ABS141

Low immunogenicity of emicizumab ▼ in persons with haemophilia A

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Disclosures

CS: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd; **TE**: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: Roche Diagnostics GmbH; **EA**: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: Finnish Health Authority, Previous employee of: F. Hoffmann-La Roche Ltd; **SC**: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd; **EF**: Employee of: F. Hoffmann-La Roche Ltd; **CP**: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd; **KY**: Employee of: Chugai Pharmaceutical Co., Ltd; **AK**: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd; **MH**: Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: Roche Canada, Previous employee of: PRO Unlimited; **MN**: Employee of: F. Hoffmann-La Roche Ltd; **IP-P**: Employee of: Genentech, Inc.; **TC**: Shareholder of: Genentech, Inc., F. Hoffmann-La Roche, Ltd, Employee of: Spark Therapeutics, Inc., Previous employee of: Genentech, Inc., F. Hoffmann-La Roche, Ltd.

Key takeaways

- Emicizumab is associated with a low incidence of anti-drug antibody (ADA) development; importantly, ADAs with neutralising potential occurred in <1% of participants in Phase III clinical trials
- The efficacy of emicizumab was not impacted by ADAs without neutralising potential and the presence of ADAs did not impact the overall safety profile of emicizumab

▼ 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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This analysis of clinical trial data assesses the immunogenicity of emicizumab and the impact of ADAs on its efficacy and safety in PwHA

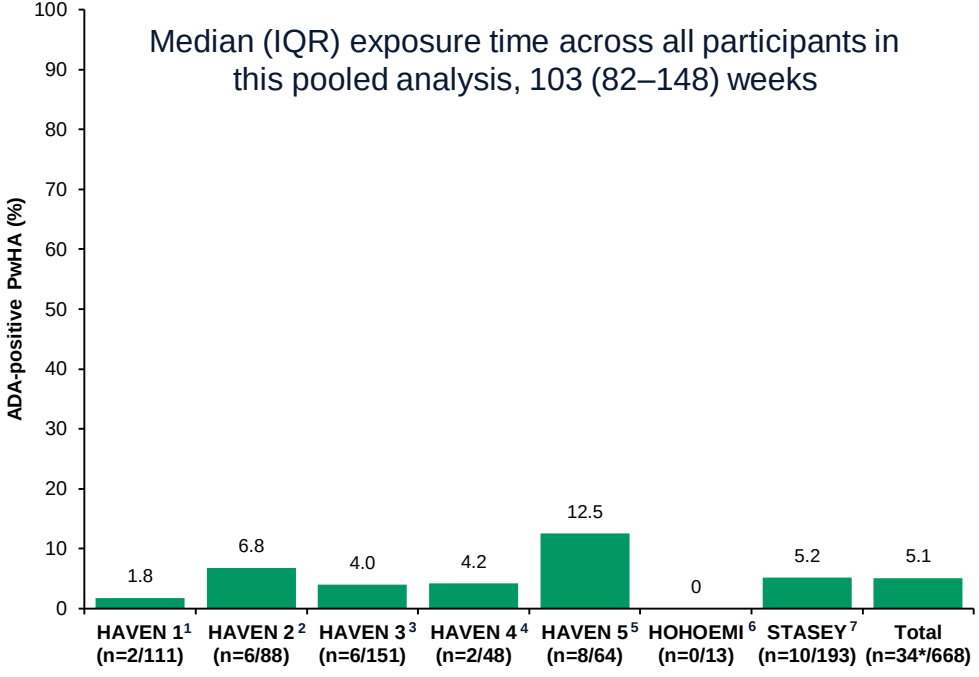
Methods

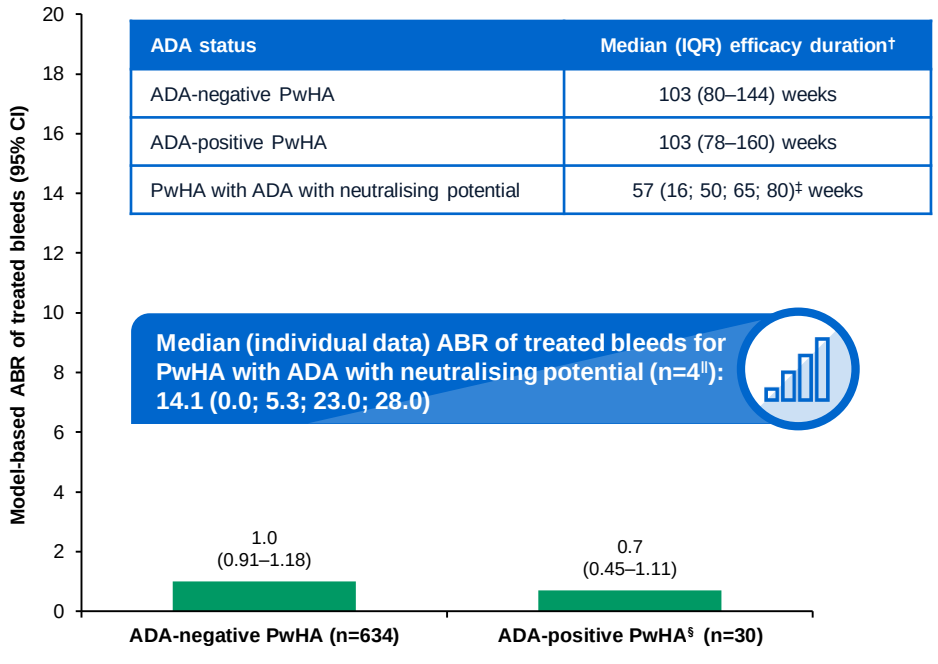
- **Studies:** HAVEN clinical development programme (HAVEN 1–4[1–4]), along with three additional Phase III/IIIb studies (HAVEN 5,[5] HOHOEMI,[6] and STASEY[7])
- **Participants:** PwHA with ≥1 ADA assessment post-emicizumab exposure were included in the analysis*
- **Sample collection:** Blood samples were collected at baseline and at regular intervals during emicizumab treatment or 24 weeks post-last dose if discontinued
- **Assays:** ADAs were detected using an ELISA†
  - ADAs associated with a decline in PK and corresponding reduced PD effects were classified as ADAs with neutralising potential
  - Association between ADAs and bleeds/AEs were examined

