Emicizumab Outcomes in Hemophilia A Using Real-World Data from the Canadian Hemophilia Bleeding Disorder Registry

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Disclosures

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Background and aims

- The CBDR is a clinical database that includes data from Canadian HTCs* to assist in the management of hemophilia and other bleeding disorders
- The CBDR launched on July 1, 2015 and integrates the data entry platform for patients, myCBDR, allowing direct entry of treatments, bleeding events, and other PRO data
- Health Canada approved emicizumab in August 2018 for the treatment of PwHA with FVIII inhibitors, and for PwHA without FVIII inhibitors in 2019,† enabling some individuals without FVIII inhibitors to be provided compassionate access beginning November 2019[1]

The aim of this analysis was to use the CBDR data to describe the demographics of the emicizumab-treated HA population in Canada and assess the effectiveness, safety, treatment patterns, and impact on disease burden of the therapy

*Includes all HTCs in Canada, with the exception of those located in British Columbia; †emicizumab was funded from September 2021 for PwHA with FVIII inhibitors and from October 2021 for PwHA without FVIII inhibitors.
CBDR; Canadian Hemophilia Bleeding Disorders Registry; F, factor; HA, hemophilia A; HTC, Hemophilia Treatment Center; PRO, patient-reported outcome; PwHA, people with hemophilia A

1. Hemlibra Product Monograph; available from: https://www.rochecanada.com/PMs/Hemlibra/Hemlibra_PM_E.pdf, accessed Nov 2021

Methods

- De-identified data were extracted from the CBDR database for all registered PwHA who had received emicizumab at least once up to December 31, 2020
- Effectiveness outcomes include:
  - Number (%) of PwHA with zero bleeds, zero joint bleeds or zero spontaneous bleeds
  - ABR, calculated as (total number of bleeds/duration of follow-up [days])*365.25
  - PROBE score and EQ-5D-5L index and VAS scores
- All analyses were performed based on the observed values, without imputation
- Reported cases of AEs of special interest were assessed, including TEs, TMAs, and allergic and other acute reactions

ABR, annualized bleed rate; AE, adverse event; CBDR; Canadian Hemophilia Bleeding Disorders Registry; EQ-5D-5L, EuroQoL 5 dimensions, 5 levels; PwHA: people with hemophilia A; TE, thromboembolic event; TMA, thrombotic microangiopathy; VAS, visual analog scale

Baseline characteristics

- Characteristics of PwHA enrolled in the CBDR who received emicizumab at least once prior to December 31, 2020

	Total (N=73)	Severity of hemophilia A*		
		Severe (n=64)	Moderate (n=7)	Mild (n=2)
Age, years				
Mean ± SD	26.9 ± 22.2	24.4 ± 20.7	47.3 ± 28.0	36.8 ± 15.9
Median (IQR)	19.7 (10.0–40.6)	19.4 (8.5–36.9)	57.8 (17.3–75.2)	36.8 (25.5–48.0)
<18 years, n (%)	33 (45.2)	31 (48.4)	2 (28.6)	0 (0.0)
FVIII inhibitor status,† n (%)				
Current inhibitors	49 (67.1)	45 (70.3)	2 (28.6)	2 (100.0)
History of inhibitors	12 (16.4)	10 (15.6)	2 (28.6)	0 (0.0)
No inhibitors	12 (16.4)	9 (14.1)	3 (42.9)	0 (0.0)
Emicizumab regimen, n (%)				
Weekly	59 (80.8)	51 (79.7)	7 (100.0)	1 (50.0)
Every 2 weeks	11 (15.1)	10 (15.6)	0 (0.0)	1 (50.0)
Other	3 (4.1)	3 (4.7)	0 (0.0)	0 (0.0)
ITI while on emicizumab, n (%)	5 (6.8)	5 (7.8)	0 (0.0)	0 (0.0)
Median follow-up, weeks (IQR)	62.0 (47.3–77.0)	63.4 (46.0–79.1)	50.1 (47.3–68.0)	83.5 (25.1–141.9)

