



Factor Nine News

The Coalition for Hemophilia B

Topics in Hemophilia B

Summer 2019



- Generation IX Mentorship Program in Portland
- Benjamin Shuldiner - A One-Man Dynamo
- Parker Feagins Uses His Love of the Music Business To Create Community
- 7-Year-Old Champ Learns How to Self-Infuse with Confidence
- The Coalition Goes *On The Road*
 - Minneapolis, Minnesota
 - St. Louis, Missouri
 - Boston, Massachusetts
 - Dallas, Texas
 - Ann Arbor, Michigan
- Treatment News
- Hemophilia Treatment Pioneer Dr. Shelby Dietrich Dies at 95
- Hemophilia Update
- BCares
- BConnected
- Hemophilia, Mental Health, and Heart Disease
- Young Entrepreneur
- Save the Date!
- Annual Holiday Fund
- Kidz Korner



GENERATION IX
MENTORSHIP
PROGRAM IN
PORTLAND



GENERATION IX MENTORSHIP PROGRAM IN PORTLAND, OR

From June 4–9, Camp Collins in beautiful Portland, OR played host to a mentorship training program for young leaders in the hemophilia B community. Camp Collins is a YMCA camp that has accommodated many youth education programs for more than 90 years. Our program was the latest in the Generation IX Project. Earlier sessions focused on leadership and advocacy.

Generation IX Project is a joint effort of the Coalition for Hemophilia B and GutMonkey, with sponsorship from Aptevo Therapeutics. GutMonkey is an experiential learning company with a long history of working with the hemophilia community.

The June program incorporated two categories of attendees. The mentors, ages 18–30, arrived first for two days of their own training. They were followed by the arrival of the teens, ages 14–17, who were assigned to the young adult mentors so that they could receive training and learn from them.

Each of the two groups had specific objectives. For the mentors, it was about acquiring the tools, skills, and the experience needed to be successful in mentoring the teens. Their learning focused on how to share their personal stories as a source of information and inspiration. For the

teens, the objectives were learning about hemophilia and their own self-care, leading to improved health outcomes.

The groups accomplished their objectives by participating in various activities designed to encourage teamwork, cooperation, creative problem solving, and leadership. For example, in one activity, participants had to construct “blanket forts” and were given a lot of leeway to decide how to accomplish this task. They were divided into four groups and had the option of building four forts but decided instead to work together and build one giant fort. In another activity, participants created an original show called Gen IX’s Got Talent. They tapped into their own creativity in designing costumes and staging musical numbers. Everyone also had the opportunity to engage in physical challenges using the beautiful outdoor





setting of Camp Collins.

The closing activity was a campfire where all the participants celebrated their accomplishments together and cemented the new friendships they had formed during this very special week.



New Gen IX programs will be coming in 2020, so please stay tuned and check our website, www.hemob.org, for more information as it becomes available. The Coalition for Hemophilia B would like to thank Atevo for its generous sponsorship of this program.





IXINITY[®]
coagulation factor IX
(recombinant)



**Discover more
about IXINITY[®]**

Visit IXINITY.com



© 2017 Aptevo BioTherapeutics LLC.
All rights reserved. CM-FIX-0258

Aptevo BioTherapeutics LLC, Berwyn, PA 19312

IXINITY[®] [coagulation factor IX (recombinant)] and any and all Aptevo BioTherapeutics LLC brand, product, service and feature names, logos, and slogans are trademarks or registered trademarks of Aptevo BioTherapeutics LLC in the United States and/or other countries.

7-YEAR-OLD CHAMP LEARNS HOW TO SELF-INFUSE WITH CONFIDENCE

By Rose, Community Member

While attending the 2019 Coalition for Hemophilia B Symposium, our seven-year-old son Benjamin had an experience that was both empowering and inspirational.

He met Nurse Hope Woodcock-Ross who runs the infusion table at many Coalition events, Nurse Hope's gentle and caring manner drew him in and, for the first time, he showed genuine interest in learning how to self-infuse. He spent a lot of his free time at Hope's table, using a fake hand to practice doing a "stick," watching others self-infuse, and even learning how to infuse us, his mom and dad, and succeeding on the first try! This achievement gave him the confidence to start practicing on himself.

Upon our return home, Benjamin could not stop talking about the

conference. He shared about how "cool" it was to see a documentary about a guy with hemophilia B "just like him" who had climbed the tallest mountains in the world. He also talked about meeting a girl with hemophilia and sitting next to her while she self-infused.

All these experiences contributed to inspiring him to fearlessly self-infuse, with a deep belief in himself and his ability to achieve it. He is now able to infuse himself whenever he needs to and looks forward to attending camp and getting his "Big Stick" award. We are very proud of our remarkable seven-year-old.



HEMOPHILIA TREATMENT PIONEER DR. SHELBY DIETRICH DIES AT 95

Shelby Dietrich, MD, a true pioneer in the treatment of hemophilia, died on August 12, 2019, in her hometown of Pasadena, CA at the age of 95. Dietrich started one of the first hemophilia treatment centers in 1976, located at Children's Hospital Los Angeles. She was one of the leading clinicians during the height of the tainted blood crisis who went on to do important research in the search for a cure for HIV/AIDS.

Dietrich earned her undergraduate and medical degrees at the University of Michigan, where she was one of only 15 women in her medical school class of 118.

She is predeceased by Irving Rector, her husband of 51 years who died in 2002. Dietrich is survived by daughters Sarah Rector Aguilar, Lucy Rector Filppu, and Ann Chapin Rector; son-in-law Len Filppu; daughter-in-law Nancy

Megli; and grandchildren Albert Aguilar, Arthur Filppu, Dori Filppu, and Alexi Seale.

In lieu of flowers, please make donations to Young and Healthy of Pasadena (<https://yhpasadena.org>), an organization Dietrich helped start in 1990. The group provides medical, dental, and psychosocial care to underserved and uninsured children in the greater Pasadena area.

Hemophilia, Mental Health, and Heart Disease

By Dr. David Clark

A 2007 study of depression in adult male hemophilia patients conducted by the Arizona Hemophilia Treatment Center (HTC) in Tucson found that 37% of patients experienced depression.¹ This is about twice the incidence in the normal population and has rightly become an important issue in the hemophilia community.

It is not surprising that mental health issues, especially anxiety and depression, arise in people dealing with a major disorder like hemophilia. However, if not treated, such issues can lead to other problems, both social and medical. Feeling anxious and/or depressed can lead to problems with school or work and interfere with relationships. Depression is also linked to an increased risk of suicide. It can also affect physical health, as we'll see below.

We always say that hemophilia affects the whole family, and that holds true for any related mental health issues. Not only the individual patient but also parents, other caregivers, and other family members can be affected. A very depressed caregiver may not be able to properly help his/her child with their hemophilia. A depressed adult with hemophilia may not adhere properly to their treatment regimen. A depressed patient may display unhealthy behaviors such as smoking, alcohol/drug abuse, eating/drinking too much or too little, lack of exercise—behaviors that contribute to poor overall health.

Thus it is very important for patients and caregivers with mental issues to seek treatment. Unfortunately, many affected people also have a lot of anxiety about seeking treatment, which only adds to their problems. Although both hemophilia and a number of mental conditions may all be caused by genetic defects, a physical disorder is somehow seen as something unfortunate (“You’re having a knee bleed? How can I help you?”) while a mental disorder is often blamed on the patient (“You’re crazy! Leave me alone!”). In our supposedly enlightened society, there is often a stigma attached to mental illness by otherwise well-meaning people. This can drive the sufferers to avoid people and just try to get by with a disease that might be easily treatable. By focusing more on mental health, the hemophilia community hopes to bring our affected brothers and sisters the help they need.

However, getting proper treatment can also be a challenge. (My own experiences as a non-hemophiliac with serious mental health issues inform the comments



here. I'll write more about that in a future issue.) There is a shortage of mental health providers in the United States, and insurance issues can further limit the options available. Although insurance companies are required to cover mental health the same as they do physical health, the companies have many ways to limit coverage—for instance, by only covering a small network of mental health providers.

Those who receive their hemophilia treatment from an HTC have an advantage. Under their comprehensive care model, most HTCs employ social workers to help patients and families deal with their disorder. If you have an HTC social worker, please be open with them about the problems you're having.

They can do a lot—everything from helping you themselves to getting you to people who can help you with more serious issues.

Depression and anxiety often go together. Many times it's difficult to tell which you're experiencing. They are different, though, in that depression can often be well controlled (mine is) but anxiety is much harder to treat (mine is a constant problem). Both can be treated with drugs and/or counseling, preferably both. Psychiatrists are medical doctors (MDs) who can prescribe antidepressants and other drugs. Today, most psychiatrists only prescribe drugs—they don't do counseling. Psychologists, social workers, therapists, and other mental health professionals do the counseling. Don't be misled by degrees and titles (although in many states mental health professionals must be licensed or certified). Knowledge helps, but what's more important is how you and the counselor relate to each other. If you feel like you can't speak openly or don't think they understand your problems, they might not be the right one for you. You may need to interview several therapists (usually free consultations) to find the right one.

LINK TO PHYSICAL HEALTH

Now that I've given you a pep talk about getting treated, I want to focus on some of the reasons this could help your physical health also. A group of Belgian researchers from the University of Leuven recently published a review of studies on the relationship between mental disorders and heart disease.² They first point out that depression is expected to become the leading cause of disability

worldwide by 2030. Also, about 14% of all deaths worldwide are attributable to mental disorders. Of course, people with heart disease tend to have higher rates of anxiety and depression, just like hemophilia patients and anyone suffering from any major medical issue would. The intriguing thing is that conversely, people with anxiety and depression tend to have higher rates of heart disease. The

researchers suggest that there may be a common physiological connection between the two.

It has always been thought that hemophilia would protect you from heart disease because heart attacks are caused by clotting in the blood vessels supplying the heart. However, until recently, there haven't been enough older hemophilia patients

to fully test out this theory. Recent studies suggest that hemophilia patients have just as many heart attacks; they just don't die from them as often. However, heart attacks still cause damage and impact a patient's quality of life.

The authors of the Belgian study report that depression causes about a 30% increased risk of heart attacks and a 36% increased risk of death from one. Anxiety also seems to cause a higher risk of heart attacks, but less than depression does. It is very difficult to tease out the separate effects of depression and anxiety since they often occur together. Another disorder, post-traumatic stress disorder (PTSD), is usually associated with soldiers in combat, but it can arise from any traumatic event, including bad experiences with hemophilia. PTSD appears to increase the chances for heart attacks by about 27%. Interestingly, a study on 281 pairs of twins, where only one twin suffers from PTSD, showed that PTSD more than doubled the incidence of heart disease (22.6% vs. 8.9%).

The authors go on to speculate about what the physiological connections might be between mental health and heart disease. There are a number of possibilities that need to be studied further—it's not just "all in your head." Mental illness, including anxiety and depression, is a real illness—just as real as hemophilia. It needs to be taken seriously and can be treated. When you're already dealing with hemophilia, you shouldn't needlessly suffer from mental issues, too. If you have these problems, talk to somebody!



