COMPARABILITY OF PHARMACOKINETICS IN ADULTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY RECEIVING FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN: A PHASE 3 STUDY DESIGN

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INTRODUCTION

- Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase (HyQvia) is hyaluronidase-facilitated subcutaneous immunoglobulin (fSCIG; Baxalta US Inc., a Takeda company, Cambridge, MA, USA) that comprises a dual-vial unit of immunoglobulin G (IgG) 10% and recombinant human hyaluronidase (rHuPH20).[1,2]
  - rHuPH20 depolymerizes hyaluronan in the extracellular matrix, transiently increasing subcutaneous tissue permeability, and thereby permitting high-volume immunoglobulin administration.[3]
  - Compared with conventional subcutaneous immunoglobulin (SCIG), fSCIG therapies allow less frequent (monthly) infusions. Subcutaneous therapies enable at-home self-administration via infusion devices.[4,5]
- fSCIG 10% is approved in the USA as maintenance treatment in adults with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and in the EU as maintenance treatment in patients with CIDP after intravenous IgG stabilization,[1,2] based on the findings of the ADVANCE-CIDP 1 trial.[4]
- fSCIG 20%, also known as TAK-881, is an infusion of IgG 20% and rHuPH20.
  - The higher concentration of IgG in fSCIG 20% versus fSCIG 10% reduces IgG infusion volumes by 50% for equivalent doses, which can shorten the duration of infusion.[6]
- A phase 1 study with fSCIG 20% affirmed initial safety and tolerability in adult healthy participants.[7]
- A pharmacokinetic (PK) comparison in healthy adult participants revealed no clinically relevant differences in total IgG concentrations between fSCIG 20% and fSCIG 10%.[8]

OBJECTIVE

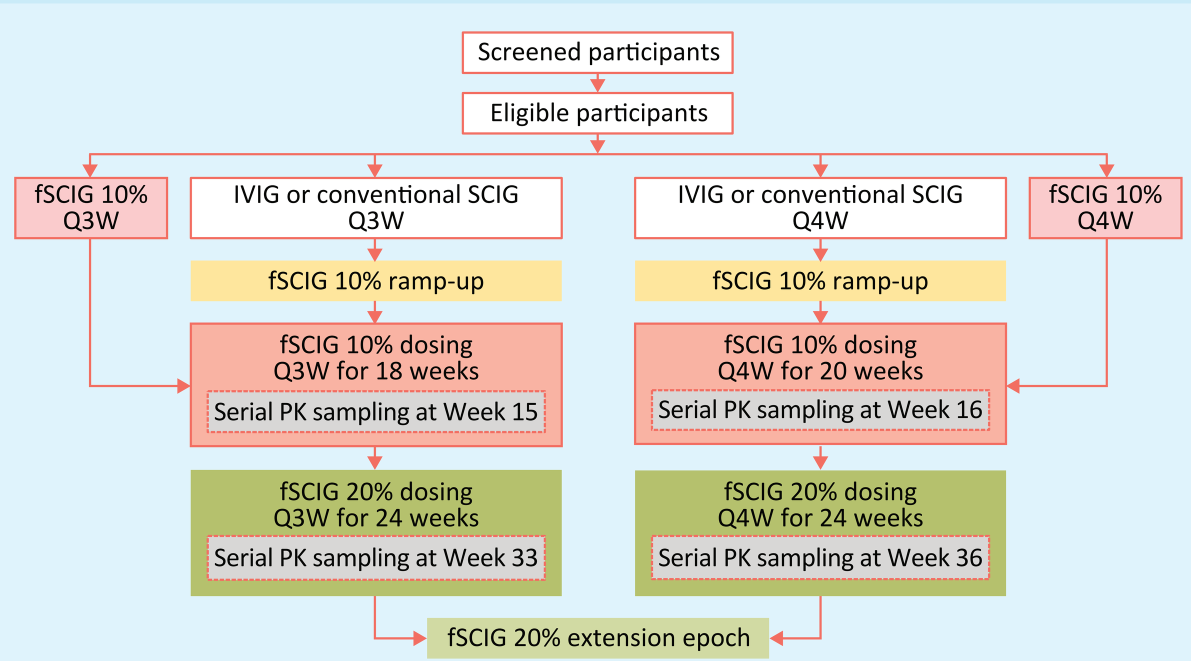
- The aim of this phase 3 trial is to assess the PK comparability of fSCIG 20% and fSCIG 10% and the safety and tolerability of fSCIG 20% in adults with CIDP.

