfilgrastim 12 mg group) [111]. The trial was subsequently discontinued early because of futility. However, another study of patients with MM or NHL undergoing mobilization with either a flat dose of pegfilgrastim 12 mg or G-CSF 10 μg/kg/day demonstrated that pegfilgrastim resulted in higher day 4 PB $CD34^+$ cell count (28.7×10^6 cells/L versus 18.1×10^6 $CD34^+$ cells/L) [112]. There are more published data supporting the use of pegfilgrastim as part of a CM regimen, with reported failure rates of 0 to 21% and cell yields and transplantation outcomes comparable to those for CM + G-CSF [76,113-121].

CM

CM may be incorporated into the initial induction or salvage therapy cycles, or may be administered as a stand-alone cycle apart from standard therapy. The most common stand-alone regimens include cyclophosphamide at a range of doses. Higher doses of cyclophosphamide (3-7 g/m^2) are associated with higher cell yields, lower failure rates, and improved engraftment kinetics [122-125], but also may result in more toxicity and higher costs.

The published literature on the various CM approaches is vast (Table 1). In general, studies demonstrate that CM will mobilize more stem cells than G-CSF alone but with a similar failure rate [20-25], suggesting that CM works best in those patients already destined to mobilize well. Exceptions to this rule may exist, however; several recent studies have shown that CM improves mobilization in traditionally difficult-to-mobilize patients, such as those with lymphoma [75,126,127]. In fact, treatment plans for lymphoma that incorporate mobilization into the initial 3 to 6 cycles of chemotherapy may reduce failure rates to <3% [126,127]. CM as a distinct cycle apart from standard chemotherapy may be a more costly approach than G-CSF alone, however [22]. Furthermore, although CM intuitively would seem to reduce graft contamination by malignant cells, in practice it has demonstrated no impact on transplantation outcomes, such as complete response rate, time to progression, event-free survival, or overall survival [25,128].

Plerixafor in initial mobilization

Table 3 summarizes the available data on plerixafor-containing mobilization regimens.

Upfront mobilization

In a phase II trial, the addition of plerixafor to G-CSF mobilization increased rates of successful mobilization (defined as $\geq 5 \times 10^6$ $CD34^+$ cells/kg) and was associated with fewer apheresis sessions compared with G-CSF alone [129]. Two subsequent large Phase III trials of upfront plerixafor + G-CSF (P + G-CSF) mobilization confirmed that the combination was associated with higher $CD34^+$ cell yields, better achievement of collection targets, lower failure rates, and fewer apheresis sessions compared with G-CSF alone [66,67,130-133].

Those Phase III trials assessed steady-state mobilization (P + G-CSF versus placebo + G-CSF), and did not include a prospective comparison of P + G-CSF versus CM + G-CSF. Nonetheless, the available nonrandomized data suggest that P + G-CSF has similar or improved cell yields and failure rates and improved resource utilization compared with CM alone [134-136]. A retrospective comparison of patients participating in the expanded access protocol of P + G-CSF with matched historical controls mobilized with CM + G-CSF showed 100% successful mobilization in both cohorts with similar median total $CD34^+$ cells counts collected and similar mobilization costs in the 2 groups. P + G-CSF was associated with reduced resource utilization, more patients completing apheresis in 1 day, and fewer hospitalizations, transfusions, and G-CSF doses [134]. Other retrospective analyses have confirmed that upfront P + G-CSF has similar or reduced costs compared with CM + G-CSF, along with lower failures rates (6% to 12.5% versus 21% to 29%) [135,136].

Preemptive and risk-adapted plerixafor use

A common trend in mobilization involves the preemptive addition of plerixafor to steady- state G-CSF in patients known to mobilize poorly based on preapheresis PB $CD34^+$ cell counts or to collect poorly based on early daily apheresis yields. Various institutional approaches have been published [95-99,131,137]. Costa et al. [95] used center-specific cost simulation to develop preestablished PB $CD34^+$ thresholds at which plerixafor would be added to improve collection efficiency and reduce the cost of mobilization attempts [95]. This resulted in significantly lower mobilization failure rates of 2% to 3% compared with the 22% observed with

Table 3
Initial Mobilization Failure Rates with Plerixafor-containing Approaches

Author	Patient Population	Regimen	$CD34^+$ Yield, $\times 10^6$/kg	FD	Failure Rate, %
First-line mobilization					
DiPersio et al. [66]	NHL	n = 150 UP + G-CSF	5.7	O	41/10
		n = 148 G-CSF	2		80/45
DiPersio et al. [67]	MM	n = 148 UP + G-CSF	13	O	28
		n = 154 G-CSF	7.3		66
Shaughnessy et al. [134]	MM, NHL	n = 33 CM + G-CSF	11.6	O	0
		n = 33 P + G-CSF	10.7		0
Isola et al. [130]	MM	n = 25 G-CSF	8.4	NA	NA
		n = 25 UP	16.1		NA
Campen et al. [136]	NHL	n = 34 Cy + G-CSF	NR	M	29.4
		n = 8 UP	NR		12.5
Dugan et al. [139]	MM, NHL	n = 40 UP + CM + G-CSF (various schedules)	NR	O	0
Adel et al. [135]	MM	n = 98 Cy + G-CSF	NR	M	21
		n = 35 UP	NR		6
Risk-adapted					
Shapiro et al. [133]	High-risk MM, lymphoma	n = 124 G-CSF	NR	M	Group 1, 62 Group 2, 79 Group 3, 61
	Group 1: 3 + lines of chemotherapy; group 2: 4 + cycles of HCVAD; group 3: 4 + cycles of lenalidomide	n = 72 UP	NR		Group 1, 23 Group 2, 53 Group 3, 0
Li et al. [131]	MM, lymphoma	n = 23 UP (high-risk patients)	11.7	M	4
Preemptive mobilization					
Costa et al. [95]	MM, lymphoma	n = 34 PEP	6.3	O	3
Costa et al. [138]	MM, lymphoma	n = 81 CM + G-CSF	7.74	M	22.2
		n = 50 PEP	7		2
Roberts et al. [75]	MM, lymphoma	n = 155 G-CSF	NR	O	38
		n = 97 CM	NR		30
		n = 18 UP	NR		39
		n = 63 PEP	NR		24%
Abhyankar et al. [96]	MM, lymphoma, other	n = 159 PEP	5.8	M	5
Micallef et al. [99]	MM, lymphoma, other	n = 147 PEP or UP if high risk	5.5	M	5
Micallef et al. [98]	MM, lymphoma, other	n = 278 G-CSF	5.6	M	19
		n = 216 PEP1	6.1		5
		n = 98 PEP2	7.8		1
LaPorte et al. [97]	MM	n = 68 PEP	8.71	M	1
Vishnu et al. [137]	MM, NHL	n = 46 PEP	4.9 (patients requiring P) 5.9 (patients not requiring P)	M	5
Li et al. [131]	MM, lymphoma	n = 165 PEP + G-CSF, ± CM	6.8 (patients requiring P) 11.7 (patients not requiring P)	M	7 0
Awan et al. [149]	Various	n = 16 CM + G-CSF + PEP	3.9	M	0
Varmavuo et al. [151]	NHL	n = 20 CM + G-CSF/PEG + PEP	3.4	M	15
Basak et al. [143]	Various	n = 48 CM + G-CSF + PEP	4.1	M	29
Jantunen et al. [144]	MM, NHL	n = 16 CM + G-CSF + PEP	2.9	M	19
Costa et al. [112]	MM, lymphoma	n = 74 G-CSF + PEP	7.26	M	1.3
		n = 57 PEG + PEP	7.54		1.7

FD indicates failure definition; M, minimal number of $CD34^+$ cells required for transplantation; MM, multiple myeloma; NA, not applicable; NR, not reported; O, optimal number of $CD34^+$ cells required for transplantation; PEG, pegfilgrastim; PEP, preemptive plerixafor; UP, upfront plerixafor.

CM + G-CSF mobilization [95,138]. Other published reports of preemptive plerixafor use have shown similar low failure rates, below 10% [96,97,99,131,137].

Plerixafor also has been used in risk-adapted strategies in which patients with high-risk baseline characteristics are mobilized with P + G-CSF. One single-center report of P + G-CSF use in patients at high risk for mobilization failure based on previous chemotherapy regimens showed significantly improved mobilization compared with historical controls who received G-CSF alone [133]. Another retrospective study of P + G-CSF in patients at high risk for failure based on medical history found a failure rate of only 4%; however, it should be noted that one-third of the patients in this cohort had previously failed mobilization [131].

CM + P + G-CSF

Limited data exist on the upfront combination of plerixafor with CM + G-CSF (CM + P + G-CSF). One small pilot study of upfront CM + P + G-CSF in patients with MM and NHL demonstrated that the combination is safe and results in a 2-fold increase in PB $CD34^+$ cell collection; all patients had successful collection (defined as $\geq 2 \times 10^6$ $CD34^+$ cells/kg) [139]. Another recent study found a success rate of 73% in patients predicted to be poor mobilizers based on either baseline characteristics or previously failed mobilization [140].

