Post ASH 2024

Haemophilia - emicizumab

Haemophilia A
Portfolio

M-CZ-00004523

Agenda of ASH 2024 - emicizumab

Those particular data are not sponsored by Roche

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- **Pediatric population**
  - ✓ ***RWD Ireland – emicizumab in PUPs/MTPs (Poster P3976)*** *– Ahmed S, et al. – Safety and outcome of early start of emicizumab in neonates and infants with severe hemophilia A, a real-world experience*
  - ✓ ***HAVEN 7 study and bleed patterns (Poster P1214)*** *– Carpenter SL, et al. – Bleed patterns in infants, from birth to 12 months of age, with hemophilia A treated with emicizumab: exploratory analysis of the HAVEN 7 study*
  - ✓ ***HAVEN 7 study and FVIII exposure (Poster P2589)*** *– Young G, et al. – FVIII exposure analysis from the HAVEN 7 study of emicizumab in infants with severe hemophilia A*
- **Special population**
  - ✓ ***Risk of TE on emicizumab (Oral presentation 130)*** – Vemuru S*, et al.* – Comparing the risk of thrombotic events in older person with hemophilia A on emicizumab prophylaxis to non-emicizumab products: A single center observational cohort study
  - ✓ ***TSUBASA study finaly analysis (Poster P1211)*** *– Nogami K, et al.* – TSUBASA study: A prospective study evaluating the association between physical activity and bleeding events, quality of daily life, and safety in people with hemophilia A without FVIII inhibitors
- **Quality of life**
  - ✓ ***Adherence and persistence to emicizumab (Poster P3699) –*** *Shapiro A, et al. – Real-world adherence and persistence to emicizumab using national claims database*
  - ✓ ***Experiences of US physicians and PwHA with emicizumab (Poster 5078)*** *– Recht M, et al. – Real-World Experience With Emicizumab for Hemophilia A From the Physician Perspective Based on Survey Data*
  - ✓ ***Mental liberation (Poster P1205)*** *– Hermans C, et al. – Impact of emicizumab on mental liberation in adult patients with severe and moderate factor VIII deficiency*

Safety and outcome of early start of emicizumab in neonates and infants with severe hemophilia A, a real-world experience

Upraveno podle posteru P3976 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024

Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/3976/529313/Safety-and-Outcome-of-Early-Start-of-Emicizumab-in

Introduction

- Prophylaxis is the recommended treatment for all patients with severe hemophilia
- Emicizumab is a bispecific humanized monoclonal antibody that binds to activated FIX and FX mimicking the function of FVIII
- In Ireland, emicizumab widely replaced CFC as the prophylaxis of choice in severe hemophilia A
- The risk of ICH in neonates diagnosed with hemophilia is 3·5 – 4·0%, which is 40–80 times higher than expected in the normal population

Aim

- There is no consensus on the ideal time to start emicizumab prophylaxis in newly diagnosed children with severe HA
- We aim to evaluate the outcomes of very early start of emicizumab prophylaxis in neonates and infants with severe HA treated in the Paediatric Coagulation Centre in Dublin, Ireland
- This is facilitated by the ease of administration of emicizumab via the subcutaneous route compared to the intravenously administered CFC

CFC, coagulation factor concentrate; F, factor; ICH, intracerebral hemorrhage; HA, hemophilia A.

Ahmed S. et al. ASH 2024; prezentace posteru P3976.

Method

- We retrospectively evaluated 15 children who started emicizumab during infancy
- Seven children (46.7%) were diagnosed at birth as their mothers were known carriers of severe HA
- The remaining eight infants (53.3%) were diagnosed between the first and 41rst weeks of life (Median 19 weeks)
- 50% (4 out of 8) children were investigated due to unusual bruising and prolonged aPTT
- All children received the standard loading dose of subcutaneous emicizumab 3mg/kg weekly for four weeks followed by 6mg/kg every 4 weeks

aPTT, activated parcial tromboplastine time; HA, hemophilia A.

Ahmed S. et al. ASH 2024; prezentace posteru P3976.

Results

Patients	Age of diagnosis (months)	Age at start of emicizumab (months)	Duration of follow up on emicizumab (months)	CFC prior to start on emicizumab	FVIII inhibitor status
1	Diagnosed at birth	0.7	21.3	6 exposure days	Negative
2	Diagnosed at birth	1	12	PUP	Negative
3	Diagnosed at birth	2.3	39.7	PUP	Negative
4	Diagnosed at birth	0.9	15.1	One exposure day	Negative
5	Diagnosed at birth	3.7	20.3	PUP	Negative
6	0.13	1	34	PUP	Negative
7	7.2	7.4	23.6	PUP	Negative
8	1.4	8.8	25.2	PUP	Negative
9	0.7	4.6	9.4	PUP	Negative
10	1.2	7.5	27.5	PUP	Negative
11	0.17	3	15	CFC prophylaxis for 3 months	Negative
12	1.3	11	38	One exposure day	Negative
13	Diagnosed at birth	0.2	4	PUP	Negative
14	Diagnosed at birth	0.2	1	One exposure day	Negative
15	0.63	4.4	1	PUP	Negative

CFC, coagulation factor concentrate; F, factor; ICH, intracerebral hemorrhage; PUPs, previously untreated patients.

Table 1: A total of 15 neonates and infants studied; 7 diagnosed at births as their mothers were known carriers; 10 are previously PUPs

- Fifteen neonates and infants enrolled in the study with a median age at start of emicizumab prophylaxis of 13 weeks (2 months), range 1-48 weeks
- The median follow up is 20.3 months (1-39.7)
- During follow up on emicizumab prophylaxis, no child develope spontaneous or traumatic bleeds including ICH
- None of the children in the study developed FVIII inhibitors while on emicizumab

Ahmed S. et al. ASH 2024; prezentace posteru P3976.

Results

Patients	Adverse event post emicizumab	Bleeding event post emicizumab	CFC treatment post emicizumab
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	Mild skin reaction	0	0
6	0	0	0
7	0	0	0
8	0	0	Two doses after two head injuries
9	0	0	0
10	Mild skin reaction	0	0
11	0	0	Peri CVC removal
12	0	0	One dose post head injury
13	0	0	0
14	0	0	0
15	0	0	One dose post head injury

Table 2: No adverse events reported apart from mild skin reaction in 2 children; no bleeding events reported; 3 children received CFC due to head injuries, however none of the children developed ICH. One child received CFC to cover removal of a CVC

- 73.3% (11/15) of the children in the study have not received CFC since starting emicizumab prophylaxis. One child was given to cover central line removal and three children received CFC after head injury
- Apart from mild transient skin reaction in two children, no other adverse events were related to emicizumab prophylaxis
- No child stopped emicizumab due to adverse events

CFC, coagulation factor concentrate; ICH, intracerebral hemorrhage; CVC, central venous catheter.

Ahmed S. et al. ASH 2024; prezentace posteru P3976.

Conclusions

- In infants diagnosed with severe HA, early start of emicizumab as soon as the diagnosis is made and during the first two months of life is a safe, well tolerated and effective strategy to prevent spontaneous as well as traumatic bleeding including ICH
- After a median follow up of 20.3 months, no child developed spontaneous or traumatic bleeding; no FVIII inhibitor was detected and no adverse events reported apart from mild skin reaction in 2 children
- The long-term outcome of very early start of emicizumab is not yet known

HA, hemophilia A; F, factor; ICH, intracerebral hemorrhage.

Ahmed S. et al. ASH 2024; prezentace posteru P3976.

Bleed patterns in infants, from birth to 12 months of age, with hemophilia A treated with emicizumab: exploratory analysis of the HAVEN 7 study

Upraveno podle posteru P1214 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024
Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/1214/532241/Bleed-Patterns-in-Infants-from-Birth-to-12-Months

Key takeaways

- In the exploratory analysis of the HAVEN 7 trial, there were no treated spontaneous bleeds, and joint and muscle bleed rates were low
- Most bleeds occurred on the head, but there were no intracranial hemorrhages
- Treated bleeds increased with age, consistent with motor development, and were similar to previously published bruising/injury patterns observed in infants without a bleeding disorder

Background and methods

- HAVEN 7 is a phase 3b, multicenter, open-label study, designed to evaluate the safety, efficacy, pharmacokinetics and pharmacodynamics of emicizumab **in infants aged 0–12 months with severe HA without FVIII inhibitors**
- This exploratory analysis of HAVEN 7 investigated the type and location of bleeds, and bleed patterns relative to age
- Recruited participants had no history of, or minimal exposure (≤5 days) to, hemophilia-related treatments containing FVIII
- Participants were excluded if they had any **prior use of emicizumab or evidence of ICH**
- ABRs (95% CI) were estimated using a **negative binomial regression model** and excluded surgical bleeds
- A new bleed was defined as a bleed occurring >72 hours after the last treatment for the original bleed. Any symptoms of bleeding that occurred ≤72 hours after the last treatment in the same location were considered the same bleed

ABR, annualized bleeding rate; CI, confidence interval; F, factor; HA, hemophilia A; ICH, intracranial hemorrhage.

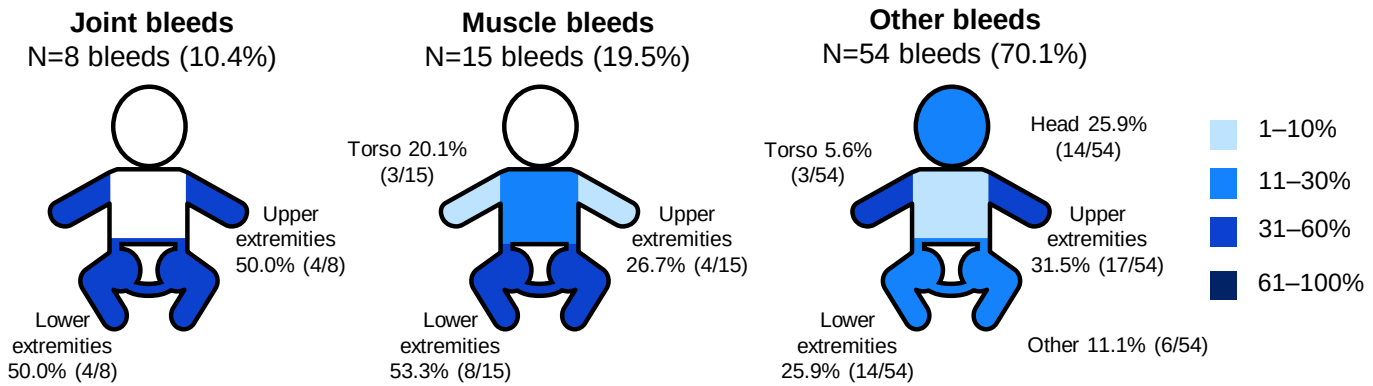
Carpenter SL. et al. ASH 2024; prezentace posteru P1214.

Overall, 195 bleeds were reported in 46 participants during the study

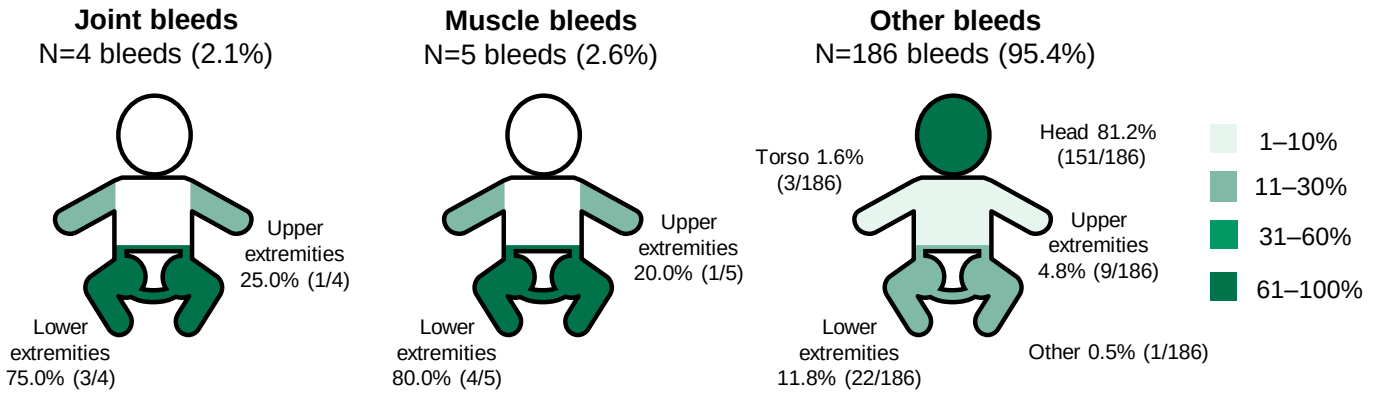
- In total, **55 male infants** were enrolled in the study, and had completed 52 weeks of emicizumab treatment*
- Median treatment duration was 100.3 weeks (range: 52–112)
- Prior to study entry, most bleeds (26/77 [33.8%]) had occurred at the **lower extremities**
- During the study, most bleeds (151/195 [77.4%]) occurred on **the head**

No ICH occurred

Bleed types and locations prior to the study†



Bleed types and locations during emicizumab treatment



*Clinical cut-off was May 22, 2023.

