PO056

rIX-FP prophylaxis use in paediatric patients with haemophilia B: French real-world evidence

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Introduction

- Recombinant factor IX albumin fusion protein (rIX-FP, IDELVION®; CSL Behring) is an extended half-life (EHL) factor IX (FIX) whose improved pharmacokinetic properties are due to genetic fusion with recombinant human albumin[1,2]
- In France, rIX-FP has been commercially available since April 2021, whilst recombinant factor IX Fc fusion protein (rFIXFc) has been available since 2018
- Clinical trials have shown that rIX-FP provides a good level of protection against bleeding in paediatric patients (<12 years old), as evidenced by low annualised bleeding rates (ABR) with prophylaxis every 7 days[2,3]
- Long-term follow-up is needed to assess the efficacy and safety of rIX-FP in routine clinical practice

Objective

The aim of this interim analysis was to gather real-world data on the efficacy and safety of rIX-FP for prophylactic use in paediatric patients with haemophilia B

Methods

- The OrPHEe study (NCT05086575) is a national, ambispective, observational, real-world study, which includes patients with haemophilia B in France, regardless of severity, who are currently receiving or have previously received rIX-FP for:
  - Long-term prophylaxis
  - Short-term prophylaxis to cover periods of high bleeding risk
  - On-demand treatment
  - Treatment during surgery
- Patients who met the inclusion criteria were enrolled for a period of two years and followed up for three years
- Data on treatment in the year prior to rIX-FP initiation were collected
- Dosing frequency, weekly consumption, and bleeds before and after switching to rIX-FP were analysed
- ABR and annualised spontaneous bleeding rates (AsBR) were calculated in patients on prophylaxis with a follow-up period of ≥6 months
- Data on the haemostatic efficacy of rIX-FP in preventing and treating non-surgical and surgical bleeding were collected
- The nature and incidence of adverse events (AEs), in particular serious AEs and treatment-related AEs, were recorded

Results

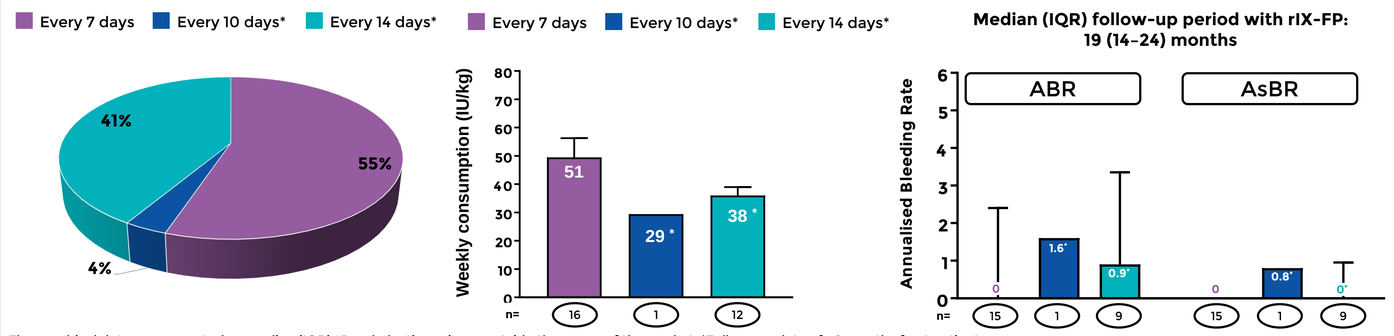
- Data were collected between October 2021 and February 2024
- In total, 166 patients receiving rIX-FP (including 106 patients receiving prophylaxis) were enrolled across 29 centres
- This interim analysis focused on the 29 patients aged <12 years old treated with rIX-FP prophylaxis
- Overall, 22 (76%) patients previously received prophylaxis
- One patient, previously treated 'on-demand', had a damaged joint when prophylaxis with rIX-FP was initiated
- Patient characteristics are shown in **Table 1**

Table 1. Characteristics of paediatric patients treated with rIX-FP prophylaxis

Characteristic	<12 years n=29
Median age of initiation of rIX-FP, years (range)	6 (0.8–11)
Median weight, kg (range)	24 (11–60)
Haemophilia B severity, n (%)	
Severe (<1 IU/dL)	26 (90)
Moderate (1–≤5 IU/dL)	3 (10)
Mild (5–<40 IU/dL)	0 (0)
Patients with target joints at initiation, n (%)	1 (3)
Previously on-demand, n (%)	7 (24)
Previous prophylaxis, n (%)	22 (76)
pdFIX (SHL)	0 (0)
rFIX (SHL)	4 (18)
rFIXFc	18 (82)

