Patient – Hemlibra Use in Hemophilia A with Inhibitors

This letter contains information you requested on the use of Hemlibra® (emicizumab-kxwh) to treat people with hemophilia A with factor VIII (factor 8 or FVIII) inhibitors. This letter includes studies with the strongest and most relevant data from clinical trials.

This information is provided only for educational purposes and not for use in treatment decisions. You should talk with your healthcare provider for specific information and advice about your condition, your individual situation, healthcare coverage, and any current or potential treatments.

Glossary

Activated prothrombin complex concentrates (aPCC): A bypassing agent also known as FEIBA® that contains active and inactive clotting factors.

Inhibitors: In hemophilia A, inhibitors are antibodies against infused FVIII clotting proteins. These antibodies make the infused FVIII products not effective.

Loading dose and maintenance dose: A loading dose is a higher dose given at the beginning of treatment to make sure that the amount of drug in the body reaches a therapeutic level before dropping down to a lower maintenance dose that will keep the amount of drug in the body at the therapeutic level.

On-demand: On-demand refers to a treatment that is given as needed. For example, when bleeding occurs.

Prophylaxis: Also known as "prophy", it is a treatment given on a regular schedule to prevent bleeds.

Spontaneous bleed: A spontaneous bleed is a bleed that happens without an obvious cause.

Subcutaneous injection: Injection that is given under the skin in the subcutaneous space (in the fatty layer between the skin and muscle). The medicine is then absorbed into the small vessels of the subcutaneous space and goes into the blood where it works.

Target joint: A target joint is a joint that has frequent and recurrent bleeds resulting in joint damage.

Thrombotic microangiopathy (TMA): Thrombotic microangiopathy is a potentially life-threatening condition in which blood clots form in small blood vessels that may result in damage to the kidneys and/or other organs.

Treated bleed: A treated bleed is any bleed that requires treatment with infused clotting factor.

What is Hemlibra?

Hemlibra is a medicine that is approved by the Food and Drug Administration (FDA) for prophylaxis in adults and children with hemophilia A, with or without FVIII inhibitors.[1]

Hemlibra is given as a loading dose of 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose of either 1.5 mg/kg once weekly, or 3 mg/kg once every 2 weeks, or 6 mg/kg once every 4 weeks.[1]

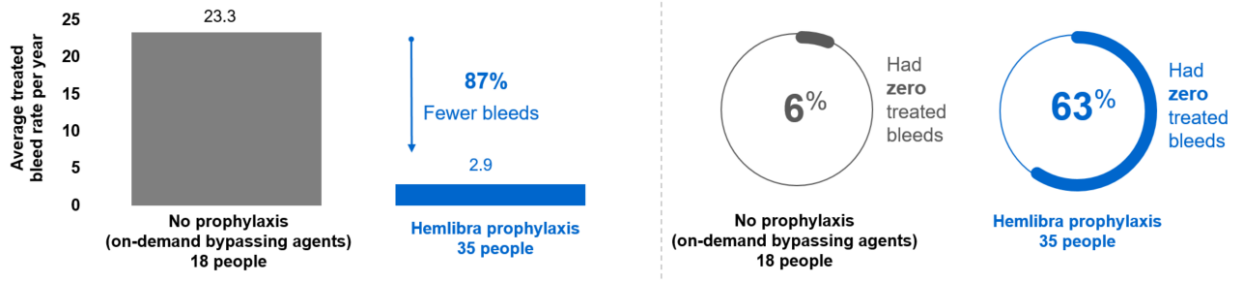
What is the HAVEN 1 study?

HAVEN 1 was a clinical trial that studied how safe and how well Hemlibra prophylaxis worked to prevent bleeds in 109 males (ages ranged from 12-75 years old) with hemophilia A with FVIII inhibitors.[2] The effect of Hemlibra 3 mg/kg once weekly for 4 weeks, then 1.5 mg/kg once weekly was compared with no prophylaxis after at least 6 months on the study. People who used on-demand bypassing agents before entering HAVEN 1 were randomly assigned to take either Hemlibra prophylaxis or no prophylaxis (continue on-demand bypassing agent to treat bleeds). Results from 35 people who used Hemlibra prophylaxis were compared with results from the 18 people who used on-demand bypassing agents (no prophylaxis).

What was the effect of Hemlibra on bleeding in HAVEN 1?

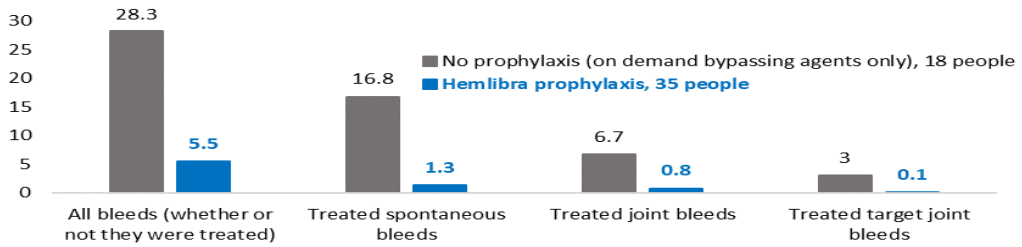
People who took Hemlibra prophylaxis had fewer treated bleeds compared with people on no prophylaxis.[2] Most people treated with Hemlibra prophylaxis (63%) did not have any treated bleeds, compared to 6% of people who used on-demand bypassing agents.

Figure 1: Treated Bleed Results in HAVEN 1[2]



In addition, Hemlibra reduced the number of all bleeds (whether the bleed was treated or not), treated spontaneous bleeds, treated joint bleeds, and treated target joint bleeds.[2]

Figure 2: All Bleed, Treated Spontaneous Bleed, Treated Joint Bleed, and Treated Target Joint Bleed Results in HAVEN 1[2]



Did Hemlibra prophylaxis prevent more bleeds than bypassing agent prophylaxis?

