DISCOVER THE FIRST AND ONLY ERYTHROID MATURATION AGENT

FDA APPROVED FOR ANEMIA

IN MDS

Reblozyl®

(luspatercept-aamt)

for injection 25mg • 75mg

for patients with ring sideroblasts who are failing an ESA and require ≥2 RBC units/8 weeks[1]

REBLOZYL is indicated for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

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%) 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 click here for full Prescribing Information for REBLOZYL.

Myelodysplastic syndromes (MDS) are a heterogeneous group of myeloid malignancies characterized by multilineage cytopenias, including anemia[2]

THE WORLD HEALTH ORGANIZATION (WHO) CLASSIFIES MDS AS NEOPLASTIC AND THEREFORE CANCER[3]

- MDS are characterized by:
  - Bone marrow dysfunction[3,4]
  - Dysplasia[3,4]
  - Genomic instability[3]
  - Peripheral blood cytopenias[3,4]
  - Ineffective hematopoiesis[4]

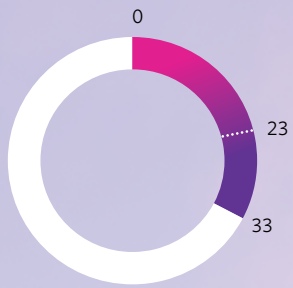
ANEMIA IS PRESENT IN THE MAJORITY OF PATIENTS WITH MDS[2]

- At diagnosis, anemia is the most common cytopenia present in patients with MDS[2]*
- 94% of patients with MDS received red blood cell (RBC) transfusions in the SEER-Sound registry of 783 patients from 2001 to 2007[5]
  - 13% of all patients with MDS requiring RBC transfusions had ring sideroblasts[5]

*Determined in a database analysis of 7012 patients with untreated MDS from 11 countries for the International Working Group for the Prognosis of MDS (IWG-PM) project.[2]

BASED ON THE NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®), MDS MANAGEMENT APPROACHES DIFFER ACCORDING TO MDS SUBTYPE AND SEVERITY OF DISEASE[6]

Patients with MDS may also have ring sideroblasts[7]



23%–33%

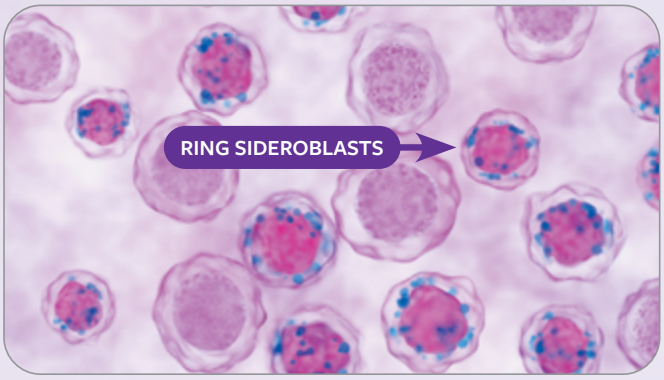
of patients with MDS have ring sideroblasts[7]

RING SIDEROBLASTS ARE PART OF THE WHO 2016 CLASSIFICATION OF MDS[8]

- The WHO 2016 recognizes 2 MDS subtypes specific to ring sideroblasts[8]:
  - MDS-RS with single lineage dysplasia (MDS-RS-SLD)
  - MDS-RS with multilineage dysplasia (MDS-RS-MLD)
- MDS-RS subtype is identified with <5% bone marrow blasts and either[8]:
  - ≥15% ring sideroblasts in the bone marrow
  - ≥5% ring sideroblasts in the bone marrow and the presence of an *SF3B1* mutation (identified through molecular testing)
- MDS-RS is recognized as part of the ICD-10-CM coding system[9]
- Ring sideroblasts may also be present at any level in other subtypes of MDS[10]
- MDS/MPN-RS-T is a rare subtype recognized by the WHO 2016. It has similarities to MDS-RS but is characterized by specific clinical features[8,11]
  - These include anemia, bone marrow dysplasia with ring sideroblasts, and persistent thrombocytosis ≥450 × 10^9/L with proliferation of large and morphologically atypical megakaryocytes[8]

ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

RING SIDEROBLASTS ARE ERYTHROBLASTS WITH IRON-LOADED MITOCHONDRIA ASSOCIATED WITH ANEMIA[10]



For illustrative purposes only.

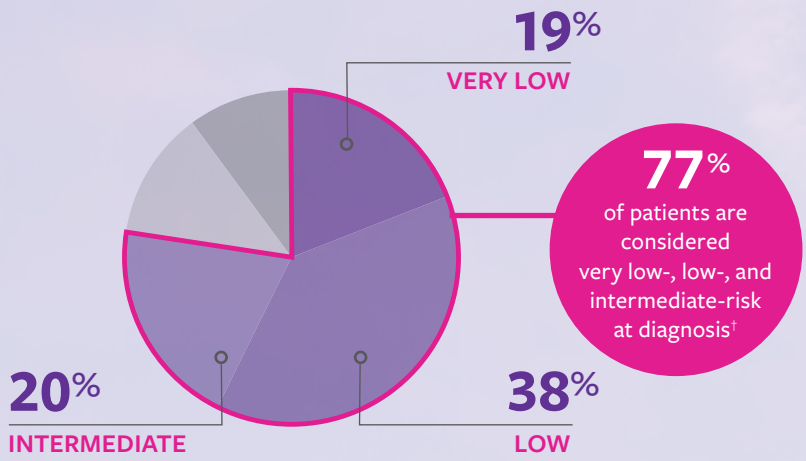
- Ring sideroblasts are identified by iron staining and the results can be found on pathology reports[10]
- There is variability in how pathologists describe the presence of ring sideroblasts in pathology reports[12]

Consult with your pathologist about how ring sideroblasts are reported in your patients with MDS

The IPSS-R categorization is the preferred* prognostic system of the NCCN Guidelines®[6]

THE MAJORITY OF PATIENTS WITH MDS HAVE IPSS-R VERY LOW- TO INTERMEDIATE-RISK DISEASE AT DIAGNOSIS[2]

Distribution of patients with MDS by IPSS-R risk status (N = 7012)†



*The NCCN Guidelines for MDS also note that other risk stratification systems have good value.[6]

†Distribution of the IPSS-R risk scores at time of diagnosis evaluated in the recently diagnosed patient cohort; (N = 7012) for the patient population included in the IPSS-R analysis.[2]

IPSS-R IS BASED ON BONE MARROW CYTOGENETICS, MARROW BLAST PERCENTAGE, AND PRESENCE AND DEPTH OF CYTOPENIAS[2]

Prognostic score values[2]							
Prognostic variable	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**
BM blasts, %	≤2	—	>2 to <5	—	5 to 10	>10	—
Cytogenetics	Very good	—	Good	—	Intermediate	Poor	Very poor
Hgb, g/dL	≥10	—	8 to <10	<8	—	—	—
Platelets, × 10^9 cells/L	≥100	50 to <100	<50	—	—	—	—
ANC, × 10^9 cells/L	≥0.8	<0.8	—	—	—	—	—

IPSS-R prognostic risk categories/scores[2]				
Very low	**Low**	**Intermediate**	**High**	**Very high**
≤1.5	>1.5–3	>3–4.5	>4.5–6	>6

AN IPSS-R SCORE IS CALCULATED BY ADDING THE VALUES FOR THE PROGNOSTIC FACTORS TOGETHER. AN EXAMPLE OF AN IPSS-R LOW-RISK SCORE:

- 2% blast count = 0
- Good cytogenetics = 1
- 8 g/dL Hgb = 1
- Platelets 75 x 10^9 cells/L = 0.5
- ANC 0.9 x 10^9 cells/L = 0

Total values added together = 2.5

ANC, absolute neutrophil count; BM, bone marrow; Hgb, hemoglobin; IPSS-R, Revised International Prognostic Scoring System.

Ineffective erythropoiesis is an underlying cause of anemia in MDS[13]

ANEMIA IN MDS IS LINKED TO BONE MARROW DYSFUNCTION CHARACTERIZED AS INEFFECTIVE ERYTHROPOIESIS[14]

- In MDS, stem cells lack the ability for differentiation and maturation, resulting in bone marrow dysfunction and poor blood cell production, in particular RBCs

INEFFECTIVE ERYTHROPOIESIS IN MDS MAY LEAD TO ANEMIA REQUIRING RBC TRANSFUSIONS, AND IS CHARACTERIZED BY[13,15]:

