Long-term efficacy and safety of rIX-FP prophylaxis in adult patients with haemophilia B on a 21-day dosing regimen

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Introduction

- rIX-FP is a fusion protein genetically linking recombinant human coagulation factor IX with recombinant human albumin
- rIX-FP has an improved pharmacokinetic profile compared with standard FIX products, allowing a prolonged dosing interval in patients with haemophilia B

Aim

- To assess the efficacy and safety of a 21-day individualized prophylactic dosing interval in patients ≥18 years with severe haemophilia B

Methods

- As part of the PROLONG-9FP phase 3 clinical trial, patients received episodic treatment or routine prophylaxis with rIX-FP
  - In the extension study, all patients were on routine prophylaxis
- Patients began weekly treatment intervals with rIX-FP (35–50 IU/kg) and after 6 months, if they were well controlled, could extend to every 10 or 14 days (50–75 IU/kg)
  - Dosing intervals could be changed at any 6-month follow-up
- In the extension study, patients ≥18 years of age could switch to a 21-day regimen (100 IU/kg) if they were well controlled on a 14-day regimen for ≥6 months

Results

Patient characteristics

- In total, 59 adult/adolescent patients were treated with rIX-FP in the extension study
- Of those, 11 adults switched to a 21-day regimen; basic characteristics are shown in Table 1

Table 1. Patient characteristics

	21-day regimen (N=11)
Age, years	
Mean (SD)	40.2 (12.8)
Weight, kg	
Mean (SD)	69.4 (9.8)

SD, standard deviation

Change in dosing regimens during the clinical trial program

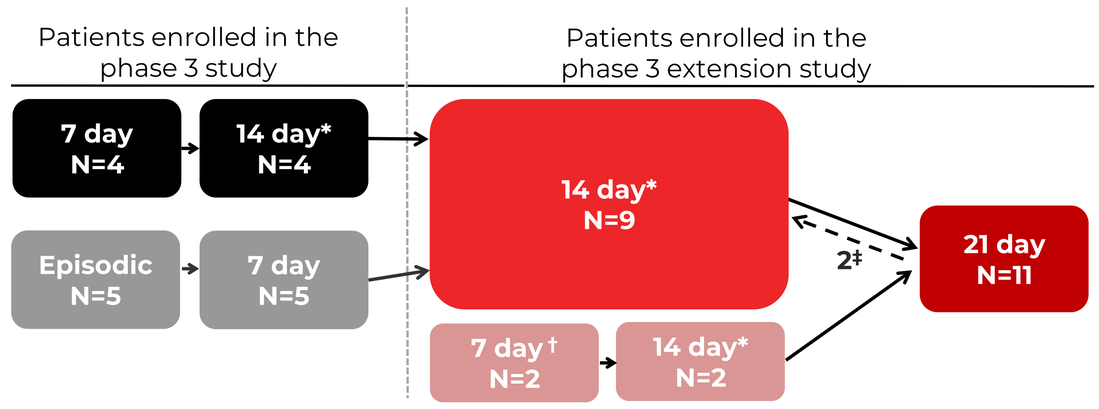
- Of the 11 adults who switched to a 21-day regimen, five patients were initially treated episodically (Figure 1)
- After 6 months on the 21-day regimen, two patients switched to a 14-day regimen
  - One patient chose to switch to a more frequent regimen after one traumatic bleed
  - One patient switched due to the occurrence of breakthrough bleeding

Bleeding rates

- Patients who switched to the 21-day regimen had a median annualized spontaneous bleeding rate of 0.0 throughout the study (Table 2)
  - 64% of these patients reported zero spontaneous bleeds

Results

Figure 1. Change in regimens as patients moved through the clinical trial program



*Prior to switching to the 14-day regimen, patients were required to have ≥6 months of rIX-FP treatment on their 7-day regimen, with no dose adjustments or spontaneous bleeding in the prior month
†Two patients were enrolled directly into the extension study following surgery
‡After 6 months of treatment on the 21-day regimen, two patients switched back to the 14-day regimen to reduce the frequency of bleeding

FIX consumption

- For all patients on the 21-day regimen, the total mean monthly consumption of rIX-FP was 146.9 IU/kg/month for a median of 21.5 months (range 5–37) of treatment (Table 2)
  - The mean monthly consumption of rIX-FP for these patients (n=11) treated on a 7-day regimen was 178.7 IU/kg/month, and on a 14-day regimen was 166.6 IU/kg/month (Table 2)

Safety data

- 10 patients reported adverse events (AEs) on the 21-day regimen with 89.7% (26/29) considered mild and 6.9% (2/29) considered moderate in intensity; 3.4% (1/19) were considered severe (peritonsillar abscess) and was reported 8 days after the last rIX-FP dose
- All AEs were unrelated to rIX-FP treatment
- No inhibitor, anaphylactic reaction or thromboembolic events were reported

Table 2. Treatment duration and bleeding rates in patients switching to a 21-day regimen

	Episodic (N=5)	7-day regimen (N=11)	14-day regimen (N=11)	21-day regimen (N=11)
Duration on regimen, days				
Mean (SD)	187.0 (10.2)	308.1 (145.4)	516.2 (413.5)	654.5 (333.8)
AsBR				
Mean (SD)	13.9 (7.9)	0.1 (0.5)	0.2 (0.6)	0.6 (1.4)
Median (range)	15.6 (11.7, 16.7)	0.0 (0.0, 1.6)	0.0 (0.0, 2.0)	0.0 (0.0, 4.7)
Patients with zero spontaneous bleeds, n (%)	0	8 (73)	6 (55)	7 (64)
ABR				
Mean (SD)	16.2 (9.0)	0.5 (0.8)	0.4 (0.8)	1.2 (1.6)
Median (range)	17.6 (2.0, 27.0)	0.0 (0.0, 1.9)	0.0 (0.0, 2.0)	0.3 (0.0, 4.7)

ABR, annualized bleeding rate; AsBR, annualized spontaneous bleeding rate; SD, standard deviation

Conclusion

This study demonstrated that a 21-day prophylaxis regimen with 100 IU/kg rIX-FP is an additional treatment option, with good efficacy and safety, for patients ≥18 years of age who are well controlled on a 14-day prophylaxis regimen

Author disclosures

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