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# High-titer IVIG 10 % (human)–slra reduces infections and hospitalizations over 6 to 12 months: A retrospective quality improvement study

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ABSTRACT

Patients with primary or secondary immunodeficiencies are at an increased risk for recurrent respiratory infections despite standard intravenous immunoglobulin (IVIG) therapy. This retrospective quality improvement review evaluated the clinical impact of a high-titer IVIG product enriched with pathogen-specific antibodies in 14 patients after failing conventional IVIG. The primary outcomes were changes in infection frequency and hospitalization rates during the 6 months before and after treatment initiation, and from 6 months post-treatment to the present. Ten patients (71%) showed clinical improvement, with infections decreasing from 36 to 8 and hospitalizations from 14 to 5 in the first 6 months post-treatment; benefits were more pronounced when excluding one clinical outlier. Two patients discontinued therapy due to mild adverse effects or lack of efficacy. High-titer IVIG was associated with meaningful reductions in infection burden and hospitalizations, supporting its consideration for high-risk patients unresponsive to standard IVIG.

## 1. Introduction

Intravenous immunoglobulin (IVIG) therapy is a cornerstone in the management of patients with humoral primary immunodeficiencies. While standard IVIG formulations provide broad-spectrum antibody support, some patients continue to experience frequent infections despite treatment. A novel commercially available intravenous immunoglobulin (IVIG) (ASCENIV®) product enriched with high-titer antibodies against respiratory pathogens, including respiratory syncytial virus (RSV), has shown promise in treating patients with immunodeficiencies who remain symptomatic despite standard IVIG therapy [1,2].

Immunodeficiencies represent a diverse group of disorders characterized by an impaired immune response, leading to increased susceptibility to infections, autoimmune diseases, and malignancies. These conditions pose significant clinical burdens and are broadly categorized into primary immunodeficiencies (PIDs). Patients with PIDs often experience recurrent, severe infections which may lead to chronic health issues and require lifelong management including immunoglobulin replacement therapy. PIDs contribute to increased morbidity, healthcare utilization, and reduced quality of life, underscoring the need for early diagnosis and tailored therapeutic strategies [3].

Immunoglobulin replacement therapy (IgRT) is the current standard of care for primary antibody deficiency patients, providing essential immunoglobulins to help reduce the frequency and severity of infections [4]. While IVIG is generally effective and well-tolerated, patients experience varying degrees of treatment burden, which can influence therapy adherence and quality of life.

High-titered IVIG was developed for patients with immunodeficiencies with recurrent infections who failed other IVIG treatments. This IVIG product is derived from human plasma containing naturally occurring polyclonal antibodies, including plasma from donors determined to have high levels of neutralizing antibodies to RSV. This high-tittered IVIG is an ideal choice for inpatient use due to the added high titer RSV protection, and the technique to specifically screen donors for these specific antibodies has been patented by ASCENIV®. This highlights the potential benefit of high-titer IVIG products in targeting difficult-to-manage infections, particularly in patients with ongoing respiratory morbidity despite conventional immunoglobulin replacement. This retrospective practice quality improvement study reviews real-world outcomes of this high-titer IVIG product in immunocompromised patients who previously failed to achieve adequate infection control with conventional IVIG therapy.

*Abbreviations:* IVIG, intravenous immunoglobulin; IgRT, immunoglobulin replacement therapy; RSV, respiratory syncytial virus.

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## 2. Materials and methods

This study took place at Allergy/Immunology Associates in Mayfield Heights, Ohio. We performed a retrospective quality improvement review of 14 patients treated at this outpatient center with the high-titer IVIG product between May 2023 and July 2024. The patients included in the study had either primary or secondary immunodeficiencies and a history of recurrent respiratory infections, defined as infections requiring medical intervention within a six-month period. The patient information concerning this study was compiled into a structured table for analysis (Table A.1). The dataset recorded in the table includes the following variables: start date of IVIG therapy, whether the patient remained on treatment at the time of review, indication for initiation, prior IVIG treatment experience, and infection burden. The patients were selected based on referrals for persistent infections despite prior standard IVIG therapy or other immunomodulatory treatments.

