Safety and efficacy of B-domain deleted 3rd generation recombinant factor VIII (GreenGene F™) in Korean patients with haemophilia A: Data from a post-marketing surveillance study

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INTRODUCTION

To reduce the risk of transmission of blood-borne infections as well as to overcome the shortage of plasma concentrate, recombinant FVIII (rFVIII) concentrates have been developed, and have been more widely available now in the world, greatly replacing the human plasma-derived products. GreenGene F™, new B-domain deleted 3rd generation recombinant factor VIII, was launched in 2010.

OBJECTIVE(S)

This clinical trial evaluated the safety and efficacy of the drug in patients with haemophilia A.

METHODS

From July 2010 to July 2014, a total 135 hemophilia A patients were enrolled in the post marketing surveillance (PMS) study and were analyzed for safety of the drug. Among them, 114 patients were analyzed for efficacy. Subjects with differing haemophilia A severities and medical histories were monitored during 12 months of prophylactic and/or on-demand therapy. Efficacy for hemostasis and hemorrhage prevention effect was rated by their doctors with 4 scales as excellent, good, moderate, or no effect.

Those with 0-3 ED were considered PUPs, while those with > 50 EDs were referred to as PTPs. Hemophilia was classified as follows: severe, FVIII <1%; moderate, 1% ≤ FVIII ≤5%; mild, FVIII >5 IU/dL.

Data analysis was performed with IBM SPSS Statistics 19 software program.

RESULTS (1)

Among 135 evaluable subjects, 85 (63.0%) had severe haemophilia, 35 (25.9%) had moderate haemophilia and 15 (11.1%) had mild haemophilia. Twelve subjects reported 13 adverse drug reactions (ADRs), which were recovered without sequelae. The frequent ADRs were gastrointestinal disorders, nervous system, vascular disorders and general disorders. In 113 previously treated patients (PTP), two patients (1.8%) developed inhibitors after intensive FVIII treatment for pseudotumor removal and for nephrolithiatomy, respectively. The incidence of inhibitors in PUPs was 9.1% (2/22). Excellent/good efficacy rate was 91.3% for hemostasis and 89.4% for hemorrhage prevention.

RESULTS (2)

Table 1. Demographic and baseline characteristics by initial treatment regimen according to the previously treated patients or not.

Characteristic	PTP (n=113)	PUP (n=22)	Total
Gender			
Male	113	22	135
Female	0	0	0
Age (years)			
Median	24	22	24
Mean (SD)	27.99+15.69	18.61+16.78	26.42+16.18
Range	0.92~73	0~56	0~73
Numbers by life stage			
<12 yr-old	18	9	27
>65 yr-old	2	0	2
Disease severity			
Mild	9	6	15
Moderate	27	8	35
Moderately severe	16	3	19
Severe	77	8	85
Family history (yes:no)	56:57	5:17	61:74
Haemophilic arthropathy	44 (38.9%)	4 (18.2%)	48 (35.6%)
Assigned therapy			
Prophylaxis	76	16	92
On-demand	37	6	43

Abbreviations: PTP, previously treated patients; PUP, previously untreated patients.

Table 2. Demographic and baseline characteristics by initial treatment regimen according to the prophylaxis and on-demand.

Characteristic	Prophylaxis (n=92)	On-demand (n=43)	Total (n=135)
Age (years)			
Median	24	24	24
Mean (SD)	24.97+15.93	29.65+16.46	26.42+16.18
Range	0.044~59	0~73	0~73
Disease severity			
Mild	10	5	15
Moderate	20	15	35
Moderately severe	9	10	19
Severe	62	23	85
Time since diagnosis (years)			
Median	11.12	12.5	11.56
Mean (SD)	11.98+9.29	12.37+7.7	12.12+8.72
Range	0~57	0~23	0~57
Prior FVIII product			
Recombinant	19	11	30
Plasma-derived	57	28	85
No use	16	4	20
FVIII exposure history			
0-3 EDs	7	4	11
4-50 EDs	28	29	57
>50 EDs	57	10	67

RESULTS (3)

Table 3. Adverse drug reactions during the use of GreenGene F treatment.

Characteristic	PTP, n=113	PUP, n=22	Total, n=135
General or nonspecific symptoms			
Chest discomfort	2 (1.8%)		2 (1.5%)
Nausea	1 (0.9%)	1 (4.6%)	2 (1.5%)
Vomiting		1 (4.6%)*	1 (0.7%)
Dizziness	1 (0.9%)		1 (0.7%)
Headache	1 (0.9%)		1 (0.7%)
Facial flushing	1 (0.9%)		1 (0.7%)
Syncope		1 (4.6%)	1 (0.7%)
Inhibitors			
Development	2 (1.8%)	2 (9.1%)*	4 (3.0%)

Table 4. Efficacy of hemostasis response and hemorrhage prevention effect to GreenGene F treatment

	Patients numbers	%
Hemostatic effect (n=92)		
Excellent	49	53.3
Good	35	38.0
Moderate	8	8.7
None	0	0
Hemorrhage preventive effect (n=94)		
Excellent	26	27.7
Good	58	61.7
Moderate	10	10.6
None	0	0

CONCLUSION(S)

The results of this PMS study support that GreenGene F™ is safe and efficacious in the treatment and prevention of patients with hemophilia A. The results of this study are consistent with the previously published GreenGene F™ studies. .

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