*Severe (FVIII <0.01 IU/mL), moderate (0.01 ≤ FVIII ≤ 0.05 IU/mL) and mild (0.05 < FVIII ≤ 0.40 IU/mL); †current inhibitor, inhibitor at the time of receipt of the first dose of emicizumab; history of inhibitors, inhibitor detected prior to emicizumab but no current inhibitor; no inhibitors, none detected or observed yet.
CBDR; Canadian Hemophilia Bleeding Disorders Registry; F, factor; IQR, interquartile range; ITI, immune tolerance induction; SD, standard deviation

HA severity and bleeding outcomes

Median (IQR) ABR

- The ABR was 0 (0–0) for the total population
- ABRs according to HA severity were:
  - Mild: 11 (0–23[†] [n=2 (both with FVIII inhibitors)]
  - Moderate: 0 (0–2) [n=7]
  - Severe: 0 (0–0) [n=64]

Median (IQR) ABR for PwHA with ≥1 bleed

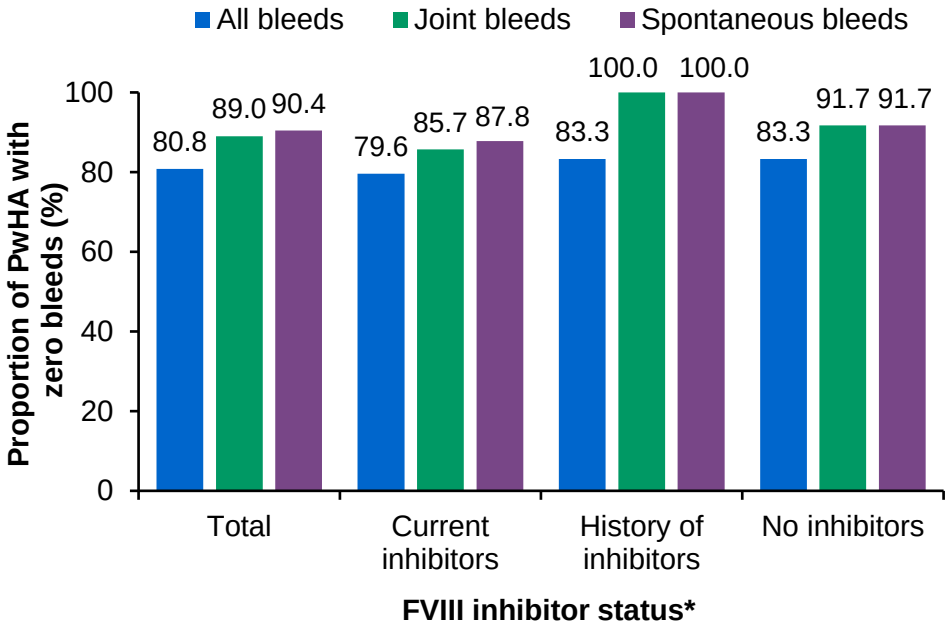
- The ABR for PwHA with bleeds was 2 (1–3) [n=14]
- ABRs according to HA severity were:
  - Mild: 23 [n=1[†]]
  - Moderate: 2 (1–2) [n=3]
  - Severe: 1 (1–3) [n=10]

Intrapatient comparison of bleeding before and after emicizumab initiation

- There were 10 PwHA with current inhibitors where data pre- and post-emicizumab initiation were available
- Rate ratios for all bleeds, joint bleeds and spontaneous bleeds more than halved, but the small sample size did not allow for in-depth analysis

*Severe (FVIII < 0.01 IU/mL), moderate (0.01 ≤ FVIII ≤ 0.05 IU/mL) and mild (0.05 < FVIII ≤ 0.40 IU/mL); [†]one participant, who had current inhibitors, experienced 11 bleeds during 176 days of follow-up; 8 were related to sporting injuries and 3 were spontaneous.
ABR, annualized bleed rate; F, factor; HA, hemophilia A; IQR, interquartile range; PwHA, people with hemophilia A

