010

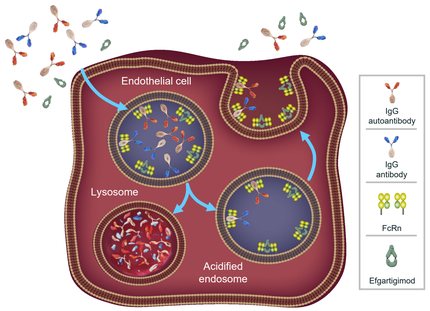
Fixed Cycle and Every-Other-Week Dosing of Intravenous Efgartigimod for Generalized Myasthenia Gravis: Part A of ADAPT NXT

Vera Bril,[1,2] Yessar Hussain,[3] Kelly Gwathmey,[4] Gregory Sahagian,[5] Ali A. Habib,[6] Kristl G. Claeys,[7] Elena Cortés-Vicente,[8] Edward Brauer,[9] Deborah Gelinas,[9] Anne Sumbul,[9] Rosa H. Jimenez,[9] Daniela Hristova,[9] Renato Mantegazza[10]

[1]Ellen & Martin Prosserman Centre for Neuromuscular Diseases, University Health Network, Toronto, Ontario, Canada; [2]University of Toronto, Toronto, Ontario, Canada; [3]Austin Neuromuscular Center, Austin, Texas, USA; [4]Department of Neurology, Virginia Commonwealth University, Richmond, Virginia, USA; [5]The Neurology Center of Southern California, Carlsbad, California, USA; [6]Department of Neurology, University of California, Irvine, Irvine, California, USA; [7]Department of Neurology, University Hospitals Leuven, Leuven, Belgium; [8]Neuromuscular Diseases Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [9]argenx, Ghent, Belgium; [10]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn

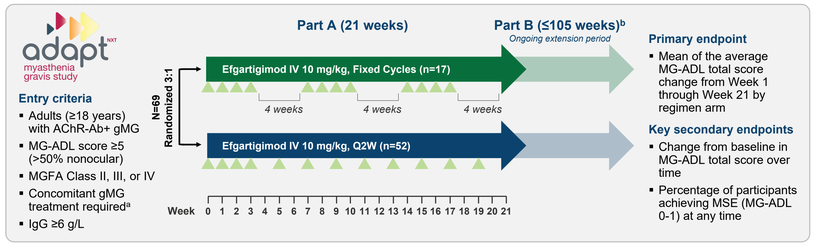


- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as albumin recycling, as well as IgG-dependent phagocytosis and antigen presentation[2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[3,4]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, reducing IgG levels without impacting IgG production[3-6]
  - Targeted reduction of all IgG subtypes[3,5]
  - No impact on levels of IgM, IgA, IgE, or IgD[3,6]
  - No reduction in albumin or increase in cholesterol levels[5-7]

METHODS

ADAPT NXT is a phase 3B, randomized, open-label, parallel-group study designed to evaluate 2 dosing regimens of efgartigimod IV to maximize and maintain clinical benefit in participants with gMG

- Both study arms initially receive 1 cycle of 4 once-weekly infusions. Subsequently, the Fixed Cycles arm receives 3 cycles of 4 once-weekly infusions (with 4 weeks between cycles), and the Q2W arm receives infusions once every other week



Note: Green triangles indicate efgartigimod infusion.
[a]Including NSISTs, corticosteroids, and/or AChEIs. If receiving corticosteroids and/or NSISTs, must be on a stable dose for ≥1 month prior to screening. [b]All participants entering Part B will be transitioned to Q2W with the option to extend to Q3W dosing.