More data are available on the use of preemptive plerixafor to salvage CM + G-CSF patients who have failed to mobilize sufficient PB $CD34^+$ cells, or who demonstrate declining PB $CD34^+$ cell counts during apheresis [32,141-150]. In a small 2-center study, 16 patients received plerixafor salvage after CM + G-CSF for either a PB $CD34^+$ cell count $<10/\mu L$ after WBC recovery or poor cell yield ($<1 \times 10^6$ $CD34^+$ cells/kg) after 2 apheresis sessions [149]. A mean 2.4-fold increase in PB $CD34^+$ cell counts was seen after plerixafor administration, and all 16 patients successfully collected $\geq 2 \times 10^6$ $CD34^+$ cells/kg. Another study of 20 patients with NHL receiving preemptive plerixafor after poor mobilization with CM showed a success rate of 85% [151]. Although most of the published literature on

preemptive plerixafor in CM involves small single-center retrospective analyses or case reports, most demonstrate successful collection comparable to that in patients who are good mobilizers [141-147,150]. One study failed to show an additional benefit with the combination of CM + P compared with historical controls [148].

Recommendations for initial mobilization attempts

Prevention of mobilization failure

- The goals of mobilization should be to reduce overall failure rates to <5%, to minimize mobilization-related complications, and to optimize resource utilization.
- The use of preapheresis PB $CD34^+$ cell count monitoring is recommended to identify poor mobilizers before failure.
- Preemptive plerixafor use based on PB $CD34^+$ cell count monitoring, although not evaluated in a Phase III trial, appears to prevent mobilization failure and may avoid unnecessary use of plerixafor.
- Upfront steady-state mobilization with P + G-CSF is a reliable strategy for preventing remobilization.
- CM + P + G-CSF is an emerging mobilization strategy that merits further evaluation in prospective trials.

First-line mobilization strategies

For patients with MM:

- Steady-state mobilization with G-CSF alone in doses of 10-16 μg/kg/day is an option, but should be limited to patients with no more than 1 previous line of therapy, not previously treated with melphalan or >4 cycles of lenalidomide. In such patients, PB $CD34^+$ cell count monitoring with preemptive plerixafor will allow for successful collection in the vast majority of patients.

For patients with NHL:

- Steady-state mobilization with G-CSF alone in doses of 10-16 μg/kg/day, although associated with higher failure rates in some patient populations, may be an option owing to low toxicity and ease of scheduling. It should be limited to those at low risk for mobilization failure. Again, PB $CD34^+$ count monitoring with preemptive plerixafor will allow successful collection in the vast majority of patients.
- CM, either incorporated into the initial 3 to 6 cycles of planned chemotherapy or as part of a salvage regimen, is appropriate.

General recommendation for all patients:

- CM versus steady-state cytokine mobilization remains an ongoing debate, but data on head-to-head comparisons are equivocal. Patient with MM and patients with NHL respond differently to mobilization regimens. Although growth factor alone is often adequate for patients with early-stage MM, it is often suboptimal for those with NHL and late-stage MM. Although success rates are similar to those seen in steady-state mobilization with G-CSF, CM as a stand-alone cycle apart from standard chemotherapy is associated with higher costs and toxicities.
- Consider limiting stand-alone CM to patients who have not responded optimally to salvage therapy or in patients who have failed other strategies.
- Data to support the use of higher cyclophosphamide doses (>4 g/m^2) are limited, in light of increased toxicity.
- Upfront plerixafor is a suitable option for all patients, particularly in the following circumstances: if the goal is the highest possible $CD34^+$ cell collection yield, if real-time PB $CD34^+$ cell counts are not available, or if fewer apheresis days is the top priority. Preemptive use of plerixafor based on PB-CD34 + measurements is reasonable in other cases.
- Firm recommendations regarding the use of CM versus P + G-CSF cannot be made owing to a lack of data; controlled prospective trials comparing the 2 strategies should be considered.

Impact of Novel Therapies on Stem Cell Mobilization

Lenalidomide is an effective and commonly used agent for induction in patients with MM, but has consistently shown a negative impact on stem cell collection [74,77,83-85,152]. This effect may be linked to the duration of lenalidomide exposure, given that stem cell yields may be significantly lower in patients receiving more than 4 to 6 cycles [74,84,152]. Both CM and plerixafor-containing mobilization strategies have been shown to overcome this negative effect and result in successful collections [133,152-156].

Most studies of bortezomib-containing induction regimens have shown no significant impact on total stem cell yield or failure rates [157-162], although a review of International Myeloma Foundation 2005-01 trial data has revealed trends toward reduced overall collections and slightly higher failure rates [163]. Bendamustine is an even more recent addition to the treatment arsenal for both lymphoid malignancies and MM, and information on the its ability to mobilize stem cells after exposure is limited. There are some data suggesting the feasibility of stem cell collection in patients with NHL or MM previously treated with bendamustine [164-166]. Fludarabine is often used in the treatment of hematologic malignancies, and has been shown to impair collection of PB CD34 + cells [86,87], particularly at lifetime cumulative doses >150 mg/m^2 [87].

Recommendations for mobilization after treatment with novel agents or agents known to inhibit stem cell collection

- Early collection (between the second and fourth cycles of lenalidomide) should be performed whenever possible.
- Most experts recommend a washout period of 2 to 4 weeks between the last lenalidomide dose and the start of apheresis.
- There are insufficient data on which to recommend a single mobilization strategy in patients with lenalidomide exposure, but P + G-CSF and CM have been shown to be effective approaches.
- Mobilization with G-CSF alone is insufficient in patients with extensive (>4 to 6 cycles) lenalidomide pretreatment and should be avoided.

Remobilization Options

Cytokine-only strategies are inadequate for remobilization attempts. One study has shown that the combination of growth factors is less costly and equally as effective as high-dose G-CSF in remobilization [167], but these strategies are still associated with an 82% failure rate [20]. CM historically has been recommended as the primary remobilization option in patients failing G-CSF alone [168]. Unfortunately, the

failure rate of CM remobilization is still as high as 74% [20]. The remaining traditional option for those previously failing mobilization is bone marrow harvest; however, this approach is associated with increased costs and reduced quality of life [102,169,170]. Furthermore, this approach is rarely successful in the event of failed PBSC collection.

Of the currently available remobilization options, steady-state mobilization with P + G-CSF is associated with the lowest failure rates, below 30% [20,171,172]. The single-center series that reported remobilization failure rates of 82% with G-CSF and 74% with CM found a failure rate of only 28% with P + G-CSF [20]. Data on the use of plerixafor in combination with CM for remobilization are limited and insufficient for drawing any conclusions regarding its utility [173]; this may be a promising strategy, but appropriate timing of plerixafor administration remains to be determined, owing to the variable mobilization kinetics with CM regimens.

Recommendations for remobilization

- Cytokine-alone strategies should not be used for remobilization.
- Plerixafor should be included in the remobilization regimen for patients failing a non–plerixafor-containing mobilization attempt, and also may be effective in patients who have failed previous plerixafor-based mobilization [174]. Remobilization options include P + G-CSF and CM + G-CSF + P.
- The addition of plerixafor to CM for remobilization should be explored in prospective trials.
- CM is an acceptable remobilization strategy for patients who have failed cytokine-only mobilization.
- Bone marrow harvest should be reserved as a third-line approach in patients ineligible for mobilization clinical trials and in whom the benefit of aHSCT is sufficiently compelling to outweigh the potential drawbacks.

Mobilization Algorithms to Optimize Mobilization Outcomes

Given the current mobilization options and the differences in failure rates, costs, resource utilization, and clinical outcomes among these options, numerous investigators have performed pharmacoeconomic analyses to identify the most cost-effective mobilization strategies [75,130-132,134,136,137,175,176]. Their findings may have limited application to other institutions, however, given the differing costs, patient populations, transplantation goals, and mobilization strategies among centers. Without pharmacoeconomic data from a multicenter controlled trial, centers have developed algorithms to guide the use of plerixafor within steady-state G-CSF mobilization based on PB $CD34^+$ cell counts, daily apheresis yields, and the presence of risk factors for failure [96,98,99,133,138]. In these algorithms, the most common approach requires performing PB $CD34^+$ cell analysis on day 4 of G-CSF administration; if the count is below a predetermined threshold, then plerixafor is administered on the evening of day 4, and the start of apheresis is delayed until day 5. Many algorithms also incorporate criteria for optimal daily apheresis yields, and allow for the addition of plerixafor if a daily collection is suboptimal. The use of these algorithms has reduced mobilization failure rates to below 10% (Table 4).

Recommendations for algorithm development

- Each center should develop and implement its own algorithms for applying various mobilization strategies, with the goal of optimizing collection yields.