References

1. Information in the first part of this article comes from Rita Colorito, "Putting the Spotlight on Mental Health and Bleeding Disorders," HemAware, the magazine of the National Hemophilia Foundation, available at <https://hemaware.org/mind-body/putting-spotlight-mental-health-and-bleeding-disorders>. The article includes a lot of good information from Debbie de la Riva, a licensed counselor and member of the hemophilia community, plus links to many useful resources.
2. The Belgian study is published (in English) in M. DeHert, J. Detraux, and D. Vancampfort, "The Intriguing Relationship Between Coronary Heart Disease and Mental Disorders," *Dialogues in Clinical Neuroscience* (2018) 20 (1):31–40.



LONG-LASTING BLEED PROTECTION FOR THE HERO WITHIN

THE ONLY EXTENDED HALF-LIFE FACTOR IX THERAPY THAT DELIVERS

0 SPONTANEOUS BLEEDS*

Whether dosed every 7 or 14 days in clinical trials

UP TO **14** DAY DOSING†
FDA APPROVED

Dosing schedules that fit your lifestyle

20% STEADY-STATE TROUGH LEVELS WITH 7-DAY PROPHYLACTIC USE‡

High and sustained steady-state FIX levels

*Zero median annualized spontaneous bleeding rate when dosed at 7 or 14 days in clinical trials.

†Once well controlled (1 month without spontaneous bleeding or requiring dose adjustments on a weekly dose of ≤ 40 IU/kg), people 12 years and older can be transitioned to 14-day dosing.

‡The average dose for people receiving prophylaxis every 7 days was 37 IU/kg and every 14 days was 73 IU/kg.

§Hemophilia FIX Market Assessment. Third-Party Market Research.

Is it time for a switch? Learn more at IDELVION.com



Important Safety Information

IDELVION is used to control and prevent bleeding episodes in people with hemophilia B. Your doctor might also give you IDELVION before surgical procedures. Used regularly as prophylaxis, IDELVION can reduce number of bleeding episodes.

IDELVION is administered by intravenous injection into the bloodstream, and can be self-administered or administered by a caregiver. Do not inject IDELVION without training and approval from your healthcare provider or hemophilia treatment center.

Tell your healthcare provider of any medical condition you might have, including allergies and pregnancy, as well as all

medications you are taking. Do not use IDELVION if you know you are allergic to any of its ingredients, including hamster proteins. Tell your doctor if you previously had an allergic reaction to any FIX product.

Please see additional Important Safety Information and brief summary of prescribing information on adjacent page and full prescribing information including patient product information at IDELVION.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call **1-800-FDA-1088**.

IDELVION is manufactured by CSL Behring GmbH and distributed by CSL Behring LLC. IDELVION® is a registered trademark of CSL Behring Lenggau AG. Biotherapies for Life® is a registered trademark of CSL Behring LLC.

©2019 CSL Behring LLC 1020 First Avenue, PO Box 61501, King of Prussia, PA 19406-0901 USA
www.CSLBehring.com www.IDELVION.com IDL-0307-MAY19

Biotherapies for Life® **CSL Behring**

Important Safety Information (cont'd)

Stop treatment and immediately contact your healthcare provider if you see signs of an allergic reaction, including a rash or hives, itching, tightness of chest or throat, difficulty breathing, lightheadedness, dizziness, nausea, or a decrease in blood pressure.

Your body can make antibodies, called inhibitors, against Factor IX, which could stop IDELVION from working properly. You might need to be tested for inhibitors from time to time. IDELVION might also increase the risk of abnormal blood clots

in your body, especially if you have risk factors. Call your healthcare provider if you have chest pain, difficulty breathing, or leg tenderness or swelling.

In clinical trials for IDELVION, headache was the only side effect occurring in more than 1% of patients (1.8%), but is not the only side effect possible. Tell your healthcare provider about any side effect that bothers you or does not go away, or if bleeding is not controlled with IDELVION.

IDELVION®, Coagulation Factor IX (Recombinant), Albumin Fusion Protein

Initial U.S. Approval: 2016

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IDELVION safely and effectively. Please see full prescribing information for IDELVION, which has a section with information directed specifically to patients.

What is IDELVION?

IDELVION is an injectable medicine used to replace clotting Factor IX that is absent or insufficient in people with hemophilia B. Hemophilia B, also called congenital Factor IX deficiency or Christmas disease, is an inherited bleeding disorder that prevents blood from clotting normally.

IDELVION is used to control and prevent bleeding episodes. Your healthcare provider may give you IDELVION when you have surgery. IDELVION can reduce the number of bleeding episodes when used regularly (prophylaxis).

Who should not use IDELVION?

You should not use IDELVION if you have had life-threatening hypersensitivity reactions to IDELVION, or are allergic to:

- hamster proteins
- any ingredient of IDELVION

Tell your healthcare provider if you have had an allergic reaction to any Factor IX product prior to using IDELVION.

What should I tell my healthcare provider before using IDELVION?

Discuss the following with your healthcare provider:

- Your general health, including any medical condition you have or have had, including pregnancy, and any medical problems you may be having
- Any medicines you are taking, both prescription and non-prescription, and including any vitamins, supplements, or herbal remedies
- Allergies you might have, including allergies to hamster proteins
- Known inhibitors to Factor IX that you've experienced or been told you have (because IDELVION might not work for you)

What must I know about administering IDELVION?

- IDELVION is administered intravenously, directly into the bloodstream.
- IDELVION can be self-administered or administered by a caregiver with training and approval from your healthcare provider or hemophilia treatment center. **(For directions on reconstituting and administering IDELVION, see the Instructions for Use in the FDA-Approved Patient Labeling section of the full prescribing information.)**
- Your healthcare provider will tell you how much IDELVION to use based on your weight, the severity of your hemophilia B, your age, and other factors. Call your healthcare provider right away if your bleeding does not stop after taking IDELVION.
- Blood tests may be needed after you start IDELVION to ensure that your blood level of Factor IX is high enough to properly clot your blood.

What are the possible side effects of IDELVION?

Allergic reactions can occur with IDELVION. Call your healthcare provider right away and stop treatment if you get a rash or hives, itching, tightness of the chest or throat, difficulty breathing, light-headedness, dizziness, nausea, or decrease in blood pressure.

Your body can make antibodies, called inhibitors, against Factor IX, which could stop IDELVION from working properly. Your healthcare provider may need to test your blood for inhibitors from time to time.

IDELVION might increase the risk of abnormal blood clots forming in your body, especially if you have risk factors for such clots. Call your healthcare provider if you experience chest pain, difficulty breathing, or leg tenderness or swelling while being treated with IDELVION.

A common side effect of IDELVION is headache. This is not the only side effect possible. Tell your healthcare provider about any side effect that bothers you or does not go away.

Based on May 2018 revision

Please see full prescribing information, including FDA-approved patient labeling.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

IDELVION is manufactured by CSL Behring GmbH and distributed by CSL Behring LLC. IDELVION® is a registered trademark of CSL Behring Lengnau AG. Biotherapies for Life® is a registered trademark of CSL Behring LLC.

©2019 CSL Behring LLC 1020 First Avenue, PO Box 61501, King of Prussia, PA 19406-0901 USA
www.CSLBehring.com www.IDELVION.com IDL-0307-MAY19



IDELVION®
 Coagulation Factor IX (Recombinant), Albumin Fusion Protein

BENJAMIN SHULDINER

A ONE-MAN DYNAMO



By Michael Perlman

At 41, Benjamin Shuldiner has earned his titles of principal, professor, educator, and ultimately an innovator and humanitarian. He is past president of the Association for Supervision and Curriculum Development (ASCD), a distinguished lecturer of Education Leadership at Hunter College, was an adjunct lecturer at Baruch College, School of Public Affairs, and was the founder and principal of the High School for Public Service in Brooklyn. This Harvard University graduate was raised in New York and later lived in Los Angeles, California prior to relocating to Brooklyn. In 2005, he was the recipient of the prestigious *Jefferson Award for Public Service for an Individual 35 Years of Age and Under*.

Shuldiner is an active member of the hemophilia community and has an engaging presence at The Coalition for Hemophilia B symposiums and conferences, where he often discusses, from educational perspective, how to advocate for your child who has a bleeding disorder.

He explained, “I cover Individualized Education Programs (IEPs) and 504s relating to how parents and students can use the system to get their needs met. IEPs encompass how you get educational support for the students, and 504s involve acquiring physical and mobility support for students.” That was the topic of his most recent seminar in Pittsburgh, Pennsylvania, as well as in Portland, Maine a couple months earlier. Shuldiner was the key note speaker at the National Hemophilia Foundation in 2003. “I have

presented for many chapters countrywide, telling them the story of my life including my career,” he continued.

Shuldiner was diagnosed with hemophilia B at birth, after he was predisposed to the condition from his grandfather. He explained, “There are always challenges, and hemophilia is just one challenge. I never saw it as a hindrance, but as a community that I was part of, and something I needed to take care of. I had incredible support along the way, and it helped me grow as a person to know I am loved and supported by not only friends, family, doctors, and nurses, but by the hemophilia community.” His active lifestyle continues with being a Mets fan, hiking and international travels.

One of Shuldiner’s greatest influences is his family, which impacts his work ethic and humanitarian spirit. He said, “My parents worked in public service. My mother was an English teacher and my father worked in public housing. My grandmother ran a nursery school and my grandfather worked in rehabilitation to help people with job training. My family has always been an inspiration for me to do well, give back to the community and support people as much as I can.”

In 2016, he was elected president of ASCD, the largest education professional organization countrywide, comprised of over 125,000 members from over 138 countries, including 52 affiliate organizations. Members include superintendents, principals, teachers, and

advocates. He was elected to the board of directors in 2015, and his leadership led to his position as president a year later. He said, "My role is to shepherd the mission and vision of the organization, and we help support teachers and educators to support students to achieve success. It is an honor and a privilege, and I am humbled."

His work at Hunter involves supporting the training of individuals who wish to become principals and superintendents. His expertise has taken him to destinations as near as the Bronx and Arkansas, and internationally to India and Norway. He said, "I am very thankful I am able to help schools and districts around the world. For 4 consecutive years, I have visited India and consulted school principals to improve teachings, and worked with students to support their learning and growth. My goals are to continue to help as much as I can during the brief time I have on this planet."

One of Shuldiner's most rewarding achievements is founding and becoming principal of the High School for Public Service, a position he held for 10 years. He reminisced, "It was located in a building that had a 23% graduation rate. When the school was shut down, we came in, serving the same population. In our first graduating class, we had a 98% graduation rate, and that really set the standard proving students can learn no matter where they are. Believing in education and having great schools can change an entire community."

The vision originated while in graduate school. He explained, "I was working with another student, and we formulated this idea of having a high school focused on academic excellence and creating better citizens by requiring students to do public service and support their

community. All students are required to do 200 hours of community service in order to graduate. In 2003, we put together a team of educators, parents, students, and community members, and applied to start a school in New York City. The Department of Education approved it and the rest is history."

“ There are always challenges, and hemophilia is just one challenge.”

Throughout his tenure as principal and after he left, the school was a recipient of numerous awards. It was named the top *Title 1 School in New York*. "It was the first time a high school ever won the award," he said. It was also named a top *50 High School* citywide and received a bronze medal from U.S. News & World Report for being a high achiever.

