Branded Episode 2:
An Approach to Complex Cases in Hemophilia B
(Runtime: 21:33)

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This podcast is intended for US healthcare professionals only.

An Approach to Complex Cases in Hemophilia B

HOST:
Hello! My name is Ben Barker, and I'm a Thought Leader Liaison at Sanofi, Rare Blood Disorders. I'm happy to be hosting THE FACTOR FORUM podcast today, a series *for* healthcare professionals, *by* healthcare professionals. Today, I am joined by hematologist Dr. Guy Young. Dr. Young is being compensated by Sanofi for his participation in this podcast, and the content was developed in conjunction with him.

He is sharing his personal experiences from his practice and with ALPROLIX® [Coagulation Factor IX (Recombinant), Fc Fusion Protein]. Over the course of this podcast, you will hear Important Safety Information about ALPROLIX. Now, let's welcome Dr. Young.

GY:
Hello, Ben. Thank you for having me and it's great to be here.

HOST:
In today's episode, we will be exploring some common challenges that can arise when treating patients with moderate to severe hemophilia B. In his own practice, Dr. Young has found that comorbidities, age, and concomitant medications are just a few of the complexities that can impact these patients. We'll be discussing his perspective and how he manages some of his more intricate cases.

Dr. Young, tell us a little bit about yourself

GY:
I'm the Director of the Hemostasis and Thrombosis Center at Children's Hospital Los Angeles, and I'm also a Professor of Pediatrics at the University of Southern California Keck School of Medicine. I've been at this institution for 17 years and have been taking care of patients with hemophilia for about 22 years. I've been involved in the community for a long time, including patient care, research, and education.

MUSIC BUG

HOST:
In your experience, what makes treating hemophilia B complicated or challenging?

GY:
Well, I think there's a number of challenges. Some of those are just the nature of available treatments and others are really more patient specific.

When it comes to hemophilia B, there is no one-size-fits-all treatment, which frankly is the same for hemophilia A. Patients may require different types of treatments at different times, but the goal is as close to zero bleeds as possible. Finding the right treatment that works for a particular patient and, subsequently, the right regimen can be complex.

Factor infusions will continue to be a very real part of the hemophilia treatment landscape, and it's my job to make the process of maintaining factor levels as simple as possible for my patients. Although gene therapy was recently approved, there are some limitations that need to be considered. Certainly, it's not going to be right for every patient.

HOST:
Can you elaborate a little more about the complications certain patients face?

GY:
One example that's top of mind is the complexity of education. In my practice, we recently saw a newborn with hemophilia who was just a few weeks old. No family history. His parents had never heard of the word hemophilia and had no idea how to handle the diagnosis—where to begin, what to do. It's tough, because when you're responsible for educating and comforting them but also helping them understand the importance and benefits of prophylactic treatment. We want to help them see that their child can still have a normal life, but it's a big educational lift because they are really starting from zero.

It was a team effort to get them prepared and organized. We familiarized the parents with our individual roles and how we contribute to the overall care of their child. Providing the family with information about the disease and guidance on how to administer the infusions is, of course, extremely important.

If we take that same child and put them in a single-caregiver home where there are three other kids, it becomes even more difficult—for example, a mom who has two jobs, just trying to keep things going is challenging. That creates even more challenges, and having team members like social workers on hand really helps that situation.

HOST:
So, Dr. Young, what are some of the challenges when treating older patients?

GY:
I would say that the complex part of treating older patients with hemophilia is dealing with both chronic joint disease and chronic pain. In my opinion, the biggest obstacles to overcome with older patients is that most of them have established joint disease, and often times, the treatment options aren't ideal.

For knees, we have good options. You can have a knee replacement, which has proven to be effective. However, when it comes to elbows, or ankles, the two most commonly affected joints, there are really no similar alternatives. Instead of replacement, we have to manage the pain, which means long-term pain medicine that has its own risks and dangers.

That's one of the reasons why it's so important to protect patients against joint damage early. Getting patients on prophylaxis and making sure they are on a treatment that protects against joint bleeds is critical.

