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Pharmacoeconomic impact of up-front use of plerixafor for autologous stem cell mobilization in patients with multiple myeloma

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Abstract

Background aims. Stem cell collection can be a major component of overall cost of autologous stem cell transplantation (ASCT). Plerixafor is an effective agent for mobilization; however, it is often reserved for salvage therapy because of its high cost. We present data on the pharmacoeconomic impact of the use of plerixafor as an up-front mobilization in patients with multiple myeloma (MM). *Methods.* Patients with MM who underwent ASCT between January 2008 and April 2011 at the Mount Sinai Medical Center were reviewed retrospectively. In April 2010, practice changes were instituted for patients with MM to delay initiation of granulocyte-colony-stimulating factor (G-CSF) support from day 0 to day +5 and to add plerixafor to G-CSF as an up-front autologous mobilization. Targets of collection were $5–10 \times 10^6$ $CD34^+$ cells/kg. *Results.* Of 50 adults with MM who underwent ASCT, 25 received plerixafor/filgrastim and 25 received G-CSF alone as an up-front mobilization. Compared with the control, plerixafor mobilization yielded higher $CD34^+$ cell content (16.1 versus 8.4×10^6 $CD34^+$ cells/kg; $P = 0.0007$) and required fewer sessions of apheresis (1.9 versus 3.1; $P = 0.0001$). In the plerixafor group, the mean number of plerixafor doses required per patient was 1.8. Although the overall cost of medications was higher in the plerixafor group, the cost for blood products and overall cost of hospitalization were similar between the two groups. *Conclusions.* Up-front use of plerixafor is an effective mobilization strategy in patients with MM and does not have a substantial pharmacoeconomic impact in overall cost of hospitalization combined with the apheresis procedure.

Key Words: *autologous stem cell transplantation, mobilization, multiple myeloma, plerixafor, stem cell collection*

Introduction

Autologous stem cell transplantation (ASCT) is an effective treatment for multiple myeloma (MM) [1,2]. The most commonly used up-front mobilizing agent for autologous stem cell collection is granulocyte-colony-stimulating factor (G-CSF), which is associated with approximately 25% of unsuccessful mobilization [3,4]. Strong predictors for poor mobilization include advanced age, bone marrow (BM) failure, extensive prior chemotherapy treatment and previous treatment with lenalidomide or alkylating agents. Another common mobilization strategy is to combine chemotherapy, such as cyclophosphamide, with G-CSF [5,6]. This approach is associated with an unpredictable stem cell yield and, in some patients, neutropenic fever requiring hospitalization [7]. Mobilization of stem cells is induced through the interaction between stem cells and cells of the BM microenvironment. The binding of stromal cell–derived factor 1 (SDF-1), a chemokine expressed in BM stromal cells, to CXCR-4 plays a major role in regulating trafficking and retaining hematopoietic stem cells (HSC) in the BM [8]; however, the predominant source of SDF-1 (ie, osteoblasts, reticular cells in endosteal and vascular niches, endothelial cells and bones) is not clearly understood [9]. G-CSF promotes HSC mobilization by altering the BM niche; it downregulates osteoblast SDF-1 by altering the signaling of sympathetic nervous system to osteoblast, thereby attenuating CXCR signaling [10–12]. Plerixafor promotes HSC mobilization by reversibly blocking the binding of SDF-1 to its receptor, CXCR-4. Concurrent administration of plerixafor and G-CSF was shown to exert a synergistic effect on the mobilization of $CD34^+$ progenitor cells [13]. Plerixafor, in combination with G-CSF, was granted US Food and Drug Administration approval in 2008. Its approval was based on the improved rate of successful mobilization when used up-front for ASCT in patients with

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non-Hodgkin's lymphoma and multiple myeloma (MM). Because of its high cost, plerixafor is often reserved for patients who failed previous standard mobilization [14–16]. The use of plerixafor as a salvage mobilization strategy can increase the number of apheresis sessions required to achieve an adequate peripheral blood stem cell (PBSC) collection and potentially impose delays on the timing of ASCT, especially for patients with MM who often require sufficient $CD34^+$ cells for two ASCTs.

