NHF News Briefs

July 13 – July 19, 2018

This report includes selected news items from the past week on issues of concern to the bleeding disorders community. It is designed to help keep NHF national and local leadership and staff informed of the latest information from the news media. It will be distributed by email on Thursday of each week, covering important news items from the previous seven days. Subjects covered will include hemophilia, other bleeding disorders, gene therapy, hepatitis, HIV/AIDS, and others.

July 15, 2018
Mdjonline.com (Marietta, GA)

Camp Inspires Confidence in Marietta Boy

When 8-year-old Ethan Welsch packed his bags for summer camp this month, he also packed his tourniquet and syringe, along with the medication he'll infuse into his left arm. All by himself.

The Marietta boy has received a weekly infusion of medicine for hemophilia, an inherited bleeding disorder, for the past seven years.

Ethan was just three months old when his parents, Emily and Andrew, noticed the first bruise, a thumbprint-sized mark with a knot underneath on the inside of his right arm. The bruises increased, some causing the entire inside of his arm to be purple. He was diagnosed with hemophilia shortly after his first birthday, and he started a treatment plan of weekly infusions to help enhance his blood's ability to clot.

Last summer, Ethan visited Camp Wannaklot, a summer camp hosted by Hemophilia of Georgia in partnership with Camp Twin Lakes in Rutledge. He was inspired by the kids he saw who could mix their own factor and do their own infusions. After camp, he told his parents he was ready to learn. His mom and dad would do whatever it took to help him — even going so far as to let him practice needle sticks on their own veins.

After practicing on his parents for over a month, he was able to do it all by himself for the first time. At age eight, he's able to fully mix the medicine, apply the tourniquet, find the vein, stick himself with a syringe and push the infusion. He got it on his first solo try.

"It took me six months to learn to do his weekly infusions, and Ethan had it down in six weeks," said his mother, Emily Welsch, Ethan's biggest cheerleader. "That's what is so great about camp is he's there with everyone who is in a situation like his. They all cheer each other on and support each other, which I think is truly the main focus of camp. Camp is not just the fun stuff, but it's also about feeling comfortable with his disease, knowing how to talk about it and being around other people with it."

This week, Ethan is back at Camp where he will join the ranks of the "Mighty Stickers," a group of campers capable of treating themselves and who demonstrate full understanding of their diagnosis and treatment. Ethan and his fellow Mighty Stickers perform their treatment at the Camp Twin Lakes medical lodge under the supervision of medical staff trained to meet the unique needs of children diagnosed with hemophilia.

"The impact of our intentionally-designed camp programs reaches far beyond a child's time spent at camp," said Dan Mathews, COO, Camp Twin Lakes. "We teach campers how to overcome their unique obstacles as they learn new skills to more independently manage their every-day challenges and actively participate in their own treatment."

The rising third-grader at Chatham Hill Elementary School has become more comfortable explaining his diagnosis to others. According to his mother, Ethan, an avid tennis player, met his new tennis coach, and asked him, "Do you know what hemophilia is?" Ethan told his coach, "'My blood doesn't clot like yours does. If I get hurt I need ice right away. I don't bleed more than other people, it just takes my boo boos longer to heal."

These are the moments when Emily says she is reminded of just how independent her little boy has become. “He is so confident and comfortable, not only talking about, but also managing his disease. He truly is capable of extraordinary things,” says Welsch shaking her head proudly.

Camp Wannaklot is one of the 39 weeklong camps happening in partnership with Camp Twin Lakes this summer, each serving a unique diagnosis or life challenge. For more information, visit www.camptwinlakes.org.

July 18, 2018
Medscape.com

FDA Approves *Symtuza* for Treatment of HIV Infection

By Troy Brown, RN

The US Food and Drug Administration (FDA) has approved what its manufacturer calls "the first and only complete, darunavir-based single-tablet regimen (STR) for the treatment of human immunodeficiency virus type 1 (HIV-1) in treatment-naive and certain virologically suppressed adults." Using the brand name Symtuza and made by Janssen Pharmaceuticals, the drug combo "combines the proven high barrier to resistance of darunavir with a formulation designed for improved tolerability and the convenience of an STR."

The combination tablet contains darunavir 800 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir alafenamide 10 mg. The once-daily STR is expected to improve patient compliance, which will also help prevent drug resistance.

"The approval of Symtuza…will provide patients with yet another one-tablet regimen with excellent potency, tolerability, and a high genetic barrier to resistance," Antonio Urbina, MD, associate professor of infectious diseases at the Icahn School of Medicine at Mount Sinai in New York City, told Medscape Medical News.

"At the Institute for Advanced Medicine at Mount Sinai, it will become one of our antiviral options for our immediate start program, which provides same-day HIV treatment to patients newly diagnosed with HIV," he added.

Urbina said there are currently eight other one-tablet regimens for HIV, but they "do not include a protease inhibitor [such as darunavir]. The use of a protease inhibitor-based regimen may be preferable in certain patient populations, for example, patients with suboptimal adherence," Urbina explained.

