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Short Communication

Autologous Stem Cell Harvest and Transplantation for Hematological Malignancies: Significance of Plerixafor

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ABSTRACT

Autologous Stem Cell Transplantation (ASCT) is one of the most effective treatment strategies for hematological malignancies. Before ASCT, hematopoietic stem cells must be stimulated to move from the bone marrow to the peripheral blood for harvesting. Plerixafor is used to increase stem cell harvests. No physicians have questions about the power of plerixafor for promoting more efficient harvest. Many studies have examined the optimal strategies for hematopoietic stem cell mobilization, and the clinical criteria for using plerixafor have gradually been elucidated. However, the effects of plerixafor on post-ASCT outcomes remain unclear. Thus, using a dual-center, retrospective, cohort study of 43 adult patients who received ASCT, we compared transplantation outcomes in patients who underwent stem cell mobilization with granulocyte colony-stimulating factor with or without plerixafor. The number of days to neutrophil and platelet engraftment was significantly shorter with plerixafor than without plerixafor, as assessed by univariate, subgroup, and propensity score matching and inverse probability weighting analyses. Although the cumulative incidence of fever was comparable with or without plerixafor that of sepsis was significantly lower with plerixafor than without. Therefore, we concluded that plerixafor leads to earlier neutrophil and platelet engraftment and a reduction of infectious risk.

Keywords: Autologous stem cell transplantation; Hematological malignancy; Plerixafor

DESCRIPTION

Autologous Stem Cell Transplantation (ASCT) is powerful means of treating multiple myeloma and non-Hodgkin lymphoma [1,2]. However, the peripheral blood contains only a small number of Hematopoietic Stem Cells (HSCs), meaning that HSCs must be stimulated to move from bone marrow to the peripheral blood before harvesting [3]. The conventional means of mobilizing HSCs is by administration of Granulocyte Colony-Stimulating Factor (G-CSF) either alone or in combination with chemotherapy [4]. However, it is sometimes difficult to harvest sufficient HSCs, particularly in patients who have received many lines of therapy [5]. Plerixafor is a C-X-C Chemokine Receptor type 4 (CXCR4) antagonists that promotes release of HSCs from the bone marrow to the peripheral blood by blocking the connection between HSCs and the bone marrow niche [6]. No physicians have questions about the power of plerixafor for promoting more efficient harvest. Many studies have examined the optimal strategies for hematopoietic stem cell mobilization, and the clinical criteria for using plerixafor have gradually been elucidated [7]. However, some physicians feel that plerixafor increases the risk of contamination of the apheresis product by malignant cells [8]. Recently, several studies have shown that plerixafor has positive effects on post-ASCT outcomes; however, further examinations are needed [9,10].

Thus, we performed a dual-center retrospective cohort study to evaluate the effect of plerixafor on post-ASCT outcomes in Japanese patients with hematological malignancies [11]. We compared transplantation outcomes in patients who underwent stem cell mobilization with G-CSF with (n=25) or without (n=18) plerixafor. The number of days to neutrophil and platelet engraftment was significantly shorter with plerixafor than without plerixafor, as assessed by univariate (neutrophil, P=0.004,

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platelet, P=0.002), subgroup, propensity score matching and inverse probability weighting analyses. Although the cumulative incidence of fever was comparable with or without plerixafor (P=0.31), that of sepsis was significantly lower with plerixafor than without (P<0.01). Thus, the present data indicate that plerixafor leads to earlier neutrophil and platelet engraftment and a reduction of infectious risk.

Expression of CXCR4, the target receptor of plerixafor, has been identified in many malignancies-not only solid cancers, such as breast cancer, ovarian cancer, and melanoma, but also several hematological malignancies, such as diffuse large B-cell lymphoma, follicular lymphoma, and multiple myeloma [12-14]. In addition, CXCR4 has been implicated in the migration and trafficking of malignant B cells [15]. It is reported that overexpression of CXCR4 is closely related to distal metastasis and poor prognosis [16]. Moreno, et al. reported that administration of a CXCR4 antagonist suppressed proliferation of diffuse large B-cell lymphoma cells in a xenograft mouse model [17]. However, it has also been suggested that the risk of relapse is increased in multiple myeloma because multiple myeloma cells express CXCR4 and plerixafor leads to residual malignant cells being released from the bone marrow niche. Future studies are needed to clarify the true effects on ASCT outcome.

There are various stages of maturation in HSCs. It is reported that immature HSCs (i.e., long-term HSCs) have higher and more prolonged proliferative and pluripotent activity [18]. Relatively a lot of long-term HSCs are included in cord blood [19]. Immunological fever (pre-engraftment syndrome) is often observed in cord blood transplantation. We hypothesize that plerixafor may mobilize higher-quality HSCs, like long-term HSCs, for harvest compared with mobilization without plerixafor. In our study, non-infectious fever was often observed in the patients harvested with plerixafor. This is consistent with a report made at the 45th Annual Meeting of the European Society for Blood and Marrow Transplantation [20].

CONCLUSION

The fact that risk of non-infectious fever increases has in common in ASCT cases harvested with plerixafor and in cord blood transplantation case. We think this supports our hypothesis that plerixafor may mobilize long-term HSCs. Future studies about difference of maturity and quality of HSCs harvested with or without plerixafor both *in vitro* and *in vivo* are needed.

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