Increased proliferation of erythroid progenitors

Increased death of erythroid precursors

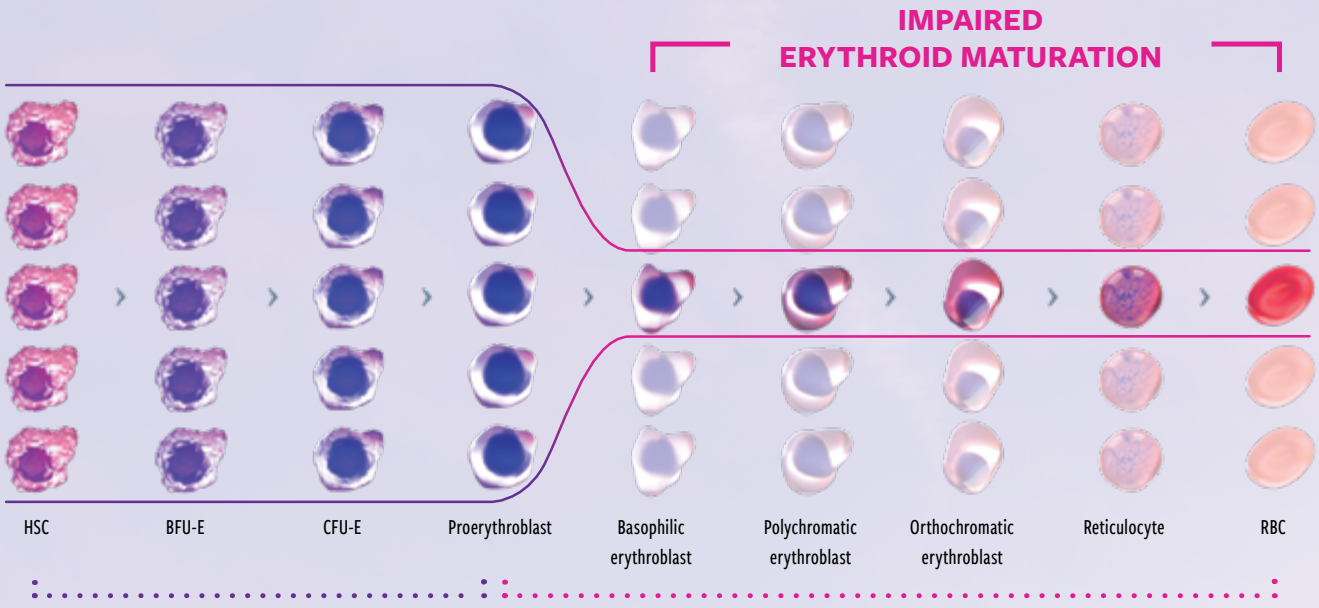
Impaired erythroid maturation

The presence of anemia despite increased proliferation of progenitor cells is indicative of ineffective erythropoiesis in MDS

There is a need to help address anemia due to ineffective erythropoiesis in patients with MDS requiring RBC transfusions

MECHANISM OF DISEASE

Impaired erythroid maturation contributes to ineffective erythropoiesis, resulting in low production of RBCs and anemia[16,17]



EARLY-STAGE ERYTHROPOIESIS[18]

Endogenous erythropoietin regulates proliferation

LATE-STAGE ERYTHROPOIESIS[19,20]

Select TGF-β superfamily ligands help regulate maturation

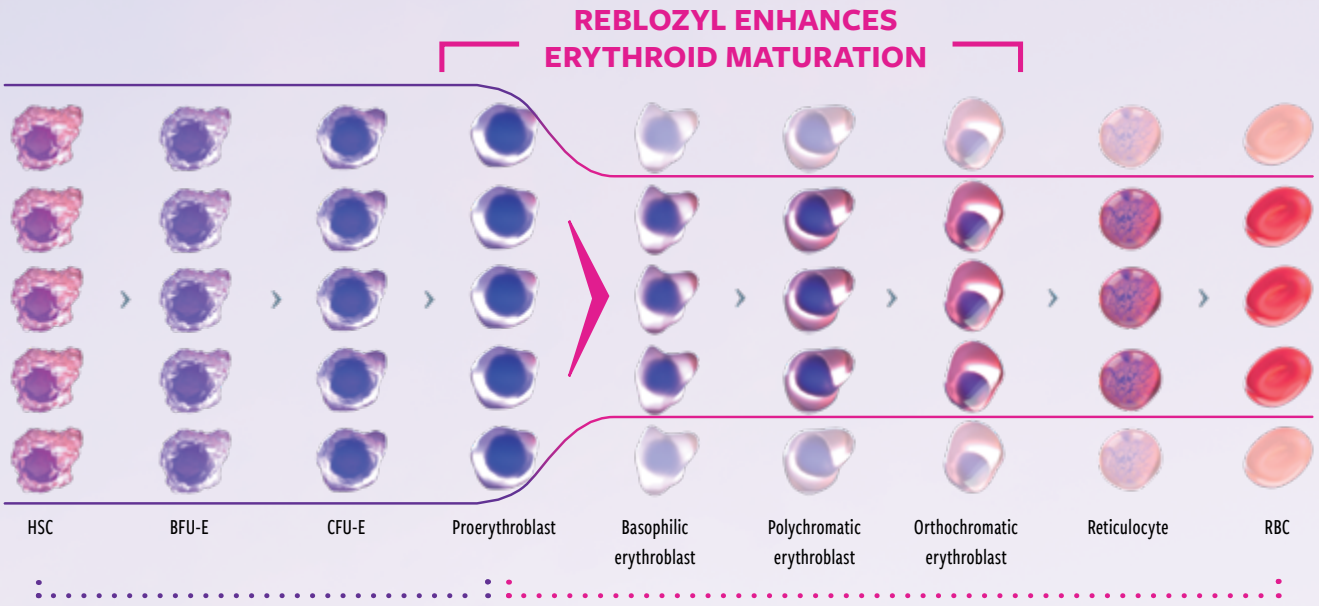
TGF-β superfamily signaling through Smad2/3 is abnormally high in diseases characterized by ineffective erythropoiesis, which leads to impaired erythroid maturation of RBCs

For illustrative purposes only.

BFU-E, burst-forming unit erythroid; CFU-E, colony-forming unit erythroid; HSC, hematopoietic stem cell; TGF-β, transforming growth factor beta.

MECHANISM OF ACTION

REBLOZYL restores erythropoiesis by increasing the number and improving the quality of mature RBCs[1,17]



For illustrative purposes only.

In preclinical models, REBLOZYL improved Hgb levels, RBC morphology, and other hematology parameters* associated with ineffective erythropoiesis[1,20,21]

*Other hematology parameters include reducing oxidative stress in erythrocytes, reducing accumulation of α-globin aggregates in erythrocyte membranes, and improving RBC life span.[21]

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Hypertension

Hypertension was reported in 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. In adult patients with MDS with normal baseline blood pressure, 26 (29.9%) patients developed SBP ≥130 mm Hg and 23 (16.4%) 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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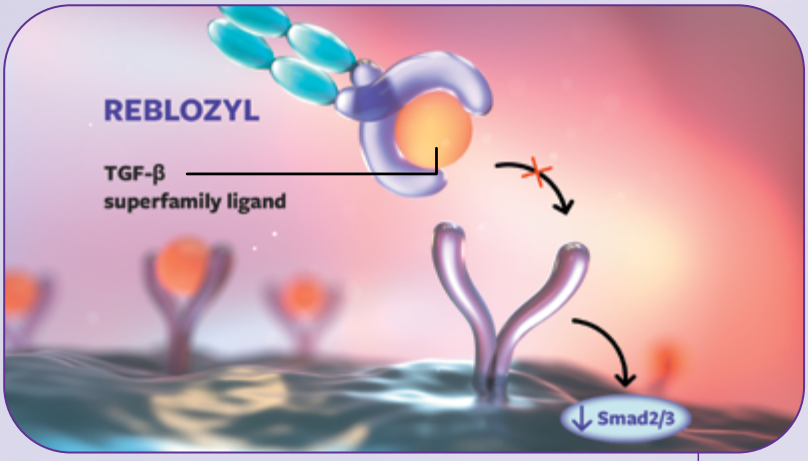
MECHANISM OF ACTION

How REBLOZYL works is based on preclinical studies[1]



REBLOZYL is a recombinant fusion protein that binds several endogenous TGF-β superfamily ligands, thereby diminishing Smad2/3 signaling

REBLOZYL PROMOTED ERYTHROID MATURATION

through differentiation of late-stage erythroid precursors (normoblasts)

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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REBLOZYL was studied in the multicenter, randomized, double-blind, placebo-controlled, phase 3 MEDALIST trial[1,22]

Patient population (N = 229)[1,22]

Key inclusion criteria:

- Adults ≥18 years of age
- IPSS-R very low-, low-, or intermediate-risk MDS
- <5% bone marrow blasts
- Presence of ring sideroblasts
  - ≥15% ring sideroblasts or ≥5% ring sideroblasts with an *SF3B1* mutation
- RBC transfusion burden ≥2 units over 8 weeks
- ESA exposure
  - Inadequate response (response that is no longer maintained after at least 8 doses of recombinant human erythropoietin or 4 doses of darbepoetin alfa)
  - Ineligible for ESAs (serum EPO >200 U/L)
  - Intolerant of ESA treatment

Key exclusion criteria:

- del 5q MDS
- White blood cell count >13 Gi/L
- Neutrophils <0.5 Gi/L
- Platelets <50 Gi/L
- Prior use of a disease-modifying agent for treatment of MDS

Randomized 2:1[1]

REBLOZYL[1]

SC every 3 weeks (n = 153) for at least 24 weeks or until unacceptable toxicity, loss of efficacy, or disease progression*

- **Starting dose:** 1 mg/kg
- Patients could have dose increased to 1.33 mg/kg and then to 1.75 mg/kg

Data cutoff: **48 weeks**[22]

Placebo[1]

SC every 3 weeks (n = 76)

All patients received best supportive care (BSC), including RBC transfusions as needed[1]

*The primary efficacy assessment was conducted after completion of 24 weeks on study drug. Patients with a decrease in transfusion requirement or increase in Hgb could continue on blinded study drug thereafter until unacceptable toxicity, loss of efficacy, or disease progression.[1]

del 5q, deletion 5q; EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; SC, subcutaneous injection.

