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Poster #P170

Long-Term Outcomes with Immune Globulin Subcutaneous 16.5% in Treatment of Primary Immunodeficiency

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Background

Immune globulin subcutaneous (IGSC) 16.5% solution (Cutaquig®) is indicated to manage primary humoral immunodeficiency (PID) in adults and pediatric patients aged 2 years and older [1-3]. Unlike treatments using immune globulin intravenous (IGIV), IGSC treatments offer fewer systemic adverse reactions and a more consistent pharmacokinetic profile in patients with PID [4]. Additionally, IGSC can be self-administered and has been associated with a better quality of life and treatment compliance in patients with PID. [5,6]

Administration of IGSC therapy provided specifically through a physician office infusion center with nursing and pharmacy services has shown efficacy in addition to high medication adherence [7,8]. A recent study demonstrated positive tolerability, safety and efficacy in 100 patients who received a year of therapy with IGSC 16.5% [9]. Building upon these findings, the aim of this study was to evaluate the first long-term outcomes of IGSC 16.5% in patients with PID over 18 months.

Objective

The objective of this study is to evaluate effectiveness, safety, and tolerability of IGSC 16.5% in patients with PID receiving 18 months of therapy.

Methods

A retrospective, observational study was conducted in adult patients with PID who received 18 months of IGSC 16.5% from June 2019 to March 2023. Patients were eligible if they had a diagnosis of PID, initiated IGSC 16.5% treatment in infectious disease or immunology practices and completed 18 months of treatment. Patients were included in the study who previously utilized IGIV or IGSC therapies or who were naïve to therapy (minimum of six months with no immunoglobulin therapy).

Patient initiation was conducted by IGSC-trained pharmacists and nurses. The treatment initiation and training occurred in the physician offices. Pharmacists dispensed the medication, devices and supplies, typically on a monthly basis and performed monthly assessments to capture patient-reported outcomes.

Primary endpoints were:

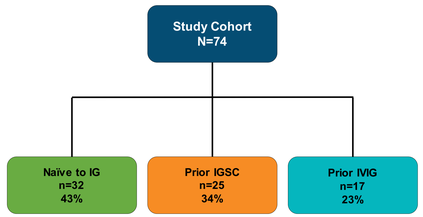
- Tolerability of treatment, defined as local infusion site reactions (ISRs)
- Safety, defined as systemic adverse events (AEs)
- Efficacy, defined by rate of serious bacterial respiratory tract infections (SBIs) per person-year, SBIs were defined as respiratory infections that required hospitalization. Overall rates of respiratory tract infections (RTIs) per person-year were also captured.

Other data included:

- Baseline demographics and disease characteristics
- IGSC 16.5% therapy parameters
- Treatment adherence (e.g., utilization within ±2 days of scheduled treatment)

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. Linear regression modeling was used for the incidence of ISRs and AEs as a function of infusion number.

Study Cohort



- The study included three sub-groups of patients who all received IGSC 16.5%
  - The largest group was the treatment-naïve group.
  - Those on prior IGSC received IG therapy for a median of 3.1 years.
  - Those on prior IGIV received IG therapy for a median of 4.4 years.

Results

Study Patients

- A total of 74 patients received IGSC 16.5% over an 18-month period.

Table 1. Baseline Demographics and Disease Characteristics

Parameter	IGSC 16.5% N=74
Age in years, median (min, max)	52 (18, 73)
Female gender, n (%)	63 (85%)
Body weight in kg, median (min, max)	77.1 (44.5, 165.0)
Body mass index in kg/m^2, median (min, max)	28.2 (16.8, 66.2)
PI primary diagnosis, n (%)	
Common variable immunodeficiency (CVID)	47 (63.5%)
Selective deficiency of IgG subclasses	10 (13.5%)
Nonfamilial hypogammaglobulinemia	9 (12.2%)
Other*	8 (10.8%)
IG treatment-experienced, n (%)	42 (56.8%)
Transitioned from alternative IGSC, n (%)	25 (59.5%)
Transitioned from IVIG, n (%)	17 (40.5%)
IG treatment-naïve, n (%)	32 (43.2%)

*Other includes antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia (n=5), hereditary hypogammaglobulinemia (n=2), other immunodeficiencies with predominantly antibody defects (n=1)

- As with previously reported data, most of our patients were female [2,7,8].
- The predominant PID diagnoses were common variable immunodeficiency, followed by selective deficiency of IgG subclasses.

