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Difficulties of Mobilization and Harvesting of Hematopoietic Stem Cells in Heavily Pre-Treated Patients

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ABSTRACT

This study presents a new method of combined growth factor mobilization with increased dose (15 μg/kg) of filgrastim and standard mono dose of plerixafor in subjects with multiple myeloma, Hodgkin or non-Hodgkin lymphoma. Efficient mobilization is a key factor in the treatment of this group of patients, because autologous transplantation can be performed in cases in which we succeed to obtain a minimally sufficient number of stem cells. Autologous stem cell transplantation is included in the current standard treatment of multiple myeloma and in the relapsed cases of lymphomas.

Keywords: mobilization, plerixafor, autologous transplantation

INTRODUCTION

Stem cell mobilization in patients with multiple myeloma and lymphomas can be a challenge for transplant physicians. Autologous stem cell transplantation has a major role in the treatment of these malignant hematologic diseases. In multiple myeloma, stem cell transplantation is part of the treatment for all fit patients practically by the age of 70 years if there are no serious comorbidities.[1] In both Hodgkin and non-Hodgkin lymphoma, autologous transplantation is indicated in relapsed cases or in cases of residual disease post-chemotherapy and/or radiotherapy.[2,3]

The yield of stem cells in autologous transplantation is $2.6*10^6$ CD34+/kg (stem cells)/patient. This number is, in many cases, difficult to obtain due to the large number of chemotherapy cycles received by the patients, the administered chemotherapy, and the biologically active disease.

In most of the centers, these patients do not benefit from autologous transplantation due to the insufficient quantity of stem cells. The new combined mobilization method with granulocyte colony stimulating growth factor (GCS-F) and plerixafor helps in obtaining a minimally sufficient number of stem cells,

thus ensuring the possibility of an autologous stem cell transplantation.[4,5]

Plerixafor has been shown to improve mobilization by increasing the number of stem cells in patients with lymphoma and multiple myeloma. This drug is an inhibitor of the CXCR4 chemokine receptor and blocks the binding of its cognate ligand stromal cell-derived factor 1 (SDF-1α) and CXCR4.[6]

Due to the fact that it is a standard indication of care, it is very important to perform at least one auto-transplantation in these diseases.

AIM OF STUDY

The aim of our study was to show the efficiency of stem cell mobilization method used in the BMT Unit of Tîrgu Mureș that allows us to mobilize a sufficient number of stem cells in patients who do not mobilize with the conventional methods.

MATERIAL AND METHODS

The study included a number of 15 patients, diagnosed with multiple myeloma and non-Hodgkin or Hodgkin lymphoma with double mobilization using GCS-F + plerixafor. All patients were poor mobilizers, meaning that on day +4 (GCS-F mobilization) or on day +9 (chemo-mobilization + GCS-F) the CD34+ stem cell count was below $10*10^6$/kg on peripheral blood.

The patients received increased doses of filgrastim (15 μg/kg/day) and 0.24 mg/kg of plerixafor on day +5 or +10 from mobilization.

We present the mobilization results of 15 cases from our recent clinical experience from October 2016 until April 2017, performing the above presented double mobilization technique in order to obtain a minimum sufficient number of stem cells for autologous transplantation.

RESULTS

The study population had a mean age of 51 years (range 21 to 64 years) and included 9 female and 6 male patients. The study group was comprised of 10 patients with multiple myeloma, 3 patients with B-cell non-Hodgkin lymphoma, 1 case with T-cell non-Hodgkin lymphoma and 1 case with Hodgkin lymphoma. An increase in the filgrastim dose from 10 μg/kg to 15 μg/kg and the administration of 0.24 mg/kg of plerixafor on day +5 or +10 of the mobilization, showed improved mobilization rates.

We present the number of stem cells obtained with the increased dose of filgrastim and a monodose of plerixafor in patients with myeloma and lymphomas, as well as the number of apheresis procedures used in order to harvest the minimal quantity of stem cells necessary to be able to perform a safe autologous transplantation. We can observe the peak of stem cells obtained by this method on day +5 and +10 of the mobilization. By this method all mobilized

TABLE 1. Number of CD34+ cells/kg before and after combined mobilization with filgrastim + plerixafor

No	Diagnosis	No. of apheresis	No. of CD34+/kg before plerixafor	No. of CD34+/kg after plerixafor	Total no. of CD34+/kg
1	HL	2	0.35	3.45	3.80
2	NHL	2	0.27	2.39	2.66
3	NHL	2	0.74	1.39	2.13
4	NHL	2	0.43	1.83	2.26
5	T-NHL	2	0.72	2.97	3.69
6	MM	2	0.71	1.34	2.05
7	MM	2	0.45	2.56	3.01
8	MM	2	0.76	3.21	3.97
9	MM	2	1.32	5.56	6.88
10	MM	2	0.9	3.35	4.25
11	MM	2	0.96	3.36	4.92
12	MM	2	1	3.84	4.84
13	MM	3	0.4	1.52/0.73	2.69
14	MM	2	0.85	3.08	3.93
15	MM	2	0.47	1.81	2.28