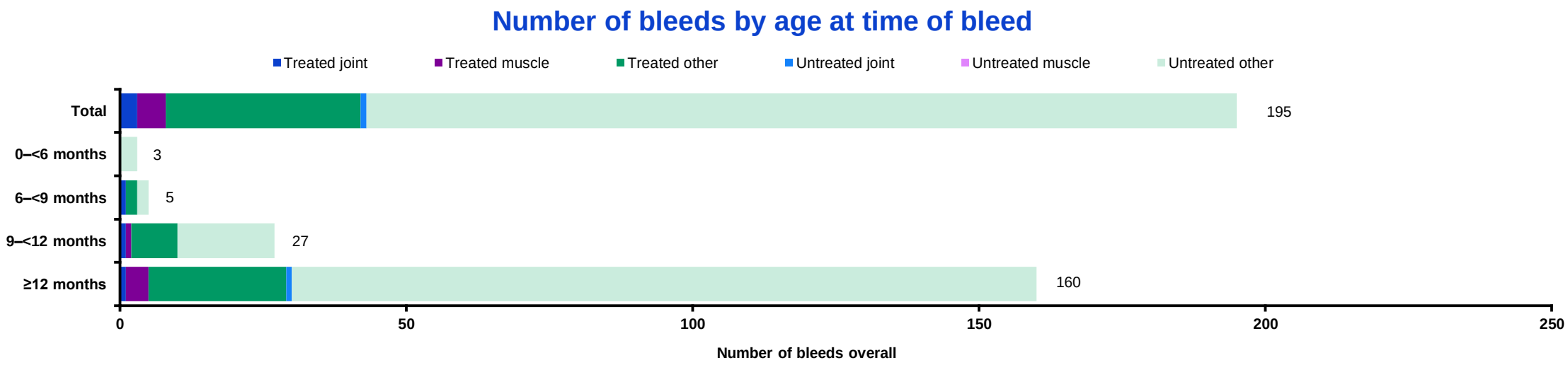
†Historical bleeds (since birth) were captured through medical history records and therefore may be underrepresented.

ICH, intracranial hemorrhage.

Carpenter SL. et al. ASH 2024; prezentace posteru P1214.

All treated joint, muscle, and other bleeds were traumatic

- **Model-based ABRs** (95% CI) for **treated bleeds** and **all bleeds** were **0.40 (0.30–0.63)** and **2.0 (1.49–2.66),** respectively
- There were **42 treated bleeds** in 25/46 (54.3%) participants, **all traumatic**
  - Zero (0%) occurred in participants aged 0–<6 months at time of bleed, and 3 (7.1%), 10 (23.8%), and 29 (69.0%) in those aged 6–<9, 9–<12, and ≥12 months, respectively



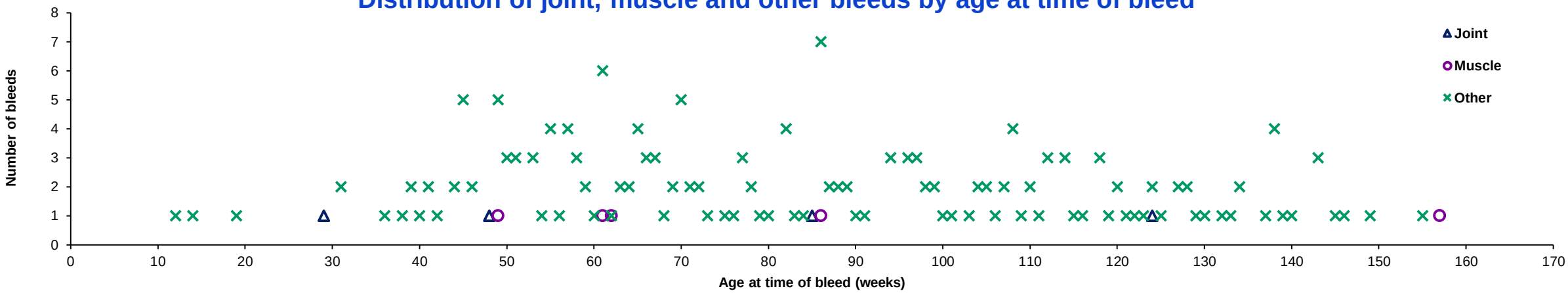
No treated spontaneous bleeds were reported during the study

ABR, annualized bleeding rate; CI, confidence interval.

Carpenter SL. et al. ASH 2024; prezentace posteru P1214.

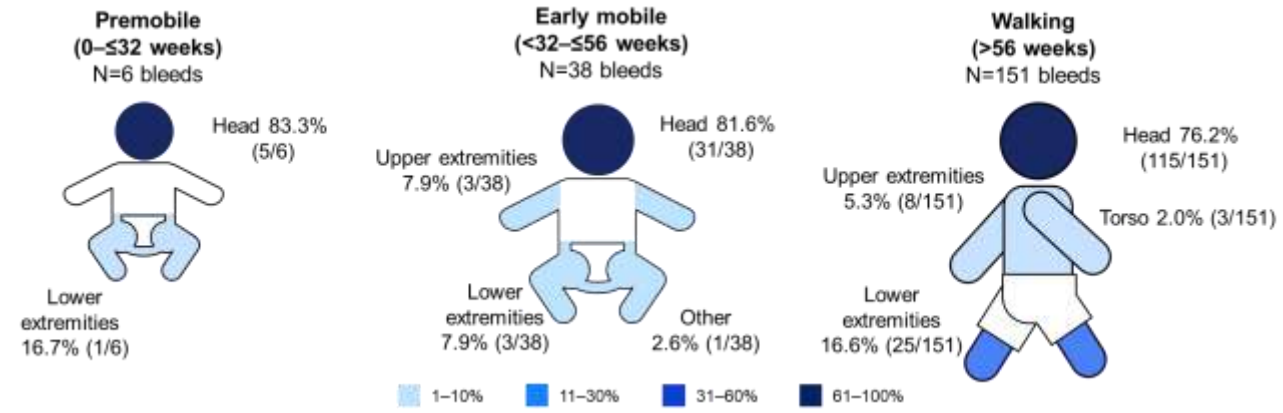
More bleeds occurred as infants gained mobility

Distribution of joint, muscle and other bleeds by age at time of bleed*



- Most spontaneous and traumatic bleeds occurred on the head (151/195 [77.4%])
- The most common were **mouth bleeds** (57/151 bleeds [37.7%]; 12 treated) and **nose bleeds** (37/151 bleeds [24.5%]; all untreated)
- The majority of bleeds occurred in participants **aged >56 weeks**, consistent with motor development and also bruising/injury patterns observed in non-hemophilic infants

Treated and untreated bleeds by location and mobility at time of bleed†



*Surgical bleeds were not included.
†Mobility of infants was estimated using data from a previous pediatric hemophilia study.

Carpenter SL. et al. ASH 2024; prezentace posteru P1214.

Conclusions

This is one of the first analyses describing in detail bleeding patterns in infants with HA receiving emicizumab

At the primary analysis of HAVEN 7, no treated spontaneous bleeds were reported during emicizumab treatment, and joint and muscle bleed rates were low

All treated bleeds reported were traumatic and bleed events increased with age as infants gained mobility and motor development

No ICH was reported with emicizumab prophylaxis; HAVEN 7 was not designed to investigate ICH

In this exploratory analysis, the pattern and location of bleeding displayed during emicizumab treatment were similar to previously published analyses of bruising and injury in infants without a bleeding disorder

ICH, intracranial hemorrhage.

Carpenter SL. et al. ASH 2024; prezentace posteru P1214.

FVIII exposure analysis from the HAVEN 7 study of emicizumab in infants with severe hemophilia A

Upraveno podle posteru P2589 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024
Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/2589/529501/FVIII-Exposure-Analysis-from-the-HAVEN-7-Study-of

Key takeaways

- During the HAVEN 7 clinical trial, **two previously untreated infants** with hemophilia A receiving emicizumab developed **FVIII inhibitors**
- Both participants who developed inhibitors had **FVIII exposure** and ***F8* genotypic risk factors.** One of the participants also had a **family history of inhibitors**

Background and methods

- Subcutaneous emicizumab enables prophylaxis from birth, potentially reducing bleed risk and delaying FVIII inhibitor development associated with FVIII administration in infants
- HAVEN 7 (NCT04431726), a Phase 3b, multicenter, open-label study, is the first clinical trial of emicizumab dedicated to infants (aged ≤12 months) with HA
- Eligible infants had severe HA with no history of FVIII inhibitors and were PUPs or minimally treated participants (MTPs; defined as having 1–5 EDs with a hemophilia-related treatment containing FVIII)
- Inhibitors are measured by chromogenic Bethesda assay, and were assessed in MTPs at baseline, as well as in any infant after 3 FVIII EDs or a block of EDs (≥2 consecutive doses) during the study

Here, we present data on **total FVIII EDs pre- and on-study**, providing additional context on the incidence of inhibitor development at primary analysis of HAVEN 7

ED, exposure day; F, factor; HA, hemophilia A; MTP, minimally treated participant; PUP, previously untreated participant

Young G. et al. ASH 2024; prezentace posteru P2589.

Baseline demographics

- At data cut-off (May 22, 2023), **55 male infants had received emicizumab for at least 52 weeks**
- The median duration of emicizumab treatment was 100.3 (range: 52–118) weeks
- Prior to study entry, 30 (54.5%) infants had ≥1 FVIII ED (median: 1 ED [range: 0–6])*

Participant demographics and baseline characteristics by number of EDs at data cut-off

	0 EDs (n=11)	1–3 EDs (n=27)	4–6 EDs (n=12)	7–9 EDs (n=3)	10–13 EDs (n=2)	Total (N=55)
Median (min–max) age at CCOD, months	20 (12–34)	31 (16–38)	32 (16–39)	33 (29–39)	23 (16–30)	29 (12–39)
Age of the youngest participant at study entry, days	14	9	17	84	61	9
Baseline treatment status, n (%)						
MTP	0	17 (63.0)	9 (75.0)	3 (100.0)	1 (50.0)	30 (54.5)
PUP	11 (100.0)	10 (37.0)	3 (25.0)	0	1 (50.0)	25 (45.5)

*The participant with 6 EDs was eligible for study entry as although they had FVIII administrations over six calendar days, two of these were within 24 hours, despite the maximum of 5 EDs allowed. CCOD, clinical cut-off date; ED, exposure day; F, factor; MTP, minimally treated participant; PUP, previously untreated participant

