Value of Hemophilia Drug Treatment Using Analysis of the Area Under the Curve

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CONCLUSION

- **Results from this updated analysis show larger area under the plasma level curves (AUCs) for extended half-life (EHL) compared with standard half-life (SHL) products in all scenarios modeled, with damoctocog alfa pegol having the largest AUC**
- **These results suggest that EHLs may offer longer infusion intervals due to greater Factor VIII (FVIII) levels over time**

INTRODUCTION

- **Standard of care for hemophilia A is prophylaxis with recombinant FVIII replacement therapy[1,2]**
- **Conventional SHL products for the treatment of hemophilia have similar characteristics and thus are considered similar in effect[1]**
- **Due to the advent of EHL products, the relationship between dose, dosing intervals, and treatment outcomes is likely to differ between products[1]**
- **AUC quantifies FVIII levels over time after infusion and provides an outcome-oriented approach to product comparison[2]**
- **This poster aims to present an updated analysis using AUCs to indirectly compare most marketed products, now with additional data[3]**

References

1. Berntorp E, et al. *Haemophilia*. 2016;22:389–96.
2. Persson S, et al. *Haemophilia*. 2022;1–11.
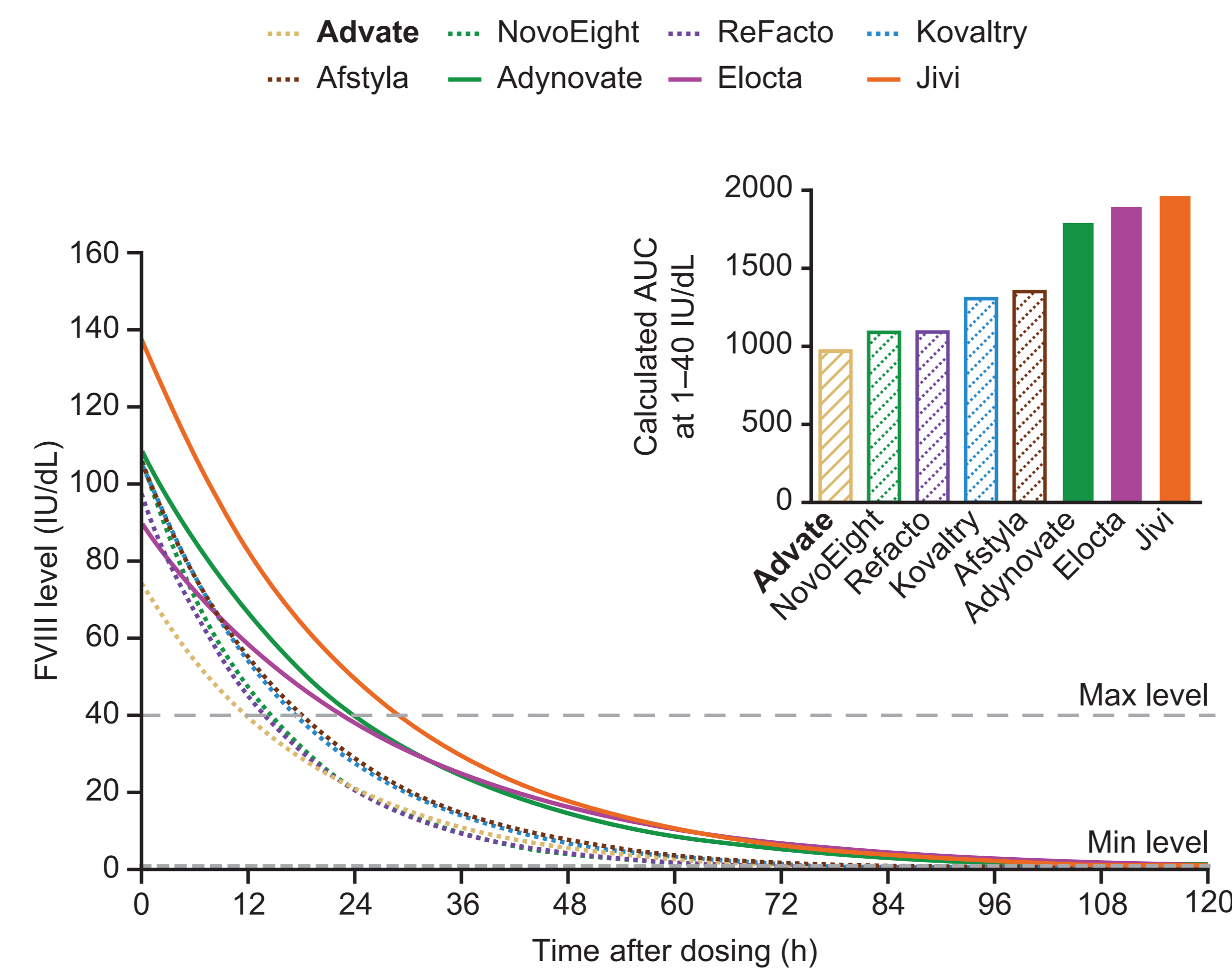3. Solms A, et al. EAHAD 2022. *Haemophilia* (P092).