Table 4
Algorithms for Preemptive Plerixafor Use in Stem Cell Mobilization

Study	Target $CD34^+$ Cell Yield, cells/kg	Criteria for Plerixafor Administration	Regimen	FD	Failure Rate, %
Costa et al. [95]	6×10^6 (some MM) 3×10^6 (all others)	Preestablished PB $CD34^+$ threshold derived from cost simulation, for example, threshold of 14 for a target of 3×10^6/kg, and threshold of 25 for a target of 6×10^6/kg	n = 34 PEP (n = 11 G-CSF alone, n = 23 P + G-CSF)	O	3
Costa et al. [138]	6×10^6 (some MM) 3×10^6 (all others)	Preestablished PB $CD34^+$ threshold derived from cost simulation, for example, threshold of 14 for a target of 3×10^6/kg, and threshold of 25 for a target of 6×10^6/kg	n = 50 PEP n = 81 CM + G-CSF	M	2 22
Abhyankar et al. [96]	2.5×10^6 (single) 5×10^6 (tandem)	Day 5 PB $CD34^+$ <10 cells/μL: Administer P, begin apheresis on day 6 Day 5 PB $CD34^+$ ≥10 but < 20 cells/μL: If target is 2.5, begin apheresis without P; if target is 5, begin apheresis but administer P that night Day 5 PB $CD34^+$ ≥20 cells/μL: Begin apheresis without P Apheresis day 1 cell yield <50% of desired collection: Administer P	n = 159 PEP (n = 104 G-CSF alone, n = 55 P + G-CSF)	M	5
Micallef et al. [99]	2×10^6 (minimum)	Day 5 PB $CD34^+$ <10 cells/μL or daily apheresis yield of $<0.5 \times 10^6$/kg	n = 147 UP for high risk, PEP for all others	M	5
Micallef et al. [98]	2×10^6 (minimum)	PEP1: Same as above PEP2: Day 4 PB $CD34^+$ <10 (single) or <20 cells/μL (tandem) or apheresis day 1 yield $<1.5 \times 10^6$/kg or any subsequent daily yield $<0.5 \times 10^6$/kg	n = 278 G-CSF alone n = 216 PEP1 + G-CSF n = 98 PEP2 + G-CSF	M	19 5 1
LaPorte et al. [97]	4×10^6 (target) 2×10^6 (minimum)	Day 4 PB $CD34^+$ <12 cells/mm^3 or daily apheresis yield of $<1 \times 10^6$ or ≤50% of previous day's yield	n = 68 PEP (n = 38 G-CSF alone, n = 30 P + G-CSF)	M	1
Devine (unpublished data)	4×10^6 (MM) 2×10^6 (others)	Day 4 PB $CD34^+$ <7 cells/μL, give P; day 5 PB $CD34^+$ <10/L, give P, begin apheresis on day 6 or day 1 yield <50% target collection	PEP	U	6

FD indicates failure definition; FN, febrile neutropenia; M, minimal number of $CD34^+$ cells required for transplantation; MM, multiple myeloma; O, optimal number of $CD34^+$ cells required for transplantation; P, plerixafor; PEP, preemptive plerixafor; U, unknown; UP, upfront plerixafor.

- Algorithms should include center-specific data regarding priorities of the transplantation center (eg, highest possible cell yield versus fewest apheresis days), priorities of patients and caregivers (eg, reduced hospitalizations, fewer days missed from work, less time spent in/around the transplantation and collection center), relationship of PB $CD34^+$ cell count to collection yield in the center, center-specific cost assessments, and minimum and target cell collections.

FUTURE DIRECTIONS

Novel mobilization regimens have changed the climate of stem cell transplantation such aHSCT may now be performed in more than 90% of those patients in whom the procedure is indicated, with a minimal need for remobilization strategies. The precise regimen that is most effective remains to be determined, however, and may vary depending on patient population and the specific goal of stem cell collection. Extensive Phase III clinical trial data on mobilization approaches are lacking (Table 5) [13], and further prospective studies are needed to answer important questions regarding first-line and secondary mobilization strategies.

The effect of mobilization strategy, particularly mobilization strategies containing plerixafor, on tumor cell mobilization remains unknown and should be explored in future trials. Plerixafor is known to displace acute leukemia cells from their microenvironment into the PB (reviewed in [177]), a phenomenon that has been therapeutically explored as a chemotherapy sensitization strategy [178-180]. Similarly, cancer cell mobilization with plerixafor has been detected in patients with MM in some [181], but not all [182,183], studies. Mobilization of cancer cells also occurs with growth factor alone [184,185] and with chemotherapy plus growth factor [184,186]. It is unknown whether the mobilization of MM or NHL cells to the PB will differ in different mobilization strategies, or whether the contamination of apheresis products with tumor cells will have any influence on the frequency or timing of relapse [187].

Table 5
Published Phase III Mobilization Data

Author	Patient Population	Regimen	$CD34^+$ Yield, $\times 10^6$/kg	FD	Failure Rate, %
Shpall et al. [198]	BC	n = 100, SCF + G-CSF	5.3	O	37
		n = 103, G-CSF	4.8		53
André et al. [199]	BC, MM, lymphoma	n = 66, G-CSF 5 μg/kg	7.2	M	7
		n = 62, G-CSF 10 μg/kg	12.0		7
Weaver et al. [200]	BC, MM, lymphoma	n = 51, CM + G-CSF	12	O	12
		n = 52, CM + GM-CSF	5.4		47
		n = 53, CM + G-CSF + GM-CSF	10.5		19
DiPersio et al. [66]	NHL	n = 150, UP + G-CSF	5.7	O	41/10
		n = 148, G-CSF	2		80/45
DiPersio et al. [67]	MM	n = 148, UP + G-CSF	13	O	28
		n = 154, G-CSF	7.3		66

BC indicates breast cancer; FD, failure definition; M, minimal number of $CD34^+$ cells required for transplantation; MM, multiple myeloma; O, optimal number of $CD34^+$ cells required for transplantation; SCF, stem cell factor; UP, upfront plerixafor.

Investigations of both clinical effectiveness and cost-effectiveness are needed for CM versus steady-state mobilization with P + G-CSF, for preemptive plerixafor versus upfront plerixafor, and for the role of CM + G-CSF + P in first-line and secondary mobilization. Pharmacoeconomics and cost endpoints should be incorporated into all future plerixafor trials, and are warranted for existing trial data.

The bone marrow microenvironment and stem cell trafficking mechanisms also merit further study. Interestingly, when plerixafor is added to stromal cells, CXCR4 expression increases owing to blockade of SDF-1–mediated CXCR4 internalization, with the effect of sending a "survival signal" to the mobilized stem cells to return to the marrow [188]. In contrast, G-CSF down-regulates CXCR4 and SDF-1, potentially blocking the rehoming process and resulting in persistent mobilization of hematopoietic stem cells. Manipulation of this rehoming signal has ramifications both for increasing or prolonging stem cell mobilization, as well as improving the efficiency of engraftment post-transplantation. Various other chemokines that may be useful in the mobilization of stem cells are in early stages of investigation [189], including the small-molecule inhibitor of VLA-4, BIO5192, which in mouse models has demonstrated additive mobilization effects in combination with plerixafor [190]. These investigations likely will result in the introduction of additional chemokine molecules to the mobilization arsenal, requiring continuing reassessment of mobilization standards.

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REFERENCES

1. Barlogie B, Kyle RA, Anderson KC, et al. Standard chemotherapy compared with high-dose chemoradiotherapy for multiple myeloma: final results of phase III US intergroup trial S9321. *J Clin Oncol*. 2006; 24:929-936.
2. Attal M, Harousseau J, Facon T, et al. Single versus double autologous stem-cell transplantation for multiple myeloma. *N Engl J Med*. 2003; 349:2495-2502.
3. Attal M, Harousseau J, Stoppa A, et al. A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. *N Engl J Med*. 1996;335:91-97.
4. Child JA, Morgan GJ, Davies FE, et al. High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. *N Engl J Med*. 2003;348:1875-1883.
5. Bladé J, Rosiñol L, Sureda A, et al. High-dose therapy intensification compared with continued standard chemotherapy in multiple myeloma patients responding to the initial chemotherapy: long-term results from a prospective randomized trial from the Spanish cooperative group PETHEMA. *Blood*. 2005;106:3755-3759.

