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Real-World Utilization of Immune Globulin Subcutaneous 16.5% in Treatment-Naïve Primary Immunodeficient Patients

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Abstract

Introduction: Immune Globulin Subcutaneous (Human) 16.5% (IGSC 16.5%) is a subcutaneous immunoglobulin (IG) approved for the treatment of primary immunodeficiency diseases (PIDD) in adults and pediatric patients ≥2 years old. We evaluated clinical outcomes in IG treatment-naïve patients with PIDD who utilized IGSC 16.5% as initial therapy.

Methods: A retrospective review was conducted in IG treatment-naïve patients who received 24 weeks of IGSC 16.5% from 5/2019-4/2022. Data included demographics, IGSC 16.5% utilization, adverse reactions, respiratory tract infections (RTIs), and treatment adherence defined as self-administering within two days of the scheduled treatment.

Results: Thirty-five IG treatment-naïve patients (mean age 49±11.8 years, 94% female) utilized IGSC 16.5% during the study period. The predominant PIDD diagnosis was common variable immunodeficiency (40%). All patients infused weekly, with a mean dose of 122±31.8 mg/kg/week. The initial infusion rate was 26.5±6.9 mL/hr/all sites, and the maximum rate was 55.7±19.9 mL/hr/all sites (min 22.1, max 86.1). During infusions 1-24, local reactions were reported in 27 patients (77%), most commonly swelling, redness and itching. Local reactions were highest at infusion 1 and decreased significantly over time (p<0.01). Systemic reactions were reported in 15 patients (43%), most commonly fatigue and headache. Systemic reactions also diminished significantly over time (p<0.05). Seventeen bacterial RTIs occurred in 13 patients (33%); none were serious. Patients were adherent in 833/840 infusions (99% adherence rate).

Conclusion: Our real-world study confirmed effectiveness and excellent adherence with IGSC 16.5% in IG treatment-naïve patients with PIDD. Local and systemic reactions were highest at treatment initiation and then decreased significantly over time.

Introduction

Immune globulin subcutaneous (IGSC) therapy is commonly used in the treatment of primary humoral immunodeficiency disease (PIDD) [1]. IGSC therapy has been associated with a low adverse reaction profile and predictable IgG pharmacokinetics in patients with PIDD [2]. IGSC therapy can be effectively provided through a physician clinic with nursing and pharmacy services, demonstrating high medication adherence [2,3].

IGSC 16.5% (Cutaquig®) is a human immune globulin (IG) subcutaneous product approved in the US for the treatment of PIDD in adults and children two years old and younger [4]. A phase 3 clinical trial showed treatment efficacy, safety with no serious bacterial infections, stable IgG plasma levels, and tolerability in IG treatment-experienced patients [5]. A long-term, prospective study also reported maintained efficacy and low rates of adverse events [6].

Our previous real-world assessments of IGSC 16.5% indicate safe and effective therapy at six months and twelve months in patients who were primarily treatment-experienced [7-8]. The purpose of the present study was to evaluate clinical outcomes in IG naïve patients receiving IGSC 16.5% as their initial therapy for the treatment of PIDD.

Methods

A retrospective, observational review was conducted in IG treatment-naïve patients who initiated therapy with IGSC 16.5%. Patients had not received either intravenous or subcutaneous IG prior to the start of IGSC 16.5%.

All patients were required to have at least 6 months (i.e., 24 weeks) of IGSC 16.5% use. Data was collected from May 2019 to April 2022.

Patients initiated IGSC 16.5% at immunology and infectious disease physician clinics. IGSC-trained pharmacists and nurses provided training in self-administration and therapy management. Pharmacists dispensed medications and conducted monthly assessments to capture patient-reported outcomes.

Study data included:

- Baseline demographics and disease characteristics
- IGSC 16.5% therapy details
- Bacterial respiratory tract infections (RTIs)
- Local and systemic adverse reactions
- Treatment adherence (e.g., utilization within ±2 days of scheduled treatment)

Descriptive statistics included means, standard deviations (SD), medians, interquartile ranges (IQR), frequencies, and percentages. Repeated measures linear regression was used to assess the change in local and systemic reactions over time.