Project-based and hands-on learning was essential, and the grading curriculum was based on mastery and proficiency. He said, "What they worked on, they continued to work on throughout their high school career. It was much more than just 'do an assignment and move on.' Things were not based just on a grading formula associated with a curve. It depended on whether they met the expectations their teacher set out for them. It is about supporting the student with a deep understanding of the subject, rather than a cursory understanding."

Since there were not a lot of options for fresh fruits and vegetables, the school is located in what is considered a food desert. Shuldiner explained, "We had an acre front yard and I asked the custodian if we could turn it into a farm. He said, 'You're the principal, so you can do what you want.' We created a fully functioning acre organic farm where our students plant and harvest, and use it as a classroom for biology to learn about cells and growth. We also have a farmers market every Wednesday where we can sell produce to the community. The farmers market takes food stamps, so all community members have access. It has really helped teach and show our students about healthy eating." Produce included varieties of tomatoes, eggplant, strawberries, and cucumbers among many others.

"You name the vegetable, we probably grew it!" he concluded.



THE COALITION FOR HEMOPHILIA B GOES “ON THE ROAD”

Even if you didn't make it to our Annual Symposium in Orlando, that doesn't mean you can't attend a terrific educational meeting with other families in your area. That's because the Coalition for Hemophilia B also hosts a year-long series of programs called "Family Meetings on the Road." We hold these one-day free family programs in cities across the country throughout the year, with a record 13 meetings scheduled for 2019. Five of these meetings have already taken place. These events allow families affected by hemophilia B in each locale to connect, share support, and receive valuable information and education. Families who attend these programs report that they become more knowledgeable and self-assured, leading to better health outcomes. All meetings also feature an exhibit area with opportunities to learn about available products and services offered by manufacturers and specialty pharmacies who serve the hemophilia B community.

OUR KICKOFF IN MINNEAPOLIS, MINNESOTA

The *On the Road* series kicked off May 18th in Minnesota at the Hilton Minneapolis/St. Paul Airport Hotel. The program featured a variety of sessions designed to give the families in attendance tools and information to help them manage their own hemophilia or that of a family member. Participants also had many opportunities to meet other families, share experiences, and make new friends.

One of the highlights was a presentation called *Learning from Experiences: Living with Hemophilia B*, presented by Sue Geraghty, RN. Sue served as Nurse Coordinator at the University of Colorado Denver Hemophilia and Thrombosis Center for 25 years. She talked about how we can use our own experiences and the experiences shared by others to grow and improve our strategies for managing hemophilia B and its complications on a day-to-day basis.

Families gained additional tools in a session on *Constructive Conversations*, led by Joe Schuch, Patient Affairs Liaison-Rare Disease at Pfizer. Participants learned how to get the most out of their interactions with healthcare providers and others. In another session, attendees learned about the findings of the B-HERO-S study, *Bridging Hemophilia B Experiences, Results and Opportunities into Solutions*. The session was led by Penny Smith of Novo Nordisk, which funded the study. The B-HERO-S study documents survey responses from 290 hemophilia B patients and 150 caregivers. One of the most significant findings is that most respondents, including those with mild or moderate hemophilia B, report a negative impact on things like education, work life, and participation in recreational activities.



Several sessions directly addressed some of the issues raised by the study. Felix Garcia led a session on *Rebuilding the Body with Diet*, offering strategies on using what we eat to build a strong resilient body. Another session led by Rick Starks offered participants ways to promote their own health and wellness through a system of coordinated body postures and subtle movements, breathing, and meditation known as Tai Chi.

The program concluded with an update called *What's New in Hemophilia B* presented by Coalition for Hemophilia B Chair Dr. David Clark. This is an unprecedented time for the community with more approved therapies than ever before, and even more on the way. Participants benefit greatly from Dr. Clark's deep understanding of the science and medicine behind hemophilia B therapy, as well as his gift for making complex subjects easily understandable to everyone.

The Coalition would like to thank Pfizer for its generous support of the Minneapolis program.





NEXT STOPS: ST. LOUIS AND BOSTON...

ST. LOUIS, MISSOURI

On Saturday, June 1, it was time to “hit the road” again with simultaneous meetings in St. Louis and Boston. The Missouri meeting was at the St. Louis Airport Marriott. The program featured several of the most popular sessions from the Minneapolis meeting, including *Constructive Conversations* with Pfizer’s Joe Schuch, as well as the B-HERO-S study update with Penny Smith of Novo Nordisk. Participants appreciated the tools and knowledge they gained from these two important sessions.

The meeting also had sessions on fitness, joint health, and pain management. These included a *Tai Chi Movements and Meditation* workshop led by Rick Starks and a *Kinesiology and Joint Support Workshop* led by physical therapist and sports medicine expert Dr. Doug Stringham. Participants learned easy joint stretches they can do at home or in an office setting. They also learned how kinesiology taping can assist in reducing joint pain. Dr. David Clark again provided participants with a comprehensive update on the latest in hemophilia B treatment. As treatment advances at a record rate, these types of updates are more important than ever.



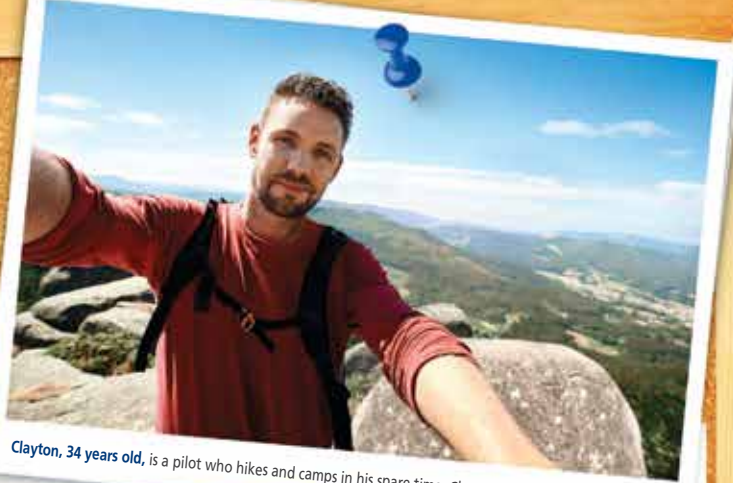
Kids in attendance had the opportunity to visit the St. Louis Zoo, where they saw gorillas, cheetahs, and many other animals. Perhaps most important, the meeting gave families the opportunity to share their own experiences and lend each other strength and support.

The Coalition for Hemophilia B would like to thank Pfizer for its generous sponsorship of the St. Louis meeting.





In hemophilia B
**TAKE CONTROL TO A
HIGH LEVEL
WITH REBINYN®**



Clayton, 34 years old, is a pilot who hikes and camps in his spare time. Clayton lives with hemophilia B.

Rebinyn® elevates factor levels above normal levels^a

+94% Factor IX (FIX) levels achieved immediately after an infusion^b

17% FIX levels sustained after 7 days^a

With a single dose of Rebinyn® 40 IU/kg in adults with $\leq 2\%$ FIX levels^a

^aIn two phase 3 studies, factor levels were evaluated for 1 week after the first dose of Rebinyn® 40 IU/kg. The average levels after 7 days were 16.8% in 6 adults, 14.6% in 3 adolescents, 10.9% in 13 children ages 7 to 12 years, and 8.4% in 12 children up to age 6 years.

Image of hemophilia B patient shown is for illustrative purposes only.

^bBased upon a 2.34% increase in factor levels per IU/kg infused in adults.

INDICATIONS AND USAGE

What is Rebinyn® Coagulation Factor IX (Recombinant), GlycoPEGylated?

Rebinyn® is an injectable medicine used to replace clotting Factor IX that is missing in patients with hemophilia B. Rebinyn® is used to treat and control bleeding in people with hemophilia B. Your healthcare provider may give you Rebinyn® when you have surgery. Rebinyn® is not used for routine prophylaxis or for immune tolerance therapy.

IMPORTANT SAFETY INFORMATION

What is the most important information I need to know about Rebinyn®?

- **Do not attempt to do an infusion yourself unless you have been taught how by your healthcare provider or hemophilia treatment center.** Carefully follow your healthcare provider's instructions regarding the dose and schedule for infusing Rebinyn®.

Who should not use Rebinyn®?

Do not use Rebinyn® if you:

- are allergic to Factor IX or any of the other ingredients of Rebinyn®.
- are allergic to hamster proteins.

What should I tell my health care provider before using Rebinyn®?

Tell your health care provider if you:

- have or have had any medical conditions.
- take any medicines, including non-prescription medicines and dietary supplements.
- are nursing, pregnant, or plan to become pregnant.
- have been told you have inhibitors to Factor IX.

How should I use Rebinyn®?

- Rebinyn® is given as an infusion into the vein.
- **Call your healthcare provider right away if your bleeding does not stop after taking Rebinyn®.**
- Do not stop using Rebinyn® without consulting your healthcare provider.

What are the possible side effects of Rebinyn®?

- **Common side effects include** swelling, pain, rash or redness at the location of the infusion, and itching.
- **Call your healthcare provider right away or get emergency treatment right away if you get any of the following signs of an allergic reaction:** hives, chest tightness, wheezing, difficulty breathing, and/or swelling of the face.
- **Tell your healthcare provider about any side effect that bothers you or that does not go away.**
- Animals given repeat doses of Rebinyn® showed Polyethylene Glycol (PEG) inside cells lining blood vessels in the choroid plexus, which makes the fluid that cushions the brain. The potential human implications of these animal tests are unknown.

Please see Brief Summary of Prescribing Information on the following page.

Rebinyn® is a prescription medication.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Learn more at rebinyn.com



Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, New Jersey 08536 U.S.A.

Rebinyn® is a registered trademark of Novo Nordisk Health Care AG.

Novo Nordisk is a registered trademark of Novo Nordisk A/S.

© 2018 Novo Nordisk All rights reserved. USA18BIO00594 August 2018

rebinyn®

Coagulation Factor IX
(Recombinant), GlycoPEGylated

rebinyn®

Coagulation Factor IX (Recombinant), GlycoPEGylated

Brief Summary Information about: REBINYN® Coagulation Factor IX (Recombinant), GlycoPEGylated

Rx Only

This information is not comprehensive.

- Talk to your healthcare provider or pharmacist
- Visit www.novo-pi.com/REBINYN.pdf to obtain FDA-approved product labeling
- Call 1-844-REB-INYN

Read the Patient Product Information and the Instructions For Use that come with REBINYN® before you start taking this medicine and each time you get a refill. There may be new information.

This Patient Product Information does not take the place of talking with your healthcare provider about your medical condition or treatment. If you have questions about REBINYN® after reading this information, ask your healthcare provider.

What is the most important information I need to know about REBINYN®?

Do not attempt to do an infusion yourself unless you have been taught how by your healthcare provider or hemophilia treatment center.

You must carefully follow your healthcare provider's instructions regarding the dose and schedule for infusing REBINYN® so that your treatment will work best for you.

What is REBINYN®?

REBINYN® is an injectable medicine used to replace clotting Factor IX that is missing in patients with hemophilia B. Hemophilia B is an inherited bleeding disorder in all age groups that prevents blood from clotting normally.

