MG32

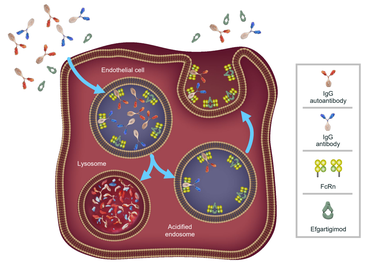
Efficacy, Safety, and Pharmacodynamics of Efgartigimod PH20 SC Across Bodyweight Quartiles: A Post hoc Analysis of the ADAPT-SC+ Trial

Jeffrey Guptill,[1] Yuebing Li,[2] Tuan Vu,[3] Denis Korobko,[4] Li Liu,[1] Sophie Steeland,[1] Benjamin Van Hoorick,[1] Jana Podhorna,[1] Edward Brauer,[1] Jan Noukens,[5] Tonke van Bragt,[5] Kimiaki Utsugisawa,[6] Jan L. De Bleecker,[7] James F. Howard, Jr,[8] and the ADAPT-SC Study Group

[1]argenx, Ghent, Belgium; [2]Cleveland Clinic, Cleveland, Ohio, USA; [3]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, Florida, USA; [4]State Budgetary Healthcare Institution of Novosibirsk Region "State Novosibirsk Regional Clinical Hospital," Novosibirsk, Russia; [5]Curare Consulting BV, The Netherlands; [6]Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; [7]Ghent University Hospital, Ghent, Belgium; [8]Department of Neurology, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

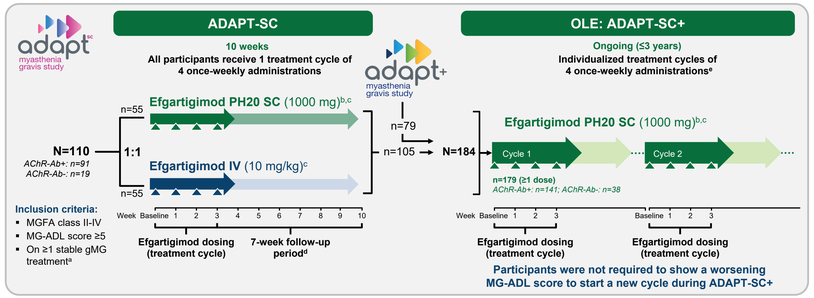
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG antibodies and albumin. This recycling and salvage from lysosomal degradation results in IgG antibodies having the longest half-life and being the most abundant of all immunoglobulins[1-3]
- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn, 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, albumin levels, or other parts of the immune system[1,4,5]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[6,7]
- PK/PD modeling and phase 3 data (ADAPT-SC) have demonstrated 4 once-weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[6,8]

METHODS



[a]AChEIs, steroids, and/or NSISTs. [b]Coformulated with 2000 U/mL rHuPH20. [c]Arrows indicate efgartigimod administration. [d]Participants could not receive treatment in the 7-week follow-up period. [e]Participants who are not in need of retreatment at study entry will instead start with an intertreatment period.

SUMMARY

- Efgartigimod PH20 SC treatment resulted in consistent reductions in IgG levels and improvements in MG-ADL total scores across bodyweight quartiles in participants with gMG in the ADAPT-SC+ trial
- Efgartigimod PH20 SC was well tolerated over a total of 193.4 PYFU with no new safety signals observed compared with ADAPT-SC
- All injection-site reactions were mild or moderate, decreased with subsequent cycles, and none led to treatment discontinuation
- The ADAPT-SC+ study is ongoing

RESULTS

Table 1. Baseline Demographics and Disease Characteristics for ADAPT-SC/ADAPT-SC+

Overall Population

	ADAPT-SC		ADAPT-SC+
Characteristics	**Efgartigimod IV (n=55)**	**Efgartigimod PH20 SC (n=55)**	**Efgartigimod PH20 SC (n=179)**
Age, y, mean (SD)	55.8 (15.4)	50.9 (15.8)	50.7 (15.5)
Sex, n (%)			
Female	34 (61.8)	31 (56.4)	119 (66.5)
Male	21 (38.2)	24 (43.6)	60 (33.5)
AChR-Ab+, n(%)	46 (83.6)	45 (81.8)	141 (78.8)
Weight, kg, median (range)	78.0 (45.0-139.3)	78.3 (42.0-150.2)	76.9 (42.0-148.8)
Total MG-ADL score, mean (SD)	8.7 (2.6)	8.7 (2.5)	7.9 (3.4)
Commonly prescribed therapies, n (%)			
NSIST	25 (45.5)	23 (41.8)	89 (49.7)
Steroid	33 (60.0)	40 (72.7)	128 (71.5)
AChEI	47 (85.5)	48 (87.3)	150 (83.8)

