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Tolerability and Persistence with Subcutaneous Immunoglobulin Provided Through Physician Clinics for the Treatment of Primary Immunodeficiencies

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Abstract

Rationale: Investigate effectiveness, tolerability and persistence of 5 brands of subcutaneous immunoglobulin (SCIG) in patients with primary immunodeficiencies (PID) in a real-world physician clinic setting.

Methods: Medical and pharmacy records were extracted from 2 physician clinics with pharmacy services of patients receiving SCIG in 2017. Data collected included demographics, SCIG therapy, infection rates, adverse reactions and hospitalizations. Persistence was assessed as time from first dose of SCIG to discontinuation during the study period.

Results: 42 pts (mean age 52, 78% female) received various SCIG therapies for treatment of PID, including Cuvitru™, Gammagard®, Gamunex®-C, HyQvia®, and Hizentra®. Three patients had drug changes and 11/42 had drug dosage increases. Adverse reactions occurred in 31/42 (74%) of patients. The reactions were primarily mild, with infusion site reactions, fatigue and headache most common. All were managed without drug discontinuation. Serious bacterial infections were observed in 3/42 patients (7%), resulting in hospitalizations. Persistence with therapy was achieved in 98% of patients (41/42).

Conclusion: Self-administration of various brands of SCIG for PID provided through physician clinics proved effective and tolerable, even with reported adverse reactions. Persistence of therapy was remarkedly high, suggesting positive patient experiences when managed through a physician clinic setting.

Introduction

Subcutaneous immune globulin (SCIG) is indicated for the treatment of adult and pediatric patients with primary immunodeficiencies [1-5]. Compared to intravenous IgG, SCIG is equally effective in prevention of infections, however, with a more favorable safety profile [6]. In addition, SCIG allows for convenient home-based self administration and improved quality of life.

In an immunologist office, appropriate candidates for SCIG home infusions are selected. Patients receive thorough training by skilled infusion nurses and pharmacists in the immunology clinic. A comprehensive assessment is performed monthly and/or prior to each SCIG dispense by a pharmacist to ensure efficacy, safety and compliance to therapy. Oversight is maintained by the immunologist.

Our goal was to investigate overall efficacy, tolerance and persistence of various SCIG products provided through immunologist clinics with dedicated nurses and pharmacists.

Methods

A retrospective chart review was conducted of PID pts receiving SCIG in 2017 through two large immunology physician clinics.

Sample size: n=42

Patient and disease characteristics: demographics including gender, age (≤18, 18-64, >65 years), body mass index, primary PID diagnosis, length of diagnosis, prior IgG therapy including intravenous (IVIG) and SCIG.

SCIG utilization and therapy characteristics: SCIG product use, dose interval, no. of infusion sites, infusion volume per site and dose per patient calculated as mg/kg per month.

Efficacy/hospitalizations:
Incidence of respiratory infections in 2017 and hospitalizations due to infections were recorded.

Tolerability/adverse reactions:
All adverse reactions were extracted from regular monthly pharmacy assessments and shown as overall adverse event rate (%). Local infusion-site reactions and systemic adverse reactions are presented for each SCIG product.

Patient persistence:
Persistence was defined as continued use of SCIG over 12 months as ordered by the immunologist and dispensed by the pharmacist. This was confirmed by pharmacist assessment and dispensing records. Reasons for non-persistence were documented.

Statistical Analysis:
Data were analyzed using descriptive statistics (mean, median, standard deviation). Frequencies and percentages were calculated for qualitative variables.

Results

Study Patients & SCIG Utilization

Table 1. Baseline Characteristics

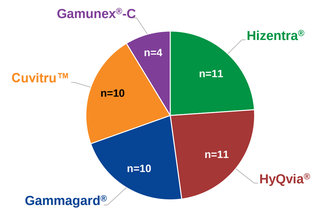
Variable	Results (n = 42)
Gender, n (%)	
Female	33 (78.6%)
Male	9 (21.4%)
Mean age (years) ±SD	52±18
Age groups, n (%)	
≤18 years	3 (7%)
19 to <64 years	31 (74%)
≥65 years	8 (19%)
Body mass index (kg/m^2)	
Mean±SD	28±7.6
Median (range)	25.4 (16 - 48.5)

