



Efficacy and Safety of Luspatercept in patients with anemia: A Systematic Review

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Background

Luspatercept is an erythroid maturation agent that has been shown to improve anemia by influencing late onset erythropoiesis.

Design

Systematic Review

Methods

A literature search was performed on PubMed, Embase, clinicaltrials.gov, Web of Science and Cochrane using mesh terms “anemia” and “Immunoglobulin fc fragments”, from the inception of literature till 4/20/2021. After screening 420 articles, 2 randomized clinical trials (RCT, N=565), and 2 phase II trials (N=122) were included.

Objective

To determine safety and efficacy of luspatercept in patients aged > 18 years of age and diagnosed with either Myelodysplastic syndrome or Beta-Thalassemia.

Results

Table 1: Baseline Characteristics of luspatercept in patients with anemia

Author	Study Type/ Year	Number of Pt.	BASELINE CHARACTERISTICS						
			Median age in yrs. (range)	Type of Anemia	Time since diagnosis	Median pre-transfusi on HB level	Median red cell transfusion burden	Iron chelation %	Median Follow up time
M.D. Cappellini	Phase 3CT/2020	224	30	Beta-Thal		9.3g/dl	14 rbc units/24 weeks	99.6%	48 weeks
A. Piga	Phase 2CT/2019	64	38.5	Beta-Thal		9-10g/dl	8.0 rbc unit/12 weeks	100%	NA
U.Platzbecker	Phase 2CT/2017	LD-L (0.125-0.5mg/kg) N=9	72	MDS	4.6 yrs.	8.7g/dl	8 rbc units/8weeks	67%	6.8 months
		HD-L (0.75-1.75mg/kg) N=49	71		2.3 yrs.		6 rbc units/8weeks	41%	
P. Fenaux	Phase 3CT/2020	153	71	MDS	3.7 yrs.	7.6g/dl	5 rbc units/8weeks	71%	48 weeks

Table 2: Subcutaneous luspatercept (0.125mg/dl to 1.75 mg/dl) administered every 21 days for at least 48 weeks or 5 cycles to treat anemia in beta-thalassemia (N=288) and MDS (N=211) patients

4 Clinical Trials- (N=687)	MDS	Beta-thalassemia
Median Pre-transfusion Hemoglobin	7.6g/dl	10g/dl
Median Red Cell Transfusion	14 RBC units/24 weeks	8 RBC/8 weeks