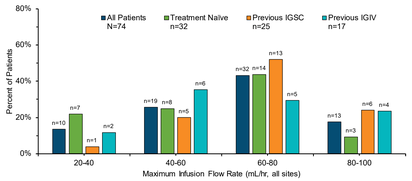
Therapy Parameters

Table 2. Dosing and Administration

Parameter	IGSC 16.5% N=74
IGSC 16.5% Doses	**median (min, max)**
Weekly dose (mg/kg)	136.7 (48.1, 293.7)
Monthly dose (mg/kg)	546.9 (192.5, 1174.7)
IGSC 16.5% Infusions	
Total infusions	5,772
IGSC 16.5% Administration	**median (min, max)**
Initial rate per infusion site (mL/hr)	7.9 (4.2, 24.9)
Initial rate per all infusion sites (mL/hr)	24.5 (21.6, 60.8)
Initial volume per infusion site (mL)	20 (14,54)
Maximum rate per all infusion sites (mL/hr)	61.8 (22.1, 93.5)
Maximum volume per infusion site (mL)	18 (14, 54)
Number of infusion sites	3 (2, 6)

- All patients received weekly infusions.
- The median weekly dose was 136.7mg/kg, equating to a monthly dose of 546.9 mg/kg. Median conversion factor for those transitioning from IGIV was 1.3.
- Initial median infusion rate for all sites was 24.5 mL/hr with a maximum rate of 62 mL/hr and 3 median infusion sites.

Figure 1. Maximum Infusion Flow Rate for All Infusion Sites



- Most patients (43%) across all treatment groups achieved a maximum infusion rate of 60-80ml/hr for all sites.
  - The median maximum infusion rate for the treatment sub-groups were:
    - Treatment naïve 60.8 mL/hr
    - Prior IGSC 73.5 mL/hr
    - Prior IGIV 60.3 mL/hr
- The ramp up for the infusion rate change following initiation of IGSC 16.5% occurred at a median of the 7th infusion for all treatment groups.

Tolerability

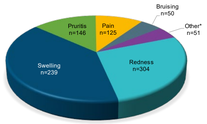
Table 3. Patients with ISRs

ISR	Total N (%) N=74	Treatment naive n(%) n=32	Prior IGSC n(%) n= 25	Prior IGIV n(%) n=17
Swelling	32 (43.2%)	14 (43.8%)	8 (32%)	10 (58.8%)
Redness	27 (36.5%)	14 (43.8%)	5 (20%)	8 (47.1%)
Pain	25 (33.8%)	10 (31.3%)	8 (32%)	7 (41.2%)
Pruritis	19 (25.7%)	10 (31.3%)	4 (16%)	5 (29.4%)
Bruising	12 (16.2%)	6 (18.8%)	3 (12%)	3 (17.6%)
Other*	14 (18.9%)	6 (18.8%)	4 (16%)	4 (23.5%)

* other included: burning (n=6), warm:th (n=6), leaking (n=5), nodules (n=5) and bleeding (n=4)

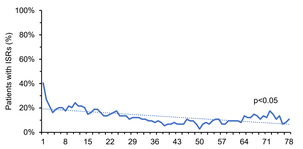
- ISRs were reported in 55 patients (74.3%).
- Patients who are treatment naïve were more likely to experience local ISR: n=27 (84.4 %), followed by those transitioning from IGIV: n=3 (76.4%) and fewest in those who were previously on an alternative IGSC: n= 15 (60%).

Figure 2. Total ISRs



- A total of 1098 ISRs were reported in 5772 infusions for an overall rate of 0.2.

Figure 3. Incidence of ISR Over Time



- ISRs were highest at infusion 1 and decreased over time.
- A slight increase in reporting of reactions occurred in the second year following implementation of a real-time online patient reporting tool.