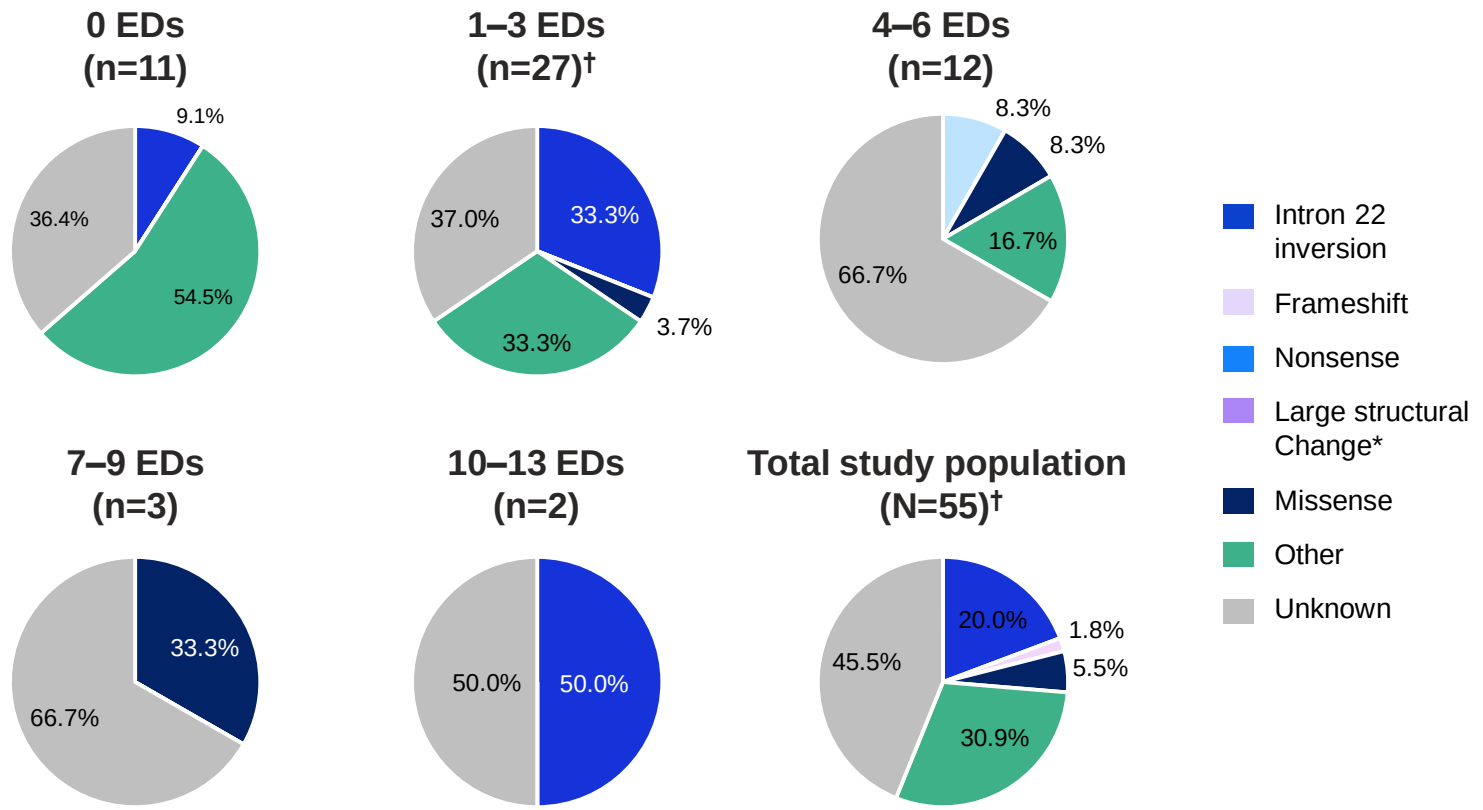
Young G. et al. ASH 2024; prezentace posteru P2589.

Two participants who had genotypic risk factors developed FVIII inhibitors during the study

- One infant in the 1–3 EDs subgroup with large *F8* deletion and no family history of inhibitors **developed inhibitors after 3 non-consecutive FVIII EDs** for the treatment of two traumatic mouth bleeds

- One infant in the 10–13 EDs subgroup with an intron 22 inversion and a family history of inhibitors **developed an inhibitor after 10 non-consecutive FVIII EDs** for a traumatic mouth bleed and surgical procedures (adenoidectomy and tonsillectomy)

F8 genotypes in each ED subgroup



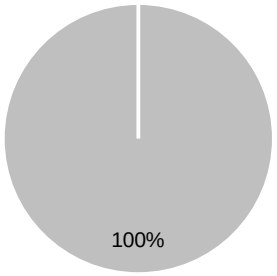
*A large structural change was defined as being >50 base pairs
†Categories are not mutually exclusive. Two participants with 'other' genotype also had an intron 22 inversion
ED, exposure day; F, factor; HA, hemophilia A

Young G. et al. ASH 2024; prezentace posteru P2589.

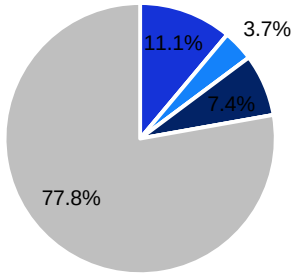
Participants were diagnosed with HA from a range of bleeds and procedures, in addition to family history

Reasons for HA diagnosis in each ED subgroup

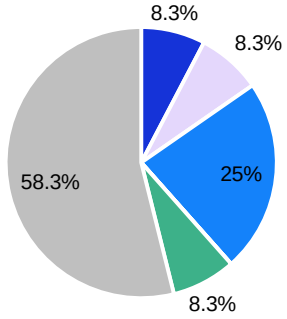
0 EDs (n=11)



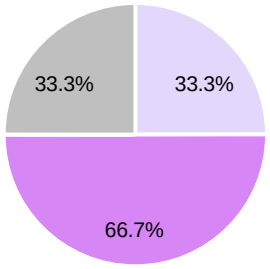
1–3 EDs (n=27)



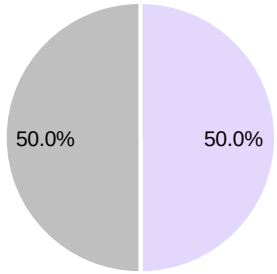
4–6 EDs (n=12)*



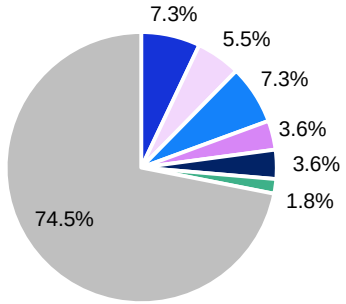
7–9 EDs (n=3)*

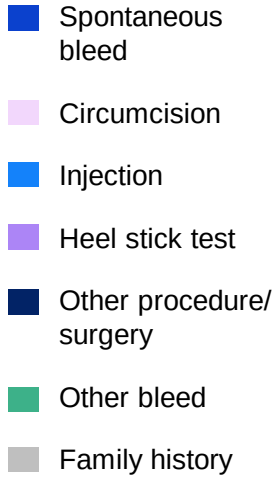


10–13 EDs (n=2)



Total study population (N=55)*

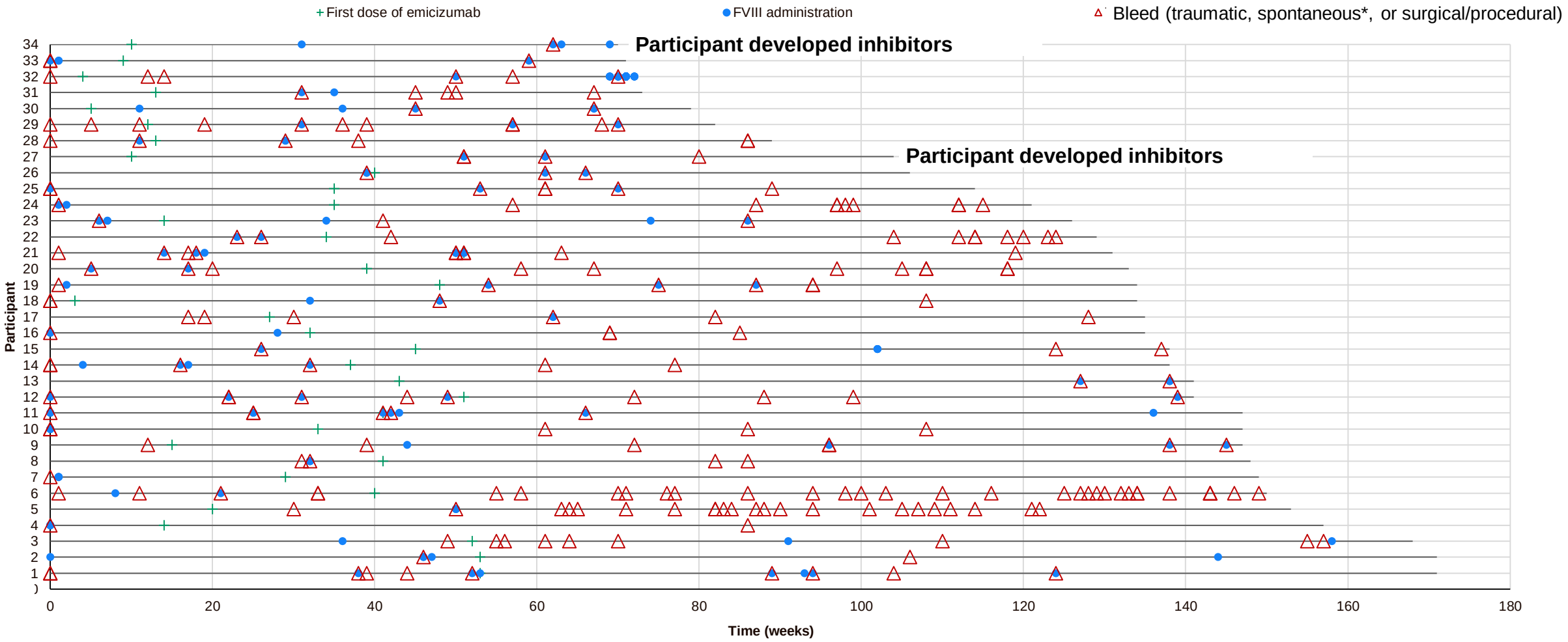




*Categories are not mutually exclusive.
ED, exposure day; HA, hemophilia A

Young G. et al. ASH 2024; prezentace posteru P2589.

Bleeds and FVIII administrations since birth in participants with ≥2 pre- and/or on-study EDs (n=34)



*There were no on-study spontaneous bleeds recorded.

ED, exposure day; F, factor

Young G. et al. ASH 2024; prezentace posteru P2589.

Limitations

- As most people with HA develop FVIII inhibitors after a median of 9–36 EDs, it will take more time to determine the inhibitor rate in people who start emicizumab alone as infants

- Although female infants were eligible for inclusion, no female infants were enrolled due to the low frequency of severe HA in females and the typically later diagnosis than males

EDs, exposure days; F, factor; HA, hemophilia A

Young G. et al. ASH 2024; prezentace posteru P2589.

Conclusions

In HAVEN 7, 25/55 (45.5%) infants receiving emicizumab had treated bleeds, none of which were spontaneous

Over two thirds of the participants (69%) had ≤3 EDs during a follow-up period of 100.3 weeks

Two (3.6%) participants developed FVIII inhibitors, after 3 and 10 non-consecutive EDs, respectively

Participants are continuing emicizumab prophylaxis during a 7-year long-term follow-up in HAVEN 7, in which inhibitor testing will continue

Future analyses may provide further data on rate, timing of, and risk factors for, FVIII inhibitor development in this population

ED, exposure day; F, factor

Young G. et al. ASH 2024; prezentace posteru P2589.

Comparing the risk of thrombotic events in older person with hemophilia A on emicizumab prophylaxis to non-emicizumab products: A single center observational cohort study

Upraveno podle ústní prezentace 130 přednesené na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024

Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/130/530491/Comparing-the-Risk-of-Thrombotic-Events-in-Older

Emicizumab

- A recombinant humanized bispecific monoclonal antibody that binds to both FIXa and FX, ultimately resulting in the activation of FX
- Approved by the FDA for PwHA both with and without FVIII inhibitors in 2017 and 2018, respectively
- Dosing ranges from weekly to monthly infusions

Concern for thrombosis with emicizumab use

- Theoretical increased risk of thrombosis in emicizumab compared to FVIII replacement products
  - Lack of inactivation by activated protein C
- This increased risk of thrombotic events is of particular concern in patients with cardiovascular risk factors, including older age, and atherosclerosis
- Among the original clinical trials, thrombotic events reported only in HAVEN 1
  - 3 TMAs and 2 TE were reported, all in the setting of concomitant aPCC infusions
  - Median age: 29 years

PwHA, people with hemophilia A; F, factor; TMA, thrombotic microangiopaties; TE, thrombotic events; aPCC, activated prothrombin complex concentrate.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Prior real-world study in an older population

Emicizumab prophylaxis in hemophilia patients older than 50 years with cardiovascular risk factors: Real-world data

- Observational prospective study conducted in Israel
  - 17 patients with HA on emicizumab
  - 2 patients had inhibitors
  - >50% of patients had multiple cardiovascular risk factors
  - No thrombosis or TMA
  - Median follow-up of 400 days
  - Lack of inactivation by activated protein C

HA, hemophilia A; TMA, thrombotic microangiopaties.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Research aim

- To determine thrombotic risk while on emicizumab compared to while not on emicizumab in people ≥ 50 years of age with severe and moderately severe hemophilia A (FVIII levels <2%)

Study design

- Retrospective observational cohort study
- Data source: Electronic Health record at a Single Hemophilia Treatment Center, Emory University

