Trough Levels of IgG Antibodies to Encapsulated Pathogens
After Infusion of a 5% or 10% IVIG Formulation

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BACKGROUND

• Patients with primary immunodeficiencies (PI) are susceptible to a wide variety of infectious pathogens.1,2
• Due to an inability to produce adequate amounts of immunoglobulin G (IgG) antibodies to prevent infection, these patients are often dependent on immunoglobulin therapies to provide passive antibodies.1,2
• Two major infectious encapsulated pathogens that can result in significant and serious infectious complications in immunocompromised individuals are Haemophilus influenzae type b (the most common serotype b) and numerous serotypes of Streptococcus pneumoniae.3
• In this analysis, we measured trough levels of H. influenzae type b and seven S. pneumoniae serotypes (serotypes 14, 18C, 19F, 23F, 4, 6B, and 9V) in patients with PI treated with 5% intravenous immunoglobulin (IVIG) and/or 10% IVIG formulations. Results are reported here.

PURPOSE

GMX®07 was a phase 3 open-label study to evaluate the pharmacokinetics, safety, and tolerability of IVIG 5% and 10% in patients with PI.4

METHODS

In this bioequivalence trial comparing Gammaplex® IVIG 5% and 10%, adult patients received 10 infusions through random assignment to either a sequence of five infusions of the 5% IVIG formulation followed by five infusions of the 10% IVIG formulation or to the opposite sequence. Pediatric patients received five infusions of the 10% IVIG formulation only. In both cohorts, IVIG was given on either 28- or 21-day cycles, according to the frequency of the patient’s previous IVIG preparation. All patients were dosed at the investigator’s discretion within a 300 mg/kg to 600 mg/kg per infusion dose range.5

Blood samples were taken up to 21 or 20 days after the fifth infusion (all patients) and tenth infusion (adult patients only). Samples for clinical laboratory testing were shipped to a central laboratory.4

Trough levels of H. influenzae type b and seven S. pneumoniae serotypes (serotypes 14, 18C, 19F, 23F, 4, 6B, and 9V) were quantified after each patient’s last infusion of assigned treatment with 5% IVIG (adult patients only) and/or 10% IVIG (adult and pediatric patients).4

Statistical Analysis: The ITT analysis set was defined as all subjects who received at least one infusion of IVIG 5% or IVIG 10%. Analysis of trough levels of total IgG and IgG antibodies to specific antigens was conducted using the ITT population.4

Data from adult (16 years of age and older) and pediatric patients (2 to 15 years of age) were summarized separately as well as in overall analyses.4

RESULTS

• Patient characteristics are described in Table 1.4

Table 1. Patient Characteristics4

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adults</th>
<th>Pediatrics</th>
<th>All Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>33</td>
<td>15</td>
<td>48</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>12 (36)</td>
<td>6 (33)</td>
<td>20 (41.7)</td>
</tr>
<tr>
<td>Age, years</td>
<td>Mean ± SD</td>
<td>35.5 ± 11.99</td>
<td>6.6 ± 4.15</td>
</tr>
<tr>
<td>Height (Range)</td>
<td>42.0 (17.00)</td>
<td>6.0 (3.16)</td>
<td>35.5 (0.00)</td>
</tr>
<tr>
<td>Age range, n (%)</td>
<td>2-8</td>
<td>0</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td></td>
<td>6-12</td>
<td>0</td>
<td>7 (46.7)</td>
</tr>
<tr>
<td></td>
<td>12-15</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>16-25</td>
<td>33 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
<td>White - Not Hispanic or Latino</td>
<td>32 (97.0)</td>
<td>13 (86.7)</td>
</tr>
<tr>
<td></td>
<td>Hispanic or Latino</td>
<td>1 (3.0)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>CVID</td>
<td>30 (90.9)</td>
<td>7 (46.7)</td>
<td>37 (77.1)</td>
</tr>
<tr>
<td>XLA</td>
<td>3 (9.1)</td>
<td>3 (20.0)</td>
<td>6 (12.9)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Clinical laboratory analysis. XLA, X-linked agammaglobulinemia.

• Results were available for 31 adult patients who received the 5% IVIG formulation and for 32 adults who received the 10% IVIG formulation; results were available for 14 pediatric patients who received the 10% IVIG formulation only.4

• The median trough titers of IgG antibodies to the subject pathogens after dosing with 5% IVIG or 10% IVIG in adult patients and with 10% IVIG in pediatric patients ranged from 0.60 μg/mL (range: 0.2-2.3) to 6.85 μg/mL (patients) and 0.7-2.61 (Fig 1).4

• In adults, median trough levels of IgG antibodies to H. influenzae were 2.80 μg/mL (range: 1.29-6.0) for 5% IVIG and 2.76 μg/mL (range: 1.29-9.0) for 10% IVIG; corresponding data in pediatric patients treated with 10% IVIG were 2.46 (range: 1.16-7.1).4

• Trough levels of IgG antibodies to all seven S. pneumoniae serotypes were consistent between the 5% and 10% formulation, and between adult and pediatric patients receiving the 10% formulation. No clinically meaningful differences in trough concentrations were noted between the 5% and 10% formulation, or between adult and pediatric patients.4

DISCUSSION

• Patients with PI require passive immunity with infused IgG antibodies to protect against infectious pathogens.1,2
• While specific thresholds for protective IgG antibody levels for either H. influenzae or S. pneumoniae have not been clearly defined, delivering these antibodies to patients with PI is important.
• Our results indicate that there were no clinically relevant differences in the levels of specific antibodies to H. influenzae and S. pneumoniae provided by the 5% and 10% formulations of this IVIG product.4
• Adult and pediatric patients with PI achieved similar results.4

CONCLUSIONS

• Trough levels of IgG antibodies to problematic serotypes of H. influenzae and S. pneumoniae were measurable and consistent in PI patients receiving this 5% or 10% IVIG treatment.
• Delivery of these passive antibodies is critical in limiting infectious complications in PI patients.

References


Acknowledgments and Disclosures

Bio Products Laboratory, Ltd., Elstree, UK provided funding for medical writing and editorial support of this poster.
S. Russ-Gilliam, E. Wolford and M. Norton are employees of Bio Products Laboratory, Ltd.
Presented at the National Home Infusion Association (NHIA) Conference, Washington, DC, March 29-31, 2023

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1.5 mg/kg
2.5 mg/kg
9.5 mg/kg
7.5 mg/kg
5.5 mg/kg
4.5 mg/kg
3.5 mg/kg
2.5 mg/kg
1.5 mg/kg
0.5 mg/kg
0.0 mg/kg

Figure 1. Median Trough Titers of IgG Antibodies to Specific Antigens4

IVIG 5% - Adult
IVIG 10% - Adult
IVIG 10% - Pediatric

CONCLUSIONS

• Trough levels of IgG antibodies to problematic serotypes of H. influenzae and S. pneumoniae were measurable and consistent in PI patients receiving this 5% or 10% IVIG treatment.
• Delivery of these passive antibodies is critical in limiting infectious complications in PI patients.