PO115

# Assessment of treatment schedule, factor VIII trough level, and area under the curve for efanesoctocog alfa vs an extended half-life FVIII comparator: a modelling approach

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## CONCLUSIONS

- Model results demonstrate that **AUC and trough levels are greater using a once-weekly efanesoctocog alfa** 50 IU/kg prophylaxis schedule versus 50 IU/kg of efmoroctocog alfa every 4 days, **while reducing injection frequency and weekly IU consumption.**
- **The injection frequency of efmoroctocog alfa would have to be increased 3.0- to 3.5-fold, with a 3.2-fold increase in weekly IU consumption,** in order to achieve the AUC and trough level observed with efanesoctocog alfa over a 1-week period.

## INTRODUCTION

- Haemophilia A (HA) is a rare, congenital bleeding disorder caused by deficiency in clotting factor VIII (FVIII), classified as mild (>5-40 IU/dL), moderate (1-5 IU/dL) or severe (<1 IU/dL).[1]
- HA often results in bleeding, primarily into joints and muscles, causing swelling and acute pain,[2] with risk of spontaneous bleeding in severe or moderate forms.[3–5]
- Repeated joint bleeding can lead to haemophilic arthropathy, causing chronic pain, mobility restrictions and joint deformity, diminishing health-related quality of life and increasing the psychosocial burden of HA.[3,6–9]
- Standard of care (SoC) for severe haemophilia A (SHA) comprises routine prophylaxis (PPx) with replacement FVIII concentrates or non-factor replacement therapies.
- PPx with replacement FVIII aims to maintain FVIII levels ≥3-5 IU/dL, to avoid breakthrough bleeding events.[2]
- Currently available FVIII PPx approaches can sustain FVIII levels in the non-haemophilia range (>40 IU/dL) for a limited time and require frequent administration, causing considerable treatment burden.[10]
- In clinical trials, efanesoctocog alfa has sustained higher FVIII levels for longer durations versus SoC, with the non-haemophilia range maintained in adults for approximately 4 days and a trough of 18 IU/dL, on a once weekly (QW) 50 IU/kg schedule.[11]

## AIMS

- The primary aim was to investigate the differences in area under the curve (AUC) and trough levels between QW 50 IU/kg efanesoctocog alfa (Altuvoct) and a SoC prophylaxis regimen.
- Secondary aims were to estimate dosage and frequency of injection for SoC comparator treatment to achieve equivalent AUC / trough levels to QW 50 IU/kg efanesoctocog alfa.
- Here we present the results of a PK comparison with efmoroctocog alfa (Elocta) in adults with SHA on PPx.

## METHODS

- A pharmacokinetic simulation model was developed to compare weekly AUC (h*IU/dL) and trough level for QW 50 IU/kg efanesoctocog alfa and differing treatment schedules of efmoroctocog alfa in adults with SHA on PPx.
- Steady-state (SS) peak and trough FVIII levels for efmoroctocog alfa were estimated using half-life (HL) and incremental recovery from the Summary of Product Characteristics (SmPC) alongside dose (IU/kg) and injection frequency and were calculated based on the number of HLs elapsed between injections.[11]
- Peak and trough levels were modelled for 10 injections for comparator FVIII regimens, accounting for accumulation with each injection, at which point the regimen's peak and trough were observed to have stabilised and reached SS. A FVIII level of 0 IU/dL trough was assumed at first injection.
- SS-HL for efanesoctocog alfa was calculated using SS peak (150 IU/dL) and trough (18 IU/dL) in adult patients sourced from the SmPC, as SS-HL was not available within the SmPC.[12]
- Weekly AUC was calculated using SS peak and trough FVIII levels. For efanesoctocog alfa, AUC was calculated over a single administration, while for efmoroctocog alfa it was calculated as the total AUC for all administrations occurring within the examined week.
- Regimens required for efmoroctocog alfa to achieve AUC and trough levels equivalent to efanesoctocog alfa were calculated by estimating AUC and trough levels for all possible comparator treatment regimens (within SmPC ranges) and identifying those providing levels equivalent to QW 50 IU/kg efanesoctocog alfa.