## 3. Theory/calculation

Clinical data were extracted from a comprehensive review of electronic medical records (EMR), and included infection type (e.g., pneumonia, sinusitis, urinary tract infections), frequency and severity in the 6 months before and after starting the high-titer IVIG, concurrent use of antibiotics or corticosteroids, respiratory medications, and past infusions. Additional variables included the number and duration of hospitalizations, use of adjunctive respiratory medications, and concomitant immunosuppressive therapies. Special attention was paid to patients with prior failures of standard IVIG formulations, documented adverse reactions, or comorbid conditions such as bronchiectasis, asthma, or COPD

Any reported adverse events, therapy discontinuation, or need for dose adjustments during the treatment period were documented. The patient records were retrospectively reviewed from 6 months prior to treatment to the present after starting the enriched IVIG product to assess trends in clinical response and treatment tolerability. The results were sectioned into 3 groups: 6 months prior to treatment, 6 months following treatment, and the time 6 months following treatment to the present. This review was conducted under a retrospective quality improvement framework.

## 4. Results

Among the 14 patients included in the study (Table A.1, A.2, A.3), 8 of whom had previously failed other IVIG formulations and started the new IVIG therapy, 10 demonstrated clinical improvement defined by reduced infection frequency or severity post-IVIG treatment. This accounted for 71% of the sample population. The total number of infections in the cadre of patients we studied notably decreased from 36 in the 6 months prior to treatment to 8 in the 6 months following initiation. Similarly, the total number of hospitalizations declined from 14 to 5 during the same period (Fig. A.1). The patients with underlying severe asthma, bronchiectasis, or combined immunodeficiencies reported clinical improvement in baseline symptoms and fewer exacerbations requiring systemic intervention. Two patients discontinued treatment due to mild adverse effects (headaches, GI symptoms, and poor appetite) or lack of efficacy.

One patient in our cohort presented as an outlier. This patient continued to experience frequent infections and required ongoing hospitalizations due to prior comorbidities, which skewed the overall outcome data. To address this, a secondary analysis was performed excluding this outlier (Fig. A.2) to better represent the therapeutic effect of the high-titer IVIG in the remaining patients. When this patient was excluded, the reduction in infection burden and hospitalization rate was even more pronounced, further supporting the potential efficacy of this product in appropriately selected populations.

Infections and hospitalizations were compared across three time periods: (A) 6 months before the high-titer IVIG (ASCENIV) treatment, (B) the first 6 months after starting treatment, and (C) the period from 6 months after treatment to the present. Significant reductions in infections were observed between A and C ($n = 14$, $p = 0.009$) and between B and C (n = 14, $p = 0.001$) when all patients were included. These results became even more statistically robust when the clinical outlier was excluded, with $p$-values of 0.003 ($n = 13$, A vs. C) and 0.001 ($n = 13$, B vs. C). While the reduction between A and B did not reach significance in the full cohort ($n = 14$, $p = 0.187$), it approached significance after removing the outlier ($n = 13$, $p = 0.056$), suggesting a possibly early treatment effect.

Hospitalization rates showed a similar trend, with improvements most notable when the outlier was excluded. Although comparisons between A and B ($n = 14$, $p = 0.095$) and A and C (n = 14, $p = 0.085$) were not statistically significant in the full dataset, both reached significance after removing the outlier (n = 13, $p = 0.40$ and $p = 0.018$, respectively). No significant difference in hospitalizations was observed between B and C in either analysis (n = 14, $p = 0.165$ with outlier; n = 13, $p = 0.337$ without). These findings suggest that ASCENIV treatment may have the greatest impact on reducing hospitalizations within the first 6 months, with more stable outcomes thereafter.

## 5. Discussion

The findings from this retrospective quality improvement review suggest that the high-titer IVIG product may be an effective therapeutic option for patients with primary or secondary immunodeficiencies and recurrent respiratory infections, particularly those who have failed conventional IVIG therapy. The overall reduction in infections, antibiotic use, and hospitalizations indicates a favorable clinical response in the majority of patients.

