Analysis of Pooled Real-world Utilisation and Outcomes Data of rVIII-SingleChain Compared with Standard and Extended Half-Life FVIII Products for Prophylaxis of Haemophilia A in France, Germany and Italy

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Introduction

- Haemophilia A (Haem A) is a rare clotting disorder caused by factor VIII (FVIII) deficiency, which can manifest in life-threating bleeding episodes[1,2]
- In clinical trials, prophylaxis with recombinant FVIII products, including recombinant factor VIII single-chain (rVIII-SingleChain), has shown efficacy in preventing breakthrough bleeds, which can lead to joint and muscle damage and have a negative impact on patient quality of life[1,3]
- Comparative real-world data of varied patient populations is essential for efficient utilisation across rFVIII products for Haem A prophylaxis[1]

Objectives

To evaluate real-world utilisation and outcomes of rVIII-SingleChain prophylaxis in patients with moderate or severe Haem A versus extended half-life (EHL; recombinant factor VIII Fc fusion protein [rFVIIIFc]) and standard half-life (SHL; octocog alfa and BAY 81-8973) FVIII products in France, Germany and Italy

Methods

- De-identified patient chart data of people with Haem A on prophylactic (≥6 months) rVIII-SingleChain, rFVIIIFc, octocog alfa or BAY 81-8973, were collected from France, Germany and Italy
- Patients with FVIII inhibitors, unknown bleed data, or known congenital or acquired coagulation disorders were excluded
- Endpoints included FVIII consumption (based on most recent infusion history), annualised bleeding rate (ABR), dosing frequency and percentage of patients with zero bleeds throughout the study period

STATISTICAL ANALYSIS

- Descriptive analyses were conducted for pooled data from all three countries, and participant cohorts were separated by country, disease severity and age (all patients and patients aged ≥18 years)
- Generalised linear models adjusted for covariates (age, weight, disease severity and country) were performed for FVIII consumption and ABR
- No adjustments were made for dose frequency or zero bleed data

Results

- A total of 549 patients with Haem A aged ≥12 years were included. Patient characteristics are shown in **Table 1**

Table 1: Patient characteristics

Patient characteristics	rVIII-SingleChain	rFVIIIFc	Octocog alfa	BAY 81-8973
n, pooled	118	175	117	139
n, France	34	61	46	33
n, Germany	42	42	42	44
n, Italy	42	72	29	62
Age (years), mean ± SD	35.0±13.7	30.3±16.0	30.5±14.3	29.5±18.1
Sex, male, n (%)	108 (91.5)	166 (94.9)	112 (95.7)	129 (92.8)
Weight (kg), mean ± SD	74.2±11.5	70.3±12.5	73.8±10.7	71.2±14.9
Severe Haem A, n (%)	76 (64.4)	114 (65.1)	60 (51.3)	87 (62.6)
Moderate Haem A, n (%)	42 (35.6)	61 (34.9)	57 (48.7)	52 (37.4)
Observation period (months), mean ± SD	31.9±13.7	34.1±12.8	37.3±11.9	30.9±12.4

Haem A, haemophilia A; kg, kilogram; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain; SD, standard deviation.

DOSING FREQUENCY

- ≤2x weekly dosing was seen in 47.4% of patients treated with rVIII-SingleChain compared with 63.4%, 23.1% and 36.0% of patients treated with rFVIIIFc, octocog alfa and BAY 81-8973, respectively
- In all three countries, rVIII-SingleChain demonstrated a similar rate of ≤2x weekly dosing (mean range: 42.9–53.0% of patients)

FVIII CONSUMPTION

- Adjusted mean FVIII consumption with rVIII-SingleChain, rFVIIIFc, octocog alfa and BAY 81-8973 was 84.2 IU/kg/week, 85.4 IU/kg/week, 100.4 IU/kg/week and 87.2 IU/kg/week, respectively (**Figure 1**)
- In patients with moderate Haem A, adjusted mean FVIII consumption with rVIII-SingleChain was **significantly** lower versus rFVIIIFc (58.4 IU/kg/week vs 76.8 IU/kg/week, p=0.018)
- By country analysis is shown in **Figure 2**

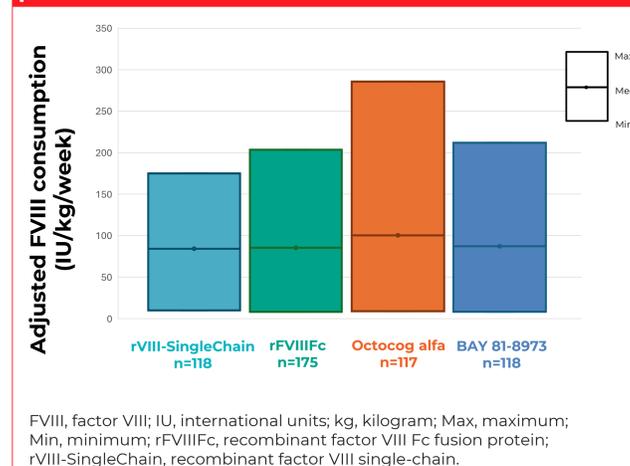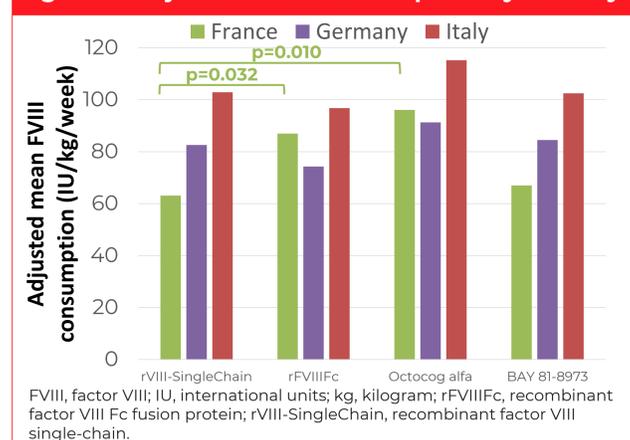#### Figure 1: Adjusted FVIII consumption by FVIII product

FVIII, factor VIII; IU, international units; kg, kilogram; Max, maximum; Min, minimum; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain.

