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Evolution of joint health and physical activity in people with hemophilia A without factor VIII inhibitors switching to emicizumab prophylaxis: A second interim analysis of the BEYOND ABR study

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Summary

Advances in hemophilia A (HA) treatment have led to lower bleeding rates, shifting the focus towards functional endpoints such as joint health and physical activity

BEYOND ABR aims to evaluate joint health and physical activity outcomes in people with HA switching from factor VIII prophylaxis to emicizumab. Here, we report data after 12 months of treatment with emicizumab

The proportion of participants reporting high physical activity increased, while the proportion reporting low physical activity decreased. Additionally, most participants preferred emicizumab over their previous treatment

During the first 12 months after switching to emicizumab, participants had low bleeding rates, with most demonstrating improved or stabilized joint health, and overall numerical improvements measured by Hemophilia Joint Health Score and the number of problem and target joints

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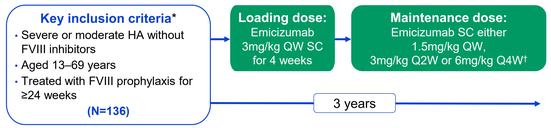
Background

- Advances in hemophilia A (HA) treatment have led to lower bleeding rates,[1] shifting focus toward functional endpoints such as joint health and physical activity, for which data are lacking and a systematic approach to data collection is needed.
  - Despite treatment with factor (F)VIII prophylaxis, joint health has been observed to deteriorate over time.[2]
- BEYOND ABR (NCT05181618) aims to evaluate joint health and physical activity outcomes in people with HA (PwHA) switching from FVIII prophylaxis to emicizumab.
- This second interim analysis reports data analyzed after 12 months of treatment with emicizumab.

BEYOND ABR is a 3-year, Phase IV, multicenter, open-label study conducted in 12 countries

- Eligible participants were PwHA aged 13–69 years with moderate/severe HA without FVIII inhibitors, who had been treated with FVIII prophylaxis for at least 24 weeks prior to enrollment (**Figure 1**).

Figure 1. Study design



Key assessments in this interim analysis

- Joint health was evaluated using:
  - **HJHS 2.1**‡
  - Numerical changes in **problem joint counts**§, captured by both participants and investigators
  - **Target joint resolution**¶ (in participants with ≥52 weeks of follow-up)
- **Physical activity** data were obtained using the **IPAQ-SF**
- The number of participants with **zero treated bleeds** was determined using data from a BMQ
- The **EmiPref survey**[3] was conducted after 6 months of treatment
- Safety was measured through **incidence and seriousness of AEs**

*Patients who had joint replacement, joint procedure, synovectomy or synoviorthesis less than 2 years before recruitment were excluded. †Maintenance dose was based on participant preference and agreement with the investigator. ‡Participants or single joints with a history of joint surgery/procedure were not included in the HJHS analysis. Meaningful changes in HJHS were ≥2 points at the single joint level and ≥4 points at the participant level.[4] §Defined as chronic joint (neck, shoulders, elbows, wrists, knees, hips, ankles, spine) pain and/or limited range of movement due to compromised joint integrity with or without persistent bleeding.[3,5] ¶A baseline target joint with <3 spontaneous or traumatic bleeds in a 52-week period was considered resolved.
AEs, adverse events; BMQ, Bleed and Medication Questionnaire; EmiPref, Emicizumab Preference survey; F, factor; HA, hemophilia A; HJHS, Hemophilia Joint Health Score; IPAQ-SF, International Physical Activity Questionnaire-Short Form; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous.

Overall, 136 PwHA were enrolled with varying levels of joint status/impairment[6]

- At data cut-off (Nov 29, 2024), 130 (95.6%) participants were still being treated with emicizumab (**Table 1**).
- The median (range) duration of follow-up was 76 (13–122) weeks.

