Post EAHAD 2024

Haemophilia - emicizumab

Haemophilia A
Portfolio

M-CZ-00003811

Agenda of EAHAD 2024 - emicizumab

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- **Safety**
  - ✓ ***TEs, TMA (Poster PO126)*** *– Sarouei K, et al. – Emicizumab prophylaxis in people with hemophilia A: Summary of 10 years of safety data on thromboembolic events and thrombotic microangiopathy*
- **Special population**
  - ✓ ***PUPs (Poster P0130)*** *– Fischer K, et al. – Uptake of emicizumab in PUPs with severe haemophilia A and changes in inhibitor incidence*
  - ✓ ***PwHA older than 40 years (Poster PO031)*** *– Hermans C, et al. – Cardiovascular safety and brain protective effect of emicizumab in people with haemophilia A older than 40 yea*
  - ✓ ***Mild and moderate PwHA (Poster PO122****) – Jiménez-Yuste V, et al. – Emicizumab in people with moderate or mild haemophilia A aged ≥40 years, with and without comorbidities*
- **Joint health**
  - ✓ ***Children with SHA on emicizumab and HJHS (Poster PO157)*** *– Jaffer Z, et al. – The use of the haemophilia joint health score as a monitoring tool for children with severe haemophilia a on emicizumab prophylaxis*

TEs, thrombotic events; TMA, thrombotic microangiopathies; PUPs, previously untreated patients; PwHA, people with haemophilia A; SHA, severe haemophilia A; HJHS, Haemophilia Joint Health Score

Emicizumab prophylaxis in people with hemophilia A: Summary of 10 years of safety data on thromboembolic events and thrombotic microangiopathy

Upraveno podle posteru PO126 předneseného na kongresu Evropské asociace pro hemofilii a přidružené choroby (EAHAD),
6. – 9. únor 2024
Abstrakt je dostupný na: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14919

Background

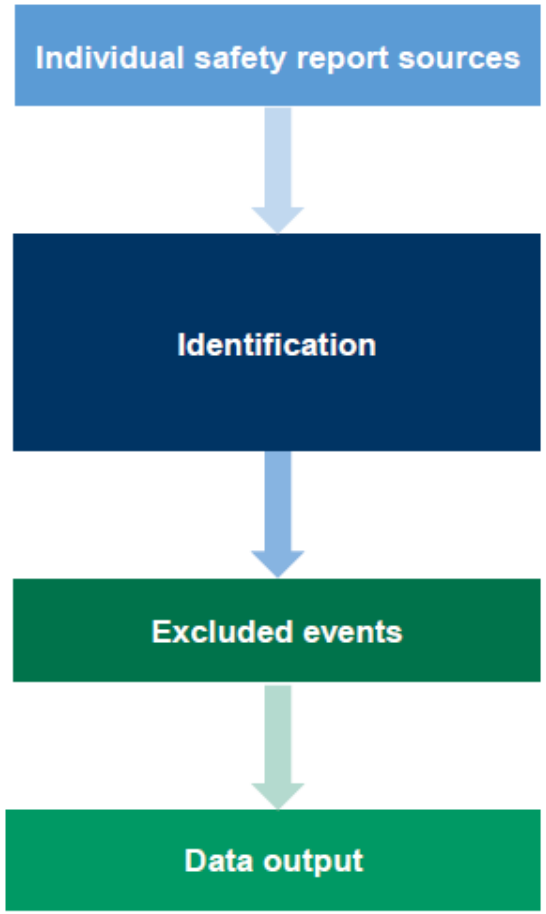
- As of July 2023, more than 24,000 people have been treated with emicizumab worldwide, with this number continually growing
- In 2017, the HAVEN 1 clinical trial outlined TEs and TMAs as risks when taking emicizumab alongside aPCC at doses of >100 U/kg/24 hours for ≥24 hours in PwHA
- Subsequently, these events have been monitored on an ongoing basis in all individuals receiving emicizumab, with or without concurrent aPCC, and routine risk minimisation activities have been included in the label
- This poster presents an updated safety evaluation of emicizumab prophylaxis, focusing on TEs and TMAs

TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Methods

Figure 1. Methodology



Clinical trials, registries, expanded access programmes, compassionate use and spontaneous post-marketing reports (cut-off date: 1 August 2023)

TEs were identified using the MedDRA v26.0 search strategy: „Embolic and Thrombotic Events“ SMQ

TMAs were defined as haemolytic uraemic syndrome, microangiopathic haemolytic anaemia, microangiopathy, thrombotic microangiopathy, thrombotic thrombocytopenic purpura, and renal-limited thrombotic microangiopathy

Individual cases were reviewed to exclude non-TEs and duplicate reports

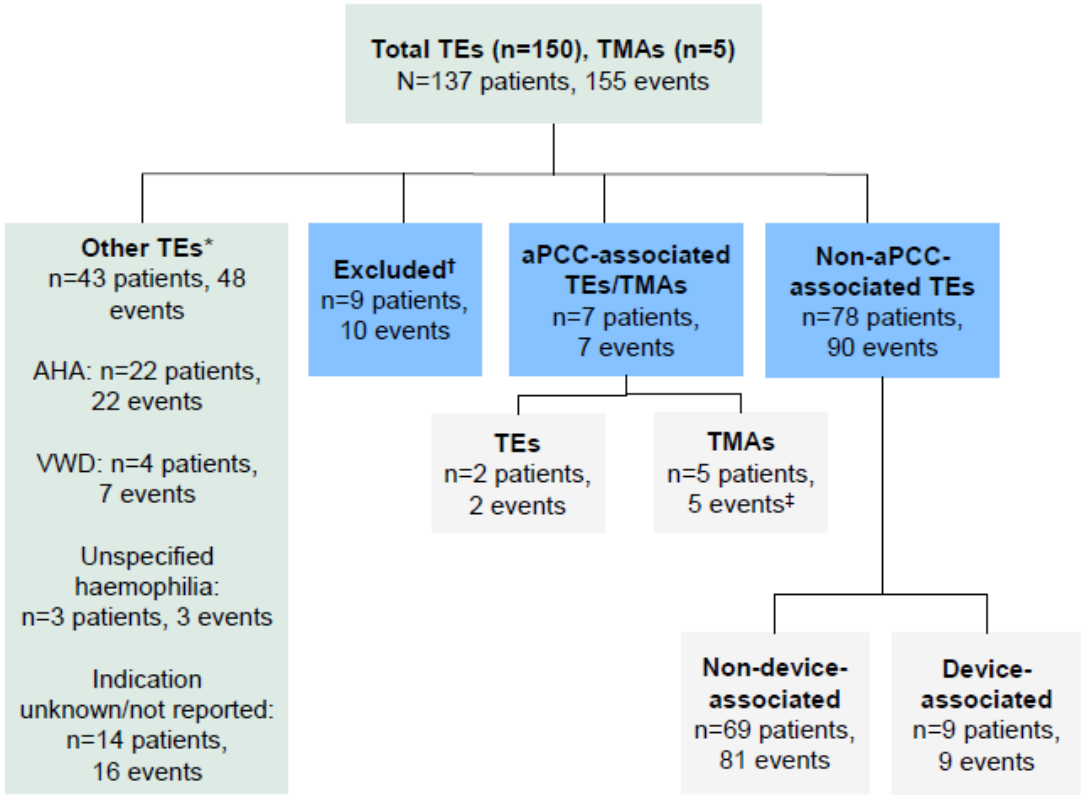
Number of TEs/TMAs, clinical factors (indication, age, FVIII inhibitor status, comorbidities) and drug factors are presented from individual reports