PRIMARY ENDPOINT[1]

- RBC transfusion independence (RBC-TI), defined as the absence of any RBC transfusion during any consecutive 8-week period occurring entirely within the first 24 weeks of treatment

KEY SECONDARY ENDPOINT[1]

- RBC-TI for ≥12 weeks (during weeks 1–24 and 1–48)

ADDITIONAL SECONDARY ENDPOINTS[22]

- RBC-TI for ≥8 weeks at 48 weeks, to capture potential late responders
- Modified hematologic improvement-erythroid (mHI-E) defined by the International Working Group (IWG) for any consecutive 56-day period
  - Reduction in RBC transfusion burden ≥4 RBC units/8 weeks
  - Mean Hgb increase of ≥1.5 g/dL/8 weeks
- Duration of response
- Hgb change from baseline

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Grade ≥3 (≥2%) adverse reactions included fatigue, hypertension, syncope and musculoskeletal pain. A fatal adverse reaction occurred in 5 (2.1%) patients.

The most common (≥10%) adverse reactions included fatigue, musculoskeletal pain, dizziness, diarrhea, nausea, hypersensitivity reactions, hypertension, headache, upper respiratory tract infection, bronchitis, and urinary tract infection.

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The MEDALIST trial included patients with very low- to intermediate-risk MDS with ring sideroblasts[1,22]

BASELINE DISEASE CHARACTERISTICS OF PATIENTS IN PIVOTAL PHASE 3 MEDALIST TRIAL[1,22]

Demographic and disease characteristics	REBLOZYL (n = 153)	Placebo (n = 76)
Age, years		
Median (min, max)	71.0 (40, 95)	72.0 (26, 91)
Time since original MDS diagnosis,[a] months		
Median (min, max)	44.0 (3, 421)	36.1 (4, 193)
Serum EPO (U/L) categories,[b] n (%)		
<200	88 (57.5)	50 (65.8)
200 to 500	43 (28.1)	15 (19.7)
>500	21 (13.7)	11 (14.5)
Missing	1 (0.7)	0
RBC transfusions/8 weeks over 16 weeks, n (%)		
<4 units	46 (30.1)	20 (26.3)
≥4 and <6 units	41 (26.8)	23 (30.3)
≥6 units	66 (43.1)	33 (43.4)

- Baseline characteristics were balanced between arms[22]

36% (83/229) of all patients in the trial were 75 years of age or older, including patients up to 95 years[1,22]*

While 39% of patients had serum EPO >200 U/L, 95.2% of all patients in the trial were ESA-exposed and only 4.8% were ESA-naive (EPO >200 U/L)[1,22]*

57% of patients had <6 RBC units/8 weeks[1]*

*Numbers in callouts are based on the entire clinical trial population.[1,22]

(continued on following page)

[a]Time since original MDS diagnosis was defined as the number of months from the date of original diagnosis to the date of informed consent.[1]

[b]Baseline EPO was defined as the highest EPO value within 35 days of the first dose of study drug.[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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The MEDALIST trial included patients with very low- to intermediate-risk MDS with ring sideroblasts (cont'd)[1,22]

BASELINE DISEASE CHARACTERISTICS OF PATIENTS IN PIVOTAL PHASE 3 MEDALIST TRIAL (CONT'D)[1,22]

Demographic and disease characteristics	REBLOZYL (n = 153)	Placebo (n = 76)
Diagnosis per WHO 2016 criteria,[c] n (%)		
MDS-RS[d]	135 (88.2)	65 (85.5)
MDS/MPN-RS-T	14 (9.2)	9 (11.8)
Other[e]	4 (2.6)	2 (2.6)
***SF3B1*, n (%)**		
Mutated	141 (92.2)	65 (85.5)
Nonmutated	12 (7.8)	10 (13.2)
Missing	0	1 (1.3)
IPSS-R classification risk category, n (%)		
Very low	18 (11.8)	6 (7.9)
Low	109 (71.2)	57 (75)
Intermediate	25 (16.3)	13 (17.1)
High	1 (0.7)	0

All patients had ring sideroblasts[1]*

The majority of patients had an *SF3B1* mutation[22]*

All patients except 1 had very low- to intermediate-risk MDS[1]*

*Numbers in callouts are based on the entire clinical trial population.[1,22]

[c]MEDALIST enrolled patients with MDS with ring sideroblasts per the WHO 2008 criteria; however, these data are based on post hoc reclassification of patients by the FDA using the WHO 2016 diagnostic criteria (MDS-RS [n = 200; 87.3%], MDS/MPN-RS-T [n = 23; 10.0%], and Other [n = 6; 2.6%]).[22]

[d]Includes MDS-RS-MLD and MDS-RS-SLD.[1]

[e]Includes MDS-EB-1, MDS-EB-2, and MDS-U, which met the criteria for inclusion of ring sideroblasts ≥15% of erythroid precursors in the bone marrow or ≥5% (but <15%) if *SF3B1* mutation was present.[1,22]

FDA, Food and Drug Administration; MDS-EB-1, myelodysplastic syndromes with excess blasts (5%–9% in the bone marrow or 2%–4% in the blood); MDS-EB-2, myelodysplastic syndromes with excess blasts (10%–19% in the bone marrow or 5%–19% in the blood); MDS-U, myelodysplastic syndromes, unclassifiable.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) 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.

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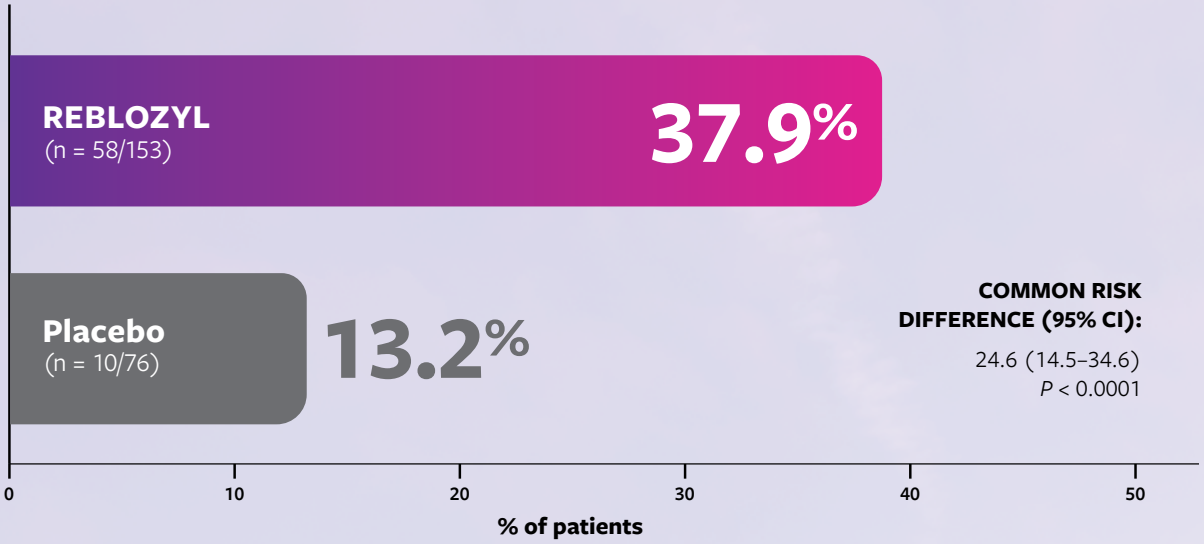
REBLOZYL provided substantial clinical benefit through RBC transfusion independence vs placebo[1]

PRIMARY ENDPOINT: RBC-TI ≥8 WEEKS DURING WEEKS 1 TO 24[1]



APPROXIMATELY

3X greater percentage of patients receiving REBLOZYL achieved RBC transfusion independence (primary endpoint) than placebo

CI, confidence interval.

The NCCN Guidelines recommend luspatercept-aamt (REBLOZYL) for anemia in very low- to intermediate-risk MDS with ring sideroblasts after 3–4 months of no response to ESAs (Category 2A)[6]

This recommendation is for patients with ring sideroblasts ≥15% or ring sideroblasts ≥5% with an *SF3B1* mutation*

*And with serum EPO ≤500 mU/mL.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Hypertension

Hypertension was reported in 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. In adult patients with MDS with normal baseline blood pressure, 26 (29.9%) patients developed SBP ≥130 mm Hg and 23 (16.4%) 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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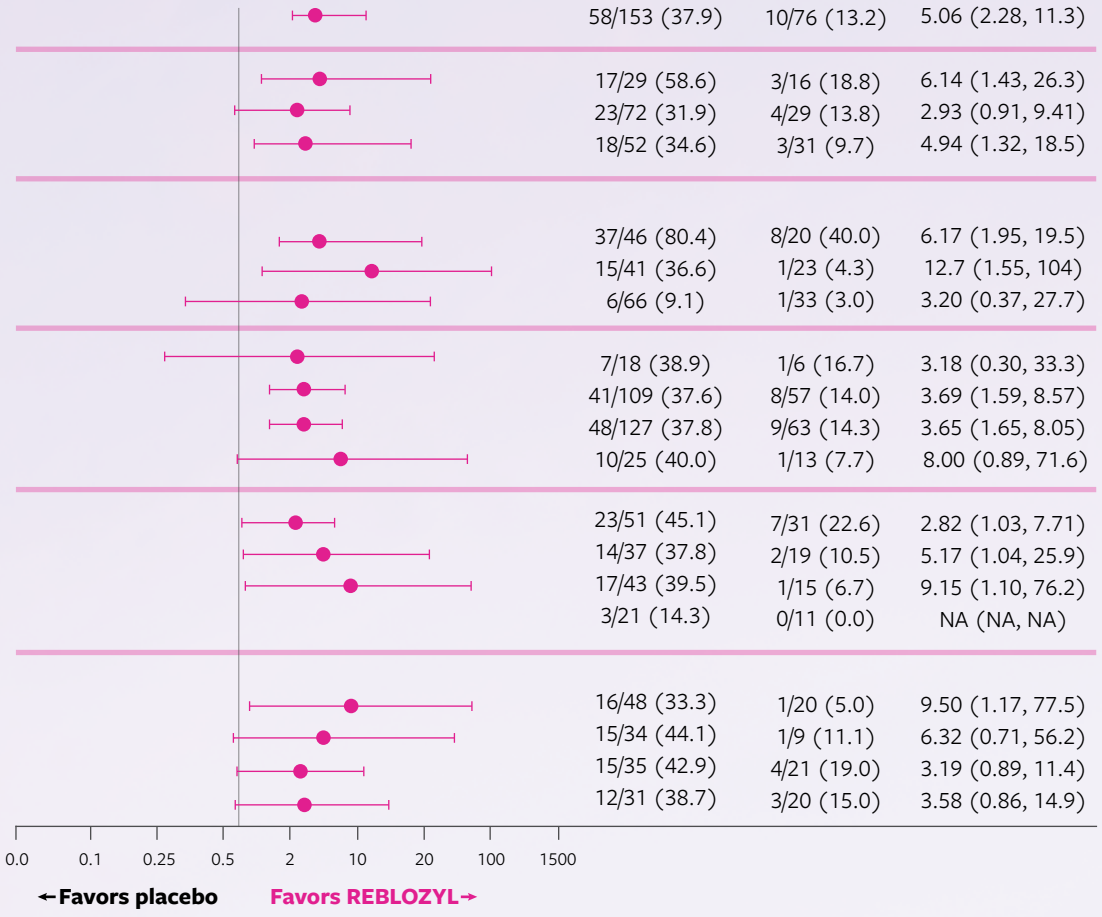
Primary endpoint subgroup analysis: Rates of RBC transfusion independence with REBLOZYL[22]

