Branded Episode 1:
Factoring in SHLs and EHLs for Hemophilia B Patients
(Runtime: 31:14)

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Factoring in SHLs and EHLs for Hemophilia B Patients

HOST:
Hello! My name is Ben Barker, and I am 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 Courtney Carr, a Nurse Practitioner at Novant Health. Courtney is being compensated by Sanofi for her participation in this podcast, and the content was developed in conjunction with her.

She is sharing her personal experiences from her 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 Courtney Carr.

CC:
Thanks for having me!

HOST:
Why don't we start off with an introduction? Tell us a little about yourself.

CC:
Well as you said, I'm a nurse practitioner at Novant Health in Charlotte, North Carolina. I've been working with hemophilia patients for 10 years, and I'm certified in hemostasis nursing, working mostly in pediatrics. Before Novant, I worked at Atrium Health.

HOST:
I'm really interested in hearing your perspective on today's podcast. We're going to be discussing factor therapy, one of the foundations of hemophilia treatment. Specifically, the benefits of EHL products. Unlike hemophilia A, there is a big difference between how long EHLs are able to extend the half-life of their factor product compared to SHLs in patients with hemophilia B. We're going to be touching a little bit on why that is, when and why physicians

use EHLs vs SHLs, and what are some ways that different factors are able to get those extended half-lives.

CC:
I'm excited to get started.

MUSIC BUG

HOST:
In the first segment of today's podcast, we will discuss the history of hemophilia treatment options from our guest's personal experience. Courtney, can you tell us more about what has changed, especially in the past decade, and how that has affected your patients with hemophilia?

CC:
Yes, absolutely. The introduction of recombinant SHLs and EHLs has made treatment options better for people living with hemophilia. We've come a long way since the 60s and 70s! In the past, drugs weren't as potent, so patients would come into the hospital and spend weeks there. I remember a grandfather of one of my patients recalled how as a child, he spent a month in the hospital recovering from a spontaneous knee bleed. An entire month! Obviously, extended hospital stays diminish the quality of life for patients. They are away from their families, they avoid sports, they miss birthdays. Their lives aren't the lives that they'd hoped for.

So, when some of the first plasma-derived factor products came to the market, people were thrilled. A lot of those treatments were promising but ended up being tainted in one way or another. This led to distrust within the hemophilia community and patients wondered if the treatment was worse than the disease at that point. Even today, there's a legacy of distrust. Patients are hesitant to try new treatments, or they don't want to switch if something is working for them. Which makes sense—a lot of the patients I've seen have family members with personal experience being on old treatments. So, I understand how my patients may question their options now—"why trust this or that one? I'm okay on this treatment—why change now?"

Today we have third- and fourth-generation recombinant factor treatment options for hemophilia B, each addressing different needs of the patients. As an NP, I'm still working on helping the community overcome their past treatment disappointments. For some patients, there's a real fear of switching products. But you also have to look at the data. When I see a lot of breakthrough bleeds on a current treatment, I remind my patients that it's okay to switch something out. In fact, it's more than okay—it's vital for their future health.

MUSIC BUG

HOST:
So, you've walked us through a little bit about the emotional legacy of the treatment from the 60s and 70s to today. Now let's talk about your practical experience with SHLs and EHLs.

CC:
I began working with hemophilia patients in 2012, so SHLs were a huge part of my patients' treatment regimens, and the standard of care for all hemophilia B patients without inhibitors. I found them safe, and patients loved being able to infuse at home. It was such an improvement from earlier treatments. Not so much my patients, but my patients' grandparents couldn't believe how different things are for their grandchildren, who have access to SHLs.

During this time, every person with hemophilia in my practice seemed to be on the same SHL medications. With limited options available, we purchased factor at one specialty pharmacy. I used to work in pediatric Urology, so I was used to using different specialty pharmacies and treatments. This one-size-fits-all approach was odd. I was really shocked to see that! But there didn't seem to be a lot of options out there—reps weren't coming by, and it really surprised me.