Safety

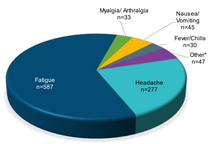
Table 4. Patients with AEs

AE	Total N (%) N=74	Treatment naive n(%) n=32	Prior IGSC n(%) n= 25	Prior IGIV n(%) n=17
Fatigue	26 (35.1%)	10 (31.3%)	13 (52%)	3 (17.6%)
Headache	22 (29.7%)	10 (31.3%)	6 (24%)	6 (35.3%)
Fever/Chills	4 (5.4%)	3 (9.4%)	0 (0%)	1 (5.9%)
Nausea/ vomiting	7(9.4%)	3 (9.4%)	1(4%)	3 (17.6%)
Myalgia/arthralgia	6 (8.1%)	3 (9.4%)	2 (8%)	1 (5.9%)
Other*	5 (6.8%)	2 (6.3%)	3 (12%)	0 (0%)

* other included: paraspinal muscle spasm (n=2), dyspepsia (n=2), angina (n=1), cervical rigidity(n=1), tight headedness(n=1) and oral ulcers (n=1)

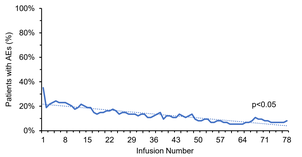
- Systemic AEs were reported in 36 patients (48.6%).
- Prior IGSC patients were more likely to experience systemic AEs: n= 15 (60 %) compared to who were treatment naïve: n=14 (43.8%) and those previously on IGIV: n=7 (41.2%).

Figure 4. Total AEs



- A total of 960 AEs were reported in 5772 infusions for an overall rate of 0.17.

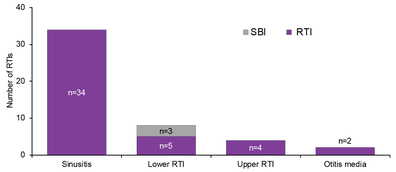
Figure 5. Incidence of AEs Over Time



- Systemic reactions were highest at infusion 1 and decreased over time.

Efficacy

Figure 6. Respiratory Tract Infections

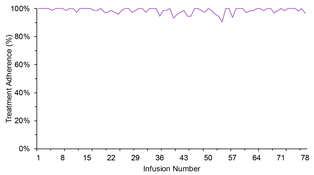


- Efficacy was measured by the rate of serious bacterial infections.
  - Three serious bacterial infections occurred. All were pneumonia and all resolved following hospital discharge.
  - Rate of SBIs was 0.02 per person-year.
  - Rate of non-serious RTI's per person-year was 0.40.

Adherence

Figure 7. Treatment Adherence

- 5703 of 5772 infusions were self-administered within ±2 days of the treatment window, resulting in an overall treatment adherence of 98.8%.
- Infusions were delayed or missed outside of the treatment window due to patient non-adherence or was delayed because of payor-related reasons



Discussion

We present outcomes of IGSC 16.5% through 18 months of treatment.

- A total of 74 PID patients self-administered IGSC 16.5% through immunology and infectious disease physician office infusion centers.
- The majority of patients were female (85%) and median age was 52 years, similar to the adult population in the pivotal phase 3 clinical trial for IGSC 16.5% [2].
- Predominant diagnosis was common variable immunodeficiency and 43% were treatment naïve to therapy prior to initiating IGSC 16.5%.
- Standard dosing was observed, and administration was weekly in all patients, with the majority achieving a maximum infusion rate of 60-80 mL/hr.
- The median infusion rate increase occurred at infusion 7, consistent with the initial labeling of the drug following approval. Currently, IGSC 16.5% can be increased as early as infusion 2 but our patients were initiated prior to this change in the prescribing information.
- The safety profile was favorable with IGSC 16.5% with an overall low rate of reported ISRs. This was similar to the clinical trial and extension study [10], although those patients were transitioned from IGIV. The highest occurrence of ISRs occurred in the treatment-naïve population with significant decreases over time in all patients.
- Systemic reactions were also low with a significant decrease over time. In the sub-groups, those previously receiving another IGSC product had the highest incidence of systemic AEs.
- IGSC 16.5% was effective with a low incidence of SBIs. The overall rate of infections was lower than that reported in the long-term study and supporting maintenance of efficacy over time [10].
- The patient population was remarkedly adherent to therapy, with almost 99% of doses administered within ± 2 days of schedule. This may be attributed to the consistent oversight by the physician, nurses and pharmacists.
- The limitations of study included the retrospective nature of the study and potential inconsistencies with patient-reported outcomes.

Conclusion

This real-world study demonstrates tolerability, safety and efficacy with IGSC 16.5% through 18 months of infusions in both IG treatment-naïve and patients with prior experience.

IGSC 16.5% was successfully initiated in patients treated by immunologists and infectious disease physicians with training and management provided by specialty-trained IG nurses and pharmacists.

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

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