Transfusion and Apheresis Science 56 (2017) 845–849

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Original Article

Autologous hematopoietic progenitor cell mobilization and collection in adult patients presenting with multiple myeloma and lymphoma: A position-statement from the Turkish Society of Apheresis (TSA)

Emre Tekgündüz[a,*], Mutlu Arat[b], Hakan Göker[c], Hakan Özdoğu[d], Leylagül Kaynar[e], Seçkin Çağırgan[f], Mehmet Ali Erkurt[g], Filiz Vural[h], İlhami Kiki[i], Fevzi Altuntaş[a,j], Fatih Demirkan[k], on behalf of Turkish Society of Apheresis (TSA)

[a] Ankara Oncology Hospital, Hematology and HCT Clinic, Ankara, Turkey
[b] Sisli Florence Nightingale Hospital, HSCT Unit, İstanbul, Turkey
[c] Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Ankara, Turkey
[d] Baskent University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Adana, Turkey
[e] Erciyes University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Kayseri, Turkey
[f] Medikalpark Hospital, Hematology and HCT Clinic, İzmir, Turkey
[g] Inonu University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Malatya, Turkey
[h] Ege University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Izmir, Turkey
[i] Ataturk University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Erzurum, Turkey
[j] Yildirim Beyazit University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Ankara, Turkey
[k] Dokuz Eylul University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, HCT Unit, Izmir, Turkey

ARTICLE INFO

Keywords:
Autologous hematopoietic cell transplantation
Lymphoma
Myeloma
Mobilization

ABSTRACT

Autologous hematopoietic cell transplantation (AHCT) is a routinely used procedure in the treatment of adult patients presenting with multiple myeloma (MM), Hodgkin lymphoma (HL) and various subtypes of non-Hodgkin lymphoma (NHL) in upfront and relapsed/refractory settings. Successful hematopoietic progenitor cell mobilization (HPCM) and collection are the rate limiting first steps for application of AHCT. In 2015, almost 1700 AHCT procedures have been performed for MM, HL and NHL in Turkey. Although there are recently published consensus guidelines addressing critical issues regarding autologous HPCM, there is a tremendous heterogeneity in terms of mobilization strategies of transplant centers across the world. In order to pave the way to a more standardized HPCM approach in Turkey, Turkish Society of Apheresis (TSA) assembled a working group consisting of experts in the field. Here we report the position statement of TSA regarding autologous HPCM mobilization strategies in adult patients presenting with MM and lymphoma.

1. Introduction

Autologous hematopoietic cell transplantation (AHCT) is a routinely used procedure in the treatment of adult patients presenting with multiple myeloma (MM), Hodgkin lymphoma (HL) and various subtypes of non-Hodgkin lymphoma (NHL) in upfront and relapsed/refractory settings [1,2]. On the other hand the application of second AHCT is recommended in MM patients with high-risk cytogenetic features as part of a tandem approach [3] or relapsed disease following a reasonable duration (>18 months) of initial remission following upfront AHCT [4]. There is a global shift from bone marrow to peripheral blood (PB) as the preferred source of $CD34^+$ hematopoietic progenitor cells because faster engraftment kinetics and better quality of life compared to bone marrow harvesting.

Successful hematopoietic progenitor cell mobilization (HPCM) and collection are the rate limiting first steps for application of AHCT. Although there are recently published consensus guidelines addressing critical issues regarding autologous HPCM [5–8], there is a tremendous heterogeneity in terms of mobilization strategies

* Corresponding author.
E-mail address: emretekgunduz@yahoo.com (E. Tekgündüz).

https://doi.org/10.1016/j.transci.2017.11.025
1473-0502/

of transplant centers across the world. Mobilization policies of centers depend not only on institutional perception of up-to-date data regarding HPCM or preference of a specific guideline-driven strategy but also on resource availability and local regulations of each country, where the center is located. In order to pave the way to a more standardized HPCM approach in Turkey, Turkish Society of Apheresis (TSA) assembled a working group consisting of experts in the field. Here we report the position statement of TSA regarding autologous HPCM mobilization strategies in adult patients presenting with MM and lymphoma.

