AAAAI 2020
Poster #101

Real-World Evaluation of Efficacy and Tolerability of Immune Globulin Subcutaneous 16.5% in the Treatment of Patients with Primary Immunodeficiency

Richard F. Herrscher, MD, FACAAI[1]; Jeffrey W. Langford, MD, AE-C[2]; Samantha A. Mehta, PharmD[3]; Lucinda J. Van Anglen, PharmD[3]

[1]AIRCare: Asthma, Allergy, and Immunology, Dallas, Texas; [2]Langford Allergy, LLC, Macon, GA; [3]Healix Infusion Therapy, LLC, Sugar Land, TX

Abstract

Rationale: Immune Globulin Subcutaneous (Human), 16.5% solution (IGSC 16.5%) is a new subcutaneous immunoglobulin for the treatment of primary immunodeficiencies (PID). Available from Octapharma as Cutaquig® since May 2019, we report the first real-world data regarding use of IGSC 16.5%.

Methods: Data were collected from all patients receiving at least one dose of IGSC 16.5% who were either naïve to immunoglobulin (IG) therapy or previously receiving intravenous or subcutaneous IG. Patients were initiated and trained in a physician clinic setting. Specialty pharmacists provided therapy and performed comprehensive assessments upon initiation and monthly to capture efficacy, tolerability, and treatment compliance. Data collection included demographics, IGSC 16.5% therapy regimen, adverse reactions, and infection rates.

Results: Thirty-three patients (age 52±10 years, 91% female) were administered a total of 154 IGSC 16.5% weekly infusions (range 1-9 infusions/patient). All patients were treated for PID, of which 17 were transitioned from another IGSC product, 13 were transitioned from intravenous IG (mean dose conversion factor 1.14±0.29), and 3 were treatment-naïve. Mean dose was 155±49.2 mg/kg/week (619±197 mg/kg/monthly). A total of 22/33 (67%) patients reported local-site reactions (rate 0.60/infusion), with injection pain and swelling most common. Systemic reactions were reported in 20/33 (61%) of patients (0.47/infusion), with headache and fatigue most common. Incidence of reactions was highest with the first infusion. Therapy was discontinued in one per patient request. There have been no serious infections to date.

Conclusions: This first real-world data suggests that IGSC 16.5% for PID is effective and tolerable, to be confirmed in this ongoing study.

Introduction

Subcutaneous immune globulin (IGSC) is indicated for the treatment of primary immunodeficiencies (PID).[1] Compared to intravenous immunoglobulin (IVIG), IGSC is equally effective in preventing infections and offers a more favorable safety profile. Additionally, IGSC can be self-administered, is cost-effective, and has been associated with better quality of life scores and treatment compliance in patients with PID.[2-3]

Immune Globulin Subcutaneous (Human) - hipp, 16.5% solution (IGSC 16.5%) is a new human immunoglobulin product for subcutaneous administration approved in December 2018 for the treatment of PID in adults.[4] Data from the phase 3 trial of patients transitioned from IVIG to IGSC demonstrated efficacy with no serious bacterial infections, acceptable rates of other infections, and stable IgG plasma levels during the study period.[5]

Given the recent approval for the US market, real-world assessment of post-marketing clinical experience is lacking. The objective of this study is to retrospectively evaluate post-marketing clinical outcomes in a real-world setting.

Methods

Retrospective chart review of all PID patients receiving IGSC 16.5% through outpatient immunology and infectious disease physician clinics June 2019 through December 2019.

- At the time of IGSC initiation, all patients and/or caregivers received routine counseling on proper self-administration of subsequent doses, medication storage, common side effects, and adherence. A comprehensive assessment was performed monthly and/or prior to each IGSC dispense by a pharmacist.
- Data collection included:
  - Baseline demographics
  - IGSC 16.5% therapy details, including dose, number of infusion sites, infusion volume, and infusion rate
  - Incidence of respiratory infections
  - Patient-reported local site and systemic adverse reactions
  - Patient adherence was defined as the use of IGSC as ordered by the physician and dispensed by the pharmacist. Missed or delayed doses were captured if administered outside of the treatment window of ±2 days.
  - IGSC 16.5% treatment discontinuation, and reasons for discontinuation
- Descriptive analyses were reported as frequencies and proportions for categorical variables, and as mean ± standard deviation (SD) or median (interquartile range, IQR) for continuous variables.