Table 1. Baseline characteristics

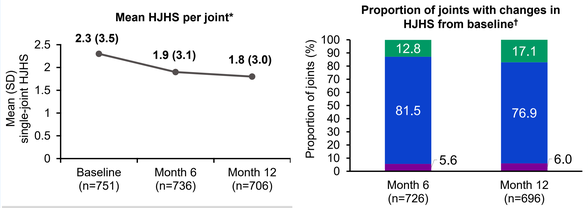
	Total (N=136)*
Age, years	
Mean (SD)	**29.3 (11.6)**
Median	**26.5**
Min–Max	**13–63**
Age group, years, n (%)	
13–17	**24 (17.6)**
18–29	**60 (44.1)**
30–49	**43 (31.6)**
50–69	**9 (6.6)**
Male, n (%)†	**136 (100)**
Mean BMI (SD)	**25.5 (6.0)**
HA severity, n (%)	
Moderate	**25 (18.4)**
Severe	**111 (81.6)**
Total no. of participants with ≥1 joint with surgery/procedure (%)	**33 (24.3)**

*Four participants discontinued the study; two discontinued treatment. Four discontinued by participant decision, two by physician decision. The two who discontinued treatment were included in the safety follow up at cut-off. †Female sex was not an exclusion criterion.
BMI, body-mass index; HA, hemophilia A; SD, standard deviation.

HJHS scores showed overall numerical trends of improvement at the single joint and participant level

- At the single joint level, the mean (standard deviation [SD]) Hemophilia Joint Health Score (HJHS; maximum: 20 points per joint) was 2.3 (3.5) at baseline and had improved by 0.3 (1.7) at Month 6 and 0.5 (1.9) at Month 12 (**Figure 2**).
- At Month 6, 93/726 (12.8%) joints showed an improvement of ≥2 points, increasing to 119/696 (17.1%) at Month 12; 41/726 (5.6%) joints and 42/696 (6.0%) joints showed a worsening of ≥2 points at Month 6 and Month 12, respectively.

Figure 2. HJHS scores at the single joint level

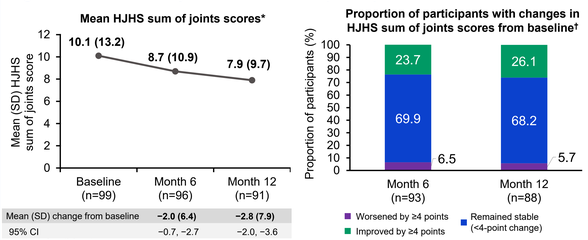


	Month 6	Month 12
Mean (SD) change from baseline	−0.3 (1.7)	−0.5 (1.9)
Number of joints, n	726	696

*Mean scores are calculated from all joints with data at that timepoint; change from baseline is calculated in joints with data at both baseline and Month 6 or Month 12. †Total percentages may not equal 100% due to rounding.
HJHS, Hemophilia Joint Health Score; SD, standard deviation.

- At the participant level, the mean (SD) HJHS sum of joints score (excluding Global Gait Score; max score: 120 = 6 joints × 20 points each) was 10.1 (13.2) at baseline and had improved by 2.0 (6.4) at Month 6 and 2.8 (7.9) at Month 12 (**Figure 3**).
- In total, 23/88 (26.1%) participants reported an improvement of ≥4 points in HJHS sum of joints from baseline to Month 12 and 5/88 (5.7%) reported worsening of ≥4 points at Month 12.

Figure 3. HJHS sum of joints scores at the participant level



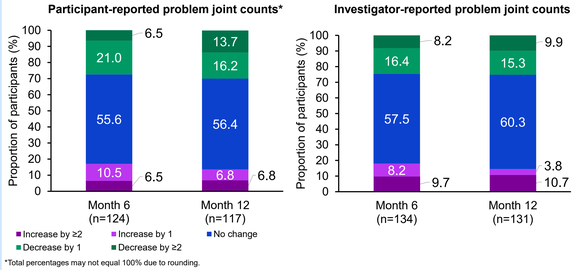
	Month 6	Month 12
Mean (SD) change from baseline	−2.0 (6.4)	−2.8 (7.9)
95% CI	−0.7, −2.7	−2.0, −3.6
Number of participants, n	93	88

*Mean scores are calculated from all participants with data at that timepoint; change from baseline is calculated in participants with data at both baseline and Month 6 or Month 12. †Total percentages may not equal 100% due to rounding.
CI, confidence interval; HJHS, Hemophilia Joint Health Score; SD, standard deviation.

