Comparison of historic on-demand versus prospective on-demand and prophylaxis bleeding episodes in hemophilia A and B patients with inhibitors treated with FEIBA NF

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Introduction

- A recently completed phase 3, prospective, open-label, parallel arm, randomized clinical trial evaluated the efficacy of prophylactic versus on-demand therapy with FEIBA NF in hemophilia patients with inhibitors to factors VIII or IX.
- Subjects receiving FEIBA prophylactically had a 72.5% reduction in annualized bleed rates (ABR) (median ABR: 7.9; n=17) compared to on-demand therapy (median ABR: 28.7; n=19) over a 12-month treatment period; P= 0.0003.[1]

Objective

A post hoc analysis compared the number of historical bleeds in the 12 months prior to study enrollment (all treated on-demand) with prospective bleeds using FEIBA NF on-demand and prophylactically in the two study arms during the 12-month treatment period.

Methods

- All subjects were treated on-demand in the 12 months prior to study entry. Historical bleeding data was based on medical records.
- Median percent changes (historical vs. prospective) in the numbers of: total bleeds, joint bleeds, and target joint bleeds for the on-demand and prophylaxis arms were computed.
- Analyses included subjects who had ≥12 historical bleeding episodes (BEs) in the 12 months prior to enrollment.
- Target joints were defined as ≥4 new bleeds in a specific joint within a period of 6 months: ankles, knees, elbows, and hips.
- Thirty-five (35) subjects (19 in the on-demand and 16 in the prophylaxis arm) qualified for comparison of historical and prospective number of bleeds. One subject in the ITT analysis set (020001) did not qualify for this analysis because the subject withdrew after only 17 days in the prophylaxis treatment arm.

Results

- Paired (historical vs. prospective) analyses were computed of median percent change of total, joint, and baseline target joint bleeds in subjects randomized during the study to prophylactic FEIBA NF treatment compared to on-demand treatment.
- In the on-demand arm, median (interquartile range [IQR]) percent change in the total number of bleeds was 14.1 (79.3), joint bleeds was 0 (88), and baseline target joint bleeds was 20.8 (131.1).
- In the prophylaxis arm, median (IQR) percent change in the total number of bleeds was 64.4 (36.0), joint bleeds was 69 (38), and baseline target joint bleeds was 72.9 (89). See Table 1 and Figures 1, 2, and 3.
- A significant median percent reduction in total number of BEs (p**= 0.0001), number of joint bleeds (p**=0.0001) and number of bleeds at target joints (p**=0.0215) was observed in subjects receiving prophylactic treatment.

Table 1: Descriptive and statistical analyses of median percent change of total, joint, and target joint bleeds (historical, prospective), by treatment arm

On-Demand					
Parameter	N	Number of Bleeds		Median % Change	IQR*
		Historical	Prospective		
% Change of Total Bleeds [a]	19	626	629	14.1	79.3
% Change of Joint Bleeds [b]	18	435	572	0.00	88.03
% Change of Baseline Target Joint Bleeds [c]	14	190	214	20.8	131.1
Prophylaxis					
Parameter	N	Number of Bleeds		Median % Change	IQR*
		Historical	Prospective		
% Change of Total Bleeds [a]	16	550	196	64.4	36.0
% Change of Joint Bleeds [b]	16	484	171	68.75	37.8
% Change of Baseline Target Joint Bleeds [c]	12	200	81	72.9	89.0

*IQR = interquartile range
a [(prospective bleeds - historical bleeds)/historical bleeds]*100.
b [(prospective joint bleeds - historical joint bleeds)/historical joint bleeds]*100.
c [(prospective baseline target joint bleeds - historical baseline target joints bleeds)/ historical baseline target joints bleeds]*100.
Median % changes are expressed as absolute values.
**Two-sample two-sided Mann-Whitney U test was used at significance level of 5%.

Results (continued)

Figure 1: Number of Total Bleeds (Historical, Prospective) by Treatment Arm (Study 090701: Modified Efficacy Intent-to-Treat Analysis Set[a])

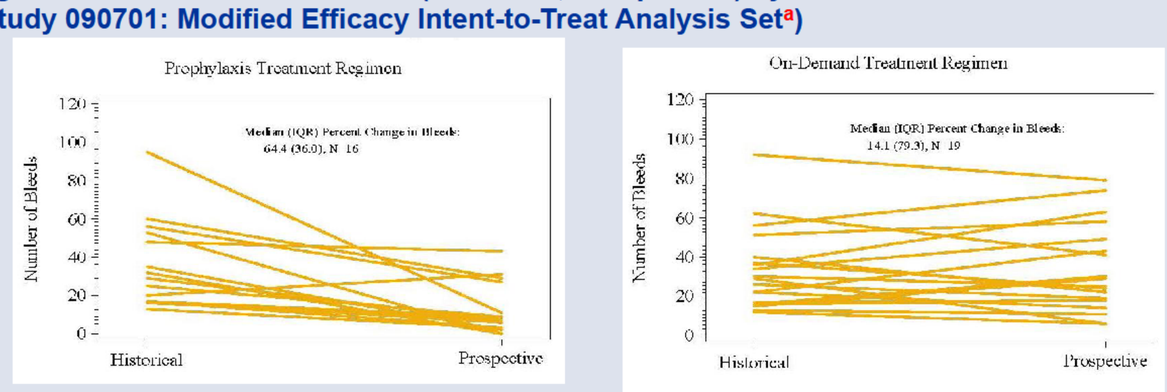


Figure 2: Number of Bleeds in Joints (Historical, Prospective) by Treatment Arm (Study 090701: Modified Efficacy Intent-to-Treat Analysis Set[a])