Hyperimmune globulins (HIGs) or high-titer gammaglobulin are immunoglobulin preparations derived from human plasma donors who have unusually high levels of antibodies against a specific pathogen or toxin. They provide passive immunity—either prophylactically or therapeutically—by delivering a concentrated dose of antibodies. Because of the selection of donors (e.g. vaccinated, naturally immune, or boosted), the antibody titers against the target antigen are markedly higher than those found in standard IVIG. HIGs are used for specific infectious diseases or toxin-mediated indications (Table A.4). These high-titer products are used via intramuscular route and are used for very specific infectious etiologies.The IV product discussed in this manuscript is derived using a donor-selection process conceptually similar to that of the products listed in Table A.4.

Recurrent respiratory tract infections (RRIs) are common in immunocompromised and can be life-threatening due to impaired host defenses. Patients with RRIs experience more frequent, prolonged, and severe infections compared to immunocompetent individuals. These infections often indicate an underlying immune deficiency and are associated with significant morbidity. RRIs can impair lung function, contribute to long-term structural damage such as bronchiectasis, and lead to repeated hospitalizations. Patients with RRIs have an increased risk of opportunistic infections and antimicrobial resistance due to frequent antibiotic use. Early recognition and interventions like immunoglobulin therapy are essential to improving quality of life and reducing complications [5].

The unique properties of high-titer immunoglobulin formulations may offer distinct clinical advantages for immuno-compromised patients, particularly those experiencing recurrent respiratory infections despite adequate conventional IVIgG therapy. As reviewed by Pati et al., high-titer IVIG products differ fundamentally from standard preparations by incorporating elevated and targeted levels of pathogen-specific IgG, particularly against respiratory viruses like RSV and influenza. These preparations are generated from donor plasma enriched through targeted selection or vaccination to ensure high antibody levels to specific viruses. They provide immediate passive immunity in

immunocompromised patients who cannot mount adequate humoral responses. In addition to direct pathogen neutralization, high-titer IVIG may enhance Fc-mediated clearance mechanisms. Clinical evaluations, especially in RSV prophylaxis and treatment contexts, suggest these targeted products may reduce infection severity and hospitalization rate. In the context of our patient population, which includes individuals with chronic respiratory conditions and histories of recurrent infection, the use of high-titer IVIG may contribute to improved infection control and a reduction in hospitalization frequency, as supported by the mechanistic and clinical insights in previous research [6].

Our findings are consistent with prior case reports utilizing high-titered IVIG, which led to clinical improvement in primary immunodeficiency patients with ongoing viral respiratory infections despite conventional IVIG therapy. Together, these studies suggest that high-titer IVIG formulations may provide added benefit in patient subsets inadequately protected by standard preparations [2]. Most patients who failed other IVIG formulations substantially improved after 6 months of high-titer IVIG use.

In clinical practice, high-titer IVIG should be considered for patients who remain at high risk for severe respiratory infections despite conventional immunoglobulin replacement, especially those with conditions such as primary immunodeficiency, bronchiectasis, chronic lung disease, or immunosuppression from therapy. Clinicians should particularly consider this product in individuals with repeated bacterial or viral respiratory infections, such as RSV or influenza, or those who continue to experience breakthrough infections after switching IVIG brands. High-titer IVIG offers not only a higher concentration of pathogen-specific antibodies compared to conventional IVIG but also enhanced capacity for direct neutralization and Fc-mediated immune activation [7]. This targeted immunoglobulin strategy may improve clinical outcomes by reducing infection severity, hospitalizations, and antibiotic use in real-world patient cohorts.

Primary immunodeficiency disorders are increasingly managed with therapies tailored to the particular immune defect, but antibody deficiencies remain the most common group, and standard first-line treatment typically involves IgRT. Both IVIG and subcutaneous IgG (SCIG) preparations are used; SCIG offers more flexibility, fewer systemic adverse events, and better patient satisfaction in many cases. [8]. For SCID and other combined T-cell immunodeficiencies, first-line or definitive therapy is hematopoietic stem cell transplantation (HSCT), often combined with supportive care (infection control, prophylactic antimicrobials, IgRT) [9]. In secondary immunodeficiency (due to malignancy, immunosuppressive therapy, chronic disease, etc.), the management focuses first on identifying and correcting underlying reversible causes and preventing or treating infections [10]. When patients have hypogammaglobulinemia, recurrent or severe infections, or fail to adequately respond to prophylactic antimicrobials, IgRT is increasingly used as first-line adjunctive therapy [11].

