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Dramatically Decreased Transfusion Dependency With Luspatercept in a Case of High-Risk MDS

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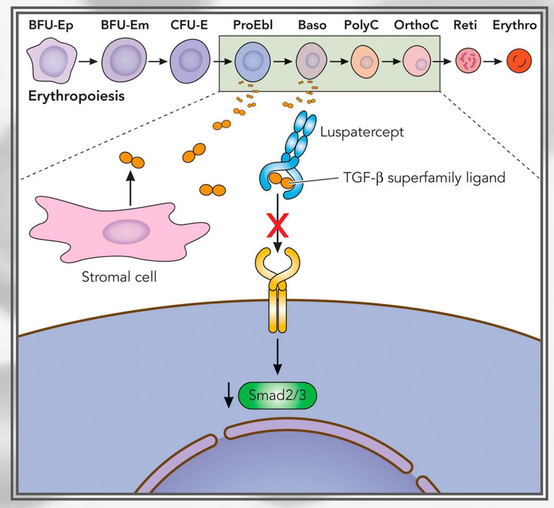
INTRODUCTION

- Myelodysplastic syndrome (MDS) patients require frequent red blood cell (RBC) transfusions due to defective erythrocyte maturation.
- Luspatercept has shown to reduce transfusion-dependence in low- to intermediate-risk MDS.
- We present a case of high-risk MDS where frequency of RBC transfusions reduced from weekly to monthly after initiating luspatercept.

CASE

81 yr old man diagnosed with High-Risk MDS in July 2018

- BM biopsy: multilineage myelodysplasia with myelofibrosis.
- JAK2 V617F mutation positive. SF3B1 not tested.
- Initiated on Darbepoetin alpha but the disease progressed. Also, EPO levels were high.
- Received 10 cycles of azacitidine from February to October 2019.
- Repeat BM biopsy showed persistent MDS with myelofibrosis and he was switched to ruxolitinib.
- Tolerated ruxolitinib well but required weekly to bi-monthly blood transfusions.
- Luspatercept started at 1 mg/kg in April 2023. Eventually increased to 1.33 mg/kg.
- Transfusion frequency decreased to every 1 to 1.5 months, improving his quality of life.

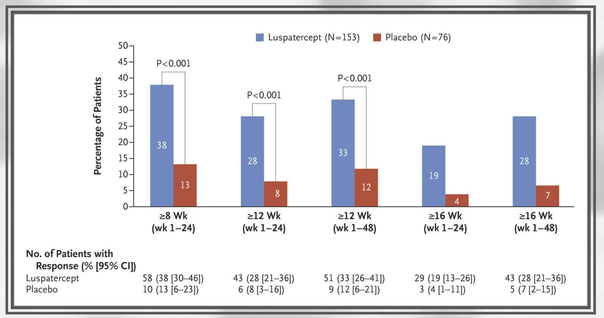


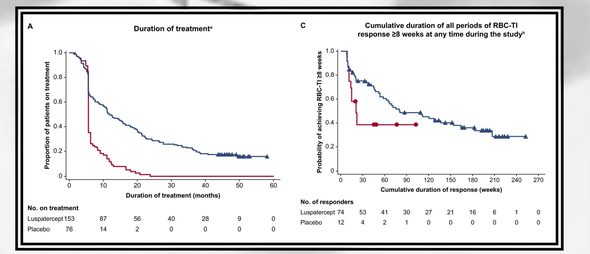
LUSPATERCEPT

- Ineffective erythropoiesis in MDS has been associated with excessive transforming growth factor β, (TGF-β) signaling pathway activation, leading to increased downstream SMAD2 and SMAD3 signaling.
- Luspatercept is a novel activin receptor type IIB fusion ligand trap agent, which neutralizes the TGF-β superfamily ligands before binding to the receptor, thus improving hematopoiesis.

DISCUSSION

- 2023 MEDALIST study: RBC transfusion independence after ≥8 weeks with luspatercept in patients with low- to intermediate-risk MDS who had ring sideroblasts and could not receive or did not respond to erythropoiesis-stimulating agents (ESA).
- Primary endpoint responders also experienced continued benefit over 24 months as well as multiple separate RBC TI ≥ 8 weeks response periods on long term follow up.
- COMMAND trial: Superiority of luspatercept in RBC transfusion dependence compared to erythropoietin alpha in ESA-naive patients with low-risk MDS with or without ringed sideroblasts.





CONCLUSION

Patients with high-risk MDS should also be evaluated for this novel drug, and further trials can be done to evaluate for efficacy and quality-of-life improvement in this patient population.

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