METHODS

- Pooled pharmacokinetic data from 9 clinical cross-over, head-to-head studies, were indirectly compared[2]
- In this scenario, comparators included 3 EHL and 5 SHL products. Octocog alfa (Advate) was defined as the common comparator (anchor) (**Figure 1**)
- Data were extracted from the studies as the mean FVIII level in the blood at each sampling point, and AUC was calculated for all products using a loglinear continuous function
- Results are presented at 5 ranges of predefined minimum and maximum levels of FVIII (0–40 IU/dL). A sensitivity analysis was performed to investigate the effects of assay type and dose-adjustment to 50 IU/kg

Figure 1: INVESTIGATED DRUGS INCLUDED IN THE COMPARISON (WITH ADVATE AS ANCHOR)
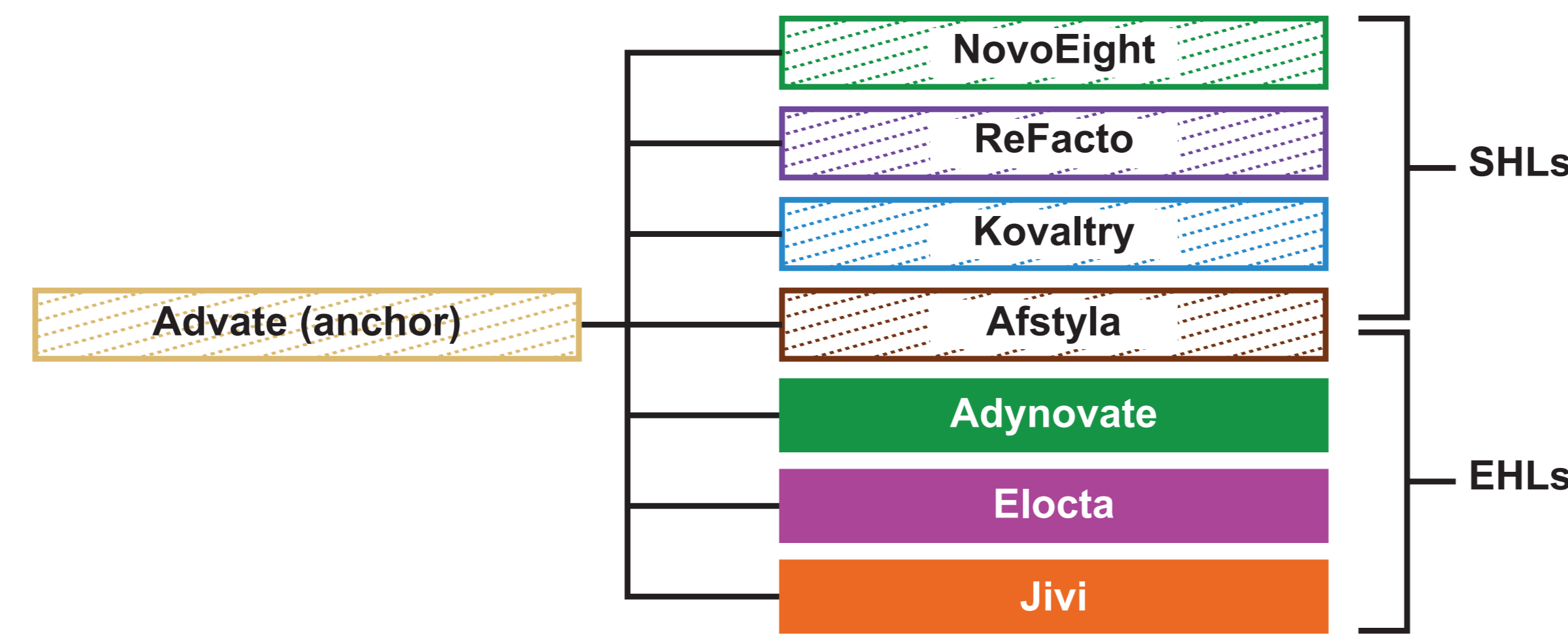
EHL, extended half-life; SHL, standard half-life.