We started hearing about various medicines that were in the pipeline for hemophilia B, and they were going to be longer acting—the possibility of infusions once a week versus 2 or 3 times a week. I remember thinking, Okay, I'll believe it when I see it; just knowing the history of the treatment for hemophilia. At the same time, if you find a way to provide longer-acting half-life, I'll be really impressed.

HOST:
Fast forward to a few years later, when EHLs come on the scene…

CC:
It totally changed the landscape! We can treat patients more individually now, and a large part of that comes from more readily available treatment options. In the old days, we'd see a patient every 2 years. Can you imagine giving factor regimen adjustments every 2 years?

The introduction of EHL products really reenergized the hemophilia community, and we started thinking about hemophilia treatment in a different way. And, especially for my younger patients, it truly made an impact to have a treatment option with significantly fewer infusions.

It was great for me—I want to give these patients as much attention as possible, because these patients are my family. I want what is best for them. Advocating and pushing for personalized approaches to treatment is important.

MUSIC BUG

HOST:
Courtney, you mostly work with pediatric patients. I'm curious how today SHL and EHL therapies are used in younger patients—is one used more often than another? Can you share some

personal experiences about what has worked best or if you have had patients switch from one to the other?

CC:
Right off the bat, I generally prescribe EHLs for my patients because of the lower infusion burden and the strong efficacy and safety profiles. That includes my pediatric patients. SHLs are generally used when a patient or their parent doesn't want to switch, or they have a strong preference, and I want to be respectful of their voice.

As far as switches go, I usually see patients switch from SHLs to EHLs. In my practice, switches between different EHL therapies happen, but are more rare. No matter what kind of switch I'm dealing with, my main job is managing emotions. When working with a patient who is ready to change treatments, I try to ease any anxiety about making a change. Patients who are on SHLs may be fearful of switching because often they haven't tried anything else.

Since I mostly work with pediatric patients, I interact with a lot of parents. And parents are VERY hesitant about switching their child's treatment. They read everything, so no matter what treatment you suggest, they are likely to discover an anecdote about a negative experience with a specific medication—sometimes on social media, on a blog, or maybe stories they heard.

I get it—parents carry a huge burden of responsibility, and they want to protect their child at all costs. So, it is not my place to say they should do this or do that. Ultimately, the parents know their child best. But as a nurse practitioner, it's my responsibility to share my knowledge and provide them with all the information so they can make the right decision for them. I can challenge disinformation, but at the end of the day, all I can do is give them guidance and encourage them to take time to sit with all the options.

MUSIC BUG

HOST:
Now that we've discussed your history with recombinant factor products in general, I'd love to dive into your history with ALPROLIX; the first factor IX EHL on the market.

Before we begin, 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.

When ALPROLIX arrived, what was the general mood?

CC:
I was excited when I heard about the launch of ALPROLIX in 2014, because I knew how many of my patients struggled with frequent infusions. I think less-frequent dosing was the first thing people in my practice were excited about. Pediatric patients won't hold still and have small veins, and some of our older patients can have collapsed veins or comorbidities. So fewer infusions are great for everyone, but way better for some!

ALPROLIX has flexible dosing options for patients—and can be used on-demand or prophylactically, in children, adolescents, and adults. It can be used in previously untreated patients, previously treated patients, and even in surgery.

HOST:
Now let's take a moment to review some Safety Information for ALPROLIX. 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.

CC:
In the beginning, my Hemophilia Treatment Center, or HTC, was hesitant to prescribe ALPROLIX, despite the data. But once my colleagues started using ALPROLIX, it quickly caught on. It allowed us to bring over a new generation of patients to prophylaxis, who were hesitant before of frequent injections. I mean, for children under 12, they can begin with a 60 IU/kg dose every week. No more trying to infuse in school or fitting it into a crowded week. Saturday or Sunday, it's once and done!

The ALPROLIX 50 IU/kg weekly dose was also the most popular dose for the adult and adolescent hemophilia B patients. But there was added flexibility too with additional doses. 100 IU/kg doses every 10 days for patients 12 years of age and older was a great option for patients who had to travel frequently, it just gave them more freedom.

