Using sEPO ≤200 as a parameter in the LR-MDS treatment algorithm

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REBLOZYL 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 cells transfusion.

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

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Hello, I'm George Yaghmour from USC Norris Comprehensive Cancer Center and Hospital in Los Angeles, California. Today I'm excited to talk about REBLOZYL and why it has emerged as a strong first-line treatment option for patients in my practice with symptomatic anemia due to non-deletion, (5q) lower-risk MDS.

We will also discuss the use of REBLOZYL in the exploratory subgroup of patients with baseline serum erythropoietin less than or equal to 200 unit per liter. REBLOZYL was approved for first-line use in adult patients, regardless of ring sideroblasts status, and the serum erythropoietin levels. Approval was based on data from the commands clinical trial.

The accentuates the clinical value of REBLOZYL, giving health care professional the opportunity to improve treatment outcomes for their patients. It's great when you have broad indication for a medication like REBLOZYL.

The commands trial was a phase 3 open label, randomized, active, controlled clinical trial of REBLOZYL versus epoetin alfa in ESA-naive adult patient with anemia due to low-risk MDS.

Patients were randomly assigned in a 1 to 1 fashion to receive REBLOZYL at starting dose of 1 mg/kg subcutaneously, with titration up to 1.75 mg/ kg once every 3 weeks, or epoetin alfa at starting dose of 450 international unit per kilogram with titration up to 1050 international units per kilogram weekly for 24 weeks.

The primary composite endpoint was RBC transfusion independence for 12 consecutive weeks during weeks 1 to 24, and mean hemoglobin increase of greater than or equal to 1.5g/dL. Other secondary endpoints, along with the eligibility criteria are also shown on screen.

Now let's have a look at the efficacy data. As you can see, 60.4% of patients in the REBLOZYL arm were transfusion independent for at least 12 weeks and had a mean hemoglobin increase of greater than or equal to 1.5g/dL, compared to 34.8% of the patient in the EPO alfa arm.

This data demonstrates superiority of REBLOZYL versus EPO alfa, with nearly twice as many patients showing clinical response. Let's now discuss the secondary endpoints.

When we review the duration of transfusion independence the median was 2.5 years for patients who responded to treatment with REBLOZYL, versus 1.5 years for patients on EPO alfa.

This is a durable, transfusion free period and an important treatment consideration for me. Note that the analysis limitation of duration of RBC-TI ≥ 12 was not powered to detect statistical significance.

REBLOZYL also demonstrated higher response rates across all secondary efficacy endpoints. Now let's switch to subgroup analysis data from the commands trial, specifically for patients with low serum erythropoietin less than or equal to 200 units per liter at baseline.

As shown, the REBLOZYL arm had a response rate of 66.2%, and the EPO alfa arm had a response rate of 41%.

However, please note that the exploratory analysis shouldn't be interpreted to determine treatment difference between arms in this subgroup because of limited sample size, lack of statistical hypothesis testing, and the increased probability of false positive finding.

Next to the duration of transfusion independence was 140.1 weeks for REBLOZYL and 89.7 weeks for EPO alfa. While the subgroup analysis was not powered to detect statistically significant difference in response rate to draw conclusions, this data helps me feel confident in treating my patients.

Since we reviewed the efficacy information for REBLOZYL, let's go over some of the safety data from the full analysis of the commands trial.

As you may have noticed, most adverse events in the clinical trial were grade 1 or 2. The most common more than 10% all grade adverse events included fatigue, diarrhea,

peripheral edema, nausea, dyspnea, asthenia, dizziness, headache, back pain, Covid 19, and anemia.

The most common 2% or more grade 3 or more adverse events included hypertension, dyspnea, Covid 19, pneumonia, thrombocytopenia, neutropenia, and anemia.

Selected lab abnormalities that change from grade 0 to 2 at baseline to grade 2 or more at any time during the studies in at least 10% of patients were glomerular filtration rate and total bilirubin increased.

Other clinically relevant adverse events reported in less than 5% of patients are injection site reaction, including erythema, pruritus, and rash.

Given the superior efficacy, long lasting transfusion dependance, and demonstrated safety in the intent to treat population with REBLOZYL,

I can confidently prescribe and recommend its use in the first-line setting for appropriate patients with symptomatic anemia due to non deletion (5q) low-risk MDS. REBLOZYL is indicated for the treatment of anemia without previous erythropoiesis stimulating agent use in adult patients with very low to intermediate risk myelodysplastic syndromes who may require regular red blood cell transfusions.

REBLOZYL is not indicated for use as a substitute for red blood cell transfusions 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. From embolic events include a deep vein thrombosis, pulmonary embolism, portal vein thrombosis, and ischemia 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 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.

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 for the effects of 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.