F, factor.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Study design

- Population
  - Severe and moderately severe hemophilia A (FVIII levels <2%)
  - ≥ 50 years as of January 1, 2017, or later
  - Followed through December 31, 2023
- Exposure
  - Time on emicizumab measured as the data a person began emicizumab until they discontinued its use, or the study period ended
- Outcome
  - Thrombotic events
    - Defined as myocardial infarction, transient ischemic attack (TIA), cerebrovascular accident (CVA), deep venous thrombosis (DVT), or pulmonary embolism (PE)

F, factor.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Study analysis

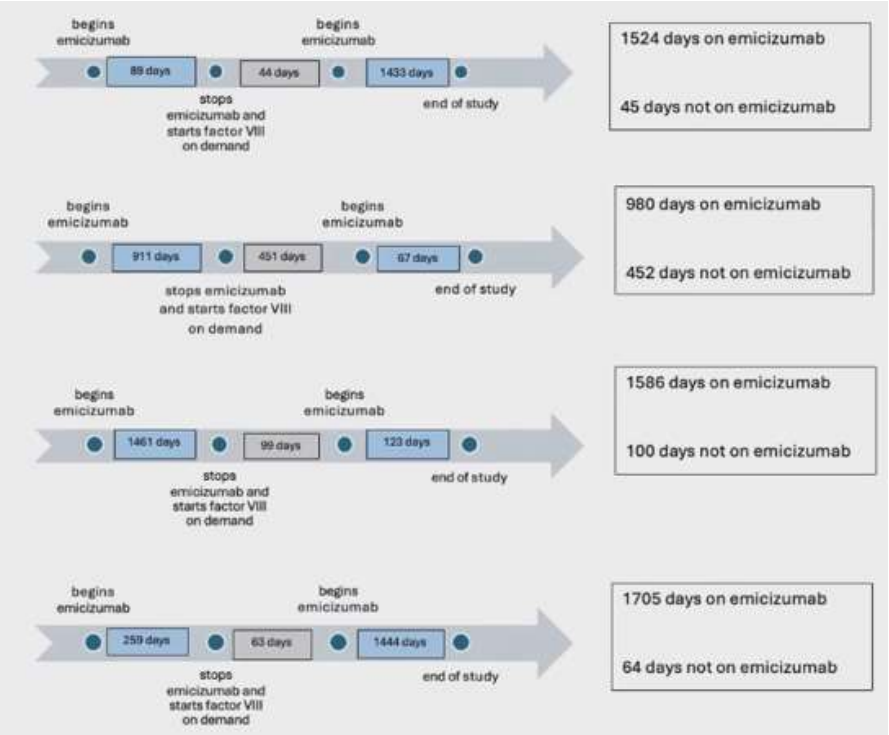
- Descriptive statistics were computed with Fischer's exact and t-tests
- Kaplan Meier Curves were used to estimate the cumulative probabilities
- Cox proportional models were used to estimate unadjusted (HR) and adjusted hazard ratios (aHR) of thrombotic risk
  - Accounted for intermittent use
  - Accounted for 30-day loading period of emicizumab
  - Accounted repeated observations

Results

- **32** patients included in total
- **27** patients contributed to time on emicizumab and time off emicizumab
  - **23** patients used emicizumab continuously
  - **4** patients used emicizumab intermittently
- **5** patients contributed ONLY to time not on emicizumab
- **0** patient contributed to time ONLY on emicizumab

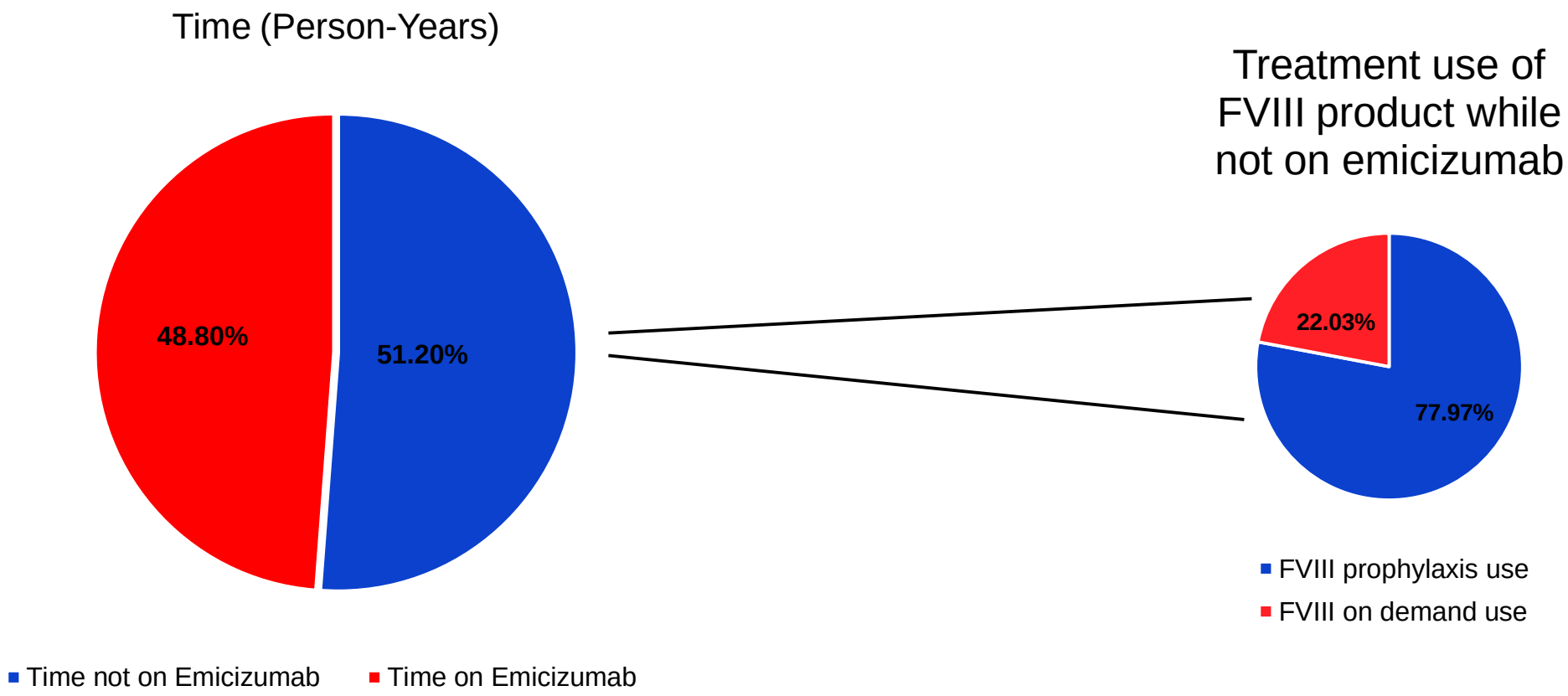
Intermittent use of emicizumab

- **4** patients used emicizumab intermittently
- They contributed **15.87** person-years to time on emicizumab
- They contributed to **1.81 person-years** to time off emicizumab



Vemuru S. et al. ASH 2024; ústní prezentace 130.

Observation time



F, factor.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Results-demographics

Categories	Total	Not emicizumab	Emicizumab	p-value
	N=32	N=5	N=27	
	N (%)	N (%)	N (%)	
Sex				
Male	32 (100)	5 (100)	27 (100)	
Race				.623
Asian/PI	1 (3.13)	0 (0)	1 (3.7)	
Black	5 (15.63)	0 (0)	5 (18.52)	
White	26 (81.25)	5 (100)	21 (77.78)	
Inhibitor history				.047
Current	1 (3.13)	0 (0)	1 (3.7)	
Never	26 (81.25)	3 (60)	23 (85.19)	
Past	3 (9.38)	0 (0)	3 (11.11)	
Unknown	2 (6.25)	2 (40)	0 (0)	
HIV viral load suppresion				
Suppressed	16 (50)	1 (20)	15 (55.65)	.173
Unsuppressed	4 (12.5)	0 (0)	4 (14.81)	
Past hepatitis C infection	31 (96.9)	4 (80)	27 (100)	.156

HIV, human immunodeficiency viruses.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Results-prevalence of cardiovascular risk factors

Categories	Total	Not emicizumab	Emicizumab	p-value
	N	**N (%)**	**N (%)**	
Hypertension	22 (68.75)	4 (80)	18 (66.67)	1.000
Hyperlipidemia	15 (46.88)	4 (80)	11 (40.74)	.161
Diabetes	4 (12.5)	1 (20)	3 (11.11)	.407
Current smoker	3 (9.38)	0 (0)	3 (11.11)	1.00
Formerly smoker	13 (40.63)	2 (40)	11 (40.74)	
Obese (BMI ≥30)	5 (15.6)	2 (6.3)	3 (9.4)	.163
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
BMI	26 (4.43)	28.2 (5.18)	25.6 (4.27)	.948
Age at baseline	55.0 (9.4)	59.8 (14.7)	54.1 (8.2)	.059

BMI, body mass index; SD, standard deviation.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Thrombotic events while not on emicizumab

- One thrombotic event, a TIA, occurred in a 56-year-old patient, during treatment time not on emicizumab and while on factor VIII prophylaxis
  - Remained on aspirin post-thrombotic event
  - Underwent carotid endarterectomy post-thrombotic event
- Of those never initiated on emicizumab, no thrombotic events were observed
- No thrombotic event occured while off emicizumab in patients who used emicizumab intermittently

TIA, transient ischemic attack; F, factor.

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Thrombotic events while on emicizumab

Left thalamic stroke
273 days after
Emicizumab initiation

Dysarthria secondary
836 days after
Emicizumab initiation

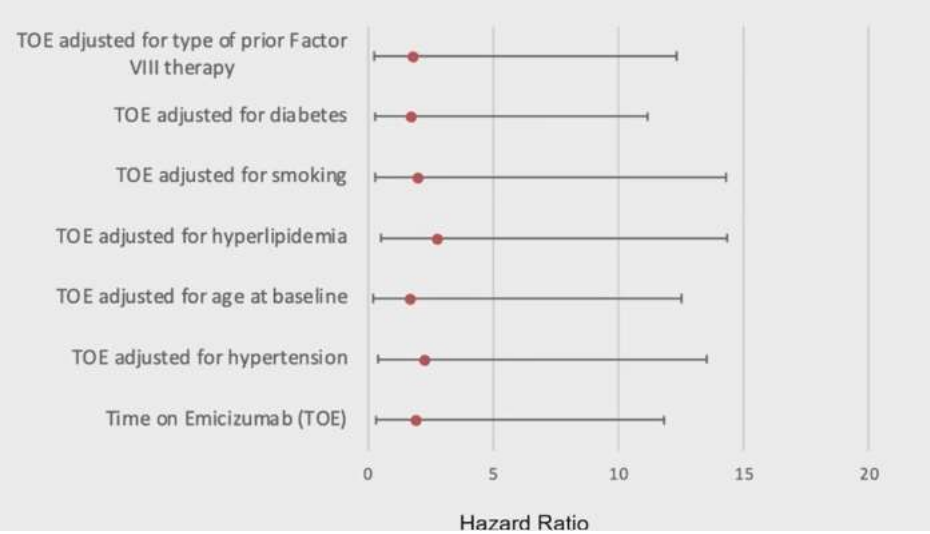
Both patients continued on emicizumab without a subsequent thrombotic event, with average time from thrombotic event to last clinic follow-up of 387 days

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Cumulative probabilities

- The cumulative probability of a thrombotic event was 0.104 while on emicizumab and 0.041 while not on emicizumab

The risk of thrombotic events on emicizumab



No significant increase in thrombotic events while on emicizumab

Vemuru S. et al. ASH 2024; ústní prezentace 130.

Limitations

- Unable to determine causation due to nature of study
- Small sample size
- Use of loading period and stoppage period
- Long time varying exposure
  - Large confidence intervals

Conclusions

- In this real-world cohort study with 174 person-years of follow up time and a high prevalence of cardiovascular risk factors, there was a **small, non-significantly** increased thrombotic risk while people were on emiczumab vs. not on emicizumab
- The thrombotic events described were particularly CVA and TIA, which were not observed in the initial clinical trials
- Among those with a thrombotic event, all subjects were on emicizumab for greater than 200 days prior to their event and continued on emicizumab without a subsequent thrombotic event
- Most patients, even those with cardiovascular risk factors, did not have thrombotic events after initiation of emicizumab
- Given this possible trend towards an increase risk of thrombotic events, despite adjusting for cardiovascular risk factors, larger-scale studies comparing real-world data of older patients on emicizumab to those on non-emicizumab treatment should be conducted to more precisely estimate the thrombotic risk and support shared decision making
- **At this time, emicizumab appears to be safe in this population**

TIA, transient ischemic attack; CVA, cerebrovascular accident.

