The Influence of Luspatercept on Bone Marrow Mesenchymal Stromal Cells in Allogeneic Hematopoietic Stem Cell Transplantation for Patients With Myelodysplastic Neoplasms and Acute Myeloid Leukemia

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INTRODUCTION

Problems related to poor graft function are linked to the altered mesenchymal stromal cells (MSCs). The drug luspatercept has demonstrated efficacy for anemia treatment in patients with MDS, affecting also the ability of MSCs to support normal hematopoiesis. It is assumed that these effects could be translated to the post-transplant period.

AIM

To demonstrate the established [1] effect of luspatercept on MSCs in HSCT setting.

METHOD

The study included 23 adult patients with established diagnoses of AML or MDS. The median age was 52 years. MSCs were isolated from patients' bone marrow at two time points: before HSCT (median 17 days) and after HSCT (median 57 days). At both time points MSCs were cultured in duplicate: an experimental sample with luspatercept and a control sample without luspatercept. Quantitative PCR was performed to assess the expression levels of the genes ITGB1, KITLG, CDH2, VCAM1, THPO, and CXCL12.

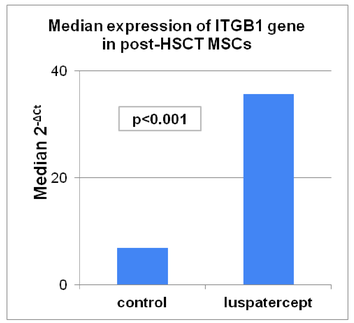
CONCLUSIONS

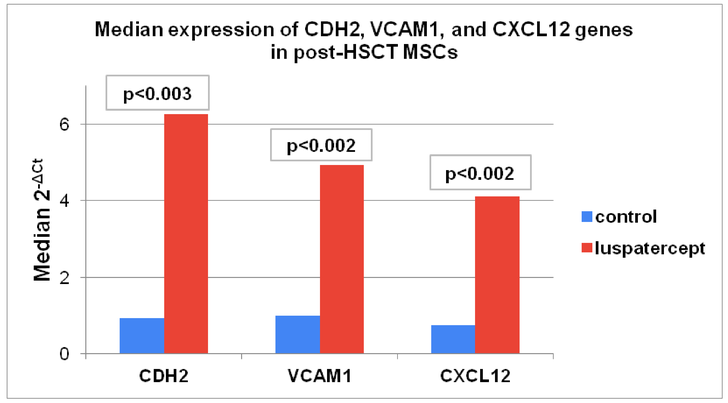
The obtained in vitro data indicate the ability of luspatercept to enhance the expression of genes responsible for hematopoietic support in bone marrow MSCs of patients with MDS and AML. Further studies are needed to confirm these results and determine the clinical significance of luspatercept use after HSCT.

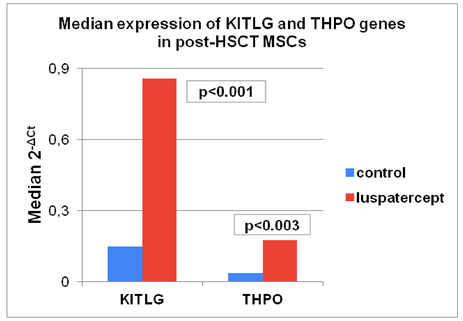
RESULTS

When comparing gene expression levels before HSCT, an increase in the expression of ITGB1 (p<0.02), KITLG (p<0.02), VCAM1 (p<0.03), and CXCL12 (p<0.007) genes was revealed in the luspatercept group compared to the control. When comparing gene expression levels after HSCT, an increase in the expression of ITGB1 (p<0.001), KITLG (p<0.001), CDH2 (p<0.003), VCAM1 (p<0.002), THPO (p<0.003), and CXCL12 (p<0.002) genes was found in the luspatercept group compared to the control. No significant correlation was found between the expression of the studied genes and the time to blood count recovery or the number of transfusions after HSCT. No cases of graft failure were observed, and the incidence of severe poor graft function (the need for red blood cell and/or platelet transfusions after engraftment) was 61% (38-77) at 1 year after HSCT. In univariate proportional hazard model we found no significant association between gene expression levels and overall or progression-free survival.

Median gene expression levels after HSCT







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REFERENCES

1 **Wobus M et al.** Luspatercept restores SDF-1-mediated hematopoietic support by MDS-derived mesenchymal stromal cells. *Leukemia*. *2021;35(10):2936-2947*