For the B-LONG trial, which was the main clinical trial for ALPROLIX, the median dosing interval for prophylactic patients over 12 was 12.5 days. That had a range of 10.4 to 13.4 days. And in that study, more than half of patients in the individualized prophylaxis group extended to 14 days or more during the last 3 months of the study. So instead of one-size-fits-all, we discovered that ALPROLIX was a flexible tool that we could use for more individualized care.

MUSIC BUG

HOST:
You mentioned the B-LONG trial, and for context, I wanted our listeners to know that B-LONG was a phase 3, open-label clinical trial of 123 previously treated patients with severe hemophilia B.

These patients were divided into 4 arms: a weekly (or fixed interval) arm with 63 patients, an interval-adjusted (or fixed dose) arm with 29 patients, an on-demand arm with 27 patients, and finally, a surgical arm with 12 patients.

For references on this and other claims and data shared during the podcast, please see our podcast description.

CC:
Another thing that was great about the arrival of ALPROLIX and other new products, and this is going to seem weird for me to say, but it also brought sales representatives! We get to see reps more often, which has helped with treatment diversity in my practice, which I think is a good thing.

Rep visits are great because I can keep up on the latest data and ask questions. One of the questions I received clarity on, for example, was the mechanism of extension for ALPROLIX. Unlike some other mechanisms of extension, Fc Fusion utilizes a naturally occurring pathway, which allows ALPROLIX to stay in the body longer.

We were also able to discuss the circulation of ALPROLIX after infusion. One way to see if factor is moving outside the blood vessel is to look at the volume of distribution or VD. The International Society on Thrombosis and Haemostasis recommends that multiple PK parameters should be evaluated, including half-life, Vd, and clearance. Together, all of these PK tools can help us make sure we're getting the right EHL for the right patients.

HOST:
Thanks for sharing your experiences. Now, here's some more Safety Information our audience should know about ALPROLIX.

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.

MUSIC BUG

I'd like to return to something you said earlier about counseling patients or their family members with regard to switches. If a parent comes to you with questions or incorrect information about treatment with ALPROLIX, how do you handle it?

CC:
I always try and give patients and families as much information as I can so that they can make the choice that's right for them. Sometimes, I can handle disinformation about ALPROLIX head on. Let's say I see on-demand patients taking SHLs who are worried about switching to an EHL because they think SHLs start working faster. In their minds, shorter half-life, shorter bleeding time, right? In cases like this, I share that ALPROLIX reaches its peak activity level as quickly as BeneFIX does. Peak activity doesn't mean that bleeds are resolved in 10 minutes, just that they start working at roughly the same time.

How do we know that? In the B-LONG trial, a pharmacokinetic subgroup of 22 patients was studied to determine a direct PK comparison. They received consecutive single IV doses of 50 IU/kg of BeneFIX and ALPROLIX at the beginning of the study for direct comparison. For both ALPROLIX and BeneFIX, peak activity was reached approximately 10 minutes after the start of the infusion. Studies have not been conducted to assess the safety or efficacy of ALPROLIX compared with BeneFIX. But we do know that when it comes to peak activity, they are very similar.

HOST:
What about questions about efficacy and safety for ALPROLIX?

CC:
A misconception I've noticed around efficacy is emotional: because SHL patients infuse more frequently, they say they feel more protected. If I encounter this misconception, I share what I know about the data. Let's say I'm talking with a parent—I'd point out that in the Kids B-LONG trial, the median overall ABR with prophylaxis was 1.1 for children 1 to 5 years old, with an interquartile range, or IQR, of 0 to 2.9. When you look at children from 6 to 11 years of age, you'll see similar results: 2.1 ABR, with an IQR from 0 to 4.2. The median spontaneous ABR for all children under 12 was 0, with an IQR of 0 to 1.1 in children 1 to 5 years old, and 0 to 2.1 in children 6 to 11 years old.