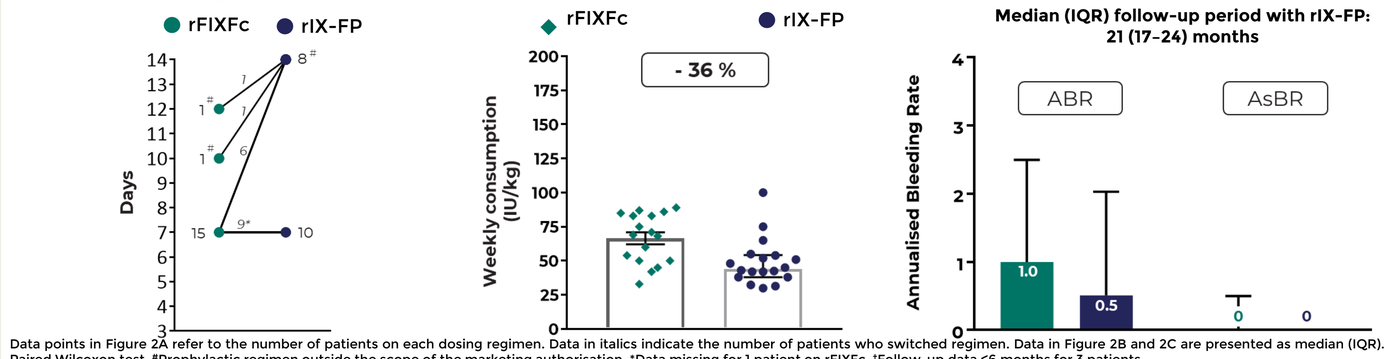
IU, international unit; pdFIX, plasma-derived factor IX; rFIX, recombinant factor IX; rIX-Fc, recombinant factor IX Fc fusion protein; rIX-FP, recombinant factor IX albumin fusion protein; SHL, standard half-life.

Figure 1. Overview of paediatric patients on rIX-FP prophylaxis



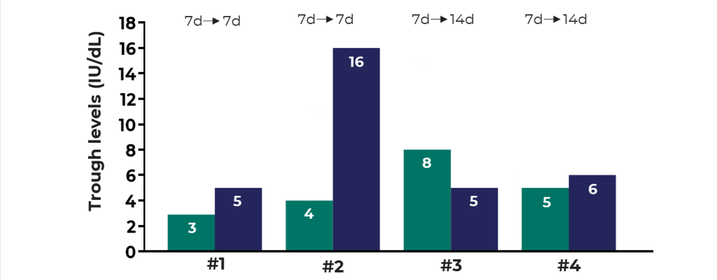
The graphical data are presented as median (IQR).*Prophylactic regimen outside the scope of the market. †Follow-up data of <6 months for 4 patients.
ABR, annualised bleeding rate; AsBR, annualised spontaneous bleeding rate; FIX, factor IX; IQR, interquartile range; IU, international unit; n, number; rIX-FP, recombinant factor IX albumin fusion protein.

Figure 2. Effect of switching from rFIXFc to rIX-FP prophylaxis



Data points in Figure 2A refer to the number of patients on each dosing regimen. Data in italics indicate the number of patients who switched regimen. Data in Figure 2B and 2C are presented as median (IQR). Paired Wilcoxon test. #Prophylactic regimen outside the scope of the marketing authorisation. *Data missing for 1 patient on rFIXFc. †Follow-up data <6 months for 3 patients.
ABR, annualised bleeding rate; AsBR, annualised spontaneous bleeding rate; IQR, interquartile range; IU, international unit; rFIXFc, recombinant factor IX Fc fusion protein; rIX-FP, recombinant factor IX albumin fusion protein.

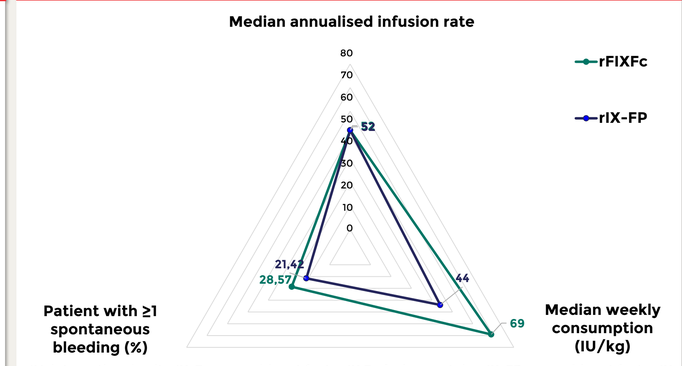
Figure 3. Changes in FIX trough levels in six patients



Weekly consumption (IU/kg)	71	65	89	100	83	48	85	42,5

Injection frequency and weekly FIX consumption are shown above and below the histogram, respectively. The number in each histogram represents the minimum level of FIX in that patient (#).
d, day; FIX, factor IX; IU: international unit.