TSUBASA study: A prospective study evaluating the association between physical activity and bleeding events, quality of daily life, and safety in people with hemophilia A without FVIII inhibitors

Upraveno podle posteru P1211 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024
Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/1211/532114/TSUBASA-Study-A-Prospective-Study-Evaluating-the

Key takeaways

- In the study, 73 participants receiving emicizumab prophylaxis performed 968 exercise events, including a wide range of activities, with only two events associated with bleeding
- Participants reported improvements in physical activity and motivation for school/work, as well as reduced anxiety around bleeding

Background and methods

- Limited data are available on the relationship between bleeding and physical activity in PwHA receiving emicizumab, as well as their QoL
- The **TSUBASA study** (UMIN-CTR ID: UMIN000037448) investigated the **association between bleeding and exercise** in PwHA receiving emicizumab
  - Type of physical activity and bleeding events were captured using the ePRO application
  - All participants ≥6 years of age wore a CentrePoint® Insight Watch activity tracker for five specified 8-day monitoring periods at Weeks 5, 25, 49, 73, and 97. Exercise events were classified as low, moderate, and high risk according to the National Bleeding Disorders Foundation
- **QoL** and **safety** outcomes were also assessed
  - QoL was measured using the SF-36, IPAQ, and a questionnaire on daily life completed by participants or caregivers
  - Safety endpoints included occurrence of AEs and FVIII inhibitors

Here we present the final analysis results of the TSUBASA study

AEs, adverse events; ePRO, electronic patient-reported outcomes; F, factor;
IPAQ, International Physical Activity Questionnaire; PwHA, people with hemophilia A; QoL, quality of life;
SF-36, 36-item short form

Nogami K, et al. ASH 2024; prezentace posteru P1211.

Exercise in participants ≥6 years old

- Of the 129 participants, 104 were ≥6 years old, with **73 recording ≥1 activity event**
- A total of **968 activity events** were documented (median [IQR] duration: 30 [15–60] minutes)
- The most common physical activities performed were walking (low risk, 38.6% of activities), cycling (moderate risk, 11.6%), and radio calisthenics (low risk, 8.7%)

Physical activity reported in participants ≥6 years old

Risk categorization (n=number of participants)	Number of instances	Median (IQR) exercise time, minutes	Median (IQR) activity intensity, mean METs	Median (IQR) activity intensity, max METs
Overall (n=73)	**968**	**30.0 (15.0–60.0)**	**2.39 (1.64–3.34)**	**4.30 (3.08–5.88)**
No hemorrhage (n=71)	**966**	**30.0 (15.0–60.0)**	**2.39 (1.65–3.33)**	**4.30 (3.08–5.88)**
Hemorrhage (n=2)	**2**	**90.0 (15.0–165.0)**	**2.70 (1.20–4.20)**	**6.57 (3.22–9.92)**
Basketball (moderate)	1	15.0	4.20	9.92
Fishing (low)	1	165.0	1.20	3.22
Low (n=58)	**556**	**30.0 (10.5–45.0)**	**2.42 (1.70–3.32)**	**4.32 (3.10–5.63)**
Moderate (n=27)	**182**	**36.5 (15.0–60.0)**	**2.81 (2.08–3.83)**	**4.62 (3.52–8.07)**
High (n=14)	**58**	**45.0 (20.0–55.0)**	**2.97 (1.59–4.16)**	**7.51 (3.50–9.31)**

Two (0.2%) of the 968 exercise events were associated with bleeding; both participants had severe HA, no reported bleeding events in the 24 weeks prior to the study, and no target joints

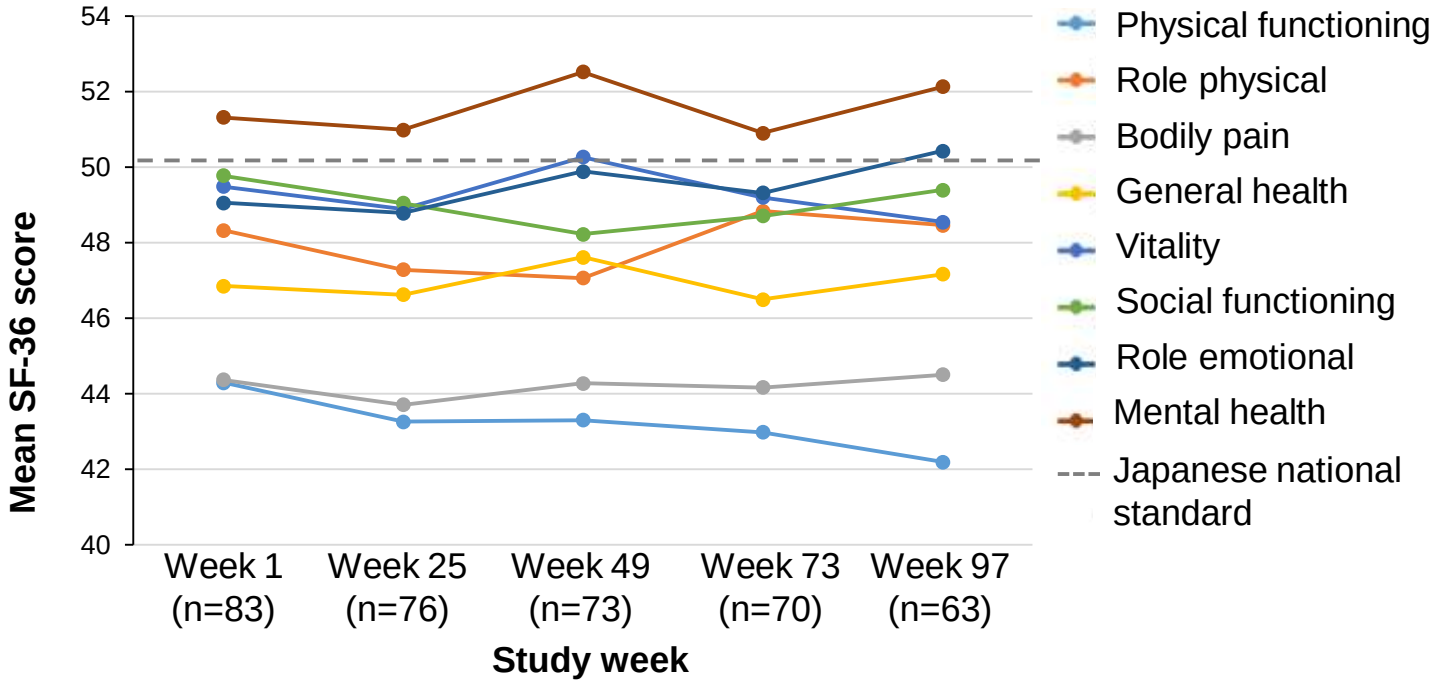
There were 172 instances of exercises that were not on the risk categorization list (median METs: 1.79 [mean] and 3.64 [maximum]).
MET is the ratio of working metabolic rate relative to resting metabolic rate. One MET is equal to the energy expended when at rest.
HA, hemophilia A; IQR, interquartile range; max, maximum; METs, metabolic equivalent of tasks.

Nogami K, et al. ASH 2024; prezentace posteru P1211.

QoL outcomes in study participants

- At Week 97, scores across domains of the SF-36, except physical functioning and bodily pain, were **comparable with the Japanese national standard**
- According to IPAQ, the proportion of participants with low physical activity decreased from 44.4% at Week 1 to 39.0% at Week 97, while participants reporting high physical activity increased from 20.2% to 27.3%
- Participants who completed the daily-life questionnaire reported improvements in physical activity and motivation for school/work, as well as reduced anxiety about bleeds

SF-36 domain scores over the study period



IPAQ, International Physical Activity Questionnaire; QoL, quality of life; SF-36, 36-item short form

Nogami K, et al. ASH 2024; prezentace posteru P1211.

Safety outcomes in study participants

- A total of 137 AEs were reported in 62 (48.1%) of the 129 study participants
- There were **no emicizumab-related serious AEs, intracranial hemorrhages, or thromboembolic events,** and no participant developed FVIII inhibitors on study
- There were ten adverse drug reactions on study (n=7):
  - Two cases of injection-site erythema
  - Five injection-site reactions
  - One case each of headache, vertigo and alopecia in the same participant
- No participant discontinued emicizumab due to an adverse drug reaction

Emicizumab was well tolerated, with no new safety signals

AEs, adverse events; F, factor

Nogami K, et al. ASH 2024; prezentace posteru P1211.

Conclusions

Many types of exercise were performed during emicizumab treatment, including some activities considered as high risk, and only two bleeds associated with physical activity were recorded

Questionnaire results showed that activity, frequency of exercise, motivation for school/work, and anxiety about bleeding improved after starting emicizumab

Emicizumab was well tolerated in both adults and children, and no new safety signals arose. There were no intracranial hemorrhages or thromboembolic events

This final analysis of TSUBASA suggests that PwHA receiving emicizumab may be able to engage in physical activity, with a low risk of associated bleeding

PwHA, people with hemophilia A

Nogami K, et al. ASH 2024; prezentace posteru P1211.

Real-world adherence and persistence to emicizumab using national claims database

Upraveno podle posteru P3699 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024

Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/3699/534065/Real-World-Adherence-and-Persistence-to-Emicizumab

Background

- Estimates of adherence to standard-of-care prophylaxis in people with hemophilia range from 47% to 82%
- Approximately 35% of PwHA receiving FVIII replacement products are nonadherent, although better adherence is associated with fewer bleeding events and better quality of life
- Emicizumab is the first bispecific FIXa- and FX-directed antibody approved in the US for routine prophylaxis in adult and pediatric PwHA with or without FVIII inhibitors
  - Emicizumab can be self-administered subcutaneously with maintenance dosing options of every 1, 2 or 4 weeks
- More real-world adherence and persistence data on emicizumab and other new hemophilia treatments are needed to better inform decisions on population healthcare and individualized treatments for PwHA

Objective

- To describe real-world adherence to and persistence with emicizumab prophylaxis in a US population of PwHA

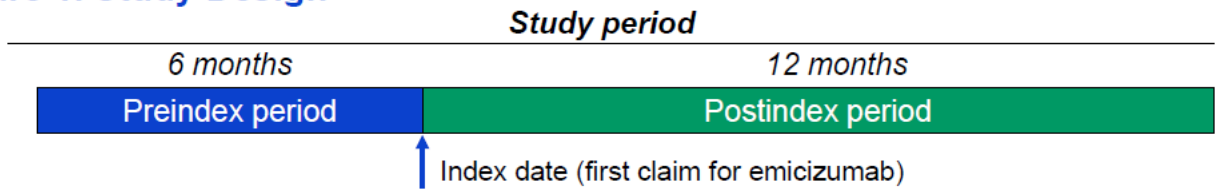
PwHA, people with hemophilia A; F, factor.

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Methods – study design

- This retrospective, observational cohort study used adjudicated health plan claims data from IQVIA PharMetrics® Plus
- PwHA were included if they had:
  - ≥1 *International Statistical Classification of Diseases, Tenth Revision* (*ICD-10*) code for hemophilia A between 5/1/2017 and 9/30/2023
  - ≥2 emicizumab prescription fills ≥2 days apart (first fill was the index date) between 11/1/2017 and 9/30/2023
    - Fills dated <2 days apart were assumed to be part of the same fill as some PwHA require multiple strengths and vials (which are each a separate claim) to receive their entire dose
  - Continuous medical and pharmacy insurance benefit coverage for ≥6 months before and ≥12 months after the index date (Figure 1.)

Figure 1. Study Design



- PwHA were excluded if they had any *ICD-10* code for hemophilia B or other rare bleeding disorders (eg, von Willebrand disease, acquired hemophilia A)

PwHA, people with hemophilia A.