RBC-TI ≥8 WEEKS DURING WEEKS 1 TO 24

Subgroups	REBLOZYL n/N (%)	Placebo n/N (%)	Odds ratio (95% CI)
Overall	58/153 (37.9)	10/76 (13.2)	5.06 (2.28, 11.3)
Age group			
≤64	17/29 (58.6)	3/16 (18.8)	6.14 (1.43, 26.3)
65–74	23/72 (31.9)	4/29 (13.8)	2.93 (0.91, 9.41)
≥75	18/52 (34.6)	3/31 (9.7)	4.94 (1.32, 18.5)
Average baseline RBC transfusion requirements			
<4 units/8 weeks	37/46 (80.4)	8/20 (40.0)	6.17 (1.95, 19.5)
4–<6 units/8 weeks	15/41 (36.6)	1/23 (4.3)	12.7 (1.55, 104)
≥6 units/8 weeks	6/66 (9.1)	1/33 (3.0)	3.20 (0.37, 27.7)
Baseline IPSS-R risk			
Very low	7/18 (38.9)	1/6 (16.7)	3.18 (0.30, 33.3)
Low	41/109 (37.6)	8/57 (14.0)	3.69 (1.59, 8.57)
Very low or low	48/127 (37.8)	9/63 (14.3)	3.65 (1.65, 8.05)
Intermediate	10/25 (40.0)	1/13 (7.7)	8.00 (0.89, 71.6)
Baseline serum EPO (U/L)			
<100	23/51 (45.1)	7/31 (22.6)	2.82 (1.03, 7.71)
100–<200	14/37 (37.8)	2/19 (10.5)	5.17 (1.04, 25.9)
200–500	17/43 (39.5)	1/15 (6.7)	9.15 (1.10, 76.2)
>500	3/21 (14.3)	0/11 (0.0)	NA (NA, NA)
Longest duration prior ESA (months)			
<6	16/48 (33.3)	1/20 (5.0)	9.50 (1.17, 77.5)
6–12	15/34 (44.1)	1/9 (11.1)	6.32 (0.71, 56.2)
>12–24	15/35 (42.9)	4/21 (19.0)	3.19 (0.89, 11.4)
>24	12/31 (38.7)	3/20 (15.0)	3.58 (0.86, 14.9)



The odds ratio is shown in the table. Odds ratio is the probability of an event (transfusion independence) occurring in a group, divided by the probability of that event not occurring. NA, not available.

ANALYSIS LIMITATIONS

- These exploratory analyses should not be interpreted to determine treatment difference between arms in these select subgroups because of potential selection bias, insufficient sample size, and a higher probability of making a false positive finding

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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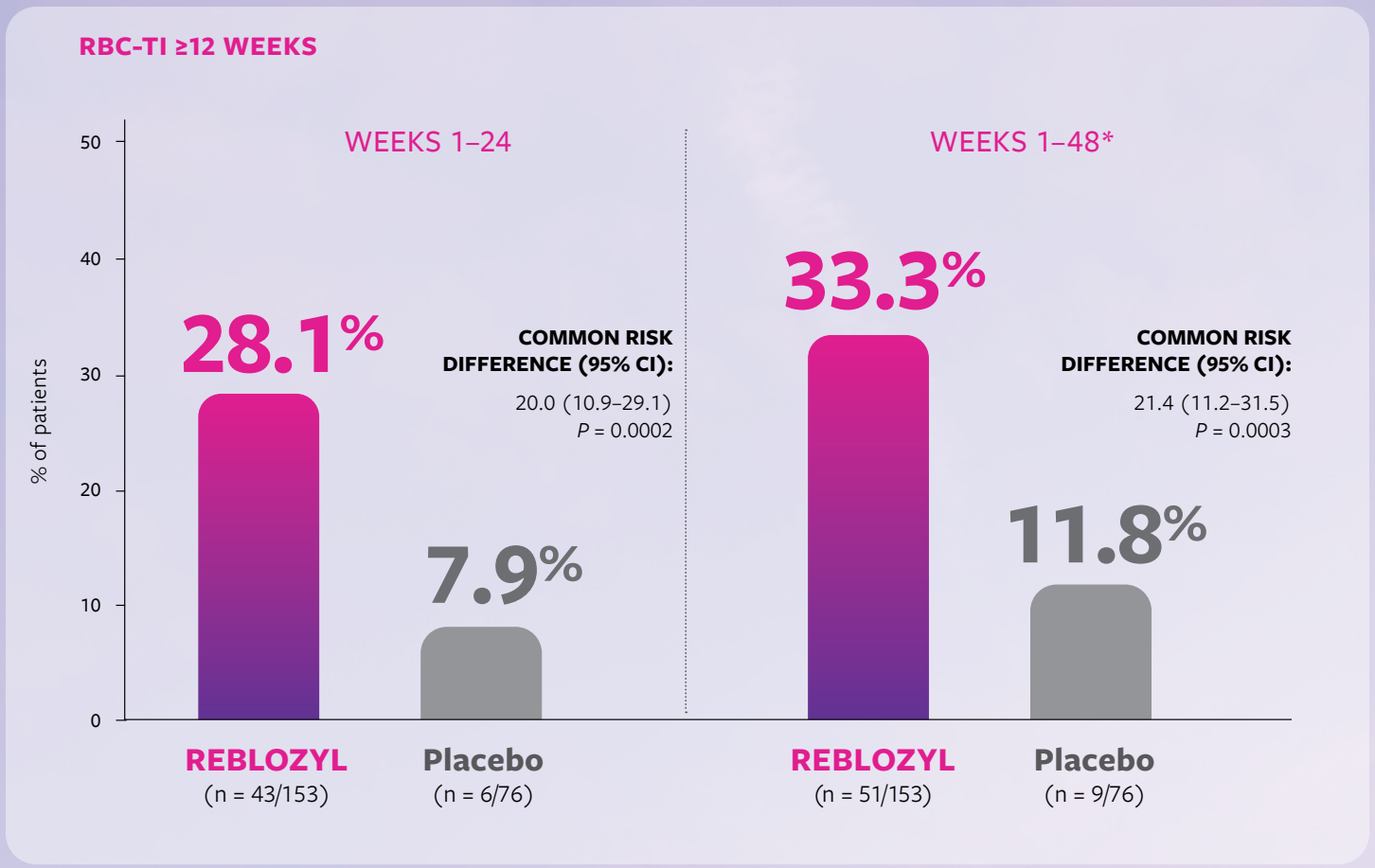
Key secondary endpoints: REBLOZYL had a significantly higher rate of RBC transfusion independence vs placebo for 12 weeks or more[1]



*The median (range) duration of treatment was 49 weeks (6–114 weeks) on the REBLOZYL arm and 24 weeks (7–89 weeks) on the placebo arm.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Grade ≥3 (≥2%) adverse reactions included fatigue, hypertension, syncope and musculoskeletal pain. A fatal adverse reaction occurred in 5 (2.1%) patients.

The most common (≥10%) adverse reactions included fatigue, musculoskeletal pain, dizziness, diarrhea, nausea, hypersensitivity reactions, hypertension, headache, upper respiratory tract infection, bronchitis, and urinary tract infection.

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

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Additional endpoints: REBLOZYL provided RBC-TI vs placebo in patients with MDS-RS and MDS/MPN-RS-T[1]

RBC-TI ≥8 WEEKS DURING WEEKS 1 TO 24 BY DIAGNOSIS AND BASELINE TRANSFUSION BURDEN IN MEDALIST

	Responders/N		% Response (95% CI)	
	REBLOZYL	Placebo	REBLOZYL	Placebo
WHO 2016 diagnosis				
MDS-RS	46/135	8/65	**34.1%** (26.1, 42.7)	**12.3%** (5.5, 22.8)
MDS/MPN-RS-T	9/14	2/9	**64.3%** (35.1, 87.2)	**22.2%** (2.8, 60.0)
Other[a]	3/4	0/2	**75.0%** (19.4, 99.4)	**0.0%** (0.0, 84.2)
Baseline RBC transfusion burden				
2–3 units/8 weeks[b]	37/46	8/20	**80.4%** (66.1, 90.6)	**40.0%** (19.1, 63.9)
4–5 units/8 weeks[c]	15/41	1/23	**36.6%** (22.1, 53.1)	**4.3%** (0.1, 21.9)
≥6 units/8 weeks	6/66	1/33	**9.1%** (3.4, 18.7)	**3.0%** (0.1, 15.8)

[a]Includes MDS-EB-1, MDS-EB-2, and MDS-U.
[b]Includes patients who received 3.5 units.
[c]Includes patients who received 5.5 units.