Figure 2: Adjusted FVIII consumption by country

FVIII, factor VIII; IU, international units; kg, kilogram; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain.

BLEEDING OUTCOMES

- Adjusted mean ABR with rVIII-SingleChain was **significantly** lower versus BAY 81-8973 (1.06 vs 1.41; p=0.024) and comparable with octocog alfa (1.25; p=0.306) and rFVIIIFc (1.10; p=0.614)
- In patients with severe Haem A, adjusted mean ABR with rVIII-SingleChain was **significantly** lower versus BAY 81-8973 (1.09 vs 1.69, p=0.013). Comparisons with other products were not significantly different
- By country data (full data presented in **Figure 3**) found the adjusted mean ABR with rVIII-SingleChain to be **significantly** lower versus octocog alfa (p=0.013) and BAY 81-8973 (p=0.002) in Italy
- The percentage of patients with zero bleeds is shown in **Figure 4**
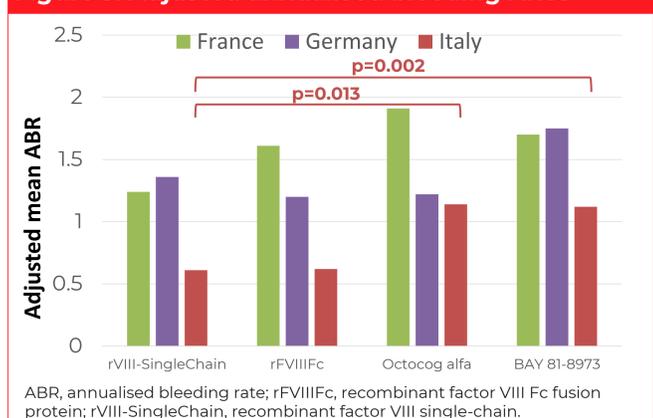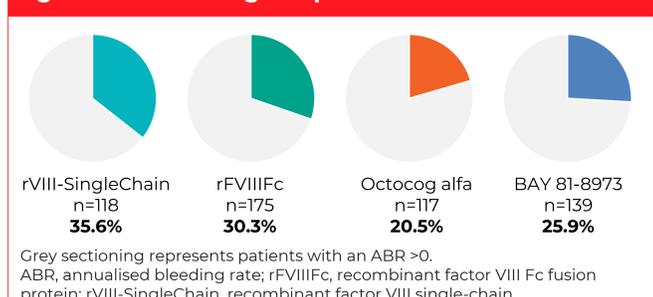
Figure 3: Adjusted annualised bleeding rates

ABR, annualised bleeding rate; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain.

Figure 4: Percentage of patients with zero bleeds

rVIII-SingleChain n=118 **35.6%** | rFVIIIFc n=175 **30.3%** | Octocog alfa n=117 **20.5%** | BAY 81-8973 n=139 **25.9%**

Grey sectioning represents patients with an ABR >0.
ABR, annualised bleeding rate; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain.

PATIENTS AGED ≥18 YEARS

- The sub-analysis of patients aged ≥18 years (n=415) supported the overall findings (**Table 2**)

Table 2: Sub-analysis of patients aged ≥18 years

Endpoint	rVIII-SingleChain (n=104)	rFVIIIFc (n=131)	Octocog alfa (n=91)	BAY 81-8973 (n=89)
Mean FVIII consumption (IU/kg/week)	82.2±46	88.4±36.2	89.4±52.9	90.9±37.9
p value	N/A	0.6044	**0.0425**	0.2407
Mean ABR ± SD	1.0±1.3	1.1±1.6	1.2±1.3	1.5±2.1
p value	N/A	0.4642	0.3841	**0.0211**
Patients with zero bleeds, n (%)	37 (35.6)	40 (30.5)	14 (15.4)	18 (20.2)
Patients treated with ≤2x weekly dosing, n (%)	49 (47.1)	79 (60.3)	25 (27.5)	29 (32.6)

ABR, annualised bleeding rate; FVIII, factor VIII; IU, international units; kg, kilogram; N/A, not applicable; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain; SD, standard deviation.

Conclusions

- **Real-world data from France, Germany and Italy show prophylaxis with rVIII-SingleChain may reduce consumption and improve bleed protection compared with SHL FVIII products, while providing comparable consumption and bleed protection to EHL FVIII products**

References

1. Olivieri M, et al. Curr Med Res Opin. 2022;38(7):1133–1139; 2. Olivieri M, et al. Eur J Haematol. 2020;104(4):310–317; 3.Mahlangu J, et al. Blood. 2016;128(5):630–637.

Acknowledgements

Abbreviations

ABR, annualised bleeding rate; EHL, extended half-life; FVIII, factor VIII; Haem A, haemophilia A; IU, international units; kg, kilograms; N/A, not applicable; rFVIIIFc, recombinant factor VIII Fc fusion protein; rVIII-SingleChain, recombinant factor VIII single-chain; SD, standard deviation; SHL, standard half-life.

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