

Safety and Efficacy of Emicizumab ▼ in Persons With Haemophilia A With / Without FVIII Inhibitors: Pooled Data from Four Phase III Studies (HAVEN 1–4)

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Key takeaways

- With nearly 3 years of follow-up, emicizumab maintained low bleed rates in persons with haemophilia A of all ages, with and without FVIII inhibitors; almost all target joints resolved
- Emicizumab remains well tolerated over long-term follow-up, and no new safety concerns were identified in this analysis

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. These should be reported to the Regulatory Authorities in your country according to your national requirements.



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INTERACTIVE

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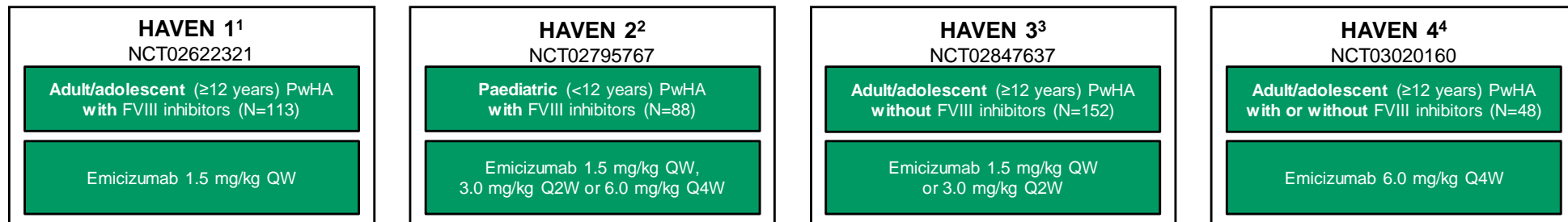
Disclosures*

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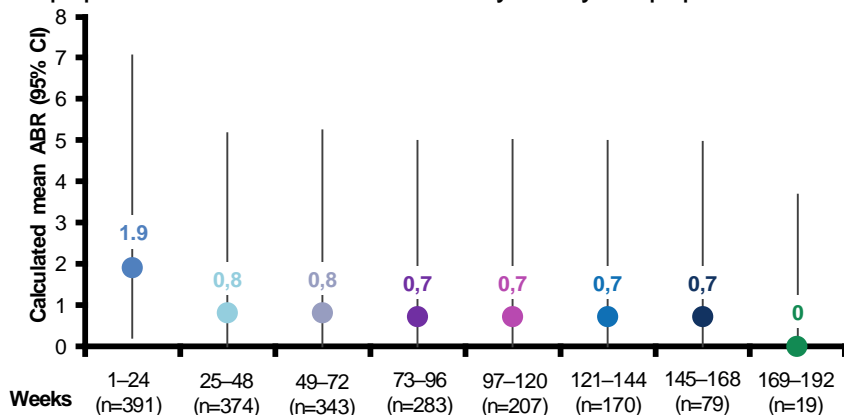
*See manuscript (Callaghan MU, et al. *Blood* 2020; published online) for all authors' disclosures.



Pooled data from HAVEN 1–4 Phase III studies demonstrated durable efficacy of emicizumab in PwHA (data cut-off 15 May, 2020) following 970.3 patient-years of exposure



- Participants (N=401) had a median (range) age of 28.0 (1–77) years; in total, 400* participants were included in the efficacy-analysis population and 399* in the safety-analysis population



- At clinical cut-off, 95.1% (n=504/530) of target joints in 226 evaluable PwHA resolved[‡] with emicizumab prophylaxis
- Among 226 evaluable PwHA who had at least one target joint at baseline and received at least 52 weeks of emicizumab prophylaxis, 89.4% (n=202/226) had zero target joint bleeds
- The percentage of PwHA with zero treated bleeds increased over the first year and remained >80% thereafter. After Week 24, at least 97% of PwHA had ≤3 bleeds in each 24-week treatment interval

*One participant in HAVEN 3 assigned to 'no prophylaxis' was lost to follow-up prior to the switch to emicizumab and was, therefore, not treated and excluded from the efficacy and safety analysis. One participant in HAVEN 1 discontinued prior to emicizumab treatment and was excluded from the safety analyses. [‡]Determined using a negative-binomial regression model. [‡]Target joint resolution: ≤2 spontaneous or traumatic bleeding events in an existing target joint within a continuous 52-week period.⁵ ABR, annualised bleed rate; CI, confidence interval; FVIII, factor VIII; PwHA, persons with haemophilia A; QW, once weekly; Q2W, once every 2 weeks; Q4W, once every 4 weeks.

