Is switching from a pdFIX (Immunine®) to a rFIX (Bax326*) safe?

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Introduction

- Safe switching from plasma-derived to recombinant concentration factors is of general interest to the haemophilia community due to a potential increase in immunogenicity due to introduction of neoantigens.
- There are limited published data on product switching from plasma-derived (pd) to recombinant concentration factors due to the low disease prevalence and low variety of factor IX concentrates on the market. Until recently, only one recombinant FIX (rFIX) product was commercially available.
- This is the first formal, prospective, comparative evaluation of safety, efficacy and incremental recovery (IR) of a pdFIX and a rFIX in the same haemophilia B patients.[1]

Objective

Evaluate the safety, efficacy and incremental recovery of a pdFIX and a rFIX following a switch from pdFIX (Immunine®) to a recently developed rFIX (Bax326*) product.

Methods

Study Design

Patients completed a pre-treatment study with Immunine® prior to entering the Bax326 pivotal[2] (aged 12-65 years) or pediatric (aged < 12 years) clinical studies, in order to prospectively document exposure during twice-weekly prophylaxis with Immunine® (20-40 IU/kg) and Bax326 (pivotal: 40-60 IU/kg; pediatric: 40-80 IU/kg).

Analysis

- Incremental recovery
  - Assessed 30 minutes post-infusion (optional for subjects < 12 years)
  - To evaluate the potential effect of patient age on FIX recovery, samples were categorized in two age groups: 12-65 years, and <12 years
- Haemostatic efficacy assessments:
  - Annualized bleeding rate (ABR)
  - Overall efficacy rating at resolution of bleed by treatment
- Safety assessments:
  - Adverse events (subject diary)
  - Clinical assessments
  - Inhibitory and treatment related binding antibodies to FIX
  - Severe allergic reactions (eg, anaphylaxis)
  - Thrombotic events

Patients

- Severe (FIX < 1%) or moderately severe (FIX level ≤ 2%) haemophilia B
- Previously treated with plasma-derived or recombinant FIX concentrate(s) for a minimum of 150 EDs (6-65 years) or for >50 EDs (subjects <6 years of age)
- No history of FIX inhibitors

Results

Patients

- 44 Immunine® PTP patients transitioned to Bax326 treatment

Safety

- No deaths, no related SAEs
- No FIX inhibitors, and no treatment-related specific binding anti-FIX antibodies during treatment with Immunine® or Bax326
- No severe allergic reactions or cases of anaphylaxis
- No thrombotic events
- Only 2 AEs (2 episodes of dysgeusia) in 1 (2.3%) subject related to Bax326 (Table 1)

Results (continued)

Table 1 Overview of Non-Serious Adverse Events

		Number and percent of Subjects	
Severity	Relationship	rFIX N=44 subject n [%]	pdFIX N=44 subject n [%]
Mild	Unrelated	19 [43.2]	15 [34.1]
	Related	1 [2.3]	0 [0.0]
	Total	19 [43.2]	15 [34.1]
Moderate	Unrelated	12 [27.3]	8 [18.2]
	Related	0 [0.0]	0 [0.0]
	Total	12 [27.3]	8 [18.2]
Severe	Unrelated	0 [0.0]	0 [0.0]
	Related	0 [0.0]	0 [0.0]
	Total	0 [0.0]	0 [0.0]
Total	Unrelated	25 [56.8]	20 [45.5]
	Related	1 [2.3]	0 [0.0]
	Total	25 [56.8]	20 [45.5]

Haemostatic Efficacy

- No bleeds in 40.6% (13/32) of subjects treated with Immunine® and 47.7% (21/44) treated with Bax326
- Slightly lower ABR during treatment with Bax326 (≥3 months of prophylactic treatment) than with Immunine® (median 1.9 vs. 4.5), likely due to the fact that patients enrolled in the Immunine® pre-treatment study were treated on-demand before study entry

Excellent	Full relief of pain and cessation of objective signs of bleeding after a single infusion. No additional infusion is required for the control of bleeding. Administration of further infusions to maintain hemostasis would not affect this scoring.
Good	Definite pain relief and/or improvement in signs of bleeding after a single infusion. Possibly requires more than 1 infusion for complete resolution.
Fair	Probable and/or slight relief of pain and slight improvement in signs of bleeding after a single infusion. Required more than 1 infusion for complete resolution.
None	No improvement or condition worsens.

Table 3 Hemostatic Efficacy Rating at Resolution of Bleed

	<12 Years Old		12+ Years Old	
Hemostatic Efficacy at Resolution of Bleed	rFIX N=11 n (%)	pdFIX N=12 n (%)	rFIX N=37 n (%)	pdFIX N=45 n (%)
Excellent	7 (63.6)	4 (33.3)	11 (29.7)	20 (44.4)
Good	4 (36.4)	7 (58.3)	24 (64.9)	24 (53.3)
Fair	0 (0.0)	0 (0.0)	2 (5.4)	1 (2.2)
None	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Not Reported	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)

Incremental Recovery

- Lower IR (IU/dL : IU/kg) was observed following infusion of BAX 326 than Immunine® in both age categories (median 0.89 vs. 1.07 in patients aged ≥ 12 years and median 0.67 vs. 0.90 in patients <12 years) confirming results of previous studies in which the IR for rFIX was reported to be 68-86% of that expected for pdFIX concentrates[3,4,5]
- Lower IR for younger children (<12 years; n=12) than for older children/adults (≥12 years; n = 32) (consistent with previous reports)[5,6] for both Bax326 and Immunine®

Conclusions

The results of this analysis provide evidence for a safe and efficacious transition from a pdFIX (Immunine®) to a newly developed rFIX (Bax326*) for prophylaxis and treatment of bleeding in PTPs of all age cohorts with severe or moderately severe haemophilia B.

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If you have any additional questions, please feel free to contact Baxter Bioscience Medical Information at medinfo@baxter.com.

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Clotting Factor Concentrates

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