As we talk about treating older patients, we also need to be mindful of increased comorbidities. You have more arthritis, more cardiovascular issues. Cardiovascular issues are probably one of the more complicated issues I deal with every day. I have to balance the hemophilia treatment—which is meant to improve clotting—with their cardiovascular treatment, which in some cases is meant to thin the blood to minimize arterial blockages. How do you balance it? It's very, very challenging.

MUSIC BUG

HOST:
We know obesity is a growing problem for many countries around the world. How does excess weight impact your patients?

GY:
Obesity is a significant issue especially when it comes to the impact on joints. I see an increase in patients with elevated body mass index, and I believe that some of the joint bleeds are a direct result from excess weight. Unlike other joints, hips do not typically sustain frequent bleeds. They do on occasion, but not as often as knees, elbows, hands, and ankles. In my overweight patients, I see much higher incidents of hip bleeds, as well as higher-than-normal bleeds in other weight bearing joints like the ankles. This of course can lead to joint pain and chronic joint dysfunction.

For me, obesity is the one comorbidity that has a direct impact on patients with hemophilia. CV patients are a bit more challenging when it comes to really getting the dosage right, because you're balancing other medications. For overweight or obese patients, dosage isn't really the issue, as starting dosages are based on weight. It's really more about trying to keep those bleed rates low. So that means high adherence to treatment, working with the patient to lower their BMI, and making sure they're on a treatment to reduce joint bleeds.

HOST:
You touched on heart disease. Dr. Young, in your experience, what are some diseases, medications, or conditions that can make hemophilia B more difficult to treat?

GY:
In addition to cardiovascular disease, hypertension in general, seems to be a little bit more common in aging hemophilia patients. The common course of action is to treat hypertension first, by using antihypertensives. I treat each of my patients with CV on a case-by-case basis and work with their cardiologist or primary care physician to develop an individualized management plan for them. This helps ensure we balance the bleeding risk with antithrombotic protection, based on the cardiovascular risk profile and the severity of factor deficiency and/or bleeding phenotype. The cardiologist may put the patient on aspirin, an antiplatelet agent, or even an anticoagulant. Then, we try to optimize the hemophilia side of things, trying to get them as close as possible to normal factor levels and zero bleeds. So, if a patient were on an extended dosing regimen with an EHL, we might consider switching to a more frequent weekly regimen. The idea there is to minimize peaks and troughs and try to keep a steady state of factor with less drastic fluctuations. You don't really increase the peak level, but it's important to improve

the trough levels. Instead of their intravascular FIX levels going from 50% to 2%, they go from 50% to 15% by giving factor infusions more frequently than they might normally do.

MUSIC BUG

HOST:
Now that we've discussed some of the comorbidity complexities that can impact patients with hemophilia B, I'd love to talk about your experience with ALPROLIX as a treatment option.

As we begin to talk about ALPROLIX, a reminder that ALPROLIX is a recombinant DNA derived, coagulation Factor IX concentrate indicated in adults and children with hemophilia B for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes.

ALPROLIX is not indicated for induction of immune tolerance in patients with hemophilia B.

ALPROLIX is contraindicated in patients who have a known history of hypersensitivity reactions, including anaphylaxis, to the product or its excipients. Additional Important Safety Information will be shared throughout the podcast.

Dr. Young, we discussed the effects of obesity on patients. When you treat with ALPROLIX in obese patients, what influences and drives that approach?

GY:
Well, for me, joint data is a huge focus. Every joint bleed matters and can lead to further damage of the joints, so the goal is to try and strive for low joint bleeds, as well as low ABRs. That's a big reason why I advocate for prophylaxis. For example, we're talking about ALPROLIX today—adult and adolescent patients taking ALPROLIX prophylaxis saw big differences in the number of ABRs versus those using an on-demand regimen.

I want to make sure—especially in overweight or obese people with hemophilia—that their joints are protected as much as they can be. ALPROLIX has been shown effective in reducing the frequency of bleeds overall and in joint bleeds when used prophylactically. In the B-LONG clinical trial, the 26 patients aged 12 and older on individualized prophylaxis had a median joint ABR of 0.4, with an interquartile range, or IQR, between 0 and 3.2. They also had an overall median ABR of 1.4, with an IQR of 0 to 3.4, and had a median joint AsBR of 0, with an IQR of 0 to 1.7. It helps me feel confident that these bleed rates can help protect my patient's joints today and that we're protecting against long-term damage caused by recurrent bleeds.