6. Fermand J, Katsahian S, Divine M, et al. High-dose therapy and autologous blood stem-cell transplantation compared with conventional treatment in myeloma patients aged 55 to 65 years: long-term results of a randomized control trial from the Group Myelome-Autogreffe. *J Clin Oncol*. 2005;23:9227-9233.
7. Palumbo A, Bringhen S, Petrucci MT, et al. Intermediate-dose melphalan improves survival of myeloma patients aged 50 to 70: results of a randomized controlled trial. *Blood*. 2004;104:3052-3057.
8. Segeren CM, Sonneveld P, van der Holt B, et al. Overall and event-free survival are not improved by the use of myeloablative therapy following intensified chemotherapy in previously untreated patients with multiple myeloma: a prospective randomized phase 3 study. *Blood*. 2003;101:2144-2151.
9. Oliansky DM, Czuczman M, Fisher RI, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the treatment of diffuse large B cell lymphoma: update of the 2001 evidence-based review. *Biol Blood Marrow Transplant*. 2011;17:20-47.
10. Oliansky DM, Gordon LI, King J, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the treatment of follicular lymphoma: an evidence-based review. *Biol Blood Marrow Transplant*. 2010;16:443-468.
11. Copelan EA. Hematopoietic stem-cell transplantation. *N Engl J Med*. 2006;354:1813-1826.
12. Center for International Blood and Marrow Transplantation Research. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR summary slides, 2011. Available from: http://www.cibmtr.org/. Accessed March 11, 2012.
13. Sheppard D, Bredeson C, Allan D, Tay J. Systematic review of randomized controlled trials of hematopoietic stem cell mobilization strategies for autologous transplantation for hematologic malignancies. *Biol Blood Marrow Transplant*. 2012;18:1191-1203.
14. Kessinger A, Armitage JO, Landmark JD, Weisenburger DD. Reconstitution of human hematopoietic function with autologous cryopreserved circulating stem cells. *Exp Hematol*. 1986;14:192-196.
15. Juttner CA, To LB, Ho JQ, et al. Early lympho-hemopoietic recovery after autografting using peripheral blood stem cells in acute non-lymphoblastic leukemia. *Transplant Proc*. 1988;20:40-42.
16. Gianni AM, Siena S, Bregni M, et al. Granulocyte-macrophage colony-stimulating factor to harvest circulating haemopoietic stem cells for autotransplantation. *Lancet*. 1989;334:580-585.
17. Socinski MA, Cannistra SA, Elias A, et al. Granulocyte-macrophage colony stimulating factor expands the circulating haemopoietic progenitor cell compartment in man. *Lancet*. 1988;331:1194-1198.
18. Lane T, Law P, Maruyama M, et al. Harvesting and enrichment of hematopoietic progenitor cells mobilized into the peripheral blood of normal donors by granulocyte-macrophage colony-stimulating factor (GM-CSF) or G-CSF: potential role in allogeneic marrow transplantation. *Blood*. 1995;85:275-282.
19. Petit I, Szyper-Kravitz M, Nagler A, et al. G-CSF induces stem cell mobilization by decreasing bone marrow SDF-1 and up-regulating CXCR4. *Nat Immunol*. 2002;3:687-694.
20. Pusic I, Jiang SY, Landua S, et al. Impact of mobilization and remobilization strategies on achieving sufficient stem cell yields for autologous transplantation. *Biol Blood Marrow Transplant*. 2008;14:1045-1056.
21. Alegre A, Tomas JF, Martinez-Chamorro C, et al. Comparison of peripheral blood progenitor cell mobilization in patients with multiple myeloma: high-dose cyclophosphamide plus GM-CSF vs G-CSF alone. *Bone Marrow Transplant*. 1997;20:211-217.
22. Chao NJ, Grima DT, Carrum G, et al. Chemo-mobilization provides superior mobilization and collection in autologous stem cell transplants but with less predictability and at a higher cost. ASH Annual Meeting Abstracts. *Blood*. 2011;118:4048.
23. Desikan KR, Barlogie B, Jagannath S, et al. Comparable engraftment kinetics following peripheral-blood stem-cell infusion mobilized with granulocyte colony-stimulating factor with or without cyclophosphamide in multiple myeloma. *J Clin Oncol*. 1998;16:1547-1553.
24. Desikan KR, Tricot G, Munshi NC, et al. Preceding chemotherapy, tumour load and age influence engraftment in multiple myeloma patients mobilized with granulocyte colony-stimulating factor alone. *Br J Haematol*. 2001;112:242-247.
25. Dingli D, Nowakowski GS, Dispenzieri A, et al. Cyclophosphamide mobilization does not improve outcome in patients receiving stem cell transplantation for multiple myeloma. *Clin Lymphoma Myeloma*. 2006;6:384-388.
26. Hoggatt J, Pelus LM. Hematopoietic stem cell mobilization with agents other than G-CSF. *Methods Mol Biol*. 2012;904:49-67.
27. Harvey RD, Kaufman JL, Johnson HR, et al. Temporal changes in plerixafor administration and hematopoietic stem cell mobilization efficacy: results of a prospective clinical trial in multiple myeloma. *Biol Blood Marrow Transplant*. 2013;19:1393-1395.
28. Larochelle A, Krouse A, Metzger M, et al. AMD3100 mobilizes hematopoietic stem cells with long-term repopulating capacity in nonhuman primates. *Blood*. 2006;107:3772-3778.
29. Fruehauf S, Veldwijk MR, Seeger T, et al. A combination of granulocyte-colony-stimulating factor (G-CSF) and plerixafor mobilizes more primitive peripheral blood progenitor cells than G-CSF alone: results of a European Phase II study. *Cytotherapy*. 2009;11:992-1001.
30. Cuzzola M, Spiniello E, Martino M, et al. Plerixafor (AMD3100) and granulocyte colony-stimulating factor mobilize different cell populations based on immunophenotype and global gene experssion signatures [abstract P1082]. *Bone Marrow Transplant*. 2011;46(Suppl 1):S335.
31. Devine SM, Vij R, Rettig M, et al. Rapid mobilization of functional donor hematopoietic cells without G-CSF using AMD3100, an antagonist of the CXCR4/SDF-1 interaction. *Blood*. 2008;112:990-998.
32. Varmavuo V, Mäntymaa P, Kuittinen T, et al. Blood graft lymphocyte subsets after plerixafor injection in non-Hodgkin's lymphoma patients mobilizing poorly with chemotherapy plus granulocyte colony-stimulating factor. *Transfusion*. 2012;52:1785-1791.
33. Gazitt Y, Freytes CO, Akay C, et al. Improved mobilization of peripheral blood $CD34^+$ cells and dendritic cells by AMD3100 plus granulocyte colony-stimulating factor in non-Hodgkin's lymphoma patients. *Stem Cells Dev*. 2007;16:657-666.
34. Fruehauf S, Seeger T, Maier P, et al. The CXCR4 antagonist AMD3100 releases a subset of G-CSF–primed peripheral blood progenitor cells with specific gene expression characteristics. *Exp Hematol*. 2006;34:1052-1059.
35. Hess DA, Bonde J, Craft TC, et al. Human progenitor cells rapidly mobilized by AMD3100 repopulate NOD/SCID mice with increased frequency in comparison to cells from the same donor mobilized by granulocyte colony-stimulating factor. *Biol Blood Marrow Transplant*. 2007;13:398-411.
36. Uchida N, Bonifacino A, Krouse AE, et al. Accelerated lymphocyte reconstitution and long-term recovery after transplantation of lentiviral-transduced rhesus $CD34^+$ cells mobilized by G-CSF and plerixafor. *Exp Hematol*. 2011;39:795-805.
37. Giralt S, Stadtmauer EA, Harousseau JL, et al. International Myeloma Working Group (IMWG) consensus statement and guidelines regarding the current status of stem cell collection and high-dose therapy for multiple myeloma and the role of plerixafor (AMD 3100). *Leukemia*. 2009;23:1904-1912.
38. Kumar S, Giralt S, Stadtmauer EA, et al. Mobilization in myeloma revisited: IMWG consensus perspectives on stem cell collection following initial therapy with thalidomide-, lenalidomide-, or bortezomib-containing regimens. *Blood*. 2009;114:1729-1735.
39. Bensinger W, Appelbaum F, Rowley S, et al. Factors that influence collection and engraftment of autologous peripheral-blood stem cells. *J Clin Oncol*. 1995;13:2547-2555.
40. Weaver C, Hazelton B, Birch R, et al. An analysis of engraftment kinetics as a function of the CD34 content of peripheral blood progenitor cell collections in 692 patients after the administration of myeloablative chemotherapy. *Blood*. 1995;86:3961-3969.
41. Oran B, Malek K, Sanchorawala V, et al. Predictive factors for hematopoietic engraftment after autologous peripheral blood stem cell transplantation for AL amyloidosis. *Bone Marrow Transplant*. 2005;35:567-575.
42. Perez-Simon JA, Martin A, Caballero D, et al. Clinical significance of $CD34^+$ cell dose in long-term engraftment following autologous peripheral blood stem cell transplantation. *Bone Marrow Transplant*. 1999;24:1279-1283.
43. Carral A, de la Rubia J, Martin G, et al. Factors influencing hematopoietic recovery after autologous blood stem cell transplantation in patients with acute myeloblastic leukemia and with non-myeloid malignancies. *Bone Marrow Transplant*. 2002;29:825-832.
44. Ketterer N, Salles G, Raba M, et al. High $CD34^+$ cell counts decrease hematologic toxicity of autologous peripheral blood progenitor cell transplantation. *Blood*. 1998;91:3148-3155.
45. Glaspy JA, Shpall EJ, LeMaistre CF, et al. Peripheral blood progenitor cell mobilization using stem cell factor in combination with filgrastim in breast cancer patients. *Blood*. 1997;90:2939-2951.
46. Stiff PJ, Micallef I, Nademanee AP, et al. Transplanted $CD34^+$ cell dose is associated with long-term platelet count recovery following autologous peripheral blood stem cell transplant in patients with non-Hodgkin lymphoma or multiple myeloma. *Biol Blood Marrow Transplant*. 2011;17:1146-1153.
47. Benedetti G, Patoia L, Giglietti A, et al. Very large amounts of peripheral blood progenitor cells eliminate severe thrombocytopenia after high-dose melphalan in advanced breast cancer patients. *Bone Marrow Transplant*. 1999;24:971-979.
48. Snyder EL, Baril L, Cooper DL, et al. In vitro collection and post-transfusion engraftment characteristics of MNCs obtained by using a new separator for autologous PBPC transplantation. *Transfusion*. 2000;40:961-967.
49. Snyder EL, O'Donnell L, Dengler TJ, et al. Ex vivo evaluation of PBMNCs collected with a new cell separator. *Transfusion*. 2001;41:940-949.
50. McLeod BC, editor. *Apheresis: principles and practice*, 3rd ed. Bethesda (MD): AABB Press; 2010.
51. McGee DC, Gould MK. Preventing complications of central venous catheterization. *N Engl J Med*. 2003;348:1123-1133.
52. Cecyn KZ, Seber A, Ginani VC, et al. Large-volume leukapheresis for peripheral blood progenitor cell collection in low body weight