I'm working with children every day; treatment safety is always top of mind. Parents ask me about it a lot. In clinical trials of PTPs, no cases of inhibitor development were reported, and in trials of PUPs, 1 case was reported out of 33 patients. Inhibitors have been detected outside of clinical trials. I usually counsel my patients about common reactions before they infuse with ALPROLIX for the first time: there's a chance of headache, dizziness, or an unusual taste in their mouth. We also instruct them to stop using ALPROLIX immediately and get in touch with us if they notice early signs of hypersensitivity reactions, like hives, chest tightness, difficulty breathing, or facial swelling. Any signs of anaphylaxis or thrombosis should be taken very seriously, as they are life-threatening.

MUSIC BUG

HOST:
Courtney, you mentioned the Kids B-LONG trial, and I just wanted to build on that for a moment. The Kids B-LONG trial was a phase 3, open-label study that investigated the safety and efficacy of ALPROLIX in 30 previously treated pediatric patients with severe hemophilia B. All 30 patients were treated with ALPROLIX on an individualized prophylactic regimen. Fifteen patients were 1 to 5 years of age; 15 patients were 6 to 11 years of age.

Here's some additional Important Safety Information:
The use of Factor IX products has been associated with the development of thromboembolic complications.

Now that you've given your overview of SHLs and EHLs in treatment, do you have any examples from your practice that can reinforce your insights? As a reminder, results may vary, and results from one case study are not necessarily predictive of results in other cases.

CC:
I had a patient, I'll call him Simon, who was an athletic and extremely social high school student, who was on an SHL. Simon was coming in multiple times for leg bleeds. And, one time, his bleeds became so severe, he came in using a wheelchair. While on his SHL, he was probably getting treatment every other day. That is an incredible burden to place on a teenager.

It's so important to make sure our patients are on a treatment that allows them to continue to follow their passions—treatments that offer protection, while reducing infusion burden. Simon switched to ALPROLIX and was infusing once a week. After starting his new treatment, he experienced fewer bleeds than before. If Simon had switched from an on-demand regimen, the difference might have been even greater.

ALPROLIX can protect him from bleeds and joint bleeds, and he can continue treating with ALPROLIX and, therefore, benefitting from that protection as he gets older. In the interval adjusted prophylaxis arm of the B-LONG trial, the median overall annual bleed rate was 1.4 for adult and adolescent patients, with an IQR of 0 to 3.4. The spontaneous ABR for that same group was 0.9, with an IQR of 0 to 2.3. And finally, the median joint ABR was 0.4, with an IQR of 0 to 3.2.

HOST:
That's amazing to hear what a difference switching from an SHL to an EHL made for that patient's life. I know, that as a nurse practitioner, you are so close to your patients. So, I imagine that felt like a big win—for him but also for you!

For references on this and other claims and data shared during the podcast, please see our podcast description. We'd also like to share some Important Safety Information about ALPROLIX. 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.

Returning to our conversation, how does the infusion schedule play a role in a patient's decision about a treatment in practice?

CC:
In my opinion, if possible, I recommend that my patients schedule infusions every 7 days. If I tell them every 10 days, then I notice the wheels spinning in their head—counting out the days. And I totally understand. If I had to take a medication that wasn't daily, I would want to make it easy for myself. However, if they are successful on 10 days, we can always try extending them to 14 days.

With a 7- or 14-day regimen, a patient will know, for example, every Sunday or every other Sunday, I need to schedule time for my infusion. It's simpler, easier, and less confusing. Obviously, dosing is a personal journey. In real life, just as in the trial, dose and dosing frequency depend on the severity of patient's factor IX deficiency, the location and extent of bleeding, the individual patient's PK profile, and/or the patient's clinical condition. And that's what's great about ALPROLIX: personalized dosing. Patients have the option of starting on a 7 or 10-day schedule—and then if successful, they can extend even further.

No matter what dosing regimen my patients choose, I try and support them. I always recommend that patients add their infusion schedule to their calendar to help them remember. But also, this will help them make future plans—family get-togethers, a weekly or monthly club, vacations, etc. As I've mentioned earlier, I want to do whatever I can to support them and help them see how their life does not need to revolve around their hemophilia.