Results

Study Patients

Study Population

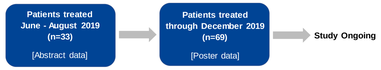
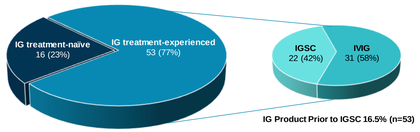


Table 1. Baseline Characteristics

Parameter	IGSC 16.5% n=69
Age in years, median (min, max)	52 (19, 70)
Female gender, n (%)	56 (81%)
Body mass index in kg/m^2, median (min, max)	26.8 (15.4, 47.7)
PID primary diagnosis, n (%)	
Common variable immunodeficiency (CVID)	39 (56%)
Nonfamilial hypogammaglobulinemia	13 (19%)
Selective deficiency of IgG subclasses	13 (19%)
Other*	4 (6%)

*Other includes 3 cases of antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia and 1 case of hereditary hypogammaglobulinemia

Figure 1. Prior IG Therapy



- Almost one-fourth of patients were naïve to IG therapy
- 53 patients initiated on IGSC 16.5% were previously treated with IG products for a median of 2.7 (min 0.1, max 26.7) years
- In treatment-experienced patients, 22 were transitioned from another IGSC product and 31 were transitioned from IVIG with a mean dose conversion factor of 1.19±0.24

IGSC 16.5% Therapy

Table 2. IGSC 16.5% Infusions and Dosing

Parameter	IGSC 16.5% n=69
Number of Infusions to Date*	
Total number of infusions	1270
Number of infusions per patient, median (min, max)	20 (1, 32)
Infusions Per Patient to Date*	
Less than 8 infusions, n (%)	10 (14%)
Between 8 and 16 infusions, n (%)	17 (25%)
Greater than 16 infusions, n (%)	42 (61%)
IGSC 16.5% Dose	
Dose in mg/kg, mean ± SD	
Weekly	143 ± 43
Monthly	570 ± 176

*Study is ongoing. Data is reported through December 31, 2019.

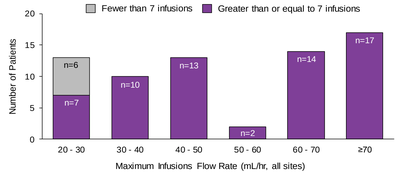
- All patients received weekly infusions, with the exception of one on every other week infusions

IGSC 16.5% Therapy

Table 3. IGSC 16.5% Administration Parameters

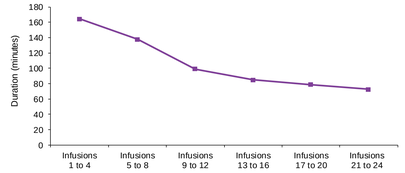
Administration Parameter	IGSC 16.5% n=69 median (min, max)
Maximum number of infusion sites	3 (2, 6)
Maximum volume per infusion site in mL	20 (13.3, 40)
Maximum rate per infusion site in mL/hr	16.1 (6.1, 30.9)
Maximum rate for all infusions sites in mL/hr	49.9 (23.6, 93.5)

Figure 2. IGSC 16.5% Maximum Infusion Flow Rate for All Infusion Sites



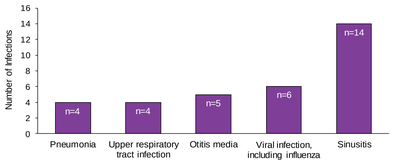
- 55 of 69 patients ramped up on or following the 7th infusion
- Median maximum rate for patients receiving greater than or equal to 7 infusions was 56.3 (min 23.6, max 93.5)

Figure 3. IGSC 16.5% Average Duration of Infusion, Through 6 Months



IGSC 16.5% Efficacy

Figure 4. Respiratory Infections, Through 6 Months



- A total of 38 respiratory infections have been reported in 29 (42%) patients
- Antibiotics were prescribed for 31 of the 38 respiratory infections
- Two infections resulted in urgent care or emergency department visits, and one pneumonia resulted in hospitalization

