Reblozyl®

(luspatercept-aamt)

for injection 25mg • 75mg

Based on the **head-to-head** trial vs epoetin alfa,

REBLOZYL redefines first-line treatment for patients with LR-MDS[1]

Superior Efficacy

NEARLY

2X

more patients

58.5%* of patients achieved RBC-TI and Hgb increase vs epoetin alfa (31.2%† of patients)[1]

Lasting Durability

APPROX.

2.5 years (126.6 weeks)‡

median duration of TI ≥12 weeks, 1.5 years (77.0 weeks) with epoetin alfa§

Analysis limitations: Duration of RBC-TI ≥12 weeks was not powered to detect statistical significance.

Dosing Convenience‖

EVERY

3

weeks¶

subcutaneous administration vs QW for epoetin alfa[1]

QW=once a week; TI=transfusion independence.

*n=86/147; 95% CI: 50.1, 66.6. †n=48/154; 95% CI: 24.0, 39.1. ‡108.3, NR; n=98. §39.0, NR; n=71.

‖See complete REBLOZYL dosing in the accompanying full Prescribing Information.

¶Timing of administration may be impacted by dose modifications (eg, AEs, rapid Hgb rise).

INDICATION

REBLOZYL (luspatercept-aamt) is indicated for the treatment of anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular red blood cell (RBC) transfusions.

REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) of REBLOZYL-treated patients. TEEs included deep vein thrombosis, pulmonary embolus, portal vein thrombosis, and ischemic stroke. Patients with known risk factors for thromboembolism (splenectomy or concomitant use of hormone replacement therapy) may be at further increased risk of thromboembolic conditions. Consider thromboprophylaxis in patients at increased risk of TEE. Monitor patients for signs and symptoms of thromboembolic events and institute treatment promptly

Please see additional Important Safety Information throughout and full Prescribing Information for REBLOZYL.

REBLOZYL is the only agent to be studied head-to-head against an ESA for MDS-associated anemia[1-3]

COMMANDS: A Phase 3 open-label, randomized, active-controlled trial of REBLOZYL vs epoetin alfa in anemia due to LR-MDS for ESA-naive patients

Patient Population (N=356)[1-3]

- Adults ≥18 years of age
- IPSS-R very low-, low- or intermediate-risk MDS
- **RS-Positive and RS-Negative**
- **ESA-naive**
- Endogenous sEPO <500 U/L
- Requiring RBC transfusions for Hgb ≤9 g/dL with symptoms or Hgb ≤7 g/dL without symptoms and 2 to 6 units of RBCs within 8 weeks prior to randomization
- Excluded: patients with del(5q) and those previously treated with disease-modifying agents or HMAs

Randomized 1:1

REBLOZYL[1]
1 mg/kg **SC Q3W**, with titration up to max 1.75 mg/kg if needed to achieve response (n=178)

Epoetin Alfa[2*]
450 IU/kg SC QW max total dose 40K IU, with titration up if needed to 1050 IU/kg max total dose 80K IU (n=178)

All patients received BSC, which included RBC transfusions as needed

Composite primary endpoint[1]

For any consecutive **12-week** period during Weeks 1 to 24:

- **RBC-TI**

  AND
- Mean improvement in **Hgb by at least 1.5 g/dL**

Key secondary endpoints[1]

- HI-E response per IWG ≥8 weeks (Weeks 1-24)
- RBC-TI for 24 weeks (Weeks 1-24)
- RBC-TI for ≥12 weeks (Weeks 1-24)

Other secondary endpoints[1,2]

- Hgb increase ≥1.5 g/dL (Weeks 1-24)
- **Duration of RBC-TI ≥12 weeks (Weeks 1-EOT)**
- Time to first RBC transfusion (Weeks 1-EOT)
- Hgb change from baseline over 24 weeks (Weeks 1-24)

*>90% of study participants were outside of the United States and used a non-US-licensed epoetin alfa product. Direct comparisons between REBLOZYL and US-licensed epoetin alfa have not been established.

Interim analysis of COMMANDS reported.

BSC=best supportive care; EOT=end of treatment; HI-E=hematologic improvement-erythroid; HMA=hypomethylating agent; IPSS-R=Revised International Prognostic Scoring System; IWG=International Working Group; LR-MDS=lower-risk myelodysplastic syndromes; QW=once a week; Q3W=every 3 weeks; RBC=red blood cell; SC=subcutaneous; sEPO=serum erythropoietin.

