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HEALIX

Poster #17

Real-World Immune Globulin Subcutaneous 16.5% Use in Treatment-Naïve Patients with Primary Immunodeficiency

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Abstract

Introduction: Immune Globulin Subcutaneous (Human), 16.5% solution (IGSC 16.5%) is approved for the treatment of primary immunodeficiencies (PID) in adults and pediatrics patients. We have previously reported good safety, effectiveness, and tolerability with IGSC 16.5% in a real-world setting, primarily with treatment-experienced patients. The purpose of this study was to evaluate clinical outcomes in immune globulin (IG) treatment-naïve patients who used IGSC 16.5% as initial therapy.

Methods: We performed a retrospective chart review from product availability in May 2019 through April 2022 of IG treatment-naïve patients receiving at least six months (24 weekly infusions) of IGSC 16.5% (Cutaquig®). Patients naïve to IG therapy were initiated on IGSC 16.5% in their physician's clinics, with patient training conducted by the clinic nurses. Pharmacists dispensed IGSC 16.5% and supplies and performed initial and monthly comprehensive assessments. Study data included patient demographics, IGSC 16.5% therapy utilization, adverse reactions, respiratory tract infections (RTIs), and treatment adherence through 24 infusions. IGSC 16.5% administered outside of the window of ±2 days were defined as delayed or missed treatments.

Results: Thirty-nine IG treatment-naïve patients initiated IGSC 16.5% during the study period. Mean age was 49±13 years with 90% females. All patients were diagnosed with PID, with common variable immunodeficiency (CVID) predominant at 44%. All patients were on weekly dosing. The mean initiation dose was 124±31.6 mg/kg/week (495±126.5 mg/kg/month). The initial infusion rate was <30 mL/hr/all sites in 33 (85%) patients and 30-50 ml/hr/all sites in 6 patients. The mean maximum infusion rate was 53.5±20.7 mL/hr/all sites (min 22.1, max 86.1). Approximately half of patients (54%) reported local reactions at the first infusion followed by a drop in reactions of 26% at the second infusion. Local reactions continued to decrease over time. Over the course of 24 infusions, the most common local reactions were swelling, redness and itching. Thirty-three percent of patients reported systemic reactions at the first infusion, which declined by 18% at the second infusion. These also continued to decline over time. The most commonly reported systemic reactions were fatigue and headache. There were 18 bacterial RTIs in 14 (36%) patients, none of which required hospitalization. Thirty-five (90%) patients completed therapy through the 24-week study window. Four patients discontinued therapy prior to 24 infusions, 2 for tolerability issues, 1 for payor issues, and 1 for patient preference. Of 871 total infusions, 864 were self-administered within ±2 days of the scheduled treatment window. Delayed doses and missed infusions accounted for 2 visits and 4 visits, respectively. Overall, treatment adherence was 99%.

Discussion: A total of thirty-five IG treatment-naïve PID patients completed six months of IGSC 16.5% infusions. Standard dosing and infusion rates were observed. The overall rates of reactions were comparable to the clinical trial. A large decline in both local and systemic reactions was seen from the first to second infusion. In IG treatment-naïve patients, the discontinuation rate of IGSC 16.5% was low, and treatment adherence was extremely good at six months.

Conclusions: Our real-world study demonstrates effectiveness, tolerability, and treatment adherence with IGSC 16.5% in IG treatment-naïve patients.

Introduction

Immune globulin subcutaneous (IGSC) therapy is used for the treatment of primary humoral immunodeficiency (PI) [1]. Compared to immune globulin intravenous (IGIV) therapy, IGSC therapy results in fewer systemic adverse reactions and more predictable pharmacokinetic profile in patients with PI. IGSC therapy can be effectively provided through a physician clinic with nursing and pharmacy services, demonstrating high medication adherence [1-3].

IGSC 16.5% (Cutaquig®) is a human immune globulin subcutaneous product approved for the treatment of PI 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 [5].

Initial real-world assessments of IGSC 16.5% indicated good safety and efficacy at six months and twelve months. These studies were primarily composed of treatment-experienced patients [6-7]. The purpose of this study was to evaluate clinical outcomes in immune globulin (IG) treatment-naïve patients who used IGSC 16.5% as initial immune globulin therapy for PI.

Methods

A retrospective, observational review from May 2019 through April 2022 of IG treatment-naïve patients who initiated IGSC 16.5% was conducted. All patients were required to have at least six months (i.e., 24 weeks) of study data for review.

