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Annualized bleed rates in severe hemophilia A after switch to emicizumab▼based on CHESS II data, including an oversample of emicizumab patients

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Summary

This analysis utilized data from **Cost of Haemophilia in Europe: a Socioeconomic Survey II (CHESS II)**, including the base study and an oversample of participants who initiated emicizumab

Overall, **146 people with hemophilia A (PwHA)** were included

Annualized bleed rates (ABRs) decreased in all groups after switching to emicizumab

- The mean pre-emicizumab ABR was **3.37**
- The mean post-emicizumab ABR was **1.42**

Both PwHA previously receiving factor (F)VIII prophylaxis and those previously treated on demand had a **lower mean ABR after emicizumab initiation**

PwHA who were **fully adherent** to their treatment had a **lower mean ABR** than those who were not fully adherent to their treatment

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Background

- Hemophilia A (HA), a bleeding disorder characterized by deficiency of FVIII, is associated with substantial morbidity.[1]
- This condition may result in frequent spontaneous bleeding and prolonged bleeds from trauma or surgery, which are more common in severe hemophilia or in the absence of treatment.
- Emicizumab, a bispecific monoclonal antibody that substitutes for deficient activated FVIII, has proven efficacious for bleeding prevention in clinical trials in PwHA with or without FVIII inhibitors.
- Here, we examine the effectiveness of emicizumab in a real-world setting.

This analysis utilizes data on all bleeds from CHESS II, a retrospective, burden-of-illness questionnaire-based study, including the base study and an oversample of participants who initiated emicizumab

- CHESS II is a cross-sectional survey study of adult men (≥18 years of age) with HA or hemophilia B (HB) of any severity, with or without inhibitors, across eight European countries (Germany, Spain, France, Italy, Romania, the Netherlands, Denmark and the United Kingdom) conducted in 2019–2020. People with HB were not included in this analysis.
- The oversample was defined as an increased selection of participants, which was used to increase the sample size of the target population.
- The methods and primary findings from these studies have been reported previously.[2,3]
- Informed consent and ethics approval were obtained; safety data were not captured. Follow-up times were 12 months in both the pre-emicizumab and post-emicizumab period.

Overall, 146 PwHA with severe disease (Italy n=81; Germany n=26; Spain n=26; France n=10; UK n=3), 22 from the base study and 124 from the oversample, were included in the analysis

- Of these, 78 adults received emicizumab for ≥12 months, including 49 (62.8%) previously treated with FVIII prophylaxis, 28 (35.9%) treated on demand and one who previously received gene therapy.
- In total, 22/78 (28.2%) PwHA had either a history of, or current, FVIII inhibitors (**Table 1**).

Table 1. Baseline characteristics of PwHA treated with emicizumab with ≥12 months of follow-up (n=78)

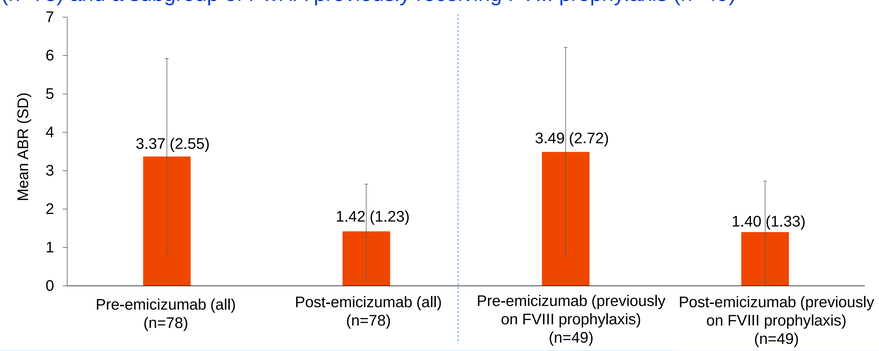
	Previously on prophylactic FVIII treatment (n=49)	Previously on on-demand FVIII treatment (n=28)	All (N=78)*
Mean age (SD), years	38.44 (15.84)	29.25 (10.37)	35.22 (14.65)
Mean BMI (SD), kg/m^2	19.33 (2.17)	19.65 (2.82)	19.48 (2.41)
Inhibitor presence, n (%)			
Never	34 (69.39)	22 (78.57)	56 (71.79)
Current/previous	15 (30.61)	6 (21.43)	22 (28.21)