F, factor; MedDRA, Medical Dictionary for Regulatory Activities; SMQ, Standardised Medical Query; TEs, thrombotic events; TMA, thrombotic microangiopathies.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Results

Figure 2. Summary of TEs and TMA events



*Includes off-label or unknown indication. †Excluded case reports include intracranial haemorrhage (n=6), blood clot in urine (n=1), duplicate report (n=1), and invalid case report (n=1). ‡One new TMA case reported since last analysis.[3]
Blue shading in the figure indicates congenital haemophilia A.

- From 28 June 2012 to 1 August 2023, 155 events in 137 patients meeting the search criteria were identified, from 24 countries, in the Roche Global Safety Database (Figure 2)
- In people with congenital HA and other non-approved indications, there were 18 clinical trial events in 18 patients, 112 post-marketing events in 97 patients, and 25 non-interventional study events in 22 patients
- Of these, 97 events were identified in people with congenital HA (34 since the previous analysis3): two TEs and five TMAs associated with aPCC, and 90 TEs not associated with aPCC use

AHA, acquired haemophilia A; VWD, von Willebrand disease; TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

One new TMA associated with aPCC was reported since the last analysis

- The new TMA event observed since the previous data cut (15 May 2022) was from a report in the Roche Global Safety Database in October 2022
  - A patient with severe HA was given aPCC above the dosage specified in the treatment guidelines in a risk-benefit decision to treat a diverticular haemorrhage. The patient subsequently recovered

HA, haemophilia A; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

A total of 81 non-aPCC-associated and non-device-associated Tes were reported in congenital PwHA received emicizumab

Table 1. Characteristics of congenital PwHA who experienced non-device-associated TEs

	Non-aPCC-associated and non-device-associated TEs N=81
Median (range) age at event, years	48 (0.8–84)*
Medically confirmed, n (%) Consumer reported, n (%)	71 (87.7) 10 (12.3)
Sources, n (%) Post-marketing† Non-interventional study Clinical trials‡	 48 (59.3) 13 (16.0) 8 (9.9)
Presence of FVIII inhibitors, n (%)	23 (28.4)
Associated with ≥1 CV risk factor§ or other risk factor for thrombosis,¶ n (%)	55 (67.9)
Led to discontinuation of emicizumab, n (%)	11 (13.6)
TEs with fatal outcome,** n (%)	5 (6.2)

*Age was provided for 50 of 69 cases. †Post-marketing events included 44 spontaneous reports and 4 events reported in the literature. ‡Clinical trial events included six SAEs: acute myocardial infarction (MO39129), acute coronary syndrome (BH37001), acute myocardial infarction (BH37001), myocardial infarction (unknown study, patient-reported), venous limb thrombosis (YO39309), cerebrovascular accident (YO39309), and two non-serious AEs: haemorrhoids thrombosed (BO41423) and renal infarct (BO41423). §Previous myocardial infarction, ischaemic heart disease, coronary artery disease, hypertension, hyperlipidaemia, smoking, advanced age. ¶Sepsis/bacteraemia, coinciding injury, hepatitis C, thrombosis.[4,5] **Two myocardial infarctions and one cerebrovascular event in three people with multiple risk factors; two disseminated intravascular coagulation events related to pneumonia in two people >70 years old.

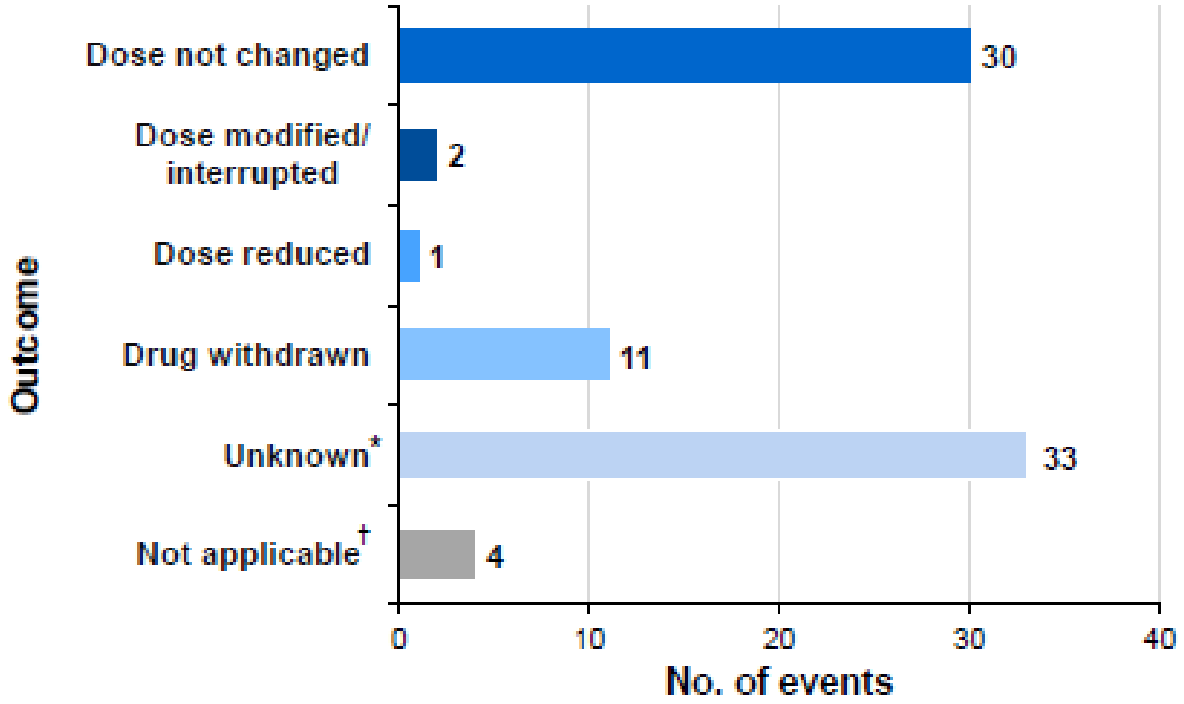
- The median (range) age at event was 48 (0.8-84) years
- A total of 71 (87.7%) Tes were medically confirmed and 10 (12.3%) were consumer reported; sources includedspontaneous (44 TEs), non-interventional studies (13 TEs), literature (4 TEs), and clinical trials (8 TEs)
- Twenty-three (28.4%) TEs occurred in 16 people with HA with known FVIII inhibitors
- There was a new fatality since the previous analysis, a cerebrovascular event in a person with multiple cardiovascular risk factors