2. Methods

TSA established a working group consisting of experts in the field of adult clinical hematopoietic cell transplantation (HCT). The position statement included frequently asked questions, relevant issues regarding HPCM and organized in a user-friendly way for transplant physicians. A core panel of experts prepared a draft including most current data and local regulations in Turkey regarding HPCM, which was thoroughly evaluated by all members of the working group to finalize the manuscript.

3. Position statement

3.1. The choice and schedule of the myeloid growth factors

Original filgrastim (Neupogen®) with its various biosimilars and lenograstim (Granocyte®) are currently available in Turkish market. Although we have robust data indicating similarity in terms of efficacy and safety of pegylated G-CSF compared to non-pegylated G-CSF [9], pegylated G-CSF is not licensed yet in the country. Equivalence of biosimilar filgrastim as originator G-CSF or lenograstim in terms of safety and efficacy has been reported in steady-state [10–15], chemomobilization [16–21] and G-CSF + plerixafor HPCM [22] settings in patients who underwent autologous HCT and healthy donors of allogeneic HCT recipients. All available G-CSFs (original/biosimilar filgrastim and lenograstim) can be used in approved doses and schedules for steady-state (10 μg/kg/day subcutaneously) and chemomobilization (5 μg/kg/day subcutaneously) as recommended by guidelines [8].

Although widely used, one study conducted in breast cancer patients found no advantage of split dose injection of filgrastim over once daily schedule [23]. Because of cost savings compared to lenograstim, original or biosimilar filgrastim seems to be the most feasible agent for steady-state HPCM in Turkey.

3.1.1. Position statement on the choice and schedule of the myeloid growth factors

Original filgrastim, biosimilar forms of filgrastim and lenograstim in recommended doses and schedules are reasonable G-CSF options for steady-state mobilization and chemomobilization in patients undergoing HPCM. Original or biosimilar filgrastim may be preferred over lenograstim because of cost-effectivity.

3.2. Progenitor cell dose and duration of leukapheresis

There is general agreement that infusion of at least 2×10^6/kg $CD34^+$ cells are needed for successful engraftment, although restoration of normal hematopoiesis is possible below this threshold [7]. Because the infusion of higher dose of progenitor cells result in faster engraftment and decreased transfusion support, optimal dose of $CD34^+$ cells needed to support one AHCT were accepted as $>4 \times 10^6$/kg [24] or $>5 \times 10^6$/kg [7,25–27]. There are also centers using disease-specific targets for $CD34^+$ cells ($>4 \times 10^6$/kg for MM and $>5 \times 10^6$/kg for lymphoma patients required for supporting one AHCT) [28]. In fact, two phase-III trials, which resulted the approval of plerixafor in combination with G-CSF for HPCM in patients with MM and NHL defined achievement of $>6 \times 10^6$/kg and $>5 \times 10^6$/kg $CD34^+$ cells as the primary end point for target stem cell yield in patients presenting MM and NHL, respectively [29,30]. Although an evidence-based threshold for optimal stem cell dose cannot be defined at this moment, targeting optimal progenitor cell dose for one AHCT as $4-5 \times 10^6$/kg seems to be reasonable. Even in the era of novel agents, AHCT is an indispensible treatment option for MM patients in upfront and relapsed/refractory settings. Indeed, many MM patients may need two AHCT procedures during the course of their disease either as a tandem approach (patients with high-risk cytogenetic features at diagnosis) or in relapsed disease with a long remission duration following first AHCT [3,4]. Therefore, achievement of minimal stem cell yield required for supporting two AHCT procedures should be aimed in patients presenting with MM.

Currently, there is no consensus on the maximal duration of leukapheresis. Defining the optimal trade-off between prolonged HPCM procedure and higher progenitor cell yield is an important issue for all transplant centers. It is often difficult to decide whether to stop or continue leukapheresis to reach the optimal cell dose in a patient after achievement of minimal stem cell dose. Italian Group for Stem Cell Transplantation (GITMO) defined proven poor mobilization as inability to harvest at least 2×10^6/kg $CD34^+$ cell dose in $\leq$3 apheresis sessions [31]. With judicious use of plerixafor in almost one third of the patients, City of Hope group was able to collect at least 2×10^6/kg $CD34^+$ cells in 2.8 days (mean) [28]. In the plerixafor era, keeping the duration of progenitor cell collection at a maximum of 4 days seems to be rational [8,29,30,32].