## RESULTS

### Standard of care comparison

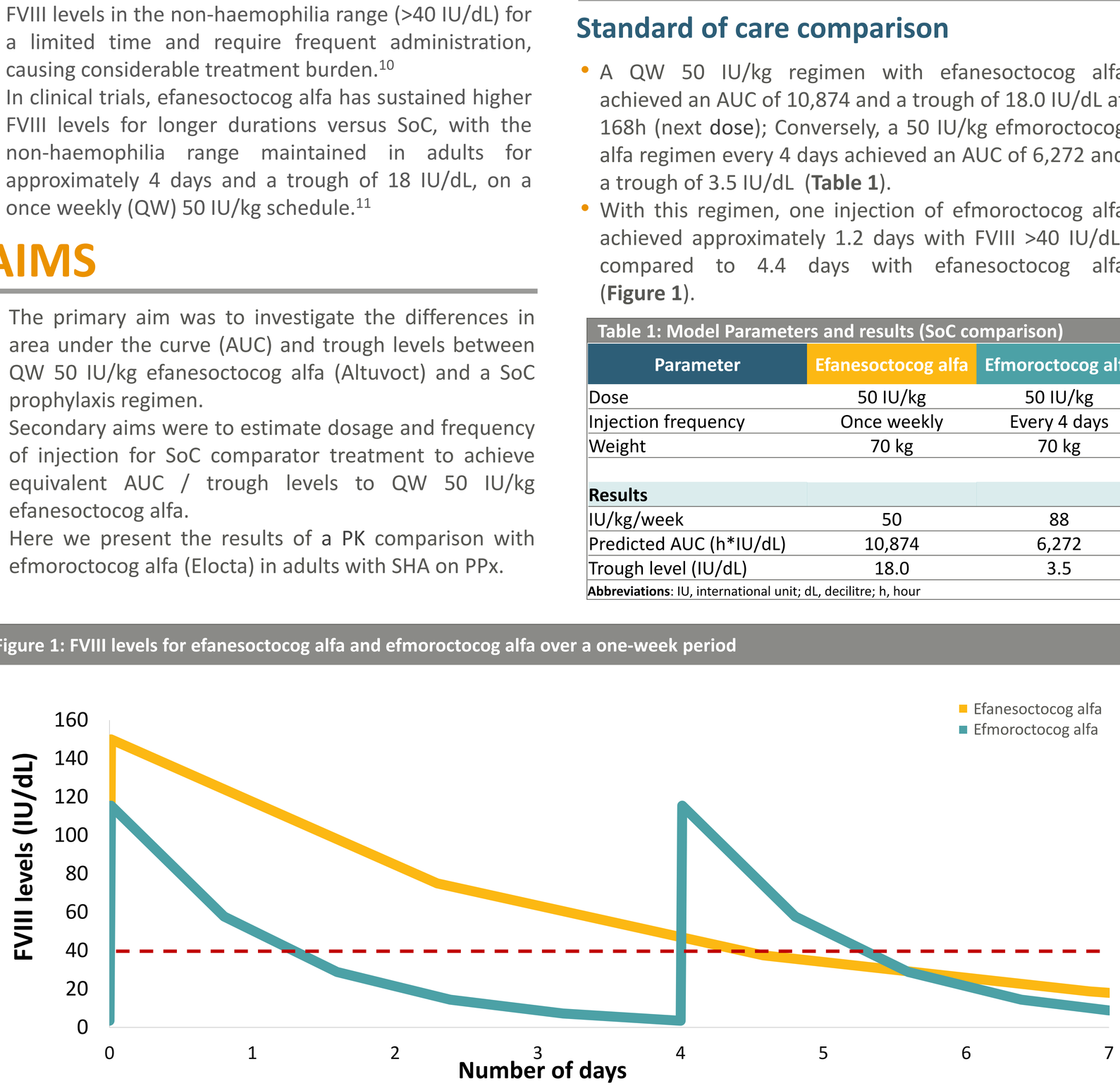
- A QW 50 IU/kg regimen with efanesoctocog alfa achieved an AUC of 10,874 and a trough of 18.0 IU/dL at 168h (next dose); Conversely, a 50 IU/kg efmoroctocog alfa regimen every 4 days achieved an AUC of 6,272 and a trough of 3.5 IU/dL (**Table 1**).
- With this regimen, one injection of efmoroctocog alfa achieved approximately 1.2 days with FVIII >40 IU/dL, compared to 4.4 days with efanesoctocog alfa (**Figure 1**).

**Table 1: Model Parameters and results (SoC comparison)**

| Parameter | Efanesoctocog alfa | Efmoroctocog alfa |
|---|---|---|
| Dose | 50 IU/kg | 50 IU/kg |
| Injection frequency | Once weekly | Every 4 days |
| Weight | 70 kg | 70 kg |
| **Results** | | |
| IU/kg/week | 50 | 88 |
| Predicted AUC (h*IU/dL) | 10,874 | 6,272 |
| Trough level (IU/dL) | 18.0 | 3.5 |

**Abbreviations**: IU, international unit; dL, decilitre; h, hour

**Figure 1: FVIII levels for efanesoctocog alfa and efmoroctocog alfa over a one-week period**




### Equivalent AUC

- More frequent injections of efmoroctocog alfa using a regimen of 46 IU/kg every other day (weekly consumption 161 IU/kg) would be required to achieve an AUC equivalent to once-weekly efanesoctocog alfa; in this scenario, the trough level for efmoroctocog alfa would be 21.6 IU/dL compared to 18.0 IU/dL for efanesoctocog alfa (**Table 2**).
- This efmoroctocog alfa regimen would provide 1.3 days at FVIII levels >40 IU/dL with one injection (**Figure 2**).