Study patients initiated IGSC 16.5% at physician clinics. IGSC-trained pharmacists and nurses provided training in self-administration and therapy management. Pharmacists also dispended 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-site and systemic AEs
- 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.

Results

Study Patients

- A total of 39 IG treatment-naïve patients with PI initiated IGSC 16.5%.

Table 1. Baseline Demographics and Disease Characteristics

Parameter	IGSC 16.5% N=39
Age in years, mean±SD	49±12.5
Female gender, n (%)	35 (90%)
Body mass index in kg/m^2, median (IQR)	29 (26-33)
PI primary diagnosis, n (%)	
Common variable immunodeficiency	17 (44%)
Selective deficiency of IgG subclasses	10 (26%)
Nonfamilial hypogammaglobulinemia	6 (15%)
Other*	6 (15%)

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

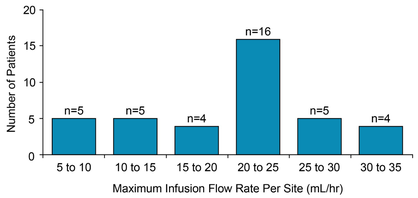
IGSC 16.5% Utilization

Table 2. IGSC 16.5% Dosing and Administration

Parameter	IGSC 16.5% N=39
IGSC 16.5% Initiation Dose	**mean ± SD**
Mean weekly dose (mg/kg)	124 ± 31.6
Mean monthly dose (mg/kg)	495 ± 126.5
IGSC 16.5% Administration	**mean ± SD**
Mean initial rate per infusion site (mL/hr)	9 ± 3.0
Mean initial volume per infusion site (mL)	19 ± 3.1
Mean maximum rate per infusion site (mL/hr)	19 ± 6.9
Mean maximum volume per infusion site (mL)	20 ± 4.1
Mean maximum number of infusion sites	3 ± 0.7

- All patients received IGSC 16.5% infusions weekly.
- On average, patients utilized 22±5.5 infusions each over the study period.
- Four discontinued therapy prior to week 24 due to payor requirements (n=1), infusion reaction (n=1), and unrelated medical conditions (n=2).

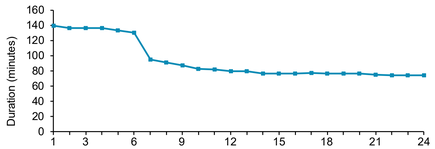
Figure 1. IGSC 16.5% Maximum Infusion Flow Rate Per Site



- Thirty-four IG-naive patients (87%) had at least 1 infusion rate increase during the study.
- The majority (68%, n=23) had their first ramp-up at infusion 7.

IGSC 16.5% Utilization

Figure 2. IGSC 16.5% Average Duration of Infusion, Through 24 Weeks*

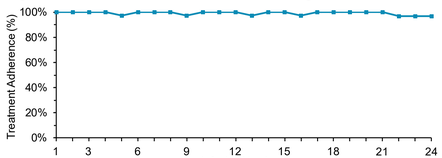


*Four patients discontinued IGSC 16.5% at infusions #3 (n=1), #5 (n=1), #6 (n=1), #22 (n=1).

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

IGSC 16.5% Adherence

Figure 3. IGSC 16.5% Treatment Adherence, Through 24 Weeks*

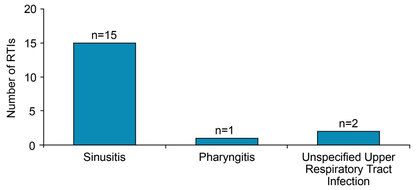


*Four patients discontinued IGSC 16.5% at infusions #3 (n=1), #5 (n=1), #6 (n=1), #22 (n=1).

- 865 of 872 infusions were self-administered within ±2 days of the treatment window, resulting in an overall treatment adherence of 99%.
- Six infusions were delayed or missed outside of the treatment window due to patient non-adherence. One infusion was delayed because of payor-related reasons.

IGSC 16.5% Efficacy

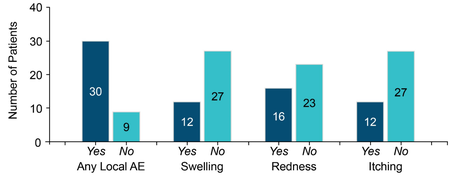
Figure 4. Bacterial RTIs, Through 24 Weeks



- A total of 18 bacterial RTIs were reported in 14 patients over 24 weeks.
- No RTIs were serious or required hospitalization.