pediatric patients: a single-center experience. *Transfus Apher Sci*. 2005;32:269-274.
53. Bojanic I, Dubravcic K, Batinic D, et al. Large volume leukapheresis: efficacy and safety of processing patient's total blood volume six times. *Transfus Apher Sci*. 2011;44:139-147.
54. Dubrovsky L, Wong ECC, Perez-Albuerne E, et al. CD34$^+$ collection efficiency as a function of blood volumes processed in pediatric autologous peripheral blood stem cell collection. *J Clin Apher*. 2011; 26:131-137.
55. Gašová Z, Marinov I, Vodvářková Š, et al. PBPC collection techniques: standard versus large-volume leukapheresis (LVL) in donors and in patients. *Transfus Apher Sci*. 2005;32:167-176.
56. Gašová Z, Bhuiyan-Ludvíková Z, Böhmová M, et al. PBPC collections: management, techniques and risks. *Transfus Apher Sci*. 2010;43: 237-243.
57. Malachowski ME, Comenzo RL, Hillyer CD, et al. Large-volume leukapheresis for peripheral blood stem cell collection in patients with hematologic malignancies. *Transfusion*. 1992;32:732-735.
58. Menichella G, Lai M, Serafini R, et al. Large volume leukapheresis for collecting hemopoietic progenitors: role of CD34$^+$ precount in predicting successful collection. *Int J Artif Organs*. 1999;22:334-341.
59. Murea S, Goldschmidt H, Hahn U, et al. Successful collection and transplantation of peripheral blood stem cells in cancer patients using large-volume leukaphereses. *J Clin Apher*. 1996;11:185-194.
60. Accorsi P, Dell'Isola M, Bonfini T, et al. Large-volume leukapheresis with AMICUS cell separator in peripheral blood stem cell autologous transplant. *Transfus Apher Sci*. 2001;24:79-83.
61. Bojko P, Scharifi M, Stossel K, Seeber S. Comparison of processing four and five times the patients' blood volume during peripheral blood stem cell collection and analysis of CD34$^+$38$^-$ and CD34$^+$49d$^+$ subsets during apheresis. *J Cancer Res Clin Oncol*. 2002;128:19-28.
62. Humpe A, Riggert J, Munzel U, et al. A prospective, randomized, sequential, crossover trial of large-volume versus normal-volume leukapheresis procedures: effect on progenitor cells and engraftment. *Transfusion*. 1999;39:1120-1127.
63. Smolowicz AG, Villman K, Tidefelt U. Large-volume apheresis for the harvest of peripheral blood progenitor cells for autologous transplantation. *Transfusion*. 1997;37:188-192.
64. Abrahamsen JF, Stamnesfet S, Liseth K, et al. Large-volume leukapheresis yields more viable CD34$^+$ cells and colony-forming units than normal-volume leukapheresis, especially in patients who mobilize low numbers of CD34$^+$ cells. *Transfusion*. 2005;45:248-253.
65. Cassens U, Barth IM, Baumann C, et al. Factors affecting the efficacy of peripheral blood progenitor cells collections by large-volume leukaphereses with standardized processing volumes. *Transfusion*. 2004; 44:1593-1602.
66. DiPersio JF, Micallef IN, Stiff PJ, 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;27:4767-4773.
67. DiPersio JF, Stadtmauer EA, Nademanee A, 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;113:5720-5726.
68. Lin JS, Burgstaler EA, Pineda AA, Gertz MA. Effects of whole blood flow rates on mononuclear cell yields during peripheral blood stem cell collection using Fenwal CS 3000 Plus. *J Clin Apher*. 1995;10:7-11.
69. Humpe A, Riggert J, Munzel U, Köhler M. A prospective, randomized, sequential crossover trial of large-volume versus normal-volume leukapheresis procedures: effects on serum electrolytes, platelet counts, and other coagulation measures. *Transfusion*. 2000;40:368-374.
70. Bolan CD, Leitman SF. Management of anticoagulation-associated toxicity during large-volume leukapheresis of peripheral blood stem cell donors. *Blood*. 2002;99:1878.
71. Bensinger W, DiPersio JF, McCarty JM. Improving stem cell mobilization strategies: future directions. *Bone Marrow Transplant*. 2009;43: 181-195.
72. Pavone V, Gaudio F, Console G, et al. Poor mobilization is an independent prognostic factor in patients with malignant lymphomas treated by peripheral blood stem cell transplantation. *Bone Marrow Transplant*. 2006;37:719-724.
73. Gertz MA, Wolf RC, Micallef IN, Gastineau DA. Clinical impact and resource utilization after stem cell mobilization failure in patients with multiple myeloma and lymphoma. *Bone Marrow Transplant*. 2010;45:1396-1403.
74. Paripati H, Stewart AK, Cabou S, et al. Compromised stem cell mobilization following induction therapy with lenalidomide in myeloma. *Leukemia*. 2008;22:1282-1284.
75. Roberts C, Sabo R, Shickle L, et al. Cost-effective stem cell mobilization: a novel early plerixafor salvage strategy is optimally resource-effective compared to chemotherapy, G-CSF or initial plerixafor strategies [abstract O378]. *Bone Marrow Transplant*. 2011;46(Suppl 1): S60-S61.
76. Russell N, Mesters R, Schubert J, et al. A phase 2 pilot study of peg-filgrastim and filgrastim for mobilizing peripheral blood progenitor cells in patients with non-Hodgkin's lymphoma receiving chemotherapy. *Haematologica*. 2008;93:405-412.
77. Mazumder A, Kaufman J, Niesvizky R, et al. Effect of lenalidomide therapy on mobilization of peripheral blood stem cells in previously untreated multiple myeloma patients. *Leukemia*. 2008;22:1280-1281. author reply 1281-1282.
78. Micallef IN, Apostolidis J, Rohatiner AZ, et al. Factors which predict unsuccessful mobilisation of peripheral blood progenitor cells following G-CSF alone in patients with non-hodgkin's lymphoma. *Hematol J*. 2000;1:367-373.
79. Stiff PJ. Management strategies for the hard-to-mobilize patient. *Bone Marrow Transplant*. 1999;23(Suppl 2):S29-S33.
80. Hosing C, Saliba RM, Ahlawat S, et al. Poor hematopoietic stem cell mobilizers: a single-institution study of incidence and risk factors in patients with recurrent or relapsed lymphoma. *Am J Hematol*. 2009; 84:335-337.
81. Wuchter P, Ran D, Bruckner T, et al. Poor mobilization of hematopoietic stem cells—definitions, incidence, risk factors, and impact on outcome of autologous transplantation. *Biol Blood Marrow Transplant*. 2010;16:490-499.
82. Haas R, Mohle R, Fruhauf S, et al. Patient characteristics associated with successful mobilizing and autografting of peripheral blood progenitor cells in malignant lymphoma. *Blood*. 1994;83:3787-3794.
83. Popat U, Saliba R, Thandi R, et al. Impairment of filgrastim-induced stem cell mobilization after prior lenalidomide in patients with multiple myeloma. *Biol Blood Marrow Transplant*. 2009;15:718-723.
84. Kumar S, Dispenzieri A, Lacy MQ, et al. Impact of lenalidomide therapy on stem cell mobilization and engraftment post-peripheral blood stem cell transplantation in patients with newly diagnosed myeloma. *Leukemia*. 2007;21:2035-2042.
85. Cavallo F, Bringhen S, Milone G, et al. Stem cell mobilization in patients with newly diagnosed multiple myeloma after lenalidomide induction therapy. *Leukemia*. 2011;25:1627-1631.
86. Tournilhac O, Cazin B, Leprètre S, et al. Impact of frontline fludarabine and cyclophosphamide combined treatment on peripheral blood stem cell mobilization in B-cell chronic lymphocytic leukemia. *Blood*. 2004; 103:363-365.
87. Waterman J, Rybicki L, Bolwell B, et al. Fludarabine as a risk factor for poor stem cell harvest, treatment-related MDS and AML in follicular lymphoma patients after autologous hematopoietic cell transplantation. *Bone Marrow Transplant*. 2011;47:488-493.
88. Ferraro F, Lymperi S, Méndez-Ferrer S, et al. Diabetes impairs hematopoietic stem cell mobilization by altering niche function. *Sci Transl Med*. 2011;3:104ra101.
89. Hoelig K, Kroschinsky F, Kramer M, et al. Predictors for the efficacy of peripheral blood progenitor cell (PBPC) collection-results from 4050 harvests performed in a single centre. ASH Annual Meeting Abstracts. *Blood*. 2008;112:4131.
90. Livingston D, Motlagh D, Debelak J, et al. Phase 2 study of intramyocardial injection of autologous CD34$^+$ cells to treat subjects with refractory chronic myocardial ischemia (CMI): factors influencing mobilization and apheresis. ASH Annual Meeting Abstracts. *Blood*. 2009;114:3227.
91. Jantunen E, Kuittinen T, Nousiainen T. Is chemotherapy scoring useful to predict progenitor cell mobilisation in patients with non-hodgkin's lymphoma? *Bone Marrow Transplant*. 2003;32:569-573.
92. Sutherland DR, Stewart AK, Keating A. CD34 antigen: molecular features and potential clinical applications. *Stem Cells*. 1993;11(Suppl 3):50-57.
93. Sutherland DR, Keeney M, Gratama JW. Enumeration of CD34$^+$ hematopoietic stem and progenitor cells. *Curr Protoc Cytom*. 2001;. http://dx.doi.org/10.1002/0471142956.cy0604s25. Unit 6.4.
94. Gambell P, Herbert K, Dickinson M, et al. Peripheral blood CD34$^+$ cell enumeration as a predictor of apheresis yield: an analysis of over 1000 collections. *Biol Blood Marrow Transplant*. 2012;18:763-772.
95. Costa LJ, Alexander ET, Hogan KR, et al. Development and validation of a decision-making algorithm to guide the use of plerixafor for autologous hematopoietic stem cell mobilization. *Bone Marrow Transplant*. 2011;46:64-69.
96. Abhyankar S, Dejarnette S, Aljitawi O, et al. A risk-based approach to optimize autologous hematopoietic stem cell (HSC) collection with the use of plerixafor. *Bone Marrow Transplant*. 2011;47:483-487.
97. LaPorte J, Solomon SR, Bashey A, et al. An effective hematopoietic stem cell mobilization algorithm for adding plerixafor to G-CSF for multiple myeloma patients undergoing autologous transplantation. ASH Annual Meeting Abstracts. *Blood*. 2011;118:4389.
98. Micallef IN, Sinha S, Gastineau DA, et al. Cost-effectiveness analysis of a risk-adapted algorithm for plerixafor use in autologous peripheral blood stem cell mobilization. *Biol Blood Marrow Transplant*. 2013;19:87-93.
99. Micallef IN, Inwards DJ, Dispenzieri A, et al. A risk-adapted approach utilizing plerixafor in autologous peripheral blood stem cell mobilization. *Biol Blood Marrow Transplant*. 2010;16(Suppl 2):S197-S198.
100. Narayanasami U, Kanteti R, Morelli J, et al. Randomized trial of filgrastim versus chemotherapy and filgrastim mobilization of

