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Investigating the Pharmacokinetics, Injection Speed, and Usability of Subcutaneous Efgartigimod PH20 Administration Using a Prefilled Syringe

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INTRODUCTION

- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared to endogenous IgG, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[1]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production or other parts of the immune system, and does not decrease albumin[1-3]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20, which allows for rapid SC administration of larger volumes[4,5]
- The 1000-mg fixed-dose formulation of efgartigimod PH20 SC utilized in ADAPT-SC and ADAPT-SC+, which is provided in a vial and administered via a separate syringe (V+S), has been shown to be well tolerated and efficacious[6]
- To improve patient convenience, a prefilled syringe (PFS) has been developed to ease the injection procedure

Efgartigimod Mechanism of Action: Blocking FcRn

1. Efgartigimod and IgG are internalized[1,7]
2. Efgartigimod competes with endogenous IgG for binding to FcRn[1]
3. Unbound IgG enters the lysosomal degradation pathway[1,7]
4. Efgartigimod and fewer IgGs are recycled back into the bloodstream[1]

METHODS

Bioequivalence

Phase 1, open-label, randomized, single-dose, 2-period crossover, bioequivalence study

Healthy Participants: N=72
1:1 randomization

Efgartigimod PH20 SC 1000 mg
Administered via PFS or V+S[a]

Study duration: 13 weeks

Injection Speed

Phase 1, single center, randomized, open-label, crossover study

Healthy participants: N=48
Randomized to 1 of 12 randomized sequences[c]

Efgartigimod PH20 SC 1000 mg
Administered over 20, 30, 45, or 60 seconds[d,e]

Study duration: 92 days

Human Factors Validation

Simulated-use human factors validation study to evaluate the efgartigimod PH20 SC PFS and associated instructions for use (IFU)[b]

Participants with gMG: n=15
Lay caregivers: n=15

Tasks included storage, unaided administration, and understanding of the PFS and IFU

Simulated-use human factors validation study to evaluate the efgartigimod PH20 SC PFS and associated IFU[b]

Participants with CIDP: N=15

Tasks included storage, unaided administration, and understanding of the PFS and IFU

[a]Participants were randomized in a 1:1 ratio to 1 of 2 treatment sequences, which defined the order in which they received the 2 presentations of efgartigimod PH20 SC (PFS and V+S) on day 1 in treatment periods 1 and 2. [b]The efgartigimod PH20 SC single-dose PFS is administered by attaching a separate 25G safety needle. [c]Each sequence included 2 dosing periods. [d]Participants were administered efgartigimod PH20 SC 1000 mg at 2 different injection times in the 2 dosing periods. The administration times of efgartigimod PH20 SC for participants in groups A, B, C, and D were 20, 30, 45, and 60 seconds, respectively. [e]To allow delivery of efgartigimod PH20 SC at specified injection durations, contents of the PFS were transferred to an administration syringe and administered via syringe pump with a 27G needle under the supervision of site staff members. A different PFS batch was used for this study with a minor difference in formulation; this is not expected to impact the conclusions of the injection speed study.

SUMMARY

- **Efgartigimod PH20 SC administered via PFS was shown to be bioequivalent to efgartigimod PH20 SC administered via V+S**
- **The feasibility, safety, and tolerability of efgartigimod PH20 SC injection at a speed of 20 seconds is comparable to injections administered at 30, 45, or 60 seconds**
- **Most participants had favorable responses when asked if they would be willing to have administration via PFS again**
- **The safety profile of the PFS was consistent with the previously reported safety profile of efgartigimod PH20 SC administered via V+S**
- **Human factor validation studies demonstrated that both participants with gMG/CIDP and lay caregivers can safely and successfully prepare and administer efgartigimod PH20 SC PFS**
- **Efgartigimod PH20 SC administered via PFS may be a convenient option for patients with gMG or CIDP to ease the injection procedure**

RESULTS

Bioequivalence Study in Healthy Participants

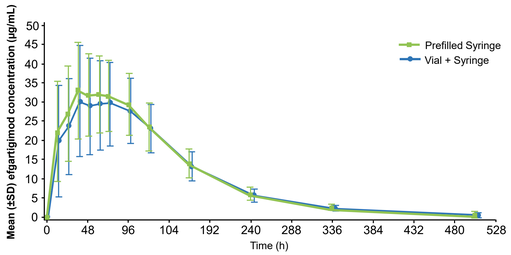
- **Design**: Healthy participants were randomized to receive a single injection of efgartigimod PH20 SC via PFS or V+S, and switched to receive the other treatment ≥2 weeks later
- **Results:** Following a single administration of efgartigimod PH20 SC via PFS or V+S, efgartigimod serum concentrations indicated that the 90% CI around the GMR of C_{max} and $AUC_{0\text{-}inf}$ was within the predefined bioequivalence criteria of 80.00% to 125.00% **(Table 1; Figure 1)**
- **Safety:** The frequency of AEs was similar between participants in both groups. The majority of AEs were mild to moderate in severity; most frequently reported AEs[a] were injection site discoloration, injection site reaction, and injection site hemorrhage. No SAEs or deaths were seen in the study

[a]Occuring in ≥10% of participants in either treatment group.