FVIII inhibitor status and bleeding outcomes



N	73	49	12	12
Median follow-up period, weeks (IQR)	62.0 (47.3–77.0)	70.0 (56.0–85.0)	49.1 (29.0–66.1)	48.1 (31.6–50.0)

*Current inhibitors, inhibitor at the time of receipt of the first dose of emicizumab; history of inhibitors, inhibitor detected prior to emicizumab but no current inhibitor; no inhibitors, none detected or observed yet.
ABR, annualized bleed rate; F, factor; A; IQR, interquartile range; PwHA, people with hemophilia A

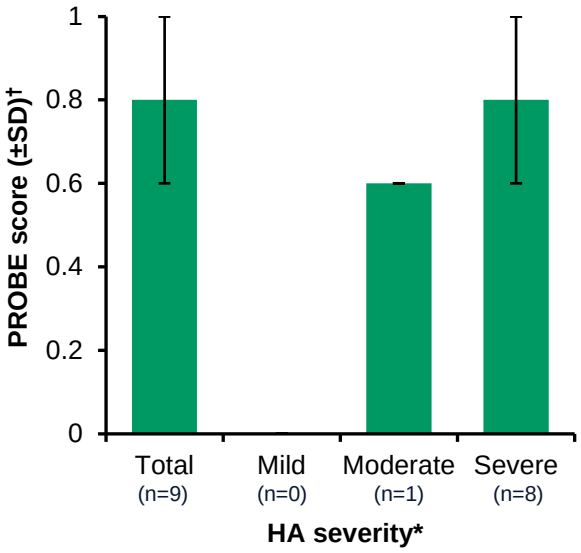
Median (IQR) ABR

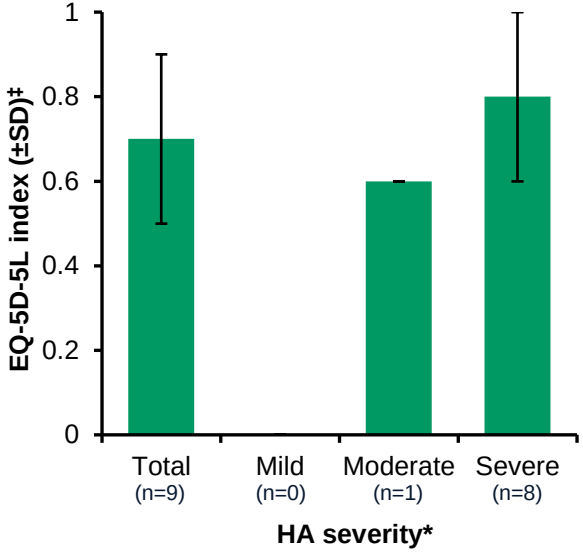
- The ABR was 0 (0–0) for the total population and when divided according to inhibitor status

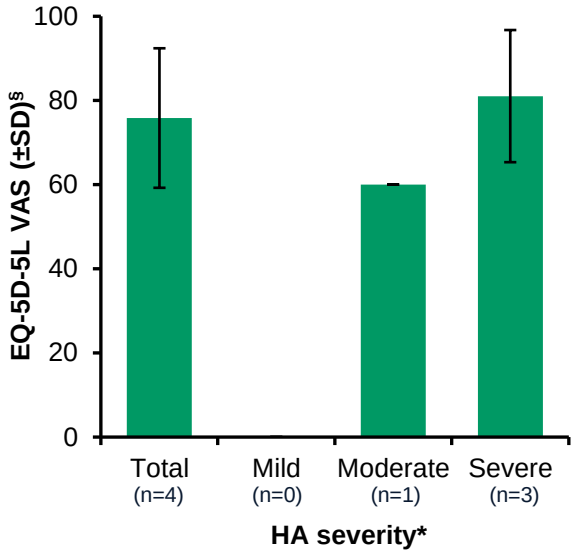
Median (IQR) ABR for PwHA with ≥1 bleed

- The ABR for PwHA with ≥1 bleed was 2 (1–3) [n=14]
- ABRs according to inhibitor status were:
  - Current inhibitors: 2 (1–3) [n=10]
  - History of inhibitors: 1 (1–1) [n=2]
  - No inhibitors: 2 (2–2) [n=2]