Patients who experience adverse events during IVIG therapy should have alternative treatment options discussed as part of their care plan. A 2024 review of subcutaneous immunoglobulin use in patients with chronic lymphocytic leukemia and secondary antibody deficiency reported that many patients were transitioned from IVIG to SCIG due to infusion-related adverse reactions, and that SCIG demonstrated significantly fewer systemic reactions and better tolerability [12]. Additionally, SCIG is often considered to be an patient-friendly alternative treatment due to its ability to be administered at home. These findings underscore that discussion of alternative options, especially SCIG, forms an important part of managing adverse events in IVIG-treated patients.

In a study by Libster et al., the concept of using high-titer immunoglobulin therapies is reinforced by clinical trial data applied in acute infectious settings. The study followed treatment of older adults with early mild COVID-19 with high-titer convalescent plasma; results supported significantly reduced progression to severe disease when given within 72 h of symptom onset [13]. In another study by Billi et al., high-risk patients with B-cell deficiencies showed real-world benefits to high-titer immunoglobulin therapy. This 2024 case series reported that hyperimmune IVIG led to rapid symptom improvement and reduced inflammatory markers in B-cell depleted individuals with persistent COVID-19 [14].

Despite the encouraging results, our study has limitations, including the small sample size, retrospective design, and short follow-up period. Further, as this was a real-world review, concomitant treatments may have influenced individual outcomes. The consistency of improvement across a diverse set of patients suggests that this formulation may play an important role in managing complex cases of immunodeficiency with a respiratory component. Future prospective studies with larger cohorts and longer follow-up are needed to confirm these findings and to better define the patient populations that would benefit most from this targeted IVIG therapy.

## 6. Conclusion

This retrospective quality improvement review demonstrates that high-titer IVIG therapy enriched with pathogen-specific antibodies can offer substantial clinical benefit for patients with primary or secondary immunodeficiencies who remain highly susceptible to respiratory infections despite use of standard IVIG therapy. The observed reductions in infection burden, hospitalizations, and respiratory exacerbations, particularly in those with bronchiectasis, chronic lung disease, or frequent viral infections, highlight the therapeutic potential of a targeted immunoglobulin approach. Our findings suggest that this product reduces infection burden and hospitalization rates, and its therapeutic effects may also become more pronounced over time, with substantial improvement after 6 months of use. By combining broad-spectrum antibody coverage with elevated titers against clinically relevant respiratory pathogens, this formulation addresses a critical unmet need in infection prevention for high-risk immunodeficient populations. These real-world findings reinforce prior mechanistic and clinical evidence and position high-titer IVIG as a valuable consideration in personalized immunoglobulin replacement strategies. Prospective studies with larger cohorts are warranted to confirm efficacy, optimize patient selection, and further define its role in improving long-term outcomes in complex immunodeficiency care. In the interim, clinicians should consider high-titer IVIG for patients with recurrent or severe respiratory infections unresponsive to conventional IVIG.

## CRediT authorship contribution statement

**Gabrielle Tan:** Writing – review & editing, Writing – original draft, Visualization, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kiran Sehmi:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Sarah Azzi:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Robert Hostoffer:** Visualization, Validation, Supervision, Project administration, Conceptualization.

## Declaration of competing interest

The authors disclose that there were no conflicts of interest or financial support in the development of this project.

## Data availability

Data will be made available on request.

