Real-life patient showcasing clinical best practices for dosing REBLOZYL

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Welcome to Real-life patient cases showcasing clinical best practices for dosing REBLOZYL.

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Hi, I'm Doctor Chris Benton, a board-certified hematologist/oncologist at Rocky Mountain Cancer Centers in Colorado. I've been in practice for 20 years and specializing in the treatment of hematologic malignancies. Working with patients with these types of malignancies feels like something I was born to do. I love coming to work every day, I love treating our MDS patients and I love growing our blood cancer programs.

Over the years, I've felt very connected and invested in the advancement of current treatments for patients with anemia due to lower-risk myelodysplastic syndromes, or low-risk MDS.

I am motivated by the scientific advances and the profound impact that blood cancers like low-risk MDS have on my patients. In my personal practice, I use REBLOZYL, also known as luspatercept-aamt, for patients with anemia due to low-risk MDS. REBLOZYL® (luspatercepts-aamt) is indicated for the treatment of anemia without previous erythropoiesis stimulating agent use, or 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 red blood cell transfusions, and patients who require immediate correction of anemia. In my experience, REBLOZYL has now become the standard of care for the first-line treatment of my patients with anemia due to low-risk MDS. The head-to-head superior efficacy of REBLOZYL over epoetin alfa was demonstrated in the phase 3 COMMANDS study, which showed nearly double the response compared to that of patients treated with epoetin alfa. Today, I will share how

REBLOZYL dose escalation, and dose reduction have helped my patients achieve response, which is defined as Hgb increase and transfusion independence.

Prior to starting my patients on a REBLOZYL or any other therapy, I always discuss the efficacy and safety associated with the treatment, along with the treatment plan that can guide our discussion and help patients understand their treatment goals. In terms of efficacy, I set expectations that we are targeting Hgb increase and patients transfusion independence. Overall, my mission is to help get patients to their treatment goals. In terms of the safety profile of REBLOZYL, I highlight that REBLOZYL has potential side effects. The most common adverse reactions include fatigue, peripheral edema, diarrhea, nausea, hypertension, dyspnea, and Covid 19. Then we set up their first appointment, which always includes labs. REBLOZYL dosing begins with a recommended starting dose of 1mg/kg, administered by way of subcutaneous injection every three weeks. The starting dose is just that, a starting dose. Finding a therapeutic dose for each patient is critical. For most patients, this will actually mean a dose increase, and for some other patients, a dose reduction. It's important to highlight that doses were escalated to achieve responses in the COMMANDS trial.

Now let's discuss one of my patients, Walter, who is being treated with REBLOZYL and needed a dose increase to achieve the goals of increasing Hgb levels and achieving transfusion independence. Walter is 72 years old, has low-risk MDS, which is ring sideroblast negative. He used to enjoy playing golf and staying physically active, but his anemia caused persistent fatigue and shortness of breath, which made it difficult for him to continue with these activities. He also has gastrointestinal polyposis and is under the care of a GI specialist. So this is a patient with real complexities. Walter presented with a Hgb of 9.2 and a baseline serum EPO level of 104.

At one point, he required blood transfusions based on his symptoms and labs, I opted to treat him with REBLOZYL to give him a better chance than with epoetin alfa at achieving the Hgb increase and transfusion independence, based on the COMMANDS data that we previously discussed. Based on the Prescribing Information for REBLOZYL, in the absence of transfusion, the predose Hgb should not exceed 11.5g/dL. Additionally, according to the National Comprehensive Cancer Network, or NCCN, the recommendation is to treat to a Hgb range of 10-12 g/dL--not exceeding 12g/dL. In my practice, my team and I closely monitor patients. In the beginning of treatment, I schedule a clinic visit with my patients around Weeks 7-9, typically before the third dose, where they would be eligible for a dose increase if needed. But of course, before each dose, my team is running a CBC, checking his Hgb, asking that patient if he had a transfusion, and asking about his tolerance to REBLOZYL.

When I started Walter on a REBLOZYL treatment, he initially responded well, he was transfusion free for approximately 18 weeks, with Hgb levels maintaining around 11.3g/dL. However, after 6 doses of 1 mg/kg every three weeks, I noticed that his Hgb level was

declining and he appeared to be losing his initial response to REBLOZYL. Based on my clinical judgment, his falling Hgb levels, and his symptoms, I believed he required a transfusion. It is important to consider the clinical need for transfusion rather than the ability to provide one. As you know, different institutions may only allow transfusions for patients with a Hgb below a certain level. For Walter, his Hgb was too high to transfuse, but based on his lost response, we increased the dose to 1.33 mg/kg. Of course, we continued to monitor his Hgb weekly following this dose increase, after 9 weeks his Hgb levels rose to 10.6 g/dL and we were able to regain a response once again. We plan to continue him on this dose while my team and I monitor his progress closely based on an every-12-week basis. If Walter loses response again and it is determined that he requires transfusions, I would increase the dose of REBLOZYL to the maximum of 1.75 mg/kg and continue treatment for at least 3 doses.