Results

Study Patients

- A total of 35 IG treatment-naïve patients received IGSC 16.5% over a 24-week period

Table 1. Baseline Demographics and Disease Characteristics

Parameter	IGSC 16.5% N=35
Age in years, mean±SD	49 ± 11.8
Female gender, n (%)	33 (94%)
Body mass index in kg/m^2, median (IQR)	30 (27-34)
PI primary diagnosis, n (%)	
Common variable immunodeficiency	14 (40%)
Selective deficiency of IgG subclasses	10 (29%)
Nonfamilial hypogammaglobulinemia	6 (17%)
Other*	5 (14%)

*Other includes antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia (n=4), hereditary hypogammaglobulinemia (n=1), other immunodeficiencies with predominantly antibody defects (n=1)

- The predominant PIDD diagnoses were common variable immunodeficiency (40%) and selective deficiency of IgG subclasses (29%)

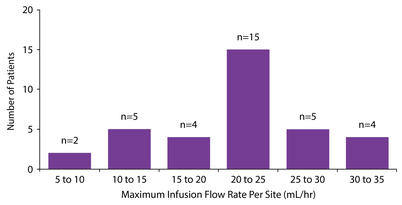
IGSC 16.5% Utilization

Table 2. IGSC 16.5% Dosing and Administration

Parameter	IGSC 16.5% N=35
IGSC 16.5% Doses	**mean ± SD**
Weekly dose (mg/kg)	122 ± 31.8
Monthly dose (mg/kg)	489 ± 127.1
IGSC 16.5% Administration	**mean ± SD**
Initial rate per infusion site (mL/hr)	9 ± 3.1
Initial rate per all infusion sites (mL/hr)	27 ± 6.9
Initial volume per infusion site (mL)	19 ± 3.1
Maximum rate per infusion site (mL/hr)	20 ± 6.4
Maximum rate per all infusion sites (mL/hr)	56 ± 19.9
Maximum volume per infusion site (mL)	21 ± 4.1
Number of infusion sites	3 ± 0.7

- All patients received weekly dosing for a total of 24 infusions
- The mean weekly dose was 122 mg/kg, equating to a monthly dose of 489 mg/kg
- Initial infusion rate per infusion for all sites was 27 mL/hr with a maximum rate of 56 mL/hr (min=22, max=86) and 3 infusion sites

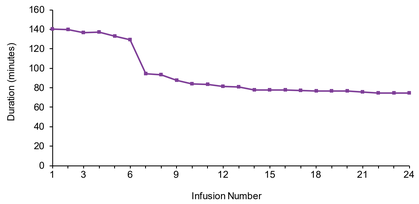
Figure 1. IGSC 16.5% Maximum Infusion Flow Rates Per Site



- Thirty-four IG-naive patients (97%) had at least 1 infusion rate increase during the study
- The majority (60%, n=21) increased their maximum infusion rate at infusion 7

IGSC 16.5% Utilization, cont.

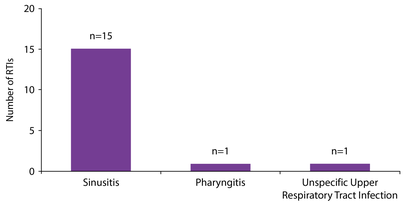
Figure 2. IGSC 16.5% Average Duration of Infusion



- Average infusion duration shortened over time, most notably at infusion 7

IGSC 16.5% Efficacy

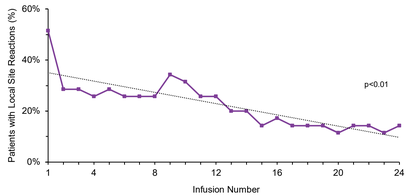
Figure 3. Bacterial Respiratory Tract Infections



- A total of 17 bacterial RTIs were reported in 13 patients (33%) during the study period
- No RTIs were deemed serious or required hospitalization

IGSC 16.5% Tolerability

Figure 4. IGSC 16.5% Local Site Reactions



- Local reactions were highest at infusion 1 and decreased significantly over time (p<0.01)

IGSC 16.5% Tolerability, cont.