## Appendix A. Appendix

**Table A.1**
Clinical course and infection history of patients receiving high-titer IVIG therapy

| Patient | Start Date | Still on High-Titer IVIG? | Reason for Use | Past Infusion Experiences: Conventional IVIG | Infections 6 months Before | Infections 6 months after | Infections 6 months after to present |
|---|---|---|---|---|---|---|---|
| 1 | Oct-23 | No (ended 11/1/23) | Chronic Pseudomonas/ *Gordonia Bronchialis*. AFB cx negative | Received only 2 doses in Oct/Nov, restarted 09/04/23; stopped again due to increased infections | 0 | 2 sinus infections, 1 MAC | 4/17/24–1 PNA; 08/7/24-sinusitis |
| 2 | Jul-23 | Yes | Bacterial sinusitis | Fewer infections than before | 6 sinus infections | 1 COVID infection, 3 sinus | 0 |
| 3 | Jun-23 | Yes | Refractory sinusitis | Headaches after infusion; switched due to infections | 3 sinus infections | 2 sinus infections, requiring multiple rounds of antibiotics, 1 IV | GI infection 03/29/24 |
| 4 | Nov-23 | Yes | Recurrent infections | Poor appetite, vomiting | 2 PNA, skin abscesses, boils | 3 sinus | 05/1/24- UTI 1 week; UTI 5/22/24 |
| 5 | May-23 | Yes | Recurrent pneumonia | Switched due to infections | 2 PNA (1 ICU) | 0 | 0 |
| 6 | Nov-23 | Yes | Recurrent infections | Hx of other brand | 2 PNA (1 admission), 1 UTI | 1 PNA (ICU), 1 UTI | 0 |
| 7 | Feb-24 | Yes | Lung nodule history | Prior other brand; frequent infections | 2 PNA (1 admission) | 1 GI issue | 0 |
| 8 | Jul-24 | Yes | Stable bronchiectasis | Switched from another brand | Bronchitis | 0 | 0 |
| 9 | Apr-24 | Yes | ACOS | Switched from another brand | 1 PNA | 0 | 0 |
| 10 | Oct-23 | Yes | Severe asthma + ABPA | Trialed and failed many other IVIGs | BL PNA (hospitalized), hospitalized 8 times within 1 year prior to starting treatment | Sinusitis, bronchitis, PNA (hospitalized x3), oral thrushes | 04/11/25- LLL PNA (1 hospitalization); 7 months into using IVIG; 11/24- PNA (1 hospitalization); 04/1/25- UTI |
| 11 | Oct-23 | Yes | Bronchiectasis | Prior IVIGs failed | Bronchitis, sinusitis | Bronchitis, sinusitis | 0 |
| 12 | Feb-24 | No (last 6/26/24) | COPD | Prior Other IVIG | 2 PNA (hospitalized) | Bronchitis, aspiration PNA (hospitalized) | N/A |
| 13 | Oct-2023 | Yes | Recurrent infections | Anaphylaxis to Other IVIG | Pyelonephritis, sinusitis x3 | Sinusitis/bronchitis x2, mastoiditis | 0 |
| 14 | Mar-24 | Yes | Recurrent pneumonia | Standard IVIG failed | PNA x2 | PNA | 0 |

Abbreviations: IVIG = intravenous immunoglobulin; AFB = acid-fast bacillus; cx = culture; MAC = *Mycobacterium avium* complex; PNA = pneumonia; ICU = intensive care unit; UTI = urinary tract infection; GI = gastrointestinal; ACOS = asthma–COPD overlap syndrome; ABPA = allergic bronchopulmonary aspergillosis; BL = bilateral; LLL = left lower lobe; Hx = history; N/A = not applicable.

**Table A.2**
Supplemental data. Demographics, infectious history, treatment characteristics, and immunologic testing in patients receiving high-titer IVIG.

| | Demographics | | | | Infectious History | IVIG Treatment History & Rationale | | Immunologic Testing | |
|---|---|---|---|---|---|---|---|---|---|
| Patient | Age at Dx | Age at IV | Sex | Ethnicity | Previously isolated bacterial and viral pathogens | Prior standard IVIG use | Rationale for switching to high-titer IVIG in patients who did NOT fail standard IVIG | Serum IgG/IgM/IgA levels (Normal Range: IgA 60–400 mg/dL; IgM 40–250 mg/dL; IgG 600–1600 mg/dL) | Specific IgG titers to past vaccines (prior to IVIG tx) |
| 1 | 63 | 63 | F | Caucasian | None | 600 mg/kg q 4 | Recurrent viral | IgA 187<br>IgM 47<br>IgG 944 | Absent |
| 2 | 61 | 61 | F | Caucasian | None | 800 mg/kg q 3 | Infections despite IVIG | IgA 194<br>IgM 62<br>IgG 1103 | Absent |
| 3 | 35 | 36 | F | Caucasian | *Strep. pneumo* | 1000 mg/kg q 3 | Infections despite IVIG | IgA <5<br>IgM <5<br>IgG 1203 | Absent |
| 4 | 32 | 33 | F | Caucasian | None | 500 mg/kg q 3 | Infections despite IVIG | IgA 46<br>IgM 82<br>IgG 1440 | Absent |
| 5 | 69 | 69 | F | Caucasian | *Strep. pneumo* | 800 mg/kg q 4 | Infections despite IVIG | IgA 55<br>IgM 1453<br>IgG 749 | Absent |

