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Improvement in Annualized Bleed Rate in Patients with Hemophilia A Initiating Emicizumab – Physician Reported Outcomes from the Adelphi Hemophilia A Disease Specific Programme™

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Summary

There is a paucity of research on real-world effectiveness of emicizumab in PwHA

Data were captured via the Adelphi Hemophilia A Disease Specific Programme™ through physician-completed questionnaries

19 Emicizumab Patients
13 severe patients and 6 mild/moderate patients

This real-world survey is one of the first to examine the change in annualized bleed rate in PwHA pre and post emicizumab initiation

Significant bleed reductions were seen after initiating emicizumab, regardless of patient's disease severity or inhibitor status

Background

- Emicizumab (trade name Hemlibra®) is indicated for prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A (PwHA) with or without factor VIII inhibitors, since it is a method of substitution therapy
- Emicizumab allows for the bridging of the activated factor IX and factor X, replacing the function normally performed by factor VIII, thus restoring hemostasis[1]
- There is a paucity of research on real-world effectiveness of emicizumab in PwHA, particularly in non-severe hemophilia A (HA). HA is categorized as severe when the PwHA has less than 1% baseline of factor VIII clotting activity
- We aimed to describe characteristics of PwHA initiating emicizumab, and examine the change in annualized bleed rate (ABR) in these patients after initiating emicizumab in the real world

Methods

- Data were collected from the Adelphi Hemophilia A Disease Specific Programme™, a point-in-time survey of physicians and their PwHA. A complete description of the methods of the survey has been previously published and validated [2]
- Data were captured in the USA between February 2020 and April 2021
- Participating physicians completed a physician-reported questionnaire for their next consulting eligible PwHA using information from their medical charts and physician recall. Data on socio-demographics, clinical characteristics and treatment were collected
- Patients were included in this analysis if they:
  - had been receiving emicizumab for at least 12 months at the time of data collection with the index date defined as the date of emicizumab initiation
  - Had complete data on bleeding events in the 12 months prior to and ≥12 months after emicizumab initiation
- The annual bleed rate in the pre-index period was calculated, and the bleed rate in the post-index period was annualized for those with >12 months follow-up
- Change in proportion of patients with zero bleeds pre- and post-emicizumab initiation was evaluated using the McNemar test
- Changes in ABR over time in the overall cohort and subgroups of disease severity (severe vs. mild/moderate) and inhibitor status were examined using unadjusted negative binomial regression models

Results

- A total of 19 patients met the inclusion criteria. 18 patients were adult (94.7%) with a mean age of 30.5 (standard deviation [SD] = 11.5) years; 15 (78.9%) patients were White (**Table 1**)
- 13 (68.4%) patients were severe and 6 (31.6%) were mild/moderate. 8 (42.1%) patients had active inhibitors at the time of survey completion [5 (38.5%) of the 13 severe, and 3 (50.0%) of the 6 mild/ moderate patients] (**Table 1**)
- 14 (73.7%) patients previously received prophylactic treatment, 14 (73.7%) were commercially insured, and 12 (63.2%) received at least some care at a Hemophilia Treatment Center (**Table 1**)

Table 1: Physician-Reported Patient Characteristics

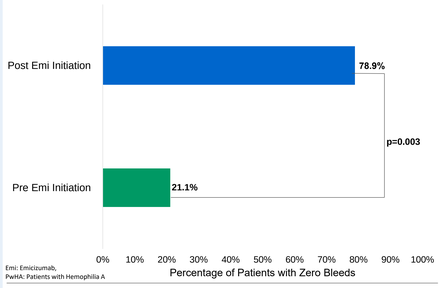
	PwHA (n=19)
HA Disease Severity, n (%)	
Mild/Moderate (≥1% baseline FVIII activity)	6 (31.6)
Severe (<1% baseline FVIII activity)	13 (68.4)
With Active Inhibitors, n (%)	8 (42.1)
Mild/Moderate (≥1% baseline FVIII activity)	3/6 (50.0)
Severe (<1% baseline FVIII activity)	5/13 (38.5)
Adult PwHA, >18 years of age, n (%)	18 (94.7)
Age at Time of Study Completion, years, mean (SD), median (IQR)	30.5 (11.5), 27.0 (22.0,39.0)
Age at Diagnosis, years, mean (SD)	4.1 (8.9)
Mild/Moderate (≥1% baseline clotting factor activity)	11.6 (12.3)
Severe (<1% baseline clotting factor activity)	0.1 (0.3)
Ethnicity, n (%)	
White	15 (78.9)
Previously Received Prophylactic Treatment, n (%)	14 (73.7)
Commercially Insured, n (%)	14 (73.7)
Been Treated in a Hemophilia Treatment Center, n (%)	12 (63.2)
Most Common Comorbidities, n (%)	
Hypertension	3 (15.8)
Anxiety	2 (10.5)
Depression	2 (10.5)
Time Since Starting Emicizumab, months, mean (sd)	20.8 (7.0)

Active inhibitors: inhibitors which are present at the time of data collection, PwHA: Patients with Hemophilia A

Results (Continued)