The efficacy of REBLOZYL in ESA-naive adult patients with MDS was established at the time of the interim efficacy analysis based upon the proportion of patients who experienced RBC-TI with an associated mean improvement in hemoglobin by at least 1.5 g/dL for any consecutive 12-week period during Weeks 1 to 24.[1]

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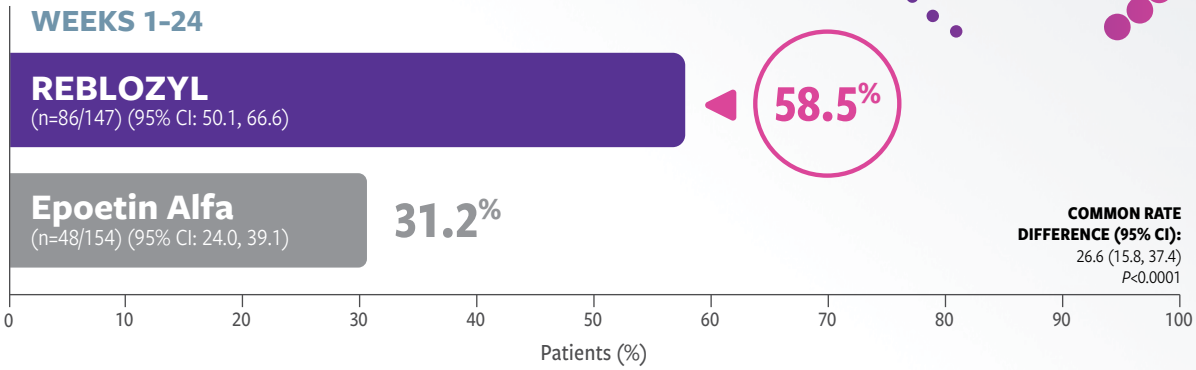
REBLOZYL demonstrated superiority with nearly 2X the patients achieving RBC-TI with Hgb increase vs epoetin alfa[1]

Primary composite endpoint: RBC-TI for at least 12 weeks with concurrent mean Hgb increase ≥1.5 g/dL[1]

NEARLY 2X THE RESPONSE RATE VS EPOETIN ALFA



The prespecified interim analysis included 301 patients who had either completed 24 weeks of treatment or discontinued prior to completing 24 weeks of treatment. This represents 85% of the total patient population contributing data for the primary endpoint.[1]

Key secondary endpoints included HI-E per IWG ≥8 weeks (Weeks 1-24): REBLOZYL 74.1% (109/147), epoetin alfa 51.3% (n=79/154); RBC-TI for 24 weeks (Weeks 1-24): REBLOZYL 47.6% (n=70/147), epoetin alfa 29.2% (n=45/154); and RBC-TI for ≥12 weeks (Weeks 1-24): REBLOZYL 66.7% (n=98/147), epoetin alfa 46.1%(n=71/154).[1]

IMPORTANT SAFETY INFORMATION (CONT)

WARNINGS AND PRECAUTIONS (CONT)

Hypertension

Hypertension was reported in 11.4% (63/554) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 2% to 9.6%. In ESA-naïve adult patients with MDS with normal baseline blood pressure, 23 (36%) patients developed SBP ≥140 mm Hg and 11 (6%) patients developed DBP ≥80 mm Hg. Monitor blood pressure prior to each administration. Manage new or exacerbations of preexisting hypertension using anti-hypertensive agents.

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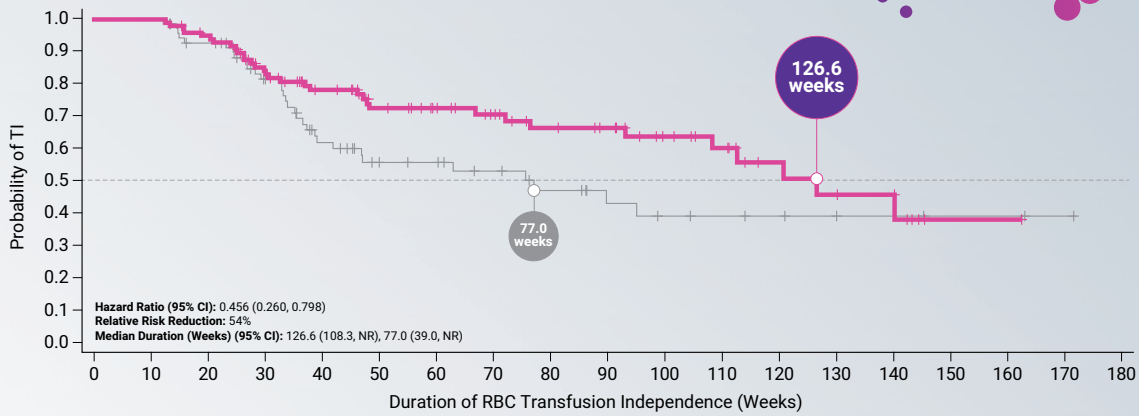
Responders on REBLOZYL had lasting transfusion independence[2]

Secondary endpoint: Median duration of RBC-TI ≥12 weeks (Week 1-EOT)

Analysis limitations: Duration of RBC-TI ≥12 weeks was not powered to detect statistical significance.