Figure 4. Effect of switching to rIX-FP



IU, international unit; rIX-Fc, recombinant factor IX Fc fusion protein; rIX-FP, recombinant factor IX albumin fusion protein.

Results

POSOLOGY, EFFICACY AND SAFETY DATA OF rIX-FP PROPHYLAXIS

- Injection frequency, FIX consumption, ABR and AsBRs on rIX-FP prophylaxis are shown in **Figure 1**
- Median (IQR) interval between rIX-FP infusions was 7 (7–14) days
  - 13 patients had an infusion frequency of every ≥10 days
- Median (IQR) weekly rIX-FP consumption was 42.0 (38.0–53.0) IU/kg (n=29)
- Median (IQR) ABR and AsBR were 0.5 (0.0–2.2) and 0.0 (0.0–0.2), respectively
- During this period, 13 (45%) and 25 (86%) patients did not experience any total bleeds or spontaneous bleeds, respectively
- Overall, 26/27 (96%) investigators evaluated the effectiveness of rIX-FP prophylaxis as 'Excellent' or 'Good', and 27/27 (100%) evaluated the safety as 'Good' (data missing for two patients in both categories)
- One AE was reported and was considered related to rIX-FP (spontaneous haemarthrosis)

COMPARISON WITH PREVIOUS PROPHYLACTIC TREATMENT WITH rFIXFc

- Injection frequency, FIX consumption, and ABRs on previous prophylactic treatment (rFIXFc versus rIX-FP) are shown in **Figure 2**
- Mean (standard error of the mean) time between injections was 9.3 (0.7) days for rFIXFc and 11.6 (0.7) days for rIX-FP (p<0.01) **(Figure 2A)**
- Fourteen of seventeen patients (82%) switching from rFIXFc reduced their weekly consumption with rIX-FP
- Overall, median (IQR) weekly FIX consumption reduced from 69.0 (50.0–84.0) with rFIXFc to 44.0 (38.0–54.2) IU/kg with rIX-FP (p<0.01) (**Figure 2B**).
- Patients who switched from rFIXFc to rIX-FP prophylaxis maintained good protection against bleeds (**Figure 2C**)
- FIX trough levels increased in 3 of the 4 patients for whom data were available after switching to rIX-FP. Individual data are presented in **Figure 3**
- The effect of switching from rFIXFc to rIX-FP, in terms of annualised infusion rate, weekly consumption and percentage of patients with spontaneous bleeding, is summarised in **Figure 4**

Conclusions

- **This interim analysis of the OrPHEe study, the world's largest cohort of patients with haemophilia B treated with an EHL FIX, confirms the favourable efficacy and safety observed during clinical development in paediatric patients (<12 years old)**
- **Data also showed that some paediatric patients who switched to rIX-FP maintained a good level of protection against bleeds despite reductions in their injection frequency and FIX consumption**

References

1. Santagostino E et al. *Blood* 2012;120:2405–2411
2. Kenet G et al. *Thromb Haemost* 2016;116:659–668
3. Kenet G et al. *Thromb Haemost* 2020;120:599–606

Disclosures

FV declares COIs from Sobi, Roche, Pfizer, Takeda and CSL Behring. **AnH** has participated in clinical trials, advisory boards and symposia for CSL Behring, Roche, Sobi, LFB, Bayer, Takeda, Octapharma, Novo Nordisk and Sanofi. **YD** has received grants/research support from Bayer, Baxter, Baxalta, Novo Nordisk, CSL Behring, LFB, Pfizer, LEO Pharma, Octapharma and Stago; an educational grant from Takeda and honoraria from Bayer, Baxter, Novo Nordisk, CSL Behring, Sobi and Octapharma. **YH** has participated in clinical trials, advisory boards and symposia for CSL Behring, Roche, Sobi, LFB, Takeda, and Sanofi. **AbH** has been a consultant for Bayer, CSL Behring and Sobi. **AF** declares no COI. **CB** declares a COI for Sobi and Octapharma. **BF** declares a COI from Sobi, CSL Behring and Novo Nordisk. **COC** declares no COI. **MP** declares no COI. **HC** and **CM** are employees of CSL Behring. **AR** has received research support for his institution from CSL Behring and Roche/ Chugai, participated in clinical trials, advisory boards and symposia for Biomarin, CSL Behring, LFB, Novo Nordisk, Octapharma, Roche-Chugai and Sobi.

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