PB0698

Emicizumab▼ prophylaxis improves long-term Physical Health scores in persons with haemophilia A (PwHA) with or without inhibitors: update from the HAVEN 3 and HAVEN 4 studies

Mark Skinner,[1] Claude Negrier,[2] Ido Paz-Priel,[3] Sammy Chebon,[4] Victor Jiménez-Yuste,[5] Michael Callaghan,[6] Michaela Lehle,[4] Markus Niggli,[4] Johnny Mahlangu,[7] Amy Shapiro,[8] Midori Shima,[9] Avrita Campinha-Bacote,[3] Gallia G. Levy,[3] Johannes Oldenburg,[10] Steven Pipe[11]

[1]Institute for Policy Advancement Ltd, Washington DC, DC, USA; [2]Edouard Herriot University Hospital, Lyon, France; [3]Genentech Inc., South San Francisco, CA, USA; [4]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [5]La Paz University Hospital, Madrid, Spain; [6]Children's Hospital of Michigan, Detroit, IL, USA; [7]University of the Witwatersrand and NHLS, Johannesburg, South Africa; [8]Indiana Hemophilia and Thrombosis Center, Indianapolis, IN, USA; [9]Nara Medical University Hospital, Kashihara, Japan; [10]Universitätsklinikum Bonn, Bonn, Germany; [11]University of Michigan, Ann Arbor, MI, USA

