The Immunoglobulin Diagnosis, Evaluation and Key Learnings (IDEaL) Patient Registry: Clinical Profiles, Dosing and Quality-of-Life Measures in the Primary Immune Deficiency Population

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Introduction

Long-term outcomes and patient-reported quality-of-life assessments are not widely available for patients on immunoglobulin (Ig) therapy for different disease types. The Immunoglobulin Diagnosis, Evaluation and Key Learnings (IDEaL) Patient Registry collects longitudinal information on subjects receiving Ig replacement therapy from Coram CVS/specialty infusion services in the home. Patients from our participating investigators are eligible to enroll in the Registry. For this study, we examined the IDEaL primary immune deficiency (PID) patient population, reviewing data for treated patients. Data included baseline immunoglobulin levels and pneumococcal vaccine response as well as dosing, infection rates and quality-of-life assessments over time.

Table 1: IDEaL Demographics

Ig Naïve, Avg Age at Admission - Allergy/Immunology	
Under 18	9 Years
18 and over	59 Years
Age Distribution - Allergy/Immunology	
Under 18	32/364 (9%)
18 and over	332/364 (91%)
65 and over	127/364 (35%)
Gender Distribution - Allergy/Immunology	
Male	89/367 (24%)
Female	278/367 (76%)
PIDD Diagnosis Distribution	
279.0 - Deficiency humoral immunity*	3/367 (0.8%)
279.00 - Hypogammaglobulinem unsp	41/367 (12%)
279.03 - Oth select immunoglobulin deficient	16/367 (4%)
279.04 - Cong hypogammaglobulinem	4/367 (1%)
279.05 - Immunodeficiency w/hyper-IgM	1/367 (0.2%)
279.06 - Common variable immunodeficiency	284/367 (78%)
279.09 - Oth deficiency humoral immunity	1/367 (0.2%)
279.2 - Combined immunity defic	5/367 (0.8%)
279.3 - Unsp immunity deficiency	11/367 (3%)

Methods

As of Q3 2015, the Registry had 410 enrolled patients. The study is approved by Schulman and Associates IRB; each patient was enrolled using an approved informed consent. Information that Coram nurses and pharmacists collected was entered into the IDEaL database. Additionally, subjects were asked to complete an SF-36 questionnaire and a Life Quality Index Questionnaire (LQIQ) every six months.

Results

Table 1 shows the breakdown of age and gender in our primary immune deficiency disease (PIDD) population. The average age of our Ig-naïve patients who started on treatment with us was 59 for those above the age of 18, and 9 for those under the age of 18.

Figure 1 shows the distribution of patients' baseline of serum IgG levels. A total of 75 percent of PIDD patients had IgG levels below a reference minimum of 700 mg/dl. The remaining 25 percent of patients who had IgG levels above the minimum showed deficiencies in specific IgG subclasses.

Figure 2 shows the status of all immunoglobulins in our PIDD patient population. For patients with all lab values present, 38 percent (60/159) had low serum IgG and low IgA. Twenty-three percent of patients had low serum IgG and low IgM, and 19 percent had low levels of all three immunoglobulins. We did note that 13 percent (n=20) of patients did only have low IgG levels, with normal IgA and IgM levels.

Figure 1. Baseline Serum IgG Level Distribution

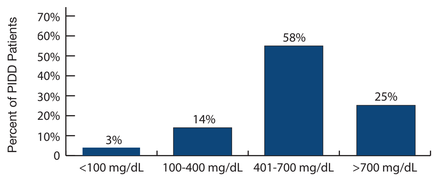
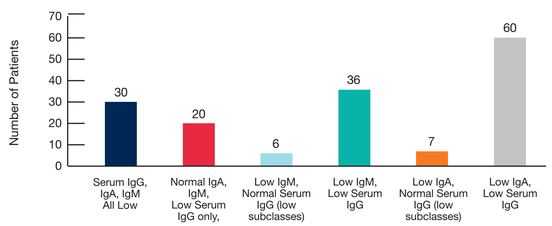


Figure 2. Immunoglobulin Status in PIDD Patient Population



We analyzed the correlation between serum IgG levels and patients' responses to pneumococcal vaccine challenge. We noted a weak, but positive, correlation between IgG levels and response to pneumococcal vaccine (R2=0.12). See Figure 3.