*One individual previously received gene therapy.
BMI, body mass index; SD, standard deviation

Mean ABR for all bleeds in the 78 participants decreased from 3.37 at last treatment pre-emicizumab to 1.42 post-emicizumab (all p-values <0.001; Figure 1)

- In the 78 participants, median ABR decreased from 3.00 to 1.19 at last treatment pre-emicizumab to post-emicizumab.
- In the 49 participants previously receiving FVIII prophylaxis, mean ABR decreased from 3.49 to 1.40 after switching to emicizumab. Median ABR decreased from 3.00 to 1.09.

Figure 1. Mean (SD) ABR pre-/post-emicizumab for PwHA with ≥12 months of follow-up (n=78) and a subgroup of PwHA previously receiving FVIII prophylaxis (n=49)

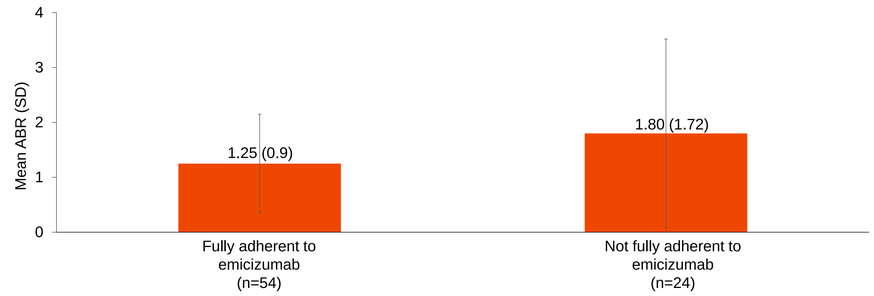


- A sensitivity analysis including 123 PwHA who received emicizumab for ≥6 months showed a decrease in mean ABR from 4.33 pre-emicizumab to 1.91 post-emicizumab; median ABR decreased from 3.00 to 1.33.

The mean post-emicizumab ABR in the 54 physician-rated fully adherent PwHA was 1.25 compared with 1.80 for the 24 PwHA who were not fully adherent to emicizumab treatment (Figure 2)

- Data on physician-rated adherence were available in the questionnaire for 78 participants.
- Fully adherent was defined as missing <15% of infusions/injections, and non-fully adherent was defined as missing ≥15% of infusions/injections.

Figure 2. Mean (SD) post-emicizumab ABR for PwHA who were or were not fully adherent to emicizumab



Conclusions

- Mean ABRs decreased in all groups after switching to emicizumab based on physician-reported data from the CHESS II study, both in PwHA previously receiving FVIII prophylaxis and those previously treated on-demand.
- PwHA who were fully adherent to their emicizumab treatment had a lower mean ABR than those who were not fully adherent to their emicizumab treatment.
- Nonetheless, there are limitations inherent within a cross-sectional design and the retrospective nature of data collection, and further analyses should explore wider elements of burden and unmet need.

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▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. These should be reported to the Regulatory Authorities in your country according to your national requirements.

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Disclosures

MEM reports consultancy with Bayer, CSL Behring, Novo Nordisk, F. Hoffmann-La Roche Ltd, Octapharma, Pfizer, Sanofi, Sobi, Kedrion, Grifols, BioMarin, Catalyst, UniQure and LFB, and is a member of the speaker's bureau for Bayer, CSL Behring, Novo Nordisk, F. Hoffmann-La Roche Ltd, Octapharma, Pfizer, Sobi, Kedrion, Grifols, BioMarin and Spark Therapeutics; FN is an employee of F. Hoffmann-La Roche Ltd, holds stock in F. Hoffmann-La Roche Ltd, and has provided consultancy for Novartis and Actelion; HZ, RO-A and KM are employees of F. Hoffmann-La Roche Ltd; EFG and TB are employees of HCD Economics; JO'H is an employee of HCD Economics, holds stock in HCD Economics, and has provided consultancy for F. Hoffmann-La Roche Ltd.