IGSC 16.5% Tolerability

Figure 5. IGSC 16.5% Local Site Adverse Reactions, Through 6 Months

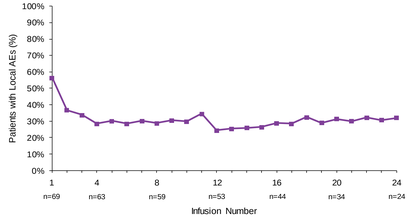


Table 4. IGSC 16.5% Local Site Adverse Reactions, Through 6 Months

Local Site Reaction	By Patient (N=69) n (%)	By Infusion (N=1196) n (rate)
Redness	29 (42%)	119 (0.10)
Pain	29 (42%)	80 (0.07)
Swelling	28 (41%)	190 (0.16)
Itching	16 (23%)	91 (0.08)
Bruising	11 (16%)	37 (0.03)

- Incidence of local site reactions was highest with the first infusion and diminished over time
- 17 (25%) patients reported no local site reactions with IGSC 16.5% therapy, more commonly with treatment-experienced patients (16/53 vs. 1/16)

Figure 6. IGSC 16.5% Systemic Adverse Reactions, Through 6 Months

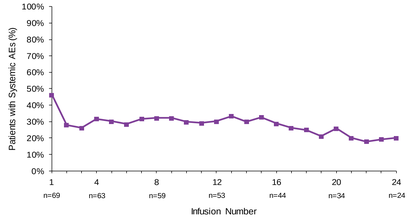


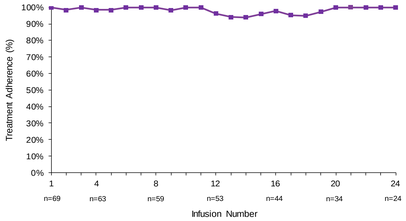
Table 5. IGSC 16.5% Systemic Adverse Reactions, Through 6 Months

Systemic Adverse Reaction	By Patient (N=69) n (%)	By Infusion (N=1196) n (rate)
Fatigue	27 (39%)	209 (0.17)
Headache	24 (35%)	150 (0.13)
Nausea/vomiting	12 (17%)	49 (0.04)
Myalgia/arthralgia	11 (16%)	61 (0.05)
Fever/chills	7 (10%)	40 (0.03)

- Again, the incidence of systemic adverse reactions was highest with the first infusion and diminished over time
- 27 (39%) patients reported no systemic adverse reactions with IGSC 16.5% therapy, more commonly with treatment-experienced patients (23/53 vs. 4/16)

IGSC 16.5% Adherence

Figure 7. IGSC 16.5% Treatment Adherence, Through 6 Months



- Of 1196 infusions through 6 months, a total of 20 infusions in 7 patients were missed and/or delayed. Overall treatment adherence was 98%.

Treatment Discontinuation

- 10 patients discontinued IGSC 16.5% therapy prior to December 31, 2019 at a median time (min, max) of 2.8 (0.2, 5.3) months
- Reasons for IGSC 16.5% discontinuation were:
  - 3 drug-related adverse events: 2 systemic, 1 local
  - 5 patient preference: 3 transitioned back to IVIG, 2 transitioned back to prior IGSC product
  - 1 IG drug holiday
  - 1 payor denial

Discussion and Conclusion

This is the first post-marketing data of IGSC 16.5% in a real-world clinical setting:

- A total of 69 PID patients were initiated on IGSC 16.5% therapy through December 31, 2019, including almost a quarter of patients naïve to IG therapy.
- Standard dosing and administration were observed, with the majority of patients following the recommended ramp-up schedule.
- A total of 38 respiratory infections have been reported to date, though most were mild-to-moderate in severity. Only one infection required hospitalization.
- The incidence of adverse reactions was similar to previously reported data on alternative IGSC products, and diminished over time.[6] The most common local site reactions were redness and pain. The most common systemic adverse reactions were fatigue and headache. Adverse reactions led to therapy discontinuation in 4% of patients.
- IGSC 16.5% treatment adherence at 6 months was 98%.

In conclusion, home self-administration of IGSC 16.5% provided through outpatient immunology and infectious disease physician clinics with continuous pharmacist oversight has demonstrated good efficacy, tolerability, and treatment adherence. This retrospective study is ongoing.

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. Hoboken, NJ: 2017.
5. Kobayashi RH, et al. *Front Immunol* 2019; 10: 40.
6. Herrscher RF, et al. *J Allergy Clin Immunol* 2019; 143(2): AB115.

This study was sponsored by Octapharma USA, Inc. Hoboken, NJ.