33% Reduction in RBC Transfusion Burden

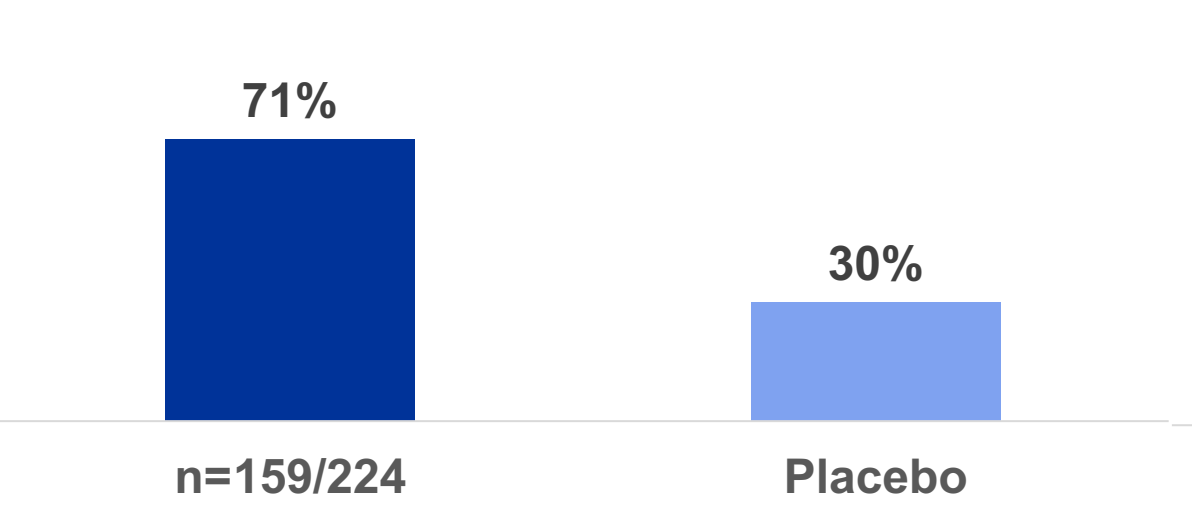


Fig. 1: Cappellini et al. (N=224), Beta-thalassemia Patients

20% Reduction in RBC Transfusion Burden



Fig. 2: Piga et al. (N=64), Beta-thalassemia Patients

>4 RBC Unit Reduction/8 Weeks

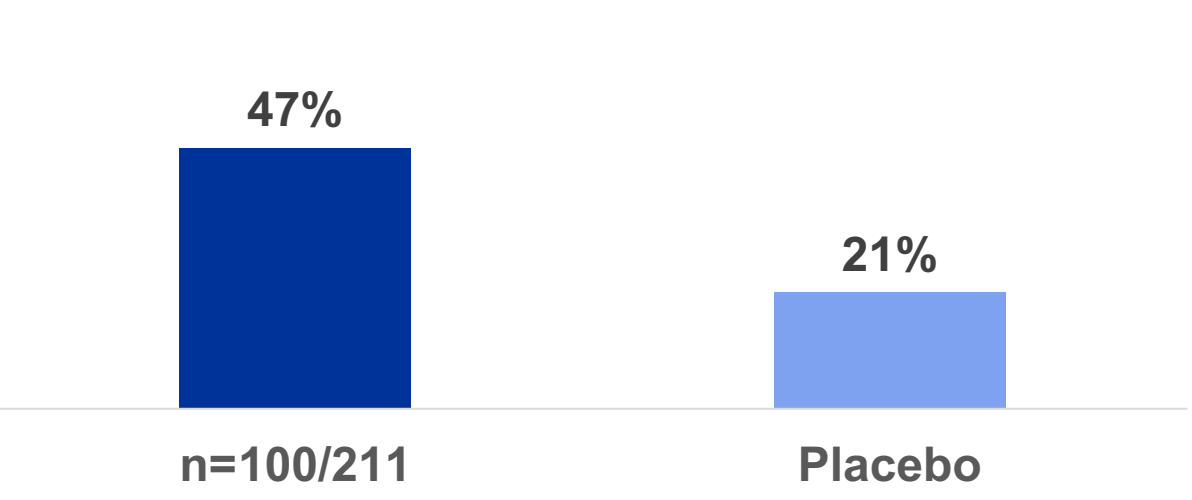


Fig. 3: Platzbecker et al. and Fenaux et al. (N=287), MDS patients treated with luspatercept

