Clinical response and duration in the RS-subgroups

Jamie Koprivnikar, MD
John Theurer Cancer Center Hackensack University Medical Center
Hackensack, NJ

REBLOZYL or luspatercept is indicated for the treatment of anemia without previous erythropoiesis stimulating agent use in adult patients with very low to intermediate risk myelodysplastic syndrome, who may require regular red blood cell transfusions. REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

This promotional educational activity is brought to you by Bristol Myers Squibb and is not certified for continuing medical education. I am a paid speaker for Bristol Myers Squibb and must present information in compliance with FDA requirements applicable to Bristol Myers Squibb.

Hi, I'm Jamie Koprivnikar, a hematologist oncologist at the John Theurer Cancer Center at Hackensack University Medical Center.

Erythropoiesis stimulating agents, also known as ESAs have been commonly used for the treatment of anemia in patients with non-deletion (5q) lower risk myelodysplastic syndromes. However, data from a real-world retrospective analysis study demonstrated that approximately 7 out of 10 patients failed to respond to ESAs and 53% of patients in this analysis were RS negative.

With the approval of REBLOZYL as a first-line option versus an active comparator, the treatment paradigm has shifted, making it possible to fulfill long standing unmet needs and low-risk MDS having this treatment choice with a broad indication where you don't need to think about specific subgroups, allows healthcare professionals like myself to competently prescribe REBLOZYL for my eligible ESA-naive patients regardless of their ring sideroblasts status or serum erythropoietin levels.

When I'm making treatment decisions, I'm always looking for appropriate, efficacious and safe options for my patients. In the case of REBLOZYL, the safety and efficacy were demonstrated in commands, a phase 3 open label randomized active controlled clinical trial of REBLOZYL versus epoetin alfa in ESA-naive adult patients with anemia due to lower risk MDS.

The clinical trial met the composite primary endpoint of red blood cell transfusion independence for 12 weeks and a mean hemoglobin increase of greater than or equal to 1.5g per deciliter. As the data show, nearly twice as many patients achieved RBC transfusion independence with REBLOZYL and a mean hemoglobin increase demonstrating superiority versus epoetin alfa.

Patients who responded well to treatment with REBLOZYL also had lasting transfusion independence, with a median duration of 2.5 years, compared with 1.5 years for patients on epoetin alfa. That additional year of transfusion independence has proved quite meaningful to my patients with low-risk MDS.

REBLOZYL also demonstrated higher response rates across all secondary efficacy endpoints. When you review the data from the subgroup analysis of the commands trial, you'll notice that the clinical trial included 99 patients who were ring sideroblasts negative. Notably, this is the most of any phase 3 study conducted in patients with lower risk MDS.

The durable responses observed with REBLOZYL in the intention to treat population are also reflected in the subgroup data for RS negative patients. As you can see, the response rate among patients in the RS negative subgroup was 46.9% with REBLOZYL and 50% with epoetin alfa. However, it's important that you know that the subgroup analysis was not powered to detect statistically significant differences in the response rates or to draw conclusions.

Although the response rates were numerically similar, as shown, more than 50% of patients on REBLOZYL remain transfusion independent and the median duration was not reached, whereas in the epoetin alfa group, more than 50% of RS negative patients lost transfusion independence, with the median duration being 95.1 weeks.

Also, as you formulate a treatment plan, it may be helpful to know that the 2023 NCCN Guidelines in Oncology recommend luspatercept as a category 2A therapy for the first-line treatment of RS negative patients with symptomatic anemia due to lower risk MDS.

Now let's have a look at the safety data from the full analysis of the commands trial. As you may have noticed, adverse events in the clinical trial were grade 1 or 2 mild or moderate. The most common all grade adverse events occurring in more than 10% of patients included fatigue, diarrhea, peripheral edema, nausea, dyspnea, asthenia, dizziness, headache, back pain, Covid 19, and anemia.

The most common grade 3 or higher adverse events occurring in more than 2% of patients included hypertension, dyspnea, Covid 19 pneumonia, thrombocytopenia, neutropenia, and anemia.

Selected laboratory abnormalities. The change from grade 0 to 2 at baseline to greater than grade 2 at any time during the studies, and at least 10% of patients were glomerular filtration rate and total bilirubin increased. Other clinically relevant adverse events reported and fewer than 5% of patients were injection site reactions, including erythema, pruritus, and rash.

Taking this information together with my clinical experience, I feel that REBLOZYL can be administered and managed safely. For health care professionals evaluating first-line treatment options, the superior efficacy and lasting duration of transfusion independence with REBLOZYL in the intention to treat population, combined with the demonstrated safety profile and real world evidence, help make it an appropriate treatment choice for patients with symptomatic anemia due to lower risk MDS, irrespective of ring sideroblasts status or erythropoietin level.

REBLOZYL is indicated for the treatment of anemia without previous erythropoietin stimulating agent use in adult patients with very low to intermediate risk myelodysplastic syndromes who may require regular red blood cell transfusions.

REBLOZYL not indicated for use as a substitute for red blood cell transactions in patients who require immediate correction of anemia in adult patients with beta thalassemia.

Thromboembolic events were reported in 3.6% of REBLOZYL treated patients. Thromboembolic events include a deep vein thrombosis, pulmonary embolism, portal vein thrombosis, and ischemic stroke. Patients with known risk factors for thromboembolism may be up for the risk of thromboembolic conditions.

Consider thromboprophylaxis in patients at increased risk of thromboembolic events. Monitor patients for signs and symptoms of thromboembolic events and institute treatment promptly.

Hypertension was reported in 11.4% of REBLOZYL treated patients across clinical studies. The incidence of grade 3 to 4 hypertension ranged from 2% to 9.6% in ESA-naive adult patients with MDS with normal baseline blood pressure, 36% of patients developed a systolic blood pressure of 140 millimeters of mercury or higher, and 6% of patients developed diastolic blood pressure of 80 millimeters of mercury or higher, monitor blood pressure prior to each administration.

Manage new or exacerbations of preexisting hypertension using antihypertensive agents. REBLOZYL may cause fetal harm when administered to a pregnant woman.

REBLOZYL cause increased post implantation loss, decreased litter size, and increased incidence of skeletal variations in pregnant rat and rapid 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. Group 3 or higher adverse reactions included hypertension and dyspnea. These were observed in 2% or more of patients.

The most common all grade adverse reactions included diarrhea, fatigue, hypertension, peripheral edema, nausea and dyspnea. These were observed in 10% or more patients.

It is not known whether REBLOZYL is excreted into human milk or absorbed systemically after ingestion by 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.

Abuse of REBLOZYL may be seen in athletes or the effects erythropoiesis misuse of drugs that increase erythropoiesis, such as REBLOZYL by health persons, may lead to polycythemia, which may be associated with life threatening cardiovascular complications.