Efficacy and Safety of PlasmaCap IG, a New 10% Intravenous Immunoglobulin Manufactured Using an Innovative Chromatography Process, In Adults and Children with Primary Immunodeficiency Disorders

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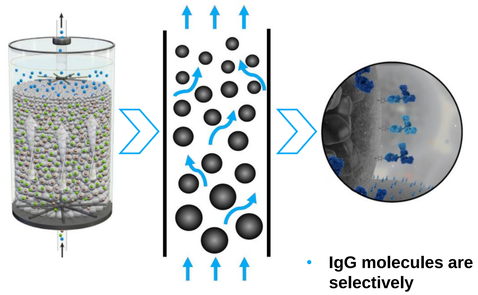
Background and Rationale

- Primary immunodeficiency disorders (PIDDs) include a heterogenous group of inherited disorders with deficiencies in one or more components of the immune system, increasing susceptibility to infections.[1,2]
- Life expectancy in PIDD patients is reduced, and recurrent infections cause significant morbidity and disability.[3,4]
- For these reasons, patients with PIDD require life-long immunoglobulin (IG) replacement therapy administered intravenously (IVIG or IGIV) or subcutaneously (SCIG) to prevent recurrent infections, notably severe bacterial infections (SBIs) of the respiratory tract.[1,3,5]
- Shortages of IVIG and SCIG continue to be reported globally[6-8], and the global need for IVIG and SCIG has grown continuously since the 1980s.[9]
- Innovative, new, and improved manufacturing technologies are needed to meet the increasing global demand for plasma-derived therapeutics, especially IG.

Innovative Manufacturing Technology

- PlasmaCap IG 10% IVIG is prepared from large pools of human donor plasma using expanded bed adsorption (EBA) chromatography (PlasmaCap EBA®) (**Figure 1**) that can enable higher yields of certain plasma proteins, including IgG, compared to traditional cold ethanol plasma fractionation.

Figure 1: PlasmaCap EBA® Technology



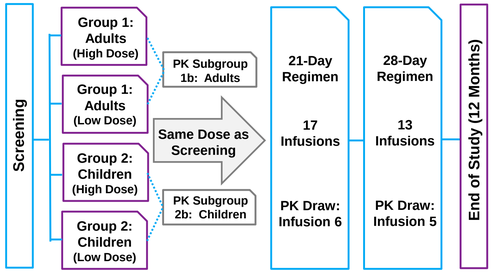
- **Expanded Bed Adsorption (EBA) columns are loaded by flowing plasma upward, exposing the ligand to the plasma proteins.**
- **The EBA resin used to capture IgG contains high- density tungsten carbide imbedded in a microporous agarose bead.**
- **IgG molecules are selectively captured and eluted.**
- **Other plasma proteins can be captured using beads with different ligands.**

Methods

Study Design

- A Phase 3 prospective, open-label, multicenter, study of the efficacy, safety, tolerability, and pharmacokinetics (PK) of PlasmaCap IG in adults and children with PIDD was conducted at 12 sites in the United States (US) and Canada.
- Following screening procedures, eligible adults (Group 1) and pediatric subjects (Group 2) received 300-900 mg/kg of PlasmaCap IG administered either every 21 or 28 days for a period of 1 year (**Figure 2**).
  - Previous dosing was used to determine placement in low-dose or high-dose subgroups.
  - A subgroup of adult and pediatric participants were also enrolled in the PK substudy.

Figure 2: Study Design



Study Endpoints

- **Primary Endpoint:**
  - The mean annual acute SBI rate (must be significantly less than 1/subject/year).
- **Secondary Efficacy Endpoints:**
  - Number of infection episodes (serious and non-serious).
  - Days of work/school/daycare missed, or days unable to perform normal daily activities due to infections.
  - Days of hospitalization due to infections, episodes of fever, and use of antibiotics to treat infections or for short-term prophylaxes.
  - Evaluation of IgG trough levels and ability to maintain stable, therapeutic IgG levels.
- **Secondary Safety Endpoints:**
  - Adverse events (AEs), viral safety, and incidence of hemolytic and thromboembolic events.
- **Secondary Pharmacokinetic Endpoints:**
  - Determination and evaluation of the PK profile plasma concentrations for each phase of the PK curve.

Results*

Study Population

- The study population (N=63) was comprised of adults (n=48 [76%]) and children (n=15 [24%]) with a confirmed diagnosis of PIDD (**Figure 3, Table 1**).