Effective, Well-tolerated in Pivotal Trials

The FDA approval follows consideration of data from two 48-week, noninferiority, pivotal phase 3 studies that compared the drug's safety and efficacy with those of a control regimen in two different populations of patients with HIV-1 infection.

The AMBER study included antiretroviral-naive adults and the EMERALD study included virologically suppressed adults. The drug combo was effective and well-tolerated in both studies, and as many as 95% of patients in the treatment groups achieved or maintained virologic suppression, defined as HIV-1 RNA less than 50 copies/mL.

The AMBER study compared the darunavir-based STR with darunavir/cobicistat plus emtricitabine/tenofovir disoproxil fumarate (F/TDF). Viral suppression rates (HIV-1 RNA < 50 copies/mL at 48 weeks, per FDA Snapshot analysis) were similar between the darunavir-based STR and control groups (91.4% vs 88.4%, respectively) and virologic failure rates were low (HIV-1 RNA ≥ 50 c/mL; 4.4% vs 3.3%) at 48 weeks.

The darunavir-based combo was associated with less bone loss than the control treatment during a substudy, although the long-term clinical significance of this finding is unclear. Renal function markers were also significantly improved compared with the control group.

Fewer patients in the darunavir-based treatment group withdrew from the study as a result of adverse events (AEs) than in the control group (AE, 2% vs 4%). Only one grade 3 adverse reaction and no grade 4 adverse reactions occurred. The most common adverse reactions that occurred in at least 2% of participants were diarrhea, rash, nausea, fatigue, headache, abdominal pain, and flatulence.

The AMBER study results were presented at the 16th European AIDS Conference in October 2017.

In the EMERALD study, researchers compared the darunavir-based treatment with continuing treatment with a boosted protease inhibitor plus emtricitabine and TDF. Virologic failure rates (HIV-1 RNA ≥ 50 copies/mL; 0.8% vs 0.5%) were low and virologic suppression rates were high (HIV-1 RNA < 50 copies/mL; 94.9% vs 93.7%) according to FDA Snapshot analysis at week 48.

No patients discontinued the study as a result of virologic failure. Those who switched to the darunavir-based treatment experienced improved bone mineral density in a substudy and significantly improved renal function markers; however, the long-term clinical significance of the bone mineral density changes is unclear.

Patients in the EMERALD study experienced few AEs in a similar manner as patients who were naïve to antiretroviral therapy, with only 1% discontinuing treatment as a result. Results from the EMERALD Study were presented at ID Week in October 2017.

The drug label will contain a boxed warning about the risk for posttreatment acute exacerbation of hepatitis B infection.

Before beginning treatment, patients should undergo testing for hepatitis B infection and renal function, with continued monitoring of renal function during treatment. Symtuza should not be given to patients whose creatinine clearance is lower than 30 mL per minute or who have severe renal impairment.

The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use recommended the combination therapy for marketing approval on July 21, 2017, and the EMA approved it on September 26, 2017.

Urbina has disclosed that he is on the scientific advisory panels for Gilead, Merck, and ViiV.

July 18, 2018
Hemophilianewstoday.com

Pfizer Launches Phase 3 Program to Test Gene Therapy for Treating Hemophilia B

By Diogo Pinto

Pfizer has partnered with Spark Therapeutics to launch a Phase 3 program to evaluate the safety and effectiveness of its factor IX replacement gene therapy for treating hemophilia B.

Replacement of factor IX (FIX), the clotting protein lacking in hemophilia B, will be done via the fidanacogene elaparvovec gene therapy (previously known as PF-06838435 and SPK-9001).

This is a gene transporter (or vector) that contains a harmless adeno-associated virus (AAV) capsid, or protein shell, and the gene that provides instructions for making factor IX.

The Phase 3 trial was designed to investigate the effectiveness of the FIX replacement gene therapy in the usual care conditons of hemophilia B patients.

An open-label, six-month lead-in Phase 3 study (NCT03587116) will measure the patients' annualized bleeding rate, or the number of bleeds over the number of days, number of adverse events and other events of special interest, as the existence of inhibitors of factor IX, thrombotic (clotting) events and hypersensitivity reactions to the treatment.

In this trial, there is no investigative product to be administered. Patients will be administering their own standard of care FIX replacement therapy.

The data from the study will be used as a control for patients who will be enrolled in the next part of the Phase 3 trial for the investigative gene therapy.

Earlier this year, Pfizer and Spark Therapeutics reported data from 15 patients participating in the Phase 1/2 study (NCT02484092) designed to treat severe or moderately severe hemophilia B (FIX levels under 2% of normal concentrations).

Results showed no serious adverse or thrombotic events. The therapy also led to significant reductions in bleeding and factor IX infusions.

"With the lead-in study now open and actively recruiting patients, we are excited to begin our Phase 3 program evaluating fidanacogene elaparvovec for the treatment of hemophilia B," Brenda Cooperstone, MD, senior vice president and chief development officer at Pfizer, said in a press release.

"The current data suggest immense promise for the use of this potential one-time treatment option. We look forward to the opportunity to continue the progress achieved by Spark Therapeutics for patients living with hemophilia B," she added.