It is important to recognize when to discontinue treatment if there is no reduction in transfusion burden from baseline or no increase in Hgb is observed after three consecutive doses at the maximum dose, I would consider stopping therapy. I want to emphasize that this approach reflects my personal practice experience with the patients I treat, and outcomes may vary depending on the patient. Let's turn our attention to another one of my patients with whom a dose reduction was necessary.

I've been treating Mary for over three years. She's 87 years old, loves spending time with her granddaughter, and enjoys tending to her backyard garden. However, since she was diagnosed with anemia due to low-risk MDS, she has been finding it difficult to engage in routine activities and hobbies that she previously enjoyed with ease. She complains that she can't rake the soil and plant flowers without having to take frequent breaks. Her Hgb was 8.3 g/dL, her baseline serum EPO was 80 and, in my clinical opinion, she was at the point of needing transfusions. Together we decided to start treatment with REBLOZYL.

Since I began treating Mary with REBLOZYL at 1 mg/kg, I have had my infusion nurses monitor her Hgb levels and transfusion needs, notifying me immediately if a dose escalation or reduction may be needed. Her Hgb has been stable at 11 g/dL this is aligned with our treatment goals of increased Hgb and transfusion independence. As with all my patients, we always check the Hgb, transfusion requirements, and tolerability before each dose. Despite adhering to my scheduling best practice, in reality, patients sometimes still miss appointments. Mary was one of those patients who missed a few appointments during her first months of treatment, which contributed to some variability in her Hgb increasing and decreasing.

However, after receiving regular doses of REBLOZYL 1 mg/kg every 3 weeks, her Hgb rapidly rose to 14.4 g/dL. The recent jump in Hgb met the criteria of more than 2 g/dL within a three-week period, and above the threshold of 11.5 g/dL per the REBLOZYL full Prescribing Information. My nurse team is actually really good about flagging high Hgb in such cases. This was a signal to pause until the Hgb fell to 11g/dL and restart treatment as soon as

possible at 0.8 mg/kg. It's important that I stay in constant contact with my team about issues like this. Treatment with REBLOZYL will likely mean dose escalation and reduction for patients along the way, so it's important that I talk to the nurse team, as well as the pharmacists, to ensure our patients are getting the best possible care. If, after reducing the dose, I observed that the patient is losing response meaning that they need a transfusion or their Hgb drops by 1 g/dL or more within 3 weeks, I may need to increase the dose by one level. On the other hand, I also find dose reduction to be an important tool to help patients stay on an every-3-week dosing schedule and avoid massive fluctuations in Hgb. Dose reduction may also be appropriate if Grade 3 or 4 side effects occur. If one of my patients has concerns about side effects prior to dose escalation or reduction, I'll happily discuss it with them. In Mary's case, she continues to maintain response and has not encountered any Grade 3 or 4 side effects at the 0.8 mg/kg dose, so I have kept her at that dose. In summary, dosing REBLOZYL requires careful consideration of the patient's response and any side effects.

It's a balance between increasing the dose to maximize efficacy and decreasing the dose if tolerability becomes a concern. Monitoring Hgb levels and transfusion needs will guide these decisions. Based on my experience with the once every-three-week dosing of REBLOZYL, most of my patients achieve Hgb increase, transfusion independence, and feel better overall. For my colleagues, this highlights how a personalized, hands-on approach helps increase Hgb while reducing the need for transfusions.

Thank you for your time today. By following these dosing techniques for REBLOZYL, I am confident that we can help our patients with low-risk MDS achieve better control of their anemia and help improve clinical outcomes.

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 (TEE) were reported in 8/223 (3.6%) of rebel cell treated patients. Thromboembolic events (TEE) include a deep vein thrombosis, pulmonary embolism, portal vein thrombosis, and ischemic stroke. Patients with known risk factors for thromboembolism may be at further increased risk of thromboembolic conditions. Considered 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-naïve adult patients with MDS with normal baseline blood pressure, 36% of patients developed a systolic blood pressure of 140mm of mercury or higher, and 6% of patients developed diastolic blood pressure of 80mm of mercury or higher. Monitor blood pressure

prior to each administration. Manage new or exacerbations of preexisting hypertension using anti-hypertensive agents. 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. Grade 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 of patients.

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.

Abuse of REBLOZYL, which 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.