P-T-83

# Post Hoc Analysis to Evaluate the Effect of Recombinant Factor IX Fc Fusion Protein (rFIXFc) Prophylaxis in Adults and Adolescents With Target Joints and Hemophilia B

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## INTRODUCTION

- The ongoing extension study B-YOND is evaluating the long-term safety and efficacy of rFIXFc among adults/adolescents and children who have completed the Phase 3 B-LONG[1-3] or Kids B-LONG[4] studies, respectively
- Among individuals with severe hemophilia, bleeding episodes frequently occur in joints; over time, recurrent bleeding in the same joint may result in joint damage and hemophilic arthropathy[5]
- Longitudinal data from subjects with target joints at entry into B-LONG, throughout the B-YOND extension study, are reported here

## OBJECTIVE

- To evaluate the sustained efficacy of rFIXFc in B-YOND subjects with target joints at entry into the B-LONG study

## METHODS

### Study Design

- Subjects completing B-LONG (ClinicalTrials.gov Identifier: NCT01027364) could enroll in 1 of 4 treatment groups in B-YOND (NCT01425723; Table 1)
- In this post hoc analysis, subjects with ≥1 target joint (major joint with ≥3 bleeding episodes in a 3-month period) at entry into B-LONG with available on-study data were evaluated

**Table 1.** B-YOND treatment groups[a]

| 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 participants in whom optimal prophylaxis could not be achieved using either individualized or weekly prophylaxis<br>– 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 |

FIX = factor IX.
[a]Subjects who changed treatment regimens during B-YOND were included in the analyses of each treatment regimen for the period they were on that regimen; thus, individual subjects may be included in >1 treatment regimen.

### Outcome Measures and Statistical Analyses

- Outcomes were analyzed over the cumulative duration of B-LONG through the first B-YOND interim data cut (October 17, 2014)
- An analysis of target joint resolution was performed. A target joint was considered resolved if there were ≤2 spontaneous bleeds in the target joint over a consecutive 12-month period[6]

## RESULTS

### Study Population

- Baseline characteristics for subjects with target joints at baseline are shown in Table 2
- For subjects with target joints at baseline (subjects who changed treatment groups during B-YOND were included in >1 treatment group), median (range) cumulative efficacy duration of rFIXFc treatment was the following:
  - Weekly prophylaxis (n = 40): 16.8 (4–43) months
  - Individualized prophylaxis (n = 12): 27.4 (11–44) months
  - Modified prophylaxis (n = 11): 27.4 (3–30) months
  - Episodic (n = 14): 10.5 (8–39) months

**Table 2.** Baseline characteristics for subjects with target joints at entry into B-LONG[a,b]

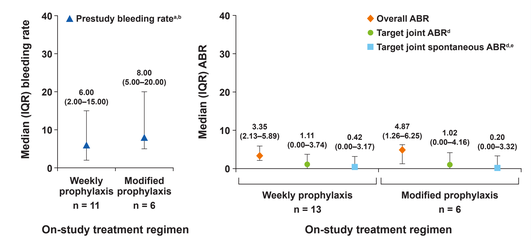
| Characteristic, n (%) | n = 60 |
|---|---|
| **Prestudy regimen** | |
| Episodic | 44 (73.3) |
| Prophylaxis | 16 (26.7) |
| **Number of target joint(s)** | |
| 1 | 20 (33.3) |
| 2 | 13 (21.7) |
| 3 | 7 (11.7) |
| >3 | 20 (33.3) |
| **Target joint location** | |
| Knee | 42 (70.0) |
| Ankle | 33 (55.0) |
| Elbow | 28 (46.7) |
| Hip | 6 (10.0) |
| Shoulder | 3 (5.0) |
| Wrist | 3 (5.0) |

[a]Includes subjects with ≥1 target joint at entry into B-LONG and with an efficacy period (defined as the sum of all intervals of time during which subjects were treated with rFIXFc according to treatment regimens of the study, excluding surgical rehabilitation periods).
[b]A target joint is defined as a major joint (eg, knee, ankle, elbow, hip, shoulder, and wrist) into which repeated bleeding occurred (frequency of ≥3 bleeding episodes into the same joint in a consecutive 3-month period).