Figure 3: Study Population

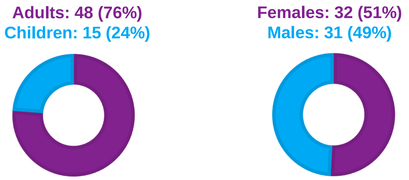


Table 1: Study Population

	No. of Subjects (%)
Adults (≥18 years): Group 1 (All)	48 (76%)
Range: 20-70 years	
Adults: Group 1 (High Dose)	22 (46%)
Adults: Group 1 (Low Dose)	26 (54%)
Adult PK Subgroup (Group 1b)	27 (56%)
Children (<17 years): Group 2 (All)	15 (24%)
Range: 2-14 years	
Children: Group 2 (High Dose)	7 (47%)
Children: Group 2 (Low Dose)	8 (53%)
Children PK Subgroup (Group 2b)	12 (80%)
Females (Groups 1 and 2)	32 (51%)
Males (Groups 1 and 2)	31 (49%)

Dosing and Infusion Summary

- More than 98% of infusions were completed without interruption, and only 1 infusion was terminated due to an AE; dosing and infusion regimens are summarized in **Table 2**.

Table 2: Dosing and Infusion Summary

Mean Previous Dose:	
Adults (Low Dose)	445.67±98.11 mg/kg
Adults (High Dose)	630.51±121.53 mg/kg
Children (Low Dose)	333.64±159.47 mg/kg
Children (High Dose)	566.79±112.47 mg/kg
Total Number of Infusions	839
Adults: Number of Infusion	613 (73%)
Children: Number of Infusions	226 (27%)

*Data is still being analyzed and final information may be subject to change prior to regulatory submission.

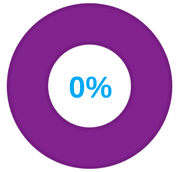
Results*

Primary Endpoint

- No SBIs occurred in any age group (**Figure 4**).
- The study met its primary endpoint (SBI rate must be significantly less than 1/subject/year).

Figure 4: Primary Endpoint

Serious Bacterial Infections (SBIs) During Study = 0%



Key Secondary Endpoints

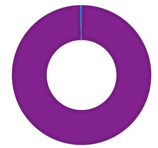
Efficacy

- Measures affecting quality of life such as days absent from work or school due to an infection (mean 6.5 days/patient/year), hospitalized due to infections (mean 0.2 days/patient/year), or with a fever >38.5ºC (mean 0.9 days/patient/year) were all low, indicating that treatment with PlasmaCap IG had a positive effect on secondary measures of efficacy (**Figure 5**).
- Antibiotic use to treat infection and for short-term prophylaxis prior to and following surgical and dental procedures was similar across both dosing subgroups (13 subjects in each of the low- and high-dose subgroups [38.2% and 44.8%, respectively]).
- IgG levels remained relatively stable throughout the treatment period of the study.

Figure 5: Key Secondary Efficacy Endpoints

Days Absent From Work or School Due to an Infection = 6.5 Days per Year

Days Hospitalized Due to an Infection or Fever = 1.1 Days per Year



Results*

Key Secondary Endpoints

Pharmacokinetics (Adults)

- PK parameters in adults were consistent with existing approved IVIG products (initial PK data results for children appear similar to that for adults).
  - The baseline-adjusted concentration of PlasmaCap IG (total IgG) is unchanged for approximately 4 hours, then declines for 21 days, with a half-life of about 180 hours.
  - No significant difference was observed between total IgG trough concentrations for the 21-day and 28-day regimens.

Safety

- **There were no treatment-related serious adverse events (SAEs) or cases of hemolysis, thromboembolism, or renal failure.**
- **Table 3** includes all AEs considered related to treatment (probably or definitely) with PlasmaCap IG in >5% of subjects; 97% of all treatment-related AEs were mild or moderate.

Table 3: Adverse Events in > 5% of Subjects

Adverse Event	Number of Subjects (%)
Headache	12 (19.0%)
Procedural Headache	6 (9.5%)
Fatigue	4 (6.3%)
Nausea	4 (6.3%)

Conclusions

- This study demonstrates that PlasmaCap IG is effective, safe, and well tolerated in the treatment of adult and pediatric patients with PIDD with no reported SBIs or related SAEs.
- PlasmaCap IG is produced using an innovative manufacturing technology, PlasmaCap EBA®, developed to enable the efficient capture of plasma proteins at high levels of purity and yield from human plasma.

References

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