Patient-Reported Outcomes in Hemophilia B Patients Treated with IB1001 [Coagulation Factor IX (recombinant)]

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INTRODUCTION

Hemophilia B is a rare bleeding disorder caused by missing or defective factor IX, a clotting protein in the coagulation cascade.[1] As an X-linked recessive genetic disorder, hemophilia is most commonly inherited through female carriers to their male offspring, although as many as one-third of all cases are due to spontaneous mutations with no family history of the disease and may also affect females.[2] Individuals with hemophilia B are at risk for bleeding, as their blood does not clot as efficiently as those without the disorder. Hemophilia B is a rare disorder, affecting an estimated 1 in every 10,000 births worldwide.

As a chronic disease, patient quality of life and satisfaction with their treatment is a fundamental component of overall patient care in hemophilia B.[3-5] Patient self-reported feedback on their disease status, perception of treatment, and other patient-reported outcome (PRO) measures are important means for optimizing patient care. Anecdotal evidence suggests that patients may experience improved clinical outcomes and increased satisfaction on specific brands of coagulation factor IX. The objective of this study was to undertake a systematic assessment of patients who have switched to IB1001 to provide a description of patient responses to measures of clinical care and quality of life that are relevant in hemophilia B.

METHODS

Study Design

This was a prospective, cross-sectional study of patients in the United States currently being treated with IB1001 (Coagulation Factor IX [recombinant], Aptevo Therapeutics, Seattle, WA) for hemophilia B. This was a pilot study to generate a descriptive analysis of patient experience.

A questionnaire was developed to capture patient-reported responses to clinical and quality of life questions of interest. In addition to basic demographic characteristics, the questionnaire contained questions relating to disease status, the number and severity of bleeding events, treatment utilization patterns, medication adherence, activity level, quality of life and treatment satisfaction. Where possible, comparisons were made between current treatment with IB1001 and previous therapy. The questionnaire was administered electronically through a readily available website (www.SurveyMonkey.com) that patients could access on their home computer or tablet device to respond.

Ethics and Patient Privacy

Personal health information for patients was protected and all data were de-identified prior to analysis. Each patient's unique identification number was used to ensure respondents cannot be individually identified, and to safeguard against multiple responses from individual patients. Unique identification numbers were not linked with patient names, and were not included in any aspects of analysis once the investigator ensured no duplication of responses occurred.

All patients provided acknowledgement of IRB-approved informed consent prior to participating in this study. Due to the unique study design in which all data was collected electronically, acknowledgement of informed consent was gathered on the initial page of the online questionnaire. Since patients are geographically dispersed, it was not practical for the investigator to personally interact with each patient in a clinic setting for the purposes of consent. Contact information for the investigator was provided to patients to address any questions throughout the study. This protocol was reviewed and approved by a central IRB (Quorum, Seattle, WA) prior to study initiation.

RESULTS

Demographics

Table 1. Demographic Characteristics of Patients Included in this Study.

N*	18
Age, years, mean (median, range)	42.6 (43; 16-73)
Male, %	13 (72.2)
Age at diagnosis, mean (median, range)	10.6 yr (7.5 mo, 0 – 60 yr)
Baseline Factor IX level at diagnosis, n (%)	
< 1%	5 (28)
1% – 5%	7 (39)
> 5% to < 40%	3 (17)
>= 40%	1 (6)
Not reported	2 (11)
Length of time on IB1001 (months), mean (median, range)	18.7 (18; 10-30)
Treatment type with IB1001, n (%)	
Prophylaxis	6 (33)
On-Demand	11 (61)
Not reported	1 (6)
Factor replacement therapy prior to IB1001, n (%)	
Alprolix	1 (6)
Benefix	8 (44)
Mononine	1 (6)
Rixubis	7 (39)
Not reported	1 (6)
Treatment type with prior therapy, n (%)	
Prophylaxis	4 (22)
On-Demand	13 (72.2)
Not reported	1 (6)

* One subject did not complete the questionnaire

Dose Patterns

Among patients who reported prior therapy with a different product, the mean dose was 249 IU lower with IB1001 compared to their previous treatment (Table 2).

Table 2. Dosage Characteristics of Treatment with IB1001 vs Prior Therapy.

	Prescribed IB1001 dose (IU)	Dose of Prior Therapy (IU)
Mean dose	4251	4500
Median dose	3760	4000
Range	1000 – 9000	2000 - 9800

Among patients who reported the actual dose of IB1001 that they were taking, the mean dose was 846 IU lower with IB1001 compared to their previous treatment (Table 3).

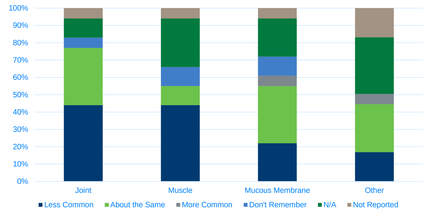
Table 3. Dosage Characteristics of Treatment with IB1001 vs Prior Therapy.

	Prescribed IB1001 dose (IU)	Actual IB1001 dose taken (IU)
Mean dose	5140	4276
Median dose	4000	4300
Range	3000 – 9000	0 - 9000

Bleeding Events

Bleeding events occurred less commonly or the same for at least 50% of subjects for joint, muscle, and mucous membrane bleeds with IB1001 compared to prior treatment.

Figure 1. Frequency of Bleeding Events for Patients Treated with IB1001 vs Prior Therapy.



- Of 15 patients who reported bleed rates with both IB1001 and their prior treatment, 11 (73%) reported a decrease in annualized bleed rate (ABR), 3 (20%) reported no change, and 1 (7%) reported increased ABR since starting treatment with IB1001.
- Three patients (17%) reported no bleeds since starting IB1001.

