

Background

The HEMLIBRA clinical development program is investigating the safety and efficacy of emicizumab-kxwh in people living with hemophilia A with and without factor VIII inhibitors.

Patients who could not enroll in one of the sponsored clinical trials and met other criteria were permitted to gain access to emicizumab-kxwh through **expanded access program** or **compassionate use**. All fatalities are evaluated through Genentech and Roche drug safety and reported to regulatory authorities in strict accordance with guidelines and requirements.¹

In the postmarketing setting, Genentech is committed to continuously monitoring the safety of HEMLIBRA through established reporting mechanisms. We collaborate with the FDA and monitor reports of adverse events experienced by patients.

Fatalities in emicizumab-kxwh clinical trials, expanded access, compassionate use, and the postmarketing setting¹⁻³

Fatalities Reported/Verified at Data Cutoff of June 30, 2020^{§1-3}

	Fatalities	Locations of Cases
<u>Clinical Trials*</u>	3 ^{†‡}	HAVEN 1, STASEY (Australia, Europe)
<u>Expanded Access*</u>	1 ^{†‡}	North America
<u>Compassionate Use*</u>	3 ^{†‡}	Europe
<u>Postmarketing</u>	37 [†]	Asia, Europe, North America

* Fatalities recorded for any patient accessing emicizumab-kxwh under an investigational new drug (IND), whether company sponsored or not, or for any ex-US pre-approval use.

† In none of the reported cases had the causality been assessed as related to emicizumab-kxwh.

‡ Causes of death for cases occurring in clinical trials, expanded access, and compassionate use were assessed as rectal hemorrhage, sepsis, intracranial hemorrhage, pre-existing pseudotumor associated with severe hemophilia A, cecal perforation, traumatic head injury, and aspiration pneumonia.

§ Patients received emicizumab-kxwh for the following indications: congenital hemophilia A with FVIII inhibitors, n=16; congenital hemophilia A without FVIII inhibitors, n=13; hemophilia A (inhibitor status not reported), n=3; acquired hemophilia A, n=9; indication not reported, n=3.

Patient safety is of the highest importance to us. We take all reports of safety events very seriously and encourage anyone who knows of an adverse event in a patient on emicizumab-kxwh to report the event to Genentech/Roche. We have systems and processes in place to collect, analyze, and monitor adverse events and report events to the FDA per regulations.

Due to the voluntary nature of postmarketing spontaneous adverse event reports, information may be missing or incomplete. Genentech/Roche has limited ability to ascertain and verify information from these adverse event reports, and reporters, including healthcare providers, are not obligated to share these details with Genentech/Roche. Furthermore, reporters themselves may not have access to all of the information regarding a patient's care for these events. Genentech/Roche does not provide additional details related to adverse events reported in the postmarketing setting, because the level of detail available and Genentech/Roche's ability to confirm individual details is variable. In addition, patient privacy is very important to Genentech/Roche, therefore we are careful not to disclose specific details about an adverse event that could jeopardize the privacy of either the patient or their family, or breach patient confidentiality. As a result of the variable level of detail in such spontaneously reported data, Genentech/Roche will provide information on the number of verified fatality reports on this website without additional reported details related to events.

If any adverse event in a person taking emicizumab-kxwh impacts the overall benefit/risk profile of the medicine, we will share this information as quickly as possible and in accordance with any FDA requirements.

Report an Adverse Event

You may report adverse events to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report adverse events to Genentech at (888) 835-2555.



References

1. Data on file. Genentech, Inc. June 2020; 2. Shima M et al. *N Engl J Med.* 2016;374:2044-2053; 3. Oldenburg J et al. *N Engl J Med.* 2017;377:809-818.