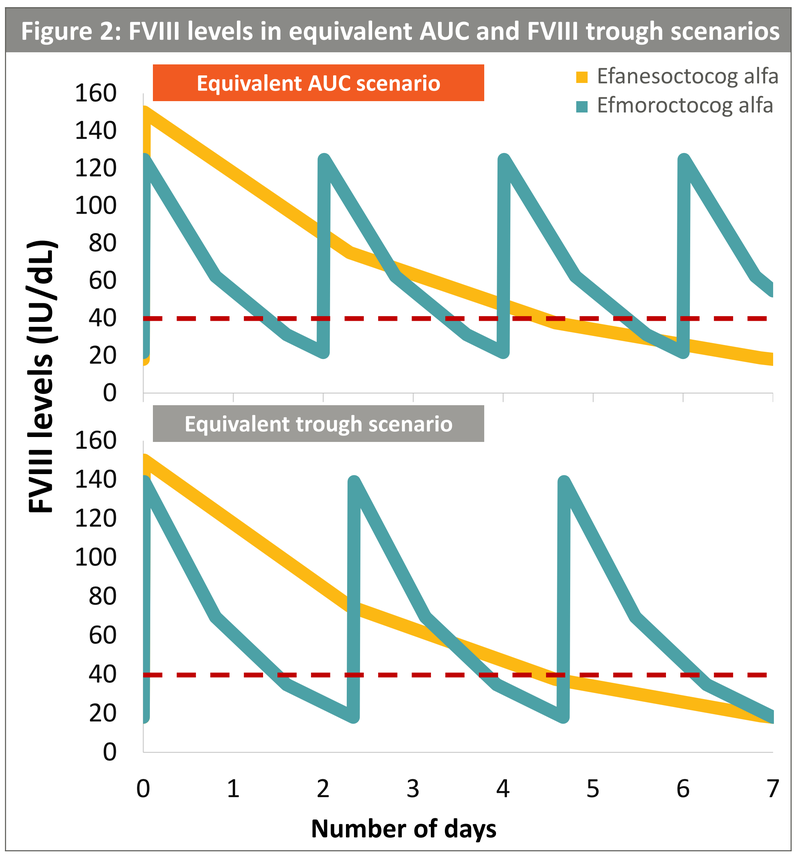
### Equivalent FVIII trough

- Efmoroctocog alfa would have to be given with a regimen of 54 IU/kg 3 times/week (weekly consumption 162 IU/kg) to achieve an equivalent FVIII trough level (18.0 IU/kg) to efanesoctocog alfa, and a weekly AUC of 10,376, compared to 50 IU/kg and 10,874 with efanesoctocog alfa (**Table 2**).
- With one injection, this regimen would achieve 1.4 days at FVIII levels >40 IU/dL (**Figure 2**).

**Table 2: Scenario analyses results**

| Parameter | Efmoroctocog alfa equivalent AUC | Efmoroctocog alfa equivalent trough |
|---|---|---|
| Weight | 70 kg | 70 kg |
| Target AUC & trough | AUC 10,874 | FVIII trough 18.0 |
| **Results** | | |
| Dosage (IU/kg) | 46 | 54 |
| Injection frequency | Every other day | 3 x week |
| IU/kg/week | 161 | 162 |
| Predicted AUC (h*IU/dL) | 10,895 | 10,376 |
| Trough level (IU/dL) | 21.6 | 18.0 |

**Figure 2: FVIII levels in equivalent AUC and FVIII trough scenarios**




## REFERENCES

**1**. Blanchette, V. S. et al. *JTH* 12, 1935–1939 (2014). **2**. Srivastava, A. et al. *Haemophilia* 26, 1–158 (2020). **3**. O'Hara, J. et al. *HRQOL* 16, 84 (2018). **4**. Iorio, A. et al. *Ann. Intern. Med.* 171, 540–546 (2019). **5**. White, G. C. et al. *Thromb. Haemost.* 85, 560 (2001). **6**. Rodriguez-Merchan, E. C. *Adv. prev. med.* 2012, 201271 (2012). **7**. Witkop, M. et al. *Haemophilia* 23, 556–565 (2017). **8**. Ferri Grazzi, E. et al. *Haemophilia* 30, 743–751 (2024). **9**. Ferri Grazzi, E. et al. *HRQOL* 22, 58 (2024). **10**. Okaygoun, D., Oliveira, D. D., Soman, S. & Williams, R. J. Biomed. Sci. 28, 64 (2021). **11**. Swedish Orphan Biovitrum AB. Package Insert ALTUVOCT. (2024). **12**. Swedish Orphan Biovitrum AB. Elocta: EPAR - Product Information. (2021).

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## DISCLOSURES

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