PB0625

Emicizumab prophylaxis in people with hemophilia A aged ≥50 years with comorbidities: experience from the ATHN 7 hemophilia natural history study

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Summary

ATHN 7 is the largest longitudinal prospective cohort study of the safety and effectiveness of treatments for people with hemophilia A (PwHA) or hemophilia B in the US.

The aim of this analysis was to examine the characteristics and real-world safety of emicizumab prophylaxis in PwHA aged ≥50 years with comorbidities from the ATHN 7 study.

There were no thromboses or emicizumab-related adverse events reported in PwHA aged ≥50 years with pre-existing comorbidities.

Overall, 15 PwHA aged ≥50 years, representing 22.4 patient-years of exposure to emicizumab, were included.

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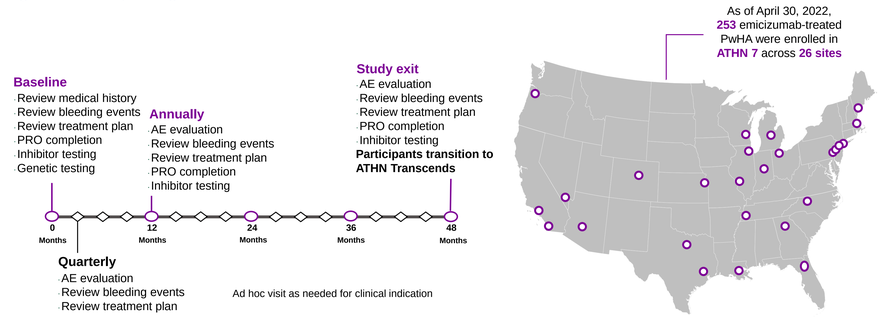
Background

- ATHN 7, A Natural History Cohort Study of the Safety, Effectiveness, and Practice of Treatment for People with Hemophilia (NCT03619863), collects real-world data describing long-term safety and effectiveness of therapies, including emicizumab, for the prevention and treatment of bleeding in people with hemophilia A (PwHA) and hemophilia B in the US.[1]
- Emicizumab is a bispecific monoclonal antibody that bridges activated factor (F)IX and FX to substitute for the function of absent or deficient activated FVIII in PwHA.[2]
- In the HAVEN and STASEY clinical trials, the efficacy and safety of emicizumab in PwHA aged ≥50 years with comorbidities was found to be consistent with PwHA in the overall population.[3–5]
- This analysis aims to examine the characteristics and real-world safety of emicizumab prophylaxis in PwHA aged ≥50 years with comorbidities from the ATHN 7 study.

ATHN 7 is a longitudinal, observational cohort study. As of April 30, 2022, 253 emicizumab-treated PwHA were enrolled at 26 American Thrombosis and Hemostasis Network (ATHN)-affiliated sites.[1]

- PwHA aged ≥50 years and receiving emicizumab at participating sites were eligible for this analysis.
- Clinical information was collected at baseline and at least quarterly through participant interview and medical record review (**Figure 1**).
- Participants were considered to have a comorbidity if they had cardiovascular (CV) risk factors (history of CV disease or current hypertension, diabetes, hyperlipidemia, or obesity), or hepatitis C virus (HCV) and/or human immunodeficiency virus (HIV) infection.
- Adverse events (AEs) were documented according to the European Haemophilia Safety Surveillance group (EUHASS) categorization.[6]
- AEs of special interest (thrombotic events, thrombotic microangiopathies, injection site reactions and allergic reactions) were also documented.
- Descriptive statistics of medical history and demographic data, as well as longitudinal data, were used to characterize the study population.

Figure 1. Study design



AE, adverse event; PRO, patient-reported outcome; PwHA, people with hemophilia A

As of the data cut-off (April 30, 2022), 15 PwHA aged ≥50 years and treated with emicizumab were enrolled in ATHN 7, representing 22.4 patient-years of exposure to emicizumab.

- Of these, 11 (73.3%) participants had severe hemophilia and 4 (26.7%) participants had moderate hemophilia.
- Five (33.3%) participants had FVIII inhibitors and 10 (66.7%) participants did not have inhibitors.
- Of the participants with CV risk factors, 10 (66.7%) participants had ≥1 CV risk factor(s) and 6 (40.0%) had ≥2 CV risk factors.
- Five (33.3%) participants had HCV infection alone and 9 (60.0%) participants had HIV/HCV co-infection (**Table 1**).

