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Poster #18

Real-World Evaluation of Immune Globulin Intravenous 10% in the Treatment of Primary Immunodeficiency

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Abstract

Introduction: Immune Globulin Intravenous (human), 10% liquid (IVIG 10%) is FDA-approved for the treatment of primary immunodeficiencies (PID). IVIG 10% was initially introduced into the US market in 2012 and voluntarily withdrawn in December 2016 by the manufacturer. Another manufacturer subsequently acquired IVIG 10%, optimized the manufacturing processes, obtained FDA approval, and reintroduced it to the US market in May 2019. Given the critical manufacturing process changes and utilization of the product in the US market, the assessment of post-marketing clinical experience is needed. The objective of this study is to evaluate post-marketing safety and tolerability of IVIG 10% in a real-world setting.

Methods: A retrospective observational review of PID patients receiving IVIG 10% (BIVIGAM®) was conducted in physician office infusion centers nationally. A random sample of patients from 18 sites was assessed in those who received IVIG 10% from August 2021 through May 2022. Study data included demographics, IVIG 10% therapy utilization, and reported drug-related adverse events (AEs).

Results: Twelve patients received IVIG 10% infusions at three clinics. The mean age was 75±4.7 years, and 83.3% were female. All patients were IG-treatment experienced and were being treated for PID. Half had a primary diagnosis for common variable immunodeficiency. Patients received a mean IVIG 10% dose of 398±98.3 mg/kg at a dosing frequency of every three or four weeks. Patients received IVIG 10% titrated over 70±22.1 minutes to a maximum rate of 150 mL/hr. To date, study patients have received a mean of 8±1.4 infusions of IVIG 10% with a total of 90 infusions administered. Three AEs (headache, fatigue, nausea) were reported in two patients (16.7%) during two infusions. The overall AE rate per infusion was 2.2%.

Discussion: Twelve PID patients who received IVIG 10% were assessed for tolerability over multiple infusions. All were treatment experienced with previous IVIG. Standard dosing was observed. IVIG 10% was well tolerated with a low rate of AEs.

Conclusions: IVIG 10% treatment at physician-led outpatient clinics demonstrated good safety and tolerability in PID patients.

Introduction

Intravenous immune globulin 10% liquid (IVIG 10%) is FDA-approved for the treatment of primary humoral immunodeficiency (PID) [1]. IVIG 10% (BIVIGAM®) was originally introduced to the US market in 2012 but was voluntarily withdrawn in December 2016 by the original manufacturer. Another manufacturer subsequently acquired IVIG 10%, optimized the manufacturing process, and obtained FDA approval for re-introduction to the US market in May 2019 [2-4].

A multicenter, open-label clinical trial was conducted prior to formulation changes demonstrating efficacy, safety, and tolerability of adverse reactions with IVIG 10% in patients with PID [1,5]. Post-marketing evidence of tolerability is needed given the manufacturing process changes that have occurred.

The objective of this study is to evaluate post-marketing safety and tolerability of IVIG 10% in a real-world setting.

Methods

A multicenter retrospective, observational review of PID patients receiving IVIG 10% from August 2021 through May 2022 was conducted in physician office infusion centers (POICs).

A random sample of patients was selected from an IVIG 10% (BIVIGAM®) population within a network of nationwide POICs from therapy start through discontinuation or the end of the study.

The following data were collected from electronic medical records:

- Baseline demographics and disease characteristics
- Pre-medication therapy
- IVIG 10% utilization and therapy details (e.g., infusion rates)
- Vital signs
- Adverse events (AEs)
- Descriptive statistics were provided as means and standard deviations for continuous variables. For categorical variables, frequencies and percentages are provided. The overall AE rate per infusion was calculated as the total number of AEs reported over the study period divided by the total number of IVIG 10% infusions utilized.

Results

Study Cohort

Figure 1. Study Population

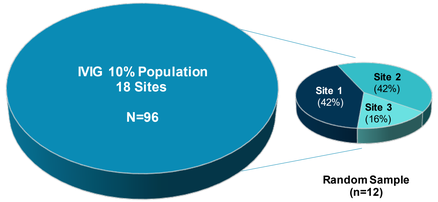


Table 1. Baseline Demographics and Disease Characteristics

Parameter	IVIG 10% N=12
Age in years, mean ± SD	75 ± 4.7
Female gender, n (%)	10 (83%)
Body mass index in kg/m^2, mean±SD	30±4.1
Common comorbidities, n (%)	
Hypertension	9 (75%)
Gastroesophageal reflux disease	8 (67%)
Cancer	7 (58%)
Hypothyroidism	6 (50%)
PID primary diagnosis, n (%)	
Common variable immunodeficiency	6 (50%)
Selective deficiency of IgG subclasses	4 (33%)
Nonfamilial hypogammaglobulinemia	2 (17%)

- All patients had a primary diagnosis of PID and were IVIG treatment-experienced.
- Individuals' doses and dosing intervals immediately prior to switching were kept the same for the first IVIG 10% infusion.
- Pre-medications were continued from the prior IVIG therapy.

