P-T-92

Long-term Safety and Efficacy of Recombinant Factor IX Fc Fusion Protein (rFIXFc) in Adults/Adolescents With Hemophilia B: Longitudinal Analysis of B-LONG and B-YOND

Mahlangu J,[1] Ragni MV,[2] Shapiro AD,[3] Pasi KJ,[4] Ozelo MC,[5] Oldenburg J,[6] Matsushita T,[7] Baker RI,[8] Feng J,[9] Ferrante F,[10] Ramirez-Santiago A,[9] Mei B,[9] Barnowski C[9,*]

[1]Haemophilia Comprehensive Care Centre, Faculty of Health Sciences, University of the Witwatersrand and NHLS, Johannesburg, South Africa; [2]Hemophilia Center of Western Pennsylvania, University of Pittsburgh, Pittsburgh, PA, USA; [3]Indiana Hemophilia & Thrombosis Center, Indianapolis, IN, USA; [4]Royal London Haemophilia Centre, Barts and the London School of Medicine and Dentistry, London, UK; [5]INCT do Sangue Hemocentro UNICAMP, University of Campinas, Campinas, Brazil; [6]Institute of Experimental Haematology and Transfusion Medicine, University of Bonn, Bonn, Germany; [7]Department of Transfusion Medicine, Nagoya University Hospital, Nagoya, Japan; [8]Western Australia Centre for Thrombosis and Haemostasis, Murdoch University, Perth, Australia; [9]Biogen, Cambridge, MA, USA; [10]Sobi, Stockholm, Sweden

*Presenting author.

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INTRODUCTION

- The safety, efficacy, and prolonged half-life of rFIXFc in previously treated adults/adolescents and children with severe hemophilia B were demonstrated in the Phase 3 B-LONG[1-3] and Kids B-LONG[4] studies, respectively
- Subjects who completed B-LONG or Kids B-LONG could enroll in the ongoing rFIXFc extension study B-YOND
- The cumulative longitudinal data from subjects who enrolled in B-YOND from B-LONG have not yet been reported

OBJECTIVE

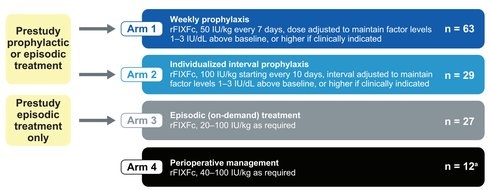
- To report the safety and efficacy of rFIXFc from the start of B-LONG to the first B-YOND interim data cut (October 17, 2014)

METHODS

Study Design

- Previously treated males aged ≥12 years with severe hemophilia B (≤2 IU/dL endogenous factor IX [FIX] activity) were eligible for B-LONG (ClinicalTrials.gov Identifier: NCT01027364; Figure 1)

Figure 1. B-LONG study design



[a]Of the 12 subjects enrolled in Arm 4, 4 subjects were only in Arm 4 during B-LONG; 2 subjects were initially enrolled into Arm 4 and then switched to Arm 1 on-study; and 6 subjects were initially enrolled into Arm 1 or 3 of B-LONG and then switched into Arm 4 on-study.

- Subjects who completed B-LONG could enroll in 1 of 4 treatment groups in B-YOND (NCT01425723; Table 1)
  - Subjects could change treatment groups at any point during B-YOND
- Data were summarized according to the treatment group in which each subject participated for the given time period; thus, subjects may be included in the analysis of >1 treatment group
- Annualized bleeding rate (ABR) by treatment regimen was analyzed by anchoring on the first date that a subject started on that treatment regimen
  - Subject ABR was summarized by year for the time period during which each subject was on that treatment regimen

Table 1. B-YOND treatment groups

Treatment group	Dosing guidance per protocol
Weekly prophylaxis	• ~20–100 IU/kg every 7 days
Individualized prophylaxis	• ~100 IU/kg every 8–16 days OR twice monthly
Modified prophylaxis	• Personalized dosing for subjects in whom optimal prophylaxis could not be achieved using either individualized or weekly prophylaxis – For example, investigators could prescribe more frequent dosing or additional prevention doses prior to strenuous activity, or target a FIX trough level >5 IU/dL, if warranted by bleeding history and/or activity level
Episodic (on-demand)	• Dosing based on type and severity of bleeding episodes

RESULTS

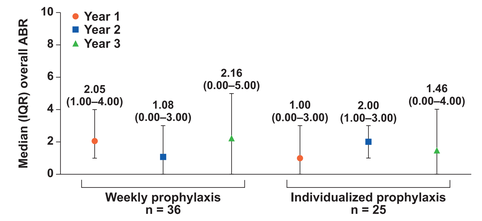
Study Population

- Among 123 subjects dosed in B-LONG, 115 completed B-LONG and 93 of those subjects enrolled in B-YOND (n = 68 ongoing at the first interim data cut)
- Among all 123 subjects from the start of B-LONG to the first B-YOND interim data cut:
  - Median cumulative duration of rFIXFc treatment = 167.43 weeks (~3.2 years)
  - Median (range) cumulative rFIXFc exposure = 123.0 (1–351) exposure days (EDs)
  - 68 subjects (55%) had ≥100 rFIXFc EDs