In the present study, we evaluated 50 patients with MM who were mobilized up-front with G-CSF with or without plerixafor. The purpose of this study was to assess the pharmacoeconomic impact of the addition of plerixafor to G-CSF as an up-front autologous mobilization regimen for patients with MM.

Methods

Study design

We performed a retrospective analysis to assess economic and clinical outcomes of 50 adult patients with MM who received ASCT between January 2008 and April 2011 at The Mount Sinai Medical Center, New York, New York. In the control group, 25 consecutive patients received single-agent G-CSF as a mobilizing agent and started G-CSF support from day 0 after PBSC infusion. In the plerixafor group, 25 consecutive patients received plerixafor in combination with G-CSF, as an up-front mobilization therapy, and started G-CSF support from day +5 after PBSC infusion.

Method for mobilization

Before April 2010, G-CSF was used as an up-front mobilizing agent as 10 μg/kg per day subcutaneously for 5 days in patients with MM scheduled to undergo ASCT. Starting in April 2010, plerixafor was added to G-CSF as an up-front mobilization strategy in patients with MM. Plerixafor was administered as 0.24 mg/kg per day subcutaneously in the evening (approximately 6–7 PM) for up to 4 days, starting on the fourth day of G-CSF. The dose of plerixafor was capped at 40 mg/d. In patients with renal insufficiency (defined as creatinine clearance $\leq$50 mL/min), the dose of plerixafor was reduced to 0.16 mg/kg per day, not exceeding 27 mg/d. Peripheral $CD34^+$ cells were not routinely measured in these patients before apheresis. Minimum and optimal collection cell targets were 5×10^6 and 10×10^6 $CD34^+$ cells/kg, respectively. If the yielded $CD34^+$ stem cell content was $>5 \times 10^6$/kg, half of the content of the collection was infused during the ASCT. Melphalan was administered intravenously at a target dosage of 200 mg/m^2 and with dose adjustment on the basis of renal function.

Method for growth factor support after ASCT

Before April 2010, G-CSF was administered as 5 μg/kg per day intravenously, starting on day 0 after PBSC infusion and until engraftment. Starting in April 2010, the initiation of G-CSF was delayed from day 0 to day +5 after PBSC infusion.

Data collection

By use of the pharmacy database, patients with MM who underwent ASCT were identified, and data collection was performed with the use of patients' electronic medical records. Data collection included patients' baseline characteristics, total $CD34^+$ cells collected, total $CD34^+$ cells infused, number of doses of G-CSF and plerixafor administered for mobilization, number of apheresis sessions, number of doses of G-CSF required for engraftment, time to engraftment, length of hospital stay from day 0 and cost analysis for the two groups.

Engraftment criteria

Center for International Blood and Marrow Transplant Research criteria were used to define engraftment. Neutrophil engraftment is defined as an absolute neutrophil count $\geq 0.5 \times 10^9$ cells/L for 3 consecutive days after HSC transplantation. Platelet engraftment is defined as a platelet count $\geq 20 \times 10^9$ cells/L for 3 consecutive days after HSC transplantation and without platelet transfusion support for the preceding 7 days.

Pharmacoeconomic analysis

All costs related to hospitalization were captured by our institution's cost accounting system. Average wholesale price was used to calculate the outpatient cost of plerixafor ($8073 per 24-mg vial) and G-CSF ($298 per 300-μg dose) required for mobilization. Expenditure for apheresis procedure was $3200 per session.

Statistical analysis

The Student's *t*-test was used to compare significance of difference between the two groups, and the two-tailed Fisher's exact test was used to compare frequencies of incidence between the two groups. A value of $P < 0.05$ was considered of statistical significance.

Results

Baseline characteristics

A total of 50 patients with MM who underwent ASCT between January 2008 and April 2011 were