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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Additional analysis in patients who achieved the primary endpoint (RBC transfusion independence ≥8 weeks) with REBLOZYL

DAY OF MEAN Hgb INCREASE OF 1.5 g/dL IN PATIENTS WHO ACHIEVED THE PRIMARY ENDPOINT (n = 58)[23]

	Day	Approximate mean Hgb increase	Number of REBLOZYL responders with an Hgb measurement at first evaluation
First evaluation for Hgb	8	1.5 g/dL	24

THE MEDIAN PEAK INCREASE IN Hgb LEVEL IN PATIENTS IN THE REBLOZYL GROUP WHO ACHIEVED THE PRIMARY ENDPOINT (n = 58)[23]

	Hgb level
Median peak increase in the Hgb level	2.55 g/dL (range, 1.0–4.1)

ANALYSIS LIMITATIONS

- The mean values and standard errors were not calculated if the number of patients was fewer than 8 in the REBLOZYL group of patients without a response or if the number was fewer than 4 in the placebo group[23]
- Hgb values that were obtained within 14 days after an RBC transfusion were censored from these analyses unless they also were within 3 days before receipt of another RBC transfusion[23]
- Patients may have experienced multiple periods of response intermittently between periods without response over the 24-week assessment period and extension phase through 25 to 48 weeks[22]
- All patients in both arms were eligible to receive BSC, which included RBC transfusions as needed[1]
- These exploratory analyses should not be interpreted to determine treatment difference between arms in these select endpoints because of potential selection bias, insufficient sample size, and a higher probability of making a false positive finding

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) 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.

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Additional analysis: Modified hematologic improvement-erythroid (mHI-E) was assessed in patients receiving REBLOZYL

mHI-E WAS DEFINED PER THE IWG CRITERIA AS THE PROPORTION OF PATIENTS WHO MET mHI-E CRITERIA SUSTAINED OVER ANY CONSECUTIVE 56-DAY (8-WEEK) PERIOD[22]:

- **For patients with baseline RBC transfusion burden of at least 4 units/8 weeks:** response was defined as a reduction in RBC transfusion burden of ≥4 RBC units/8 weeks
- **For patients with baseline RBC transfusion burden of less than 4 units/8 weeks:** response was defined as a mean Hgb increase of ≥1.5 g/dL/8 weeks in the absence of transfusions for at least 8 weeks

MODIFIED HEMATOLOGIC IMPROVEMENT-ERYTHROID (mHI-E) IN PATIENTS RECEIVING REBLOZYL VS PLACEBO[22]

	Weeks 1–24		Weeks 1–48	
	REBLOZYL (n = 153)	Placebo (n = 76)	REBLOZYL (n = 153)	Placebo (n = 76)
Modified hematologic improvement-erythroid (mHI-E)	**52.9%** (81/153)	**11.8%** (9/76)	**58.8%** (90/153)	**17.1%** (13/76)
RBC transfusion reduction of ≥4 units/8 weeks[a]	**48.6%** (52/107)	**14.3%** (8/56)	**54.2%** (58/107)	**21.4%** (12/56)
Mean Hgb increase of ≥1.5 g/dL for 8 weeks in the absence of transfusions[b]	**63.0%** (29/46)	**5.0%** (1/20)	**69.6%** (32/46)	**5.0%** (1/20)

[a]Percentage based on number of patients with baseline RBC transfusion burden of ≥4 units/8 weeks (n = 107 in the REBLOZYL arm).
[b]Percentage based on number of patients with baseline RBC transfusion burden of <4 units/8 weeks (n = 46 in the REBLOZYL arm).

ANALYSIS LIMITATIONS

- The primary endpoint of the study was transfusion independence defined as the absence of any RBC transfusion during any consecutive 8-week period occurring within weeks 1 through 24[1]
  - Primary endpoint data: 37.9% (58/153) for REBLOZYL vs 13.2% (10/76) for placebo
- The mHI-E analysis is a broader analysis than transfusion independence. The analysis included patients that did not meet the primary endpoint of transfusion independence[22]:
  - Those who achieved transfusion reduction of ≥4 units over 8 weeks (with higher baseline transfusion burden)
  - Those whose Hgb increased by ≥1.5 g/dL for 8 weeks in the absence of transfusions (with lower baseline transfusion burden)
- Patients may have experienced multiple periods of response intermittently between periods without response over the 24-week assessment period and extension phase through 25 to 48 weeks[22]
- All patients in both arms were eligible to receive BSC, which included RBC transfusions as needed[1]
- These exploratory analyses should not be interpreted to determine treatment difference between arms in these select endpoints because of potential selection bias, insufficient sample size, and a higher probability of making a false positive finding

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Hypertension

Hypertension was reported in 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. In adult patients with MDS with normal baseline blood pressure, 26 (29.9%) patients developed SBP ≥130 mm Hg and 23 (16.4%) 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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Adverse reactions with REBLOZYL

- The median time on treatment with REBLOZYL was 50.4 weeks (range, 3–221 weeks)[1]
- 67% of patients were exposed for 6 months or longer and 49% were exposed for >1 year[1]
- Among the 242 patients treated with REBLOZYL, 5 (2.1%) had a fatal adverse reaction[1]
- Selected laboratory abnormalities that changed from Grade 0 to 1 at baseline to Grade ≥2 at any time during the studies in at least 10% of patients included creatinine clearance decreased, total bilirubin increased, and alanine aminotransferase increased[1]
- Other clinically relevant adverse reactions reported in <5% of patients included bronchitis, urinary tract infection, and hypertension[1]

The majority of adverse reactions with REBLOZYL were Grade 1 or 2 (mild to moderate)[1]

ADVERSE REACTIONS (≥5%) IN PATIENTS RECEIVING REBLOZYL WITH A DIFFERENCE BETWEEN ARMS OF >2% IN MEDALIST TRIAL THROUGH CYCLE 8

Body system/adverse reaction	REBLOZYL (n = 153)		Placebo (n = 76)	
	All Grades n (%)	Grade 3 n (%)	All Grades n (%)	Grade 3 n (%)
General disorders and administration site conditions				
Fatigue[a,b]	63 (41)	11 (7)	17 (22)	2 (3)
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain[b]	30 (20)	3 (2)	11 (14)	0 (0)
Nervous system disorders				
Dizziness/vertigo	28 (18)	1 (<1)	5 (7)	1 (1)
Headache[b]	21 (14)	0 (0)	5 (7)	0 (0)
Syncope/presyncope	8 (5)	5 (3)	0 (0)	0 (0)
Gastrointestinal disorders				
Nausea[b]	25 (16)	1 (<1)	8 (11)	0 (0)
Diarrhea[b]	25 (16)	0 (0)	7 (9)	0 (0)
Respiratory, thoracic, and mediastinal disorders				
Dyspnea[b]	20 (13)	2 (1)	4 (5)	1 (1)
Immune system disorders				
Hypersensitivity reactions[b]	15 (10)	1 (<1)	5 (7)	0 (0)
Renal and urinary disorders				
Renal impairment[b]	12 (8)	3 (2)	3 (4)	0 (0)
Cardiac disorders				
Tachycardia[b]	12 (8)	0 (0)	1 (1)	0 (0)
Injury poisoning and procedural complications				
Injection site reactions	10 (7)	0 (0)	3 (4)	0 (0)
Infections and infestations				
Upper respiratory tract infection	10 (7)	1 (<1)	2 (3)	0 (0)
Influenza/influenza-like illness	9 (6)	0 (0)	2 (3)	0 (0)

[a]Includes asthenic conditions.
[b]Reaction includes similar/grouped terms.