3.2.1. Position statement on the progenitor cell dose and duration of leukapheresis

Collection of at least 2×10^6/kg $CD34^+$ cells is recommended for supporting single AHCT. In patients presenting with MM, the minimal required progenitor cell dose should be 4×10^6/kg in order to support two AHCT procedures. If feasible, we suggest targeting $4–5 \times 10^6$/kg $CD34^+$ cells for single AHCT in order to achieve faster engraftment and minimize transfusion support following AHCT. Preferentially, apheresis teams should aim to collect minimal and optimal number of $CD34^+$ cells in no more than 3 and 4 apheresis sessions, respectively.

3.3. Technical aspects and timing

Peripheral blood $CD34^+$ ($PBCD34^+$) cell count for initiating of leukapheresis is the single, most predictive parameter for progenitor cell yield [6]. Monitorization of $PBCD34^+$ cell count should begin on days 4 or 5 in patients on steady-state or plerixafor + G-CSF mobilization [7,8]. In contrast, predicting the optimal day of leukapheresis in chemomobilization setting may be complicated and vary according the chemomobilization regimen used. A recently published consensus report from United Kingdom suggested expected days of initiating leukapheresis based on chemotherapy regimen used [33]. Monitoring of PBCD34+ cell count may be started when white blood cell count (WBC) reach $4–5 \times 10^9$/L [34]. Estimating the day of leukapheresis based on $PBCD34^+$ cell count is the optimal method. Although there is no consensus on the optimal threshold for initiating leukapheresis, minimal levels are 5–20/μL $PBCD34^+$ cells [7]. In general, initiating leukapheresis when $PBCD34^+$ cell count reached >20/μL is reasonable in order to achieve at least 2×10^6/kg $CD34^+$ cells in the final product [7,8]. Even in the era of plerixafor, patients with a $PBCD34^+$ cell count <5/μL have a high risk for mobilization failure [24,35]. In recent reports, preemptive plerixafor is suggested for patients

with a PBCD34$^+$ cell count 5–10/μL [28] or ≤15/μL [33]. Based on the aforementioned facts, initiation of leukapheresis at 15-20/μL PBCD34$^+$ cell count seems reasonable, especially where preemptive plerixafor is not an option.

Splenic enlargement is frequently observed in the course of HPCM and splenic rupture is a quite rare but feared complication of patients presenting with hyperleukocytosis. Although evidence-based data is lacking, the common practice is to withhold G-CSF and plerixafor when the WBC exceeds 100×10^9/L and 75×10^9/L, respectively [7].

3.3.1. Position statement on technical aspects and timing

Monitorization of PBCD34$^+$ cell count is recommended for all patients undergoing HPCM to decide the optimal day of initiation of leukapheresis. Monitorization should begin on days 4 or 5 in patients on steady-state or plerixafor + G-CSF mobilization. In chemomobilization setting, monitorization of PBCD34$^+$ cell count may be started when WBC reach $4–5 \times 10^9$/L. Initiation of leukapheresis at 15-20/μL PBCD34$^+$ cell count seems reasonable, especially where preemptive plerixafor is not an option. It may be preferred to withhold G-CSF and plerixafor when WBC exceeds 100×10^9/L and 75×10^9/L, respectively.

3.4. Risk factors for mobilization failure

Older age (>60), irradiation to pelvis or mediastinum, marrow involvement of the primary disease, prolonged exposure to certain types of chemotherapeutic agents (fludarabine, lenalidomide, melfalan), lymphoma patients who received more than two lines of multiagent chemotherapy, bone marrow cellularity <%30 at the time of mobilization, low platelet count ($<100 \times 10^9$/L) before HPCM are known risk factors for mobilization failure [5,8,28,31]. Although very attractive, identifying poor mobilizers based solely on patient characteristics may be misleading and there is no consensus on a standard risk scoring system predicting mobilization failure. Transplants centers willing to adopt risk-based mobilization strategy may develop their own risk classification or they may prefer using proposed algorithms by experienced centers [28,31]. But in either situation we suggest using written algorithms instead of case-by-case decision making.

3.4.1. Position statement on risk factors for mobilization failure

For transplants centers willing to adopt risk-based mobilization strategy we suggest using written algorithms instead of case-by-case decision making.

