Interim results of a Phase IIIb safety and efficacy extension study of a recombinant fusion protein linking coagulation factor IX with albumin (rIX-FP) in patients with hemophilia B

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Introduction

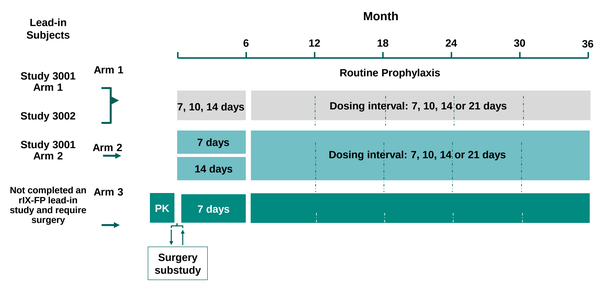
- rIX-FP is a fusion protein genetically linking recombinant human coagulation Factor IX with recombinant human albumin that has an improved pharmacokinetic profile, thus allowing less frequent dosing
- Two Phase III trials demonstrated the safety and efficacy of rIX-FP in previously treated patients (PTPs) with severe hemophilia B (FIX activity ≤2%) in those aged 12–65 years (study 3001, NCT01496274) and in those <12 years (study 3002, NCT01662531)

Objectives

- To investigate the long-term safety and efficacy of rIX-FP in patients with severe hemophilia B in a Phase IIIb, open-label, multicenter, extension study (NCT02053792)

Methods

- Patients completing studies 3001 or 3002 were included
- Treatment intervals could be extended to 10- or 14-days with 50-75 IU/kg of rIX-FP for all patients
- Adult patients (≥18 years) who were well controlled on a 14-day regimen could switch to a 21-day interval with 100 IU/kg of rIX-FP
- Primary outcome: number of patients developing inhibitors against FIX
- Secondary outcomes include clinical efficacy, monthly rIX-FP consumption, and overall adverse events (AEs)



Results

Demographics

- 83 patients from studies 3001 (n=52) and 3002 (n=24) have continued routine prophylaxis in the extension study
- 7 patients started prophylaxis following major surgery

Table 1. Baseline patient characteristics

	Adults (12–65 years) N=59	Children (<12 years) N=24	Total N=83
Age (years), mean (range)	36.0 (13–63)	7.0 (2–11)	27.7 (2–63)
<18 years, n (%)	5 (8.5)	24 (100)	29 (34.9)
≥18 years, n (%)	54 (91.5)	0	54 (65.1)
Race, n (%)			
White	45 (76.3)	23 (95.8)	68 (81.8)
Asian	12 (20.3)	0	12 (14.5)
Black	2 (3.4)	1 (4.2)	3 (3.6)
Ethnicity, n (%)			
Hispanic	0	2 (8.3)	2 (2.4)
Not hispanic	59 (100)	22 (91.7)	81 (97.6)
Geographic region, n (%)			
Africa	2 (3.4)	0	2 (2.4)
Asia	12 (20.3)	0	12 (14.5)
Europe	32 (54.2)	17 (70.8)	49 (59.0)
Middle East	11 (18.6)	4 (16.7)	15 (18.1)
North America	2 (3.4)	1 (4.2)	3 (3.6)
Oceania	0	2 (8.3)	2 (2.4)
HIV, n (%)	7 (11.9)	0	7 (8.4)
HBV, n (%)	3 (5.1)	0	3 (3.6)
HCV, n (%)	30 (50.8)	0	30 (36.1)

Safety

- Median exposure days (EDs) to rIX-FP in the extension study was 67 and was 136 in total across all rIX-FP studies
- More than 70 (84.3%) subjects have achieved 100 EDs
- No inhibitors or antibodies to rIX-FP

Prophylaxis intervals tested

- Over 45 out of 52 (87%) subjects (≥12 years) switched from weekly to 10- or 14-day interval
- 10 subjects (≥18 years) have switched from 14-day to 21-day interval
- 11 (46%) children (<12 years) have switched to 10- or 14-day interval

Disclosures

ES received honoraria for speaking and/or for consulting from CSL Behring, Bayer, Baxter/Baxalta, Pfizer, NovoNordisk, Roche, Sobi/Biogen Idec, Biotest, Kedrion, Octapharma and Grifols and received unrestricted research grants from NovoNordisk and Pfizer; CV, DW, YL, MS, GC, NB and IJ are employees of CSL Behring

Results (cont.)

Efficacy

- Low annualized spontaneous bleeding rates (AsBR) in all regimens

Table 2. AsBR rates in adults

AsBR, previous study (3001)	7-day regimen (N=40)	10-day regimen (N=7)	14-day regimen (N=21)	21-day regimen (N=0)
Median (IQR)	**0 (0, 0)**	**0 (0, 0)**	**0 (0, 1.0)**	
Estimated mean AsBR (95% CI)†	0.65 (0.37–1.13)	0.56 (0.27–1.17)	0.83 (0.38–1.77)	
Duration, median (days)	269	240	386	
AsBR, extension study (3003)	**7-day regimen (N=19)**	**10-day regimen (N=14)**	**14-day regimen (N=39)**	**21-day regimen (N=10)**
Median (IQR)	**0.85 (0, 2.9)**	**0 (0, 0.5)**	**0 (0, 1.24)**	**0 (0, 0)**
Estimated mean AsBR (95% CI)†	1.91 (1.09–3.36)	0.31 (0.14–0.70)	0.88 (0.47–1.65)	0.45 (0.07–2.98)
Duration, median (days)	309	650	491	442

AsBR, annualized spontaneous bleeding rate; CI, confidence interval; IQR, interquartile range
†Assuming Poisson distribution

- Low AsBR rates in children for all prophylaxis regimens

Table 3. AsBR rates in children

AsBR, previous study (3002)	7-day regimen (N=27)	10-day regimen (N=0)	14-day regimen (N=0)
Median (IQR)	**0.00 (0.00, 0.91)**		
Estimated mean AsBR (95% CI)†	0.56 (0.32–1.00)		
Duration, median (days)	382		
AsBR, extension study (3003)	**7-day regimen (N=20)**	**10-day regimen (N=6)**	**14-day regimen (N=8)**
Median (IQR)	**0.00 (0.00, 0.56)**	**0.00 (0.00, 3.06)**	**1.16 (0.00, 2.63)**
Estimated mean AsBR (95% CI)†	0.70 (0.30–1.60)	2.12 (0.56–8.02)	1.19 (0.56–2.54)
Duration, median (days)	415	501	483

AsBR, annualized spontaneous bleeding rate; CI, confidence interval; IQR, interquartile range
†Assuming Poisson distribution

Conclusion

- Efficacy and safety of routine prophylaxis once every 7-, 10- and 14-days with rIX-FP have been demonstrated in the pivotal Phase III studies and further validated in the extension study
- Extended treatment intervals of 21 days is possible in adults, with median AsBR of 0.0
- Extended treatment interval of 10- or 14-day are possible in young children (<12 years), with median AsBR of 0.0 and 1.16, respectively

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