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Liver function abnormalities and immunogenicity

SELECTED GRADES 2 TO 4 TREATMENT-EMERGENT LABORATORY ABNORMALITIES THROUGH CYCLE 8 IN THE MEDALIST TRIAL[1]

Parameter	REBLOZYL		Placebo	
	N[a]	n (%)	N[a]	n (%)
ALT elevated	151	13 (9)	74	5 (7)
AST elevated	152	6 (4)	76	0 (0)
Total bilirubin elevated	140	17 (12)	66	3 (5)
Creatinine clearance reduced	113	30 (27)	62	13 (21)

[a]Number of patients at Grades 0 to 1 at baseline.
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

IMMUNOGENICITY[1]

- Of 260 patients with MDS who were treated with REBLOZYL and evaluable for the presence of anti-luspatercept-aamt antibodies, 23 patients (8.9%) tested positive for treatment-emergent anti-luspatercept-aamt antibodies, including 9 patients (3.5%) who had neutralizing antibodies
- Luspatercept-aamt serum concentration tended to decrease in the presence of neutralizing antibodies
- There were no severe acute systemic hypersensitivity reactions reported for patients with anti-luspatercept-aamt antibodies in REBLOZYL clinical trials, and there was no association between hypersensitivity type reaction or injection site reaction and presence of anti-luspatercept-aamt antibodies

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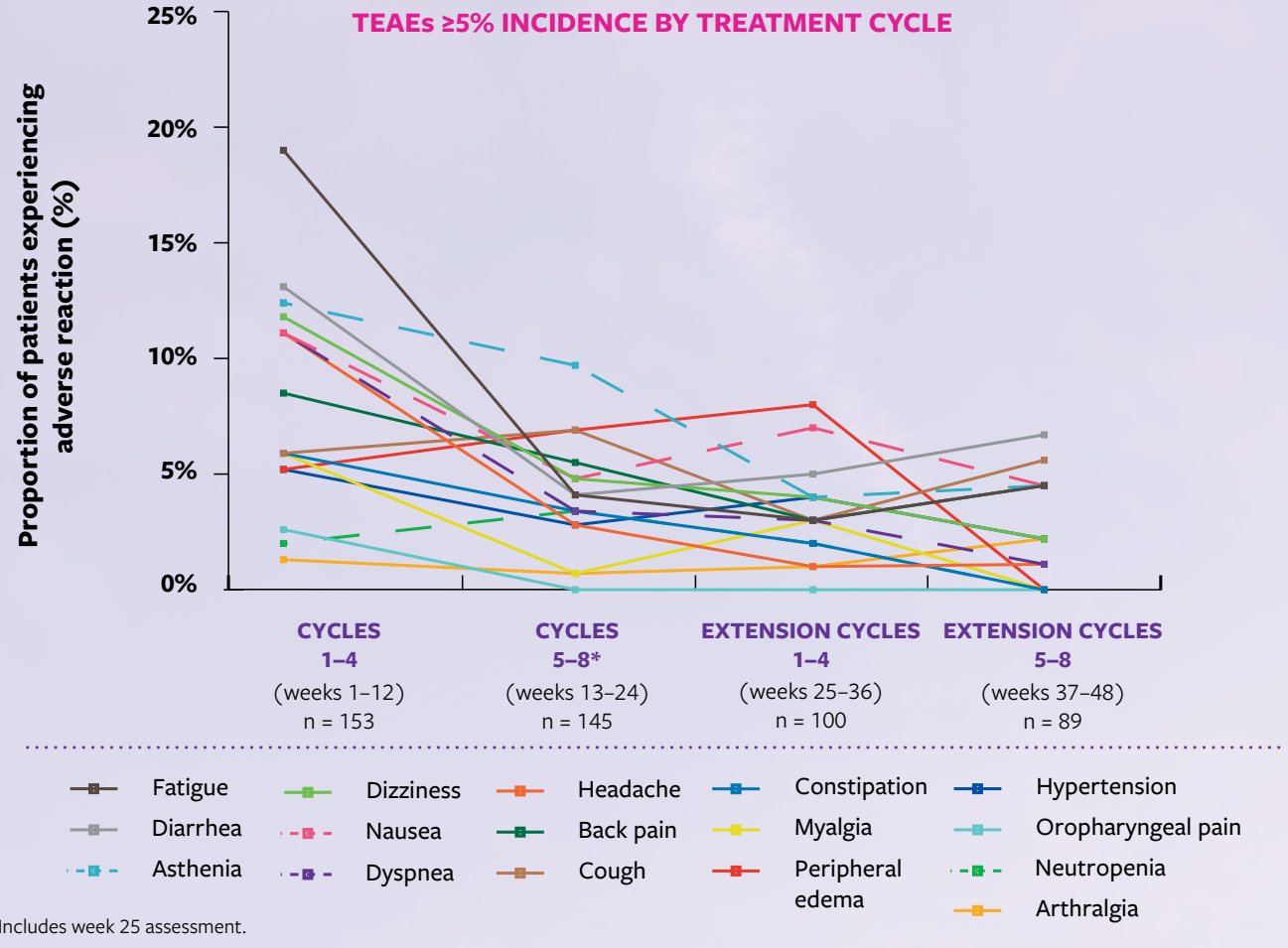
Additional analysis of treatment-emergent adverse events (TEAEs) by REBLOZYL treatment cycle[24]



*Includes week 25 assessment.

ANALYSIS LIMITATIONS

- All patients in both arms were eligible to receive BSC, including RBC transfusions as needed[1]
- Adverse events (AEs) with a duration overlapping multiple cycles were only counted in the first overlapped cycle. If an AE occurred multiple times in different cycles, it was counted once in each cycle. If an AE occurred multiple times within the same cycle, it was counted only once. If a patient experienced multiple events under the same MedDRA 20.0 preferred term, then the patient was counted only once for the preferred term[24]
- Patients who met the criteria and remained on double-blind treatment after completion of week 25 assessment may have continued dosing in the extension phase of the treatment period until the subject experienced unacceptable toxicities, disease progression, withdrew consent, or met any other discontinuation criteria[1,24]
- Fatigue TEAE does not include broader asthenic conditions adverse drug reactions (ADRs)

ADDITIONAL ANALYSIS INFORMATION

- Analysis is based on data through week 48[22]
- The chart displays TEAEs independent of attribution of treatment or disease. The percentage shown in this graph does not match the Adverse Reactions table on page 18
- TEAEs are undesirable events not present prior to medical treatment, or an already present event that worsens either in intensity or frequency following the treatment

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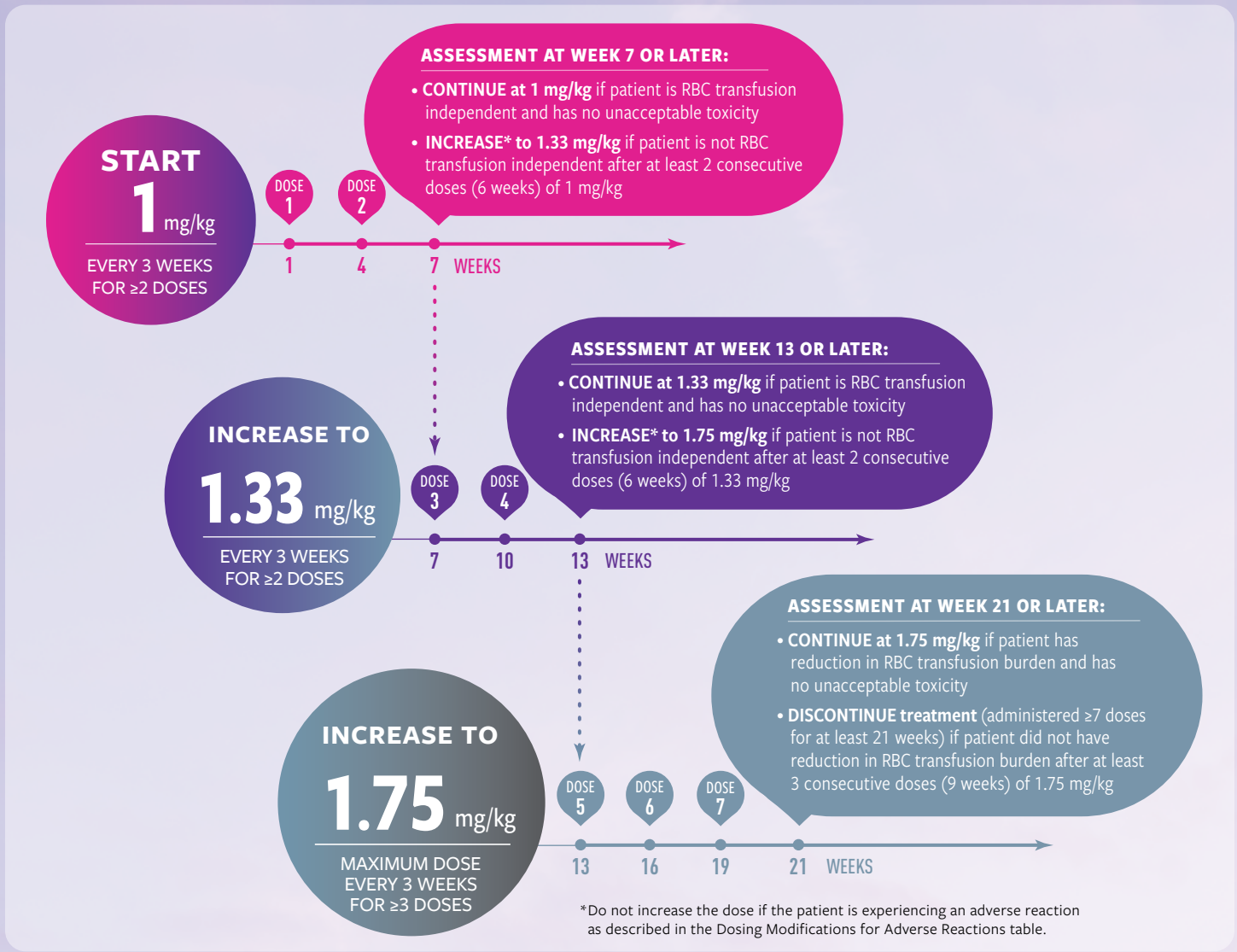
Treatment with REBLOZYL should continue as long as patients experience clinical benefit[1,22]

ASSESS AND REVIEW PATIENTS' Hgb AND TRANSFUSION RECORD PRIOR TO EACH ADMINISTRATION[1]

- If an RBC transfusion occurred prior to dosing, use the pretransfusion Hgb for dose evaluation[1]
- If a patient experiences a dose delay due to Hgb increase, measure Hgb every week[22]

REBLOZYL dose titration for response[1]

- Increase REBLOZYL dose with the goal of achieving transfusion independence, but do not increase if patient is experiencing adverse reactions. Discontinue REBLOZYL after 3 doses at the maximum dose if no transfusion burden reduction or if unacceptable toxicity occurs



