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.

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

Antifibrinolytic agents: Antifibrinolytic agents promote blood clotting by preventing blood clots from breaking down.

Interim analysis: An analysis of data that is conducted before data collection has been completed.

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).

Mucosa: Mucosa refers to the tissue that produces mucous and lines various cavities in the body (e.g. the mouth).

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 HOHOEMI study and what are the results in children <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.[2] 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.[2]

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).[2] 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.[2]

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

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

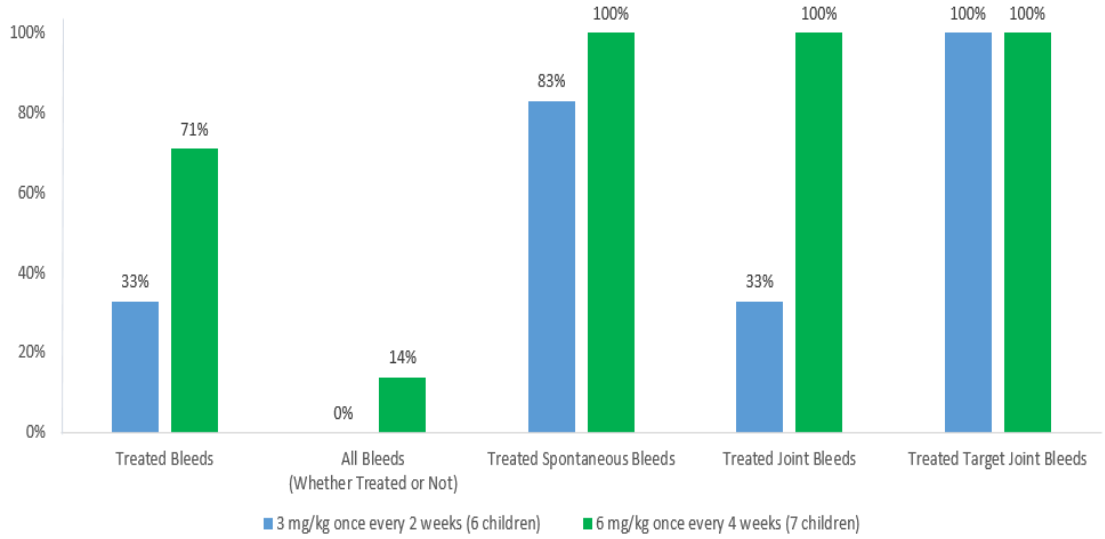
1 bleed was a spontaneous bleed in a joint

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

- 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[2]



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.[2]

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).[2]

One child had a side effect at the location that Hemlibra was injected.[2] There were no serious side effects of blood clots, thrombotic microangiopathy, or severe allergic reactions.

What is HAVEN 7 and what are the interim (early) results in infants <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.[3] Infants are 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 is 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.

Interim analysis from the study in 54 infants (all males) are available. Overall, 30 infants were between 3 and 12 months old, and 24 infants were younger than 3 months old. Before the study, 24 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 interim (early) analysis in HAVEN 7?

Results from the interim analysis showed that approximately 78% of patients had zero treated bleeds and 98% had zero treated muscle bleeds. All treated bleeds were caused by injuries and none of the infants were treated for a spontaneous bleed. Overall, approximately 43% of infants had zero bleeds (treated or not). No incidences of brain hemorrhage occurred.

How safe was Hemlibra in the interim (early) analysis in HAVEN 7?

In the interim analysis, 314 side effects were reported in 54 infants. Approximately 93% of patients reported a side effect.[3] The only side effect that was deemed by the investigators to be related to Hemlibra was injection site reactions, which occurred in 17% of infants. Approximately 15% of infants had a serious side effect that included injuries and infections. 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.

Are there other studies or reports of Hemlibra use in children less than 12 years of age with hemophilia A without FVIII inhibitors?

Three Hemophilia Treatment Centers reported their experience treating people with hemophilia A with Hemlibra (loading dose, then one of the 3 maintenance doses).[4] Among 74 people with hemophilia A without inhibitors, 49 were children less than 12 years old.

- 10 children were less than 2 years old (youngest to receive Hemlibra was 5 weeks old)
- 15 children were 2 to less than 6 years old
- 24 children were 6 to less than 12 years old

Information was collected for the 6 months before the patient switched to Hemlibra and the time on Hemlibra.[4] The median time of Hemlibra treatment for all people without FVIII inhibitors was 35 weeks.

- Before switching to Hemlibra, children less than 12 years old had an average of 1.1 bleeds each year that required treatment with FVIII.[4]

out of the 49 children (63%) had no bleeds that required treatment with FVIII 8.[4]

- After starting Hemlibra, these same children had an average of 0.3 bleeds each year that required treatment with FVIII. This is less than 1 bleed per year, on average.[4]

45 out of the 49 children (92%) had no bleeds that required treatment with FVIII while on Hemlibra prophylaxis.[4]

Over the 6 months before switching to Hemlibra, the 49 children that were less than 12 years old had 19 bleeds that did not require treatment with FVIII; nine bleeds occurred in the mucosa, seven in the muscle/soft tissue, and three in the joints.[4]

After being on Hemlibra for 6 months, these same 49 children that were less than 12 years old had 16 bleeds that did not require treatment with FVIII; twelve bleeds occurred in the mucosa, one in muscle/soft tissue, and three in the joints. Most bleeds were in the mouth and were managed with antifibrinolytic agents. There were no serious side effects, blood clots, or TMA reported in this study, and there were no new inhibitors to FVIII.

Children <12 Years with Hemophilia A without Inhibitors References

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

2. 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

3. Pipe S, Collins P, Dhalluin C, et al. Emicizumab Prophylaxis for the Treatment of Infants with Severe Hemophilia A without Factor VIII Inhibitors: Results from the Interim Analysis of the HAVEN 7 Study. Presented at the American Society of Hematology in New Orleans, Louisiana; December 10-13, 2022. ASH Poster #187. https://www.hematology.org/

4. McCary I, Guelcher C, Kuhn J, et al. Real-world use of emicizumab in patients with haemophilia A: Bleeding outcomes and surgical procedures. Haemophilia. E-pub Date: April 2020. DOI # 10.1111/hae.14005. https://www.ncbi.nlm.nih.gov/pubmed/32311809