- 184 participants rolled over from ADAPT-SC (n=105) and ADAPT+ (n=79)
- 179 participants (141 AChR-Ab+ and 38 AChR-Ab-) received ≥1 dose of efgartigimod PH20 SC in ADAPT-SC+ through December 2022, with a mean (SD), median, and maximum study duration for all participants of 412.9 (104.52), 451, and 585 days, respectively

Figure 1. Change (%) From Baseline in Total IgG Levels at Day 29 in ADAPT-SC

Overall Population

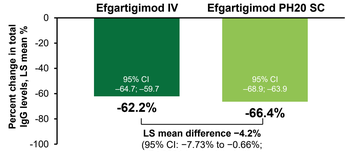


Table 2. Summary of TEAEs for ADAPT-SC/ADAPT-SC+

Overall Population

	ADAPT-SC				ADAPT-SC+	
	Efgartigimod IV (n=55) [10.5 PY]		**Efgartigimod PH20 SC (n=55)** [10.7 PY]		**Efgartigimod PH20 SC (n=179)** [193.4 PY]	
	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)
TEAEs	7.62	28 (50.9)	12.43	37 (67.3)	8.95	152 (84.9)
Serious TEAEs	0.48	4 (7.3)	0.93	8 (14.5)	0.26	33 (18.4)
Discontinued due to TEAE	0	0	0.19	2 (3.6)	0.03	4 (2.2)

[a]ER was calculated as number of events per total PY of follow-up.

Table 3. Summary of TEAEs of ADAPT-SC+ Bodyweight Quartiles

Overall Population

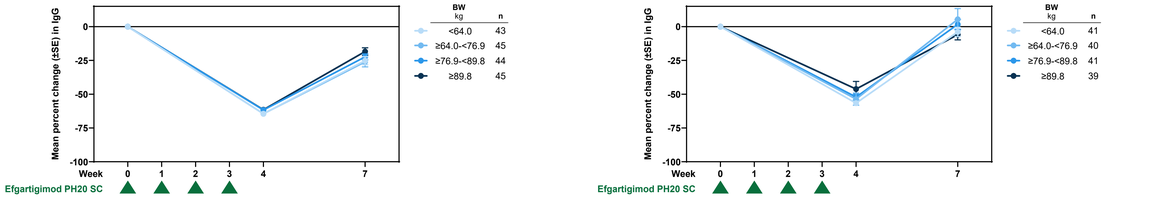
	Q1: BW <64.0 (n=44) [49.94 PY]		Q2: BW ≥64.0-<76.9 (n=45) [47.09 PY]		Q3: BW ≥76.9-<89.8 (n=44) [49.55 PY]		Q4: BW ≥89.8 (n=46) [46.78 PY]	
	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)
Any TEAEs	9.59	38 (86.4)	8.71	40 (88.9)	9.51	39 (88.6)	7.93	35 (76.1)
Any serious TEAEs	0.08	4 (9.1)	0.13	4 (8.9)	0.32	11 (25.0)	0.51	14 (30.4)
Any TEAE grade ≥3	0.08	4 (9.1)	0.25	9 (20.0)	0.40	10 (22.7)	0.86	13 (28.3)
Any infection	0.78	21 (47.7)	0.66	20 (44.4)	1.37	28 (63.6)	1.37	22 (47.8)
Any ISR	4.65	19 (43.2)	3.55	24 (53.3)	2.87	20 (45.5)	1.86	19 (41.3)
Discontinued due to TEAE[b]	0	0	0.04	1 (2.2)	0.02	1 (2.3)	0.04	2 (4.3)
Fatal event[c]	0.02	1 (2.3)	0.04	1 (2.2)	0	0	0.04	2 (4.3)

[a]ER was calculated as number of events per total PY of follow-up. [b]Treatment discontinuations were due to metastatic renal cell cancer (Cycle 1, death), cardiac arrest (Cycle 2, death), COVID-19/respiratory failure (Cycle 3, death), and MG crisis (Cycle 1). [c]Fatal events (metastatic renal cell cancer, cardiac arrest, pulmonary mass, and COVID-19/respiratory failure) were not related to efgartigimod PH20 SC treatment, as determined by investigators.