Table 4. Mean Annualized Bleed Rate for Patients Treated with IB1001 vs Prior Therapy.

	Prophylaxis mean (median; range)	On Demand mean (median; range)
IB1001	3.1 (1.6; 0.5 – 11.5)	5.4 (3.5; 0 – 20.6)
Prior Treatment	11.2 (8.5; 4.0 – 30)	6.4 (5.0; 0 – 30)

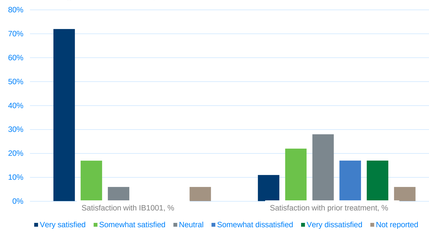
Activity Level

- Since starting IB1001, a majority of patients are very active (22%) or somewhat active (56%).
- Compared to when on their prior therapy, 40% of patients reported they are more active on IB1001, 33% reported the same activity, and 11% reported they are less active.
- Most subjects (56%) are either very satisfied or somewhat satisfied with their activity level on IB1001.
- Only 22% are either somewhat dissatisfied or very dissatisfied with their activity level.

Patient Satisfaction

89% of patients said they were either very satisfied or somewhat satisfied with IB1001 vs 33% of patients reporting the same categories with prior treatment.

Figure 2. Patient Reported Treatment Satisfaction.



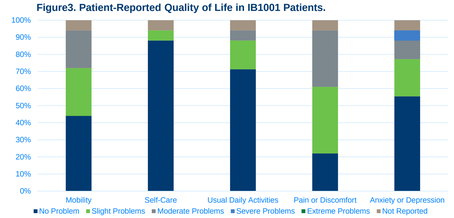
Limitations

- As a survey-based study we rely on patient recall and accuracy of reporting. This may introduce recall bias, and other variability that may not be well characterized or quantifiable.
- As participation in this study was entirely voluntary, there is potential bias derived from patient self-selection such that it is impossible to know if there are any systematic differences in patient characteristics among those who chose to participate and those who did not.
- With only 18 patient responses it is unclear whether this is a large enough sample size to reasonably reflect the experiences of the hemophilia B population in general.
- The survey was designed specifically for this study and is not a validated patient-reported outcomes instrument and therefore the results may not be transferrable to other populations or subgroups; however, this was designed as a pilot study to capture patient experience with a particular product in a systematic way, and there are likely multiple hypotheses that can be derived from this study to support future expanded studies in the hemophilia B population.

Patient-Reported Quality of Life

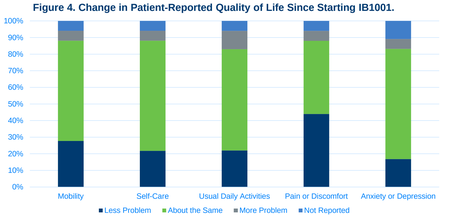
- A majority of IB1001 patients reported "No Problem" with self care (89%), usual daily activities (72%), and anxiety or depression (56%).
- The only areas where patients reported moderate or severe problems were pain or discomfort (33%), mobility (22%), and anxiety or depression (17%).

Figure3. Patient-Reported Quality of Life in IB1001 Patients.



- Despite 33% of patients reporting moderate or severe problems with pain or discomfort, 88% reported less problem (44%) or about the same (44%) since starting IB1001.
- Only 6% of patients reported more problem on IB1001 with mobility, self-care, pain or discomfort, and anxiety or depression; 11% reported more problem with usual activities.

Figure 4. Change in Patient-Reported Quality of Life Since Starting IB1001.



CONCLUSIONS

- Eighteen IB1001 patients were evaluated in this prospective cross-sectional study of clinical and quality of life; 17 patients completed the full questionnaire
- Among patients who reported a dose for their prior therapy, the mean and median prescribed IB1001 dose was lower than the dose of the prior therapy
- The median reported ABR among patients taking IB1001 for prophylaxis (1.6) was about half of the median ABR for the prior therapy (3.5); the ABR is also consistent with the median ABR seen in the pivotal clinical trial (1.52).[6]
- Compared to when on their prior therapy, 40% of patients reported they are more active on IB1001, 33% reported the same activity
- 89% of patients reported they were very satisfied or somewhat satisfied with IB1001, compared with 33% on their prior therapy
- A majority of patients reported no problems or slight problems on all domains of quality of life; a majority also reported this is the same or less problem on all domains than on their prior therapy
- Further research is necessary to fully understand these trends

REFERENCES

1. Hemophilia B. (Accessed October 26, 2016, at https://http://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-B.)
2. Srivastava A, et al. Guidelines for the management of hemophilia. Haemophilia : the official journal of the World Federation of Hemophilia 2013;19:e1-47.
3. Efficace F, et al. Patient-reported outcomes in hematology: is it time to focus more on them in clinical trials and hematology practice? Blood 2017;130:859-66.
4. Murthy HS, Wood WA. The Value of Patient Reported Outcomes and Other Patient-Generated Health Data in Clinical Hematology. Current hematologic malignancy reports 2015;10:213-24.
5. European Hematology Association Scientific Working Group: Quality of Life and Symptoms. Guidelines: Patient-Reported Outcomes in Hematology. In: Novik A, Salek S, Ionova T, eds. Genoa, Italy: Litoprint; 2012.
6. Collins PW, et al. Pharmacokinetics, safety and efficacy of a recombinant factor IX product, trenonacog alfa in previously treated haemophilia B patients. *Haemophilia*. 2017;1-9.

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