3.5. Mobilization strategy

The optimal mobilization strategy in terms of efficacy, safety and cost-effectiveness is yet to be defined. Until the Food and Drug Administration (FDA) approval of plerixafor in 2008, the main options for HPCM were steady-state mobilization with G-CSF and chemomobilization characterized by administration of G-CSF following completion of chemotherapy, either as a separate mobilization chemotherapy or as part of a disease-specific chemotherapy regimen. Compared to steady-state mobilization with G-CSF, the probability of achieving desired stem cell yield with lower number of leukapheresis procedures is higher with chemomobilization [9]. Steady-state mobilization with G-CSF alone or chemomobilization will result in mobilization failure in 15–30% of patients [36]. In the last decade many study groups exerted great afford to identify patients who will fail to achieve desired progenitor cell yield before the first mobilization attempt or at early time points in the course of HPCM in order to define the optimal strategy (chemomobilization or plerixafor + G-CSF upfront) or adding plerixafor on demand (just-in-time or preemptive), respectively [24–28,31,32,37,38]. Unfortunately, clinical risk factors before start of HPCM are frequently inaccurate to predict mobilization failure and risk-scoring systems should be validated before using in real-life decision-making [31,37,38]. The recent evidence suggest, that preemptive use of plerixafor in patients who will likely fail based on low PBCD34$^+$ cell count seems to be the most effective strategy, especially if optimal rather than minimal cell yields are desired [24–27,32,33,39].

Until early 2017, National Social Security Institution (NSSI) of Turkey covered the cost of mobilization with plerixafor + G-CSF only for patients who failed at least two mobilization attempts including steady-state mobilization and chemomobilization. Therefore, common policy in real-life was steady-state mobilization at first line, chemomobilization at second line and plerixafor + G-CSF as third line attempt (step-by-step approach). Nowadays, application of plerixafor + G-CSF is possible in patients following failed chemomobilization. On the other hand, due to current regulations the preemptive use of plerixafor (just-in-time or on-demand approach) is not option in the country. Using preemptive plerixafor in steady-state mobilization or chemomobilization settings, the required apheresis sessions to reach the desired progenitor cell yields are frequently in the range of 1–3 [33,39–41]. Currently, the cost of two vials of plerixafor (Mozobil® 20 mg/ml, 1.2 ml sc) and single AHCT to NSSI of Turkey are almost 6800 $ and 13800 $, respectively. Therefore, cost of plerixafor seems to be an important barrier for application of preemptive strategy. Using plerixafor rescue following failed chemomobilization will not change the drug-specific cost, but additionally it will negatively affect the motivation of the patient, delay a potentially curative treatment, and increase the workload of apheresis stuff.

In the era of preemptive plerixafor, upfront plerixafor + G-CSF or plerixafor + chemotherapy + G-CSF do not seem feasible in any patient including those having various risk factors for mobilization failure [33]. We suggest chemomobilization using disease specific regimens as part of induction or salvage in patients with NHL and HL, who need tumor reduction where preemptive plerixafor is not an option. In MM patients, the commonly used high-dose cyclophosphamide or etoposide-based regimens apart from induction/salvage do not have strong effect on tumor control in the era of novel agents like immunomodulatory drugs, proteasome inhibitors, monoclonal antibodies etc. [8]. As a result of current regulations in Turkey, chemomobilization at first line may still be preferred even in MM patients, because rescue attempt with plerixafor is possible if chemomobilization fails.

3.5.1. Position statement on mobilization strategy

Preemptive plerixafor following G-CSF or chemotherapy + G-CSF should be preferred, if available. Due to the current regulations in Turkey, chemomobilization may be preferred at first attempt. We suggest chemomobilization using disease specific regimens as part of induction or salvage in patients with NHL and HL, who need tumor reduction. High-dose cyclophosphamide or etoposide-based regimens apart from induction/salvage may be used in MM patients as first line of HPCM. Steady-state mobilization with G-CSF alone may still be an option for patients who do not need tumor reduction, do not accept prolonged hospitalization and risk of febrile neutropenia, and have no or limited number risk factors for mobilization failure. Clinical risk factors before start of mobilization are frequently inaccurate to predict mobilization failure and risk-scoring systems should be validated before using in real-life decision-making.