RESULTS

- Estimated AUC for all products compared with octocog alfa (Advate) in base-case analysis are shown in **Figure 2**
- Damoctocog alfa pegol (Jivi) and efmoroctocog alfa (Elocta) had the largest AUCs compared with octocog alfa (Advate) (+71%–90% and +66%–73%, respectively) depending on min/max range (**Table 1**)
- Other ranges were explored (3-40 IU/dL and 5-40 IU/dL) with similar findings
- After one-stage assay type and dose-adjustment sensitivity analyses, results remained robust and all EHLs still had larger AUC compared with Advate (**Figure 3 and Figure 4**)

Table 1: ESTIMATED AUC BY MINIMUM (0–10 IU/DL) AND MAXIMUM (40 IU/DL) FVIII LEVEL IN THE BASE-CASE ANALYSIS

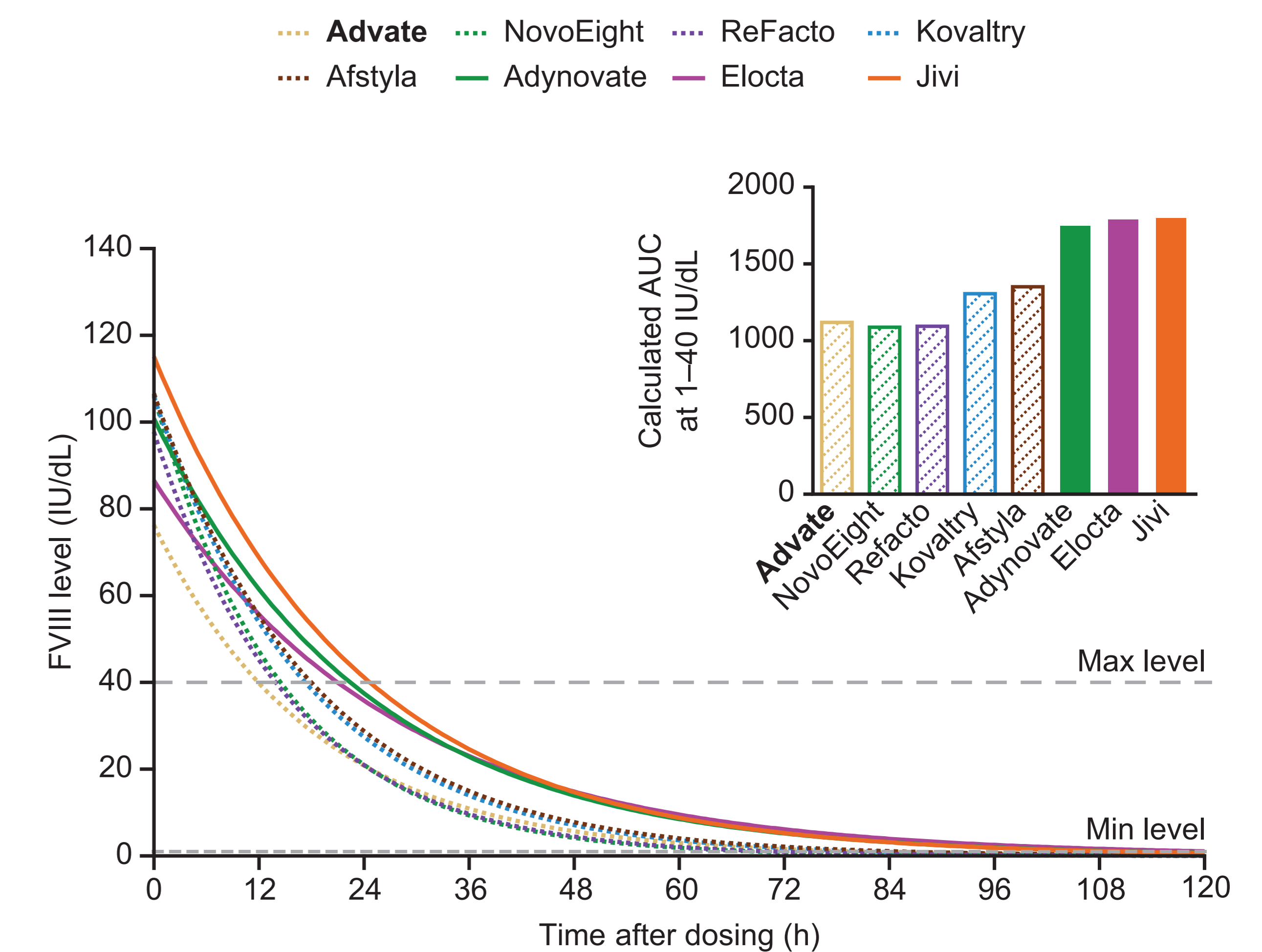| Minimum and maximum FVIII (IU/dL)						
	0-40		1-40		10-40	
	AUC	Diff. vs common comparator	AUC	Diff. vs common comparator	AUC	Diff. vs common comparator
Octocog alfa (Advate) (anchor)	1229	0%	969	0%	659	0%
EHL						
Damoctocog alfa pegol (Jivi)	2104	+71%	1965	+74%	1252	+90%
Rurioctocog alfa pegol (Adynovate)	1924	+57%	1788	+58%	1111	+69%
Efmoroctocog alfa (Elocta)	2045	+66%	1890	+68%	1142	+73%
SHL						
Turoctocog alfa (NovoEight)	1174	–4%	1090	–3%	674	+2%
Octocog alfa (Kovaltry)	1407	+15%	1306	+16%	808	+23%
Lonoctocog alfa (Afstyla)	1455	+18%	1351	+20%	836	+27%
Moroctocog alfa (Refacto)	1178	–4%	1092	–3%	668	+1%

AUC, area under the plasma level curve; EHL, extended half-life; FVIII, factor VIII; SHL, standard half-life; vs, versus.

Figure 2: GRAPH OF FVIII CURVES (1–40 IU/DL): ADVATE AS COMMON COMPARATOR

AUC, area under the plasma level curve; FVIII, factor VIII; h, hours.