hematopoietic progenitor cells for rescue in autologous transplantation. *Blood*. 2001;98:2059-2064.
101. Dazzi C, Cariello A, Rosti G, et al. Is there any difference in PBPC mobilization between cyclophosphamide plus G-CSF and G-CSF alone in patients with non-Hodgkin's lymphoma? *Leuk Lymphoma*. 2000; 39:301-310.
102. Glaspy JA. Economic considerations in the use of peripheral blood progenitor cells to support high-dose chemotherapy. *Bone Marrow Transplant*. 1999;23(Suppl 2):S21-S27.
103. Kanteti R, Miller K, McCann J, et al. Randomized trial of peripheral blood progenitor cell vs bone marrow as hematopoietic support for high-dose chemotherapy in patients with non-Hodgkin's lymphoma and Hodgkin's disease: a clinical and molecular analysis. *Bone Marrow Transplant*. 1999;24:473-481.
104. Zeller W, Gutensohn K, Stockschlader M, et al. Increase of mobilized CD34-positive peripheral blood progenitor cells in patients with Hodgkin's disease, non-Hodgkin's lymphoma, and cancer of the testis. *Bone Marrow Transplant*. 1996;17:709-713.
105. Weaver CH, Birch R, Greco FA, et al. Mobilization and harvesting of peripheral blood stem cells: randomized evaluations of different doses of filgrastim. *Br J Haematol*. 1998;100:338-347.
106. Sheridan WP, Begley CG, To LB, et al. Phase II study of autologous filgrastim (G-CSF)-mobilized peripheral blood progenitor cells to restore hemopoiesis after high-dose chemotherapy for lymphoid malignancies. *Bone Marrow Transplant*. 1994;14:105-111.
107. Stiff P, Gingrich R, Luger S, et al. A randomized phase 2 study of PBPC mobilization by stem cell factor and filgrastim in heavily pretreated patients with Hodgkin's disease or non-Hodgkin's lymphoma. *Bone Marrow Transplant*. 2000;26:471-481.
108. Weaver CH, Schulman KA, Wilson-Relyea B, et al. Randomized trial of filgrastim, sargramostim, or sequential sargramostim and filgrastim after myelosuppressive chemotherapy for the harvesting of peripheral-blood stem cells. *J Clin Oncol*. 2000;18:43-53.
109. Arora M, Burns LJ, Barker JN, et al. Randomized comparison of granulocyte colony-stimulating factor versus granulocyte-macrophage colony-stimulating factor plus intensive chemotherapy for peripheral blood stem cell mobilization and autologous transplantation in multiple myeloma. *Biol Blood Marrow Transplant*. 2004; 10:395-404.
110. Hosing C, Qazilbash MH, Kebriaei P, et al. Fixed-dose single agent pegfilgrastim for peripheral blood progenitor cell mobilisation in patients with multiple myeloma. *Br J Haematol*. 2006;133:533-537.
111. Randomized, double-blind study of peripheral blood progenitor cell (PBPC) mobilization by pegfilgrastim or filgrastim for autologous transplantation in subjects with Hodgkin's or non-Hodgkin's lymphoma. Available from: http://download.veritasmedicine.com/REGFILES/amgen/20020112.pdf. Accessed .
112. Costa LJ, Kramer C, Hogan KR, et al. Pegfilgrastim- versus filgrastim-based autologous hematopoietic stem cell mobilization in the setting of preemptive use of plerixafor: efficacy and cost analysis. *Transfusion*. 2012;52:2375-2381.
113. Bruns I, Steidl U, Kronenwett R, et al. A single dose of 6 or 12 mg of pegfilgrastim for peripheral blood progenitor cell mobilization results in similar yields of CD34+ progenitors in patients with multiple myeloma. *Transfusion*. 2006;46:180-185.
114. Zappasodi P, Nosari AM, Astori C, et al. DCEP chemotherapy followed by a single, fixed dose of pegylated filgrastim allows adequate stem cell mobilization in multiple myeloma patients. *Transfusion*. 2008;48: 857-860.
115. Steidl U, Fenk R, Bruns I, et al. Successful transplantation of peripheral blood stem cells mobilized by chemotherapy and a single dose of pegylated G-CSF in patients with multiple myeloma. *Bone Marrow Transplant*. 2005;35:33-36.
116. Fruehauf S, Klaus J, Huesing J, et al. Efficient mobilization of peripheral blood stem cells following CAD chemotherapy and a single dose of pegylated G-CSF in patients with multiple myeloma. *Bone Marrow Transplant*. 2007;39:743-750.
117. Isidori A, Tani M, Bonifazi F, et al. Phase II study of a single pegfilgrastim injection as an adjunct to chemotherapy to mobilize stem cells into the peripheral blood of pretreated lymphoma patients. *Haematologica*. 2005;90:225-231.
118. Putkonen M, Rauhala A, Pelliniemi TT, Remes K. Single-dose pegfilgrastim is comparable to daily filgrastim in mobilizing peripheral blood stem cells: a case-matched study in patients with lymphoproliferative malignancies. *Ann Hematol*. 2009;88:673-680.
119. Simona B, Cristina R, Luca N, et al. A single dose of pegfilgrastim versus daily filgrastim to evaluate the mobilization and the engraftment of autologous peripheral hematopoietic progenitors in malignant lymphoma patients candidate for high-dose chemotherapy. *Transfus Apher Sci*. 2010;43:321-326.
120. Tricot G, Barlogie B, Zangari M, et al. Mobilization of peripheral blood stem cells in myeloma with either pegfilgrastim or filgrastim following chemotherapy. *Haematologica*. 2008;93:1739-1742.
121. Cesaro S, Zanazzo AG, Frenos S, et al. A phase II study on the safety and efficacy of a single dose of pegfilgrastim for mobilization and transplantation of autologous hematopoietic stem cells in pediatric oncohematology patients. *Transfusion*. 2011;51:2480-2487.
122. Hiwase DK, Bollard G, Hiwase S, et al. Intermediate-dose CY and G-CSF more efficiently mobilize adequate numbers of PBSC for tandem autologous PBSC transplantation compared with low-dose CY in patients with multiple myeloma. *Cytotherapy*. 2007;9:539-547.
123. Hamadani M, Kochuparambil ST, Osman S, et al. Intermediate-dose versus low-dose cyclophosphamide and granulocyte colony-stimulating factor for peripheral blood stem cell mobilization in patients with multiple myeloma treated with novel induction therapies. *Biol Blood Marrow Transplant*. 2012;18:1128-1135.
124. Sizemore CA, Laporte J, Holland HK, et al. A comparison of toxicity and mobilization efficacy following two different doses of cyclophosphamide for mobilization of hematopoietic stem cells in non-Hodgkin's lymphoma patients. *Biol Blood Marrow Transplant*. 2010;16(Suppl 2):S206.
125. Sizemore CA, LaPorte J, Sanacore M, et al. A comparison of toxicity and mobilization efficacy following two different doses of cyclophosphamide for mobilization of hematopoietic stem cells in multiple myeloma patients. ASH Annual Meeting Abstracts. *Blood*. 2009;114:4229.
126. Damon LE, Johnson JL, Niedzwiecki D, et al. Immunochemotherapy and autologous stem-cell transplantation for untreated patients with mantle-cell lymphoma: CALGB 59909. *J Clin Oncol*. 2009;27: 6101-6108.
127. Geisler CH, Kolstad A, Laurell A, et al. Long-term progression-free survival of mantle cell lymphoma after intensive front-line immunochemotherapy with in vivo–purged stem cell rescue: a non-randomized phase 2 multicenter study by the Nordic Lymphoma Group. *Blood*. 2008;112:2687-2693.
128. Bacon WA, Long GD, Rizzieri DA, et al. Impact of high-dose cyclophosphamide on the outcome of autologous stem cell transplant in patients with newly diagnosed multiple myeloma, ASH Annual Meeting Abstracts. *Blood*. 2011;118:4127.
129. Flomenberg N, Devine SM, DiPersio JF, et al. The use of AMD3100 plus G-CSF for autologous hematopoietic progenitor cell mobilization is superior to G-CSF alone. *Blood*. 2005;106:1867-1874.
130. Isola L, Banoff KM, Kim SS. Pharmacoeconomic impact of upfront use plerixafor for autologous stem cell mobilization in multiple myeloma patients. ASH Annual Meeting Abstracts. *Blood*. 2011;118:2075.
131. Li J, Hamilton E, Vaughn L, et al. Effectiveness and cost analysis of "just-in-time" salvage plerixafor administration in autologous transplant patients with poor stem cell mobilization kinetics. *Transfusion*. 2011;51:2175-2182.
132. Perkins J, Bookout R, Sapiro J, et al. Retrospective comparison of secondary mobilization strategies in candidates for autologous hematopoietic cell transplantion with A focus on resource utilization: Plerixafor + G-CSF versus other regimens. *Biol Blood Marrow Transplant*. 2010;16(Suppl 2):S197.
133. Shapiro J, Perkins J, Bookout R, et al. Evaluation of a risk-based algorithm for the utilization of plerixafor as primary mobilization of $CD34^+$ cells in autologous hematopoietic cell transplant candidates, ASH Annual Meeting Abstracts. *Blood*. 2011;118:4060.
134. Shaughnessy P, Islas-Ohlmayer M, Murphy J, et al. Cost and clinical analysis of autologous hematopoietic stem cell mobilization with G-CSF and plerixafor compared to G-CSF and cyclophosphamide. *Biol Blood Marrow Transplant*. 2011;17:729-736.
135. Adel NG, Duck E, Collum K, et al. Cost analysis of using plerixafor plus G-CSF versus cyclophosphamide plus G-CSF for autologous stem cell mobilization in multiple myeloma patients treated at Memorial Sloan-Kettering Cancer Center (MSKCC), ASH Annual Meeting Abstracts. *Blood*. 2011;118:4059.
136. Campen CJ, Armstrong EP, Christian JA, et al. Comparative cost-effectiveness of plerixafor plus granulocyte-colony stimulating factor versus cyclophosphamide plus granulocyte-colony stimulating for autologous peripheral blood stem cell mobilization in patients with non-Hodgkin's lymphoma. *Biol Blood Marrow Transplant*. 2010; 16(Suppl 2):S206.
137. Vishnu P, Roy V, Paulsen A, Zubair AC. Efficacy and cost-benefit analysis of risk-adaptive use of plerixafor for autologous hematopoietic progenitor cell mobilization. *Transfusion*. 2012;52:55-62.
138. Costa LJ, Miller AN, Alexander ET, et al. Growth factor and patient-adapted use of plerixafor is superior to CY and growth factor for autologous hematopoietic stem cells mobilization. *Bone Marrow Transplant*. 2011;46:523-528.
139. Dugan MJ, Maziarz RT, Bensinger WI, et al. Safety and preliminary efficacy of plerixafor (Mozobil) in combination with chemotherapy and G-CSF: an open-label, multicenter, exploratory trial in patients with multiple myeloma and non-Hodgkin's lymphoma undergoing stem cell mobilization. *Bone Marrow Transplant*. 2010;45:39-47.
140. Attolico I, Pavone V, Ostuni A, et al. Plerixafor added to chemotherapy plus G-CSF is safe and allows adequate PBSC collection in predicted poor mobilizer patients with multiple myeloma or lymphoma. *Biol Blood Marrow Transplant*. 2012;18:241-249.
141. Nimmagadda S, Sweiss K, Mahmud N, et al. Plerixafor given before the third leukapheresis to rescue an unsuccessful stem cell mobilization with CY and G-CSF. *Bone Marrow Transplant*. 2010;45:1121-1122.