Figures 4 and 5 show the correlations between SCIg and IVIg doses, and average annual rates of non-serious bacterial infections. Overall, patients averaged about three infections a year regardless of route of treatment administration. SCIg patients averaged 130 mg/kg/week (520 mg/kg/month). IVIg patients averaged 472 mg/kg/month. For both populations, we noted no consistent trends in terms of higher dose leading to lower infections. We found two populations of interest, one subgroup that was receiving Ig infusions below the manufacturer recommended minimum, and one subgroup with doses below the population average, with infections above the population average.

Figure 6 shows the distribution of patients' perception of their health status at baseline, 6, and 12 months after starting on treatment. Patients were asked to score their perceptions of their current health on a scale of 1(best) to 5 (worst). Most patients reported scores between 3 and 4 at all time points, but we noted that the curve showed a leftward shift, towards an improved perception of health, at the 6- and 12-month time points.

Figure 3. Correlation Between Serum IgG Levels and Pneumococcal Vaccine Response

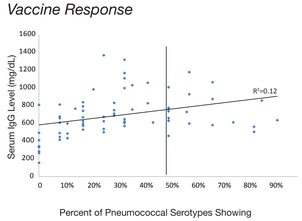


Figure 4. SCIg Dose and Non-Serious Bacterial Infection Correlation

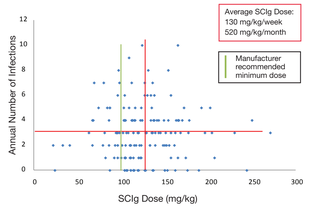


Figure 5. IVIg Dose and Non-Serious Bacterial Infection Correlation

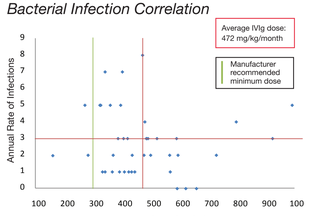
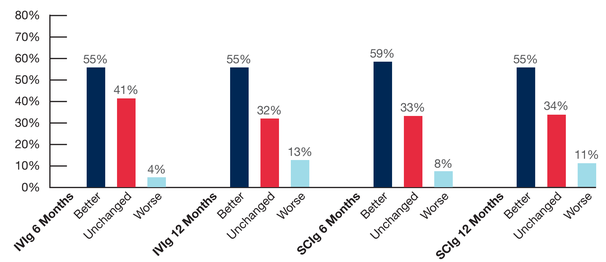


Figure 6. Health Assessment Distribution at Baseline, 6, 12 Months

In addition to current health, patients also were asked to compare their health at the current time to their health a year ago. In looking at the 6- and 12-month time points, we noted that a majority of both IVIg and SCIg patients said their health was better, or had not changed in those time periods. (Figure 7)

Figure 7. Health Transition Index: IVIg and SCIg Results at 6 and 12 months



Conclusions

- The IDEaL Patient Registry is a long-term outcomes based study designed to collect and analyze data from patients on immunoglobulin therapy in the home.
- The majority of our PIDD patients were diagnosed with CVID (ICD-279.06). We noted that adult Ig-naïve patients did not start treatment until their late 50s on average (average age of adult patients at time of start of care was 59 years old). This suggests that patients either did not develop symptoms until later in life, or that their presentation was milder. Delays in diagnosing and starting treatment of PIDD have been linked to increased risk of developing end-stage organ damage, even in milder forms.
- The majority (75) of our PIDD patients had low serum IgG levels, though most were between 401-700 mg/dl (58 percent). A significant minority (25 percent) did not have serum IgG deficiency, but did have IgG subclass deficiency. The majority of patients also showed low IgA levels, but more than 20 percent of the PIDD population with labs showed at least one normal immunoglobulin level.
- Serum IgG levels showed a weak correlation with pneumococcal vaccine responses. This suggests that normal IgG levels could be present in patients with a compromised humoral immune system, and that functional immune assessments as well as a clinical profile encompassing infection burden must be performed to accurately detect PIDD.
- We also noted weak correlations between IV and SC doses, and average annual rates of non-serious bacterial infections. We did note a number of patients with above-average numbers of infections that were below the average dose, as well as those below the manufacturer-recommended dose minimums. This suggests that some patients could benefit from increased follow-up and dose optimization.
- Overall, patients felt that their health was better and had improved while on Ig treatment.