REBINYN® is used to treat and control bleeding in people with hemophilia B.

Your healthcare provider may give you REBINYN® when you have surgery.

REBINYN® is not used for routine prophylaxis or for immune tolerance therapy.

Who should not use REBINYN®?

- You should not use REBINYN® if you
- are allergic to Factor IX or any of the other ingredients of REBINYN®
 - if you are allergic to hamster proteins

If you are not sure, talk to your healthcare provider before using this medicine.

Tell your healthcare provider if you are pregnant or nursing because REBINYN® might not be right for you.

What should I tell my healthcare provider before I use REBINYN®?

You should tell your healthcare provider if you

- Have or have had any medical conditions.
- Take any medicines, including non-prescription medicines and dietary supplements.
- Are nursing.
- Are pregnant or planning to become pregnant.
- Have been told that you have inhibitors to Factor IX.

How should I use REBINYN®?

Treatment with REBINYN® should be started by a healthcare provider who is experienced in the care of patients with hemophilia B.

REBINYN® is given as an infusion into the vein.

You may infuse REBINYN® at a hemophilia treatment center, at your healthcare provider's office or in your home. You should be trained on how to do infusions by your hemophilia treatment center or healthcare provider. Many people with hemophilia B learn to

infuse the medicine by themselves or with the help of a family member.

Your healthcare provider will tell you how much REBINYN® to use based on your weight, the severity of your hemophilia B, and where you are bleeding. Your dose will be calculated in international units, IU.

Call your healthcare provider right away if your bleeding does not stop after taking REBINYN®.

If your bleeding is not adequately controlled, it could be due to the development of Factor IX inhibitors. This should be checked by your healthcare provider. You might need a higher dose of REBINYN® or even a different product to control bleeding. Do not increase the total dose of REBINYN® to control your bleeding without consulting your healthcare provider.

Use in children

REBINYN® can be used in children. Your healthcare provider will decide the dose of REBINYN® you will receive.

If you forget to use REBINYN®

If you forget a dose, infuse the missed dose when you discover the mistake. Do not infuse a double dose to make up for a forgotten dose. Proceed with the next infusions as scheduled and continue as advised by your healthcare provider.

If you stop using REBINYN®

Do not stop using REBINYN® without consulting your healthcare provider.

If you have any further questions on the use of this product, ask your healthcare provider.

What if I take too much REBINYN®?

Always take REBINYN® exactly as your healthcare provider has told you. You should check with your healthcare provider if you are not sure. If you infuse more REBINYN® than recommended, tell your healthcare provider as soon as possible.

What are the possible side effects of REBINYN®?

Common Side Effects Include:

- swelling, pain, rash or redness at the location of infusion
- itching

Other Possible Side Effects:

You could have an allergic reaction to coagulation Factor IX products. **Call your healthcare provider right away or get emergency treatment right away if you get any of the following signs of an allergic reaction:** hives, chest tightness, wheezing, difficulty breathing, and/or swelling of the face.

Your body can also make antibodies called "inhibitors" against REBINYN®, which may stop REBINYN® from working properly. Your healthcare provider may need to test your blood for inhibitors from time to time.

You may be at an increased risk of forming blood clots in your body, especially if you have risk factors for developing blood clots. Call your healthcare provider if you have chest pain, difficulty breathing, leg tenderness or swelling.

Animals given repeat doses of REBINYN® showed Polyethylene Glycol (PEG) inside cells lining blood vessels in the choroid plexus, which makes the fluid that cushions the brain. The potential human implications of these animal tests are unknown.

These are not all of the possible side effects from REBINYN®. Ask your healthcare provider for more information. You are encouraged to report side effects to FDA at 1-800-FDA-1088.

Tell your healthcare provider about any side effect that bothers you or that does not go away.

What are the REBINYN® dosage strengths?

REBINYN® comes in three different dosage strengths. The actual number of international units (IU) of Factor IX in the vial will be imprinted on the label and on the box. The three different strengths are as follows:

Cap Color Indicator	Nominal Strength
Red	500 IU per vial
Green	1000 IU per vial
Yellow	2000 IU per vial

Always check the actual dosage strength printed on the label to make sure you are using the strength prescribed by your healthcare provider.

How should I store REBINYN®?

Prior to Reconstitution (mixing the dry powder in the vial with the diluent):

Store in original package in order to protect from light. Do not freeze REBINYN®.

REBINYN® vials can be stored in the refrigerator (36-46°F [2°C-8°C]) for up to 24 months until the expiration date, or at room temperature (up to 86°F [30°C]) for a single period not more than 6 months.

If you choose to store REBINYN® at room temperature:

- Note the date that the product is removed from refrigeration on the box.
- The total time of storage at room temperature should not be more than 6 months. Do not return the product to the refrigerator.
- Do not use after 6 months from this date or the expiration date listed on the vial, whichever is earlier.

Do not use this medicine after the expiration date which is on the outer carton and the vial. The expiration date refers to the last day of that month.

After Reconstitution:

The reconstituted (the final product once the powder is mixed with the diluent) REBINYN® should appear clear without visible particles.

The reconstituted REBINYN® should be used immediately.

If you cannot use the reconstituted REBINYN® immediately, it should be used within 4 hours when stored at or below 86°F (30°C). Store the reconstituted product in the vial.

Keep this medicine out of the sight and out of reach of children.

What else should I know about REBINYN® and hemophilia B?

Medicines are sometimes prescribed for purposes other than those listed here. Do not use REBINYN® for a condition for which it is not prescribed. Do not share REBINYN® with other people, even if they have the same symptoms that you have.

More detailed information is available upon request.

Available by prescription only.

For more information about REBINYN®, please call Novo Nordisk at 1-844-REB-INYN.

Revised: 11/2017

REBINYN® is a trademark of Novo Nordisk A/S.

For Patent Information, refer to: <http://novonordisk-us.com/patients/products/product-patents.html>

Manufactured by:

Novo Nordisk A/S

Novo Allé, DK-2880 Bagsværd, Denmark

For information about REBINYN® contact:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, NJ 08536, USA

© 2017 Novo Nordisk
USA17BI003951 12/2017





BOSTON, MASSACHUSETTS

On the same day as St. Louis, June 1, families gathered at the Holiday Inn Boston-Bunker Hill for yet another wonderful *Family Meeting on the Road*. At the Boston meeting, the B-HERO-S study update was presented by Michael F. Guerrero, MD, Director of the Comprehensive Hemostasis and Thrombosis Program at Children's National Health System in Washington, DC.

Participants received an update on advocacy and access to care in a session called *The B Voice: It Starts with You and Me*. The session was led by Glenn Mones, The Coalition for Hemophilia B's Advocacy Consultant with 20 years of experience in the hemophilia community. The attendees learned about how the Coalition's *B Voice* Advocacy Program is addressing health insurance issues and other challenges to adequate reimbursement for quality treatment. Community members were encouraged to use their own voices to help make a real difference.

Several sessions focused on attaining physical and mental well-being. A highly interactive session called *Managing the Stress of Hemophilia B* was led by Robert Lawrence Friedman, MA. Friedman is an author, speaker, trainer, and psychotherapist who has provided his unique training programs to Fortune 500 corporations, universities, and healthcare organizations throughout the United States, Europe, and Asia. He is the author of *How to Relax in 60 Seconds or Less*. Participants were offered specific and easy-to-learn techniques for instantly reducing tension and effectively managing stress.

A session on *Light Beginner Chair Yoga* was led by Mihaela Dumea, a wellness counselor, consultant, and teacher of yoga and meditation. Participants

learned centering breathing exercises, light stretching techniques, and the basis of chair yoga. The benefits of these techniques can include an increase in strength and flexibility, decreased levels of pain, and a decrease in blood pressure.

Dr. Michael Zolotnitsky, PT, DPT, an orthopedic and neurological physical therapist with severe hemophilia A, led a workshop in *Kinesiology and Joint Support*, demonstrating how the application of kinesio tape can be used to reduce pain and inflammation in almost any part of the body. Participants had the opportunity to apply tape to their own problem areas and were given tape samples to use at home.

Kids in attendance enjoyed a trip to the New England Aquarium located at Boston's Central Wharf. The young visitors had the opportunity to view the aquarium's thousands of fascinating sea creatures and other attractions.

Every *Family Meeting on the Road* includes an all-important update on the status of research and treatment, and the Boston meeting was certainly no exception. The update was given by Dr. Shelby Smoak, a former college professor with a PhD in Literature and a long-time hemophilia community advocate. His 2013 memoir *Bleeder* was published to critical acclaim and received an American Library Association book of the year award. Dr. Smoak gave a comprehensive presentation on the status of treatment as well as a peek at what is yet to come.

The Coalition for Hemophilia B would like to thank CSL Behring for its generous support of the Boston meeting.

CSL Behring



ON THE ROAD AGAIN: DALLAS AND ANN ARBOR

DALLAS, TEXAS

Saturday, June 8th was another “double header” as The Coalition for Hemophilia B headed to Dallas and Ann Arbor for two more Family Meetings on the Road. The Dallas meeting was held at the Sheraton Dallas Hotel. A session that debuted at this meeting was entitled *Braving Change*, led by Nikita Lyons, Patient Liaison with Bioverativ. The program allowed participants to explore the concept of resilience in the face of change, including ways to adapt to difficult circumstances. Other concepts included characteristics of resilient individuals and ways of fostering resilience within the family, at school, and in the larger community.



Physical and mental well-being was addressed in a chair yoga workshop led by John Avitia, a personal trainer who emphasized building stability and mobility in joints. Robert Friedman then followed up with another edition of his *Managing the Stress of Hemophilia B* workshop. This time, he also included part of a presentation called *What's So Funny*, focusing on the physical, mental, and emotional benefits of humor.



Kids in attendance had the opportunity to visit the Dallas Aquarium, where they interacted with a three-toed sloth and a variety of fascinating sea creatures. The program concluded with Dr. David Clark's update on the latest news and information regarding hemophilia B.



The Coalition for Hemophilia B would like to thank CSL Behring for its generous sponsorship of the Dallas meeting.

CSL Behring





ANN ARBOR, MICHIGAN

On the same day as the Dallas meeting, the Sheraton Ann Arbor Hotel in Michigan served as the venue for yet another Family Meeting on the Road. Ann Arbor attendees enjoyed the special participation of Ben Shuldiner. Ben has hemophilia B and is a leading educator who, at the age of 25, founded and led the High School for Public Service in New York City. Currently, he is a professor at New York City's Hunter College. Ben opened the Ann Arbor program with a session on *504 Plans and IEPs* (Individualized Education Programs). These are documents designed to protect the legal right of any child with special needs or health issues to receive special accommodations from their school. Ben advised parents on how to ask for the right things to create a document that genuinely helps their child. Later in the day, Ben also took on the *Hemophilia B Update*, providing participants with the latest information about the status of treatment for hemophilia B.

Another first-time learning session in Ann Arbor was called the *Power of Empowerment*. It was presented by Shelley Gerson, MEd, a professional educator with a long history in the bleeding disorders community and a Patient Education and Advocacy Manager at Sanofi Genzyme. Shelley taught participants ways of becoming more empowered—such as by acknowledging strengths, embracing individuality, creating safe environments, enhancing confidence, and establishing supportive partnerships.

