Patient – Hemlibra Use in Children Less than 12 Years Old with Hemophilia A without Factor 8 Inhibitors

This letter contains information you requested on the use of Hemlibra® (emicizumab-kxwh) to treat children less than 12 years old with hemophilia A without 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

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.

Median: The median is the middle number in a sorted list of numbers (example, 28 is the median of 5, 20, 28, 89, 100).

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 absorbed into the small vessels of the subcutaneous space and goes into the blood where it works.

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 HAVEN 7 study and what are the results in infants less than 12 months old with hemophilia A without inhibitors?

HAVEN 7 is an ongoing study evaluating the use of Hemlibra in infants less than 12 months old who had severe hemophilia A without FVIII inhibitors.[2] Infants were started with a loading dose of 3 mg/kg once weekly for the first 4 weeks. Following the loading dose, maintenance dose of 3 mg/kg once every 2 weeks was given for 48 weeks. After 48 weeks, parents/caregivers may elect for their child to continue with the same dose or change to 1.5 mg/kg weekly or 6 mg/kg every 4 weeks for a 7 year long-term follow-up.

Results from the study in 55 infants (all males) are available. Overall, 30 infants were between 3 and 12 months old, and 25 infants were younger than 3 months old. Before the study, 25 infants had never received any treatments for hemophilia, and 30 infants were minimally treated (less than 5 days of FVIII treatments for hemophilia).

What was the effect of Hemlibra on bleeding in the HAVEN 7 study?

Approximately 55% of patients had zero treated bleeds and 95% had zero treated joint bleeds.[2] All treated bleeds were caused by injuries and none of the infants were treated for a spontaneous bleed. Overall, approximately 16% of infants had zero bleeds (treated or not). No incidences of brain hemorrhage occurred.

How safe was Hemlibra in the HAVEN 7 study?

In this study, 631 side effects were reported in 55 infants; all patients had a side effect.[2] The only side effect that was deemed by the investigators to be related to Hemlibra was injection site reactions, which occurred in 16% of infants. Approximately 29% of infants had a serious side effect that included injuries and infections; none of them were considered related to Hemlibra. There were no deaths and no serious side effects of blood clots and thrombotic microangiopathy. None of the side effects led to treatment discontinuation or dose change. Two patients developed FVIII inhibitors after receiving FVIII treatment for injuries and surgical procedures.

What is HOHOEMI study and what are the results in children less than 12 years old with hemophilia A without inhibitors?

HOHOEMI studied the use of Hemlibra in 13 Japanese children (all boys) less than 12 years of age who had hemophilia A without FVIII inhibitors.[3] The ages of children ranged from 4 months to 11 years old.

All 13 children started with a loading dose of 3mg/kg once weekly for the first 4 weeks. After the loading dose, maintenance dosing was started. Six children took Hemlibra 3 mg/kg once every 2 weeks. Seven children took Hemlibra 6 mg/kg once every 4 weeks.

Most children (12 of the 13) used infused FVIII prophylaxis before starting HOHOEMI, except one infant (4-month old) enrolled in the Hemlibra 6 mg/kg once every 4 weeks group had never received FVIII treatment before entering HOHOEMI.[3]

The amount of time on treatment for the 6 children taking Hemlibra 3 mg/kg once every 2 weeks ranged from 38 to 41 weeks (median 40 weeks).[3] The amount of time for the 7 children taking Hemlibra 6 mg/kg once every 4 weeks ranged from 24 to 37 weeks (median 34 weeks).

What was the effect of Hemlibra on bleeding in the HOHOEMI study?