METHODS

STUDY DESIGN

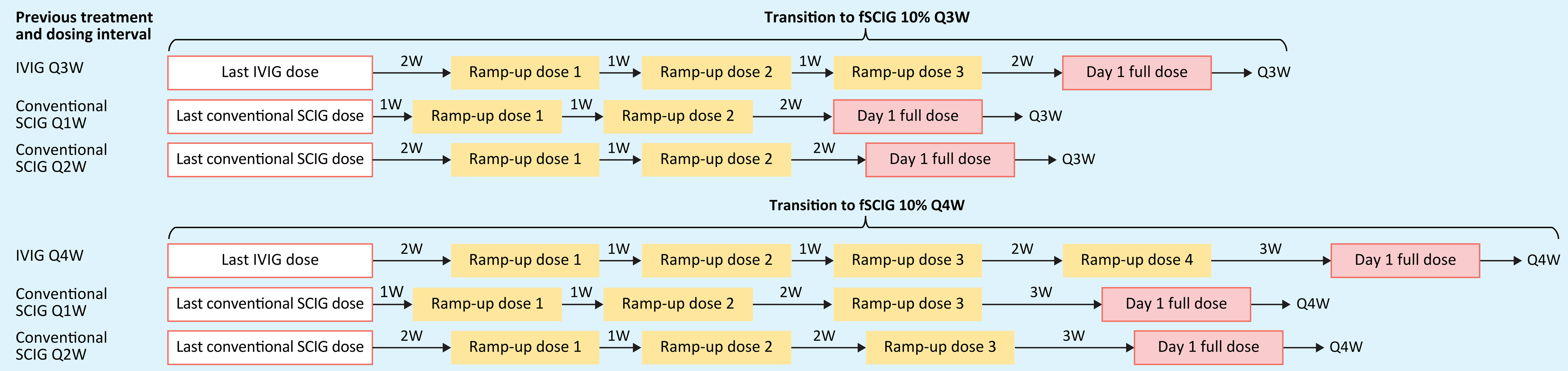
- This is a multicenter, single-arm, multi-dose phase 3 trial (NCT06747351) of fSCIG 10%/20% in adults with CIDP previously receiving intravenous IgG, conventional SCIG or fSCIG 10% (study schematic shown in **Figure 1**).
- After dose ramp-up (if applicable; **Figure 2**), eligible patients will receive fSCIG 10% every 3 weeks (Q3W) for 18 weeks or every 4 weeks (Q4W) for 20 weeks (at the weekly equivalent dose to prior therapy), and will then switch to fSCIG 20% (at the same dose and frequency as fSCIG 10%) for 24 weeks.
- Serial PK samples will be collected at Weeks 15 or 16 (for fSCIG 10% Q3W or Q4W, respectively) and Weeks 33 or 36 (for fSCIG 20% Q3W or Q4W, respectively).
- In the 3-year extension epoch, patients will receive fSCIG 20% with allowances for flexible dosing and self-administration at home (with training) at the discretion of the physician/patient/caregiver.

FIGURE 1. STUDY DESIGN



fSCIG, hyaluronidase-facilitated subcutaneous immunoglobulin; IVIG, intravenous immunoglobulin; PK, pharmacokinetic; Q3W, every 3 weeks; Q4W, every 4 weeks; SCIG, subcutaneous immunoglobulin.

FIGURE 2. fSCIG 10% RAMP-UP SCHEDULE



fSCIG, hyaluronidase-facilitated subcutaneous immunoglobulin; IVIG, intravenous immunoglobulin; Q1W, every week; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; SCIG, subcutaneous immunoglobulin; W, week(s).

PATIENT ELIGIBILITY CRITERIA

- Patients aged ≥ 18 years with a confirmed diagnosis of CIDP or possible CIDP, with stable pretrial treatment with intravenous IgG, conventional SCIG, or fSCIG 10% administered for ≥ 12 weeks before screening and who have responded to IgG treatment in the past.
  - A summary of key patient eligibility criteria is provided in **Table 1**.