PwHA, people with haemophilia A; TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate; CV, cardiovascular; SAEs, serious adverse events.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Among PwHA who had dose modification data available and experienced a non-aPCC-associated and non-device-associated TE, most had no change to emicizumab

Figure 3. Dose modifications in people with congenital HA who experienced non-aPCC-associated TEs



*Includes two fatal TEs; †Three fatal TEs and one non-fatal case of myocardial infarction that was incorrectly coded.

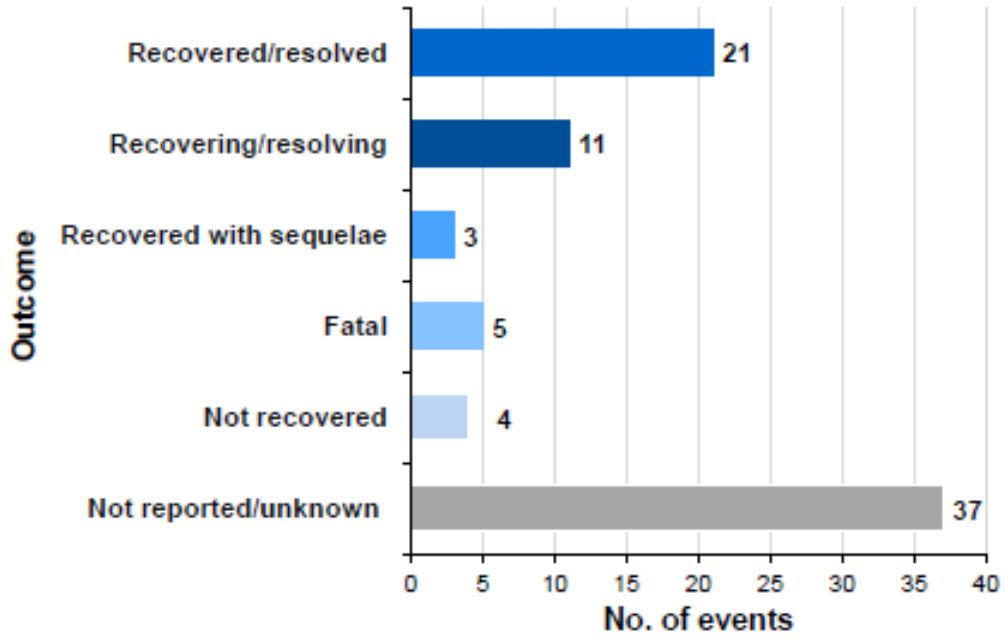
- Emicizumab prophylaxis was modified, interrupted, reduced, or withdrawn in 14/81 (17.3%) events of people with HA receiving emicizumab without concomitant aPCC experiencing a TE (Figure 3)
- There were no dose modifications in 30/81 (37.0%) events of people with HA experiencing a non-aPCC-associated TE; data are unknown for 33 events

HA, haemophilia A; TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

A total of 32/81 non-aPCC-associated and non-device-associated TEs were recovered or resolving at the time of data cut

Figure 4. Reported outcomes of Tes at the time of analysis



HA, haemophilia A; TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Clinical trial incidence and real-world data analyses

Table 2. Dose modifications in people with congenital HA who experienced non-aPCC-associated TEs

Events	Incidence rate ratio (95% CI)	Crude incidence rate/ 100 person-years (95% CI)
Arterial events		
Myocardial infarction	0.80 (0.53–1.12)	0.23 (0.15–0.32)
Ischaemic stroke*	1.03 (0.72–1.39)	0.29 (0.20–0.39)
Venous events		
Deep vein thrombosis*	0.89 (0.60–1.23)	0.25 (0.17–0.35)
Pulmonary embolism	0.29 (0.14–0.49)	0.08 (0.04–0.14)
Device-related thrombosis	1.60 (1.21–2.05)	0.46 (0.35–0.58)

*Excludes device-related thrombosis.

- The incidence rate for serious TEs (excluding aPCC-related serious AEs) in clinical trials with people with congenital HA receiving emicizumab is 0.17 events per 100 person-years (based on data from 850 patients with a median emicizumab exposure of 108 weeks; 95% confidence interval [CI]: 0.05-0.43)
- TE frequency is also monitored in numerous key emicizumab clinical trials, Phase IV HA studies, and ongoing registries including: HAVEN 1-7, STASEY, AOZORA, ACE002JP, ATHN 7/ATHN Transcends, EUHASS, PedNET, HEMNOR, and UKHCDO
- Real-world data in the overall population of people with HA, irrespective of treatment, including incidence risk for arterial, venous and device-related TEs, is shown in Table 2

HA, haemophilia A; TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate; ATHN, American Thrombosis and Hemostasis Network;

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Limitations of data collection through pharmacovigilance initiatives

- Pharmacovigilance initiatives exist for the purpose of monitoring and reporting on adverse events
- Due to the potential underreporting of events in this context, making conclusions based on incidence rates is discouraged, especially given that many events are reported in the literature for the emicizumab clinical trial programme
- Reporting events with greater detail outside clinical trials can continue to support understanding of TEs and TMA events

TEs, thrombotic events; TMA, thrombotic microangiopathies.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Conclusions

- No new safety concerns were observed since the last data cut-off and the risk-benefit profile remains positive
- All TMAs were associated with concomitant use of aPCC at >100U/kg/24 hours for ≥24 hours
- Most TEs (67.9%) were associated with pre-existing cardiovascular risk factors and/or risk factors for thrombosis
- This analysis continues to support that TEs and TMAs without concomitant aPCC at doses of >100U/kg/24 hours for ≥24 hours are not an identified risk for people with HA receiving emicizumab prophylaxis
- Health authorities no longer require special expedited safety reporting for emicizumab worldwide. However, monitoring and reporting of safety data are still ongoing

TEs, thrombotic events; TMA, thrombotic microangiopathies; aPCC, activated prothrombin complex concentrate; HA, haemophilia A.