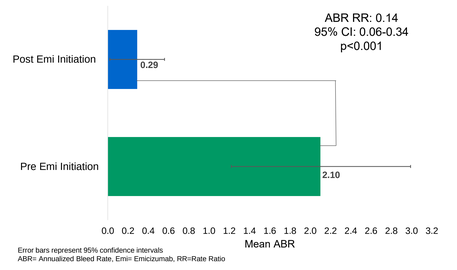
- Mean age at diagnosis was 4.1 (SD=8.90) years, 11.6 (SD=12.28) years in mild/moderate patients, and 0.1 (SD=0.28) years in severe patients
- The most common comorbidities were hypertension (n=3, 15.8%), anxiety (n=2, 10.5%), and depression (n=2, 10.5%)
- The average time since starting treatment with emicizumab was 20.8 (SD=7.04) months
- A larger proportion of patients experienced zero bleeds in the post-emicizumab compared to pre-emicizumab period (78.9% vs. 21.1%, p=0.003) (**Figure 1**)
- The mean ABR was 2.10 events (95% confidence interval [CI]: 1.22-2.99) before initiating emicizumab compared to 0.29 events (95% CI: 0.02-0.56) in the post-emicizumab period, indicating an 86% lower mean ABR after initiating emicizumab prophylaxis (ABR rate ratio [RR]: 0.14; 95% CI: 0.06-0.34; p<0.001) (**Figure 2**)

Figure 1: Percentage of PwHA with Zero Bleeds Pre- and Post-Emicizumab Initiation (n=19)



Emi: Emicizumab, PwHA: Patients with Hemophilia A

Figure 2: Mean Annualized Bleed Rate Pre- and Post-Emicizumab Initiation (n=19)



Error bars represent 95% confidence intervals
ABR= Annualized Bleed Rate, Emi= Emicizumab, RR=Rate Ratio

Results

- In the pre-emicizumab period, the ABR in severe patients was 1.69 events (95% CI: 0.62-2.76) and 3 events (95% CI: 1.61-4.39) in mild/moderate patients compared to 0.21 (95% CI: -0.08-0.50) and 0.47 (95% CI: -0.08-1.02), in the post-emicizumab period with an estimated 88% (ABR RR: 0.12; 95% CI: 0.04-0.44; p=0.001) and 84% (ABR RR: 0.16; 95% CI: 0.04-0.55; p=0.004) lower ABR in these subgroups respectively, after initiating emicizumab. 3/6 of the mild/moderate patients had inhibitors at data collection, which is usually indicative of more severe hemophilia (**Figure 3**)
- The ABR in patients with active inhibitors was 2.13 (95% CI: 0.81-3.44) and 2.09 (95% CI: 0.9-3.28) in patients without inhibitors in the pre-emicizumab period, compared to 0.21 (95% CI: -0.25-0.66) and 0.35 (95% CI: 0.00-0.71) in the post-emicizumab period, with an estimated 90% (ABR RR: 0.10; 95% CI: 0.02-0.48; p=0.004) and 83% (ABR RR: 0.17; 95% CI: 0.06-0.50; p=0.001) lower ABR in these subgroups, after initiating emicizumab (**Figure 4**)

Figure 3: Annualized Bleed Rate Pre- and Post-Emicizumab Initiation: Split By Disease Severity

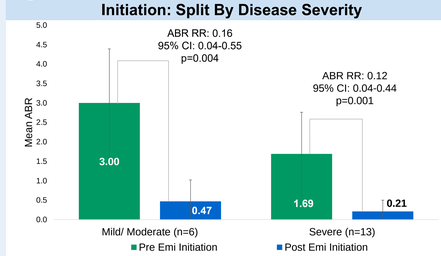
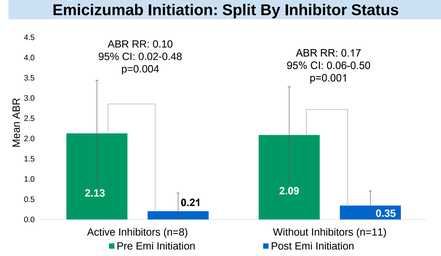


Figure 4: Annualized Bleed Rate Pre- and Post-Emicizumab Initiation: Split By Inhibitor Status



Error bars represent 95% confidence intervals. ABR= Annualized Bleed Rate, Emi= Emicizumab, RR=Rate Ratio. Changes in ABR over time were examined using unadjusted negative binomial regression models

Conclusions and Limitations

- This real-world survey is one of the first to examine the change in ABR in PwHA initiating emicizumab, including patients of different disease severity
- Significant bleed reductions were observed after initiating emicizumab, with nearly 80% having zero bleeds in the post emicizumab period
- These significant bleed reductions were seen regardless of patient's disease severity or inhibitor status, although the small sample size should be noted as a limitation to these analyses
- Given this small sample size, we could not further stratify patient outcomes by both severity and inhibitor status; therefore, further research is required to understand the impact of emicizumab in this patient population
- This study identified significant associations between factors, but given its point-in-time design, we could not make any conclusions about causal relationships

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

References

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