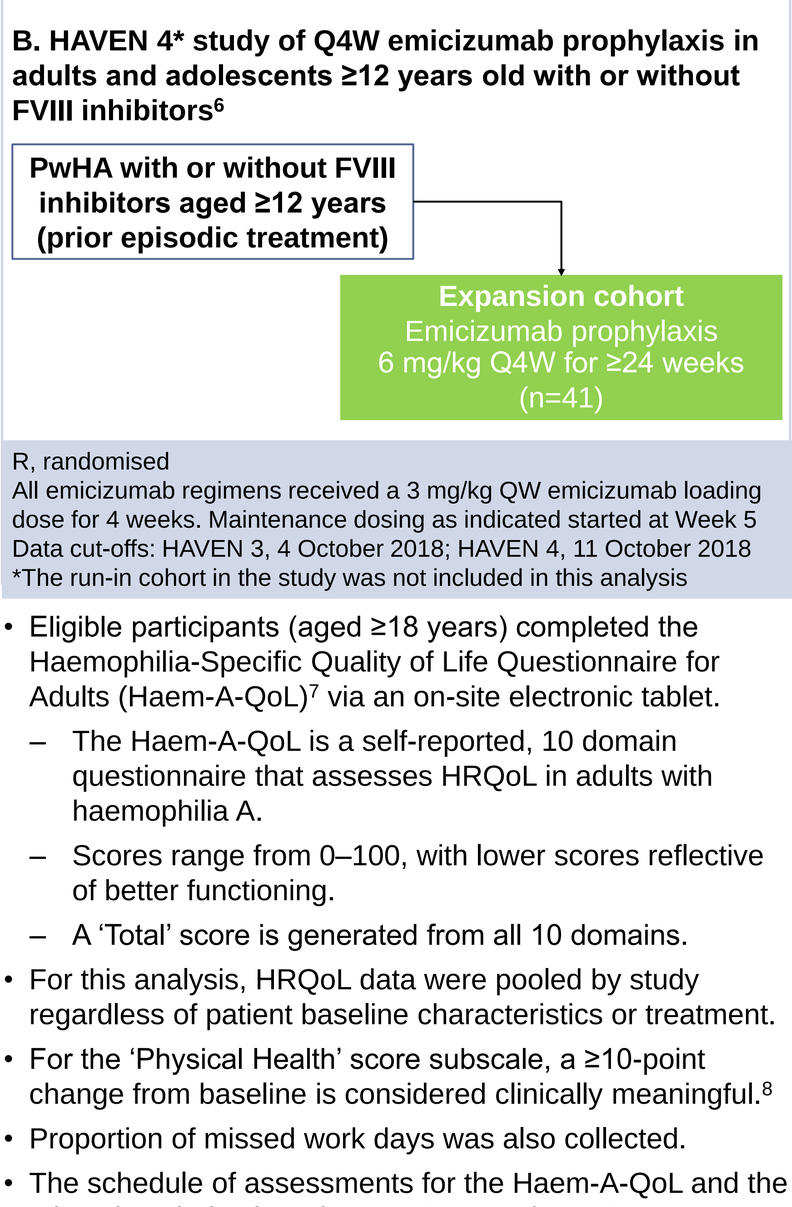
BACKGROUND

- Haemophilia A is a congenital bleeding disorder associated with a major impact on health-related quality of life (HRQoL) for those with or without factor VIII (FVIII) inhibitors.
- A greater understanding of the impact of haemophilia A disease- and treatment-related burdens on patients will provide valuable insights into patient needs.[1]
- Emicizumab, a bispecific, humanised, monoclonal antibody, binds activated FIX (FIXa) and FX to restore the function of missing FVIIIa in persons with haemophilia A (PwHA).[2]
- Emicizumab prophylaxis achieved highly efficacious bleed protection when administered once weekly (QW), once every 2 weeks (Q2W) or once every 4 weeks (Q4W) in PwHA with or without FVIII inhibitors.[3–6]
- Here we assess the impact of prophylactic emicizumab on long-term HRQoL of participants in the phase III HAVEN 3[5] (NCT02847637) and HAVEN 4[6] (NCT03020160) studies.

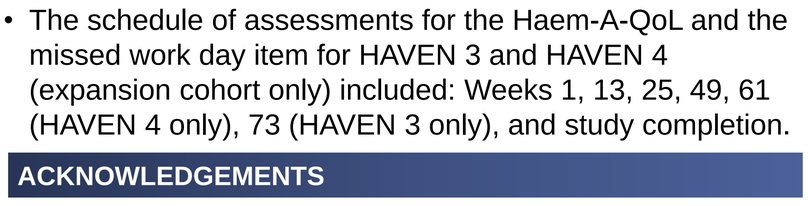
METHODS

Figure 1. HAVEN 3 and HAVEN 4 study designs

A. HAVEN 3 study of emicizumab prophylaxis in adults and adolescents ≥12 years old without FVIII inhibitors[5]



B. HAVEN 4* study of Q4W emicizumab prophylaxis in adults and adolescents ≥12 years old with or without FVIII inhibitors[6]



R, randomised
All emicizumab regimens received a 3 mg/kg QW emicizumab loading dose for 4 weeks. Maintenance dosing as indicated started at Week 5
Data cut-offs: HAVEN 3, 4 October 2018; HAVEN 4, 11 October 2018
*The run-in cohort in the study was not included in this analysis

- Eligible participants (aged ≥18 years) completed the Haemophilia-Specific Quality of Life Questionnaire for Adults (Haem-A-QoL)[7] via an on-site electronic tablet.
  - The Haem-A-QoL is a self-reported, 10 domain questionnaire that assesses HRQoL in adults with haemophilia A.
  - Scores range from 0–100, with lower scores reflective of better functioning.
  - A 'Total' score is generated from all 10 domains.
- For this analysis, HRQoL data were pooled by study regardless of patient baseline characteristics or treatment.
- For the 'Physical Health' score subscale, a ≥10-point change from baseline is considered clinically meaningful.[8]
- Proportion of missed work days was also collected.
- The schedule of assessments for the Haem-A-QoL and the missed work day item for HAVEN 3 and HAVEN 4 (expansion cohort only) included: Weeks 1, 13, 25, 49, 61 (HAVEN 4 only), 73 (HAVEN 3 only), and study completion.

ACKNOWLEDGEMENTS

Dr Sylvia von Mackensen (Department of Medical Psychology, University Medical Centre Hamburg, Hamburg, Germany) is the developer of all Haem-A-QoL questionnaires. Medical writing assistance for this poster was provided by Sophie Nobes of Gardiner-Caldwell Communications and was funded by F. Hoffman-La Roche Ltd.

RESULTS

Table 1. Baseline characteristics for all participants in HAVEN 3 and HAVEN 4 who were eligible to complete the Haem-A-QoL

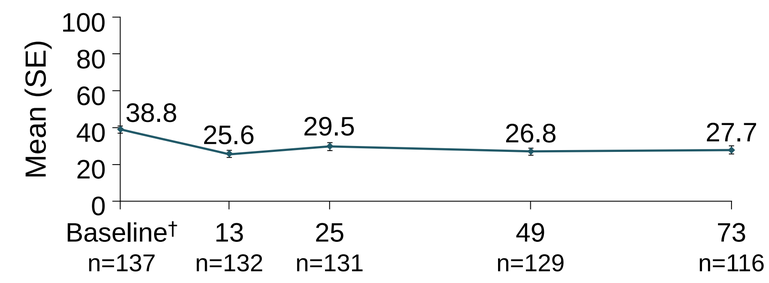
Baseline characteristic	HAVEN 3 N=143	HAVEN 4 N=38
Age (years), median (range)	39.0 (19–77)	42.0 (20–68)
Number of bleeds in the past 24 weeks, mean (SD)	13.5 (16.5)	9.6 (15.6)
Patients with target joints prior to study entry, n (%)	100 (70%)	25 (66%)
Prior episodic treatment, n (%)	87 (61%)	11 (29%)
Prior prophylactic treatment, n (%)	56 (39%)	27 (71%)