In other popular sessions, Dr. Michael F. Guerrero again



presented the findings of the B-HERO-S study on behalf of the study sponsor, Novo Nordisk. The light chair yoga session (another consistent feature of all the meetings) was led by local yoga instructor Paul Barr, founder and owner of Oxford Yoga Studio. He focused on increased balance, strength, flexibility, range of motion, and stress reduction.

Kids in attendance took an exciting trip to the Ann Arbor Hands-On Museum. As the name implies, the museum has many installations that allow kids to learn by exploring, touching, investigating, and problem solving. As always, the meeting offered many opportunities for families to interact and share their own strength and experience.

The Coalition for Hemophilia B would like to thank CSL Behring for its generous sponsorship of the Ann Arbor meeting.

CSL Behring





THANK YOU

In addition, we would like to thank the many speakers, staff team members, volunteers, exhibitors, and of course the participating families for making these first five *On the Road* meetings of the year a great success.

JOIN US AT AN UPCOMING MEETING

There are still eight meetings left for 2019. They will be held in Columbus, OH and Knoxville, TN on October 19; in Atlanta, GA and Seattle, WA on October 26; in Fort Smith, AR and Baton Rouge, LA on November 2; and in Phoenix, AZ and Schaumburg, IL on November 9. Please visit our website at www.hemob.org for more information and to register.



Benefix[®]
Coagulation Factor IX (Recombinant)
Room Temperature Storage






*Benefix was approved February 11, 1997.

Not actual patients.

EXPERIENCE MATTERS

BeneFix: The only recombinant factor IX supporting individuals with hemophilia for more than 20 years.*

More than 20 years* of experience—you've been at the heart of all we do

-  The first recombinant treatment indicated for bleed control and prevention in individuals with hemophilia B
-  Designed with viral safety in mind
-  More than 150 quality control tests are done on each batch of BeneFix
-  The flexibility to infuse on demand or preventively based on your physical activity
-  The convenience of the BeneFix Rapid Reconstitution (R2) Kit with a range of vial sizes



What Is BeneFix?

BeneFix, Coagulation Factor IX (Recombinant), is an injectable medicine that is used to help control and prevent bleeding in people with hemophilia B. Hemophilia B is also called congenital factor IX deficiency or Christmas disease.

BeneFix is **NOT** used to treat hemophilia A.

Important Safety Information

- BeneFix is contraindicated in patients who have manifested life-threatening, immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster protein.
- Call your health care provider right away if your bleeding is not controlled after using BeneFix.
- Allergic reactions may occur with BeneFix. Call your health care provider or get emergency treatment right away if you have any of the following symptoms: wheezing, difficulty breathing, chest tightness, your lips and gums turning blue, fast heartbeat, facial swelling, faintness, rash or hives.

Visit BeneFix.com to learn more

- Your body can make antibodies, called “inhibitors,” which may stop BeneFix from working properly.
- If you have risk factors for developing blood clots, such as a venous catheter through which BeneFix is given by continuous infusion, BeneFix may increase the risk of abnormal blood clots. The safety and efficacy of BeneFix administration by continuous infusion have not been established.
- Some common side effects of BeneFix are nausea, injection site reaction, injection site pain, headache, dizziness and rash.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see the Brief Summary for BeneFix on the next page.



R_x only

Brief Summary

See package insert for full Prescribing Information. This product's label may have been updated. For further product information and current package insert, please visit www.Pfizer.com or call our medical communications department toll-free at 1-800-438-1985.

Please read this Patient Information carefully before using BeneFix and each time you get a refill. There may be new information. This brief summary does not take the place of talking with your doctor about your medical problems or your treatment.

What is BeneFix?

BeneFix is an injectable medicine that is used to help control and prevent bleeding in people with hemophilia B. Hemophilia B is also called congenital factor IX deficiency or Christmas disease.

BeneFix is **NOT** used to treat hemophilia A.

What should I tell my doctor before using BeneFix?

Tell your doctor and pharmacist about all of the medicines you take, including all prescription and non-prescription medicines, such as over-the-counter medicines, supplements, or herbal remedies.

Tell your doctor about all of your medical conditions, including if you:

- are pregnant or planning to become pregnant. It is not known if BeneFix may harm your unborn baby.
- are breastfeeding. It is not known if BeneFix passes into the milk and if it can harm your baby.

How should I infuse BeneFix?

The initial administrations of BeneFix should be administered under proper medical supervision, where proper medical care for severe allergic reactions could be provided.

See the step-by-step instructions for infusing in the complete patient labeling.

You should always follow the specific instructions given by your doctor. If you are unsure of the procedures, please call your doctor or pharmacist before using.

Call your doctor right away if bleeding is not controlled after using BeneFix.

Your doctor will prescribe the dose that you should take. Your doctor may need to test your blood from time to time. BeneFix should not be administered by continuous infusion.

What if I take too much BeneFix?

Call your doctor if you take too much BeneFix.

What are the possible side effects of BeneFix?

Allergic reactions may occur with BeneFix. Call your doctor or get emergency treatment right away if you have any of the following symptoms:

wheezing	fast heartbeat
difficulty breathing	swelling of the face
chest tightness	faintness
turning blue (look at lips and gums)	rash
	hives

Your body can also make antibodies, called "inhibitors," against BeneFix, which may stop BeneFix from working properly.

Some common side effects of BeneFix are nausea, injection site reaction, injection site pain, headache, dizziness and rash.

BeneFix may increase the risk of thromboembolism (abnormal blood clots) in your body if you have risk factors for developing blood clots, including an indwelling venous catheter through which BeneFix is given by continuous infusion. There have been reports of severe blood clotting events, including life-threatening blood clots in critically ill neonates, while receiving continuous-infusion BeneFix through a central venous catheter. The safety and efficacy of BeneFix administration by continuous infusion have not been established.

These are not all the possible side effects of BeneFix.

Tell your doctor about any side effect that bothers you or that does not go away.

How should I store BeneFix?

DO NOT FREEZE BeneFix. The BeneFix kit can be stored at room temperature (below 86°F) or under refrigeration. Throw away any unused BeneFix and diluent after the expiration date indicated on the label.

Freezing should be avoided to prevent damage to the pre-filled diluent syringe.

BeneFix does not contain a preservative. After reconstituting BeneFix, you can store it at room temperature for up to 3 hours. If you have not used it in 3 hours, throw it away.

Do not use BeneFix if the reconstituted solution is not clear and colorless.

What else should I know about BeneFix?

Medicines are sometimes prescribed for purposes other than those listed here. Do not use BeneFix for a condition for which it was not prescribed. Do not share BeneFix with other people, even if they have the same symptoms that you have.

If you would like more information, talk to your doctor. You can ask your doctor for information about BeneFix that was written for healthcare professionals.

This brief summary is based on BeneFix® [Coagulation Factor IX (Recombinant)] Prescribing Information LAB-0464-10.0, revised June 2017.

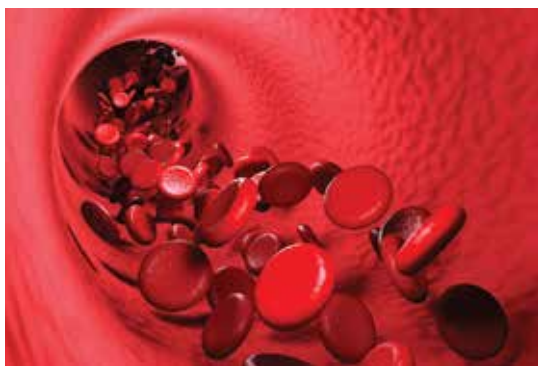
HEMOPHILIA UPDATE

By Dr. David Clark

NON-FACTOR TREATMENT AND CLOTTING

A group from France is studying the inhibition of the anticoagulant Protease Nexin-1 (PN-1) as a way of rebalancing the clotting system without using factor. PN-1 is a potent inhibitor of thrombin (factor IIa), the factor that converts fibrinogen to fibrin to form a clot. In studies in mice, the researchers showed that they can promote hemostasis (normal clotting) by inhibiting PN-1.

[ISTH abstract OC 75.3]



A group from The Netherlands has shown that the composition of microbes in the gut (intestines) has an effect on clotting. The researchers used fecal matter transplants in 35 subjects to alter their gut bacteria and then measured thrombin generation and levels of 43 clotting-related proteins. They showed that the gut microbe composition affects the body's production of a number of clotting factors, which affects clotting ability.

[ISTH abstract OC 35.3]



ORAL DELIVERY

At least two organizations are working on robotic pills that could deliver factor IX orally.

At ISTH, Takeda and Rani Therapeutics made a presentation on a robotic pill containing clotting factors or other proteins. The pill is swallowed and passes through the stomach unchanged. When the pill reaches the small intestine, a tiny balloon inside the pill inflates, pushing micro-needles out from the sides of the pill. The micro-needles

pierce the intestinal wall injecting the pill contents into the bloodstream. Takeda focused on factor VIII for the presentation, but factor IX or other proteins could just as easily be used. [ISTH abstract OC 60.5]

Novo Nordisk and the Massachusetts Institute of

Technology (MIT) are working on a similar robotic pill. Although Novo is initially focusing on insulin delivery, the pill could be used to deliver other proteins, including clotting factors. This pill has a single needle, which it uses to inject its payload through the wall of the stomach. The pill has a special mechanism to make it stand upright in the stomach to ensure that the needle pierces the stomach wall. [MIT News at news.mit.edu, 2/7/19]

GENE THERAPY

A group at the Medical College of Wisconsin has shown that gene therapy targeted to platelets can promote factor IX production by the platelets. The researchers modified hematopoietic stem cells (cells in the bone marrow that continuously produce platelets and other blood cells) with a factor IX gene and transplanted the cells into hemophilia B mice. All of the mice showed increased factor IX production and correction of their bleeding tendency.

[ISTH abstract OC 53.4]



MILD AND MODERATE HEMOPHILIA

Recent studies have shown that life expectancy for people with mild and moderate hemophilia (A or B) is the same as for the normal population. But what about quality of life? The Patient-Reported Outcomes Burdens and Experiences (PROBE) study group looked at quality of life (QoL) indicators for that population compared with normal controls (i.e., people without bleeding disorders). They found that milds and moderates have more health-related problems, more school/work issues, and lower health-related quality of life. According to the group, mild and moderate hemophilia "is not a benign disease." They found that traditional measures used for severe hemophilia, such as bleeding rates and factor levels, are less-sensitive indicators of health status for milds and moderates.

[ISTH abstract OC 32.4]

This is a summary of noncommercial research news on hemophilia. Most of the following news was presented at the 2019 Congress of the International Society on Thrombosis and Haemostasis (ISTH) in Melbourne, Australia, July 6–10, 2019. Free copies of the abstracts (summaries of the presentations) can be found at <https://onlinelibrary.wiley.com/toc/24750379/2019/3/S1>.