Pre-medications

Table 2. Medications Prior to IVIG 10%

Parameter	IVIG 10% N=90 Infusions
Pre-medications	
Infusions with premedication, n (%)	63 (70%)
Pre-medications per infusion, mean±SD	2±1.1
Medications	
Acetaminophen, n (%)	60 (67%)
Diphenhydramine, n (%)	43 (48%)
Corticosteroids, n (%)	
Hydrocortisone	3 (25%)
Methylprednisolone	12 (13%)

- Pre-medications were provided to 10 patients (83%) in 63 of 90 infusions (70%).
- The most utilized pre-medication was acetaminophen (60 of 138, 67%).
- Of those patients receiving pre-medications, 4 of 10 patients (40%) received the same pre-medications at each visit.

IVIG 10% Treatment

Table 3. IVIG 10% Dosing and Administration

Parameter	IVIG 10% N=12
IVIG 10% Dosing	
Number of infusions, mean±SD	8±1.4
Dose in mg/kg, mean±SD	398±98.3
Dosing interval	
Every 3 weeks, n (%)	18 (20%)
Every 4 weeks, n (%)	72 (80%)
IVIG 10% Administration	
Maximum infusion rate in mL/hr, median (min, max)	150 (112-150)
Infusion ramping time in minutes, mean±SD	70±22.1

- Patients could be infused to a maximum rate of 150 mL/hr per practice protocol.
- Eleven patients (92%) reached their maximum ordered infusion rate by infusion 1.

Vital Signs

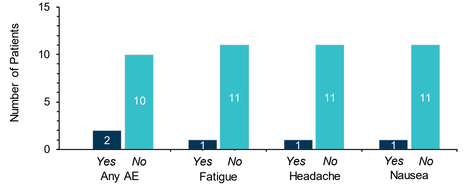
Table 4. Blood Pressure

Parameter	IVIG 10% Infusions
Pre-Infusion, n=86	**median (IQR)**
Systolic blood pressure in mmHg	130 (121-136)
Diastolic blood pressure in mmHg	69 (64-76)
Post-Infusion, n=49	**median (IQR)**
Systolic blood pressure in mmHg	135 (123-155)
Diastolic blood pressure in mmHg	72 (66-78)
Difference, n=48	**mean±SD**
Change in systolic blood pressure in mmHg	10±22.8
Change in diastolic blood pressure in mmHg	5±10.6

- Minimal changes were observed in blood pressures from pre- to post-infusion.

Tolerability

Figure 2. Adverse Events



- Three AEs occurred in 2 patients during 2 infusions: headache and nausea in one infusion and fatigue in one infusion.
- No patients discontinued IVIG 10% due to AEs.
- The overall rate of AEs per infusion was 2.2% for 90 infusions.

Discussion

We present utilization and tolerability of IVIG 10% (BIVIGAM ®) in patients receiving multiple infusions in POICs. To our knowledge, this is the first real-world IVIG 10% study in patients since the product relaunch into the US market in 2019.

- Twelve patients with PID received an average of eight IVIG 10% infusions during the study period, with expected dosing and treatment intervals and consistent with prescribing information.[1].
- All study patients were IVIG treatment-experienced and received the same dose and frequency of IVIG 10% as with the prior therapy.
- The maximum infusion rate was 150 mL/hr as established by POIC protocol. This conservative infusion rate is lower than the maximum recommended in the prescribing information and may have had a beneficial impact on tolerability.[1].
- There were no marked changes in blood pressure observed during the infusions, and no decreases in infusion rates were required during the study period.
- Pre-medications were administered in over two-thirds of infusions, most commonly acetaminophen, but also diphenhydramine and corticosteroids. This standard practice across most POICs may have also positively affected tolerability.
- Overall AE rate was 2.2%, less than that reported in clinical trials of other IVIG products [4-6].
- The limitation of the study is generalizability due to the small study population. Our results represent an interim analysis of ongoing research with PID patients utilizing IVIG 10%.

Conclusion

IVIG 10% treatment at physician-led outpatient clinics demonstrated safety and tolerability in patients with PID over multiple infusions.

Patients experienced very few infusion-related adverse reactions with IVIG 10%.

Established POIC protocols using pre-medications and slower than allowed infusion rates may have contributed to the tolerability of IVIG 10%.

Physician office infusion centers with trained nurses and physician oversight serve as an effective outpatient setting for management of treatment-experienced PID patients receiving IVIG 10%.

References

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