Table 1. Participant demographics and baseline characteristics

	Participants (N=15)
Age at baseline (years)	
n	15
Mean (SD)	61.1 (8.6)
Median (Min, Max)	60.0 (50.0, 79.0)
Baseline FVIII inhibitor status, n (%)	
Inhibitor	5 (33.3)
Non-inhibitor	10 (66.7)
Severity of hemophilia, n (%)	
Mild	0 (0)
Moderate	4 (26.7)
Severe	11 (73.3)
Exposure (weeks)	
n	14
Mean (SD)	83.5 (50.7)
Median (Min, Max)	84.4 (11.9, 148.0)
CV risk factors, n (%)	
≥1	10 (66.7)
≥2	6 (40.0)
HIV and/or HCV infection, n (%)	
HIV infection only	0 (0)
HCV infection only	5 (33.3)
HIV + HCV coinfection	9 (60.0)
Missing	1 (6.7)

CV, cardiovascular; F, factor; HCV, hepatitis C virus; HIV, human immunodeficiency virus; SD, standard deviation

Of the 15 eligible participants, three reported a total of four AEs.

- Four AEs, in three participants, were reported; all were deemed unrelated to emicizumab by the investigator **(Table 2)**.
- The four AEs were: a malignancy (metastasis of malignant prostate tumor) in one participant, a subdural hematoma in one participant, and one case of hemorrhagic shock secondary to a presumed gastrointestinal bleed, which resulted in death (previously reported) in the other participant.
- No AEs of special interest were reported.

Table 2. Participants with reported adverse events

	People with hemophilia A aged ≥50 years with reported adverse events, n (%)				
	Total (N=15)	≥1 CV risk factor (n=10)	≥2 CV risk factor (n=6)	HCV positive only (n=5)	HIV+HCV positive (n=9)
Any adverse event	3 (20.0)	3 (30.0)	3 (50.0)	2 (40.0)	1 (11.1)
Malignancy	1 (6.7)	1 (10.0)	1 (16.7)	1 (20.0)	0
Death	1 (6.7)	1 (10.0)	1 (16.7)	0	1 (11.1)
Other*	2 (13.3)	2 (20.0)	2 (33.3)	1 (20.0)	1 (11.1)

*Other adverse events were hemorrhagic shock and subdural hematoma. CV, cardiovascular; HCV, hepatitis C virus; HIV, human immunodeficiency virus

Conclusions

- No thromboses or AEs related to emicizumab were reported in PwHA aged ≥50 years and treated with emicizumab in the ATHN 7 study.
- This analysis is limited by the small study population and limited overall data in aging PwHA, regardless of prophylaxis type.
- The data contribute to the pool of evidence for emicizumab in PwHA aged ≥50 years with comorbidities, a population that is expected to grow due to increasing availability of improved prophylaxis.[7]
- Safety was consistent with previous studies of emicizumab prophylaxis in PwHA, including analyses of emicizumab in a similar population of PwHA aged ≥50 years in the HAVEN and STASEY clinical trials.[3–5]
- Continuous data collection is ongoing in the ATHN Transcends study (NCT04398628) to further evaluate the safety and effectiveness of emicizumab prophylaxis in PwHA.

Presented at the 2023 International Society on Thrombosis and Haemostasis (ISTH) Annual Meeting June 24–28 2023

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Acknowledgments

We would like to acknowledge the ATHN 7 participants, investigators and the 26 ATHN-affiliated hemophilia treatment centers for their participation in this important project. ATHN 7 was supported by a research grant from Genentech, Inc. Third party medical writing assistance, under the direction of the authors, was provided by Ella Spraggan MSc, of Ashfield MedComms, an Inizio company, and was funded by Genentech, Inc.

Disclosures

TB: Has received consulting fees from BioMarin Pharmaceutical Inc., UniQure, Tremeau Pharmaceuticals, Inc. , and has received research funding from Genentech, Inc. and the American Thrombosis and Hemostasis Network; and is listed as an advisory committee member for CSL Behring, Novo Nordisk, Pfizer, Spark Therapeutics, BioMarin Pharmaceutical Inc., Genentech, Inc., Takeda, Kedrion, HEMA Biologics, UniQure, and Tremeau Pharmaceuticals, Inc.; ND: Employee of the American Thrombosis and Hemostasis Network; LL: Employee of Genentech, Inc.; PM: Employee of Genentech, Inc.; CO: Employee of the American Thrombosis and Hemostasis Network; MW: Has received consulting fees/honoraria from Bayer, BioMarin Pharmaceutical Inc., Bioverativ (a Sanofi Company), CSL Behring, Genentech, Inc., Novo Nordisk and Takeda; MR: Has received consulting fees from BioMarin Pharmaceutical Inc., CSL Behring, Genentech, Inc., Novo Nordisk, Pfizer, Sanofi, Takeda, UniQure and has received a research grant from BioMarin Pharmaceutical Inc., Genentech, Inc., Novo Nordisk, Sanofi, Spark Therapeutics, Takeda, UniQure and has membership on an entity's Board of Directors for the Foundation for Women and Girls with Blood Disorders and Partners in Bleeding Disorders.