HEMOPHILIC ARTHROPATHY (JOINT DISEASE)

A number of studies of hemophilia joint disease were presented at the ISTH 2019 Congress. Iron accumulation after a joint bleeding episode appears to be unique to hemophilia (A or B). The iron is

apparently involved in degradation of the joint, but the exact mechanism is unknown. A group from University of California San Diego and the Scripps Institute carried out studies in hemophilic mice to look at iron transport in the joints. The researchers saw changes in a number of proteins that may influence iron clearance from the joint. Further study is necessary. [ISTH abstract OC 75.4]

A group of European and Japanese scientists have looked at the effect of Protein S, an anticoagulant, on joint damage. They found that inhibiting Protein S reduces joint damage in hemophilic mice. It is not clear whether the effect is from rebalancing the clotting system, so joint bleeding ceases more quickly, or if it depends on another action of Protein S. The group is continuing to look at the effect of Protein S on the inflammation that promotes chronic joint damage. [ISTH abstract OC 75.2]

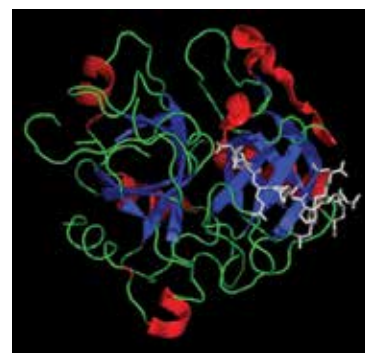
A protein called thrombin-activatable fibrinolysis inhibitor (TAFI) is activated in normal bleeding by the thrombin created during the clotting process. However, the low thrombin levels generated in hemophilic patients only activates minimal amounts of TAFI, causing easier breakdown of clots (fibrinolysis) and growth of aberrant blood vessels, leading to joint degradation. Scientists from UC San Diego and Scripps Institute found that by increasing TAFI levels, they could normalize hemostasis in the joints of hemophilic mice. They also found that increased TAFI levels prevented the formation of dysfunctional blood vessels in the joints. [ISTH abstract OC 75.1]

A study of moderate and severe hemophilia patients in Europe looked for information on joint bleeding and joint damage in children. The authors studied 785 patients ranging in age from two or younger to 17 years of age, including inhibitor patients, of which 76% were on continuous or intermittent prophylaxis and 24% were treated on demand. They found that 33% of inhibitor patients, 20% of severe non-inhibitor patients, and 11%

of moderate non-inhibitor patients had target joints and evidence of chronic joint disease. The conclusion was that there are unmet needs and opportunities for improvement in treatment of children with hemophilia. [ISTH abstract OC 70.1]

FACTOR IX ASSAYS

One of the under appreciated aspects of hemophilia is that factor IX (FIX) assays are very tricky to run. Assays are tests for the amount of FIX. Manufacturers rely on these assays in determining how much product to put in a vial, and patients and physicians rely on them to determine how much FIX is in the patient's bloodstream. A FIX assay tries to mimic in the laboratory how FIX performs in the blood. There are several different types of FIX assays and a number of different reagents (the chemicals used in the assay). They don't always give the same result, and the differences have expanded with the introduction of the extended half-life (EHL) products.



A group of German researchers looked at several assay types with several different reagents with the three current EHL products plus one standard half-life (SHL) product. With the SHL product, most of the assays agreed within about 20%, except for two that differed by 57% and 68%. With Alprolix, the assay discrepancies varied more widely with differences between 35% and 88%. With Idelvion, the differences ranged up to 78%, and with Rebinyn, the discrepancies varied up to 19.6 times (18,600%) greater potency. The study's authors recommend a need for better test procedures and standardization. [ISTH abstract OC 07.2]

A group of Dutch researchers performed a similar study comparing two types of FIX assays. In testing conducted at 144 different laboratories, they found similar large discrepancies, including large variations in repeat testing of the same sample with the same assay. [ISTH abstract OC 07.5]

These studies and others demonstrate that assay results shouldn't be given too much credibility. They are just a guide. Your bleeding behavior may be a much better indicator of how a product is working for you.

HEMOPHILIA UPDATE

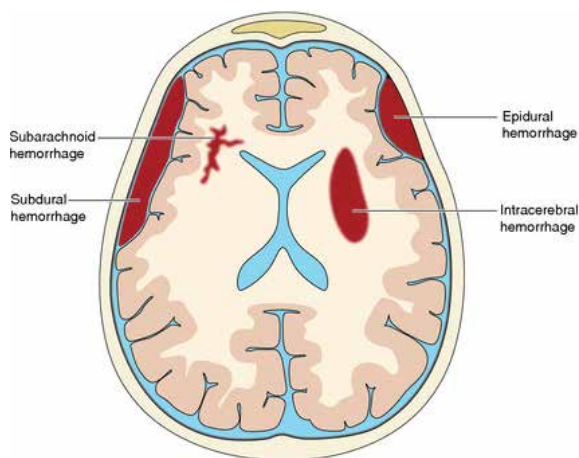
SWITCHING TO EHL PRODUCTS

Several ISTH papers focused on switching from SHL to EHL products. One group looked at hemophilia B patients in Ireland, all of whom were switched to an EHL product. Studying patient-reported outcomes, the researchers found significant improvements in most QoL measures as well as decreases in bleeding rates. Pre-switch, 29% of patients reported having eight or more bleeds per year and 41% reported having one or fewer bleeds a year. After the switch, there were no patients reporting eight or more bleeds and 59% reported one or fewer bleeds per year. [ISTH abstract OC 42.4]

A U.S. group looked at severe B patients at four hemophilia treatment centers (HTCs) who had switched to either Alprolix or Idelvion (none of the patients switched to Rebinyn). Out of 55 patients, 13 reported unexpected bleeding and/or poor bleeding control. The study's authors suggest that FIX levels themselves might not be the best guide to dosing EHL products, and that much more research is needed to really understand the mechanisms of the EHL products. [ISTH abstract OC 70.4]

INTRACRANIAL HEMORRHAGE

There have been a number of reports in the literature on intracranial hemorrhage (ICH), or bleeding in the brain, in hemophilia patients, but they report a wide range of incidence and mortality (death). A Dutch group surveyed all of the studies—56 studies, including over 82,000 patients and 1,508 ICH events—from 1960 to 2018. Pooling the studies and summarizing and analyzing all the results, they found an average incidence of 400 per 100,000 person-years for hemophilia patients compared with a rate of 25 per 100,000 person-years in the general population. Interestingly, the ICH incidence fell from 8% in the period 1960–1979 to 3% in 2000–2018 (possibly as a result of the increased use of prophylaxis). [ISTH abstract OC 70.3]



WOMEN WITH HEMOPHILIA

“Hemophilia carriers (HCs) face specific psychosocial and physical challenges related to their inherited bleeding disorder.” So says a group of Dutch researchers who surveyed all of the medical literature on carriers and pregnancy. Their primary findings:

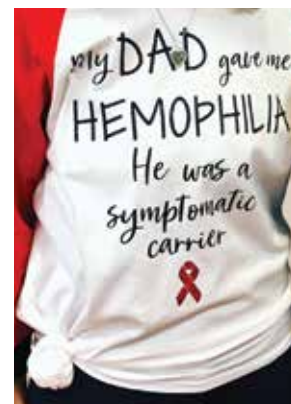
1. Genetic counseling is generally considered useful.
2. A specialized clinic focusing on issues for HCs would be valuable.
3. HCs considered prenatal diagnosis as beneficial but psychologically challenging.
4. The experiences of noninvasive prenatal diagnosis and preimplantation genetic testing were predominantly positive. The authors of this survey also bemoan the lack of more studies on the psychosocial challenges surrounding pregnancy and hemophilia. [ISTH abstract OC 19.2]

Another Dutch study looked at postpartum hemorrhage (PPH), which is excessive bleeding after giving birth, in hemophilia carriers and women with von Willebrand Disease (vWD). Overall, the rate of PPH was 36.6%. The authors state that the need for changes in post-birth management of hemophilia carriers and women with vWD is evident. The risk of PPH remains high even with clotting factor treatment. [ISTH abstract OC 19.4]

An 11-year study of hemophilia patients and carriers in Sweden showed that they have a higher risk of experiencing pain, anxiety, and depression than non-hemophiliac controls. Similar patterns were seen in carriers as well as in hemophilia patients, indicating the need for better medical attention and further research. [ISTH abstract OC 32.3]

HEMOPHILIA NEWS TODAY HAS A COLUMN ON WOMEN WITH HEMOPHILIA

Hemophilia News Today is a free online newsletter (<https://hemophilianewstoday.com/>) covering both psychosocial and medical aspects of hemophilia. Shellye Horowitz, a woman with hemophilia A, writes “*The Forgotten Factor*” column on issues for women with hemophilia. What first caught our eye was the June 4, 2019 column in which she described a T-shirt she made that said, “My dad gave me hemophilia. He was a symptomatic carrier.”



YOUNG ENTREPRENEUR PARKER FEAGINS USES HIS LOVE OF THE MUSIC BUSINESS TO CREATE COMMUNITY



A veritable Renaissance man, Parker's interests are engineering and math, robotics, bass clarinet, and the business side of music.

Fourteen-year-old Parker, a freshman who attends L&N STEM Academy in Knoxville, Tennessee, has started a business to promote young musicians —YP Entertainment, LLC. His first show was January 5, 2019, at Knoxville's Central Collective.

He called it *JAMuary the 5th*, and it was quite a way to start the year. The local bands he lined up to play included Garret Smith, Nightfly, Astro Biz, Denzel Hendricks, Indigo Age, and Vagabon Brew.

"This is the first show I've done so far," said Parker, who lives in Halls, Tennessee, with his parents, Jenifer Feagins Fraker and Jason Fraker, and four siblings. "I really like organizing shows and creating community around them." Parker donated the profits from the show's ticket sales to The Coalition for Hemophilia B.

Both Parker and his little brother Ben have hemophilia B. "Ben and I have the mildest form, so we're lucky, but it's really disabling for some people. Knowing what the Coalition has done for me with my mild hemophilia, I can imagine what they could do for someone with more severe hemophilia—they built a pool for a kid one time. Kim Phelan, Coalition's Vice President, has helped me through a lot."

Parker, who is interested in engineering and math, plays bass clarinet at school but got hooked on the business side of music when he was marketing his robotics team and learned about SoundCloud.com. "I've met great people through this work. It's interesting and very quirky, and I've learned that I don't have to be the public face of the music," he said.

When asked if he'd like to be the next Ashley Capps—the music promoter and founder of AC Entertainment, also based in Knoxville—Parker laughed and said that's his goal, "I'm thinking about applying for an internship there."

The original article, "Parker Feagins, 14, kicks off music promotion career with JAMuary," appeared in the January 2, 2019, edition of KnoxvilleToday.com. Reprinted with permission.

TREATMENT NEWS

By Dr. David Clark

APTEVO ANNOUNCES AVAILABILITY OF 3000 IU VIALS FOR IXINITY, PLUS PEDIATRIC STUDY



6/25/19 Aptevo Therapeutics has launched a new 3000 IU vial of Ixinity, its recombinant factor IX product. It will now be available in 500, 1000, 1500, and 3000 IU vials. Aptevo believes that this will offer important advantages and additional convenience for patients. Interestingly, while some of the standard half-life products, like Ixinity, have lost market share to extended half-life products, Ixinity sales more than doubled from 2017 to 2018.