A "before and after study" compared the number of bleeds that happened in 24 people when they used bypassing agents for prophylaxis, then entered HAVEN 1 and switched to Hemlibra.[2]

After this group of 24 people switched from prophylaxis with bypassing agents to Hemlibra prophylaxis, 79% fewer treated bleeds happened.[2] On bypassing agent prophylaxis, 13% did not have treated bleeds, and on Hemlibra prophylaxis, 71% did not have treated bleeds.[2]

What common side effects were seen with Hemlibra in the HAVEN 1 study?

The most common side effects were redness, tenderness, warmth, and itching where Hemlibra injection was given.[2] Other common side effects were headache, tiredness, colds, and joint pain.

What serious side effects were seen with Hemlibra in the HAVEN 1 study?

Two people had blood clots (thrombotic events) and 3 people had TMA.[2] These were reported when on average a cumulative amount of >100 U/kg/24 hours of aPCC (FEIBA®) was given for 24 hours of more to people using Hemlibra prophylaxis. Neither blood clot needed blood thinning medicine and 1 person restarted Hemlibra. In the 3 TMA cases, TMA improved after aPCC (FEIBA®) was stopped. A death occurred in 1 TMA case due to rectal bleeding. Of the other 2 TMA cases, 1 person restarted Hemlibra.

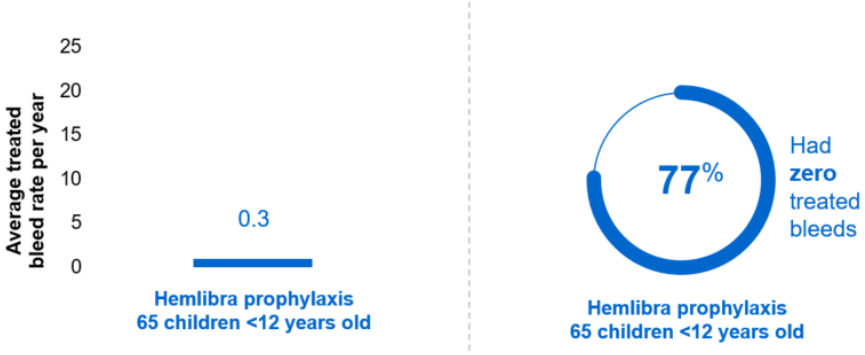
What is the HAVEN 2 study?

HAVEN 2 studied how safe and how well Hemlibra worked to prevent bleeds in children <12 years old with hemophilia A with FVIII inhibitors.[3] The study lasted for 1 year. Hemlibra was given as 3 mg/kg once weekly for 4 weeks, then 1.5 mg/kg once weekly. The study later enrolled children to receive maintenance doses of 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks after the loading dose.

What was the effect of Hemlibra on bleeds in children in HAVEN 2?

A total of 65 children <12 years took Hemlibra 1.5 mg/kg once weekly for 1 year or more, and had an average of 0.3 treated bleeds per year.[3] Most children did not have treated bleeds.

Figure 3: Treated Bleed Results in HAVEN 2[3]



Ten children received Hemlibra every 2 weeks and 10 children received Hemlibra every 4 weeks for 1 year or more, and most children did not have treated bleeds.[4] Hemlibra every 2 weeks resulted in an average of 0.2 treated bleeds per year , with 70% of children having zero treated bleeds. Hemlibra every 4 weeks resulted in an average of 1.8 treated bleeds per year, with 60% of children having zero treated bleeds.

Did Hemlibra prophylaxis prevent more bleeds than bypassing agent prophylaxis?

A "before and after study" compared the number of treated bleeds that happened in 15 children when they used bypassing agent prophylaxis, then entered HAVEN 2 and switched to Hemlibra once weekly.[3]

After this group of 15 children switched from bypassing agent prophylaxis to Hemlibra, 99% fewer treated bleeds happened. The average number of treated bleeds per year was 0.3 on Hemlibra prophylaxis compared to 21 on their prior bypassing agent prophylaxis.[3]

What side effects were seen with Hemlibra in the HAVEN 2 study?

The side effects seen in HAVEN 2 were similar to those in HAVEN 1.[3,4] The most common side effects were redness, tenderness, warmth, and itching where the Hemlibra injection was given, common cold, fever, infections of nose or throat, coughing, diarrhea, vomiting, headache, bruising, falls, and the flu. There were no blood clots or cases of TMA.

One child developed an antibody to Hemlibra, which caused Hemlibra to lose effectiveness. This child stopped taking Hemlibra and went back to using their previous bypassing agent therapy.

Hemlibra Use in Hemophilia A with Inhibitors References

1. Hemlibra® [package insert]. Genentech, Inc.; South San Francisco, CA.

2. Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab prophylaxis in hemophilia A with inhibitors [supplementary appendix appears online]. N Engl J Med 2017;377:809-818. https://www.ncbi.nlm.nih.gov/pubmed/28691557

3. Young G, Liesner R, Chang T, et al. A multicenter, open-label phase 3 study of emicizumab prophylaxis in children with hemophilia A with inhibitors. Blood 2019;134:2127-2138. https://pubmed.ncbi.nlm.nih.gov/31697801/

4. Young G, Sidonio JR, Oldenburg J, et al. Efficacy/safety in children on 2/4-weekly emicizumab prophylaxis: 52-week outcomes in HAVEN 2. Presented at the American Society of Pediatric Hematology/Oncology Conference; May 4-7, 2022. ASPHO Poster.