(*continued on next page*)

**Table A.2** (*continued*)

| | Demographics | | | | Infectious History | IVIG Treatment History & Rationale | | Immunologic Testing | |
|---|---|---|---|---|---|---|---|---|---|
| Patient | Age at Dx | Age at IV | Sex | Ethnicity | Previously isolated bacterial and viral pathogens | Prior standard IVIG use | Rationale for switching to high-titer IVIG in patients who did NOT fail standard IVIG | Serum IgG/IgM/IgA levels (Normal Range: IgA 60–400 mg/dL; IgM 40–250 mg/dL; IgG 600–1600 mg/dL) | Specific IgG titers to past vaccines (prior to IVIG tx) |
| 6 | 66 | 66 | F | Caucasian | None | 650 mg/kg q 3 | Infections despite IVIG | IgA 40<br>IgM 18<br>IgG 876 | Absent |
| 7 | 89 | 85 | F | Caucasian | None | 600 mg/kg q 3 | Infections despite IVIG | IgA 140 IgM 105 IgG 105 | Absent |
| 8 | 36 | 37 | F | Caucasian | *Strep. pneumo* | 500 mg/kg q 2 | Infections despite IVIG | IgA 11<br>IgM 18<br>IgG1032 | Absent |
| 9 | 64 | 65 | F | Caucasian | None | 400 mg/kg q 4 | Infections despite IVIG | IgA <5<br>IgM <5<br>IgG 585 | Absent |
| 10 | 36 | 37 | F | Caucasian | *Mycobacteria* | 900 mg/kg q 3 | Infections despite IVIG | IgA 82<br>IgM 35<br>IgG 2062 | Absent |
| 11 | 64 | 64 | F | Caucasian | None | 800 mg/kg q 4 | Infections despite IVIG | IgA 291<br>IgM 105<br>IgG 978 | Absent |
| 12 | 76 | 76 | M | Caucasian | None | 400 mg/kg q 4 | Infections despite IVIG | IgA 194<br>IgM 28<br>IgG 488 | Absent |
| 13 | 42 | 42 | F | Caucasian | None | 400 mg/kg q 2 | Infections despite IVIG | IgA 197<br>IgM 15<br>IgG 904 | Absent |
| 14 | 83 | 84 | F | Caucasian | None | 600 mg/kg q 4 | Infections despite IVIG | IgA 72<br>IgM 606<br>IgG 436 | Absent |

Abbreviations: F = female; M = male; Dx = diagnosis; IV = intravenous therapy initiation; IVIG = intravenous immunoglobulin; ASCENIV = high-titer IVIG; Strep. pneumo = *Streptococcus pneumoniae*; q = every.

The rationale for switching to high-titer IVIG is provided for patients who did not fail standard IVIG. In cases where patients had 0 reported infections prior to high titer IVIG, standard IVIG had not been used. For patients with adverse reactions to standard IVIG, subcutaneous immunoglobulin (SCIG) was not considered.