Spark Therapeutics transferred its investigative hemophilia B gene therapy program to Pfizer, who initiated the Phase 3 trial program.

Under the terms of the agreement, Pfizer will be responsible for the clinical studies, manufacturing, regulatory activities, and global commercialization of any products related to the hemophilia B gene therapy program.

“We are pleased to have transitioned fidanacogene elaparvovec to Pfizer following the positive results of the ongoing Phase 1/2 clinical trial,” said Katherine A. High, MD, president and head of research and development of Spark Therapeutics.

“The initiation of the Phase 3 program marks an important milestone toward our goal of one day potentially freeing patients with hemophilia B of the need for regular infusions, while potentially eliminating spontaneous bleeding,” she said.

July 19, 2018
Prnewswire.com

Working to Improve Hemophilia A Testing: Precision Biologic Presents New Data at the 64th Annual SSC Meeting

Precision BioLogic today unveiled data from a study using a new kit for a Modified Nijmegen-Bethesda Assay (MNBA) at the International Society on Thrombosis and Haemostasis' Scientific and Standardization Committee (SSC) meeting in Dublin. Recognizing the need to standardize and improve Factor VIII (FVIII) inhibitor testing for people with hemophilia A, the company developed the new MNBA kit and the recent study in collaboration with Roche and Genentech, a member of the Roche Group.

Data presented builds on findings released at the Thrombosis & Hemostasis Societies of North America (THSNA) 2018 Summit in San Diego, California and the World Federation of Hemophilia (WFH) 2018 World Congress in Glasgow, Scotland. The latest data demonstrate that a bovine-based chromogenic MNBA is suitable for FVIII inhibitor measurement in plasma samples containing HEMLIBRA® (emicizumab-kxwh), a bispecific antibody that is approved by the U.S. Food and Drug Administration (FDA) and European Commission for the prophylactic treatment of hemophilia A with factor VIII inhibitors.

"We're seeing promising advancements in the treatment of bleeding disorders," says Paul Empey, President & CEO of Precision BioLogic. "We are hopeful that combining accurate diagnosis and monitoring with potential advancements could improve the quality of life for people with bleeding disorders. Precision BioLogic is proud to be at the forefront of this promising research."

A poster of the latest study, *Emicizumab Impact on Factor VIII Inhibitor Determination in Plasma Samples from Persons with Hemophilia A (PwHA) Using a New Kit for Modified Nijmegen-Bethesda Assay (MNBA)*, as well as previous studies, can be downloaded from the publications page of the Precision BioLogic website.

Precision BioLogic's newly developed MNBA kit was used in the study. To eliminate FVIII depleted plasma as a potential source of variant and standardize inhibitor titer measurement, the kit was developed with the following components:

- Imidazole-buffered pooled normal plasma
- Imidazole-buffered bovine serum albumin
- Positive FVIII inhibitor control
- FVIII inhibitor-free human plasma

All kit components are frozen, like Precision BioLogic's line of cryocheck™ diagnostic products, which closely resemble frozen patient samples.

Precision BioLogic plans to commercialize the kit and will seek clearance from regulatory authorities around the globe beginning in late 2018. The company is actively pursuing other opportunities to innovate in the field of hemostasis and diagnostics.

About Hemophilia A and Inhibitors

Hemophilia A is an inherited bleeding disorder caused by insufficient clotting factor VIII (FVIII) in the blood. People with hemophilia A experience prolonged bleeding, which can lead to permanent joint damage and life-threatening hemorrhages. The standard treatment for people with hemophilia A without inhibitors is intravenous (IV) FVIII replacement therapy with recombinant FVIII (rFVIII) or plasma-derived FVIII (pdFVIII) concentrates. Prophylaxis, the regular infusion of clotting factor concentrates, is used to prevent bleeds thereby minimizing joint damage.

Unfortunately, up to 30% of people with hemophilia A develop inhibitors, an immune response to treatment with clotting factor concentrates. Inhibitors make it more difficult to manage and treat hemophilia. In fact, according to the World Federation of Hemophilia, apart from access to care and treatment, inhibitors are the most serious challenge in hemophilia care today.[1] While routine blood tests may suggest the presence of anti-factor FVIII antibodies, specialized testing is important to confirm not only the presence of inhibitors but also the quantitation to effectively adjust treatment. Current methods for inhibitor testing vary from lab to lab and there is not an FDA-cleared gold standard for reference.

About Precision BioLogic

Precision BioLogic is a privately-held company that develops, manufactures and markets specialized products used by medical professionals and researchers around the globe to diagnose coagulation disorders. Precision BioLogic also has several active initiatives with pharmaceutical partners who seek to ensure that the diagnostic implications for their novel therapeutic agents have been well characterized. For more information, visit www.precisionbiologic.com.

HEMLIBRA® is a registered trademark of Chugai Pharmaceutical Co., Ltd., Tokyo, Japan.

1. World Federation of Hemophilia. Current issues in inhibitors. Available at https://www.wfh.org/en/Current-issues-in-inhibitors. Accessed on February 22, 2018