2 SYNOPSIS

Name of Sponsor: CSL Behring, LLC.	Individual Study Table Referring to Part of the Dossier Volume: Page:	(For National Authority Use Only)
Name of Finished Product: Hizentra®		
Name of Active Ingredient: IgPro20		
Title of Study: Study of immune deficiency patients treated with subcutaneous immunoglobulin (IgPro20, Hizentra®) on weekly and biweekly schedules		
Coordinating Investigator: PPD CHU Sainte-Justine 3175 Chemin Côte-Sainte-Catherine Montreal, Quebec Canada H3T 1C5		

Publication (reference):
Not Applicable

Study Period:	**Phase of Development:** Phase 4
First Subject Visit: 15 Mar 2016 *Last Subject Visit*: 30 Jan 2018	

Objectives:

Primary Objective: To determine tolerability and safety of a biweekly Hizentra injection regimen and to assess pharmacokinetic (PK) characteristics of weekly and biweekly Hizentra therapy.

Secondary Objectives:

- To determine efficacy of a biweekly Hizentra injection regimen.
- To evaluate the dose of biweekly Hizentra injections needed for subjects switching from weekly Hizentra therapy to biweekly therapy.
- To assess the quality of life (QoL) of subjects on biweekly Hizentra injections.

Methodology:

In Part 1, all subjects were observed for 12 weeks on a weekly Hizentra home infusion treatment regimen. In Part 2, subjects were observed for up to 52 weeks on a biweekly Hizentra home infusion treatment regimen. Part 2 of the study began immediately after the end of Part 1, with the first biweekly Hizentra infusion occurring 2 weeks after the last weekly infusion of Hizentra.

Number of Subjects:

Planned: 25

Actual: 25

Diagnosis and Main Criteria for Inclusion:

Patients who have a documented diagnosis of primary immune deficiency (PID) and secondary immune deficiency (SID), who were on a stable dosing regimen of immunoglobulin (IgG) replacement therapy at screening.

Investigational Product, Dose and Mode of Administration, Batch Number(s):

Commercially available Hizentra was used for this study at doses that were consistent with the approved weekly and biweekly Hizentra therapy regimens for patients with immune deficiency.

Duration of Treatment:

Up to 15 months

Criteria for Evaluation:

Primary Endpoint: Annualized rate of local and systemic adverse events (AEs) during the biweekly treatment period.

Secondary Endpoints:

- Annualized rate of infections per subject during weekly and biweekly Hizentra therapies
- SF-36 (Short Form 36, v2)
- CHQ-PF28 (Child Health Questionnaire Parent Form 28): for age < 10 years
- CHQ-CF87 (Child Health Questionnaire Child Form 87): for age ≥ 10 years

Statistical Methods:

No formal statistical tests of hypothesis were planned for the primary or secondary endpoints. Statistical analyses and conclusions were based on descriptive statistics of the study data. The assessment of safety, tolerability and efficacy of biweekly Hizentra therapy, evaluation of the biweekly Hizentra therapy for subjects who switch from a weekly to a biweekly regimen, and QoL assessments were based on the review of subject listings and descriptive statistics.

Results:

Subject Disposition

A total of 25 subjects were enrolled in the study and treated in Part 1. Of these, 24 (96.0%) were treated in Part 2. A total of 16 subjects (64.0%) completed the study and 9 subjects (36.0%) withdrew: adverse event (AE; 1 subject), scheduling issues (3 subjects), out of town (2 subjects), and subject decision (3 subjects). Of the 16 subjects who completed the study, 9 subjects (36.0% of the enrolled population) completed the study per protocol.

Demographics

There were 14 male subjects (56.0%) and 11 female subjects (44.0%) in the All Treated Subjects analysis set (ATS) and almost all subjects were white (24 subjects, 96.0%). The mean (range) age was 23.6 (6 to 66) years. The mean (range) baseline body weight was 57.28 (19.0 to 96.0) kg and the mean body mass index (range) was 22.41 (13.7 to 37.0) kg/m^2. Half of the subjects in the ATS (13 subjects, 52.0%) were reported to be diagnosed with common variable immunodeficiency, 2 subjects (8.0%) were reported to be diagnosed with severe combined immunodeficiency, and 10 subjects (40.0%) were reported to be diagnosed with other immunodeficiencies.

Efficacy

The annualized rate of infections per subject during biweekly treatment for up to 52 weeks of dosing was 1.22; by age group, annualized rates were largely similar to those of the full study population. Mean IgG concentrations during biweekly dosing remained consistent with IgG concentration during pre-study treatment and weekly dosing. The biweekly treatment regimen comprising of twice the prescribed weekly dose provided adequate Hizentra exposure.

Quality of Life

Quality of life was maintained throughout the study and largely similar for weekly and

biweekly dosing.

Safety

A total of 22 subjects (91.7%) experienced any AE during Part 2 and 24 subjects (96.0%) experienced any AE during the study. The annualized rate of local AEs per patient year was 0.21 in Part 2 and 0.24 for the whole study. The mean annualized rate of local AEs per subject was 0.18 in Part 2 and 0.26 for the whole study. In subjects < 12 years old, the mean annualized rate of local AEs per subject was 0.13 for Part 2 and 0.41 for the whole study, and in subjects ≥ 18 years old, the mean annualized rate of local AEs per subject was 0.35 for Part 2 and 0.33 for the whole study. No subjects 12 to < 18 years old experienced a local AE during the whole study. The rate of AEs per infusion was 0.116 for Part 2 and 0.124 for the whole study. The rate of local AEs per infusion was the same (0.008) for Part 2 and for the whole study. The biweekly Hizentra dosing regimen offers a good safety profile comparable to or better than weekly Hizentra dosing reported in other Hizentra studies.

Conclusions:

The data from the PK substudy and the full study indicate that the Hizentra biweekly treatment regimen provides equivalent exposure, reliable protection from infections, and offers a favorable safety profile while maintaining stable overall QoL of patients receiving Hizentra.