Annualized Bleeding Rates

- Median pooled ABRs were low with rFIXFc prophylaxis (Table 2)
- Median overall ABRs remained low over time during B-LONG/B-YOND (Figure 2)
- Overall, 97.3% of bleeding episodes from the start of B-LONG to the first B-YOND interim data cut were controlled with 1–2 infusions

Figure 2. Median overall ABRs over time during B-LONG/B-YOND



Changes to Prophylactic Dosing Regimens

- With rFIXFc, 88.9% (32/36) of subjects increased and 11.1% (4/36) maintained their dosing interval compared with their prestudy FIX product (Figure 3), while median total weekly prophylactic factor consumption decreased (Figure 4)

Figure 3. Change in prophylactic dosing interval from pre–B-LONG to the first B-YOND interim data cut[a]

B-YOND dosing interval (first interim data cut: October 17, 2014)

Pre–B-LONG dosing interval	Twice weekly n = 2 (5.6%)	Once weekly n = 25 (69.4%)	Every 10 days n = 2 (5.6%)	Every 14 days n = 6 (16.7%)	Every 16 days n = 1 (2.8%)
3 times weekly n = 9 (25.0%)	2	5	–	2	–
Twice weekly n = 22 (61.1%)	–	16	1	4	1
Once weekly n = 5 (13.9%)	–	4	1	–	–

Change in dosing interval
- Lengthened (n = 32; 88.9%)
- No change (n = 4; 11.1%)
- Shortened (n = 0; 0.0%)

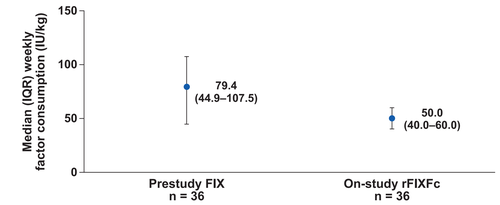
[a]Only subjects who were on prophylaxis prior to B-LONG and during B-YOND and who had both available prestudy and on-study dosing frequency data were included in this analysis.

Table 2. Summary of pooled ABRs from the start of B-LONG to the first B-YOND interim data cut[a]

Treatment group[b]	Weekly prophylaxis (n = 73)	Individualized prophylaxis (n = 33)	Modified prophylaxis (n = 13)	Episodic treatment (n = 27)
ABR, median (IQR)				
Overall	2.41 (0.60–4.35)	1.95 (1.20–5.01)	2.42 (1.26–5.40)	16.28 (10.77–23.08)
Spontaneous	0.68 (0.00–2.45)	0.84 (0.30–2.47)	0.41 (0.00–1.84)	10.74 (2.74–19.78)
Traumatic	0.68 (0.00–2.13)	0.56 (0.00–1.16)	1.75 (0.56–2.76)	2.83 (0.92–6.79)
Joint	1.24 (0.00–3.50)	1.41 (0.31–4.74)	0.92 (0.42–2.03)	12.91 (6.13–19.30)
Spontaneous joint	0.40 (0.00–1.84)	0.55 (0.00–2.47)	0.00 (0.00–0.56)	5.11 (2.21–18.97)

IQR = interquartile range.
[a]The efficacy period reflects the sum of all intervals of time during which subjects were treated with rFIXFc according to the treatment regimens of the study, excluding major and minor surgical/rehabilitation periods and large dosing intervals.
[b]Subjects could change treatment groups at any point in B-YOND; thus, subjects could be represented in >1 treatment group.

Figure 4. Total weekly prophylactic factor consumption pre–B-LONG and at the first B-YOND interim data cut[a]



[a]Only subjects who were on prophylaxis prior to B-LONG and during B-YOND and who had both available prestudy and on-study total weekly factor consumption data were included in this analysis.

Safety Summary

- No inhibitors, serious allergic reactions/anaphylaxis, or vascular thrombotic events were observed in B-LONG or through the first interim data cut of B-YOND; adverse events were typical of a population with hemophilia B

CONCLUSIONS

- Longitudinal data from B-LONG/B-YOND confirm the long-term safety and efficacy of rFIXFc in adults/adolescents with hemophilia B over a median of 3 years
- With prophylactic rFIXFc treatment, adult/adolescent subjects maintained low ABRs with extended dosing intervals and decreased weekly factor consumption relative to their prestudy FIX products

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