Sarouei K, et al. EAHAD 2024; prezentace posteru P0126.

Uptake of emicizumab in PUPs with severe haemophilia A and changes in inhibitor incidence

Upraveno podle posteru PO130 předneseného na kongresu Evropské asociace pro hemofilii a přidružené choroby (EAHAD),
6. – 9. únor 2024
Abstrakt je dostupný na: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14919

Background and aim

- Since the first publication on emicizumab in 2016, the possibility of an effective prophylaxis without the burden of venous access is appealing for infants and toddlers with SHA
- Emicizumab is increasingly used for primary prophylaxis in PUPs with SHA and consequently exposure to FVIII is reduced and/or postponed
- We aimed to quantify the uptake of emicizumab and concomitant changes in the incidence of FVIII inhibitors

SHA, severe haemophilia A; PUPs, previously untreated patients; F, factor.

Fischer K, et al. EAHAD 2024; prezentace posteru P0130.

Methods

- The EUHASS has been monitoring Aes according to concentrate in 83 European haemophilia treatment centres
- Inhibitors were reported quarterly, and PUPs completing 50 EDs without inhibitor development annually and per concentrate
- Cumulative inhibitor incidences and 95% CI were compared without adjustment for other risk factors
- For the present analysis, data on treatment and inhibitor development from 2016 until 2022 of PUPs with SHA were extracted and compared per treatment year

SHA, severe haemophilia A; PUPs, previously untreated patients; F, factor; EUHASS, European Haemophilia Safety Surveillance System; AEs, adverse events; EDs, exposure days; CI, confidence intervals

Fischer K, et al. EAHAD 2024; prezentace posteru P0130.

Results

Table 1. Data per treatment year

Year	2016	2017	2018	2019	2020	2021	2022
Treated (N)	107	131	120	143	103	124	103
Receiving emicizumab	0.0%	1.5%	9.2%	9.0%	3.9%	25.0%	43.7%
FVIII inhibitors	21.5%	22.1%	22.5%	15.4%	11.7%	9.7%	5.8%

- Since 2016, 831 PUPs were reported, of whom 131 (15.8%) developed FVIII inhibitors
- The use of emicizumab was first reported in 2017, but the proportions reaching 50 EDs on emicizumab really started to increase in 2021, when already 25% of all PUPs were primarily treated with emicizumab
- A trend was observed towards lower inhibitor incidences, from around 22% in 2016-2018 to around 6% in 2022. This is most likely related to the fact that treatment with FVIII occurs only very infrequently in patients on emicizumab, resulting in postponement of inhibitor development
- No inhibitors against emicizumab or other/thrombotic side effects were reported in these PUPs

PUPs, previously untreated patients; F, factor; EDs, exposure days;

Fischer K, et al. EAHAD 2024; prezentace posteru P0130.

Conclusions

- Primary prophylaxis with emicizumab is increasingly used in PUPs with SHA and the concomitant lower inhibitor incidence is expected to be temporary
- These trends will make it more difficult to assess inhibitor incidence for newly introduced FVIII concentrates
- It is probable that the FVIII inhibitors will eventually develop when patients are treated with FVIII, up until 50 EDs, but this will have to be studied in registries

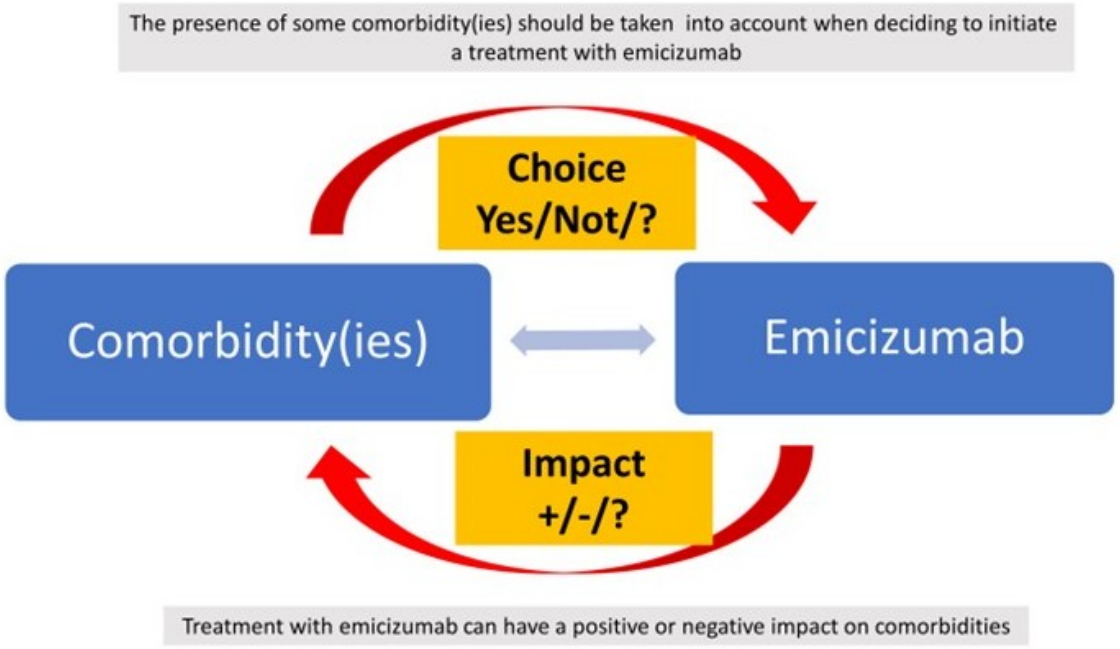
SHA, severe haemophilia A; PUPs, previously untreated patients; F, factor; EDs, exposure days.

Fischer K, et al. EAHAD 2024; prezentace posteru P0130.

