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Emicizumab and Females with Hemophilia A: Case Series from ATHN 7

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Summary

The population of females with hemophilia A (HA) is rare and under-represented in the medical literature

The safety, effectiveness, and practice of treatment were evaluated for the three females with HA receiving emicizumab in the ATHN 7 study

This analysis contributes to the body of evidence on females with HA receiving emicizumab prophylaxis

There were no adverse events reported; one participant reported a treated bleed, while the other two participants reported no bleeds

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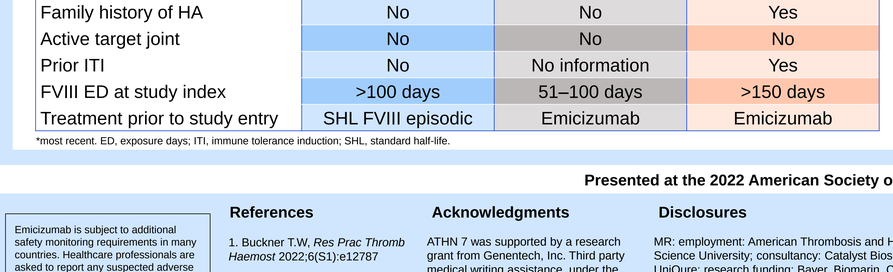
Background

- ATHN 7, A Natural History Cohort Study of the Safety, Effectiveness, and Practice of Treatment for People with Hemophilia (NCT03619863), monitors the use of current hemophilia A (HA) and B therapies, including the substitution therapy, emicizumab[1]
- Emicizumab is a bispecific monoclonal antibody, bridging activated factor (F) IX and FX, substituting for the function of activated FVIII, which is deficient in people with hemophilia A (PwHA). It is approved in the United States for prophylaxis in PwHA (ages newborn and older), with or without FVIII inhibitors
- The population of females with HA is rare and under-represented in the medical literature
- This analysis aims to characterize females with HA enrolled in ATHN 7 receiving emicizumab and present their associated experience on this therapy, including the safety profile of emicizumab in this population

ATHN 7 is a longitudinal, prospective observational cohort study conducted at 26 American Thrombosis and Hemostasis Network (ATHN)-affiliated sites

- Females (assigned sex at birth) with HA receiving care at participating sites (Figure 1) were eligible for inclusion
- Clinical and demographic information was collected at baseline, and medical history, demographic data and longitudinal data were used to characterize the study population
- There were no differences in the type of data collected for males and females

Figure 1. Study design and participants



*AEs included those events designated by the European Haemophilia Safety Surveillance group as well as AEs of special interest such as thrombotic events and thrombotic microangiopathies. AE, adverse event; PRO, patient-reported outcome.

At the data cut-off for this analysis (December 31, 2021), demographic and baseline medical history information was available for three emicizumab-treated females with HA in ATHN 7

- One of the three became post-menarchal during the study period (at age 13), while the other two were pre-menarchal throughout (Table 1)
- The participant who had baseline FVIII activity of 1% had a history of a tolerated low-titer FVIII inhibitor

Table 1. Participant demographics and characteristics

	Participant 1	Participant 2	Participant 3
Study inclusion	9/2019	7/2019	5/2019
Age at index (years)	11.4	6.6	5.9
Weight (kg)*	39.6	23.9	17.9
Ethnicity and race	Non-Hispanic white	Non-Hispanic white	Non-Hispanic white
Severity of hemophilia	Severe	Severe	Moderate
Baseline FVIII level	<1%	<1%	1%
FVIII inhibitors	No	No	Yes
FVIII mutation type	Inversion mutation intron 22, not sequenced	Frameshift c.5351delC	Inversion mutation intron 22, not sequenced
Family history of HA	No	No	Yes
Active target joint	No	No	No
Prior ITI	No	No information	Yes
FVIII ED at study index	>100 days	51–100 days	>150 days
Treatment prior to study entry	SHL FVIII episodic	Emicizumab	Emicizumab

*most recent. ED, exposure days; ITI, immune tolerance induction; SHL, standard half-life.

During study follow-up emicizumab exposure ranged from approximately 81.0 to 94.9 weeks, the longest follow-up in females with HA receiving emicizumab reported to date in the literature

- Only one participant experienced a treated bleed, which was associated with a dental procedure (Table 2)
  - This participant also reported one bleed that was not treated with coagulation factor (menses)
    - Her menstrual flow fluctuated over time, with some episodes of heavy bleeding, for which tranexamic acid was administered
- During the study, one participant underwent surgery (pressure equalization tube removal), with no unexpected bleeds associated with the procedure and no additional FVIII concentrate given

Table 2. Treatment and outcomes on emicizumab

	Participant 1	Participant 2	Participant 3
Maintenance emicizumab dosing regimen	Q2W	Q2W	Q2W
Baseline emicizumab dosing regimen	3 mg/kg Q2W	3 mg/kg Q2W	3 mg/kg Q2W
Duration of emicizumab exposure, weeks*	81.0	94.9	94.4
Concomitant hemostatic agents kept on hand†	Aminocaproic acid, tranexamic acid (for heavy menstrual flow) and SHL FVIII product for breakthrough bleeding	EHL and SHL FVIII product for breakthrough bleeding	Aminocaproic acid and SHL FVIII product for breakthrough bleeding
Treated bleeds on emicizumab	1 (for dental procedure)	0	0
Untreated bleeds on emicizumab	1 (menses)	0	0
Surgical procedures on emicizumab	None	None	Pressure equalization tube removal‡
Adverse events	None reported	None reported	None reported

*From baseline study visit date to latest follow-up visit date. †The hemostatic agents listed on participant medication list. Information as to whether they were used is unavailable. ‡Reported verbatim as "ventilating tube removal". There were no unexpected bleeds associated with this surgical procedure. EHL, extended half-life; Q2W, once every 2 weeks

Conclusions

- This analysis contributes to the body of evidence on females with HA receiving emicizumab prophylaxis
- In the largest multi-center, prospective observational experience of emicizumab-treated PwHA in the US (ATHN 7), two of the three female participants had no bleeds (treated or untreated), while the third participant had one treated bleed associated with a dental procedure and one untreated bleed associated with menses
- No AEs were reported during a total of 5.18 patient-years exposure to emicizumab
- Continued data collection is vital to further understand safety and effectiveness in this rare and under-represented population to optimize care for females with HA; as such, participants in ATHN 7 are currently transitioning to ATHN Transcends in order to maintain longitudinal data collection

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Emicizumab is subject to additional safety monitoring requirements in many countries. Healthcare professionals are asked to report any suspected adverse reactions to the regulatory authorities in your country according to your national requirements.

References

1. Buckner T.W, *Res Prac Thromb Haemost* 2022;6(S1):e12787

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Disclosures

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