(Gly60Arg)), classified as likely pathogenic. **Discussion:** The *RAP1B* gene (OMIM: 179530) is associated with the clinical phenotype of syndromic constitutional thrombocytopenia. Currently, only a few genotype-phenotype associations have been described in the literature. The previously reported variants include c.35G>T (p.Gly12Val), c.176C>G (p.Ala59Gly), c.178G>C (p.Gly60Arg), c.35G>A (p.Gly12Glu), and c.178G>A (p.Gly60Arg). RAP1B is a member of the RAS superfamily of small GTPases involved in many cellular processes. Previous studies have shown a link between RAP1B activation and platelet function in humans and mice. Our case report shares the common phenotype of thrombocytopenia (HP: 0001873), suggesting the clinical relevance of this phenotype to variants in this region of the *RAP1B* gene. Notably, 4 out of 5 (80%) described variants in public genomic databases are located in exon 4, indicating that this exon may be particularly relevant to the clinical condition. **Conclusion:** Our data support that the *RAP1B* variant detected in our patient may contribute to the phenotype through dysregulation of the MEK/ERK pathway. The effects of variants in *RAP1B* explain the divergent phenotypes observed among patients. Nonetheless, further studies are required to understand better the correlation between genotype and phenotype.

https://doi.org/10.1016/j.htct.2024.09.751

LONG-TERM EFFECTIVENESS AND SAFETY OF LUSPATERCEPT FOR ANEMIA TREATMENT IN PATIENTS WITH LOWER-RISK MYELODYSPLASTIC SYNDROMES: A SYSTEMATIC REVIEW AND META-ANALYSIS

DVS Cavalcante [a], IQC Neto [b], IO Môro [c], RGO Galvão [d], JF Abreu [e], AM Cavalcante [f], MCFLC Freitas [g], V Lopes [h], BX Mendes [i], FD Xavier [g]

[a] *Universidade Federal do Maranhão (UFMA), São Luís, Brazil*
[b] *Universidade Católica de Pernambuco (UNICAP), Recife, Brazil*
[c] *Escola Superior de Ciências da Santa Casa de Misericórdia de Vitória, Vitória, Brazil*
[d] *Escola Superior de Ciências da Saúde (ESCS), Brasília, Brazil*
[e] *Fundación Hector Alejandro Barceló, Buenos Aires, Argentina*
[f] *Universidade Cidade de São Paulo (UNICID), São Paulo, Brazil*
[g] *Universidade de Brasília (UnB), Brasília, Brazil*
[h] *Universidade Federal do Amazonas (UFAM), Manaus, Brazil*
[i] *Faculdade CHRISTUS, Fortaleza, Brazil*

Introduction: Erythropoiesis-stimulating agents (ESA) are the primary treatment for anemia in most patients with low to moderate-risk myelodysplastic syndromes. However, in some patients, ESA therapy is not effective, and emerging evidence suggests that Luspatercept may offer longstanding benefits in these patients. **Objective:** This study evaluated the long-term effectiveness and safety of luspatercept in treating anemia in patients with low-risk syndrome (MDS). It focused on achieving at least eight weeks of red blood cell transfusion independence and examined hematologic responses, particularly in relation to erythroid ring sideroblasts. **Methods:** We searched MEDLINE, Embase, and Cochrane databases for Clinical trials (CT) that assessed events of effectiveness and safety with the use of Luspatercept in patients with Low-risk Myelodysplastic Syndrome from inception to July 2024. Following the PRISMA protocol, 688 articles were screened. The primary endpoints focused on red blood cell transfusion independence for at least 8, as well as hematologic response-erythroid. Adverse events such as bone pain were also pooled and analyzed. We calculated event prevalence for binary outcomes, along with 95% confidence intervals (CI). A random-effects model was used for all outcomes, and heterogeneity was assessed with I2 statistics. **Results:** After duplicate removal and exclusion by title and abstract, 12 studies were thoroughly read, and 5 articles referring to 3 CT, encompassing 393 patients treated with luspatercept that were enrolled and evaluated in this meta-analysis. All the groups had similar demographics and clinical factors. The mean age was 72.5 years, 273 (62.2%) were male and 196 (44.65%) were previously treated with real-world erythropoiesis-stimulating agents (ESA). Among all patients, SF3B1 mutations were detected in 296 (47.28%) patients, while 330 (52.72%) were positive for ring sideroblasts. Luspatercept was associated with a proportion of hematologic response-positive erythroid ring sideroblasts, accounting for 68.13% (95% CI 56.74 to 79.52; $p < 0.01$; $I^2 = 82\%$). In addition, the proportion of patients who were independent of red cell transfusion for at least 8 weeks was 48.17% (95% CI 42.56 to 53.79; $p = 0.55$; $I^2 = 0\%$). In patients with SF3B1 mutations, the proportion of hematologic response-positive erythroid was 48.73% (95% CI 42.32 to 55.14; $p < 0.43$; $I^2 = 0\%$), and the proportion of patients who were independent of red-cell transfusion for at least 8 weeks was also 48.73% (95% CI 42.32 to 55.14; $p = 0.43$; $I^2 = 0\%$). The proportion of bone pain was 3.87% (95% CI 1.56 to 9.28; $p < 0.09$; $I^2 = 58\%$) among all patients. **Discussion:** This meta-analysis identified a significant link between luspatercept use and a positive hematologic response in erythroid ring sideroblasts, indicating notable anemia improvement in many patients. Nearly half achieved at least 8 weeks of red blood cell transfusion independence, demonstrating significant clinical benefit. Among patients with SF3B1 mutations, the hematologic response rate was slightly lower but matched the transfusion independence rate, indicating consistent efficacy across this genetic subgroup. The study also noted a low incidence of bone pain, a common adverse effect in many hematologic treatments. This low incidence, combined with the efficacy data, suggests a favorable safety profile for luspatercept. **Conclusion:** Luspatercept seems to be associated with improved hematological parameters while having a small prevalence of adverse outcomes. However, more clinical trials are necessary to completely assess its use in the long term and in comparison with other interventions.

https://doi.org/10.1016/j.htct.2024.09.752