*Do not increase the dose if the patient is experiencing an adverse reaction as described in the Dosing Modifications for Adverse Reactions table.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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Dose modifications for predose Hgb levels or rapid Hgb rise[1]

	REBLOZYL Dosing recommendation
Predose Hgb is **≥11.5 g/dL** in the absence of transfusions	• Interrupt treatment • Restart when the Hgb is no more than **11 g/dL**
Increase in Hgb **>2 g/dL** within 3 weeks in the absence of transfusions and:	
• current dose is **1.75 mg/kg**	• Reduce dose to **1.33 mg/kg**
• current dose is **1.33 mg/kg**	• Reduce dose to **1 mg/kg**
• current dose is **1 mg/kg**	• Reduce dose to **0.8 mg/kg**
• current dose is **0.8 mg/kg**	• Reduce dose to **0.6 mg/kg**
• current dose is **0.6 mg/kg**	• Discontinue treatment

Dose increases in the event of loss of response[1]

- If, upon dose reduction, the patient loses response (ie, requires a transfusion) or Hgb concentration drops by 1 g/dL or more in 3 weeks in the absence of transfusion, increase the dose by 1 dose level
- Wait a minimum of 6 weeks between dose increases
- Dose increases to 1.33 mg/kg and subsequently to 1.75 mg/kg may occur at any time during treatment after patients have received at least 2 consecutive doses at the prior lower dose level
- **Do not increase the dose more frequently than every 2 consecutive doses (6 weeks) or beyond the maximum dose of 1.75 mg/kg**

Discontinue treatment if no reduction in transfusion burden is observed[1]

- Discontinue REBLOZYL if a patient does not experience a decrease in transfusion burden after 3 doses (9 weeks of treatment) at the maximum dose level or if unacceptable toxicity occurs at any time

If a planned administration of REBLOZYL is delayed or missed[1]

- Administer REBLOZYL as soon as possible and continue dosing as prescribed, with at least 3 weeks between doses

REBLOZYL dosing modifications for adverse reactions[1]

	REBLOZYL Dosing recommendation*
Grade 3 or 4 hypersensitivity reactions	• Discontinue treatment
Other Grade 3 or 4 adverse reactions	• Interrupt treatment • When the adverse reaction resolves to no more than Grade 1, restart treatment at the next lower dose level† • If the dose delay is >12 consecutive weeks, discontinue treatment

*Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.
†Per dose reductions in table above.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Grade ≥3 (≥2%) adverse reactions included fatigue, hypertension, syncope and musculoskeletal pain. A fatal adverse reaction occurred in 5 (2.1%) patients.

The most common (≥10%) adverse reactions included fatigue, musculoskeletal pain, dizziness, diarrhea, nausea, hypersensitivity reactions, hypertension, headache, upper respiratory tract infection, bronchitis, and urinary tract infection.

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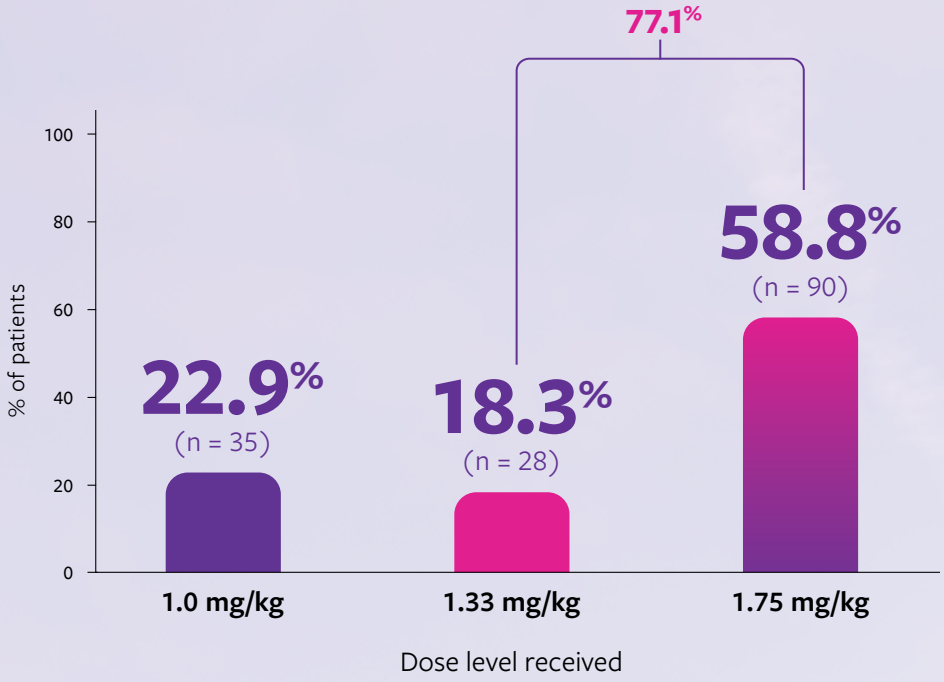
Highest dose level of REBLOZYL received by patients in the MEDALIST trial

ASSESSMENT OF HIGHEST DOSE LEVEL RECEIVED BY ALL PATIENTS RECEIVING REBLOZYL (N = 153)[25]



77.1%
(n = 118/153)

of all patients receiving REBLOZYL had their dose increased at least once

The majority of patients (58.8%, n = 90/153) received 2 dose increases

Data cutoff: May 8, 2018.

Median time to dose escalation

9 weeks (63 days) — time to dose escalation from **1 mg/kg to 1.33 mg/kg** (range 39–419 days)[25]

15 weeks (106 days) — time to dose escalation from **1 mg/kg to 1.75 mg/kg*** (range 81–359 days)[25]

*This was a stepwise increase from 1 mg/kg to 1.33 mg/kg and then to 1.75 mg/kg.

Data cutoff: May 8, 2018.[25]

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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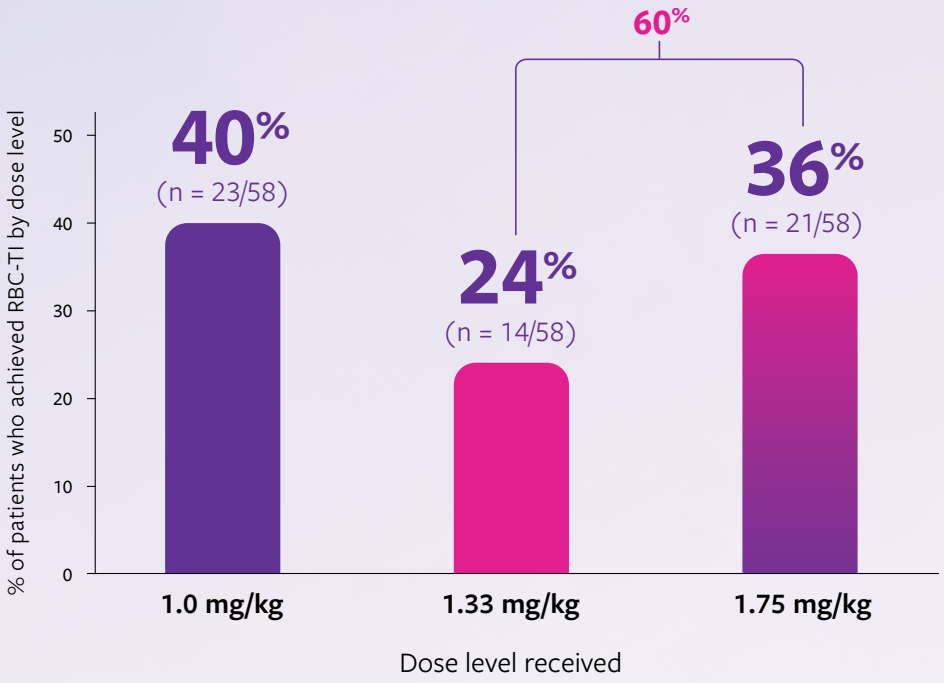
Primary endpoint responder analysis: Responses by REBLOZYL dose levels in patients achieving RBC-TI ≥8 weeks during weeks 1 to 24

ASSESSMENT OF DOSE LEVEL AT WHICH REBLOZYL RESPONDERS ACHIEVED RBC-TI ≥8 WEEKS DURING WEEKS 1 TO 24 (N = 58)[22]



60%
(n = 35/58)

of responders* required at least 1 dose increase

*Patients achieving RBC-TI ≥8 weeks during weeks 1 to 24 (n = 58/153).

ANALYSIS LIMITATIONS

- The primary endpoint of the study was transfusion independence defined as the absence of any RBC transfusion during any consecutive 8-week period occurring within weeks 1 through 24[1]
  - Primary endpoint data: 37.9% (58/153) for REBLOZYL vs 13.2% (10/76) for placebo
- Patients may have experienced multiple periods of response intermittently between periods without response over the 24-week assessment period and extension phase through 25 to 48 weeks[22]
- All patients in both arms were eligible to receive BSC, which included RBC transfusions as needed[1]
- These exploratory analyses should not be interpreted to determine treatment difference between arms in these select endpoints because of potential selection bias, insufficient sample size, and a higher probability of making a false positive finding

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) 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.