### Bleeding Rates

- Prestudy and on-study bleeding information is shown in Figure 1
- Subjects on rFIXFc prophylaxis who did not have a target joint re-bleed on-study:
  - Weekly prophylaxis: 15 of 40 (37.5%)
  - Individualized prophylaxis: 1 of 12 (8.3%)
  - Modified prophylaxis: 5 of 11 (45.5%)
  - Episodic: 0 of 14 (0.0%)

**Figure 1.** Prestudy bleeding rate (A) and on-study ABR (B) in subjects who received prestudy prophylaxis and who had target joints at baseline

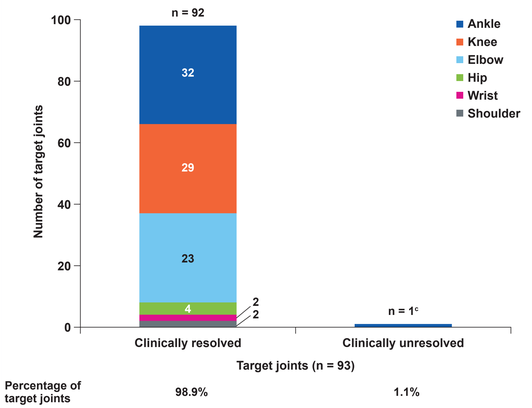



ABR = annualized bleeding rate; IQR = interquartile range.
[a]Subject-reported overall bleeding rate for the 12 months prior to the parent study.
[b]Only subjects with available prestudy bleeding information were included in this analysis.
[c]On-study median (IQR) ABRs for the individualized prophylaxis regimen (n = 2) were as follows: overall, 7.13 (5.71–8.56); target joint, 5.78 (4.57–7.00); target joint spontaneous, 5.01 (4.57–5.44).
[d]A bleeding episode was considered to involve a target joint if the bleeding joint was a target joint identified at entry to the parent study.
[e]A target joint bleeding episode was classified as spontaneous if there was no known contributing factor, such as definite trauma or antecedent strenuous activity.

### Clinical Target Joint Resolution (≤2 Spontaneous Bleeds in 12 Months)

- Overall, 98.9% (92/93) of target joints were clinically resolved (Figure 2)

**Figure 2.** Clinical target joint resolution in subjects with target joints at baseline[a,b]




[a]Evaluable target joints included those with ≥12 months of consecutive follow-up time and had not undergone joint surgery within 12 months since the start of follow up.
[b]97.3% (36/37) of B-LONG prophylaxis subjects with target joints at baseline and 12 months of follow up had target joints resolved.
[c]The subject with an unresolved target joint was in the episodic treatment arm in B-LONG and switched to individualized treatment in B-YOND (efficacy duration, 1.26 years in B-YOND; 33 IU/kg every 10 days at the first B-YOND interim data cut).

### Prophylactic Dosing

- Prestudy and on-study dosing is shown in Table 3

**Table 3.** Summary of rFIXFc prophylactic dosing among subjects who received prestudy prophylaxis and who had target joints at baseline[a]

| Treatment group[b,c,d] | Weekly prophylaxis (n = 12) | Modified prophylaxis (n = 5) |
|---|---|---|
| Prestudy average weekly dose (IU/kg), median (IQR) | 62.7 (40.0–111.3) | 95.6 (39.9–109.1) |
| On-study average weekly dose (IU/kg), median (IQR) | 47.6 (41.0–59.3) | 38.7 (33.7–61.7) |
| Prestudy dosing interval (days), median (IQR) | 3.5 (2.9–3.5) | 3.5 (3.5–3.5) |
| On-study dosing interval (days), median (IQR) | 7.0 (6.9–7.0) | 6.9 (6.9–7.0) |

[a]Only subjects with available prestudy and on-study dose and dosing interval data were included in this analysis.
[b]Subjects are included in each treatment regimen they participated in for the duration of time on that regimen and, as such, may appear in >1 B-YOND treatment regimen.
[c]The on-study average weekly dose and dosing interval for each of the 2 subjects on individualized prophylaxis were: subject 1, 92.5 IU/kg and 7.8 days, respectively; subject 2, 69.6 IU/kg and 10.4 days, respectively. The prestudy average weekly dose and dosing interval for each of these subjects were: subject 1, 30.0 IU/kg and 3.5 days, respectively; subject 2, 40.1 IU/kg and 2.3 days, respectively.
[d]Among all subjects with target joints at baseline, the median (IQR) average weekly prophylactic dose of rFIXFc was: weekly prophylaxis (n = 40), 45.3 (37.3–54.7) IU/kg; individualized prophylaxis (n = 12), 64.9 (47.1–82.3) IU/kg; modified prophylaxis (n = 11), 61.7 (38.7–139.1) IU/kg. The median (IQR) on-study dosing interval was: individualized prophylaxis (n = 12), 10.4 (8.9–13.0) days; modified prophylaxis (n = 11), 6.5 (4.7–7.0) days.

## CONCLUSIONS

- In adult/adolescent subjects with target joints, treatment with rFIXFc prophylaxis over an extended time period resulted in low target joint ABRs with prolonged dosing intervals
- Nearly all (98.9%) target joints in subjects on rFIXFc prophylaxis were clinically resolved during the follow-up period

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