Cardiovascular safety and brain protective effect of emicizumab in people with haemophilia A older than 40 years

Upraveno podle posteru PO031 předneseného na kongresu Evropské asociace pro hemofilii a přidružené choroby (EAHAD),
6. – 9. únor 2024
Abstrakt je dostupný na: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14919

Background and aim



- Frequent concerns have arisen regarding the cardiovascular safety and thrombosis risk in older PwH, particularly those who have pre-existing CRVF on emicizumab
- However, these concerns are predominantly grounded in limited real-world data
- To bridge this knowledge gap, we aimed to assess our proactive approach in adopting emicizumab across all our patients with severe haemophilia A, irrespectively of age, including older individuals with multiple comorbidities and CVRF

PwHA, people with haemophilia; CRVF, cardiovascular risk factors.

Hermans C, et al. EAHAD 2024; prezentace posteru P0031.

Population and method

- Out of the 117 patients with severe to moderately severe HA followed at the Saint-Luc university Hospital in Brussels, 52 are aged 40 or older
- In the past three years, 44 (84%) patients opted to transition to emicizumab, while 8 (16%) chose to continue their prophylactic treatment with FVIII concentrate (standard half-life [3] and extended half-life FVIII [5])
- Prior to switching to emicizumab, 34 patients were receiving FVIII prophylaxis, and 10 were on an on-demand treatment regimen.

HA, haemophilia A; F, factor; CV, cardiovascular.

Hermans C, et al. EAHAD 2024; prezentace posteru P0031.

Results

Table 1. Demographic and cardio-vascular risk factors of PwHA and ≥40 years of age on emicizumab

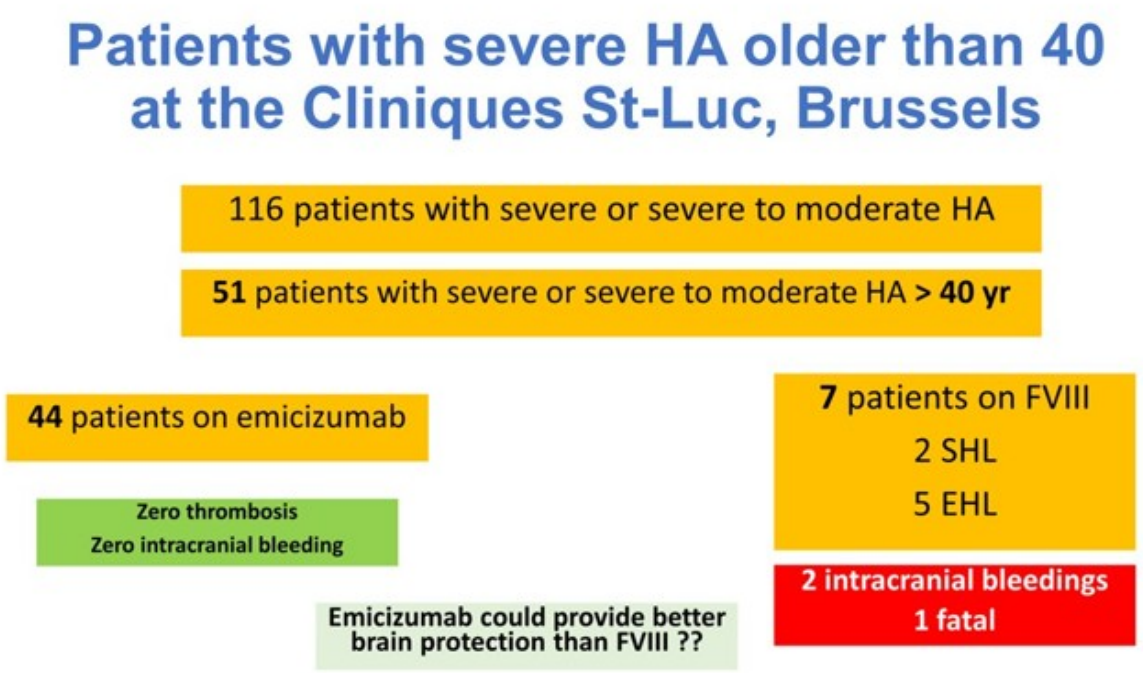
Number of patients / gender / sex	44 PWH - mean age 56 years (40-83) - males (43) and female (1)
Hemophilia severity /inhibitor status	Severe (42) - moderate to severe (2) – past history of inhibitor (2)
Hemophilia Treatment before switching to emicizumab	On-demand (10) / Prophylaxis (34)
Duration of treatment on emicizumab	Mean duration 26 months (range 8-56 months)
Frequency of administration	1x/4 weeks (42) – 1x/2 weeks (1) – 1x/week (1)
Cardiovascular risk factors	Hypertension (22) – Diabetes (5) – High cholesterol (12) – HIV treatment (7) – obesity (7) – active smoking (15)
Number of CVRF	None (5)/ at least one (39)/at least two (19)
Pre-existing CVRF	Atrial fibrillation (1) – Ischemic Heart Disease with stent (1)
FVIII equivalent activity (%) measured with chromogenic assay and human reagents on emicizumab	< 10% (7) - between 10-20% (15) - > 20% (16) not measured (6)
D-Dimers assay on emicizumab	< 500 ng/ml (26) – > 500 ng/ml (14) - not measured (4)

- During the follow-up period after the commencement of emicizumab, no cardiovascular events were observed, even in a patient aged 82 with AF and FV Leiden, who required hospitalization for severe COVID-19 infection
- In contrast, two patients on FVIII prophylaxis experienced intracranial bleeding due to uncontrolled hypertension, which was fatal in one case

PWH, people with haemophilia; HA, haemophilia A; F, factor; CRVF, cardiovascular risk factors; AF, atrial fibrilation; COVID-19, Coronavirus disease 2019.

Hermans C, et al. EAHAD 2024; prezentace posteru P0031.

Conclusions



- Our experience, characterized by a lack of selection bias, does not substantiate the assumption that emicizumab is linked to an increased incidence of thrombotic events in older PWH with multiple CVRF
- Instead, our series suggests that emicizumab may have a significant protective effect against the incidence of intracranial bleeding, although confirmation in larger-scale studies is needed

PWH, people with haemophilia; HA, haemophilia A; F, factor; CRVF, cardiovascular risk factors.

Hermans C, et al. EAHAD 2024; prezentace posteru P0031.