Categorical changes in the number of problem joints per participant showed overall improvements from baseline to Month 12

- At Month 12, the number of participant-reported problem joints had decreased from baseline in 35/117 (29.9%) participants, including a resolution of ≥2 problem joints in 16 (13.7%) participants (**Figure 4**). Problem joint counts increased in 16 (13.7%) participants, including an increase of ≥2 problem joints in 8 (6.8%) participants.
- Similar outcomes were observed for investigator-reported problem joints.

Figure 4. Overall categorical changes in problem joint counts from baseline



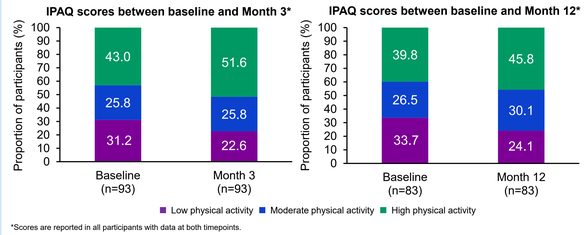
*Total percentages may not equal 100% due to rounding.

- In participants who remained in the study for at least one year, 27/27 (100%) baseline target joints in 15 participants had resolved at Month 12.

The proportion of participants reporting high physical activity increased

- In an intra-participant comparison of International Physical Activity Questionnaire (IPAQ) scores between baseline and Month 3 or Month 12, the proportion of participants in the low activity category decreased and the proportion in the high activity category increased (**Figure 5**).

Figure 5. Intra-participant comparison of IPAQ scores between baseline and Month 3 or Month 12



*Scores are reported in all participants with data at both timepoints.
IPAQ, International Physical Activity Questionnaire.

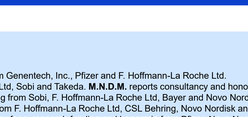
The proportion of participants with zero treated bleeds was high and remained stable during emicizumab treatment

- Zero treated bleeds were reported by 110/136 (80.9%) participants between Weeks 1 and 24, and 105/134 (78.4%) between Weeks 25 and 48.
- Throughout Weeks 1–24, 22/136 (16.2%) participants reported 1–3 treated bleeds; 26/134 (19.4%) reported 1–3 treated bleeds throughout Weeks 25–48.

Participants preferred emicizumab over their previous treatment

Figure 6. EmiPref survey outcomes

At Month 6, **125/130 (96.2%)** participants preferred emicizumab to their previous FVIII prophylaxis in the EmiPref survey, while only 1/130 (0.8%) preferred their previous treatment; 4/130 (3.1%) had no preference.



EmiPref, Emicizumab Preference survey; F, factor.

Emicizumab was well tolerated, with no new safety signals

- Overall, 113 (83.1%) participants reported an adverse event (**Table 2**).

Table 2. Safety summary

	Emicizumab (N=136)
Total number of AEs, n	372
Total number of participants with ≥1 AE, n (%)	113 (83.1)
AE with fatal outcome	0
Serious AE*	9 (6.6)
AE leading to withdrawal from treatment	0
AE leading to dose modification/interruption	2 (1.5)
Grade 3–5 AE	14 (10.3)
Related AE	18 (13.2)
AEs of special interest†	0

*Included influenza, hematemesis, hematochezia, ligament rupture, hemarthrosis, unstable angina, seizures, upper respiratory tract infection, multiple trauma; none were deemed related to treatment. †Included anaphylactic reactions, thromboembolic events, TMAs, drug-induced liver injuries.
AE, adverse event; TMA, thrombotic microangiopathy.

Limitations

- The results presented here are descriptive and not supported by formal statistical hypothesis testing or inferential analysis.

Conclusions

- During the first 12 months after switching to emicizumab, participants had low bleeding rates, with most demonstrating improved or stabilized joint health, and overall numerical improvements measured by HJHS and the number of problem and target joints.
- Overall, physical activity levels assessed with IPAQ were stable or showed a shift towards higher activity levels, and most (96.2%) participants preferred emicizumab compared with their previous treatment.
- These data support previous reports of sustained bleed protection and improved joint health with emicizumab,[7–9] enabling PwHA to lead more active lives.[7]
- Study follow-up will continue for 3 years.

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