

Analysis of Trough Levels of Total IgG, IgG Subclasses, Measles Neutralizing Antibodies and IgG Antibodies to Encapsulated Pathogens After Infusion of a 5% or 10% Intravenous Immunoglobulin

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BIOPHARMA

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BACKGROUND

- Some patients with primary immunodeficiency (PI) are at risk of infection due to low immunoglobulin (IgG) levels.^{1,2}
- We report trough levels of total IgG, IgG subclasses, and measles neutralizing antibody (MVA) titers, in addition to trough titers of IgG antibodies to *Haemophilus influenzae* type b and seven *Streptococcus pneumoniae* serotypes, in PI patients receiving a 5% and 10% intravenous immunoglobulin (IVIG) formulation.

PURPOSE

As a subanalysis of data from GMX07, a phase 3 open-label bioequivalence study, the purpose of this study was to compare protective concentrations of IgG antibodies provided by a 5% and a 10% IVIG product in patients with PI.³

METHODS

Adult patients were enrolled in a randomized, 2-period crossover study comparing Gammalex[®] 5% and 10%. Patients received 10 infusions through random assignment to either a sequence of five infusions of IVIG 5% followed by five infusions of IVIG 10%, or five infusions of IVIG 10% followed by five infusions of IVIG 5%.

Pediatric patients were enrolled in a single-arm, nonrandomized study in which they received five infusions of IVIG 10% only.

In both cohorts, IVIG was given on either 21-day or 28-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 800 mg/kg per infusion dose range.³

Blood samples were taken up to 21 or 28 days after the fifth infusion (all patients) and tenth infusion (adult patients only). Samples for clinical laboratory testing were shipped to a central laboratory.³

Trough levels of IgG antibodies to MVA were assessed at the beginning and end of treatment for 47 of the 48 subjects included in the intention-to-treat (ITT) population and compared against the level (120 mIU/mL for immunocompetent individuals or 240 mIU/mL for at-risk patients with PI) established as protective against wild measles virus.^{3,4} 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 IVIG 5% (adult patients only) and/or IVIG 10% (adult and pediatric patients).

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.³

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.³

RESULTS

Patient characteristics are described in Table 1.³

- The ITT population consisted of 33 adults who received the 5% IVIG, 32 adult patients who received the 10% IVIG, and 15 pediatric patients who received the 10% IVIG.³
- In adults, median IgG trough levels were 937.0 mg/dL for the 5% IVIG and 952.5 mg/dL for the 10% IVIG. In pediatric patients, the median IgG trough level was 879.5 mg/dL (Fig. 1). Trough levels of IgG subclasses were comparable across formulations and age groups (Table 2).³

RESULTS (Continued)

- Adult patients had a mean trough MVA titer of 2908 mIU/mL with the 5% IVIG vs 3213 mIU/mL with the 10% IVIG; pediatric patients had a mean trough MVA titer of 2122 mIU/mL (Table 3). These differences were not statistically significant, and all trough levels were above both protective levels of 120 mIU/mL and 240 mIU/mL, respectively.³

Table 1. Patient Characteristics (ITT Population)³

Characteristic	Adults	Pediatrics	All Subjects
Patients, N	33	15	48
Male, n (%)	12 (36.4)	8 (53.3)	20 (41.7)
Age, years			
Mean ± SD	39.5 ± 11.99	9.6 ± 4.15	30.1 ± 17.29
Median (Range)	42.0 (17-55)	8.0 (3-15)	30.5 (3-55)
Age range, n (%)			
2-5	0	2 (13.3)	2 (4.2)
6-11	0	7 (46.7)	7 (14.6)
12-15	0	6 (40.0)	6 (12.5)
16-55	33 (100)	0	33 (68.8)
Race/Ethnicity, n (%)			
White – Not Hispanic or Latino	32 (97.0)	13 (86.7)	45 (93.8)
Hispanic or Latino	1 (3.0)	2 (13.3)	3 (6.3)
Diagnosis, n (%)			
CVID	30 (90.9)	7 (46.7)	37 (77.1)
XLA	3 (9.1)	5 (33.3)	8 (16.7)
Hyper-IgM syndrome	0	0	0
Other	0	3 (20.0)	3 (6.3)

CVID, common variable immunodeficiency; XLA, X-linked agammaglobulinemia.