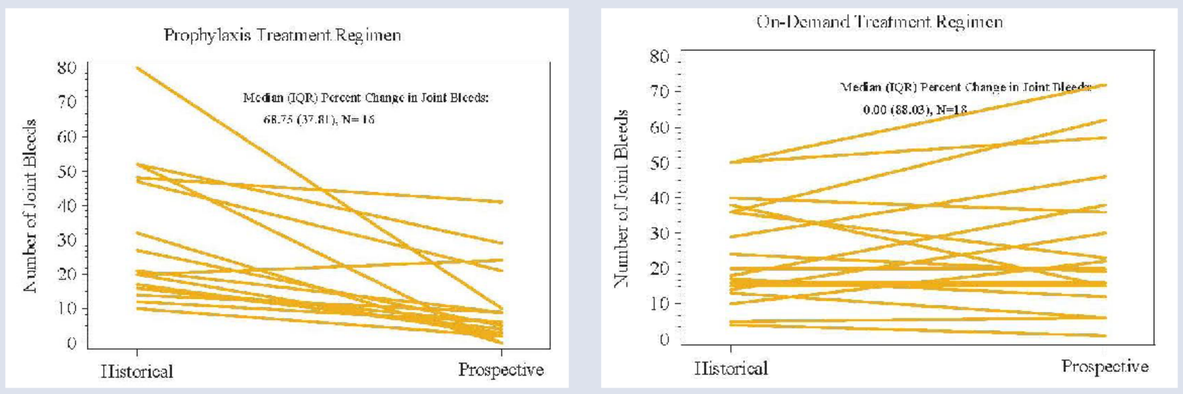
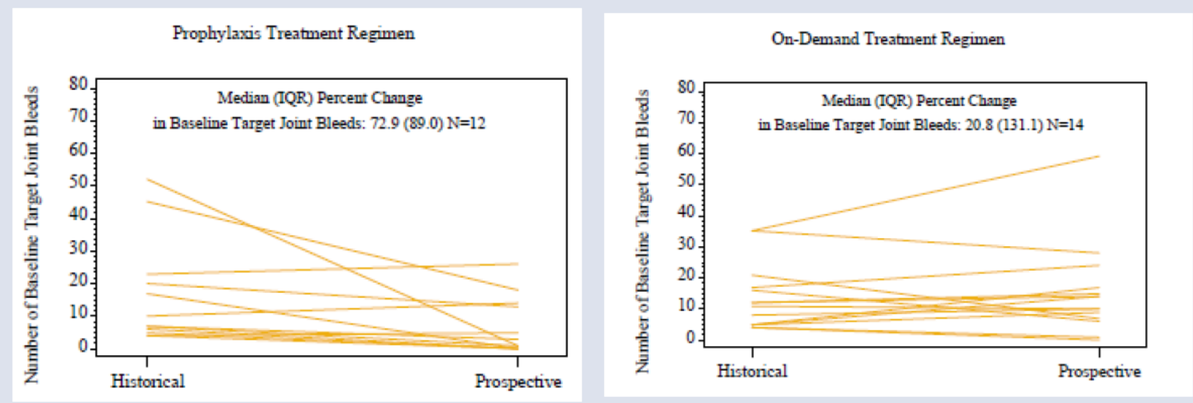


Figure 3: Number of Bleeds in Baseline Target Joints (Historical, Prospective) by Treatment Arm (Study 090701: Modified Efficacy Intent-to-Treat Analysis Set[a])



[a] Subject 020001 was excluded from this analysis since he was on regimen for 17 days. Also, subjects with an unknown number of historical bleeds (joint/target joint bleeds) were recorded as zero. These subjects were not considered in this analysis.

- As shown in Figures 1, 2, and 3, prophylaxis with FEIBA NF was demonstrated to significantly reduce total number of bleeds, joint bleeds, and target joint bleeds when historical and prospective data were compared.
- In subjects on prophylaxis, 15 of 16 had a decrease in number of total and joint bleeds; 9 of 12 had a decrease in the number of baseline target joint bleeds.

Conclusions

- Subjects remaining in on-demand therapy in the two consecutive 12-month periods showed consistent bleeding patterns.
- Subjects randomized to prophylaxis therapy demonstrated significant reduction in bleeding (overall bleeding episodes, joint bleeds, and bleeds at target joints) during the 12-month treatment period.
- Results from this post-hoc analysis demonstrate clear benefits in hemophilia A and B subjects with inhibitors receiving FEIBA NF prophylactic treatment.

Conflicts of interest:

S Tangada, N Guzmán-Becerra, J Doralt, B Ewenstein and WY Wong are employees of Baxter. SV Antunes, J Phillips, O Stasyshyn, and V Mamonov were investigators in the clinical trial.

References

1. Antunes SV, Tangada S, Stasyshyn O, Mamonov V, Phillips J, Guzmán-Becerra N, Grigorian A, Ewenstein B, Wong WY. Randomized comparison of prophylaxis and on-demand regimens with FEIBA NF in the treatment of haemophilia A and B with inhibitors. Haemophilia. 2014 Jan;20(1):65-72. doi: 10.1111/hae.12246. Epub 2013 Aug 1.

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