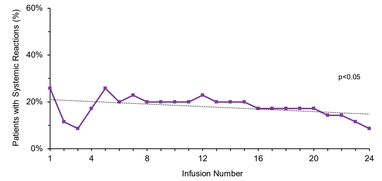
Table 3. Detailed Local Site Reactions

Local Site Reaction	By Patient (N=35) n (%)	By Infusion (N=840) n (rate)*
Redness	14 (40%)	80 (0.10)
Swelling	11 (31%)	89 (0.11)
Itching	11 (31%)	58 (0.07)
Pain	8 (23%)	32 (0.04)
Bruising	4 (11%)	10 (0.01)
Other†	2 (6%)	9 (0.01)

*Rate was calculated as number of infusions divided by 840.
†Other included flakiness in 1 patient during 8 infusions and bleeding in 1 patient during 1 infusion.

- From infusion 1-24, local reactions were reported in 27 patients (77%), most commonly swelling, redness, and itching
- 8 patients (23%) reported no local reactions during the study period
- This data is comparable to reported local site reactions in a cohort of primarily treatment-experienced patients who used IGSC 16.5% for 6 months [6], which showed:
  - 28% with no local site reactions
  - Common reactions of redness (rate=0.09), swelling (0.13), itching (0.05)

Figure 5. IGSC 16.5% Systemic Reactions



- Systemic reactions diminished significantly over time (p<0.05)

Table 4. Detailed Systemic Reactions

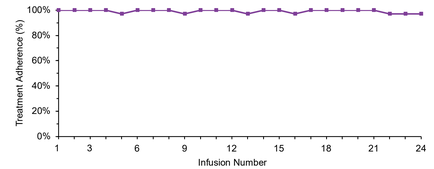
Systemic Reaction	By Patient (N=35) n (%)	By Infusion (N=840) n (rate)*
Fatigue	10 (29%)	98 (0.12)
Headache	10 (29%)	80 (0.10)
Nausea/vomiting	3 (9%)	20 (0.02)
Myalgia/arthralgia	3 (9%)	6 (0.01)
Fever/chills	2 (6%)	9 (0.01)
Other†	1 (3%)	5 (0.01)

*Rate was calculated as number of infusions divided by 840.
†Other included dizziness in 1 patient during 5 infusions.

- Systemic reactions were reported in 15 patients (43%), most commonly fatigue and headache
- 20 patients (57%) had no systemic reactions during the study period
- A previous study [6] of primarily treatment-experienced patients who used IGSC 16.5% for 6 months reported:
  - 41% with no systemic reactions
  - Predominant reactions of fatigue (rate=0.15) and headache (0.10)
- Our data indicated a low rate of systemic reactions, with over half experiencing no reactions.

IGSC 16.5% Adherence

Figure 6. IGSC 16.5% Treatment Adherence



- The overall treatment adherence rate was 99%
- 833 of 840 infusions were self-administered within ±2 days of the treatment window
- 6 infusions were delayed or missed outside of the treatment window; 1 infusion was delayed because of payor-related reasons

Discussion and Conclusion

We present IGSC 16.5% 6-month outcomes in PIDD patients naïve to IG treatment.

- A total of 35 patients completed 24 weeks of IGSC 16.5% therapy.
- Standard dosing and administration were observed.
- The ramp-up schedule was consistent with previous prescribing information recommending a dose increase at infusion 7 [8].
- No serious bacterial RTIs were reported.
- Rates of both local and systemic reactions were highest at initiation and then decreased significantly over time.
- IGSC 16.5% was very tolerable with 23% and 41% of patients having no local site reactions or no systemic reactions, respectively.
- In both the clinical trial data and our data, the most common local site reactions were swelling, redness, and itching [5].
- For systemic reactions, fatigue and headache were most reported by study patients. Systemic reactions were similar or better to previously reported data on treatment-experienced patients [6].
- Treatment adherence was exceptionally high with IGSC 16.5% [6,7].
- Clinical trials in subcutaneous IG, including those with IGSC 16.5%, have been conducted in patients receiving previous IG therapy [5,6]. Our study greatly contributes to the literature by reporting the initiation of IGSC 16.5% in IG naïve patients.

Our real-world study confirmed effectiveness and tolerability with IGSC 16.5% in IG treatment-naïve patients with PIDD.

A collaborative practice model of committed physicians and specialty-trained nurses and pharmacists resulted in excellent patient adherence with IGSC 16.5% in IG treatment-naïve patients.

References

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