In both the 3 mg/kg once every 2 weeks and the 6 mg/kg once every 4 weeks group, the average number of bleeds that required treatment each year was about 1 bleed per year.[3]

In the 3 mg/kg every 2 weeks group, 6 bleeds requiring treatment happened in 4 children.[3]

5 of these bleeds happened after an injury, of which 3 were joint bleeds

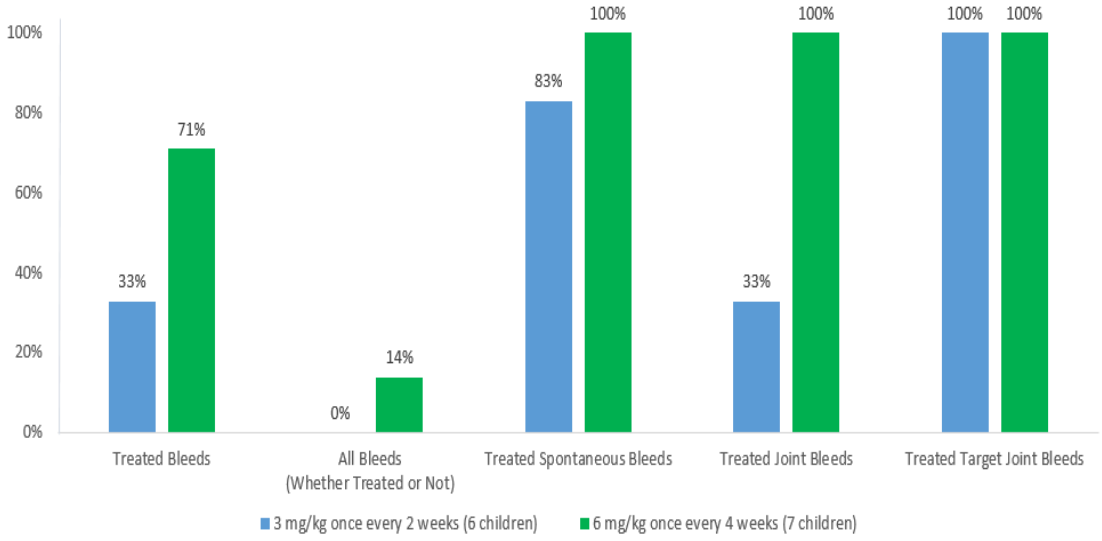
1 bleed was a spontaneous bleed in a joint

In the 6 mg/kg every 4 weeks group, 3 bleeds requiring treatment happened in 2 children.[3]

- All 3 of these bleeds happened after an injury and none were joint bleeds

Figure 1 shows the percent of children in each Hemlibra group with zero treated bleeds, all bleeds (whether or not the bleeds were treated), treated spontaneous bleeds, treated joint bleeds, and treated target joint bleeds.

Figure 1: Percent of Children with Zero Bleeds[3]



How many bleeds happened in the 4 month old infant who had never received FVIII treatment?

The infant who had never received FVIII treatment did not have a bleed requiring treatment before starting HOHOEMI or while on Hemlibra prophylaxis during the study.[3]

How safe was Hemlibra in the children enrolled in the HOHOEMI study?

The most common side effects in this study were bruising in 10 children (77% of children), swelling of nasal passages and back of throat in 5 children (39% of children), scratches or scrapes on the skin (31% of children), and fall in 4 children (31% of children).[3]

One child had a side effect at the location that Hemlibra was injected.[3] There were no serious side effects of blood clots, thrombotic microangiopathy, or severe allergic reactions.

Hemlibra Use in Children Less Than 12 Years Old with Hemophilia A without Factor 8 Inhibitors References

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

2. Pipe S, Collins P, Dhalluin C, et al. Emicizumab Prophylaxis in Infants with Severe Hemophilia A without Factor VIII Inhibitors: Results from the Primary Analysis of the HAVEN 7 Study. Presented at the American Society of Hematology Annual Meeting in San Diego, CA; December 9-12, 2023. ASH Oral presentation #505. https://www.hematology.org/

3. Shima M, Nogami K, Nagami S, et al. A multicentre, open-label study of emicizumab given every 2 or 4 weeks in children with severe haemophilia A without inhibitors. Haemophilia. E-pub Date: September 2019. DOI # 10.1111/hae.13848. https://www.ncbi.nlm.nih.gov/pubmed/31515851