HA severity and quality of life for PwHA receiving emicizumab



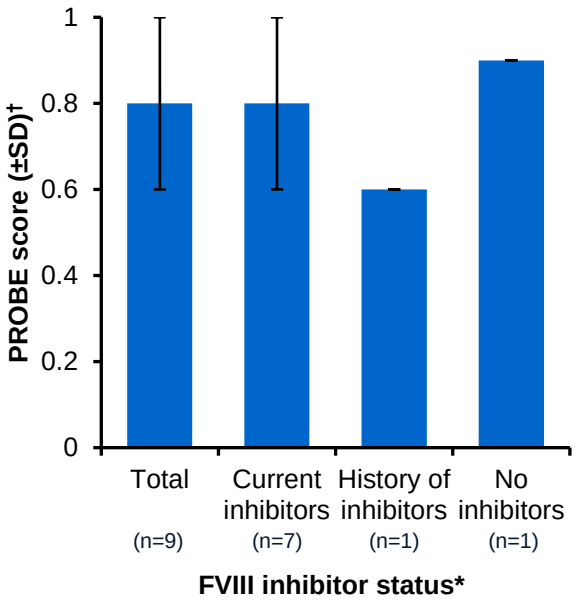


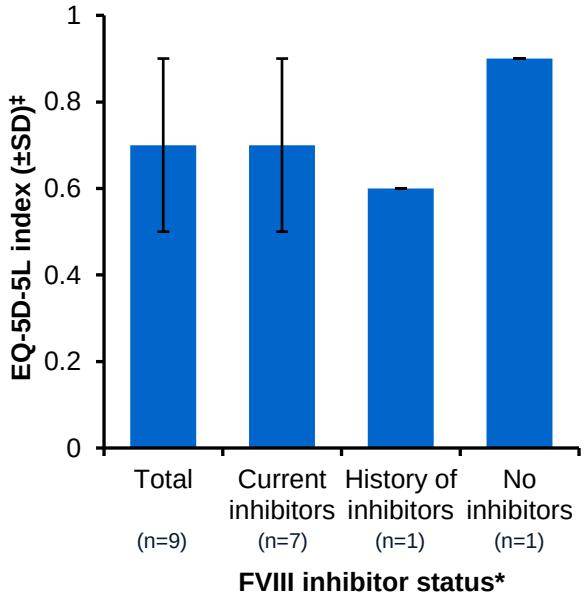


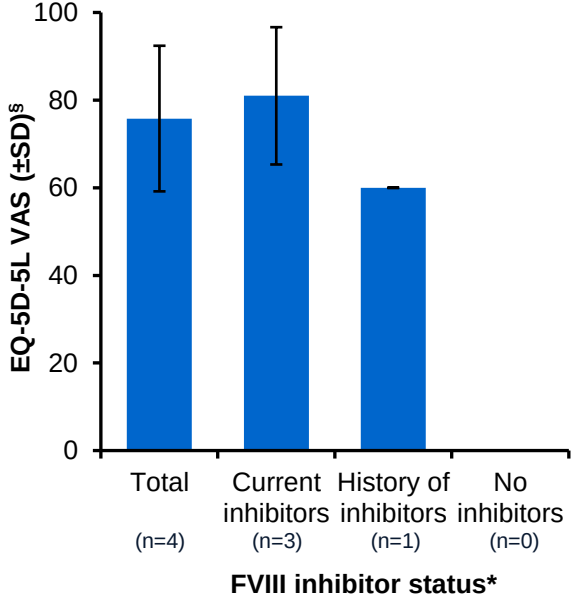
Quality of life for the individual who had moderate HA and available data was similar to that for those with severe HA, but the analysis was limited by the small sample size