SUMMARY

- **Both Fixed Cycles and Q2W dosing resulted in clinically meaningful improvements in MG-ADL scores maintained through 21 weeks**
- **Clinical improvements were observed as early as Week 1 in both groups**
- **MSE was achieved in 47.1% and 44.2% of patients receiving Fixed Cycles and Q2W dosing, respectively**
- **Efgartigimod was well tolerated across both dosing regimens**
- **ADAPT-NXT provides data on further options to individualize efgartigimod treatment (Fixed Cycles or Q2W) for the treatment of gMG**

RESULTS

Table 1. ADAPT NXT Baseline Demographics and Clinical Characteristics
Safety Analysis Set

	Efgartigimod IV Fixed Cycles (n=17)	Efgartigimod IV Q2W (n=52)
Age, years, mean (SD)	52.4 (16.1)	57.1 (16.5)
Age ≥65 years, n (%)	5 (29.4)	20 (38.5)
Sex, female, n (%)	9 (52.9)	34 (65.4)
Time since diagnosis, y, mean (SD)	7.4 (6.6)	6.9 (7.3)
MGFA classification at screening, n (%)		
Class II	6 (35.3)	17 (32.7)
Class III	11 (64.7)	33 (63.5)
Class IV	0	2 (3.8)
Total MG-ADL score, mean (SD)	8.1 (2.2)	9.8 (3.3)
Total MG-ADL categorization, n (%)		
5-12	17 (100.0)	39 (75.0)
>12	0	13 (25.0)
Baseline MG therapy, n (%)		
Any steroid	10 (58.8)	30 (57.7)
Any NSIST	8 (47.1)	19 (36.5)
Any AChEI	12 (70.6)	49 (94.2)
AChEI only	0 (0)	17 (32.7)

ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor autoantibody; AChR-Ab+, acetylcholine receptor autoantibody positive; ANCOVA, analysis of covariance; CMI, clinically meaningful improvement; ER, event rate; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IV, intravenous; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; mITT, modified intent-to-treat; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy; PYFU, participant years of follow-up; Q2W, every other week; TEAE, treatment-emergent adverse event.

Table 2. ANCOVA[a] Analysis of Primary Endpoint: Mean of the Average MG-ADL Total Score Change From Baseline During Week 1-21

	Efgartigimod IV Fixed Cycles		Efgartigimod IV Q2W		Efgartigimod IV Fixed Cycles vs Q2W
	n	LS mean (95% CI)	n	LS mean (95% CI)	LS estimate (95% CI)
mITT analysis set	17	-5.13 (-6.499; -3.767)	52	-4.61 (-5.383; -3.845)	-0.52 (-2.104; 1.067)

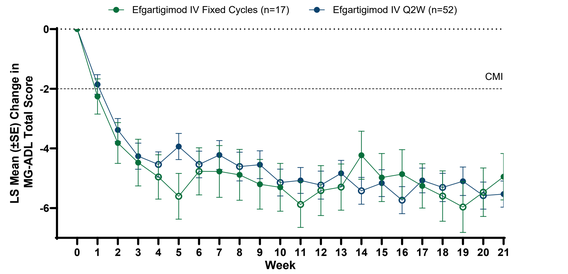
[a]The ANCOVA model includes the treatment arm as a factor and the baseline MG-ADL total score as covariates.

Table 3. Summary of TEAEs
Safety Analysis Set

	Efgartigimod IV Fixed Cycles (n=17, PYFU=6.9)			Efgartigimod IV Q2W (n=52, PYFU=20.9)			Efgartigimod IV Total population (n=69, PYFU=27.8)		
	n	%	ER[b]	n	%	ER[b]	n	%	ER[b]
TEAE	16	94.1	12.0	43	82.7	10.1	59	85.5	10.6
Serious TEAE	1	5.9	0.4	7	13.5	0.3	8	11.6	0.4
Grade ≥3 TEAE	3	17.6	1.3	7	13.5	0.4	10	14.5	0.6
Fatal TEAE	0			0			0		
Discontinued due to TEAEs	0			1	1.9	<0.1	1	1.4	<0.1
Most frequent TEAEs[a]									
COVID-19	2	11.8	0.3	11	21.2	0.5	13	18.8	0.5
Headache	5	29.4	1.2	8	15.4	0.6	13	18.8	0.8
Upper respiratory tract infection	2	11.8	0.4	5	9.6	0.4	7	10.1	0.4

[a]Reported by ≥10% of total participants. [b]ER was calculated as number of events/PYFU.