Table 2. Disease Characteristics and Previous Therapy

Parameter	Results (n = 42)
PID primary diagnosis, n (%)	
Common variable immunodeficiency	31 (74%)
Immunodeficiency w/ predominantly antibody defects	11 (26%)
Length of diagnosis (mean years±SD)	7.6±11.5
IgG level at time of diagnosis* (mean±SD)	517±185 mg/dL
IgG Therapy History Prior to 2017	
Patients only on IVIG, n (%)	3 (7%)
Patients only on SCIG, n (%)	23 (55%)
Patients on both IVIG and SCIG, n (%)	11 (26%)
Patients naïve to IgG therapy, n (%)	5 (12%)
Length of prior IgG therapies (mean years±SD)	
prior SCIG therapy	3.5±2.7
prior IVIG therapy	7.3±12.3

*: available for 38 of 42 (90%) patients.

Figure 1. Utilization of SCIG Products



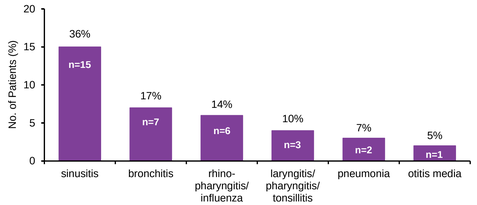
- 46 products were used in 42 patients with 4 receiving 2 products:
  - Gamunex®-C to Cuvitru™ (n=2)
  - Gammagard® to Cuvitru™ (n=2)

SCIG Therapy & Efficacy

Table 3. Therapy Characteristics by SCIG Product

SCIG Product	IgG Conc.	No. of Pts	Dose Interval	No. of Infusion Sites	Infusion Volume/Site (range)	Dose/Month Mean±SD (mg/kg)
Cuvitru™	20%	8 2	qw q2w	2 or 3	17 to 55 mL	667±261
Gammagard®	10%	8 2	qw q2w	4 to 6	12.5 to 30 mL	530±175
Gamunex®-C	10%	4	qw	4	12.5 to 25 mL	464±117
Hizentra®	20%	10 1	qw q2w	2 to 4	10 to 25 mL	550±174
HyQvia®	10%	1 3 7	q2w q3w q4w	1	225 to 400 mL	630±180

Figure 2. Incidence of Respiratory Infections



- A total of 38 respiratory infections were reported in 27 patients (64%)
- Hospitalizations were reported in 3 patients due to pneumonia

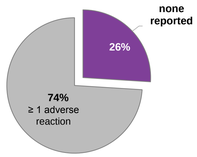
Table 4. SCIG Therapy Changes in 2017

SCIG Product	No. of Pts	Dose Change		Reason	SCIG Change Y/N (Product)
		from	to		
Cuvitru™	2	18g qw 9g qw	20g qw 12g qw	infection low IgG level	N N
Hizentra®	3	9g qw 10g qw 9g qw	12g qw 12g qw 12g qw	worsening dermatitis infection low IgG level	N N N
Gammagard®	4	15g qw 10g qw 8g qw 9g qw	18g qw 12g qw 12g qw 10g qw	infection recurrent infections recurrent infections recurrent infections	Y (Cuvitru™) N Y (Cuvitru™) N
HyQvia®	2	25g q3w 30g q3w	30g q3w 32.5g q3w	recurrent infections recurrent infections	N N

- SCIG dose changes were reported in 11 of 42 patients (26%), primarily due to increases in respiratory infections or low IgG trough levels

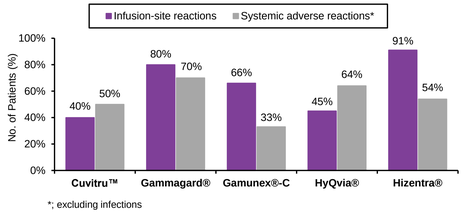
SCIG Tolerability

Figure 3. Adverse Event Rate



- 31 of 42 patients (74%) reported adverse reactions (ARs)
- 28 patients (67%) experienced local infusion-site reactions and 24 patients (57%) reported systemic ARs
- 23 patients (55%) had ≥2 ARs during the 12-month study period

