**Supplemental Materials**

**Inclusion criteria**

For inclusion in the phase 2/3 study (NCT00546871), participants were aged ≥2 years at screening, were diagnosed with primary immunodeficiency disease (PID) as defined by International Union of Immunological Societies (IUIS)/World Health Organization (WHO) criteria [1, 2], for which they had been receiving a regular regimen of intravenous immunoglobulin (IVIG) every 21±3 days or 28±3 days or subcutaneous immunoglobulin (SCIG) every 1 to 2 weeks for ≥3 months prestudy at a dose of 300–800 mg/kg body weight (BW)/4 weeks, and had a serum IgG trough level >450 mg/dL at the last documented prestudy determination [3].

For inclusion in the phase 3 study (NCT00814320), participants were aged ≥2 years at screening, had been diagnosed with PID requiring antibody replacement as defined by IUIS/WHO criteria, had completed or were about to complete the phase 2/3 study or had been receiving regular IVIG treatment every 21±3 days or 28±3 days or SCIG treatment every 5 to 16 days for ≥3 months before enrollment at a minimum dose of 300 mg/kg BW/4 weeks, and had a serum trough level of IgG >450 mg/dL at the last documented determination [4].

For inclusion in the long-term extension study (NCT01175213), participants had completed or were able to complete the phase 3 study [5]. For all studies, written informed consent obtained from either the participant or the participant’s legally acceptable representative was required before any study-related procedures and study product administration, and a negative serum pregnancy test and agreement to practice birth control measures for the duration of the study were required for female participants of childbearing potential [3-5].

**Supplemental Table 1.** Participant demographics and baseline characteristics

|  |  |
| --- | --- |
| **Characteristic** | **All participants**  **(N = 30)** |
| Gender, n (%) |  |
| Male | 17 (56.7) |
| Female | 13 (43.3) |
| Median age, y (range)a | 28.0 (4–78) |
| Participants per age group, n (%)a |  |
| Children (aged 2–11 y) | 6 (20.0) |
| Adolescents (aged 12–15 y) | 3 (10.0) |
| Adults aged 16–65 y | 17 (56.7) |
| Adults aged >65 y | 4 (13.3) |
| Participants per BMI group, n (%)a |  |
| <18 kg/m2 | 3 (10.0) |
| 18–25 kg/m2 | 20 (66.7) |
| 26–30 kg/m2 | 4 (13.3) |
| >30 kg/m2 | 3 (10.0) |
| PID diagnosis, n (%) |  |
| Common variable immunodeficiency | 18 (60.0) |
| Male | 9 (30.0) |
| Female | 9 (30.0) |
| Hypogammaglobulinemia | 7 (23.3) |
| Male | 4 (13.3) |
| Female | 3 (10.0) |
| X-linked agammaglobulinemia | 2 (6.7) |
| Male | 2 (6.7) |
| Female | 0 |
| Specific antibody deficiency | 2 (6.7) |
| Male | 2 (6.7) |
| Female | 0 |
| Hyper IgE syndrome | 1 (3.3) |
| Male | 0 |
| Female | 1 (3.3) |

aAt screening.

BMI: body mass index; IgE: immunoglobulin E; PID: primary immunodeficiency disease.

**Supplemental Table 2.** Annualized rates of infections by IgG route of administration for subgroup of participants sequentially treated with IVIG, SCIG, and fSCIG and total population from clinical studies

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Participants sequentially treated with IVIG, SCIG, and fSCIG** | | | **Total Study Populations** | | |
| **Infection rate** | **IVIG**a  **n = 30** | **SCIG**  **n = 30** | **fSCIG**  **n = 30** | **Phase 2/3 SCIG [3]**  **n = 49** | **Phase 3 fSCIG [4]**  **n = 87** | **LTE of Phase 3 fSCIG [5]**  **n = 83** |
| VASBIs/participant-year (upper limit of 99% CI) | 0 (0.60) | 0.09 (0.20)b | 0.04 (0.09) | 0.07 (0.13) | 0.03 (0.05) | 0.03 (0.05) |
| All infections/participant-year (95% CI) | 4.17 (2.73–6.05) | 3.68 (2.72–4.85) | 2.42 (1.89–3.04) | 4.1 (3.2–5.1) | 2.97 (2.51–3.47) | 2.99 (2.60–3.42) |

aDue to the short duration spent in the intravenous period, no seasonal balancing was done.

bDue to few events no seasonal balancing was done.

CI: confidence interval; fSCIG:, facilitated SCIG; IgG: immunoglobulin G; IVIG: intravenous immunoglobulin; LTE: long-term extension; SCIG: subcutaneous immunoglobulin; VASBI: validated acute serious bacterial infection.