SD, standard deviation

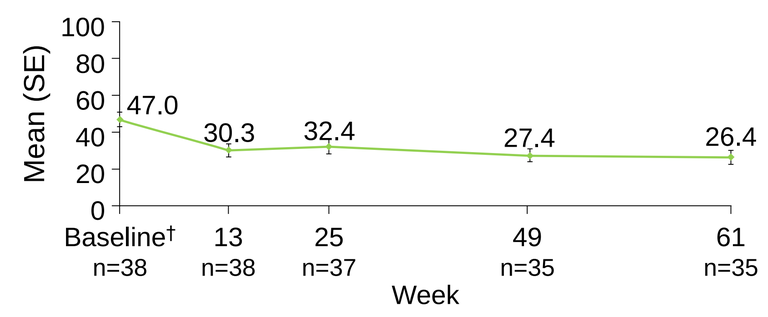
- Haem-A-QoL questionnaire compliance rates were 94.3% in HAVEN 3 (up to Week 73) and 99.1% in HAVEN 4 (up to Week 61).
- Mean Physical Health scores improved after initiation of emicizumab prophylaxis; these improvements were maintained throughout the follow-up period (Figure 2). Scores improved by ≥10 points from baseline in over 44% and 65% of participants in HAVEN 3 and HAVEN 4 respectively (Figure 3).

Figure 2. Haem-A-QoL* Physical Health score over time in eligible participants from HAVEN 3 and HAVEN 4

A. Mean Physical Health score over time in HAVEN 3



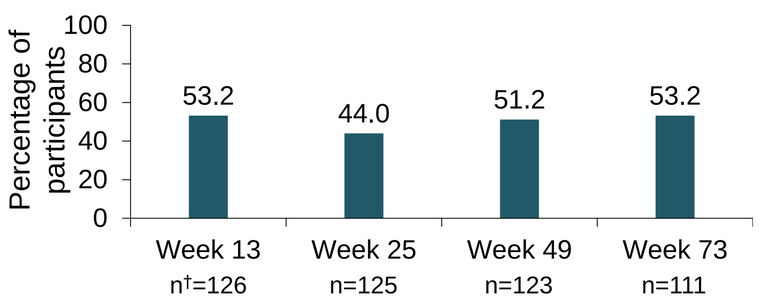
B. Mean Physical Health score over time in HAVEN 4



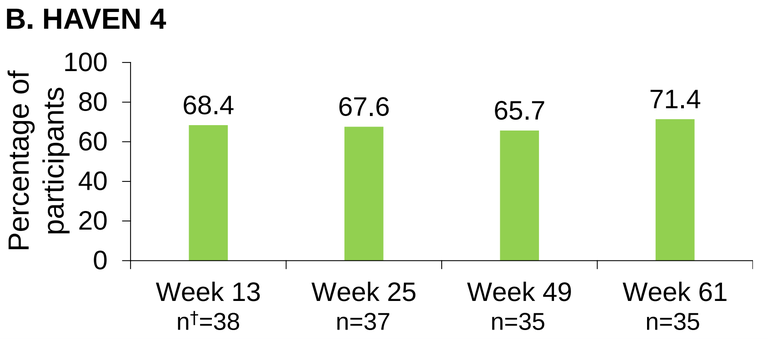
SE, standard error
*Lower scores reflect better functioning; Completed by participants aged ≥18 years only; †Baseline assessment is the last valid assessment on or before study day 1

Figure 3. Percentage of participants with improvements in Haem-A-QoL* Physical Health score greater than the responder threshold from baseline

A. HAVEN 3



B. HAVEN 4

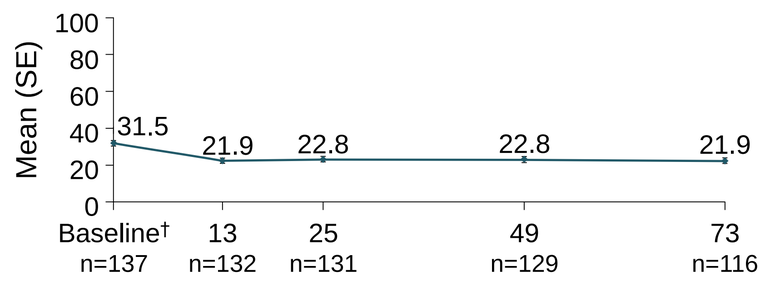


*Completed by participants aged ≥18 years only; †Number of participants with available data to calculate change from baseline