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Methods – outcomes

- Days' supply was imputed for claims with this field missing
- Adherence to emicizumab was defined as having ≥80% proportion of days covered (PDC) during the 12-month period after the index date
  - PDC was determined by calculating days covered by emicizumab divided by days in the period of interest and is a commonly used metric in adherence studies
- Persistence with emicizumab was defined as the proportion of PwHA who did not discontinue emicizumab within 12 months of the index date
  - Discontinuation was defined as a treatment gap of ≥60 days per expert clinical input
- In adherent PwHA, claims for FVIII were evaluated during the 12 months after the index date and starting after the first week of follow-up
  - Efanesoctocog alfa was not represented in the analysis given its approval in 2023

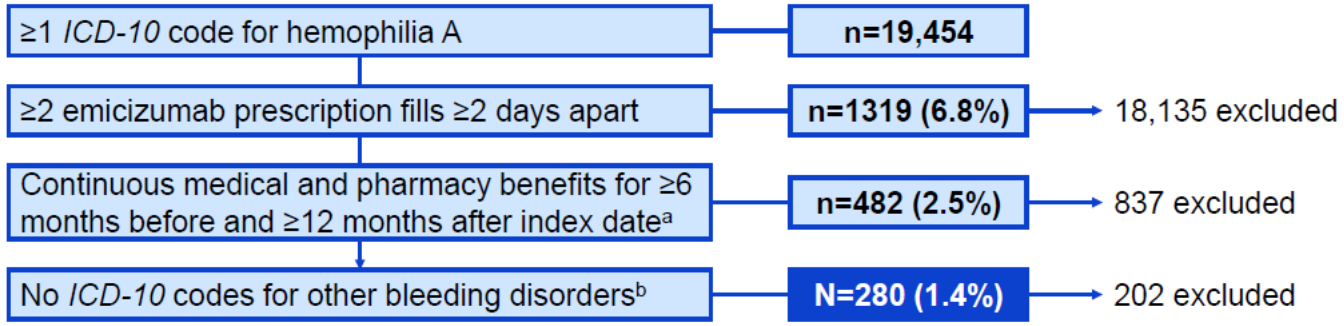
PwHA, people with hemophilia A; F, factor.

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Results

- Claims from 280 PwHA were included in the study (Figure 2.)

Figure 2. Cohort Attrition



ICD-10, International Statistical Classification of Diseases, Tenth Revision.
[a]Index date was the date of the first emicizumab prescription fill. [b]Individuals may be excluded for other rare blood disorders or using emicizumab off-label for other rare blood disorders.

PwHA, people with hemophilia A.

Results

Table 1. Baseline Characteristics of PwHA

Characteristic, n (%)	Overall cohort N=280
Age at index date	
≤12 years	66 (24)
13-18 years	34 (12)
19-30 years	73 (26)
31-50 years	89 (32)
≥51 years	18 (6)
Sex	
Female	6 (2)
Male	274 (98)
Region	
Midwest	76 (27)
Northeast	44 (16)
South	125 (45)
West	34 (12)
Missing or not applicable	1 (<1)
Insurance payer	
Commercial/self-insured	274 (98)
Medicare Advantage	4 (1)
Medicaid	2 (<1)
Plan type	
PPO	201 (72)
HMO	46 (16)
Other[a]	33 (12)
≥1 Preindex claim for:	
FVIII product	142 (51)
Bypassing agent	4 (1)

CDHP, consumer-directed health plan; FVIII, factor VIII; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; PwHA, people with hemophilia A.
[a]Includes POS, CDHP and indemnity.

- Mean (SD) age was 26 (16) years, and most PwHA were male (98%) (Table 1.)

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

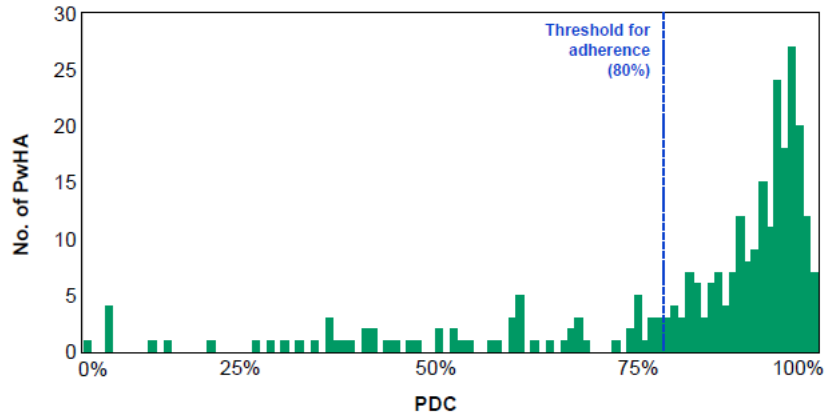
Results

Table 2. Persistence With and Adherence to Emicizumab in PwHA

Characteristic	Overall cohort N=280
Persistent, n (%)[a]	237 (85)
PDC, median (IQR), %	92 (81-96)
Adherent, n (%)[b]	213 (76)

IQR, interquartile range; PDC, proportion of days covered; PwHA, people with hemophilia A.
[a]Discontinuation was defined as a 60-day gap in emicizumab use based on expert clinical input. [b]Adherence was defined as ≥80% PDC.

Figure 3. PDC in PwHA Receiving Emicizumab (N=280)



PDC, proportion of days covered; PwHA, people with hemophilia A.

- An estimated 85% of PwHA were persistent with emicizumab therapy for the 12-month postindex period (Table 2.)
- Median PDC was 92%, and 76% of PwHA were adherent (PDC ≥80%) (Figure 3.)

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Results

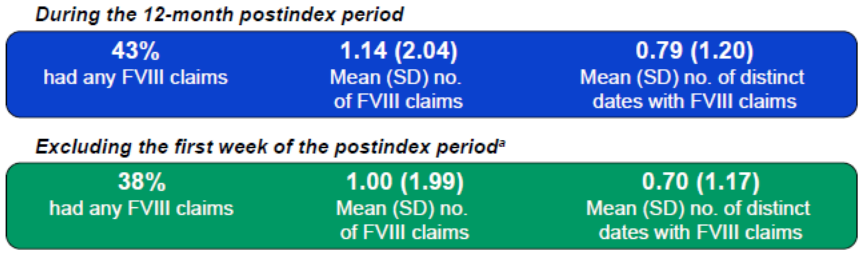
Table 3. Adherence and Persistence by Age and Region

Characteristic	Overall cohort N=280 Persistence, %[a]	PDC, median	Adherence, %[b]
Age at index date			
≤12 years	89	93	80
13-18 years	97	91	91
19-30 years	77	89	68
31-50 years	84	93	75
≥51 years	78	88	67
Region			
Midwest	88	93	80
Northeast	73	90	61
South	86	90	77
West	85	93	82

PDC, proportion of days covered; PwHA, people with hemophilia A.
[a]Discontinuation was defined as a 60-day gap in emicizumab use based on clinical inputs. [b]Adherence was defined as ≥80% PDC.

- Overall, rates of adherence and persistence were high across subgroups, ranging from 61% to 97% (Table 3.)
- Although adherence was lower in the 19- to 30-years age group, rates were not different from the ≥51-years age group

Figure 4. FVIII Claims in PwHA Adherent to Emicizumab (n=213)



FVIII, factor VIII; PDC, proportion of days covered; PwHA, people with hemophilia A.
[a]Per US prescribing information for emicizumab, prophylactic FVIII use may be continued during the first week of emicizumab use.[6]

- In the 213 PwHA who were adherent to emicizumab, most had no claims for FVIII during the postindex period (Figure 4.)
- PwHA had a mean of 1.14 (SD, 2.04) FVIII claims in the 12 months post index
- The mean number of days with FVIII claims during the postindex period was 0.79 (SD, 1.20; range, 0-5)

PwHA, people with hemophilia A.

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Limitations

- Claims data only capture medications that were dispensed and do not indicate whether the individual took the medication as indicated
- There was potential misclassification bias as the presence of a diagnosis code on a medical claim may not always be positive for the presence of the disease
- Our results are broadly from US PwHA with commercial health insurance and may not be generalizable to those with other insurance types or who are uninsured
- FVIII products have an average shelf life of 3 to 24 months, and PwHA periodically replace stock that is on hand in case of breakthrough bleeding events
- FVIII claim fills counts during the postindex period may be underestimated in PwHA who had FVIII on hand before initiating emicizumab

Strengths

- Use of a longitudinal, national database
- Long follow-up times and robust sample sizes even when excluding other bleeding disorders besides hemophilia A

PwHA, people with hemophilia A; F, factor.

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Conclusions

- Real-world adherence to emicizumab as measured by claims data continues to be high, with low discontinuation rates
- High adherence to emicizumab and few FVIII claims suggest that emicizumab treatment was well tolerated and efficacious during the study period based on the data set, which includes commercial insurance only
- The low frequency of FVIII claim fills during the 12-month postindex period can be correlated with low number of treated bleeding events
- These emicizumab adherence results are consistent with previously published self-reported adherence results in PwHA and caregivers

PwHA, people with hemophilia A; F, factor.

Shapiro A. et al. ASH 2024; prezentace posteru P3699.

Real-world experience with emicizumab for hemophilia A from the physician perspective based on survey data

Upraveno podle posteru P5078 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024
Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/5078/534165/Real-World-Experience-with-Emicizumab-for

Background

- Emicizumab is a bispecific FIXa- and FX-directed antibody approved for routine prophylaxis in adult or persons of newborn age or older with hemophilia A with or without FVIII inhibitors
- The safety and effectiveness of emicizumab have been previously evaluated in clinical and real-world studies in subpopulations of PwHA with varying inhibitor status, disease severity and/or age since its approval in the US in 2017
- Real-world data for PwHA treated in settings external to federally supported HTCs are limited

Objective

- To describe real-world characteristics and treatment experiences of US physicians and PwHA under their care receiving emicizumab at and external to federally supported HTCs

PwHA, people with hemophilia A; F, factor; HTCs, hemophilia treatment centers.

Recht M. et al. ASH 2024; prezentace posteru P5078.

Methods – study design

- The Adelphi Real World Hemophilia A Disease Specific Programme (DSP) is a cross-sectional, retrospective collection of data from physicians and male PwHA under their care in the US
- Physicians were recruited between July 2023 and April 2024 who:
  - Identified their specialty as hematologist or hematologist-oncologist (or the pediatric equivalent)
  - Were treating ≥5 individuals with hemophilia A or B at the time of the survey
- Each physician completed forms for up to 10 consecutively seen PwHA with or without inhibitors who:
  - Were male
  - Had baseline FVIII levels of <5%
  - Were not currently participating in a clinical trial
- Surveys captured demographic characteristics and hemophilia outcomes of interest, including adherence to treatment, bleeding events, joint health and healthcare resource utilization

PwHA, people with hemophilia A.

Recht M. et al. ASH 2024; prezentace posteru P5078.

Methods – surveys

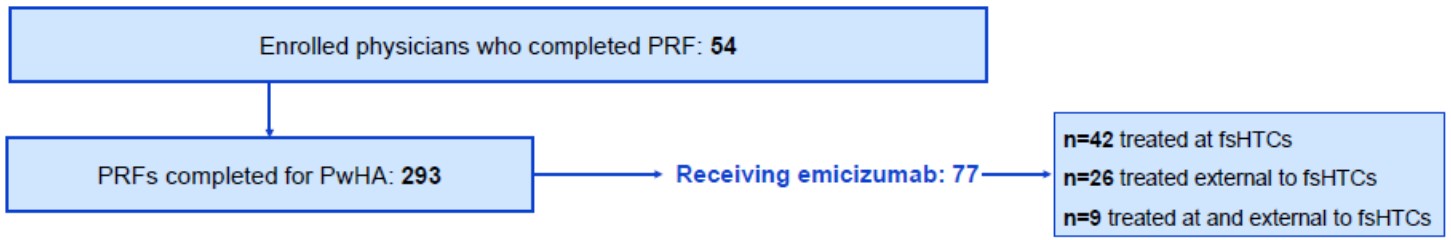
- **Physician surveys** were completed online one time by each physician participating in the study to capture perceptions and attitudes toward the management of hemophilia A and B
- **Physician-completed patient record forms (PRFs)** were completed online for individual PwHA following a consultation to capture detailed and comprehensive information
- Differences in outcomes between pre- and post-emicizumab treatment were tested for statistical significance using paired t-tests (bleeding outcomes) and Wilcoxon signed rank tests (joint health status

PwHA, people with hemophilia A; F, factor.

Results

- Overall, 54 physicians participated in the survey, resulting in completed records for 293 PwHA (Figure 1.)