Table 1. Summary of Statistical Comparisons of Efgartigimod PK Parameters After a Single Injection of Efgartigimod PH20 SC 1000 mg Administered via PFS or V+S

	PFS (test)		V+S (reference)		PFS vs V+S	
Parameter (unit)	n	Geometric LSM	n	Geometric LSM	GMR (%)	90% CI (%)
C_{max} (µg/mL)	70	34.70	72	31.63	109.70	103.40-116.39
$AUC_{0\text{-}t}$ (µg x h/mL)	70	5305.9	72	4911.2	108.04	103.72-112.54
$AUC_{0\text{-}inf}$ (µg x h/mL)	70	5389.0	72	4995.1	107.89	103.65-112.29

Figure 1. Mean (SD) Efgartigimod Serum Concentration vs Time Profiles After a Single Injection of Efgartigimod PH20 SC 1000 mg Administered via PFS or V+S

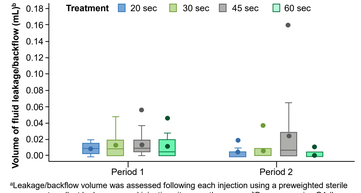


Injection Speed Study in Healthy Participants

- **Design**: Healthy participants were randomized to receive efgartigimod PH20 SC 1000 mg in 1 of 12 injection sequences, each with 2 dosing periods. In each dosing period, participants received injections over 20, 30, 45 or 60 seconds[a]
- **Results:** There was no meaningful difference in the mean fluid leakage/backflow volume at the injection site across the injection time groups **(Figure 2)**. All participants received at least 90%[b] of the entire injection volume across the injection time groups. Overall, the majority (>87%) of participants either strongly agreed or agreed to have the administration again 1 hour after injection **(Figure 3)**. No clear preference toward an injection time group was concluded
- **Safety:** All AEs were mild in severity, except for 2 moderate AEs of dysuria and pericoronitis in 2 (4.2%; 2 events) participants. No participants died during the study. Local injection-site scoring was similar and consistent across the injection time groups for the 3 assessed categories[c] at all time points

[a]To allow delivery of efgartigimod PH20 SC at specified injection durations, contents of the PFS were transferred to an administration syringe and administered via syringe pump with a 27G needle under the supervision of site staff members. A different PFS batch was used for this study with a minor difference in formulation; this is not expected to impact the conclusions of the injection speed study. [b]90% of efgartigimod PH20 SC volume administered is considered an entire dose. [c]The 3 assessed categories of local tolerability included erythema, swelling, and induration.

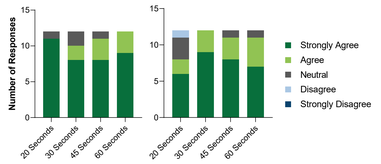
Figure 2. Volume of Leakage at Injection Site[a]



[a]Leakage/backflow volume was assessed following each injection using a preweighted sterile compress to collect leakage around injection site or on the spacer. [b]Boxes comprise Q1 (lower quartile), median (bar in the box), and Q3 (upper quartile). The dot within the box represents the mean. Bars extending from the box represent the minimum and maximum values. Dots outside of the box represent outlier values.

Figure 3. Injection Experience

Responses to
"I would be willing to have the administration again."



Human Factors Validation Studies in gMG and CIDP

- **Design**: In a simulated-use environment mimicking a home setting, participants (N=30 in the gMG study [n=15 patients with gMG and n=15 lay caregivers[a]]; N=15 in the CIDP study) were given access to the IFU and materials supplied with the PFS. No training was provided. Participants were then tasked with performing an unaided injection and were questioned on their knowledge of the PFS **(Table 2)**
- **Results:** 100% of participants (N=30/30 in the gMG study; N=15/15 in the CIDP study) were successful in preparing and delivering the full dose in an average of 30 seconds. Participants and lay caregivers had no difficulty handling the syringe and successfully identified critical information on the instructions. Residual risks were as low as possible and were not tied to the design of the prefilled syringe or instructional materials

[a]Adults who care for a family member with gMG (n=12) or CIDP (n=3).

Table 2: Patient-Reported Responses to PFS Injection

Responses to
"Would you be able to successfully inject this product weekly, if needed?"

	gMG Study		CIDP Study	
Response	Patients with gMG (n=15)	Lay caregivers[a] (n=15)	Patients with CIDP (N=15)	Overall (N=45)
Yes	15/15 (100%)	15/15 (100%)	15/15 (100%)	**45/45 (100%)**
No	0/15 (0%)	0/15 (0%)	0/15 (0%)	**0/45 (0%)**

[a]Adults who care for a family member with gMG (n=12) or CIDP (n=3).

ABBREVIATIONS

AE, adverse event; AUC, area under the curve; CI, confidence interval; CIDP, chronic inflammatory demyelinating polyneuropathy; C_{max}, maximum observed concentration; CV, coefficient of variation; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; GMR, geometric least-squares mean ratio; Ig, immunoglobulin; IFU, instructions for use; LSM, least-squares mean; PH20, recombinant human hyaluronidase PH20; PFS, prefilled syringe; PK, pharmacokinetic; SAE, serious adverse event; SC, subcutaneous; SD, standard deviation; V+S, vial and syringe.

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