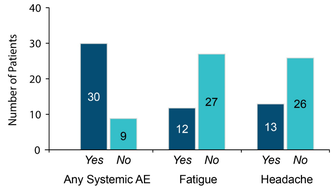
IGSC 16.5% Tolerability

Figure 5. IGSC 16.5% Local Site AEs, Through 24 Weeks



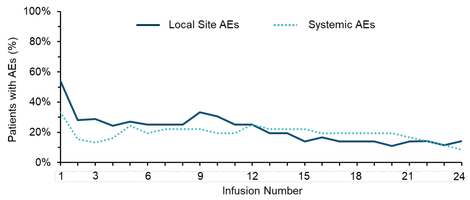
- Nine IG-naïve patients (23%) reported no local site AEs during the study.
- Of local AEs, the most common were:
  - Swelling: occurred in 90 of 872 infusions (10%) in 12 patients
  - Redness: occurred in 83 infusions (10%) in 16 patients
  - Itching: occurred in 60 infusions (7%) in 12 patients

Figure 6. IGSC 16.5% Systemic AEs, Through 24 Weeks



- Nine patients (23%) had no systemic AEs during the study period.
- Of systemic AEs, the most predominant were:
  - Fatigue: occurred in 112 of 872 infusions (13%) in 12 patients
  - Headache: occurred in 86 infusions (10%) in 13 patients

Figure 7. IGSC 16.5% Incidence of AEs Over Time



- From infusion 1 to 2, large drops in reaction rates were observed for local site reactions (54% vs. 26%) and systemic reactions (33% vs. 18%).

Discussion

We present outcomes of IGSC 16.5% through six months of treatment in an outpatient clinical setting. To our knowledge, this is the first IGSC 16.5% study focusing solely on patients who were naïve to IG treatment.

- A total of 39 patients were included with 35 completing 24 weeks of IGSC 16.5% therapy during the study period.
- Compared to the pivotal phase 3 clinical trial for IGSC 16.5% [5], our population was older and had a higher proportion of females, though specific diagnoses were common between studies (i.e., common variable immunodeficiency, selective deficiency of IgG subclasses).
- Standard dosing and administration were observed.
- The ramp-up schedule was consistent with previous prescribing information recommending a dose increase at infusion seven [8] .
- No serious bacterial RTIs were reported.
- Our study reports high treatment adherence with IGSC 16.5% in patients new to IG therapy at 99%.
- 23% of IG-naïve patients initiating IGSC 16.5% had no local site or systemic reactions.
- In both the clinical trial data and our data, the most common local site AEs were swelling, redness, and itching.[5] The rates of patients experiencing local reactions diminished with subsequent infusions.
- For systemic AEs, fatigue and headache were the most reported by study patients. Systemic AEs were also similar to our previously reported data.[6,7] Rates of these reactions also diminished over time.
- The limitations of our study include limited generalizability due to the small sample size, as well as potential response bias inherently associated with self-reported data.

Conclusion

This real-world study demonstrates effectiveness and tolerability with IGSC 16.5% through six months of infusions in IG treatment-naïve patients.

IGSC 16.5% was successfully initiated in Ig treatment-naïve patients by immunologists and infectious disease physicians, along with clinical nurses and pharmacists specialty trained to manage patients receiving IGSC.

Patients receiving IGSC 16.5% managed through physician clinics resulted in high adherence to therapy.

References

1. Jolles S, et al. *Clin Exp Immunol* 2015; 179(2): 146-160.
2. Vultaggio A, et al. *Clin Drug Investig* 2015; 35(3): 179-185.
3. Kobrynski L. *Biologics* 2012; 6: 277-287.
4. Cutaquig® (immunoglobulin human subcutaneous) [package insert]. Octapharma USA, Inc. Paramus, NJ: 2021.
5. Kobayashi RH, et al. *Front Immunol* 2019; 10: 40.
6. Langford J, et al. *Ann Allergy Asthma Immunol* 2020; 125(5): S38.
7. Herrscher RF, et al. *J Allergy Clin Immunol* 2021; 147(2): AB72.
8. Cutaquig® (immunoglobulin human subcutaneous) [package insert]. Octapharma USA, Inc. Paramus, NJ: 2017.

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