Conflict of interest statement

All authors declare that they do not have any potential conflict of interest that could inappropriately influence the present study.

References

[1] Sureda A, Bader P, Cesaro S, Dreger P, Duarte RF, Dufour C, et al. Indications for allo- and auto-SCT for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2015. Bone Marrow Transplant 2015;50(8):1037–56.

[2] Majhail NS, Farnia SH, Carpenter PA, Champlin RE, Crawford S, Marks DI, et al. Indications for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American society for blood and marrow transplantation. Biol Blood Marrow Transplant 2015;21(11):1863–9.

[3] Sonneveld P, Avet-Loiseau H, Lonial S, Usmani S, Siegel D, Anderson KC, et al. Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International myeloma working group. Blood 2016;127(24):2955–62.

[4] Giralt S, Garderet L, Durie B, Usmani S, Siegel D, Anderson KC, et al. American society of blood and marrow transplantation, European society of blood and marrow transplantation, blood and marrow transplant clinical trials network, and international myeloma working group consensus conference on salvage hematopoietic cell transplantation in patients with relapsed multiple myeloma. Biol Blood Marrow Transplant 2015;21:2039–51.

[5] Giralt S, Costa L, Schriber J, Dipersio J, Maziarz R, McCarty J, et al. Optimizing autologous stem cell mobilization strategies to improve patient outcomes: consensus guidelines and recommendations. Biol Blood Marrow Transplant 2014;20:295–308.

[6] Makar RS, Padmanabbah A, Kim HC, Anderson C, Sugrue MW, Linenberger M. Use of laboratory tests to guide initiation of autologous hematopoietic progenitor cell collection by apheresis: results from the multicenter hematopoietic progenitor cell collection by apheresis laboratory trigger survey. Transfus Med Rev 2014;28(4):198–204.

[7] Duong HK, Savani BN, Copelan E, Devine S, Costa LJ, Wingard JR, et al. Peripheral blood progenitor cell mobilization for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American society for blood and marrow transplantation. Biol Blood Marrow Transplant 2014;20:1262–73.

[8] Mohty M, Hübel K, Kröger N, Aljurf M, Apperley J, Basak GW, et al. Autologous haematopoietic stem cell mobilization in multiple myeloma and lymphoma patients: a position statement from the European group for blood and marrow transplantation. Bone Marrow Transplant 2014;49(7):865–72.

[9] Kuan JW, Su AT, Leong CF. Pegylated granulocyte-colony stimulating factor versus non-pegylated granulocyte-colony stimulating factor for peripheral blood stem cell mobilization: a systematic review and meta-analysis. J Clin Apher 2017;(May), http://dx.doi.org/10.1002/jca.21550 [Epub ahead of print].

[10] Uddin S, Russell P, Farrell M, Davy B, Taylor J, Agrawal SG. Use of biosimilar filgrastim compared with lenograstim in autologous haematopoietic stem-cell transplant and sibling allogeneic transplant. Ther Adv Hematol 2015;6(2):53–60.

[11] Pham T, Patil S, Fleming S, Avery S, Walker P, Wei A, et al. Comparison of biosimilar filgrastim with originator filgrastim for peripheral blood stem cell mobilization and engraftment in patients with multiple myeloma undergoing autologous stem cell transplantation. Transfusion 2015;55:2709–13.

[12] Elayan MM, Horowitz JG, Magraner JM, Shaughnessy PJ, Bachier C. Tbo-filgrastim versus filgrastim during mobilization and neutrophil engraftment for autologous stem cell transplantation. Biol Blood Marrow Transplant 2015;21:1921–5.

[13] León-González M, León-Peña AA, Vallejo-V.Illalobos MF, Núñez-Cortés AK, Ruiz-Argüelles A, Ruiz-Argüelles GJ. Mexican biosimilar filgrastim for autologous hematopoietic stem cell mobilization and transplantation. Rev Inves Clin 2016;68:181–3.

[14] Sivgin S, Karakus E, Keklik M, Zararsiz G, Solmaz M, Kaynar L, et al. Evaluation of the efficacy and safety of original filgrastim (Neupogen®): biosimilar filgrastim (Leucostim®) and lenograstim (Granocyte®) in CD34+ peripheral hematopoietic stem cell mobilization procedures for allogeneic hematopoietic stem cell transplant donors. Transfus Apher Sci 2016;54(3):410–5.