- Oldenburg J, et al. *N Engl J Med*. 2017;377:809–18;
- Young G, et al. *Blood*. 2019;134:2127–38;
- Mahlangu J, et al. *N Engl J Med*. 2018;379:811–22;
- Pipe SW, et al. *Lancet Haematol*. 2019;6:e295–e305;
- Blanchette VS, et al. *J Thromb Haemost*. 2014;12:1935–9.

During 970 patient-years of exposure, emicizumab had a favourable long-term safety profile with no new or unexpected signals



All AEs	Total population (N=399)
At least one AE, n (%)	381 (95.5)
Local injection-site reaction, n (%)	111 (27.8)
Treatment-related AE, n (%)	139 (34.8)*
Grade ≥3 AE†, n (%)	87 (21.8)
AE leading to withdrawal from treatment, n (%)	5 (1.3)
Serious AE, n (%)	93 (23.3)
AE with fatal outcome, n (%)	1 (0.3)‡



AEs of special interest	Total population (N=399)
Systemic hypersensitivity/anaphylactic reaction,§ n (%)	1 (0.3)
TE associated with concomitant aPCC use, n (%)	2 (0.5)
Other TE, n (%)	2 (0.5)
Device occlusion of a peripherally inserted central catheter	1 (0.3)¶
Myocardial infarction	1 (0.3)‡
TMA associated with concomitant aPCC use, n (%)	3 (0.8)€
Other TMA, n (%)	0 (0.0)

- No participants discontinued due to AEs beyond the 5 previously described in the primary analyses¹⁻⁴
- The device occlusion and MI events^{¶‡} were assessed by the Investigators as unrelated to emicizumab. Both events resolved, and each individual continued emicizumab



*One participant in HAVEN 4 was missing data on AE relationship to treatment. †Adverse events were graded according to the World Health Organization toxicity grading scale. ‡Death of one participant in HAVEN 1 was caused by rectal haemorrhage. §Assessed using Sampson criteria and includes all participants who experienced indicative symptoms. One participant was identified through algorithmic analysis as potentially having a systemic hypersensitivity/anaphylactic/anaphylactoid reaction (he had experienced symptoms of abdominal pain and cough); however, medical review of the case showed that Sampson criteria were not met. ¶The person with the non-serious device occlusion had a history of device-related thrombosis before receiving emicizumab. ‡The person with MI was >65 years, had previously undiagnosed coronary artery disease, was treated for the event, and recovered with reduced heart function. €No new cases of thrombotic microangiopathy have been reported since the primary study analyses. Data cut-off: 15 May, 2020. AE, adverse event; aPCC, activated prothrombin complex concentrate; MI, myocardial infarction; TE, thrombotic event; TMA, thrombotic microangiopathy.

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;
5. Khoo L, et al. *Haemophilia.* 2020;26:e340–42.

Conclusions



With nearly 3 years of follow-up, emicizumab maintained low bleed rates in PwHA of all ages, with and without FVIII inhibitors



ABRs decreased over time and the proportion of participants with zero treated bleeds increased; almost all target joints resolved



Emicizumab remains well tolerated over long-term follow-up, and no new safety concerns were identified in this analysis



Long-term safety and efficacy data for emicizumab are consistent with the findings of the primary analyses and indicate continued reductions in bleeding with long-term treatment

Please see full publication (Callaghan MU, et al. *Blood* 2020; doi: [10.1182/blood.2020009217](https://doi.org/10.1182/blood.2020009217)) for further details