HL – Hodgkin lymphoma, NHL – non-Hodgkin lymphoma, T-NHL – T-cell non-Hodgkin lymphoma, MM – multiple myeloma

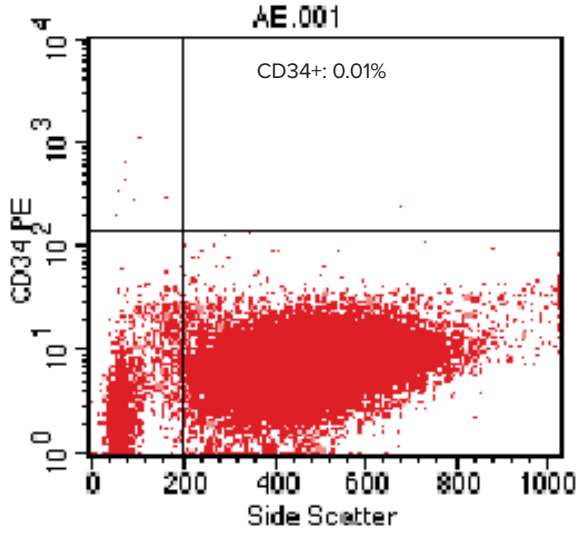

FIGURE 1. The flow cytometric examination of CD34+ colony before the plerixafor administration

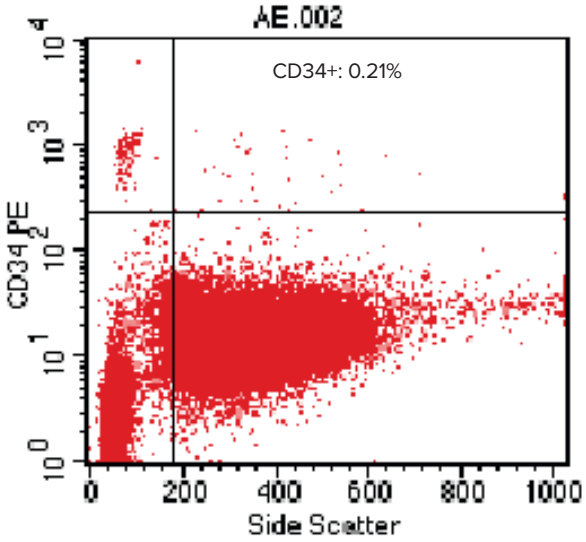

FIGURE 2. The flow cytometric examination of CD34+ colony after the plerixafor administration

patients became eligible for proceeding with the autotransplantation (Table 1).

All patients presented in this study were heavily pretreated (chemo- ± radiotherapy) for the underlying disease, and all of them had residual disease at the time of mobilization.

We present the increase in the number of CD34+ cells counted by flow cytometry after combined increased dose mobilization (Figure 1, Figure 2).

DISCUSSION

This particular mobilization technique can increase the number of stem cells in order to perform an autologous transplantation.[7] It is very important to perform autologous transplantation in this group of diseases (myeloma, lymphomas).

In multiple myeloma, autologous transplantation is included in the standard treatment for consolidation, with the indication of double autologous transplantation in case of relapse after the first transplant.[8]

In lymphomas, the transplantation needs to be performed in case of diseases relapse or in case of residual disease after chemotherapy.

Autologous transplantation is a relatively well tolerated treatment method that leads to a prolonged plateau phase in myeloma and has a curative role in lymphomas.

Autologous transplantation is preferred in this group of diseases because allotransplants have a relatively high transplant-related mortality (TRM), the graft-versus-myeloma and graft-versus-lymphoma effect is delayed, severe infectious complications may occur in the phase of aplasia, and there is a quite high incidence of acute and especially chronic graft-versus-host disease.[9,10]

CONCLUSION

We observed that mobilization with the combined treatment of growth factors and increased dose of filgrastim (15 μg/kg) + monodose of plerixafor (0.24 mg/kg) is possible, and it leads to obtaining a minimally sufficient number of stem cells in order to perform autologous transplantation. This type of mobilization is safe, well tolerated by the patients, and is also cost efficient, decreasing the rate of apheresis procedures and also the necessity of allogeneic stem cell transplantations in myeloma and lymphoma cases.

CONFLICT OF INTEREST

Nothing to declare.

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