**Supplemental Table 3.** IgG peak and trough levels by infusion interval

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **IgG level, mg/dL** | **IVIG** | | | | **SCIG** | | | | **fSCIG** | | | |
| **Weekly** | **Every**  **2 weeks** | **Every**  **3 weeks** | **Every**  **4 weeks** | **Weekly** | **Every**  **2 weeks** | **Every**  **3 weeks** | **Every**  **4 weeks** | **Weekly** | **Every**  **2 weeks** | **Every**  **3 weeks** | **Every**  **4 weeks** |
| Peak  n  Mean  SD | 0  NA  NA | 0  NA  NA | 3  2,190.0  609.1 | 19  2,212.1  607.6 | 22  1,376.0  306.3 | 0  NA  NA | 0  NA  NA | 0  NA  NA | 0  NA  NA | 0  NA  NA | 3  1,584.0  681.3 | 18  1,542.0  372.8 |
| Trough  n  Mean  SD | 0  NA  NA | 0  NA  NA | 5  1,272.6  288.2 | 23  1,064.0  292.4 | 30  1,274.0  330.6 | 0  NA  NA | 0  NA  NA | 0  NA  NA | 0  NA  NA | 13  1,203.6  3,720.1 | 6  1,065.8  367.7 | 24  1,026.0  268.8 |

fSCIG: facilitated SCIG; IgG: immunoglobulin G; IVIG: intravenous immunoglobulin; NA: not applicable; SCIG: subcutaneous immunoglobulin; SD, standard deviation.

**Supplemental Table 4.** Causally related AEs (excluding infections)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Most common systemic AEs occurring in ≥5% in any treatment arm | **IVIG**a | | **SCIG**a | | **fSCIG**a | |
| AEs/infusion | AEs/PY | AEs/Infusion | AEs/PY | AEs/infusion | AEs/PY |
| Headache | 0.12 | 1.95 | 0.01 | 0.45 | 0.01 | 0.21 |
| Chills | 0.06 | 0.91 | 0 | 0 | 0 | 0.03 |
| Heart rate increased | 0.03 | 0.52 | 0.01 | 0.24 | 0 | 0 |
| Vomiting | 0.03 | 0.52 | 0 | 0.13 | 0 | 0.05 |
| Nausea | 0.02 | 0.39 | 0 | 0.18 | 0.01 | 0.10 |
| Pyrexia | 0.02 | 0.39 | 0 | 0.15 | 0.01 | 0.09 |
| Fatigue | 0.01 | 0.13 | 0 | 0.12 | 0 | 0.04 |
| Upper abdominal pain | 0 | 0 | 0 | 0.03 | 0 | 0.04 |
| Diarrhea | 0 | 0 | 0 | 0.09 | 0 | 0 |
| Blood pressure increased | 0 | 0 | 0 | 0.03 | 0 | 0.04 |
| Dizziness | 0 | 0 | 0 | 0 | 0 | 0.03 |
| Free hemoglobin present | 0 | 0 | 0 | 0 | 0 | 0.03 |

aTotal number of infusions for IVIG, SCIG, and fSCIG = 128, 1,755, and 1,341, respectively; total PYs for IVIG, SCIG, and fSCIG = 7.7, 33.7, and 79.7, respectively; total treatment time for IVIG, SCIG, and fSCIG was 13 weeks, approximately 12 months, and 14–24 months, respectively.

AE: adverse event; fSCIG: facilitated SCIG; IVIG; intravenous immunoglobulin G; PY: participant-year; SCIG: subcutaneous immunoglobulin.

**Supplemental Table 5.** Causally related AEs (excluding infections) by IgG route of administration for subgroup of participants sequentially treated with IVIG, SCIG, and fSCIG and total population from clinical studies

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Participants sequentially treated with IVIG, SCIG, and fSCIG** | | | | | | **Total Study Populations** | | | | | |
|  | **IVIG**a  **n = 30** | | **SCIGa**  **n = 30** | | **fSCIG**a  **n = 30** | | **Phase 2/3 SCIG [3]**  **n = 49** | | **Phase 3 fSCIG [4]**  **n = 87** | | **LTE of Phase 3 fSCIG [5]**  **n = 83** | |
|  | AEs/infusion | AEs/PY | AEs/infusion | AEs/PY | AEs/infusion | AEs/PY | AEs/infusion | AEs/PY | AEs/infusion | AEs/PY | AEs/infusion | AEs/PY |
| Total local AEs | 0.01 | 0.13 | 0.02 | 0.92 | 0.09 | 1.57 | 0.03 | NR | NR | NR | NR | 2.60 |
| Total systemic AEs | 0.34 | 5.60 | 0.04 | 1.93 | 0.05 | 0.88 | NR | NR | NR | NR | NR | 1.75 |

aTotal number of infusions for IVIG, SCIG, and fSCIG = 128, 1755, and 1341, respectively; total PYs for IVIG, SCIG, and fSCIG = 7.7, 33.7, and 79.7, respectively; total treatment time for IVIG, SCIG, and fSCIG was 13 weeks, approximately 12 months, and 14–24 months, respectively.

AE: adverse event; fSCIG: facilitated SCIG; IVIG: intravenous immunoglobulin; NR: not reported; PY: participant-year; SCIG: subcutaneous immunoglobulin.

**References**

1. Picard C, Bobby Gaspar H, Al-Herz W *et al.* International Union of Immunological Societies: 2017 Primary Immunodeficiency Diseases Committee Report on Inborn Errors of Immunity. *J. Clin. Immunol.* 38(1), 96–128 (2018).

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3. Wasserman RL, Melamed I, Kobrynski L *et al.* Efficacy, safety, and pharmacokinetics of a 10% liquid immune globulin preparation (GAMMAGARD LIQUID, 10%) administered subcutaneously in subjects with primary immunodeficiency disease. *J. Clin. Immunol.* 31(3), 323–31 (2011).

4. Wasserman RL, Melamed I, Stein MR *et al.* Recombinant human hyaluronidase-facilitated subcutaneous infusion of human immunoglobulins for primary immunodeficiency. *J. Allergy Clin. Immunol.* 130(4), 951–957 (2012).

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