Subjects at Risk																	
REBLOZYL	98	98	91	74	61	49	42	37	31	28	21	17	11	8	6	1	1
Epoetin Alfa	71	71	63	47	33	24	23	19	15	11	9	8	7	5	5	2	2	1

NE=not reached; SD=standard deviation; TI=transfusion independence.

IMPORTANT SAFETY INFORMATION (CONT)

WARNINGS AND PRECAUTIONS (CONT)

Embryo-Fetal Toxicity

REBLOZYL may cause fetal harm when administered to a pregnant woman. REBLOZYL caused increased post-implantation loss, decreased litter size, and an increased incidence of skeletal variations in pregnant rat and rabbit studies. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 3 months after the final dose.

ADVERSE REACTIONS

Grade ≥3 (≥2%) adverse reactions included hypertension and dyspnea.

The most common (≥10%) all-grade adverse reactions included diarrhea, fatigue, hypertension, peripheral edema, nausea, and dyspnea.

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Safety data for REBLOZYL in ESA-naive patients[1]

Most adverse reactions in the clinical trial were Grade 1 or 2 (mild or moderate)

The most common (>10%) all-grade adverse reactions included diarrhea, fatigue, hypertension, COVID-19, peripheral edema, nausea, and dyspnea.[1]

The most common (>2%) Grade >3 adverse reactions included hypertension and dyspnea.[1]

Selected laboratory abnormalities that changed from Grade 0 to 2 at baseline to Grades 2 to 3 at any time during the studies were glomerular filtration rate and total bilirubin increased.[1]

Other clinically relevant adverse reaction reported in <5% of patients are injection-site reactions, including erythema, pruritus, and rash.[1]

Click to learn about REBLOZYL dosing

IMPORTANT SAFETY INFORMATION (CONT)

LACTATION

It is not known whether REBLOZYL is excreted into human milk or absorbed systemically after ingestion by a nursing infant. REBLOZYL was detected in milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because many drugs are excreted in human milk, and because of the unknown effects of REBLOZYL in infants, a decision should be made whether to discontinue nursing or to discontinue treatment. Because of the potential for serious adverse reactions in the breastfed child, breastfeeding is not recommended during treatment and for 3 months after the last dose.

DRUG ABUSE POTENTIAL

Abuse: Abuse of REBLOZYL may be seen in athletes for the effects on erythropoiesis. Misuse of drugs that increase erythropoiesis, such as REBLOZYL, by healthy persons may lead to polycythemia, which may be associated with life-threatening cardiovascular complications.

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In a **head-to-head** study vs epoetin alfa,* REBLOZYL provides...

Unprecedented superior efficacy. Lasting transfusion independence.[1,3]

The primary endpoint of COMMANDS was RBC-TI for ≥12 weeks along with a mean improvement in Hgb by ≥1.5 g/dL (Weeks 1-24).[1,2]

Hgb=hemoglobin; RBC-TI=red blood cell transfusion independence.

*>90% of study participants were outside of the United States and used a non-US-licensed epoetin alfa product. Direct comparisons between REBLOZYL and US-licensed epoetin alfa have not been established.

For your ESA-naive patients with MDS-associated anemia, choose REBLOZYL today[1]

Please see additional Important Safety Information throughout and full Prescribing Information for REBLOZYL.

References: 1. REBLOZYL [US Prescribing Information]. Summit, NJ: Celgene Corporation; 2023. **2.** Platzbecker U, Della Porta MG, Santini V, et el. Efficacy and safety of luspatercept versus epoetin alfa in erythropoiesis-stimulating agent-naive, transfusion-dependent, lower-risk myelodysplastic syndromes (COMMANDS): interim analysis of a phase 3, open-label, randomised controlled trial. *Lancet*. 2023;402(10399)(suppl):373-385. **3.** Platzbecker U, Della Porta MG, Santini V, et el. Efficacy and safety of luspatercept versus epoetin alfa in erythropoiesis-stimulating agent-naive, transfusion-dependent, lower-risk myelodysplastic syndromes (COMMANDS): interim analysis of a phase 3, open-label, randomised controlled trial. *Lancet*. 2023;402(10399):373-385. **4.** Garcia-Manero G, Platzbecker U, Santini V, et al. Efficacy and safety results from the COMMANDS trial: a phase 3 study evaluating luspatercept versus epoetin alfa in erythropoiesis-stimulating agent-naive transfusion-dependent patients with lower-risk myelodysplastic syndromes. Presented at: 2023 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2023; Chicago, IL. Abstract 7003.

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