HAVEN 1, NCT02622321; HAVEN 2, NCT02795767; HAVEN 3, NCT02847637; HAVEN 4, NCT03020160; HAVEN 5, NCT03315455; HOHOEMI, JapicCTI-173710; STASEY, NCT03191799.
*Cut-off dates were: 15 May, 2020 (HAVEN 1–4 and STASEY), 21 June, 2019 (HAVEN 5) and 3 July, 2019 (HOHOEMI); †ADA positivity was assessed according to the recommendations of the American Association of Pharmaceutical Scientists Therapeutic Protein Immunogenicity Focus Group.[8]
ADA, anti-drug antibody; AE, adverse event; ELISA, enzyme-linked immunosorbent assay; PD, pharmacodynamics; PK, pharmacokinetics; PwHA, persons with haemophilia A.

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. Wang S, et al. ISTH 2020;Poster # PB0957;
6. Shima M, et al. *Haemophilia.* 2019;25:979–87;
7. Jiménez-Yuste V, et al. ISTH 2020;Poster # PB0958;
8. Shankar G, et al. *AAPS J.* 2014;16:658–73.

Emicizumab is associated with a low incidence of ADAs and ADAs without neutralising potential did not impact emicizumab efficacy in PwHA





ADA status	Median (IQR) efficacy duration†
ADA-negative PwHA	103 (80–144) weeks
ADA-positive PwHA	103 (78–160) weeks
PwHA with ADA with neutralising potential	57 (16; 50; 65; 80)‡ weeks

Median (individual data) ABR of treated bleeds for PwHA with ADA with neutralising potential (n=4[‖]): 14.1 (0.0; 5.3; 23.0; 28.0)

*ADAs reported in 14/34 (41.2%) participants were detected only once; †The start of the efficacy period for each participant was the first day with available data and the end of the efficacy period was the day of clinical cut-off or treatment discontinuation; ‡Median (individual data); §Excluding PwHA with ADAs with neutralising potential; ‖HAVEN 1, n=1 participant; HAVEN 2, n=2 participants; HAVEN 5, n=1 participant (n=4/668, 0.6% of total population); of these four, one participant in HAVEN 2 discontinued emicizumab due to a lack of efficacy and resumed pre-study treatment without complication.
ADA, anti-drug antibody; CI, confidence interval; IQR, interquartile range; PwHA, person with haemophilia A.

1. Oldenburg J, et al. *N Engl J Med*. 2017;377:809–18;
2. Young G, et al. *Blood*. 2019;134:2127–38;
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No notable differences in safety profile were detected between ADA-positive and ADA-negative PwHA

	ADA-negative PwHA (n=634)	ADA-positive PwHA (n=34)
Median (IQR) duration of exposure,* weeks	103 (83–148)	100 (55–159)
PwHA with ≥1 AE, n (%)	575 (90.7)	31 (91.2)
PwHA with ≥1 treatment-related AE, n (%)	187 (29.5)	11 (32.4)
PwHA with ≥1 SAE, n (%)	122 (19.2)	7 (20.6)
PwHA with ≥1 treatment-related SAE, n (%)	6 (0.9)	1 (2.9)†
PwHA with ≥1 ISR, n (%)	132 (20.8)	10 (29.4)
PwHA with ≥1 hypersensitivity, anaphylactic or anaphylactoid reaction, n (%)	2 (0.3)	0 (0.0)

Emicizumab is associated with a low incidence of ADA development; importantly, ADAs with neutralising potential occurred in <1%‡ of participants

The efficacy of emicizumab was not impacted by ADAs without neutralising potential

ADAs did not impact the safety of emicizumab prophylaxis in PwHA

*Safety data are for the period of emicizumab prophylaxis only; †Participant (from HAVEN 2) tested positive for ADAs with neutralising potential and discontinued emicizumab due to a lack of efficacy and resumed pre-study treatment without complication; ‡A total of 4/668 (0.6%) of participants evaluable for immunogenicity analysis had ADAs with neutralising potential.
ADA, anti-drug antibody; AE, adverse event; CI, confidence interval; IQR, interquartile range; ISR, injection-site reaction; PwHA, person with haemophilia A; SAE, serious adverse event.