Mean Increase in Hb



Fig. 4: High dose receiving patients

Common Side Effects

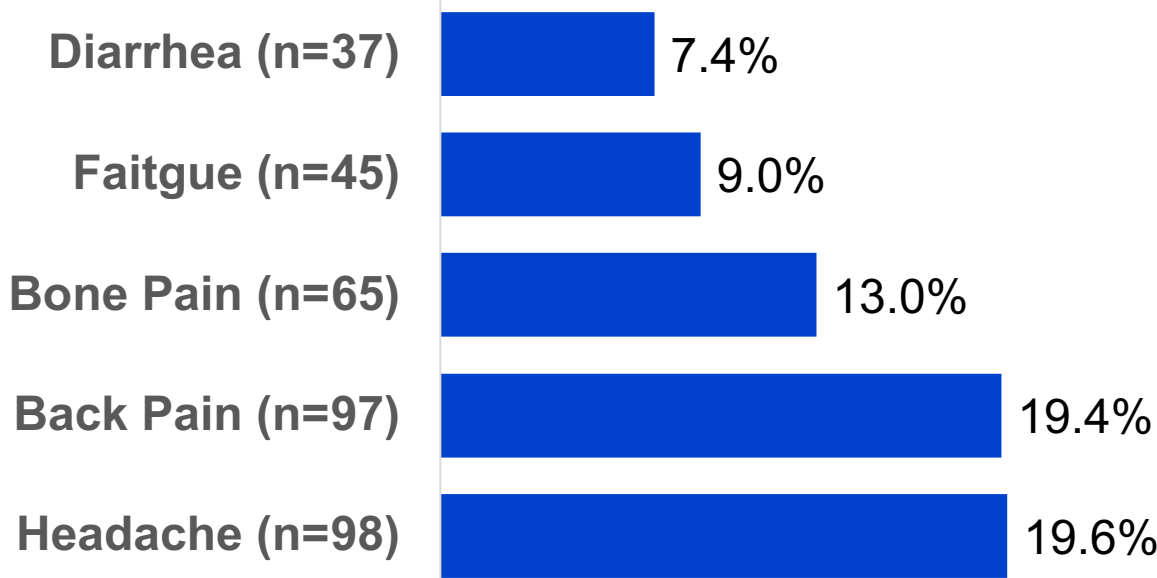


Fig. 5: Common Side Effects

Grade 3 Adverse Effects

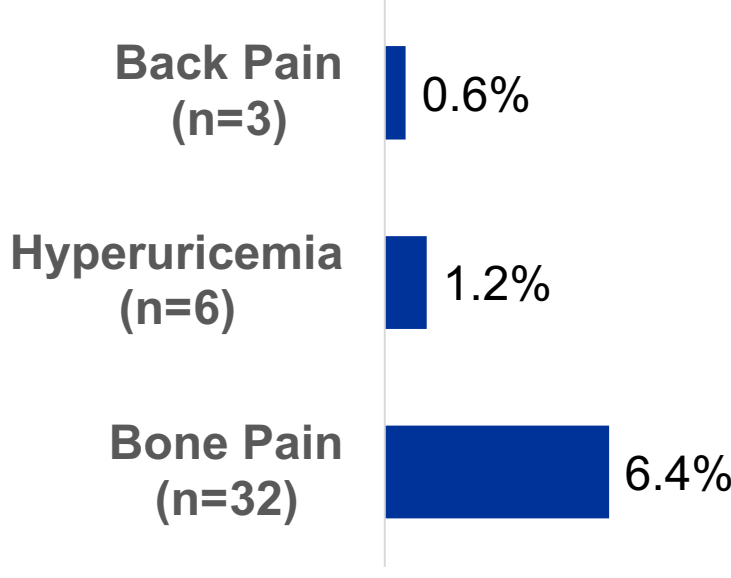


Fig. 6: Grade 3 Adverse Effects

Discussion

Based on the systematic review, we have shown luspatercept to have good response to increase in hemoglobin with tolerable side effects. It has reduced the need for transfusion in these patients which has greater risk of severe adverse effects. There was >33% reduction in RBC transfusion burden in 71% (n=159/224) of the patients (vs. 29.5% with placebo) and >20% reduction in 80%(n=51/64) of the patients with beta-thalassemia. There was >4 RBC unit reduction/8 weeks in 47%(n=100/211) of the patients with MDS treated with luspatercept (vs. 21% with placebo). High dose receiving patients had a mean increase in Hb in the range of 0.36g/dl to 1.52g/dl. Serious side effects were bone pains, hyperuricemia, and back pain.

Summary

- Luspatercept showed better efficacy than placebo in beta-thalassemia or MDS patients to treat anemia and was well tolerated by these patients
- High dose luspatercept has shown promising results in terms of erythroid response measured as either reduction in transfusion burden or mean increase in hemoglobin levels
- Number of clinical trials are ongoing to assess its efficacy in myelofibrotic disorders to further extend its usage
- This drug has a great potential to limit the need for transfusion in diseases dependent on transfusion to increase hemoglobin

References

1. Luspatercept improves hemoglobin levels and blood transfusion requirements in a study of patients with β -thalassemia, *Blood* (2019)
2. A Phase 3 Trial of Luspatercept in Patients with Transfusion-Dependent β -Thalassemia, *The New England Journal of Medicine*
3. Luspatercept in Patients with Lower-Risk Myelodysplastic Syndromes, *The New England Journal of Medicine*
4. Luspatercept for the treatment of anemia in patients with lower-risk myelodysplastic syndromes (PACE-MDS): a multicenter, open-label phase 2 dose-finding study with long-term extension study, *The Lancet Oncology*