Clinical Assessment of Safety, Pharmacokinetics, and Efficacy of Immune Globulin Intravenous 10% in Pediatric Patients

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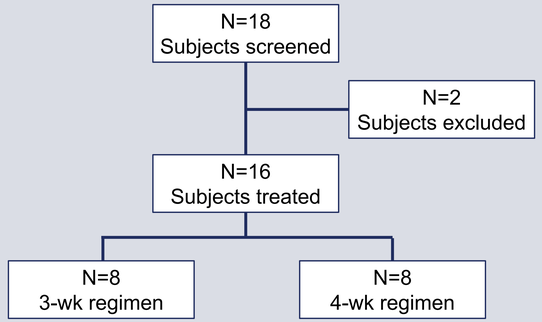
INTRODUCTION

- Immune globulin intravenous (human) 10% liquid (IGIV 10%) is FDA-approved for the treatment of primary humoral immunodeficiency (PI)[1]
- The objectives of this study were to further characterize the safety, pharmacokinetics (PK), and efficacy in children and adolescents 2-16 years old as part of post-marketing requirements[2]

METHODS

- Phase IV prospective, open-label, single-arm, multi-center clinical trial
- Six US sites enrolled subjects in this study
- Doses of 300-800 mg/kg of IGIV 10% (BIVIGAM®) were administered every 3 or 4 weeks for 5 months
- Dose adjustments were permitted during the study to maintain trough immune globulin G concentrations at >500 mg/dL
- During treatment and follow-up, subjects underwent extensive evaluations: adverse event (AE) and infection monitoring, vital signs, physical exam, routine safety blood tests, subject diaries, and PK sampling/ modeling

Figure 1. Subjects disposition



This study was sponsored by ADMA Biologics, Inc. Ramsey, NJ

RESULTS

PATIENTS

Table 1. Patient characteristics and demographics

Demographics	3-wk regimen (N=8)	4-wk regimen (N=8)	Total (N=16)
Age, Mean (SD) years	11 (5.2)	9.5 (3.1)	10.3 (4.2)
Male, *n* (%)	8 (100)	8 (100)	16 (100)
Weight, Median (min,max) kg	45.9 (16.3,119)	31.7 (18.6,67.1)	39.5 (16.3,119)
Years since PI diagnosis Median (min,max)	3.3 (1.6, 7.1)	3.2 (0.9,10.8)	3.3 (0.9,10.8)
IgG trough levels pre-study drug Median (min,max) mg/dL	1014 (761,1112)	810 (459,1022)	874 (459,1112)

IgG=immune globulin G; Max=maximum; min=minimum; wk=week

Figure 2. Age groups

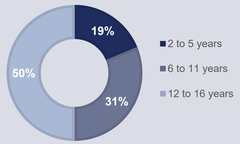
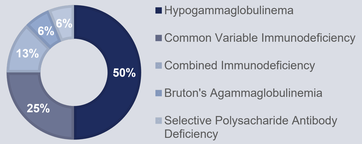


Figure 3. PI diagnosis



SAFETY

- Seven of the 96 (7.3%) infusions administered had TAAEs with the mean per subject of 6.96% (95% one-sided Confidence Limit of 12.8% that is less than the FDA safety threshold of 40%)
- TEAEs in ≥10% of subjects: headache (31.3%), upper respiratory infection (18.8%), bronchitis, cough, fatigue, influenza, nasal congestion, oropharyngeal pain, pyrexia, and sinus congestion (12.5% each)
- No AEs of special interest occurred (hemolysis or thrombosis)
- No infusion site reactions occurred

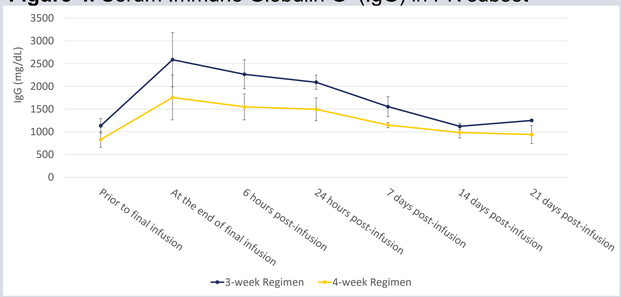
Table 2. Safety data summary

Category	3-wk regimen (N=8)		4-wk regimen (N=8)		Total (N=16)	
	Tot. Evt.	Subj. n (%)	Tot. Evt.	Subj. n (%)	Tot. Evt.	Subj. n (%)
Any AE	69	8 (100)	17	5 (62.5)	86	13 (81.3)
Any TEAE	62	8 (100)	12	5 (62.5)	74	13 (81.3)
Serious	1	1 (12.5)	0	0	1	1 (6.3)
Product-related	5	2 (25)	2	1 (12.5)	7	3 (18.8)
TAAE within 72 hours of infusion	7	3 (37.5)	2	1 (12.5)	9	4 (25)
Adverse infusion reactions	5	2 (25)	2	1 (12.5)	7	3 (18.8)

AE=adverse events; Evt.=event; Subj.=subject TAAE=temporally associated adverse event; TEAE=treatment emergent adverse event; Tot.=total

PHARMACOKINETICS

Figure 4. Serum Immune Globulin G (IgG) in PK subset



- Ten subjects had viable samples for PK analysis
- There were no apparent trends with respect to C_{max}, AUC, or clearance (CL) and age group
- There were no apparent differences in the total IgG or subclass concentrations before the first and last infusions
- None of the subjects had trough total IgG levels below 500 mg/dL

RESULTS, cont.

EFFICACY

- No hospitalizations due to infections occurred, and no subjects required intravenous antimicrobials
- One subject in the 3-wk regimen group missed a total of 9 days from school due to infection; there were no days missed from school in the 4-wk regimen group

Table 3. Efficacy outcomes

Efficacy Outcome	3-wk regimen (N=8)	4-wk regimen (N=8)	Total (N=16)
Acute SBIs (per person year)	0	0	0
Total non-serious infections	16	1	17
Non-serious infections per subject, mean (SD)	2 (2.14)	0.1 (0.35)	1.1 (1.77)
Median (min,max)	1 (0,6)	0 (0,1)	0 (0,6)

Max=maximum; min=minimum; SBI=serious bacterial infection; SD=standard deviation

DISCUSSION/CONCLUSIONS

- Treatment with IGIV 10% in pediatric patients with PI was safe and efficacious meeting all pre-specified endpoints including zero acute SBIs
- No deaths or serious AEs were attributed to the study drug, and no study discontinuation from the study
- No apparent trends were observed with respect to C_{max}, AUC, or CL and age group

REFERENCES

1. ADMA Biologics, Inc. Ramsey, NJ. BIVIGAM® (immune globulin intravenous (human) 10% liquid) [prescribing information]. Accessed July 2022.
2. S.830 - 105th Congress (1997-1998): Food and Drug Administration Modernization Act of 1997. (1997, November 21). https://www.congress.gov/bill/105th-congress/senate-bill/830