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Quality of Life in Emicizumab-treated People with Hemophilia A in the ATHN 7 Hemophilia Natural History Study – An Assessment of Baseline PROMIS®-29 Scores

Tyler W. Buckner,[1]* Nabil Daoud,[2] Lucy Lee,[3] Elise Lim,[3] Jonathan Schwartz,[2] Karina Raimundo,[3] Michael Recht[2,4,5]

*Presenting author

Summary

ATHN 7 is a longitudinal, prospective observational cohort study monitoring the use of contemporary therapies for people with hemophilia A and B, including emicizumab, in the United States (US)

Health-related quality of life (HRQoL) in 67 participants with hemophilia A taking emicizumab was measured at study entry using the PROMIS-29 and compared with the general US population

People with hemophilia A taking emicizumab reported mild symptoms of pain interference compared with the general US population

The mean PROMIS-29 domain T-scores indicated similar levels of HRQoL in this population compared with those of the general US population

Affiliations: [1]Hemophilia and Thrombosis Center, University of Colorado School of Medicine, Aurora, CO, USA; [2]American Thrombosis and Hemostasis Network, Rochester, NY, USA; [3]Genentech, Inc., South San Francisco, CA, USA; [4]Yale University School of Medicine, New Haven, CT, USA; [5]Current affiliation: National Bleeding Disorders Foundation, New York, NY, USA

Background

- People with hemophilia A (PwHA) experience frequent bleeding into joints, muscles, and soft tissues due to a deficiency of factor (F)VIII, which has a substantial negative impact on their health-related quality of life (HRQoL).[1]
- Emicizumab is a bispecific antibody approved for prophylactic treatment of hemophilia A (HA).[2]
- American Thrombosis and Hemostasis Network (ATHN): A Natural History Cohort Study of the Safety, Effectiveness and Practice of Treatment for People with Hemophilia (NCT03619863) prospectively monitors safety and effectiveness of contemporary HA and B therapies, including emicizumab, in the United States (US).
- We describe baseline scores for a subset of adults with HA enrolled in ATHN 7 who were receiving emicizumab and completed the Patient-Reported Outcomes Measurement Information System (PROMIS®)-29 Profile measure at the time of study entry, with the aim of contributing to the literature on disease burden in PwHA.

ATHN 7 is a longitudinal, prospective observational cohort study conducted at 26 ATHN-affiliated sites in the US

- Clinical and demographic information is collected at baseline.
- PwHA not receiving emicizumab at baseline were excluded from this analysis.
- The PROMIS-29 is a disease-agnostic measure capturing data across the following physical, mental, and social health domains: physical function, fatigue, sleep disturbance, pain intensity, pain interference, depressive symptoms, anxiety, and ability to participate in social roles/activities.
- The PROMIS measures are scored using a standardized T-score metric with a reference population mean of 50 and a standard deviation (SD) of 10, based on the US general population. Higher scores indicate the participant is experiencing more of the concept being measured (positive or negative). The limits for 'normal' function for each PROMIS assessment score varied between domains.[3,4]

Overall, 67 participants in ATHN 7 receiving emicizumab at study entry completed PROMIS-29 at baseline

- Participants had a median (min, max) age of 30.0 (18.0, 75.0) years (**Table 1**).
- Disease severity at diagnosis was severe for 53 (79.1%) participants and mild or moderate for 14 (20.9%) participants.
- There were 12 (17.9%) PwHA with FVIII inhibitors.

Table 1. Participant demographics and baseline characteristics.

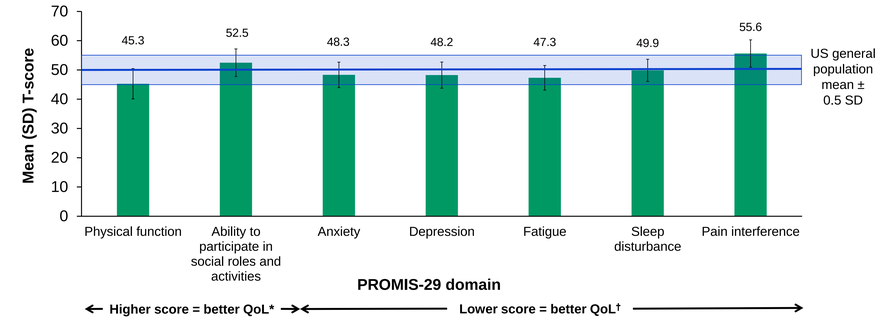
	N=67
Age at study entry, years*	
Mean (SD)	34.8 (14.5)
Median (min, max)	30.0 (18.0, 75.0)
Age (at study entry) group, n (%)	
≤24 years	17 (25.4)
25–49 years	39 (58.2)
≥50 years	11 (16.4)
Sex, n (%)	
Male	67 (100.0)
Female	0 (0.0)
Primary HA diagnosis severity, n (%)	
Severe	53 (79.1)
Mild or moderate	14 (20.9)
FVIII inhibitors, n (%)	
Yes	12 (17.9)
No	55 (82.1)
Family history of HA, n (%)	
Yes	36 (53.7)
No	29 (43.3)
Unknown	2 (3.0)

*Data on pediatric PwHA are being collected in ATHN 7 but are not reported here. ATHN, American Thrombosis and Hemostasis Network; FVIII, factor VIII; HA, hemophilia A; PwHA, people with hemophilia A; SD, standard deviation.