Figure 3: GRAPH OF ONE-STAGE ASSAY ONLY FVIII CURVES (1–40 IU/DL): ADVATE AS COMMON COMPARATOR
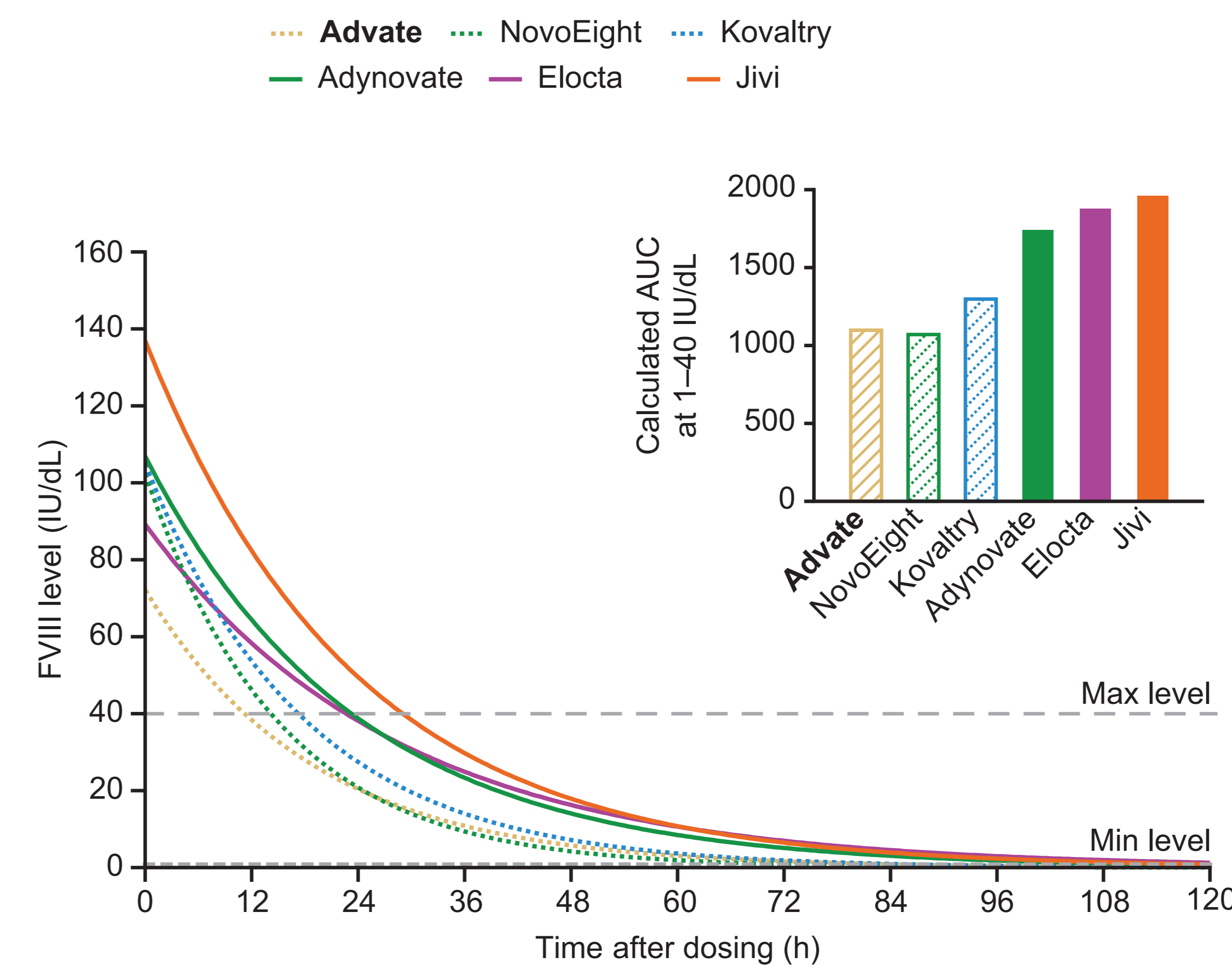
AUC, area under the plasma level curve; FVIII, factor VIII; h, hours.

Figure 4: GRAPH OF DOSE-ADJUSTED FVIII CURVES (1–40 IU/DL): ADVATE AS COMMON COMPARATOR

AUC, area under the plasma level curve; FVIII, factor VIII; h, hours.