142. Basak GW, Urbanowska E, Boguradzki P, et al. Booster of plerixafor can be successfully used in addition to chemotherapy-based regimen to rescue stem cell mobilization failure. *Ann Transplant*. 2010;15:61-67.
143. Basak GW, Mikala G, Koristek Z, et al. Plerixafor to rescue failing chemotherapy-based stem cell mobilization: it's not too late. *Leuk Lymphoma*. 2011;52:1711-1719.
144. Jantunen E, Kuittinen T, Mahlamäki E, et al. Efficacy of pre-emptively used plerixafor in patients mobilizing poorly after chemomobilization: a single-centre experience. *Eur J Haematol*. 2011;86:299-304.
145. Jantunen E, Varmavuo V, Kuittinen T, et al. Effect of plerixafor on graft lymphocyte subsets in NHL patients mobilizing poorly with chemotherapy plus G-CSF. ASH Annual Meeting Abstracts. *Blood*. 2011;118:1929.
146. Jantunen E, Varmavuo V, Valonen P, et al. $CD34^+$ subclasses of blood stem cell grafts collected after plerixafor injection in non-Hodgkin lymphoma (NHL) patients mobilizing poorly with chemotherapy plus G-CSF. ASH Annual Meeting Abstracts. *Blood*. 2011;118:2990.
147. Kochuparambil ST, Mebel ER, DeRemer DL, et al. Optimizing the efficacy of plerixafor as a salvage option in poor mobilizers following chemotherapy plus G-CSF mobilization. *Biol Blood Marrow Transplant*. 2011;17(Suppl 2):S208-S209.
148. Rosenbaum ER, Nakagawa M, Pesek G, et al. Chemotherapy does not enhance $CD34^+$ cell collection when added to growth factor and plerixafor in patients who are poor mobilizers. ASH Annual Meeting Abstracts. *Blood*. 2011;118:4388.
149. Awan FT, Kochuparambil ST, Deremer D, et al. Plerixafor salvage is safe and effective in hard-to-mobilize patients undergoing chemotherapy and filgrastim-based peripheral blood progenitor cell mobilization. *J Oncol*. 2012;2012:931071.
150. Vives S, Sancho J, Almazán F, et al. Plerixafor plus G-CSF in combination with chemotherapy for stem cell mobilization in a pediatric patient with Ewing's sarcoma. *J Clin Apher*. 2012;27:260-262.
151. Varmavuo V, Mäntymaa P, Kuittinen T, et al. Pre-emptive plerixafor injection increases blood neutrophil, lymphocyte and monocyte counts in addition to $CD34^+$ counts in patients with non-Hodgkin lymphoma mobilizing poorly with chemotherapy plus G-CSF: potential implications for apheresis and graft composition. *Transfus Apher Sci*. 2012;46:257-262.
152. Costa LJ, Abbas J, Hogan KR, et al. Growth factor plus preemptive ("just-in-time") plerixafor successfully mobilizes hematopoietic stem cells in multiple myeloma patients despite prior lenalidomide exposure. *Bone Marrow Transplant*. 2012;47:1403-1408.
153. Malard F, Kröger N, Gabriel IH, et al. Plerixafor for autologous peripheral blood stem cell mobilization in patients previously treated with fludarabine or lenalidomide. *Biol Blood Marrow Transplant*. 2012;18:314-317.
154. Mark T, Stern J, Furst JR, et al. Stem cell mobilization with cyclophosphamide overcomes the suppressive effect of lenalidomide therapy on stem cell collection in multiple myeloma. *Biol Blood Marrow Transplant*. 2008;14:795-798.
155. Micallef IN, Ho AD, Klein LM, et al. Plerixafor (Mozobil) for stem cell mobilization in patients with multiple myeloma previously treated with lenalidomide. *Bone Marrow Transplant*. 2011;46:350-355.
156. Nazha A, Cook R, Vogl DT, et al. Stem cell collection in patients with multiple myeloma: impact of induction therapy and mobilization regimen. *Bone Marrow Transplant*. 2011;46:59-63.
157. Basak GW, Jaksic O, Koristek Z, et al. Identification of prognostic factors for plerixafor-based hematopoietic stem cell mobilization. *Am J Hematol*. 2011;86:550-553.
158. Popat R, Oakervee HE, Hallam S, et al. Bortezomib, doxorubicin and dexamethasone (PAD) front-line treatment of multiple myeloma: updated results after long-term follow-up. *Br J Haematol*. 2008;141:512-516.
159. Lu S, Wang J, Xu X, et al. Bortezomib in combination with epirubicin, dexamethasone and thalidomide is a highly effective regimen in the treatment of multiple myeloma: a single-center experience. *Int J Hematol*. 2009;89:34-38.
160. Kaufman JL, Nooka A, Vrana M, et al. Bortezomib, thalidomide, and dexamethasone as induction therapy for patients with symptomatic multiple myeloma. *Cancer*. 2010;116:3143-3151.
161. Jakubowiak AJ, Kendall T, Al-Zoubi A, et al. Phase II trial of combination therapy with bortezomib, pegylated liposomal doxorubicin, and dexamethasone in patients with newly diagnosed myeloma. *J Clin Oncol*. 2009;27:5015-5022.
162. Corso A, Barbarano L, Mangiacavalli S, et al. Bortezomib plus dexamethasone can improve stem cell collection and overcome the need for additional chemotherapy before autologous transplant in patients with myeloma. *Leuk Lymphoma*. 2010;51:236-242.
163. Moreau P, Hulin C, Marit G, et al. Stem cell collection in patients with de novo multiple myeloma treated with the combination of bortezomib and dexamethasone before autologous stem cell transplantation according to IFM 2005-01 trial. *Leukemia*. 2010;24:1233-1235.
164. Ponisch W, Wiesler J, Leiblein S, et al. Successful mobilization of peripheral blood stem cells after intensive bendamustine pre-treatment in patients with multiple myeloma. ASH Annual Meeting Abstracts. *Blood*. 2010;116:4439.
165. Ponisch W, Wiesler J, Wagner I, et al. Impact of bendamustine pretreatment on stem cell mobilization and autologous stem cell transplantation in patients with multiple myeloma. ASH Annual Meeting Abstracts. *Blood*. 2011;118:1933.
166. Burchardt CA, Brugger W, Maschmeyer G, et al. Peripheral blood stem cell mobilization after bendamustine containing chemotherapy in indolent lymphomas is possible: results from the Phase III study of B-R versus CHOP-R (NHL 1-2003 trial) of the StiL (Study Group Indolent Lymphomas, Germany). ASH Annual Meeting Abstracts. *Blood*. 2009;114:2679.
167. Boeve S, Strupeck J, Creech S, Stiff PJ. Analysis of remobilization success in patients undergoing autologous stem cell transplants who fail an initial mobilization: risk factors, cytokine use and cost. *Bone Marrow Transplant*. 2004;33:997-1003.
168. Jantunen E, Kuittinen T. Blood stem cell mobilization and collection in patients with lymphoproliferative diseases: practical issues. *Eur J Haematol*. 2008;80:287-295.
169. Vellenga E, Van Agthoven M, Croockewit AJ, et al. Autologous peripheral blood stem cell transplantation in patients with relapsed lymphoma results in accelerated haematopoietic reconstitution, improved quality of life and cost reduction compared with bone marrow transplantation: The HOVON 22 study. *Br J Haematol*. 2001;114:319-326.
170. Woronoff-Lemsi MC, Arveux P, Limat S, et al. Cost-comparative study of autologous peripheral blood progenitor cells (PBPC) and bone marrow (ABM) transplantations for non-Hodgkin's lymphoma patients. *Bone Marrow Transplant*. 1997;20:975-982.
171. Calandra G, McCarty J, McGuirk J, et al. AMD3100 plus G-CSF can successfully mobilize $CD34^+$ cells from non-Hodgkin's lymphoma, Hodgkin's disease and multiple myeloma patients previously failing mobilization with chemotherapy and/or cytokine treatment: compassionate use data. *Bone Marrow Transplant*. 2008;41:331-338.
172. Duarte RF, Shaw BE, Marin P, et al. Plerixafor plus granulocyte CSF can mobilize hematopoietic stem cells from multiple myeloma and lymphoma patients failing previous mobilization attempts: EU compassionate use data. *Bone Marrow Transplant*. 2011;46:52-58.
173. Hubel K, Fresen MM, Apperley JF, et al. European data on stem cell mobilization with plerixafor in non-Hodgkin's lymphoma, Hodgkin's lymphoma and multiple myeloma patients: a subgroup analysis of the European Consortium of Stem Cell Mobilization. *Bone Marrow Transplant*. 2011;47:1046-1050.
174. Micallef IN, Stiff PJ, DiPersio JF, et al. Successful stem cell remobilization using plerixafor (Mozobil) plus granulocyte colony-stimulating factor in patients with non-Hodgkin lymphoma: results from the plerixafor NHL phase 3 study rescue protocol. *Biol Blood Marrow Transplant*. 2009;15:1578-1586.
175. Hosing C, Smith V, Rhodes B, et al. Assessing the charges associated with hematopoietic stem cell mobilization and remobilization in patients with lymphoma and multiple myeloma undergoing autologous hematopoietic peripheral blood stem cell transplantation. *Transfusion*. 2011;51:1300-1313.
176. Kymes S, Pusic I, Lambert DL, et al. Economic evaluation of plerixafor for stem cell mobilization. *Am J Manag Care*. 2012;18:33-41.
177. Schroeder MA, DiPersio JF. Mobilization of hematopoietic stem and leukemia cells. *J Leukoc Biol*. 2012;91:47-57.
178. Nervi B, Ramirez P, Rettig MP, et al. Chemosensitization of acute myeloid leukemia (AML) following mobilization by the CXCR4 antagonist AMD3100. *Blood*. 2009;113:6206-6214.
179. Uy GL, Rettig MP, Motabi IH, et al. A phase 1/2 study of chemosensitization with the CXCR4 antagonist plerixafor in relapsed or refractory acute myeloid leukemia. *Blood*. 2012;119:3917-3924.
180. Welschinger R, Liedtke F, Basnett J, et al. Plerixafor (AMD3100) induces prolonged mobilization of acute lymphoblastic leukemia cells and increases the proportion of cycling cells in the blood in mice. *Exp Hematol*. 2013;41:293-302.e1.
181. Azab AK, Runnels JM, Pitsillides C, et al. CXCR4 inhibitor AMD3100 disrupts the interaction of multiple myeloma cells with the bone marrow microenvironment and enhances their sensitivity to therapy. *Blood*. 2009;113:4341-4351.
182. Fruehauf S, Ehninger G, Hubel K, et al. Mobilization of peripheral blood stem cells for autologous transplant in non-Hodgkin's lymphoma and multiple myeloma patients by plerixafor and G-CSF and detection of tumor cell mobilization by PCR in multiple myeloma patients. *Bone Marrow Transplant*. 2010;45:269-275.
183. Tricot G, Cottler-Fox MH, Calandra G. Safety and efficacy assessment of plerixafor in patients with multiple myeloma proven or predicted to be poor mobilizers, including assessment of tumor cell mobilization. *Bone Marrow Transplant*. 2010;45:63-68.
184. Anagnostopoulos A, Aleman A, Yang Y, et al. Outcomes of autologous stem cell transplantation in patients with multiple myeloma who received dexamethasone-based nonmyelosuppressive induction therapy. *Bone Marrow Transplant*. 2004;33:623-628.

