

Patient - Hemlibra and Long-Term Effectiveness and Safety

This letter contains information you requested on long-term use of Hemlibra® (emicizumab-kxwh) to treat people with hemophilia A with or 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

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

Median: The median is the middle number in a sort 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.

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

Thrombotic events: Blood clots that form in blood vessels.

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 was treated with infused clotting factor.

What is the long-term experience from the HAVEN trials for Hemlibra?

Long-term experience for Hemlibra prophylaxis is available from the Phase 3 HAVEN 1-4 clinical trials. The HAVEN trials studied how safe and how well Hemlibra worked to prevent bleeds in people with hemophilia A. A total of 399 people participated in these studies.^{1,2}

The HAVEN 1, 3, and 4 trials enrolled adult and adolescents, 12 years or older.

- The HAVEN 2 trial enrolled children less than 12 years old (or 12-17 years old if they weighed <40 kg).

How long did people take Hemlibra in this long-term HAVEN analysis?

The median time that people took Hemlibra in this long-term assessment was 120 weeks, or about 2 years and 4 months.^{1,2}

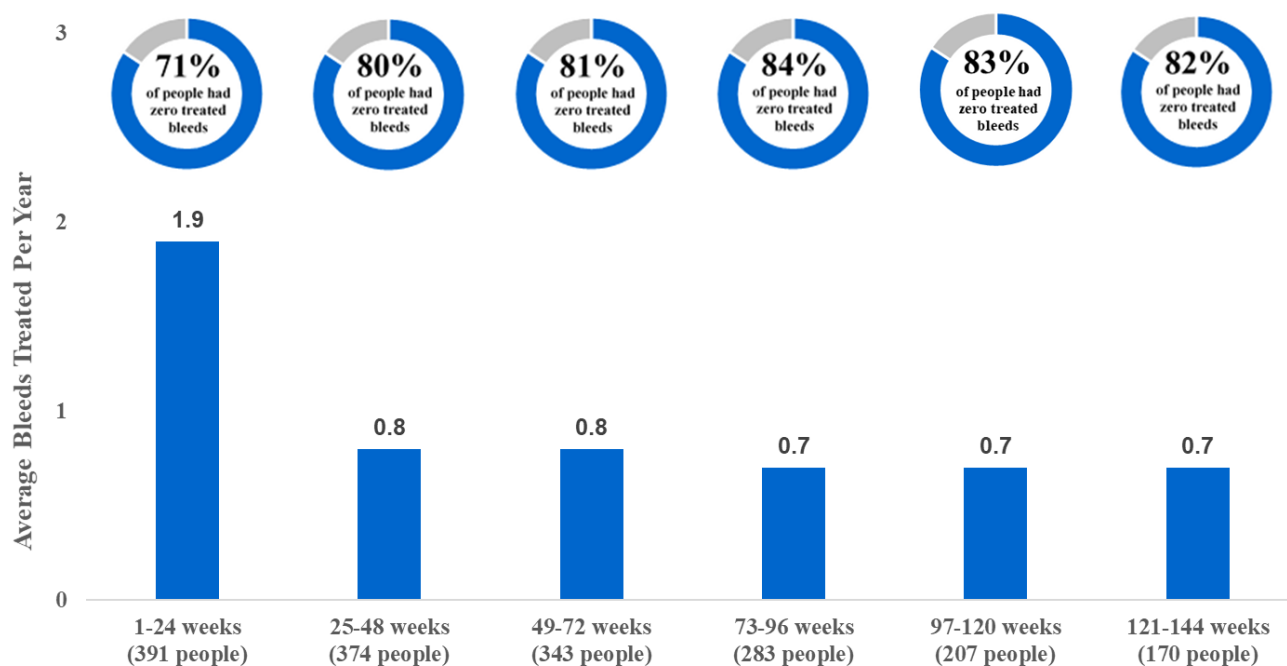
What was the long-term effect of Hemlibra on treated bleeds in the HAVEN trials?

Treated bleeds



- The average number of treated bleeds per year was less than 2 during the first 24 weeks on Hemlibra prophylaxis, and remained less than 1 for each 24 week period, through 144 weeks (bar graph in Figure 1).^{1,2}
- 71% of people had zero treated bleeds during the first 24 weeks, and this increased to over 80% in each subsequent 24 week period. (circles in Figure 1).^{1,2}

Figure 1: Long-Term Results for Bleeds Requiring Treatment^{1,2}



Treated spontaneous bleeds



- 84% of people had zero spontaneous bleeds that required treatment during the first 24 weeks, increasing to over 90% with each subsequent 24 week period.^{1,2}

What was the long-term effect of Hemlibra on treated joint bleeds in this analysis?

Treated joint bleeds



- 89.4% of people with target joints had zero target joint bleeds after receiving Hemlibra for at least 52 weeks.^{1,2}

Target joints resolved



- At the start of the studies, 226 people had a total of 530 target joints.^{1,2} 95% of these target joints resolved with Hemlibra treatment, meaning the joint had 2 or fewer bleeding events over 1 year.^{1,2}

What was the long-term safety of Hemlibra in this analysis of the HAVEN trials?



- The most common side effects related to Hemlibra were reactions at the location where Hemlibra was injected, also called injection-site reactions.^{1,2} These types of reactions occurred in 27.8% of patients.
- In this analysis, there were no additional reports of TMA or blood clots (thrombotic events) outside of the ones that were previously reported earlier in the HAVEN 1 study.^{1,2,3,4}

Hemlibra and Long-Term Effectiveness and Safety References

1. Callaghan M, Négrier C, Paz-Priel I, et al. Safety and Efficacy of Emicizumab in Persons with Hemophilia a with or without FVIII Inhibitors: Pooled Data from Four Phase III Studies (HAVEN 1–4). Presented at the 62nd American Society of Hematology Annual Meeting and Exposition in San Diego, CA; December 5–7, 2020. ASH Abstract #1800. <https://www.hematology.org/meetings/annual-meeting>
2. Callaghan M, Negrier C, Paz-Priel I. Safety and Efficacy of Emicizumab in Persons with Hemophilia A With or Without FVIII Inhibitors: Pooled Data from Four Phase III Studies (HAVEN 1-4). Presented at the 62nd American Society of Hematology Annual Meeting and Exposition in San Diego, CA; December 5–8, 2020. ASH Poster #1800.
3. Hemlibra® [package insert]. Genentech, Inc.; South San Francisco, CA. October 2018.
4. 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>