TABLE 1. KEY PATIENT ELIGIBILITY CRITERIA

Inclusion criteria
Age ≥ 18 years
Documented diagnosis of CIDP or possible CIDP, as confirmed by a neurologist specializing/experienced in neuromuscular diseases and consistent with the EAN/PNS 2021 criteria[9]
Stable pretrial treatment with IVIG, conventional SCIG, or fSCIG 10% administered ≥ 12 weeks before screening
Responded to IgG treatment in the past
INCAT disability score between 0 and 7 (inclusive)
Exclusion criteria
Documented diagnosis of focal, multifocal, distal, or sensory CIDP per the EAN/PNS 2021 criteria[9]
Neuropathy of other causes
Any chronic or debilitating disease or central nervous disorder that causes neurological symptoms
Required to take or has taken immunomodulatory/immunosuppressive agents (except IVIG, conventional SCIG, or fSCIG) within 6 months of screening
Required to take or has taken long-term systemic corticosteroids, defined as dosages > 20 mg/day prednisone-equivalent for > 30 days within 3 months of screening
Undergone plasma exchange within 3 months of screening
Pregnant or breastfeeding

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; EAN, European Academy of Neurology; fSCIG, hyaluronidase-facilitated subcutaneous immunoglobulin; IgG, immunoglobulin G; INCAT, Inflammatory Neuropathy Cause and Treatment; IVIG, intravenous immunoglobulin; PNS, Peripheral Nerve Society; SCIG, subcutaneous immunoglobulin.

STUDY OUTCOMES

- The primary endpoint is steady-state baseline-uncorrected area under the curve of total IgG during the dosing interval ($AUC_{0\text{-}\tau,ss}$) during fSCIG 20% and fSCIG 10% treatment.
  - A summary of key endpoints and associated measures is provided in **Table 2**.

STATISTICAL ANALYSIS

- $AUC_{0\text{-}\tau,ss}$ will be transformed before analysis using a logarithmic transformation. PK comparability of fSCIG 20% and fSCIG 10% will be assessed using two-sided 90% confidence intervals.
- Descriptive summaries for the change from baseline to each post-baseline visit will be presented for the adjusted Inflammatory Neuropathy Cause and Treatment disability score, hand grip strength, Medical Research Council sum score, and Inflammatory Rasch-built Overall Disability Scale centile score.

RESULTS

- Recruitment began in Q2 2025, with completion planned for Q2 2028.
- Enrollment will continue until 44 patients have received fSCIG 20%.

TABLE 2. KEY STUDY OUTCOMES

Objectives	Outcomes
Primary	
PK comparability of fSCIG 20% and fSCIG 10% at steady state after subcutaneous administration in patients with CIDP	• Steady-state baseline-uncorrected area under the curve of total IgG during the dosing interval
Secondary	
fSCIG 20% and fSCIG 10% baseline-uncorrected PK	• Baseline-uncorrected PK parameters based on total IgG levels • Trough level of total IgG
The effects of fSCIG 20% on disability and impairment	• Change in key assessments after 24 weeks relative to baseline: – INCAT score – hand grip strength – MRC sum score – I-RODS
Safety, tolerability, and immunogenicity of fSCIG 20%	• Safety: occurrence of treatment-emergent adverse events • Tolerability: occurrence of infusion withdrawals, interruptions, and infusion rate reductions • Immunogenicity: occurrence of binding and neutralizing antibodies to rHuPH20
Infusion parameters	• Number of infusions and infusion sites per month • Duration of infusions (minutes)

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; fSCIG, hyaluronidase-facilitated subcutaneous immunoglobulin; IgG, immunoglobulin G; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-built Overall Disability Scale; MRC, Medical Research Council; PK, pharmacokinetic(s); rHuPH20, recombinant human hyaluronidase PH20.

CONCLUSIONS

This is the first study to utilize PK comparability as a primary endpoint in CIDP without the need for placebo or a washout period, thereby maintaining patient centricity.

Findings are expected to provide insights into the PK comparability of fSCIG 20% and fSCIG 10% in patients with CIDP.

fSCIG 20% has the potential to reduce infusion volumes and infusion duration versus fSCIG 10%, potentially minimizing the burden of infusions for patients with CIDP.

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DISCLOSURES

CJY, **KP**, **NN**, and **ZL** are employees of Takeda Development Center Americas, Inc. and are Takeda shareholders. **AB** is an employee of Baxalta Innovations GmbH, a Takeda company, and is a Takeda shareholder. **IF** and **TL** were employees of Takeda Development Center Americas, Inc. and Takeda shareholders at the time of the study. **IF** is now affiliated with Freedman Patent, Harleysville, PA, USA and the University at Buffalo, Buffalo, NY, USA. **TL** is now an employee of Newleos Therapeutics, Boston, MA, USA.

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