MUSIC BUG

HOST:
You mentioned B-LONG. For context, B-LONG was a phase 3, open-label study that investigated the safety and efficacy of ALPROLIX in 123 previously treated patients aged ≥12 years with severe hemophilia B. The study included a fixed-interval, or weekly, arm with 63 patients; a fixed-dose, or interval-adjusted, arm with 29 patients; an on-demand arm with 27 patients; and a surgical arm with 12 patients. Listeners can see the podcast description for reference details. Now let's take a moment to review some Important Safety Information.

Allergic-type hypersensitivity reactions, including anaphylaxis, are possible with factor replacement therapies, and have been reported with ALPROLIX. Discontinue use of ALPROLIX if hypersensitivity symptoms occur, and initiate appropriate treatment.

GY:
Safety, of course, is another part of the equation for me, and ALPROLIX has a proven safety profile. I make sure to inform my patients about potential thromboembolic complications, especially if they are getting infusions through a central venous catheter. I also ensure that any of my previously treated patients starting ALPROLIX know that between 1% and 2% of patients experienced a side effect like headache, oral paresthesia, or obstructive uropathy in clinical trials.

HOST:
Along with that, here is some additional Important Safety Information. Formation of neutralizing antibodies (inhibitors) to Factor IX has been reported following administration of ALPROLIX. Patients using ALPROLIX should be monitored for the development of Factor IX inhibitors. Clotting assays (e.g., one-stage) may be used to confirm that adequate Factor IX levels have been achieved and maintained.

GY:
Let me share some insights into how I was able to help an obese patient in my practice. For privacy, we'll call him Jeremy.

Jeremy is a 34-year-old male with severe hemophilia B. He was born in a country where factor wasn't readily available and wasn't able to receive FIX until he was 12 years old. For most of his childhood and adolescence, he had many bleeds in various joints, particularly in his ankles, which developed target joints. The right ankle, in particular, was very severe. After immigrating to the US as a teenager, he was referred to our hemophilia treatment center, or HTC.

His initial evaluation revealed significant arthropathy in both ankles. He was started on prophylaxis with a recombinant SHL FIX concentrate, as there were no EHLs on the market at the time. Over the ensuing years, he continued to have intermittent bleeds in his ankles, but all in all, his target joints resolved.

When he was younger, he maintained a healthy body weight, but in his early 20s, he slowly started gaining weight. Four years ago, when he turned 30, he had a BMI of 35 which is clearly in the obesity range. At this point, after many years of relatively few ankle bleeds, Jeremy started having more frequent bleeds in his right ankle which was troublesome. This was accompanied by an increase in chronic pain to the point that he was having pain almost daily.

So we prescribed him an anti-inflammatory agent and also opiates that he used intermittently. And, with the availability of EHLs, we also prescribed ALPROLIX at a dose of 50 IU/kg once per week. We were trying to reduce the infusion burden, as he was developing problems accessing his veins.

The change in treatment to ALPROLIX improved the frequency of bleeds in his right ankle from about 6 per year down to 2 per year. He was also prescribed ankle supports and physical therapy. These adjuncts further reduced his bleeds to about once per year, but he continued to have chronic pain in his right ankle. Due to concerns for subclinical bleeding, his dose of ALPROLIX was increased to 75 IU/kg a week. And, while 75 IU/kg is not a standard dosing level, it was appropriate for Jeremy's unique circumstances, to help resolve the bleeding that contributed to this problem.

Imaging studies were done and demonstrated chronic hemophilic arthropathy. But in the past year he has lost a significant amount of weight, his BMI is now down to 26. Additionally, his joint pain improved significantly after weight loss. While he still has pain, it is more intermittent and responds to NSAIDs. After he lost weight, his dose of ALPROLIX was reduced to the 50 IU/kg a week that we started him on, and he currently continues to do relatively well. Now, these are the results I observed in my practice, and individual physicians may have different results with different patients.