Emicizumab in people with moderate or mild haemophilia A aged ≥40 years, with and without comorbidities

Upraveno podle posteru PO122 předneseného na kongresu Evropské asociace pro hemofilii a přidružené choroby (EAHAD),
6. – 9. únor 2024
Abstrakt je dostupný na: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14919

Background

- Emicizumab is a bispecific antibody licensed by the EMA and other regulatory authorities for prophylaxis in people of all ages with HA with FVIII inhibitors, and in those without FVIII inhibitors who have severe disease (FVIII activity <1%) or moderate disease (FVIII activity ≥1%–≤5%) with severe bleeding phenotype (label varies by country)

- Few data exist on the use of emicizumab in older PwHA, particularly those with comorbidities, such as CV conditions, hepatitis, and HIV, and in people with moderate or mild HA

- We present a post hoc analysis of PwHA aged ≥40 years from the HAVEN 6 trial (NCT04158648), which was conducted to evaluate the safety and efficacy of emicizumab in people with non-severe HA without FVIII inhibitors

EMA, European Medicines Agency; HA, haemophilia A; PwHA, people with haemophilia A; F, factor; CV, cardiovascular; HIV, human immunodeficiency virus.

Jiménez-Yuste V, et al. EAHAD 2024; prezentace posteru P0122.

Methods

- HAVEN 6 is a global, multicentre, open-label, single-arm, Phase III trial conducted in individuals of all ages with a diagnosis of moderate (FVIII activity ≥1%–≤5%) or mild (FVIII >5%–<40%) HA without FVIII inhibitors, warranting prophylaxis as assessed by the investigator
- The emicizumab loading dose was administered subcutaneously at 3mg/kg once weekly, for 4 weeks
  - This was then followed by the participant's choice of maintenance dose, which included the options of 1.5mg/kg weekly, 3mg/kg every 2 weeks, or 6mg/kg every 4 weeks
- The primary objective was safety, including TEs and TMA, and the primary efficacy endpoint was the ABR for treated bleeds
- An age cut-off of ≥40 years was selected for this exploratory analysis in order to obtain a population with a high proportion of comorbidities in PwHA In this analysis, comorbidities included CV risk factors (history of CV disease; hypertension; hyperlipidaemia; diabetes; BMI ≥30kg/m2), HIV, and current or previous history of HCV infection

EMA, European Medicines Agency; HA, haemophilia A; PwHA, people with haemophilia A; F, factor; TEs, thromboembolic events; TMA, thrombotic microangiopathy; ABR, annualized bleed rate; CV, cardiovascular; BMI, body mass index; HIV, human immunodeficiency virus.; HCV, hepatitis C virus.

Jiménez-Yuste V, et al. EAHAD 2024; prezentace posteru P0122.

Results

Table 1. Demographics and characteristics

	Participants aged ≥40 years
Total, N (%)	16 (100)
Median (range) age, years	50.5 (41–71)
Aged ≥50 years	8 (50.0)
Male, n (%)	16 (100)
Median (range) emicizumab treatment duration, years	1.1 (0.6–1.7)
Haemophilia severity at study entry, n (%)	
Mild	6 (37.5)
Moderate	10 (62.5)
CV risk factors, n (%)	
≥1 CV risk factor	9 (56.3)*
≥2 CV risk factors	5 (31.3)
HIV and/or HCV infection, n (%)	
HIV infection only	1 (6.3)
HCV infection only	3 (18.8)
HCV+HIV coinfection	2 (12.5)

*Of the nine participants who had CV risk factors, seven had hypertension, four had past medical history events (these included atrial fibrillation, coronary artery disease, mitral valve incompetence, and one participant having both sinus tachycardia and pelvic venous thrombosis), two had a baseline BMI ≥30kg/m², and one had diabetes.

- At data cut-off (30 October 2021), 72 participants had been treated in HAVEN 6; 16 were aged ≥40 years and were included in this analysis

CV, cardiovascular; HIV, human immunodeficiency virus.; HCV, hepatitis C virus.

Jiménez-Yuste V, et al. EAHAD 2024; prezentace posteru P0122.

There were no fatal AEs, AEs leading to treatment withdrawal/modification/interruption, or TMA

Table 2. Summary of safety outcomes by comorbidities and risk factors

		Participants aged ≥40 years					
	Participants aged <40 years (N=56)	Participants aged ≥40 years (N=16)	No CV risk factor (n=7)	≥1 CV risk factor (n=9)	≥2 CV risk factors (n=5)	No HCV or HIV (n=10)	HCV and/or HIV (n=6)
Number of AEs, n	192	56	26	30	22	39	17
Participants with ≥1 AE, n (%)							
Any AE	45 (80.4)	15 (93.8)	7 (100.0)	8 (88.9)	4 (80.0)	9 (90.0)	6 (100.0)
Serious AE	5 (8.9)	3 (18.8)	2 (28.6)	1 (11.1)	1 (20.0)	3 (30.0)	0
Fatal AE	0	0	0	0	0	0	0
AE leading to withdrawal	0	0	0	0	0	0	0
AE leading to dose modification/interruption	0	0	0	0	0	0	0
Grade 3–4 AE	3 (5.4)	1 (6.3)	0	1 (11.1)	1 (20.0)	1 (10.0)	0
Treatment-related AE	12 (21.4)	3 (18.8)	2 (28.6)	1 (11.1)	1 (20.0)	3 (30.0)	0
Injection-site reaction	10 (17.9)	2 (12.5)	1 (14.3)	1 (11.1)	1 (20.0)	2 (20.0)	0
Thromboembolic event	0	1 (6.3)	1 (14.3)	0	0	1 (10.0)	0
Thrombotic microangiopathy	0	0	0	0	0	0	0

- The median (range) duration of emicizumab exposure was 1.1 (0.6–1.7) years
- Fifteen (93.8%) of the 16 participants experienced ≥1 AE during the study. Three (18.8%) experienced a serious AE and 1 (6.3%) a Grade 3–4 AE; these were deemed unrelated to emicizumab (Table 2)
- One individual, who had no CV risk factors or HIV/HCV infection, experienced a TE (Grade 1 thrombosed haemorrhoids); this was deemed unrelated to emicizumab
- Three participants experienced a total of six treatment-related AEs: three injection-site reactions and one case each of fatigue, head discomfort, and accidental overdose

AEs, adverse events; HA, haemophilia A; PwHA, people with haemophilia A; F, factor; TEs, thromboembolic events; TMA, thrombotic microangiopathy; ABR, annualized bleed rate; CV, cardiovascular; BMI, body mass index; HIV, human immunodeficiency virus.; HCV, hepatitis C virus.