MUSIC BUG

HOST:
Courtney, you just spoke about 14-day extension, which was part of the B-YOND extension trial. B-YOND was an extension trial that studied the long-term safety and efficacy of ALPROLIX in 120 adult, adolescent, and pediatric patients previously treated in Kids B-LONG or B-LONG. The study included a fixed-interval arm of 74 patients, a fixed-dose arm of 36 patients, a modified prophylaxis arm of 17 patients, and an on-demand arm of 15 patients.

Thank you so much for sharing your experience with us, Courtney. For the last segment of our podcast, I'd like to ask you some questions about a few topics frequently discussed within the hemophilia HCP community.

Now, a reminder that Courtney is giving her opinion based on her experiences in clinical practice. Decisions surrounding patient care depend on the physician's professional judgment in consideration of all available information for the individual case.

When you're planning to recommend that a patient switch, whether that switch is from an SHL to an EHL, or from one EHL to another, how do you handle the conversation if the patient is resistant to the switch?

CC:
Well, coming from my experience in pediatrics, like I said earlier, my job is as much about managing parents as it is managing my patients! Some parents have a fear of the unknown, or there's often emotional resistance—they don't want their child to be reminded of their disease, or maybe they are wary of their child developing inhibitors.

But I have had success in that conversation about switching to ALPROLIX with adolescent patients when I focus on specific benefits and not generalities. Is infusion burden a problem? ALPROLIX offers a flexible dosing schedule—dosing every 7 or 10 days, with the potential to extend to 2 weeks or more.

Is your schedule busy? Then try a weekly schedule. This is one area that I feel strongly about. It's much easier for patients to remember.

Are parents worried about giving up on-demand treatment? Since ALPROLIX is indicated for prophylaxis, on-demand, or perioperative, they can continue on-demand if they like. ALPROLIX can be used on-demand and may help ease the transition to prophylaxis.

Out of the 19 adults and adolescents treated with ALPROLIX on-demand during B-LONG, 47% made the switch to ALPROLIX prophylaxis during the B-YOND extension trial. So, when they're ready for prophylaxis, I know ALPROLIX can help them switch.

And finally, if there is a distrust of something new, I can rely on the brand's experience. I find that patients are drawn to products with established experience on the market. And ALPROLIX was the first EHL rFIX—a treatment that gave the hemophilia community more options and flexibility in treatment.

HOST:
Here is some more Important Safety Information for ALPROLIX. 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.

Courtney, the last question is on the issue of infusion. Some doctors may have patients who are struggling to infuse properly. Have you come across this problem, and how can the hematologist community better set patients up for success? Are EHLs a solution or just the first step?

CC:
Needles can be scary. I think we can all agree on that! So, when I meet with patients who are extremely fearful of them, I know we need to act fast. It could potentially impact adherence! So,

I think just helping them overcome a phobia of needles is step 1. This is very common in children and adolescents but can linger into adulthood as well.

I think it's critical to have a patient or the patient's parents infuse in front of you the first time. That way you can monitor if they're doing everything properly. Sometimes if results aren't what they should be, I'll ask them to show me again how they infuse to eliminate improper infusion as a cause of lackluster treatment results. Sometimes just checking in once a year is all it takes to make sure patients are infusing the right way.

In general, I think a big part of proper infusion is consistent infusion. I try to encourage them to be consistent, especially about prophylaxis. I help them see the long-term benefits. I can show them the ALPROLIX ABR or joint ABR data and explain how much lower those numbers are compared to patients who are treating on-demand. I remind them that this so-called "scary" experience can help them get the benefits prophylaxis has to offer. As an NP, I see the difficulties my patients face every day. I want to do the best for my patients, which involves connecting with other members of the multidisciplinary team, especially the social worker—to help the patient identify the root cause of their anxieties and find solutions, whether it's coping mechanisms or discussing their plan in more detail with the HCP.

HOST:
This concludes this episode of THE FACTOR FORUM podcast. Thank you so much for sharing your expertise with us, Courtney! That's all the time we have for today.

CC:
Thank you 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.

FADE OUT

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