Figure 1. Median Trough Levels: Total IgG³

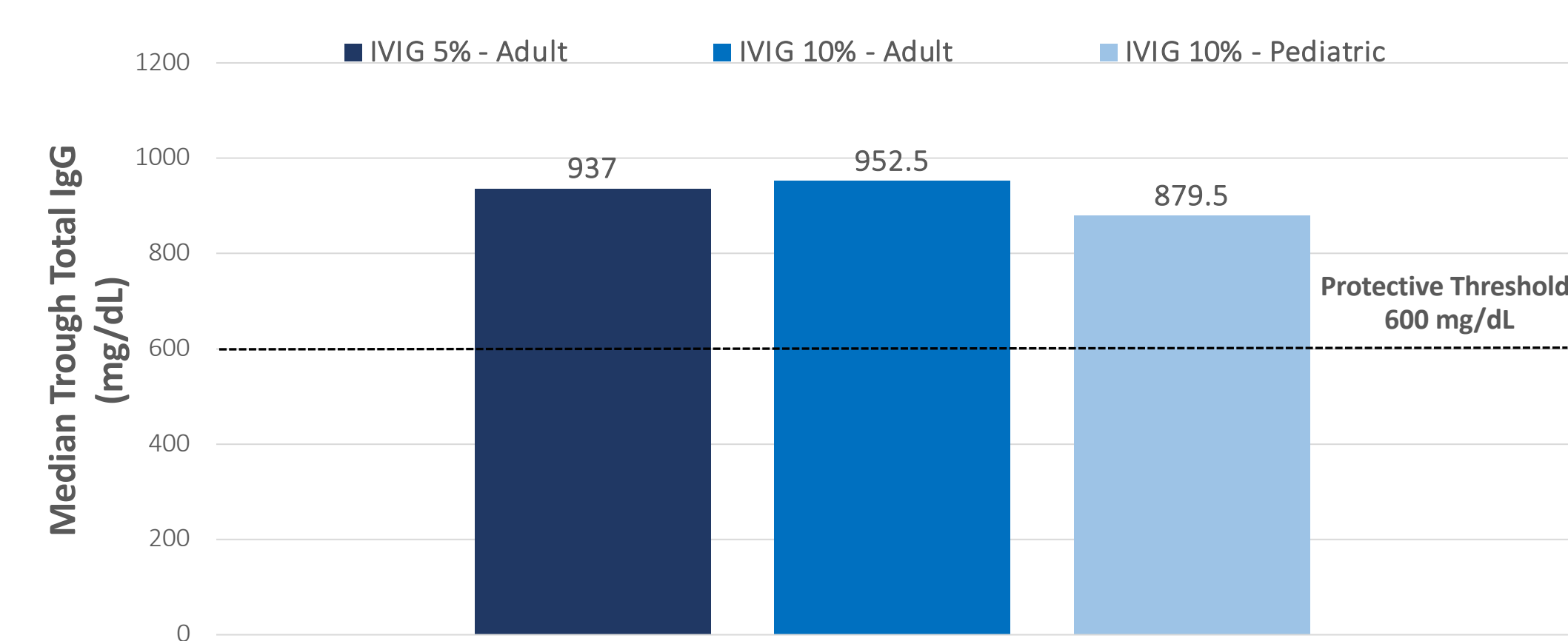


Table 2. Trough Concentrations of IgG Subclasses³

IgG Subclass	Median (Range) Trough Levels (mg/dL)		
	IVIG 5% - Adult	IVIG 10% - Adult	IVIG 10% - Pediatric
Subclass 1	570.0 (410-962)	533.5 (385-907)	512.0 (406-689)
Subclass 2	354.0 (160-680)	328.5 (175-557)	300.0 (189-396)
Subclass 3	32.0 (12-89)	33.5 (11-96)	26.0 (10-71)
Subclass 4	7.0 (2-38)	7.0 (1-28)	6.0 (3-17)

RESULTS (Continued)