Figure 1. Survey Completion



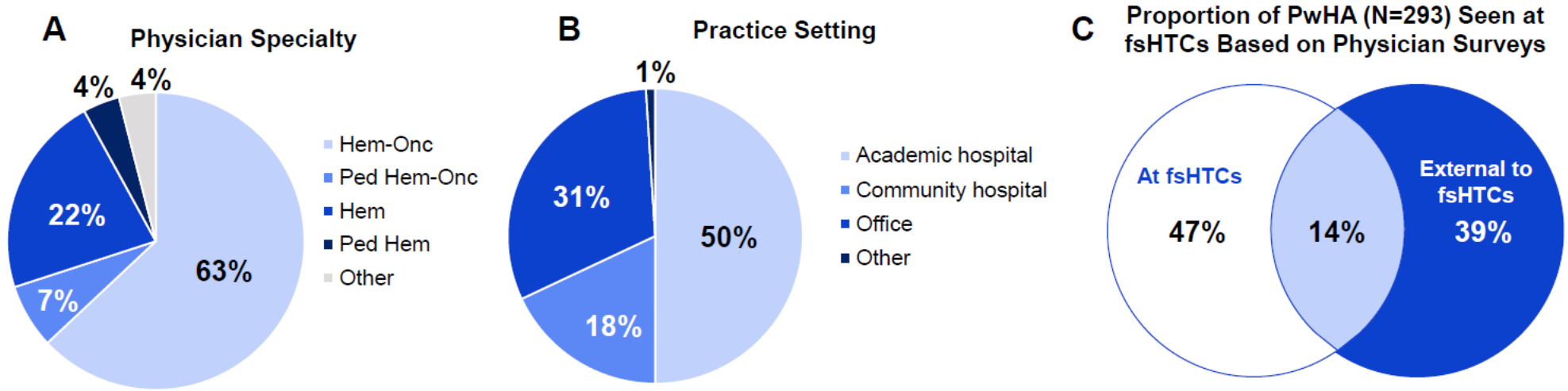
fsHTC, federally supported hemophilia treatment center; PRF, physician-completed patient record form; PwHA, people with hemophilia A.

Recht M. et al. ASH 2024; prezentace posteru P5078.

Results

- Most physicians were hematologist-oncologists (Figure 2A.) and half practiced in academic settings vs community hospital or office settings (Figure 2B.)
- Among PwHA, 39% were only treated external to federally supported HTCs (Figure 2C.)

Figure 2. Characteristics of Physicians Participating in Survey (N=54)



fsHTC, federally supported hemophilia treatment center; Hem, hematology; Ped, pediatric; PwHA, people with hemophilia A; Onc, oncology.

Recht M. et al. ASH 2024; prezentace posteru P5078.

Results

Table 1. Characteristics of PwHA Receiving Emicizumab (N=77)

Characteristic	All PwHA receiving emicizumab N=77	Seen at fsHTCs n=42	Seen external to fsHTCs n=26	Seen at and external to fsHTCs n=9
Age, mean (SD)	21.7 (11.8)	22.4 (11.8)	18.3 (8.0)	28.1 (18.3)
Age, n (%)				
≤11 years	15 (19.5)	7 (16.7)	6 (23.1)	2 (22.2)
12-17 years	6 (7.8)	1 (2.4)	4 (15.4)	1 (11.1)
18-49 years	53 (68.8)	32 (76.2)	16 (61.5)	5 (55.6)
≥50 years	3 (3.9)	2 (4.8)	0	1 (11.1)
BMI, mean, kg/m²	23.0 (4.0)	23.7 (3.6)	21.9 (4.4)	22.9 (4.4)
Ethnicity, n (%)				
Black, African American, African or Caribbean	23 (29.9)	7 (16.7)	12 (46.2)	4 (44.4)
East or Southeast Asian	2 (2.6)	1 (2.4)	1 (3.8)	0
Middle Eastern or North African	2 (2.6)	0	1 (3.8)	1 (11.1)
White	50 (64.9)	34 (81.0)	12 (46.2)	4 (44.4)
FVIII inhibitors, n (%)	8 (10.4)	3 (7.1)	3 (11.5)	2 (22.2)
Hemophilia A severity at diagnosis, n (%)	**n=64**	**n=34**	**n=24**	**n=6**
Moderate (FVIII 2%-5%)	15 (23.4)	6 (17.6)	8 (33.3)	1 (16.7)
Moderately severe (FVIII 1%-1.99%)	15 (23.4)	11 (32.4)	4 (16.7)	0
Severe (FVIII <1%)	34 (53.1)	17 (50.0)	12 (50.0)	5 (83.3)

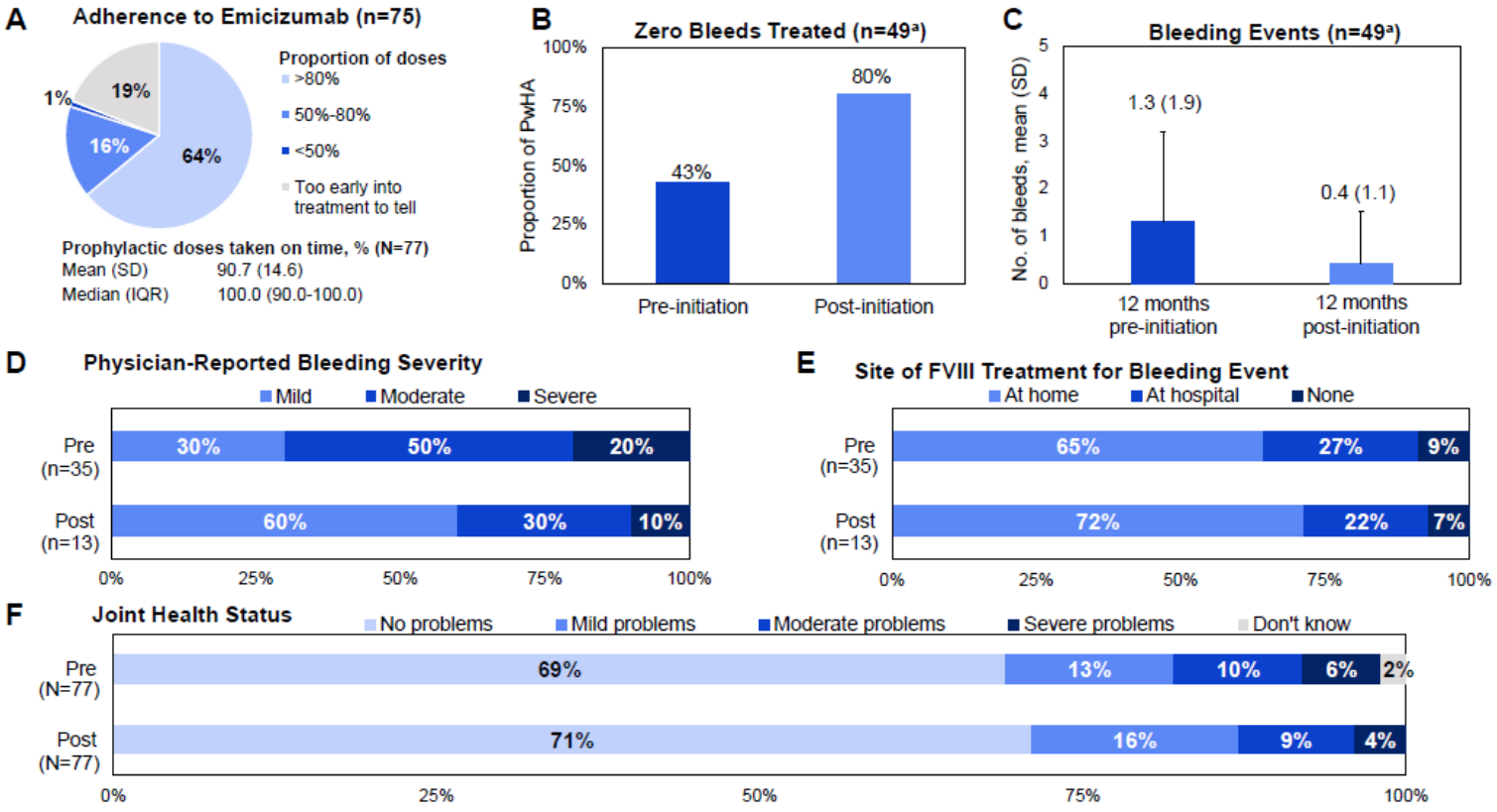
BMI, body mass index; fsHTC, federally supported hemophilia treatment center; FVIII, factor VIII; PwHA, people with hemophilia A.

- Among PwHA receiving emicizumab (N=77), the mean (SD) age was 21.7 (11.8) years, 55% were managed at federally supported HTCs, 53% had severe hemophilia A and 90% did not have inhibitors (Table 1.)
- HTCs without federal support had higher proportions of Black PwHA (46.2%) relative to federally supported HTCs (16.7%)

Recht M. et al. ASH 2024; prezentace posteru P5078.

Results

Figure 3. Physician-Reported Adherence, Bleeds and Joint Health in PwHA (N=77) Receiving Emicizumab



FVIII, factor VIII; IQR, interquartile range; PwHA, people with hemophilia A.
[a]Bleeding events were analyzed only in PwHA who had data available for both pre– and post–emicizumab initiation (n/N=49/77).

- Most PwHA (64%) were fully adherent to emicizumab (Figure 3A.), and 80% had zero treated bleed rate post initiation (Figure 3B.)
- Bleed rates decreased (Figure 3C.) and bleeds were less severe (Figure 3D., E.) after emicizumab initiation
- PwHA reported improved joint health after 12 months of emicizumab treatment (Figure 3F.)
- A decrease was observed in the number of bleeds between pre- and post-emicizumab (1.3 and 0.4, *P*=0.0001). None of the other outcomes analyzed had a statistically significant change (*P*>0.05)

Recht M. et al. ASH 2024; prezentace posteru P5078.

Conclusions

- This recent real-world survey of physicians showed that in the 12 months after initiating emicizumab, PwHA experienced an average of 0.4 bleeds and 80% of PwHA had zero treated bleeds compared with 1.3 bleeds and 43% of PwHA pre-initiation
- Real-world adherence to emicizumab is high, and 87% of PwHA receiving emicizumab had either no or mild joint problems compared with 82% before treatment
- A study limitation is the exclusion of female PwHA, who were not included as part of the survey offering; future studies should include female PwHA
- These results from physicians treating PwHA at and/or external to federally supported HTCs are consistent with the effectiveness of emicizumab reported from previous real-world and clinical studies

PwHA, people with hemophilia A; HTCs, hemophilia treatment centers.

Recht M. et al. ASH 2024; prezentace posteru P5078.

Impact of emicizumab on mental liberation in adult patients with severe and moderate factor VIII deficiency

Upraveno podle posteru P1205 předneseného na kongresu Americké hematologické společnosti (ASH), 7. – 10. prosince 2024
Abstrakt je dostupný na: https://ashpublications.org/blood/article/144/Supplement%201/1205/532342/Impact-of-Emicizumab-on-Mental-Liberation-in-Adult

Introduction

- The treatment landscape of hemophilia has been evolving rapidly over the past few decades. One of these innovations is emicizumab, a bispecific antibody that mimics the cofactor activity of coagulation FVIII
- Unlike classical replacement therapy with FVIII concentrates, emicizumab is administered subcutaneously on a weekly basis or, every 2 to 4 weeks, providing stable hemostatic activity. Several advantages of emicizumab have been reported:
  - Improved access to prophylaxis for persons with hemophilia (PWHs) unable to perform regular intravenous infusions,
  - Better hemostatic control as reflected by a lower bleeding rate,
  - A positive impact on pain and quality of life,

F, factor.

Hermans C. et al. ASH 2024; prezentace posteru P1205.

