

**Association of Hemophilia Clinic Directors of Canada
Factor IX Subcommittee**

**Report to Annual General Meeting
Montreal, Quebec
July 15, 2000**

Members:

- M-C. Poon (chair)
 - R. Card
 - D. Lillicrap
 - M.-F. Scully

1. Data analyzed for this report include those received on or before 2000-06-15.
2. Data analyzed for the attached abstract submitted to the 2000 WFH Congress include those received on or before 2000-01-24

Thrombogenicity monitoring

No case of thrombosis or DIC as a result of using factor IX concentrates has been reported from Canadian hemophilia clinics.

Recombinant factor IX (BeneFIX®) efficacy and safety monitoring

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Recovery

BeneFIX®: Data reported and analyzed: 119 infusions from 111 patients from 14 centers (Age: range 1-75, mean 26.8, median 25)

Immunine®: Data reported and analyzed: 60 infusions from 60 patients from 9 centers (Age: range 2-74, mean 27.4, median 25.5)

Analysis of RECOVERY (U per IU/kg infused)

A,B: all infusions from all patients

	Product	Infusions	Patients	min/max	Mean	Median	SD	95% CI
A	BeneFIX	119	111	0.36-1.86	0.77	0.71	0.19	0.73-0.80

B	Immunine	60	60	0.37-2.29	1.03	1.00	0.26	0.97-1.10
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A vs. B: 0.0000

C,D: only infusions from patients <= 15 years age

	Product	Infusions	Patients	min/max	Mean	Median	SD	95% CI
C	BenefIX	42	38	0.37-0.92	0.63	0.63	0.11	0.59-0.67
D	Immunine	18	18	0.37-1.25	0.89	0.90	0.17	0.81-0.97

C vs. D: 0.0001

E,F: only infusions from patients > 15 years age

	Product	Infusions	Patients	min/max	Mean	Median	SD	95% CI
E	BenefIX	77	73	0.36-1.85	0.83	0.77	0.21	0.79-0.89
F	Immunine	42	42	0.42-2.29	1.10	1.01	0.29	1.01-1.87

E vs. F: 0.0002

Comparison of age groups (<= 15 years age vs >15 years age)

BeneFIX <= 15 years age vs >15 years age: 0.0000

Immunine <= 15 years age vs >15 years age: 0.0113

Fifty-one (51) patients had values from both BeneFIX and Immunine infusions

G,H: Paired infusions from all 51 patients

	Product	Infusions	Patients	min/max	Mean	Median	SD	95% CI
G	BenefIX	51	51	0.39-1.85	0.78	0.72	0.20	0.73-0.84
H	Immunine	51	51	0.37-2.29	1.04	1.00	0.26	0.97-1.11

G vs. H: 0.0000

I,J: Paired infusions from patients <=15 years age

	Product	Infusions	Patients	min/max	Mean	Median	SD	95% CI
G	BeneFIX	14	14	0.39-0.92	0.63	0.62	0.14	0.56-0.70
H	Immunine	14	14	0.37-1.26	0.92	0.95	0.196	0.82-1.02

I vs. J: 0.0012

K,L: Paired infusions from patients >15 years age

	Product	Infusions	Patients	min/max	Mean	Median	SD	95% CI
G	BeneFIX	37	37	0.47-1.85	0.84	0.75	0.22	0.77-0.91
H	Immunine	37	37	0.42-2.29	1.09	1.00	0.29	0.99-1.18

K vs. L: 0.0000

Comparison of Age Groups

BeneFIX <= 15 years age vs >15 years age: 0.0026
 Immunine <= 15 years age vs >15 years age: 0.0745

Discussion

1. The number of infusions analysed is very reasonable
2. Recovery of BeneFIX significantly lower than Immunine overall and in both children (= 15 years age) and adults (>15 years age). Within each blood product group, overall, the recovery of those =15 year age is significantly lower than those of >15 years age
3. Multiplication factor for BeneFIX based on available overall data

	Age group	Infusions	Patients	Multiplication factor (1/mean recovery)
A	All	119	111	1.31 (95% CI: 1.25-1.37)
C	< =15 years	42	38	1.59 (95% CI: 1.50-1.68)
E	> 15 years	77	73	1.19 (95% CI: 1.13-1.26)

4. The multiplication factor is higher in younger children. All patients should have recovery studies done to help with proper dosing.
5. The influence of pre-infusion factor IX value (severity) on recovery: remains to be analyzed as we accumulate more data

6. Consistency of recovery for a given patient from year to year: needs to be determined

Half-disappearance time

90 of the 119 BeneFIX infusions and 44 of 60 Immuline infusions include factor IX values from 4 time points (pre, post 15-30 min, 1 hr, 4 hr). The $t_{1/2}$ based on manual plotting proved to be difficult. Further data manipulation is required and suggestions will be welcome.

Inhibitors

No report of factor IX inhibitors during this initial period of BeneFIX usage has been reported. The Kingston Laboratory (D. Lillicrap) has analyzed 100 post-BeneFIX infusion samples for non-neutralizing factor IX antibody by a modified ELISA technique and all samples were negative

Patient satisfaction questionnaire

Insufficient submissions for analysis

Discussion

The Factor IX Subcommittee wish to thank all centers for submitting data for analysis. We urge all centers to submit data on all their patients to allow meaningful analysis. Each patient receiving BeneFIX should have the studies done for patient care purpose, and the extra work involved include just completion of the forms for submission.