**Table A.3**
Supplemental data, continued. Clinical and diagnostic data in patients receiving high-titer IVIG.

| | Clinical & Diagnostic Data | | | | | | |
|---|---|---|---|---|---|---|---|
| Patient | Genetic Dx | Subtype of PID | SID status | Baseline lymphocyte phenotyping (Normal Ranges: CD19 96–515; CD3 678–2504; CD4 414–1679; CD8 162–1038) | CBC (Normal Range: PLT 150,000-400,000/mm$^3$) | Abnormal lymphocyte subsets (Normal Ranges: CD19 96–515; CD3 678–2504; CD4 414–1679; CD8 162–1038) | Memory B-cell subsets |
| 1 | None | SPAD | None | Normal | Normal | None | 0.073 B cells; 81.1 % naïve B cells (increased); 8.5 % nonswitched memory B cells (decreased); 6.4 % switched memory B cells (decreased); 5.7 % transitional (high) |
| 2 | None | SPAD | None | Normal | Normal | None | 0.148 B cells (wnl); Naïve B cells 69.2 % (wnl); Nonswitched mem 12 % (decreased); switched mem 13,3 (wnl); Transitional 3.1 % (wnl) |
| 3 | None | CVID | None | Normal | Normal | None | 0.003 B cells (Very Low) mostly naïve and transitional cells |
| 4 | None | SPAD | None | CD8 1568 | Normal | None | 88.6 % (increased) naïve; 4.3 % (increased) transitional; 5.2 % (decreased) memory; 0.3 % (decreased) plasmablasts |
| 5 | None | Hypogamm | None | Normal | Normal | None | 0.027 (decreased B cells); 13.2 % (decreased) non switched memory cells; 20.3 % (increased) switched memory B cells; absent transitional B cells |
| 6 | None | Hypogamm | None | Normal | Normal | None | Increased B cells; 1.7% (decreased) Naïve B |
| 7 | None | SPAD | None | Normal | Normal | None | 0.051 B cells (low);80.2 % Naïve B cells; 80.2 % non switched B cells (low); 9.1 % switched mem (low); 8.3 % transitional |
| 8 | None | CVID | None | Normal | PLT 131 | None | Not done |
| 9 | None | Agamm | B cell lymphoma | Normal | Normal | None | Not done |

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**Table A.3** (*continued*)

| | Clinical & Diagnostic Data | | | | | | |
|---|---|---|---|---|---|---|---|
| Patient | Genetic Dx | Subtype of PID | SID status | Baseline lymphocyte phenotyping (Normal Ranges: CD19 96–515; CD3 678–2504; CD4 414–1679; CD8 162–1038) | CBC (Normal Range: PLT 150,000-400,000/mm$^3$) | Abnormal lymphocyte subsets (Normal Ranges: CD19 96–515; CD3 678–2504; CD4 414–1679; CD8 162–1038) | Memory B-cell subsets |
| 10 | None | Combined | None | CD19 44<br>CD3 642<br>CD4 385 | Lymphopenia | CD19 44<br>CD3 642<br>CD4 385 | 0.005 B cells (Decreased); 10.4% (Decreased) Naïve B cells; 69% nonswitched B mem (high); 18.2% switched B cells; 0.07% Transitional mem (Low) |
| 11 | None | SPAD | None | Normal | Normal | Normal | Not done |
| 12 | None | Hypogamm | None | CD19 0.030 | Normal | CD19 0.030 | Not done |
| 13 | None | SPAD | None | Normal | Normal | Normal | 0.007 B cells (decreased); 81.7 % naïve B cells (increased); 7.8 % (decreased) non switched memory B cells; 8.7 % switched B cells (decreased); 17.9 % transitional |
| 14 | None | Hypogamm | None | Normal | Normal | Normal | 0.029 B cells (decreased); 54.5 % Naïve B cells (decreased); 25.1 % non switched mem (increased);9.2 % Transitional (increased) |

Abbreviations: Dx = diagnosis; PID = primary immunodeficiency; SID = secondary immunodeficiency; SPAD = specific antibody deficiency; CVID = common variable immunodeficiency; Hypogamm = hypogammaglobulinemia; Agamm = agammaglobulinemia; CBC = complete blood count; PLT = platelets; Ig = immunoglobulin; tx = treatment.

**Table A.4**
Selected hyperimmune globulin products and indications [14–16].

| Product | Indication/Use |
|---|---|
| Human rabies immune globulin (HRIG) | Post-exposure prophylaxis for rabies, along with vaccine |
| Hepatitis B immune globulin (HBIG) | Post-exposure prophylaxis (e.g. perinatal exposure, needle stick); transplant settings |
| Cytomegalovirus immune globulin (CMVIG) | Prevention/treatment of CMV disease in transplant recipients<br>Substantially greater neutralizing activity per gram of IgG |
| Tetanus immune globulin (TIG) | Tetanus-prone wounds; treatment of tetanus (neutralizes free toxin) |
| Varicella-zoster immune globulin (VZIG) | Post-exposure prophylaxis in immunocompromised/high-risk individuals |
| Botulism immune globulin | Treatment of infant botulism (neutralizes botulinum toxin) |
| High-titer COVID-19 convalescent globulin | Passive immunization during the COVID-19 pandemic |

Abbreviations: IgG = immunoglobulin G; COVID-19 = coronavirus disease 2019.