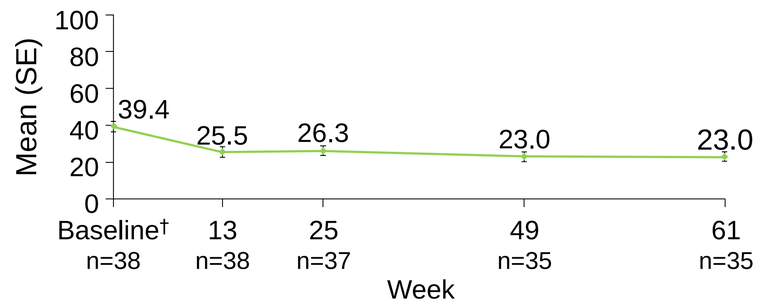
- Mean Total score (SD) improved from 31.5 (15.0) and 39.4 (17.9) at baseline to 22.8 (15.1) and 26.3 (16.6) at Week 25 for HAVEN 3 and HAVEN 4, respectively. These improvements were maintained throughout the follow-up period (Figure 4).

Figure 4. Mean Haem-A-QoL* Total score over time in eligible participants from HAVEN 3 and HAVEN 4

A. Mean Total score over time in HAVEN 3



B. Mean Total score over time in HAVEN 4

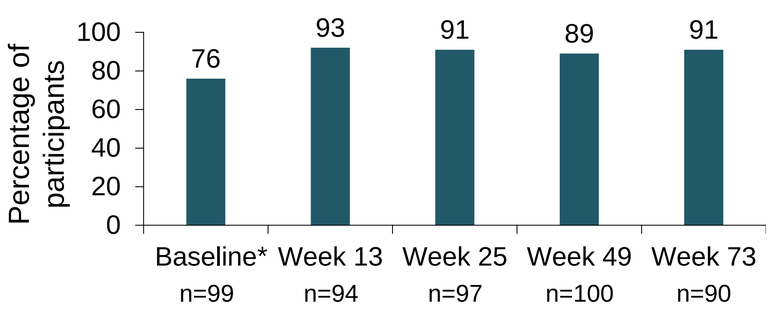


*Lower scores are indicative of better functioning. Completed by participants aged ≥18 years only; †Baseline assessment is the last valid assessment on or before study day 1

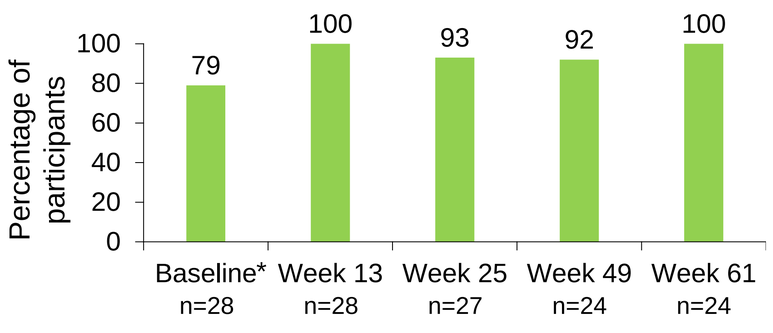
- Following administration of emicizumab, fewer employed participants missed days of work than in the 28 days prior to study enrolment (Figure 5).

Figure 5. Percentage of employed participants with no missed days of work in the previous 28 days

A. HAVEN 3



B. HAVEN 4



n is the number of participants enrolled in work at each time point
*Reflects the work period 28 days prior to enrolment

CONCLUSIONS

- **Clinically meaningful improvements were observed in Haem-A-QoL Physical Health scores with emicizumab prophylaxis in ≥44% and ≥65% of participants in HAVEN 3 and HAVEN 4, respectively.**
  - **These improvements are consistent with the demonstrated efficacy of emicizumab.[5,6]**
  - **Participants in HAVEN 3 and HAVEN 4 achieved similar Physical Health and Total scores from Week 13 onwards, regardless of baseline QoL scores.**
- **The proportion of participants with no missed work days increased to ≥90% with emicizumab prophylaxis in both HAVEN 3 and HAVEN 4.**
- **The HRQoL results seen here are consistent with those seen in the HAVEN 1 study,[3] indicating that emicizumab improves aspects of HRQoL regardless of inhibitor status.**

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