Figure 2. Median Trough Titers of IgG Antibodies to Specific Antigens³

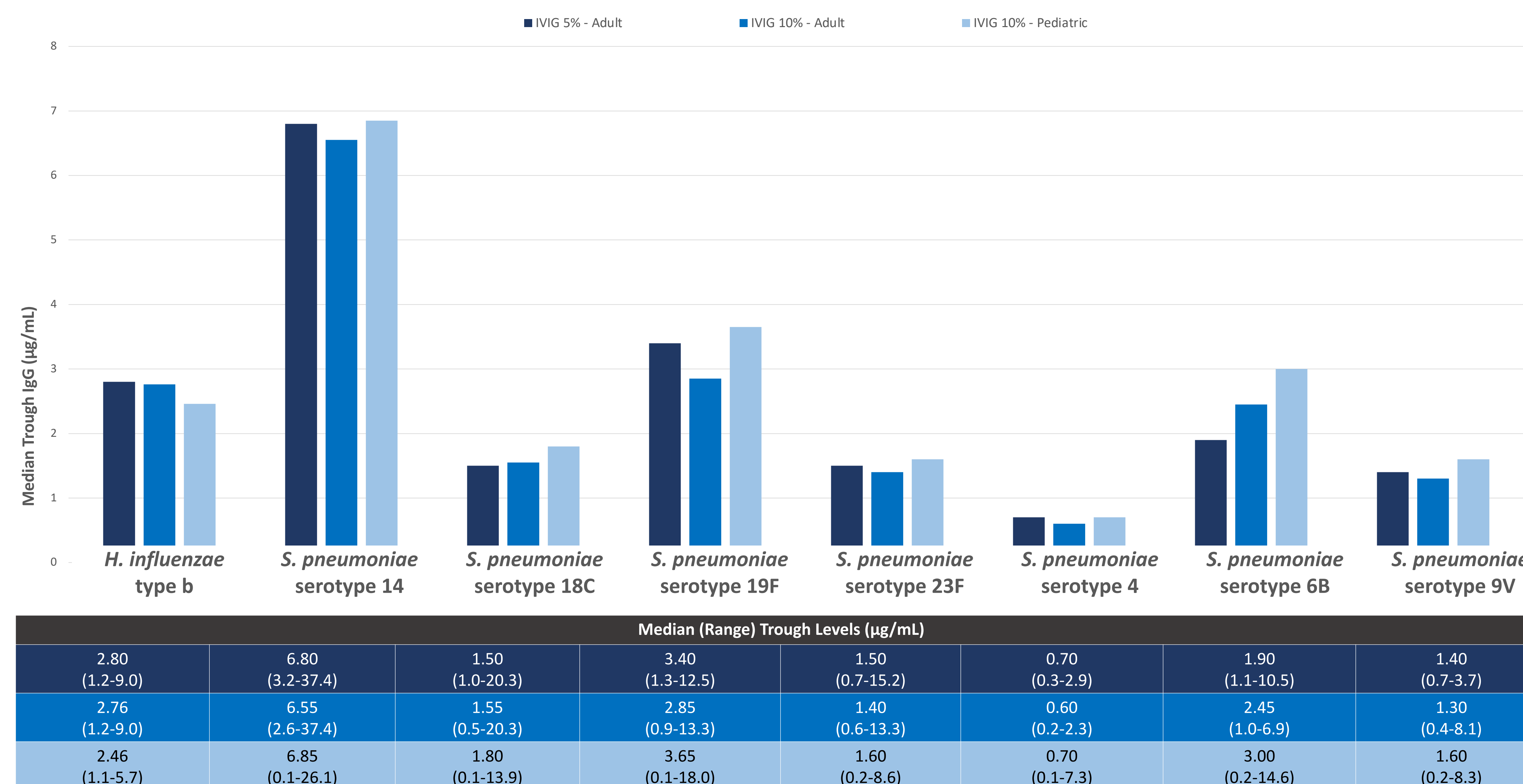


Table 3. Mean Trough Measles Neutralizing Antibody Levels³

IVIG Product	Mean (Range) Measles Antibody Levels (mIU/mL)		
	Adults	Pediatrics	All Subjects
5% IVIG	2908 (250-28,483)	--	--
10% IVIG	3213 (304-34,697)	2122 (371-12,936)	2864 (304-34,697)

- In adults, median trough levels of IgG antibodies to *H. influenzae* type b (anti-Hib) were 2.80 µg/mL for the 5% IVIG and 2.76 µg/mL for the 10% IVIG (Fig. 2).³ For anti-Hib antibodies, ≥1 µg/mL is an optimal long-term protective level as considered by World Health Organization (WHO).⁵
- Trough levels of IgG antibodies to all *S. pneumoniae* serotypes were consistent across formulations and age groups (Fig. 2).³ According to WHO recommendations, a threshold-specific pneumococcal antibody concentration of >0.35 µg/mL is assumed to be predictive for seroprotection.^{6,7}
- No clinically meaningful differences were noted between formulations, 21-day vs 28-day regimens, or age groups.³

DISCUSSION

- Maintaining IgG trough levels and mean MVA trough titers above protective thresholds is critical for some patients with PI.^{3,8}
- Trough levels of mean MVA titers, after 5 infusions of IVIG, were substantially greater than the predefined protective thresholds of 120 mIU/mL (immunocompetent individuals) or 240 mIU/mL (recommended for at-risk patients with PI), respectively.^{3,4}
- Trough levels of total IgG, after 5 infusions of IVIG, were above the predefined protective threshold of 600 mg/dL in all adult and pediatric patients.³

CONCLUSION

- Our results indicate that the 5% and 10% formulations of this IVIG product deliver protective trough levels of IgG to measles virus and to a range of specific bacterial antigens, with similar results at all dosing schedules for adult and pediatric patients with PI.³

References

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