[15] Tekgunduz E, Kaya AH, Göker H, Ozdemir E, Iskender D, Kocubaba S, et al. Biosimilar filgrastim (Leucostim®) seems to have similar efficacy in hematopoietic progenitor cell mobilization compared to original filgrastim (Neupogen®) and lenograstim (Granocyte®): a retrospective, multicenter analysis [Abstract]. Transfus Apher Sci 2018;57(1):S338. EBMT 2015Abstract Book (P429).

[16] Publicover A, Richardson DS, Davies A, Hill KS, Hurlock C, Hutchins D, et al. Use of a biosimilar granulocyte colony-stimulating factor for peripheral blood stem cell mobilization: an analysis of mobilization and engraftment. Brit J Haematol 2013;162:107–11.

[17] Manko J, Walter-Croneck A, Jawniak D, Grzasko N, Gorska-Kosicka M, Cioch M, et al. A clinical comparison of the efficacy and safety of biosimilar G-CSF and originator G-CSF in haematopoietic stem cell mobilization. Pharmacol Rep 2014;66:239–42.

[18] Martino M, Recchia AG, Moscato T, Fedele R, Neri S, Gentile M, et al. Efficacy of biosimilar granulocyte colony-stimulating factor versus originator granulocyte colony-stimulating factor in peripheral blood stem cell mobilization in the de nova multiple myeloma patients. Cytotherapy 2015;17(10):1485–93.

[19] Lisenko K, Baertsch MA, Meiser R, Pavel P, Bruckner T, Kriegsmann M, et al. Comparison of biosimilar filgrastim, originator filgrastim, and lenograstim for autologous stem cell mobilization in patients with multiple myeloma. Transfusion 2017;57(10):2359–65.

[20] Maul JT, Stenner-Liewen F, Seifert B, Pfrommer S, Petrausch U, Kiessling MK, et al. Efficacious and safe use of biosimilar filgrastim for hematopoietic progenitor cell chemo-mobilization with vinorelbine in multiple myeloma patients. J Clin Apheresis 2017;32(1):21–6.

[21] Sivgin S, Karakus E, Kaynar L, Kurnaz F, Pala C, Keklik M, et al. The comparison of filgrastim (Neupogen®), biosimilar filgrastim (Leucostim®) and lenograstim (Granocyte®) as a first line peripheral blood stem cell mobilization strategy in autologous hematopoietic stem cell transplantation: a single center experience from Turkey. Transfus Apher Sci 2013;48(3):315–20.

[22] Lanza F, Saraceni F, Pezzi A, Martino M, Bosi A, Cascavilla N, et al. A comparative analysis of biosimilar vs originator filgrastim in combination with plerixafor for stem cell mobilization in lymphoma and multiple myeloma; a propensity-score weighted multicenter approach. Am J Hematol 2017;92(9):E557–9.

[23] Carrión R, Serrano D, Gómez-Pineda A, Díez-Martín JL. A randomized study of 10ó(g/kg/day (single dose) vs 2ó¡ó5ó(g/kg/day (split dose) G-CSF as stem cell mobilization regimen in high-risk breast cancer patients. Bone Marrow Transplant 2003;32:563–7.

[24] Greil C, Kiote-Schmidt C, Fink G, Ihorst G, Hildenbeutel S, Bosse R, et al. Successful peripheral blood stem cell mobilization with a cost-efficient single fixed-dose plerixafor schedule in poor mobilizers. Leuk Lymphoma 2017;58(8):1849–58.

[25] Li J, Hamilton E, Vaughn L, Graiser M, Renfroe H, Lechowicz MJ, 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;51:2175–82.

[26] Veltri L, Cumpston A, Schillingburg A, Wen S, Luo J, Leadmon S, et al. Hematopoietic progenitor cell mobilization with 'just in time' plerixafor approach is a cost-effective alternative to routine plerixafor use. Cytotherapy 2015;17:1785–92.

[27] Afifi S, Adel NG, Devlin S, Duck E, Vanak J, Landau H, et al. Upfront plerixafor plus G-CSF versus cyclophosphamide plus G-CSF for stem cell mobilization in multiple myeloma: efficacy and cost analysis study. Bone Marrow Transplant 2016;51(4):546–52.