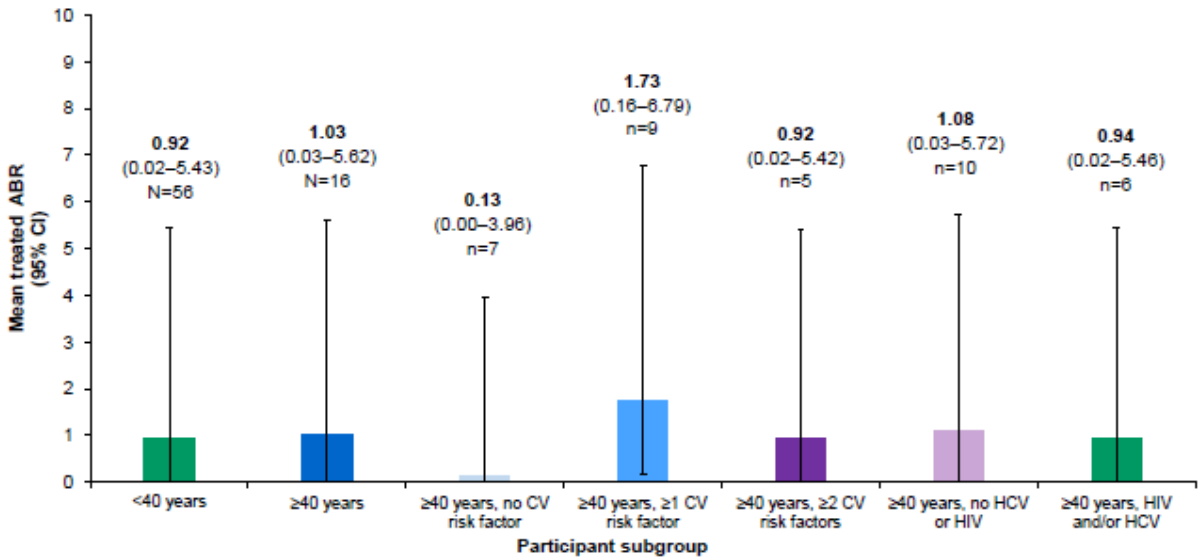
Jiménez-Yuste V, et al. EAHAD 2024; prezentace posteru P0122.

Bleed outcomes in the ≥40 years subgroup were similar to those for the overall HAVEN 6 population, and to those aged <40 years

Table 3. Summary of bleed outcomes by comorbidities and risk factors

		Participants aged ≥40 years					
	Participants aged <40 years (N=56)	Participants aged ≥40 years (N=16)	No CV risk factor (n=7)	≥1 CV risk factor (n=9)	≥2 CV risk factors (n=5)	No HCV or HIV (n=10)	HIV and/or HCV (n=6)
Total number of treated bleeds, n	54	17	1	16	5	11	6
Participants with zero treated bleeds, n (%)	37 (66.1)	11 (68.8)	6 (85.7)	5 (55.6)	3 (60.0)	6 (60.0)	5 (83.3)
Median ABR	0	0	0	0	0	0	0

Figure 1. Mean ABR for treated bleeds by age, comorbidities, and risk factors



- During the study, the mean (95% CI) and median ABR for treated bleeds for the 16 participants aged ≥40 years were 1.03 (0.03–5.62) and 0, respectively (Table 3)
  - Mean (95% CI) ABRs were similar to that of the overall population of HAVEN 6 (0.94 [0.02–5.48]) and the population aged <40 years (0.92 [0.02–5.43]; Figure 1)
- A total of 11 participants (68.8%) had zero bleeds during the study, which is comparable with the 66.7% reported for the total population and 66.1% reported for participants aged <40 years

ABR, annualized bleed rate; CV, cardiovascular; CI, confidence interval; HIV, human immunodeficiency virus.; HCV, hepatitis C virus.

Jiménez-Yuste V, et al. EAHAD 2024; prezentace posteru P0122.

Conclusions

- This post hoc analysis of the HAVEN 6 trial helps to address the existing data gap of the safety and efficacy of emicizumab in older PwHA, particularly those with comorbidities, and in people with moderate or mild HA
- Overall, emicizumab prophylaxis appeared to be well tolerated in PwHA ≥40 years with comorbidities (CV risk factor or HIV and/or HCV infection)
- The safety and efficacy of emicizumab in these participants did not differ notably from those observed in the overall population of people with moderate or mild HA in HAVEN 6, or from those aged <40 years
- However, the small number of individuals aged ≥40 years included in the current analysis (N=16) is a limitation that precludes drawing firm conclusions from the data; further studies and data from real-world evidence are therefore warranted in older PwHA with comorbidities

HA, haemophilia A; PwHA, people with haemophilia A; F, factor; CV, cardiovascular; HIV, human immunodeficiency virus; HCV, hepatitis C virus.

Jiménez-Yuste V, et al. EAHAD 2024; prezentace posteru P0122.

The use of the haemophilia joint health score as a monitoring tool for children with severe haemophilia a on emicizumab prophylaxis

Upraveno podle posteru PO157 předneseného na kongresu Evropské asociace pro hemofilii a přidružené choroby (EAHAD),
6. – 9. únor 2024
Abstrakt je dostupný na: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14919

Background

- The HJHS is an assessment tool designed for the use in patients with haemophilia for the early identification and monitoring of joint arthropathy
- Within our centre, we currently have 65 children with a diagnosis of SHA, who receive emicizumab as prophylaxis
- Every child has an annual review, during which their HJHS is evaluated as part of their physiotherapy review
- We sought to evaluate the changes in the HJHS in children with SHA receiving prophylaxis with emicizumab at our centre

SHA, severe haemophilia A; HJHS, Haemophilia Joint Health Score ; F, factor.

Fischer K, et al. EAHAD 2024; prezentace posteru P0130.

Aim

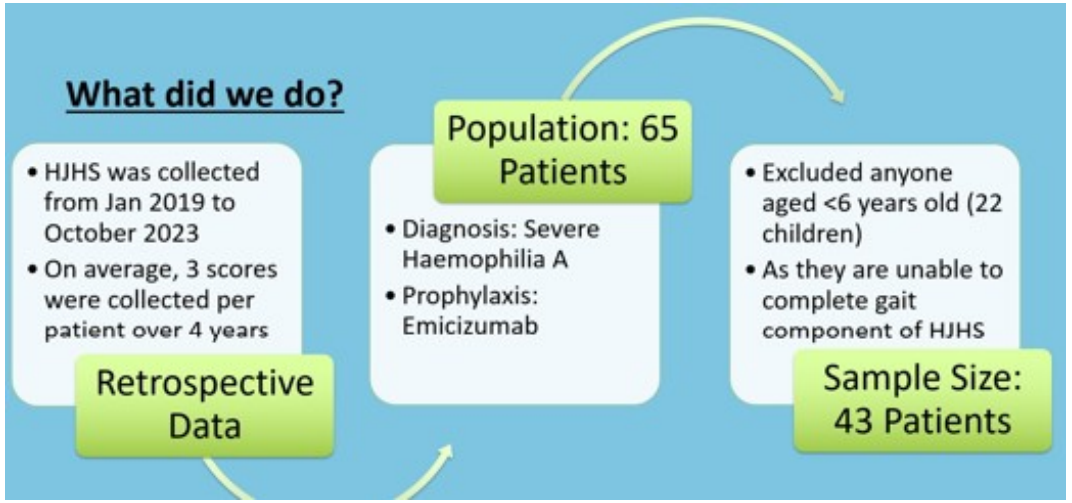
- How many joint scores were completed annually compared to the total number of eligible patients ?
  - Did the COVID-19 pandemic have an impact on this ?
- Did the HJHS change or stay the same ? If the score changed, what did we do ?
- What does this mean for the future of physiotherapy management for those on emicizumab ?