Aptevo also announced that it will begin a Phase IV (post-licensure) study of Ixinity for pediatric use. The study will enroll 20 hemophilia B patients under 12 years of age. Since about one-third of Bs are currently under 13 years of age, the company believes that this will lead to an important expansion of its market. [Aptevo press release]

ROCHE AND SPARK PUSH BACK DEADLINE FOR TAKEOVER



6/10/19 Roche is attempting to buy gene therapy company Spark Therapeutics in a deal worth \$4.3 billion. The deadline has been delayed to 4/30/20 while the U.S. Federal Trade Commission looks at any anticompetitive issues. (One concern is that Roche would delay the development of Spark's gene therapy for hemophilia A to extend the viable lifetime of Hemlibra, Roche's non-factor treatment for hemophilia A. However, with several other hemophilia A gene therapy competitors, it is unlikely that Roche would delay its own product.) With Spark, Roche will get a hemophilia A gene therapy treatment but not Spark's hemophilia B gene therapy that has been taken over by Pfizer. [Roche press release]

NEWS FROM ISTH 2019

Most of the following news was presented at the 2019 Congress of the International Society on Thrombosis and Haemostasis (ISTH) in Melbourne, Australia, July 6–10, 2019. Free copies of the abstracts (summaries of the presentations) can be found at <https://onlinelibrary.wiley.com/toc/24750379/2019/3/S1>.



CATALYST PRESENTS UPDATES ON DALCA



Catalyst Biosciences is developing Dalcinonacog Alfa (DalcA), a variant recombinant factor IX. DalcA is 22 times more potent than normal factor IX

and has a longer half-life. It will be given subcutaneously once daily. Two related patients in the Phase I/II study developed inhibitors to DalcA, but not to normal factor IX. Catalyst did an impressive and comprehensive study of the immunogenicity (tendency for inhibitor development) of DalcA, which showed that DalcA is no more immunogenic than normal factor IX. A Phase IIb study is currently underway, with results expected by the end of 2019. [ISTH abstracts PB0312 and PB0315]

CATALYST REPORTS ON PROGRESS WITH MARZAA FOR INHIBITOR TREATMENT



Catalyst is also developing Marzeptacog Alfa (Activated) (MarZAA), a variant recombinant factor VIIa for treatment of hemophilia A and B patients with inhibitors. In a Phase II study to test the possibility of subcutaneous injection, 13 subjects with inhibitors experienced a reduction in mean annualized bleeding rate (ABR) from 19.8 pre-treatment to 1.6 with MarZAA. The product appeared safe and well tolerated with no inhibitor development. One fatal adverse event occurred, an intracerebral hemorrhage in a patient with untreated high blood pressure. That event was deemed to not be related to the product. Catalyst is currently planning a Phase III study.

Catalyst also performed a related study to examine quality of life (QoL) in inhibitor patients. The study looked at patients on daily subcutaneous MarZAA compared to other inhibitor and non-inhibitor patients using validated screening tools. The baseline (prior to treatment with MarZAA) QoL scores were significantly worse than published results for non-inhibitor patients. After 28 to 50 days of MarZAA treatment, all patients showed a trend toward better scores. [ISTH abstracts OC 11.4 and PB0240]

CSL PRESENTS STUDIES ON IDELVION

CSL Behring

CSL Behring presented a number of reports on continuing studies for Idelvion, the company's licensed extended half-life factor IX product. In studies in Italy, Belgium, and Germany, 84 patients saw reductions in the mean ABR of 68–94% with Idelvion prophylaxis compared to their earlier experience on standard half-life products. Most of the patients received Idelvion every seven days or longer. Their mean weekly factor IX consumption was reduced by 56–73%. CSL is currently studying health-related quality of life (HRQoL) in these patients. [ISTH abstracts PB0281 and PB0691]

This is a summary of news from the organizations developing new and/or improved treatments for hemophilia B. Treatment News is now being updated regularly on B Connected. Look for the Treatment News channel. News will be posted online soon after it is announced.

In another study, 83 previously treated patients' dosing intervals ranged from 7 to 21 days with mean trough levels of greater than 5%. Spontaneous bleeding rates were low and no inhibitors were observed. [ISTH abstract PB1453]

In a study of patients undergoing surgery on Idelvion, hemostatic efficacy (prevention of bleeding) was rated "excellent" or "good" in 89% of cases. Use of Idelvion resulted in low factor IX consumption and infrequent need for infusions during surgery. Blood losses were lower than predicted for most patients. No patients developed inhibitors or experienced Idelvion-related adverse events. [ISTH abstract PB0734]

CSL also presented a case report of a patient who switched from a standard half-life product to Idelvion. In addition to hemophilia B, the patient had epilepsy and neurological disabilities caused by an intracerebral hemorrhage at age 4. The patient switched to Idelvion at age 24, first with infusions every 10 days, later extended to every 14 days. He maintained a trough level of >20%. His factor usage decreased from 56,000 IU to 12,000 IU every 42 days. This change greatly improved the quality of life for both the patient and his parent-caregivers. [ISTH abstract PB0684]

FREELINE ANNOUNCES UPDATED GENE THERAPY DATA



Freeline Therapeutics reported results from its Phase I/II trial of an experimental gene therapy for hemophilia B. The treatment, FLT180a, uses an AAV3 vector and the high-potency Padua variant of factor IX. After a year in the two patients who received the lowest dose, Freeline saw a sustained factor IX level of 40% with no evidence of liver inflammation. Freeline is also starting development of a gene therapy for hemophilia A. [ISTH abstract PB0309 and Freeline press release]

MITSUBISHI TANABE ENTERS HEMOPHILIA B GENE THERAPY RACE

8/6/19 Japan-based Mitsubishi Tanabe Pharma is joining with Jichi Medical University to develop a gene therapy treatment for hemophilia B. They will use an adeno-associated virus (AAV) vector, but little else has been announced. The project is being funded by a grant from the Japan Agency for Medical Research and Development. [Mitsubishi Tanabe Pharma press release]



NOVO NORDISK PRESENTS ADDITIONAL DATA ON REBINYN



Novo Nordisk presented an update on its Phase III study of Rebinyn in previously untreated patients (PUPs). Rebinyn uses polyethylene glycol (PEG) to give it an extended half-life. Novo enrolled 37 patients with ages from 0–4 years who were placed on prophylaxis with Rebinyn with a mean trough level of 15% of normal. The estimated mean ABR was 0.31. Those patients who experienced bleeds were treated with one dose of Rebinyn. Two of 33 (6.1%) patients developed inhibitors, which is consistent with the rate of inhibitor development reported in the literature for normal factor IX products. Otherwise, Rebinyn was efficacious and well tolerated. [ISTH abstract OC 42.5]

Another Phase III study looked at previously treated children (12 years old and younger) who had been treated with Rebinyn for at least five years. The study found a median ABR of 0.66, and any bleeds were treated with 1–2 doses of Rebinyn. The bleeding rates declined over the five years: 20% of the subjects were bleed-free and 64% developed no spontaneous bleeds. No inhibitors were detected. The mean concentration of PEG in the plasma reached a steady-state level in 3–6 months and then remained stable for up to five years. [ISTH abstract PB0242]

NOVO UPDATES RESULTS FOR CONCIZUMAB



Novo Nordisk is developing concizumab, a recombinant antibody that inhibits the anticoagulant tissue factor pathway inhibitor (TFPI). Inhibiting TFPI is expected to restore the balance in the clotting system that is disrupted by lack of factors VIII or IX. In Phase II studies (As, Bs, and inhibitor patients), Novo found that treatment was well tolerated with no thromboembolic events (too much clotting). Bleeding rates were comparable to those seen in hemophilia patients on prophylaxis with clotting factor. The product is injected subcutaneously. [Article from pipelinereview.com]

Continued on page 33

“One of the most important things you can do on this earth is to let people know they are not alone.”

— Shannon L. Alder



THE COALITION FOR HEMOPHILIA B PATIENT ASSISTANCE PROGRAM

The high cost of medical care is often a challenge for people with hemophilia B. Fortunately, insurance coverage, government programs and other forms of patient assistance cover much of that cost. Unfortunately, these programs do not cover the cost of non-medical emergencies, which may interfere with a family or individual's ability to deal with day-to-day life with a bleeding disorder. These emergencies may involve struggling to having enough resources for housing, food, transportation, or a range of other necessary and critical needs.

When these needs are not met, the health and well-being of the patient as well as the entire family can be negatively affected. Often, assisting a person in an immediate circumstance is all that's needed to keep the situation from spiraling out of control.

The Coalition for Hemophilia B deeply cares about families and individuals, and the urgent needs they may face. Several years ago, because of this and in order to live true to our mission statement, we established a patient assistance program for hemophilia B patients and families. We reintroduce our program as **BCares**.

BCares operates with funding generously donated by pharmaceutical manufacturers, homecare companies, business partners, and other interested supporters.

Those donating share our belief - in the case of an urgent situation, we can all do more to help. It is our obligation as a community to lend a hand and assist those in short-term, dire straits.

The Coalition for Hemophilia B is able to offer a limited amount of financial aid to our factor 9 community members who face a financial emergency. Those requesting assistance can submit a simple, confidential application. Each application will be reviewed thoroughly by a committee, who will determine and prioritize grants based on the request and level of urgency.

How you can help: We are exceedingly grateful to the donors whose charity and compassion have made this critical program possible. Please consider becoming involved by offering additional funds so we may help more hemophilia B patients through challenging times.

For more information, please contact:

Farrah Muratovic
farrahm@hemob.org
The Coalition for Hemophilia B

Tel: 212-520-8272
hemob.org



TREATMENT NEWS

NOVO REPORTS ON INCREASING THE AFFINITY OF FVIIa FOR PLATELETS

Novo Nordisk makes an activated factor VII (FVIIa) product, NovoSeven, for treatment of inhibitor patients. FVIIa improves clotting by a method that depends on platelets, which are small particles in the blood that work with the clotting system to form a plug to seal an injured blood vessel. However, FVIIa has a low affinity for binding to platelets. Novo looked at whether increasing the affinity would increase the effectiveness of FVIIa in inducing clotting. In studies in mice, and in lab studies using hemophilic blood (blood donated by a hemophilia patient), Novo found that increasing the affinity appears to increase the potency of FVIIa about 50 times. [ISTH abstract OC 35.4]



factors VIII and IX work together to activate factor X. Supplying the blood with activated factor X should eliminate the need for factors VIII and IX. However, when not regulated carefully, factor X can cause severe thrombosis (too much clotting) and even death. Pfizer has developed a variant of normal factor X— called FXa-116L—that is potentially safer and more easily controlled. In studies in hemophilia A dogs with inhibitors, hemostasis (normal clotting) was restored with no major adverse events. [ISTH abstract OC 51.5]

SANOFI PRESENTS INTERIM DATA ON FITUSIRAN

Sanofi's fitusiran inhibits the body's production of antithrombin, an anticoagulant. Reducing anticoagulant levels is an approach to restore the balance in the clotting system for patients who are deficient in clotting factors. Fitusiran, a monthly subcutaneous drug, was originally developed by Alnylam in partnership with Sanofi until Sanofi took over full responsibility for development and commercialization in 2018. Sanofi reported interim results from its ongoing Phase II study of patients with hemophilia A or B, with or without inhibitors. Thirty-three subjects treated for a maximum of over three years, experienced a median ABR of 1.5. The product was generally well tolerated, including no inhibitor development. Fitusiran is also in a Phase III study. [ISTH abstract OC 11.3]