*Severe (FVIII < 0.01 IU/mL), moderate (0.01 ≤ FVIII ≤ 0.05 IU/mL) and mild (0.05 < FVIII ≤ 0.40 IU/mL); †the PROBE score can range from 0 (worst health status) to 1 (best health status); ‡the EQ-5D-5L utility index can range from -0.28 (worst health status) to 1 (best health status); §the EQ-5D-5L VAS Score can range from 0 (worst health status) to 100 (best health status).
EQ-5D-5L, EuroQoL 5 dimensions, 5 levels; HA, hemophilia A; PROBE, Patient Reported Outcomes Burdens and Experiences; PwHA, people with hemophilia A; SD, standard deviation; VAS, visual analog scale

FVIII inhibitor status and quality of life for PwHA receiving emicizumab







Quality of life appeared to remain high, independent of FVIII inhibitor status, but available data were limited by the small sample size

*Current inhibitors, inhibitor at the time of receipt of the first dose of emicizumab; history of inhibitors, inhibitor detected prior to emicizumab but no current inhibitor; no inhibitors, none detected or observed yet;
†the PROBE score can range from 0 (worst health status) to 1 (best health status); ‡the EQ-5D-5L utility index can range from -0.28 (worst health status) to 1 (best health status); §the EQ-5D-5L VAS Score can range from 0 (worst health status) to 100 (best health status).
EQ-5D-5L, EuroQoL 5 dimensions, 5 levels; A; PROBE, Patient Reported Outcomes Burdens and Experiences; PwHA, people with hemophilia A; SD, standard deviation; VAS, visual analog scale

Safety

- Two of the 73 (2.7%) PwHA included in the analysis experienced a rash (allergic or acute reaction) that was reported in the registry
  - One of these events, which was reported 6 days after administration, was possibly related to emicizumab according to the reporting HTC
    - The individual remained on emicizumab prophylaxis after the event

No thromboembolic events or thrombotic microangiopathies were reported

HTC, Hemophilia Treatment Center; PwHA, people with hemophilia A

Conclusions

The Canadian population treated with emicizumab represented in this time period predominantly had severe disease and current or historical FVIII inhibitors

The bleed outcomes are consistent with earlier publications,[1–4] showing 80.8% had no recorded bleeds while receiving emicizumab, and there were no new safety concerns

The CBDR will allow for longitudinal follow-up of this patient population

Our results can inform healthcare practitioners and regulatory authorities on the real-world safety and effectiveness outcomes of emicizumab in PwHA with or without FVIII inhibitors

CBDR; Canadian Hemophilia Bleeding Disorders Registry; F, factor; PwHA, people with hemophilia A

1. Oldenburg J, et al. N Engl J Med 2017;377:809–18; 2. Young G, et al. Blood 2019;134:2127–38;
3. Mahlangu J, et al. N Engl J Med 2018;379:811–22; 4. Pipe SW, et al. Lancet Haematol 2019;6:e295–e305.

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Disclosures

MCP: employment: University of Calgary; honoraria and research funding: Bayer, CSL Behring; honoraria: Bioverativ, Sanofi, Novo Nordisk, Pfizer, Roche and Takeda; **AL**: research funding: Bayer, Bioverativ, Sanofi; honoraria: Bioverativ, Sanofi, CSL Behring, Novo Nordisk, Pfizer, Roche, Takeda; speaker's bureau: Bayer, Novo Nordisk and Pfizer; **FG**: employment: McMaster University; research funding: Roche, Novo Nordisk, Takeda, Bayer, Pfizer and BioMarin; **AK**: employment: McMaster University; consultancy: Novo Nordisk; **QI**: employment: McMaster University; **FN**: employment and stockholder: Roche; consultancy: Novartis and Actelion; **FS**: employment and stockholder: Roche; **MS**: employment: Roche; stockholder: Roche, Baxter and Takeda; **EI**: employment: McMaster University; **DM**: employment: McMaster University; research funding: Sanofi, Bayer, Pfizer, Octapharma; honoraria: Sanofi, Bayer, Pfizer, Octapharma, Novo Nordisk; Speaker's bureau; Sobi, Sanofi, Bayer, Pfizer and Octapharma; **AI**: employment: McMaster University; research funding: Bayer, BioMarin, Novo Nordisk, Octapharma, Pfizer, Roche, Sanofi, Sobi, Takeda and Uniqure.