COVID-19, Coronavirus disease 2019; HJHS, Haemophilia Joint Health Score.

Jaffer Z, et al. EAHAD 2024; prezentace posteru P0157.

Methods

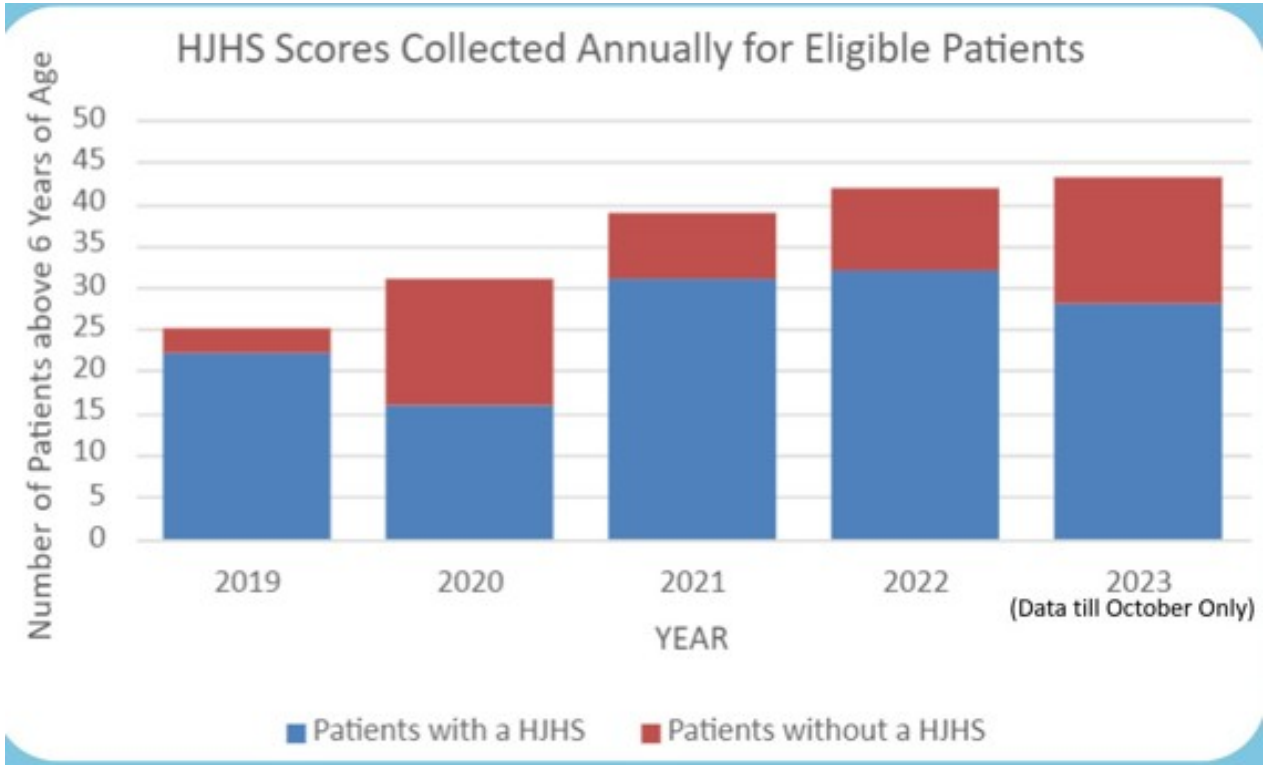
- We retrospectively collected and analysed the data of 65 children on emicizumab registered at our centre, over a period of 4 years
- Patient characteristics collected included the duration of treatment with emicizumab, current inhibitor status and annual HJHS between 2019 and 2023



COVID-19, Coronavirus disease 2019; HJHS, Haemophilia Joint Health Score.

Jaffer Z, et al. EAHAD 2024; prezentace posteru P0157.

Results



- 75% of patients >6 years of age, received a HJHS each year
- During the pandemic in 2020 this reduced to 52%
- In 2021 and 2022, this had returned to >75%

HJHS, Haemophilia Joint Health Score.

Jaffer Z, et al. EAHAD 2024; prezentace posteru P0157.

Results

- 22 patients were below the age of 6 so were excluded as they would be unable to comply with the functional components of the HJHS, and therefore would not achieve an accurate score
- Of the remaining 43 patients, there was an average of three HJHS completed over the 4-year period. All patient's scores were between 0% and 3
- 81% (35) of patients scored 0 on each of their annual HJHS, which remained consistent between 2019 and 2023. The remaining eight patients had one HJHS that scored between 1 and 3
- On each of these occasions, patients were referred for a further ultrasound or MRI scan
- The ultrasound scans showed no joint arthropathy, but all showed a degree of effusion which likely contributed to the change in their HJHS
- The MRI scan showed no abnormalities. Four of these patients have since had additional HJHS the following year where their scores returned to 0

MRI, Magnetic resonance imaging; HJHS, Haemophilia Joint Health Score.

Jaffer Z, et al. EAHAD 2024; prezentace posteru P0157.

Conclusions

- The COVID-19 pandemic resulted in a 40% loss of data. We have yet to return to our pre-pandemic levels of 88% od eligible patients having a HJHS annually
- From our population, there is a positive correlation between using emicizumab as prophylaxis and maintaining a healthy joint score (the HJHS of 3 or below)
- Therefore the role of the physiotherapist at our centre, will be to support patients on emicizumab to maintain their activity levels to continue to lead bleed-free lives

COVID-19, Coronavirus disease 2019; HJHS, Haemophilia Joint Health Score.

Fischer K, et al. EAHAD 2024; prezentace posteru P0130.

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

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