[28] Yuan S, Wang S. How to mobilize and collect autologous peripheral blood stem cells? Transfusion 2017;57(1):13–23.

[29] DiPersio JP, Stadtmauer EA, Nademanee A, Micallef IN, Stiff PJ, Kaufman JL, et al. Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma. Blood 2009;113:5720–6.

[30] DiPersio JF, Micallef IN, Stiff PJ, Bolwell BJ, Maziarz RT, Jacobsen E, et al. Phase III prospective randomized double blind placebo-controlled trial of plerixafor plus granulocyte colony-stimulating factor compared with placebo plus granulocyte colony-stimulating factor for autologous stem cell mobilization and transplantation for patients with non-Hodgkin's lymphoma. J Clin Oncol 2009;27:4767–73.

[31] Olivieri A, Marchetti M, Lemoli R, Tarella C, Iacone A, Lanza F, et al. Proposed definition of 'poor mobilizer' in lymphoma and multiple myeloma: an analytic hierarchy process by ad hoc working group Gruppo Italiano Trapianto di Midollo Osseo. Bone Marrow Transplant 2012;47:342–51.

[32] Clark RE, Bell J, Clark JO, Braithwaite B, Vithanarachchi U, McGinnity N, et al. Plerixafor is superior chemotherapy for first-line stem cell mobilization, and is effective even in heavily pretreated patients. Blood Cancer J 2014;4(10):e255.

[33] Douglas KW, Gilleece M, Hayden P, Hunter H, Johnson PRE, Kallmeyer C, et al. UK consensus statement on the use of plerixafor to facilitate autologous peripheral blood stem cell collection to support high-dose chemoradiotherapy for patients with malignancy. J Clin Apher 2017;(June), http://dx.doi.org/10.1002/jca.21563 [Epub ahead of print].

[34] Mahindra A, Bolwell BJ, Rybicki L, Elder P, Kalaycio M, Dean R, et al. Etoposide plus G-CSF priming compared with G-CSF alone in patients with lymphoma improves mobilization without an increased risk of secondary myelodysplasia and leukemia. Bone Marrow Transplant 2012;47:231–5.

[35] Wuchter P, Ran D, Bruckner T, Schmitt T, Witzens-Harig M, Neben K, et al. poor mobilization of hematopoietic stem cells-definition, incidence, risk factors, and impact of outcome of autologous transplantation. Biol Blood Marrow Transplant 2010;16:490–9.

[36] Abhyankar S, DeJarnette S, Aljitawi O, Ganguly S, Merkel D, McGuirk J. A risk-based approach to optimize autologous hematopoietic stem cell (HSC) collection with the use of plerixafor. Bone Marrow Transplant 2012;47:483–7.

[37] Rossi G, Skert C, Morello E, Almici C, Arcaini L, Basilico C, et al. PBSC mobilization in lymphoma patients: analysis of risk factors for collection failure and development of a predictive score based on the kinetics or circulating CD34+ cells and WBC after chemotherapy and G-CSF mobilization. Hematol Oncol 2015;33:125–32.

[38] Costa LJ, Nista EJ, Buadi FK, Lacy MQ, Dispenzieri A, Kramer CP, et al. Prediction of poor mobilization of autologous CD34+ cells with growth factor in multiple myeloma patients: implications for risk-stratification. Biol Blood Marrow Transplant 2014;20:222–8.

[39] Kouroukis CT, Varela NP, Bredeson C, Kuruvilla J, Xenocostas A. Plerixafor for autologous stem-cell mobilization and transplantation for patients in Ontario. Curr Oncol 2016;23(4):e409–30.
[40] Milone G, Martino M, Leotta S, Spadaro A, Zammit V, Cupri A, et al. Cost-effectiveness of on-demand plerixafor added to chemotherapy and granulocyte-colony stimulating factor for peripheral blood stem cell mobilization in multiple myeloma. Leuk Lymphoma 2018;59(1):42–8.
[41] Martin AP, Richard S, Haycox A, Houten R, McLeod C, Braithwaite B, et al. Evaluating the use of plerixafor in stem cell mobilization –an economic analysis of the PHANTASTIC trial. J Clin Apher 2016;31(5):434–42.