PROMIS-29 domain T-scores at baseline aligned with the US reference population

- Mean PROMIS-29 domain T-scores for ability to participate in social roles and activities, symptoms of anxiety, sleep disturbance, depression, and fatigue at baseline all fell within 0.5 SD of the reference population mean (**Figure 1**).
- However, PwHA did demonstrate mild symptoms of pain interference (mean baseline T-score: 55.62; [normal: <55]).

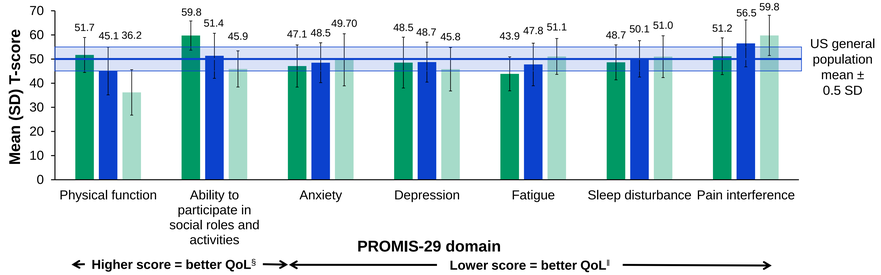
Figure 1. Baseline PROMIS-29 T-scores for the overall population of participants treated with emicizumab in ATHN 7 (N=67).



*Normal: >45; mild impairment: 40–45; moderate impairment: 30–40; severe impairment: <30; †Normal: <55; mild symptoms: 55–60; moderate symptoms: 60–70; severe symptoms: >70.[3,4] ATHN, American Thrombosis and Hemostasis Network; PROMIS, Patient-Reported Outcomes Measurement Information System; QoL, quality of life; SD, standard deviation; US, United States.

- PwHA with FVIII inhibitors had mild impairment of physical function (42.17) and mild symptoms of pain interference (58.64). People without inhibitors had physical function (45.96) and pain interference (55.00) within 0.5 SD of the reference population.
- People with severe HA without FVIII inhibitors had mild impairment of physical function (44.76) and mild symptoms of pain interference (55.49), while people with mild/moderate HA without inhibitors had physical function (49.85) and pain interference (53.46) within 0.5 SD of the reference population.
- Physical function decreased with age, from 51.71 in the group aged ≤24 years to 36.18 in the group aged ≥50 years, while pain interference increased with age, from 51.18 in the group aged ≤24 years to 59.80 in the group aged ≥50 years. There was no relationship between age group and anxiety, depression, and sleep disturbance (**Figure 2**).

Figure 2. Baseline PROMIS-29 T-scores by age group for participants treated with emicizumab in ATHN 7 (N=67).



*n=16 for ability to participate in social roles and activities; †n=38 for pain interference; ‡n=10 for anxiety, depression, pain interference; §Normal: >45; ‖Normal: <55.[3,4] ATHN, American Thrombosis and Hemostasis Network; PROMIS, Patient-Reported Outcomes Measurement Information System; QoL, quality of life; SD, standard deviation; US, United States.

Limitations

- Results should be interpreted with caution as subgroup numbers are small, therefore no statistical tests were performed.
- The exact duration of emicizumab exposure prior to study entry could not be extracted, meaning duration of treatment at the time of completing the PROMIS questionnaire could not be determined.
- The disability paradox, in which people with persistent disabilities report better quality of life outcomes than perceived by those without disabilities, should also be considered.[5]

Conclusions

- In this analysis, we observed that HRQoL in PwHA receiving emicizumab, as measured by PROMIS-29 domain T-scores, generally did not differ from that of the US reference population.
- PwHA did report mild symptoms of pain interference.
- Physical function, ability to participate in social roles/function, and pain varied between age groups.

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Disclosures

TWB: Novo Nordisk: Honoraria; Tremeau Pharmaceuticals: Consultancy; BioMarin: Consultancy; CSL Behring: Honoraria; Octapharma: Honoraria. **ND**: American Thrombosis and Hemostasis Network: Current Employment. **LL, EL**: Genentech, Inc.: Current Employment, Current equity holder in publicly-traded company. **KR**: Genentech, Inc.: Current Employment; F. Hoffmann-La Roche Ltd: Current equity holder in publicly-traded company. **JS**: no disclosures. **MR**: Hema Biologics: Consultancy, Research Funding; BioMarin: Research Funding; Grifols: Research Funding; Bayer Pharmaceuticals: Research Funding; Genentech, Inc.: Consultancy, Research Funding; CSL Behring: Consultancy, Research Funding; Pfizer: Consultancy; Sanofi: Consultancy, Research Funding; Takeda: Consultancy, Research Funding; uniQure: Consultancy, Research Funding; LFB: Research Funding; Novo Nordisk: Research Funding; Partners in Bleeding Disorders: Membership on an entity's Board of Directors or advisory committees; ATHN: Membership on an entity's Board of Directors or advisory committees.