PFIZER SHOWS QUALITY OF LIFE IMPROVEMENTS AFTER SPK-9001 GENE THERAPY

Pfizer, continuing development of the SPK-9001 gene therapy treatment that it took over from Spark Therapeutics, measured HRQoL in 15 adult hemophilia B subjects before and after treatment. Using validated questionnaires, the company found that one year after treatment, subjects exhibited significantly improved HRQoL. The median bleed rate for the subjects was zero (range 0–4) and the median number of infusions was also zero (range 0–10). [ISTH abstract OC 01.3]



SIGILON PRESENTS GENE THERAPY METHOD USING ENCAPSULATED CELLS

Sigilon Therapeutics is developing encapsulated cells, called Afibromer spheres, for hemophilia gene therapy. The Afibromer spheres will contain cells engineered to produce factor VII, VIII, or IX and would be implanted in the peritoneal cavity surrounding the stomach and liver. The Afibromer spheres protect the cells from immune rejection while being permeable to factor proteins diffusing out into the bloodstream. Sigilon presented results from animal studies showing factor production and long-term viability. The company plan to start development with hemophilia A and then move on to other bleeding disorders. [ISTH abstract OC 60.4 and Sigilon press release]



PFIZER PRESENTS DATA ON TFPI INHIBITOR

Pfizer is developing PF-06741086 as an inhibitor of TFPI, an anticoagulant. By inhibiting TFPI (that is, inhibiting the inhibitor), Pfizer hopes to restore the balance in the coagulation system. This should allow the blood to clot more easily in both hemophilia A and B patients, with or without inhibitors. The Phase Ib/II study included 26 subjects (As, Bs, and inhibitor patients) treated with increasing doses of the subcutaneous product. The annual bleed rates, depending on dose, ranged from 4.2 to 0.7, down from an average ABR of 27.7 based on historical controls. There were four serious adverse events that were unrelated to the treatment. There were no thrombotic events (too much clotting). [ISTH abstract OC 11.2]



TAKEDA REPORTS ON GENE THERAPY STUDIES

Takeda reported results for a number of gene therapy studies. To determine why production of factor IX can vary so significantly and declines in some gene therapy patients, Takeda did whole genome



PFIZER ANNOUNCES RESULTS FOR ACTIVATED FACTOR X IN DOGS

Pfizer is developing a variant activated factor X to restore clotting in hemophilia A and B patients, with or without inhibitors. In the coagulation cascade,



Continued on page 35



FREE for individuals and families with HEMOPHILIA B. To join B Connected, contact administrators Rick Starks and Shad Tullidge at: bconnected@hemob.org

THERE'S A NEW WAY

TO STAY CONNECTED TO

PEERS-FAMILIES-EXPERTS

PAST PROGRAMS FEATURING:

- » KIM MAUER, MD: PAIN MANAGEMENT
- » DONNIE AKERS, ESQ: LEGAL TOOLS ON THE ROAD TO LIFE WHILE KEEPING PUBLIC BENEFITS
- » DR. DAVID CLARK: NEW PRODUCTS IN DEVELOPMENT & GENE THERAPY
- » DEBBIE DE LA RIVA, LPC: MENTAL HEALTH & BLEEDING DISORDERS



Why B Connected?

New therapies are flooding the market. It's more important than ever that everyone in the Hemophilia B community has a way to:

- » Get critical information in a timely way.
- » Dispel false rumors immediately and get correct information from expert sources.
- » Stay engaged with the community virtually even if your hemophilia limits your mobility.
- » Ask questions and share experiences with other patients and caretakers.
- » Customize and control the content you want to receive notifications for.

contact: bconnected@hemob.org

PEER SUPPORT & ASK THE EXPERT GUESTS

Through B Connected you can also digitally join online **Ask the Expert** sessions—hour-long discussions on topics such as advocacy, depression, pain management, unaffected siblings, physical therapy and how to cut down on joint bleeds, nutrition and exercise, inhibitors, new family support, aging with hemophilia, and much more!

JOIN TODAY!

Hemophilia B Connected online discussion board is hosted on Slack and is 100% HIPAA compliant.



sequencing on a number of patients and found two important parameters that can affect the success of the treatment. One is patient differences in heterochromatinization (a type of modification of X chromosomes done by the body), which can silence the new gene. The other is protection for the liver cells that are transformed. The high viral loads used with current gene therapies can produce inflammatory stress on the cells, which can keep them from working properly and may lead to their destruction. [ISTH abstract OC 31.1]

Takeda is also developing TAK-748, a next-generation AAV vector that uses a higher-activity promoter to increase the production of factor IX from the new gene. The company has tested it in mice and rhesus monkeys and found it to be safe and efficacious. [ISTH abstract OC 22.1]

Whether a gene therapy treatment can be re-administered later in life has been a big question. Most of the current treatments rely on AAVs to deliver the new gene to liver cells. With the first treatment, the immune system develops an immunity against the AAV. The first treatment is apparently able to sneak in and do its job before full immunity is obtained, but a second dose would come up against a strong, already-developed immunity that could prevent the second dose from working. Takeda has performed a study in mice looking at whether suppressing T-cells (a type of white blood cell that is part of the immune system) could allow a second (or later) dose to be accepted. This approach appears to work, and also appears to keep memory T-cells from attacking cells that have been transformed with the new gene. [ISTH abstract OC 31.2]

Many patients already have antibodies to AAV gene therapy vectors from previous infections. Although AAV does not appear to cause disease in humans, it can still infect humans without showing symptoms. However, because of the immunity that such an earlier infection caused, those patients are not good candidates for subsequent treatment using the AAV virus. Takeda has shown that about 50% of patients cannot be treated with their AAV subtype 8 vector because of preexisting immunity. The company also found that many patients had a coexisting immunity to other AAV subtypes. This suggests that new methods are needed to deal with preexisting immunity in hemophilia patients receiving gene therapy. [ISTH abstract OC 31.4]

Takeda also announced that it has opened a new global research center in San Diego that will focus on oncology, gastroenterology, neuroscience, and rare diseases, including hemophilia, vaccines, and plasma-derived products. [Takeda press release]

UNIQURE PROVIDES UPDATES ON GENE THERAPY STUDIES

uniQure

uniQure has ongoing clinical studies of gene therapy for hemophilia B. The company currently has a Phase I/II study of AMT-060, its original AAV5 vector with a normal factor IX gene. There is a Phase IIb study of AMT-061, which is the same as AMT-060 but with the higher-potency Padua factor IX gene. The Phase IIb study is a transition study to show that AMT-061 can be used in place of AMT-060. A Phase III study of AMT-061 is also ongoing and has begun dosing patients.

The Phase I/II study of AMT-060 has followed 10 patients for up to 3.5 years. Eight of the nine patients using prophylaxis prior to the study have been able to discontinue it. The five patients in the lower-dose cohort have a mean factor IX level of 4.9% and their mean ABR decreased from 14.4 pre-study to 5.4. The five patients in the higher-dose cohort have a mean factor IX level of 7.4% and their mean ABR decreased from 4.0 pre-study to 1.0. No patient developed inhibitors or exhibited AAV-specific T-cell activation. These results help to support the viability of uniQure's gene therapy platform that is also used for AMT-061. [ISTH abstract OC 01.4]

In uniQure's Phase IIb study of AMT-061, all three patients have significant sustained increases in factor IX levels to 30%, 51%, and 54% of normal. None of the patients has experienced a loss of factor IX production, reported any bleeding events, and required any additional factor IX infusions. One patient underwent hip surgery and was treated with a short-acting factor IX product during the time of surgery. [ISTH abstract OC 01.1]

uniQure also did a study in mice to look for evidence of germline transmission of gene therapy DNA. Currently, germline transmission (transmission of a gene to offspring) is considered too risky, so gene therapy developers want to develop treatments that do not cause it. uniQure's mouse data suggests that the risk germline transmission of its AAV5 gene therapy is low. [ISTH abstract PB0303]

Reports from the financial community suggest that uniQure is exploring options including a sale of itself to pharma companies that want to get into gene therapy. No final decisions have been made. [Reports from www.bloomberg.com]

2019

Meetings on the Road

Bringing education,
advocacy, resources and
support to families
living with hemophilia B

THE COALITION FOR
HEMOPHILIA



SAVE THE DATES

Registration on our website
www.hemob.org/new-events

OCTOBER 19
Columbus, OH
Knoxville, TN

OCTOBER 26
Atlanta, GA
Seattle, WA

NOVEMBER 2
Baton Rouge, LA
Fort Smith, AR

NOVEMBER 9
Phoenix, AZ
Schaumburg, IL

Breakfast, Lunch &
Dinner served.
Childcare provided for
age infant to 5.
Fun day trip for children
age 6 and over.
Gas, tolls & parking
compliments of the
Coalition.
If you are driving 3 or
more hours, inquire with
farrahm@hemob.org
for a complimentary
room night.



SAVE THE DATE

14th Annual Symposium The Coalition for Hemophilia B Renaissance Orlando at SeaWorld

Registration available fall 2019
at www.hemob.org



MARCH 19-22, 2020

The Coalition for Hemophilia B understands there are families within our bleeding disorder community who feel the effects of the current economic situation. While the Coalition will also contribute to this fund, we ask our more fortunate Factor Nine Families to help us by making a financial donation to the Factor Nine "Holiday Fund" to help buy gifts for children with hemophilia.



To make a donation,
please send a check payable to:

The Coalition for Hemophilia B "Holiday Fund"
757 Third Avenue, 20th Floor
New York, NY 10017

Please respond by **November 18, 2019**,
so Factor Nine Santa can load his sleigh with
holiday gifts for all good girls and boys!

For families in our community in need of a little holiday cheer, we would like to help put something under the tree for your children! Fill out this form and send it to Santa's special elf, Kim, at the "East" Pole. Factor Nine Santa has a busy schedule, so please send this form no later than November 18, 2019. Your name and information will be kept strictly confidential. Send mail this form to:

The Coalition for Hemophilia B Holiday Cheer
757 Third Avenue, 20th Floor
New York, NY, 10017

Name: _____

Street Address: _____

City, State, Zipcode: _____

Phone: _____

Please give an exact description of your child's wish item.
Gifts will be purchased and sent to your home.

Child's Name and Age:

Child's Name and Age:

Child's Name and Age:

Wish List:

Wish List:

Wish List:



**We wish you all a
beautiful holiday season
filled with love, happiness
and good health!**



The Coalition for Hemophilia B

757 Third Avenue, 20th Floor; New York, New York 10017
Phone: 212-520-8272 Fax: 212-520-8501 contact@hemob.org

Visit our social media sites:

Website: www.hemob.org

Facebook: www.facebook.com/HemophiliaB/

Twitter: <https://twitter.com/coalitionhemob>

Instagram: www.instagram.com/coalitionforhemophiliab



For information, contact Kim Phelan
kimp@hemob.org or call 917-582-9077