Figure 4. Incidence of Adverse Reactions by SCIG Product



*: excluding infections

- Infusion-site reactions were most frequently reported in patients on Hizentra® (91%) and Gammagard® (80%)
- Systemic ARs were most frequently reported with Gammagard® (70%) and HyQvia® (64%)

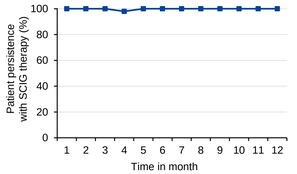
Table 5. Overview of Adverse Reactions by SCIG Product

Adverse reaction	Cuvitru™ (n=10)	Gammagard® (n=10)	Gamunex®-C (n=4)	Hizentra® (n=11)	HyQvia® (n=11)	Total (n=46)
Infusion-site reaction, n (%)						
redness	2 (20%)	3 (30%)	2 (50%)	8 (73%)	4 (36%)	**19 (45%)**
swelling	2 (20%)	3 (30%)	1 (25%)	4 (36%)	2 (18%)	**12 (28%)**
itching	2 (20%)	-	-	3 (27%)	4 (36%)	**9 (21%)**
pain	-	3 (30%)	1 (25%)	2 (18%)	-	**6 (14%)**
bruising	-	1 (10%)	-	3 (27%)	-	**4 (10%)**
bleeding	-	2 (20%)	-	1 (9%)	-	**3 (7%)**
leaking	1 (10%)	1 (10%)	-	1 (9%)	-	**3 (7%)**
burning	-	1 (10%)	-	-	-	**1 (2%)**
Systemic adverse reaction*, n (%)						
fatigue	4 (40%)	4 (40%)	1 (25%)	3 (27%)	4 (36%)	**16 (38%)**
headache	3 (30%)	3 (30%)	-	3 (27%)	4 (36%)	**13 (31%)**
body ache	1 (10%)	1 (10%)	-	1 (9%)	1 (9%)	**4 (7%)**
joint pain	-	-	-	-	3 (27%)	**3 (7%)**
fever & chills	-	1 (10%)	-	-	1 (9%)	**2 (5%)**
nausea	-	-	-	-	2 (18%)	**2 (5%)**
dizziness	-	-	-	1 (9%)	-	**1 (2%)**

*: excluding infections

Persistence with SCIG Therapy

Figure 5. 12-Month Persistence Rate



- During the 12-month observation period, 41 patients (98%) were fully persistent with SCIG therapy
- Only one patient had a delay in therapy, which was limited to 2 weeks

Discussion and Conclusion

This retrospective one-year study presents data on efficacy, tolerability and persistence with the use of SCIG products in PID patients managed by immunologists, dedicated nurses and pharmacists in 2 physician clinics.

- SCIG products included Cuvitru™ (n=10), Gammagard® (n=10), Gamunex®-C (n=4), Hizentra® (n=11), and HyQvia® (n=11)
- Respiratory infections were reported in 64% of patients, mostly mild to moderate. Hospitalizations due to infection occurred in 7% of patients.
- SCIG doses were increased in 11 patients due to infections (n=9) or low IgG trough levels (n=2). Four patients were switched from a 10% IgG product (Gammagard®, Gamunex®-C) to 20% Cuvitru™.
- Overall, 74% of patients reported an adverse reaction with 67% reporting infusion-site reactions and 57% reporting systemic reactions. Reactions were well-managed and tolerable. No patients discontinued therapy due to adverse reactions.
- Persistence was exceptionally high. The 12-month persistence rate was 98% with a delay of SCIG therapy of 2 weeks in only one patient.

In conclusion, home self-administration of SCIG provided through outpatient immunology physician clinics that provide continuous oversight and monitoring by the immunologist, nurse and pharmacist has demonstrated efficacy and tolerability with a high rate of persistence to therapy.

References

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3. GAMMUNEX-C (immune globulin subcutaneous, human, 10% solution) [package insert]. Research Triangle Park, NC: Grifols Therapeutics, Inc.; 2015.
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6. Vultaggio A, Azzari C, Milito C et al. Subcutaneous immunoglobulin replacement therapy in patients with primary immunodeficiency in routine clinical practice: The VISPO prospective multicenter study. Clin Drug Investig 35: 179-85, 2015.