MUSIC BUG

HOST:
Thank you for your insights, Dr. Young. I'm glad to hear your patient is doing better. His target joint resolution is very similar to what was observed in the B-YOND extension trial. This trial

studied the long-term safety and efficacy of ALPROLIX over 5 years in 120 adults, adolescents, and pediatric patients previous enrolled in B-LONG and Kids B-LONG. Study arms included 3 prophylaxis arms and an on-demand arm. Of the patients in the prophylaxis arms, 37 had 93 target joints, defined as a major joint with ≥3 bleeds over 3 consecutive months. 100% of these target joints resolved by the end of B-LONG, with target resolution defined as ≤2 spontaneous joint bleeds within 12 months.

Here is some additional Important Safety Information about ALPROLIX.

The use of Factor IX products has been associated with the development of thromboembolic complications. Nephrotic syndrome has been reported following attempted immune tolerance induction in hemophilia B patients with Factor IX inhibitors and a history of allergic reactions to Factor IX. The safety and efficacy of using ALPROLIX for immune tolerance induction have not been established.

The most common adverse reactions (incidence ≥1%) in previously untreated patients were injection site erythema, hypersensitivity, and Factor IX inhibition. The most common adverse reactions (incidence ≥1%) in previously treated patients were headache, oral paresthesia, and obstructive uropathy.

It's clear that good communication and perseverance are key to dealing with successful cases. Before we conclude, I want to ask you about your team. How does your team help support you and your patients, Dr. Young?

GY:

At my HTC, we work as a multidisciplinary team, or MDT, and frankly I think it's the only way to properly support patients with hemophilia. Just yesterday I met with a nurse practitioner, nurse coordinator, 2 physical therapists, 2 social workers, and a psychologist, all seeing my current patients. We saw a family with 2 working parents, difficult financial circumstances, and the children were really falling through the cracks—barely maintaining any treatment adherence. Every single member of the team met with that family, and we all worked together to figure out what would be the ideal approach in this more difficult situation. Some families really do go through a lot—I mean, they drove 14 hours to see me! They are farm workers, and they go back and forth between northern California and Oregon, so it's a challenging situation. We need to manage that and that's where the MDT comes in.

MUSIC BUG

HOST:
Can you elaborate a little more on the individual roles of the team members and how their unique perspectives contribute to the best overall care for your patients?

GY:
Absolutely, let me go through the disciplines. With our nursing team there are sometimes things that physicians may not be as involved with—especially on a more routine basis, such as making sure the patient's treatment plan actually comes to fruition. Yesterday, our nurse coordinator spent time with this family to help ensure access and adherence to factor product by arranging for a nurse to make a house call for a few weeks. And that is one of the benefits of the MDT.

Sometimes, there are financial issues, work-related issues. How do we give caregivers some time to make sure that they get their loved ones taken care of? What laws support them? That's why it is important to have a social worker as part of our care team.

One of the boys we saw developed a very problematic joint that needed special attention. Our physical therapist handles the mechanics of joint dysfunction and spent a lot of time examining him carefully. Setting a baseline, showing, and explaining to the mother what is happening and why this is very crucial. He put the injury in the context of the family business—how the boy couldn't help out on the farm if he wasn't able to straighten his arm—and that was very impactful. It helped the mom see why treatment adherence is important—that it's not just about pain now, but how important it is to consider all of the things that the child may not be able to do as they get older.

And finally, when there are treatment adherence issues, which are a big part of what we face, the psychologist gets involved. Is the patient in denial about having hemophilia? Are there some other psychological issues that are impacting the care and interfering with adherence? What other challenges are impacting adherence to their infusion schedule?

As we discussed, hemophilia is a complex disease that impacts more than just the patient. It impacts the whole family and other caregivers. And, because of that, providing a full-service care team is really invaluable.

HOST:
Thank you. As a reminder, ALPROLIX has not been studied specifically in patients with the comorbidities we've discussed. And our discussion reflects Dr. Young's experiences in his own clinical setting, and other physicians may have different experiences.

This concludes this episode of THE FACTOR FORUM podcast. Thank you, Dr. Young, for sharing your expertise with us.

GY:
Thanks for having me!

MUSIC BUG

ANNCR:
For information on references and links to the full Important Safety Information and Prescribing Information for ALPROLIX, please see our podcast description or visit ALPROLIXpro.com.

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