Aim

- Beyond these physical benefits, emicizumab should allow PWHs to be mentally liberated from the disease
- The concept of a "hemophilia-free mind" has been recently proposed to describe how new treatments for hemophilia could liberate patients not only from the physical but also the mental burden of the disease and its treatment
- In routine clinical practice, asking PWHs if they currently experience days when their minds are not preoccupied by hemophilia has been proposed as a first step to evaluate and validate this concept

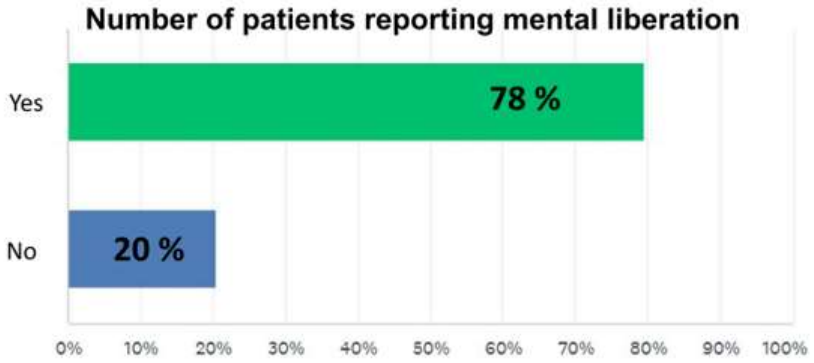
Method

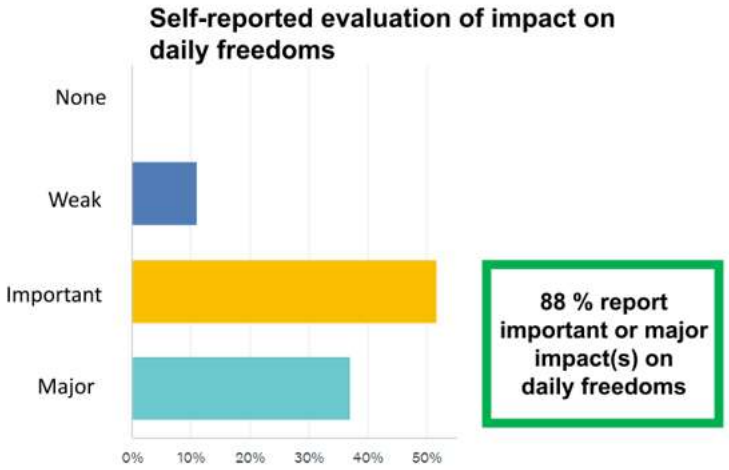
- A survey was recently conducted among all 80 adult patients (>18) with severe (69) and moderate (11) hemophilia A treated with emicizumab for at least 6 months, representing 80 % of the total number of severe and moderate PWHs followed at the Hemophilia Treatment Center of the Cliniques universitaires Saint-Luc in Brussels
- An online questionnaire via SurveyMonkey was sent to 74 patients reachable by email

PWHs, persons with hemophilia.

Hermans C. et al. ASH 2024; prezentace posteru P1205.

Results

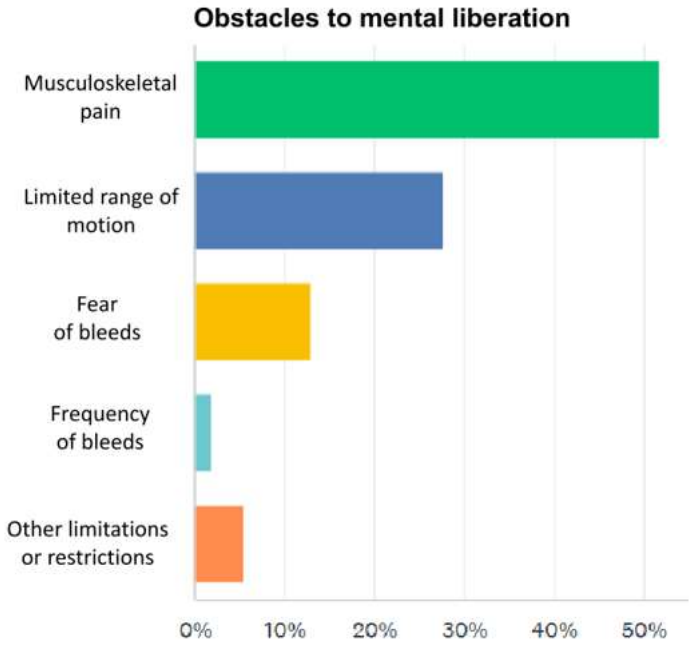




- Fifty patients (67%) provided anonymous responses that were collectively analyzed
- Thirty-nine patients (78%) reported experiencing days without thinking about hemophilia and its treatment
- The ability of emicizumab to provide more freedom to perform daily tasks and activities was rated as weak (6/50, 12%), important (25/50, 50%), or major (19/50, 38%)

Hermans C. et al. ASH 2024; prezentace posteru P1205.

Results



Number of hemophilia-free mind days :
5.2 / 5.5 (mean/median) days/week
23.2 / 27.5 (mean/median) days/month

- The number of "hemophilia-free mind" days was 5.2/5.5 (mean/median) per week and 23.2/27.5 (mean/median) per month
- The main obstacles that prevented PWHs from being totally mentally liberated were:
  - musculoskeletal pain (26/50, 52%),
  - restricted articular ranges of motion (14/50, 28%),
  - fear of bleeding (6/50, 12%),
  - bleeding events (1/50, 2%),
  - other non-specified limitations imposed by hemophilia (3/50, 6%)

PWHs, persons with hemophilia.

Hermans C. et al. ASH 2024; prezentace posteru P1205.

Conclusions

- This study clearly demonstrates for the first time the major potential of a new treatment such as emicizumab to liberate adult PWHs not only from the physical but also the mental burdens of hemophilia and supports the value of recording the number of "hemophilia-free mind" days
- Musculoskeletal pain and functional limitations represent major obstacles to this ambition, emphasizing the importance of pain and musculoskeletal management and care in the era of new therapies
- This potential for mental liberation should be evaluated in young patients on emicizumab as well as in patients of all ages currently benefiting from other new treatment options of hemophilia (rebalancing agents, ultra-long FVIII, and gene therapy)

PWHs, persons with hemophilia; F, factor.

Hermans C. et al. ASH 2024; prezentace posteru P1205.

HEMLIBRA 30 mg/ml injekční roztok, HEMLIBRA 150 mg/ml injekční roztok
– Zkrácená informace o přípravku

Účinná látka: emicizumab. **Držitel rozhodnutí o registraci:** Roche Registration GmbH, Grenzach - Wyhlen, Německo. **Registrační číslo:** EU/1/18/1271/001-004. **Indikace:** Přípravek Hemlibra je indikován k rutinní profylaxi krvácivých epizod u pacientů s hemofilií A s inhibitorem faktoru VIII, u pacientů s těžkou hemofilií A (vrozený deficit koagulačního faktoru VIII, FVIII < 1 %) bez inhibitoru faktoru VIII a u pacientů se středně těžkou hemofilií A (vrozený deficit koagulačního faktoru VIII, FVIII ≥ 1 % a ≤ 5 %) se závažným krvácivým fenotypem bez inhibitoru faktoru VIII. Přípravek Hemlibra mohou používat všechny věkové kategorie. **Dávkování a způsob podání:** Léčba musí být zahájena pod dohledem lékaře se zkušeností s léčbou hemofilie a/nebo krvácivých poruch. Den před zahájením léčby přípravkem Hemlibra musí být ukončena léčba (včetně rutinní profylaxe) bypassovými přípravky. Profylaxe faktorem VIII (FVIII) může pokračovat během prvních 7 dnů léčby přípravkem Hemlibra. Doporučená dávka je 3 mg/kg jednou týdně během prvních 4 týdnů (nasycovací dávka), po kterých následuje od týdne 5 udržovací dávka buď 1,5 mg/kg jednou týdně, nebo 3 mg/kg každé dva týdny nebo 6 mg/kg každé čtyři týdny, všechny dávky podávané formou subkutánní injekce. Režim nasycovací dávky je vždy stejný bez ohledu na režim udržovací dávky. Při sestavování celkového objemu dávky pro podání nesměšujte různé koncentrace roztoku Hemlibra (30 mg/ml a 150 mg/ml) v jedné injekční stříkačce. Nepodávejte objem větší než 2 ml na injekci. Přípravek Hemlibra je určen k dlouhodobé profylaktické léčbě. Nejsou doporučeny žádné úpravy dávkování přípravku Hemlibra. Přípravek Hemlibra je určen pouze k subkutánnímu použití a musí být aplikován pomocí vhodné aseptické techniky. Během léčby přípravkem Hemlibra mají být jiné léčivé přípravky k subkutánní aplikaci aplikovány přednostně v jiných místech. Přípravek Hemlibra je určen k používání pod vedením zdravotnického pracovníka. Po důkladném zaškolení v aplikaci subkutánní injekce jej může aplikovat pacient nebo pečovatel, uzná-li to lékař za vhodné. **Kontraindikace:** Hypersenzitivita na léčivou látku nebo na kteroukoli pomocnou látku. **Imunogenita:** U pacientů s klinickými projevy ztráty účinnosti (např. nárůst počtu průlomových krvácivých příhod) je třeba okamžitě zhodnotit etiologii a při podezření, že příčinou jsou neutralizující protilátky proti emicizumabu, je třeba zvážit jiné možnosti léčby. **Významné interakce:** S emicizumabem nebyly provedeny žádné adekvátní ani dostatečně kontrolované studie interakcí. Klinické zkušenosti naznačují, že emicizumab interaguje s aPCC. Emicizumab zvyšuje koagulační potenciál; dávka FVIIa nebo FVIII potřebná k zajištění hemostázy může být proto nižší než bez profylaxe přípravkem Hemlibra. Zkušenosti se souběžným podáváním antifibrinolytik s aPCC nebo rFVIIa u pacientů léčených emicizumabem jsou omezené. Při podávání systémových antifibrinolytik v kombinaci s aPCC nebo rFVIIa u pacientů léčených emicizumabem je však třeba vzít v úvahu možnost trombotických příhod. **Hlavní klinicky významné nežádoucí účinky:** Nejzávažnějšími nežádoucími účinky hlášenými v klinických studiích s přípravkem Hemlibra byly trombotická mikroangiopatie (TMA) a trombotické příhody včetně trombózy kavernózního splavu (CST) a trombóza povrchových žil s kožní nekrózou. Nejčastějšími nežádoucími účinky u pacientů léčených přípravkem Hemlibra byly reakce v místě vpichu, bolest kloubů a bolest hlavy. Celkem tři pacienti na profylaxi přípravkem Hemlibra v klinických studiích ukončili léčbu kvůli nežádoucím účinkům, ke kterým patřila TMA, kožní nekróza současně s povrchovou tromboflebitidou a bolest hlavy. **Druh obalu a dostupná balení:** Injekční lahvička 3 ml, Hemlibra s koncentrací 30 mg/ml obsahuje 12 mg emicizumabu v 0,4 ml injekčního roztoku, nebo obsahuje 30 mg emicizumabu v 1ml injekčního roztoku. Injekční lahvička 3ml, Hemlibra s koncentrací 150 mg/ml obsahuje 60 mg emicizumabu v 0,4 ml injekčního roztoku, nebo obsahuje 105 mg emicizumabu v 0,7 ml injekčního roztoku, nebo obsahuje 150 mg emicizumabu v 1 ml injekčního roztoku, nebo obsahuje 300 mg emicizumabu ve 2 ml injekčního roztoku. Balení obsahuje vždy jednu injekční lahvičku. **Podmínky uchovávání:** Uchovávejte v chladničce (2–8 ºC). Neotevřené injekční lahvičky lze po vyjmutí z chladničky uchovávat při pokojové teplotě (do 30 °C) až po dobu 7 dnů kumulativně. Chraňte před mrazem a před světlem.

Datum registrace: 23.2.2018 **Datum poslední úpravy textu Zkrácené informace o přípravku:** 9.11.2023. **Aktuální verze Souhrnu údajů o přípravku je dostupná na** https://www.sukl.cz, **resp.** https://www.roche.cz/cs/produkty-vpois/produkty-lekari.html

Výdej léčivého přípravku je vázán na lékařský předpis. Léčivý přípravek Hemlibra je v indikaci rutinní profylaxe krvácivých epizod u pacientů s hemofilií A (vrozený deficit koagulačního faktoru VIII) s inhibitorem faktoru VIII a v indikaci rutinní profylaxe krvácivých epizod u pacientů s těžkou hemofilií A (vrozený deficit koagulačního faktoru VIII, FVIII < 1 %) bez inhibitoru faktoru VIII hrazen z prostředků veřejného zdravotního pojištění. Léčivý přípravek zatím není hrazen u pacientů se středně těžkou hemofilií A (vrozený deficit koagulačního faktoru VIII, FVIII ≥ 1 % a ≤ 5 %) se závažným krvácivým fenotypem bez inhibitoru faktoru VIII. Podmínky úhrady viz www.sukl.cz. Další informace o přípravku získáte z platného Souhrnu údajů o přípravku Hemlibra, nebo na adrese Roche s.r.o., Sokolovská 685/136f, 18600 Praha 8, Tel: +420 220382111. Podrobné informace o tomto přípravku jsou uveřejněny na webových stránkách Evropské lékové agentury (EMA) http://www.ema.europa.eu/.