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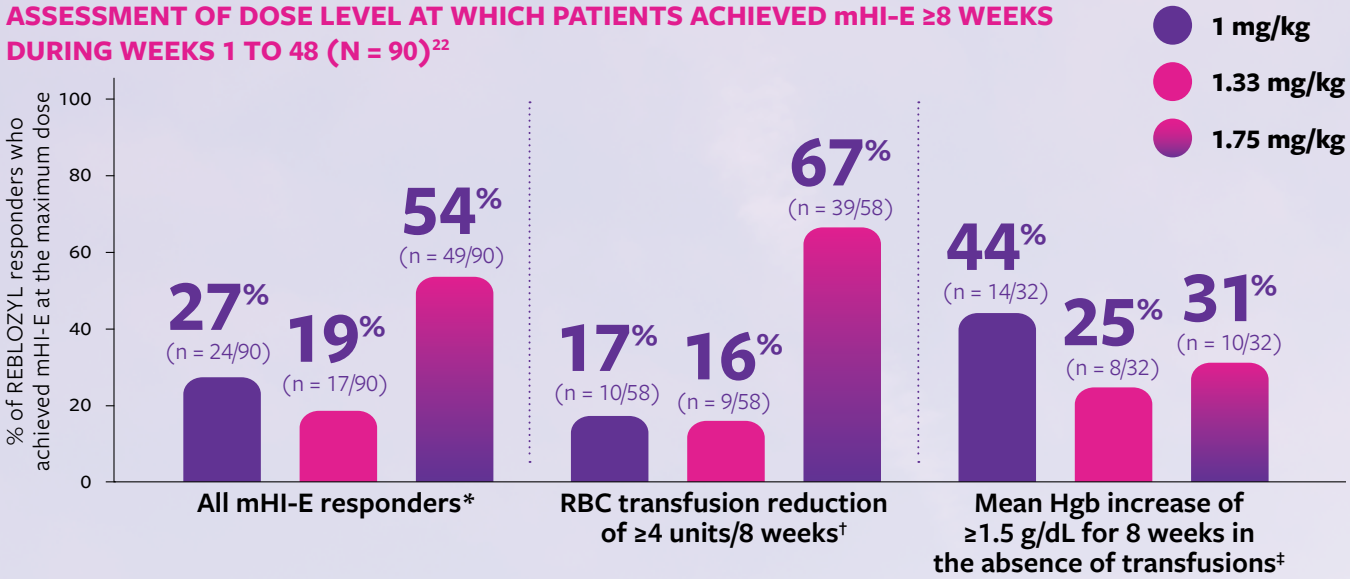
Additional analysis: Responses by REBLOZYL dose levels in patients achieving mHI-E ≥8 weeks during weeks 1 to 48 (n = 90/153)

ASSESSMENT OF DOSE LEVEL AT WHICH PATIENTS ACHIEVED mHI-E ≥8 WEEKS DURING WEEKS 1 TO 48 (N = 90)[22]



*Percentage based on number of all patients receiving REBLOZYL who achieved mHI-E during weeks 1 to 48 (n = 90/153).
†Percentage based on number of patients receiving REBLOZYL with baseline RBC transfusion burden of ≥4 units/8 weeks who achieved mHI-E during weeks 1 to 48 (n = 58/107).
‡Percentage based on number of patients receiving REBLOZYL with baseline RBC transfusion burden of <4 units/8 weeks who achieved mHI-E during weeks 1 to 48 (n = 32/46).

73% (n = 66/90) of patients who achieved mHI-E ≥8 weeks during weeks 1 to 48 received at least 1 dose increase[22]

ANALYSIS LIMITATIONS

- The primary endpoint of the study was transfusion independence defined as the absence of any RBC transfusion during any consecutive 8-week period occurring within weeks 1 through 24[1]
  - Primary endpoint data: 37.9% (58/153) for REBLOZYL vs 13.2% (10/76) for placebo
- The mHI-E analysis is a broader analysis than transfusion independence. The analysis included patients that did not meet the primary endpoint of transfusion independence[22]:
  - Those who achieved transfusion reduction of ≥4 units over 8 weeks (with higher baseline transfusion burden)
  - Those whose Hgb increased by ≥1.5 g/dL for 8 weeks in the absence of transfusions (with lower baseline transfusion burden)
- Patients may have experienced multiple periods of response intermittently between periods without response over the 24-week assessment period and extension phase through 25 to 48 weeks[22]
- All patients in both arms were eligible to receive BSC, which included RBC transfusions as needed[1]
- These exploratory analyses should not be interpreted to determine treatment difference between arms in these select endpoints because of potential selection bias, insufficient sample size, and a higher probability of making a false positive finding

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Hypertension

Hypertension was reported in 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. In adult patients with MDS with normal baseline blood pressure, 26 (29.9%) patients developed SBP ≥130 mm Hg and 23 (16.4%) 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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Discontinuations and dose modifications in the safety population

- The safety of REBLOZYL at the recommended dose and schedule was evaluated in 242 patients with MDS-RS (n = 192) or other myeloid neoplasms (n = 50)[1]

DISCONTINUATIONS AND DOSE MODIFICATIONS IN THE SAFETY POPULATION[1]

4.5% (n = 11/242)

Discontinuations due to adverse reactions

of patients who received REBLOZYL discontinued treatment due to an adverse reaction

2.9% (n = 7/242)

Dose reductions due to adverse reactions

of patients who received REBLOZYL required a dose reduction due to an adverse reaction

REBLOZYL dose delays and reductions due to Hgb levels

8.5% (n = 13/153)

of patients receiving REBLOZYL required dose delays due to predose Hgb levels ≥11.5 g/dL[25]

2.0% (n = 3/153)

of patients receiving REBLOZYL required dose reductions due to Hgb increase ≥2 g/dL vs predose Hgb level of prior treatment cycle[25]

Data cutoff: July 1, 2019.[25]

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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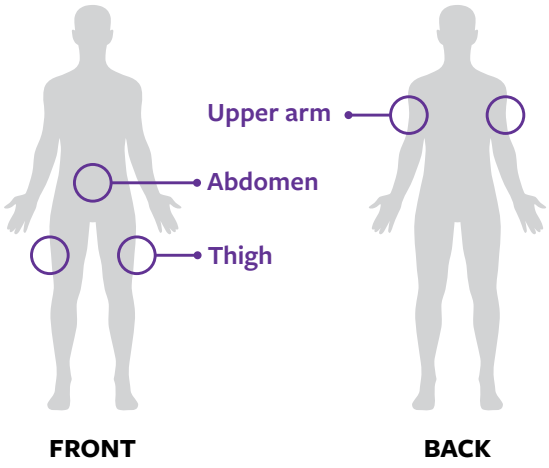
Instructions for subcutaneous administration

REBLOZYL IS ADMINISTERED SUBCUTANEOUSLY AND IS AVAILABLE IN 2 VIAL SIZES (25 mg AND 75 mg)[1]

- Prior to injection, allow solution to reach room temperature for a more comfortable injection

REBLOZYL SHOULD BE RECONSTITUTED AND ADMINISTERED BY A HEALTHCARE PROFESSIONAL[1]

Step 1: **Verify correct dose for the patient[1]**	• Calculate the exact total dosing volume of 50 mg/mL solution required for the patient
Step 2: **Plan and prep for injection[1]**	• Slowly withdraw the dosing volume of the reconstituted REBLOZYL solution from the single-dose vial(s) into a syringe • Divide doses requiring larger reconstituted volumes (ie, >1.2 mL) into separate similar-volume injections and inject into separate sites
Step 3: **Subcutaneous administration[1]**	• If multiple injections are required, use a new syringe and needle for each SC injection **Administer REBLOZYL into one or more of the following sites by SC injection:** 

NOTE: DISCARD ANY UNUSED PORTION. DO NOT POOL UNUSED PORTIONS FROM THE VIALS. DO NOT ADMINISTER MORE THAN 1 DOSE FROM A VIAL. DO NOT MIX WITH OTHER MEDICATIONS.[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Grade ≥3 (≥2%) adverse reactions included fatigue, hypertension, syncope and musculoskeletal pain. A fatal adverse reaction occurred in 5 (2.1%) patients.

The most common (≥10%) adverse reactions included fatigue, musculoskeletal pain, dizziness, diarrhea, nausea, hypersensitivity reactions, hypertension, headache, upper respiratory tract infection, bronchitis, and urinary tract infection.

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Storing REBLOZYL

REBLOZYL REQUIRES COLD STORAGE

STORAGE OF UNRECONSTITUTED VIAL[1]

- Store unreconstituted vials refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light
- Do not freeze

STORAGE OF RECONSTITUTED SOLUTION[1]

- If the reconstituted solution is not used immediately, store at room temperature at 20°C to 25°C (68°F to 77°F) in the original vial for up to 8 hours. Discard if not used within 8 hours of reconstitution
- Alternatively, store refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours in the original vial
  - Remove from refrigerated condition 15 to 30 minutes prior to injection to allow solution to reach room temperature for a more comfortable injection
  - Discard if not used within 24 hours of reconstitution
- Do not freeze the reconstituted solution

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) 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.

Hypertension

Hypertension was reported in 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. In adult patients with MDS with normal baseline blood pressure, 26 (29.9%) patients developed SBP ≥130 mm Hg and 23 (16.4%) patients developed DBP ≥80 mm Hg. Monitor blood pressure prior to each administration. Manage new or exacerbations of preexisting hypertension using anti-hypertensive agents.

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

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Please click here for full Prescribing Information for REBLOZYL.

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BMS Access Support® Can Provide Patient Access and Reimbursement Assistance

Bristol Myers Squibb is committed to helping patients gain access to their prescribed BMS medications. That's why we offer BMS Access Support. BMS Access Support provides resources to help patients understand their insurance coverage. In addition, we can share information on sources of financial support, including co-pay assistance for eligible commercially insured patients.

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Find out how BMS can work with patients and their healthcare providers to help access a prescribed BMS medication.

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Additional Resources

We provide videos, tools, and other resources that may help with your access and reimbursement needs.

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The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and the patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

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REBLOZYL is indicated for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

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

SELECT WARNINGS AND PRECAUTIONS

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