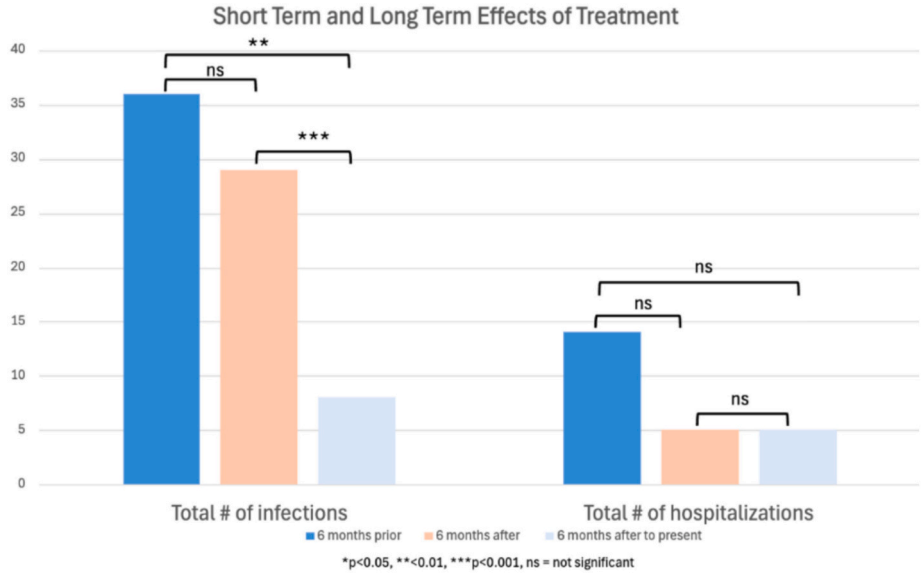


**Fig. A.1.** Short and Long Term Effects of High-Titer IVIG 10 % (Human)–slra Treatment.

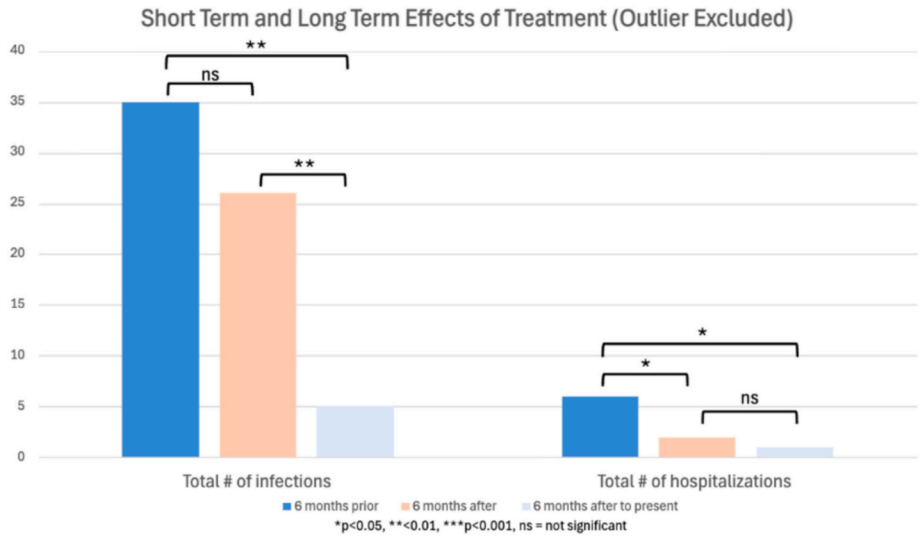


**Fig. A.2.** Short and Long Term Effects of High-Titer IVIG 10 % (Human)–slra Treatment with Outlier Excluded.

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