- The proportion of participants experiencing ISRs decreased over subsequent cycles; from 34.6% (n=62/179) in Cycle 1 to 10.3% (n=7/68) in Cycle 9
- No ISRs were grade ≥3, serious, or resulted in treatment discontinuation
- Event rates for ISRs include statistical outliers who experienced >30 ISRs (Q1 [n=3], Q2 [n=2], Q3 [n=1])

Figure 2. Mean Percent Change From Cycle Baseline in IgG Levels by Bodyweight Quartiles[a]

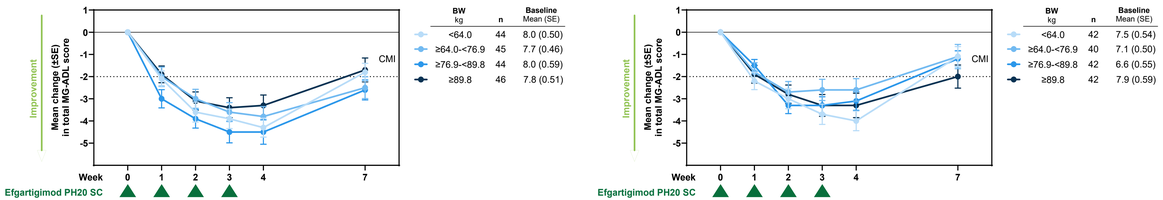
Overall Population



[a]Error bars falling within the size of the marker have been omitted.

Figure 3. Change From Cycle Baseline in MG-ADL[a] by Bodyweight Quartiles

Overall Population



[a]Values for MG-ADL range from 0-24, with higher total scores indicating more impairment.

ABBREVIATIONS

AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor antibody; BW, bodyweight; ER, event rate; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; ISR, injection site reaction; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PD, pharmacodynamic; PK, pharmacokinetic; PYFU, participant years of follow-up (sum of follow-up time of all participants expressed in years in the applicable period); rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SE, standard error; TEAE, treatment-emergent adverse event.

REFERENCES

1. Ulrichts P, et al. *J Clin Invest.* 2018;10):128:4372-4386. **2.** Ward ES, Ober RJ. *Trends Pharmacol Sci.* 2018;39(10):892-904. **3.** Vidarsson G, et al. *Front Immunol.* 2014;5:520. **4.** Howard JF Jr, et al. [published correction appears in *Lancet Neurol.* 2021;20(8):e5.] *Lancet Neurol.* 2021;20(7):526-536. **5.** Guptill JT, et al. *Autoimmunity.* 2022;55(8):620-631. **6.** Study ARGX-113-2001 (ADAPT-SC) Clinical Trial Protocol v2.0, 02 Jul 2021. **7.** Locke KW, et al. *Drug Deliv.* 2019;26(1):98-106. **8.** Casey J, et al. Poster presented at: American Academy of Neurology (AAN) Annual Meeting; April 22-27, 2023; Boston, MA.

ACKNOWLEDGMENTS AND DISCLOSURES: The authors gratefully acknowledge the ADAPT-SC and ADAPT-SC+ trial participants and investigators.

JG, LL, SS, BVH, JP, and **EB:** argenx. **YL:** argenx, UCB, Alexion, Catalyst, and Immunovant. **TV:** Alexion, argenx, CSL Behring, Alexion/AstraZeneca, Dianthus, ImmunAbs, UCB, Amgen, Immunovant, Regeneron, Johnson & Johnson, and Cartesians. **JN** and **TVB:** Curare Consulting. **KU:** UCB, Janssen, Horizon (Viela Bio), Chugai, Hanall BioPharma, Merck, Mitsubishi Tanabe, argenx, Alexion, and the Japan Blood Products Organization. **JLDB:** argenx, Alexion, CSL, UCB Pharma, Alnylam Pharmaceuticals Inc, Janssen, and Sanofi Genzyme. **JFH:** Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, UCB, AcademicCME, Biologix, CheckRare CME, F. Hoffmann-LaRoche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMB Serono, NMD, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron, Sanofi, Zai Labs, and Tolerantia AB.

The ADAPT trial was funded by argenx. Medical writing and editorial support for this presentation was provided by PRECISION AQ and funded by argenx.

Presented at Myasthenia Gravis Foundation of America (MGFA) Scientific Session at the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) Annual Meeting; October 15-18, 2024; Savannah, Georgia