185. Demirkazik A, Kessinger A, Armitage JO, et al. Progenitor and lymphoma cells in blood stem cell harvests: impact on survival following transplantation. *Bone Marrow Transplant*. 2001;28:207-212.
186. Kopp HG, Yildirim S, Weisel KC, et al. Contamination of autologous peripheral blood progenitor cell grafts predicts overall survival after high-dose chemotherapy in multiple myeloma. *J Cancer Res Clin Oncol*. 2009;135:637-642.
187. DiPersio JF, Ho AD, Hanrahan J, et al. Relevance and clinical implications of tumor cell mobilization in the autologous transplant setting. *Biol Blood Marrow Transplant*. 2011;17:943-955.
188. Rettig MP, Ansstas G, Dipersio JF. Mobilization of hematopoietic stem and progenitor cells using inhibitors of CXCR4 and VLA-4. *Leukemia*. 2012;26:34-53.
189. Bakanay SM, Demirer T. Novel agents and approaches for stem cell mobilization in normal donors and patients. *Bone Marrow Transplant*. 2011;47:1154-1163.
190. Ramirez P, Rettig MP, Uy GL, et al. BIO5192, a small-molecule inhibitor of VLA-4, mobilizes hematopoietic stem and progenitor cells. *Blood*. 2009;114:1340-1343.
191. Schiller G, Vescio R, Freytes C, et al. Transplantation of $CD34^+$ peripheral blood progenitor cells after high- dose chemotherapy for patients with advanced multiple myeloma. *Blood*. 1995;86:390-397.
192. Pavone V, Gaudio F, Guarini A, et al. Mobilization of peripheral blood stem cells with high-dose cyclophosphamide or the DHAP regimen plus G-CSF in non-Hodgkin's lymphoma. *Bone Marrow Transplant*. 2002;29:285-290.
193. Demirer T, Ayli M, Ozcan M, et al. Mobilization of peripheral blood stem cells with chemotherapy and recombinant human granulocyte colony-stimulating factor (rhG-CSF): a randomized evaluation of different doses of rhG-CSF. *Br J Haematol*. 2002;116:468-474.
194. Gojo I, Guo C, Sarkodee-Adoo C, et al. High-dose cyclophosphamide with or without etoposide for mobilization of peripheral blood progenitor cells in patients with multiple myeloma: efficacy and toxicity. *Bone Marrow Transplant*. 2004;34:69-76.
195. Lefrere F, Zohar S, Ghez D, et al. The VAD chemotherapy regimen plus a G-CSF dose of 10 μg/kg is as effective and less toxic than high-dose cyclophosphamide plus a G-CSF dose of 5 μg/kg for progenitor cell mobilization: results from a monocentric study of 82 patients. *Bone Marrow Transplant*. 2006;37:725-729.
196. Wood WA, Whitley J, Moore D, et al. Chemomobilization with etoposide is highly effective in patients with multiple myeloma and overcomes the effects of age and prior therapy. *Biol Blood Marrow Transplant*. 2011;17:141-146.
197. Wood WA, Whitley J, Goyal R, et al. Effectiveness of etoposide chemomobilization in lymphoma patients undergoing auto-SCT. *Bone Marrow Transplant*. 2013;48:771-776.
198. Shpall EJ, Wheeler CA, Turner SA, et al. A randomized phase 3 study of peripheral blood progenitor cell mobilization with stem cell factor and filgrastim in high-risk breast cancer patients. *Blood*. 1999;93:2491-2501.
199. André M, Baudoux E, Bron D, et al. Phase III randomized study comparing 5 or 10 μg per kg per day of filgrastim for mobilization of peripheral blood progenitor cells with chemotherapy, followed by intensification and autologous transplantation in patients with non-myeloid malignancies. *Transfusion*. 2003;43:50-57.
200. Weaver CH, Schulman KA, Buckner CD. Mobilization of peripheral blood stem cells following myelosuppressive chemotherapy: a randomized comparison of filgrastim, sargramostim, or sequential sargramostim and filgrastim. *Bone Marrow Transplant*. 2001;27(Suppl 2):S23-S29.