Figure 1. LS Mean Changes From Baseline in MG-ADL Total Score (Week 1-21)[a,b]



[a]Solid data points indicate weeks in which efgartigimod was administered and open data points indicate weeks in which efgartigimod was not administered in each respective dosing regimen. [b]Mixed model for repeated measurements with treatment, visit and treatment by visit interaction as fixed effects, and baseline total MG-ADL score as covariate.

Figure 2. Percentage of Participants Achieving MSE (MG-ADL 0-1; Week 1-21)

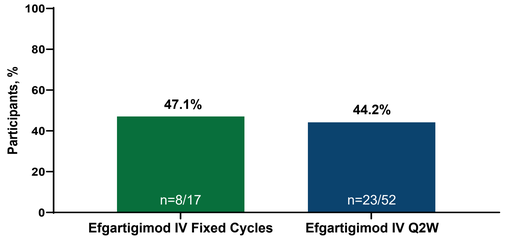
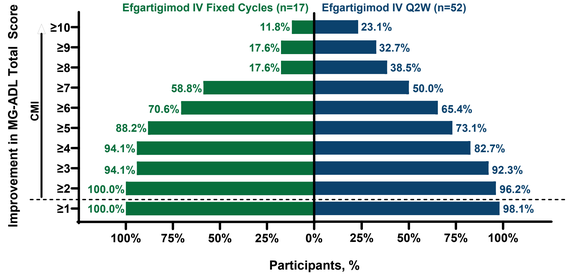


Figure 3. Proportion of Participants With Increasing MG-ADL Thresholds (Week 1-21)



Total IgG and AChR-Ab Level Changes From Baseline

- The mean (SE) percent reduction in total IgG observed at Week 4 was -64.8% (1.9) for the Fixed Cycles arm and -67.6% (1.1) for the Q2W arm
  - The mean percent changes from baseline in total IgG levels ranged between -58.0% and -67.6% for the Q2W arm across the 21 weeks
- Mean (SE) percent changes from baseline in AChR-Ab levels observed at Week 4 were -52.7% (4.1) and -58.8% (1.8) for the Fixed Cycles and Q2W arms, respectively
  - The mean percent changes from baseline in total AChR-Ab levels ranged between -45.0% and -58.8% for the Q2W arm across the 21 weeks

REFERENCES
1. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533-2550. **2.** Pyzik M, et al. *Nat Rev Immunol.* 2023;23(7):415-432. **3.** Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386. **4.** Vaccaro C, et al. *Nat Biotechnol.* 2005;23(10):1283-1288. **5.** Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536. **6.** Nixon AE, et al. *Front Immunol.* 2015;6:176. **7.** Ward ES, et al. *Front Immunol.* 2022;13:892534. **8.** Howard JF Jr, et al. *Front Neurol.* 2024;14:1284444.

ACKNOWLEDGMENTS AND DISCLOSURES: **The authors gratefully acknowledge the ADAPT NXT trial participants and investigators.**
VB: AZ-Alexion, Grifols, CSL, UCB, argenx, Takeda, Octapharma, Akcea, Momenta (J&J), Immunovant, Ionis, and Viela. **YH:** no disclosures. **KG:** Alexion, argenx, Strongbridge, and UCB. **GS:** Alexion, argenx, UCB, Immunovant, and Biogen. **AAH:** argenx, Alexion, VielaBio, UCB, Genentech, Regeneron, and Sanofi. **KGC:** Alnylam, Amicus, argenx, Biogen, CSL Behring, Ipsen, Janssen, Lupin, Pfizer, Roche, Sanofi-Genzyme, and UCB. **EC-V:** argenx, UCB, Alexion, and Janssen. **EB, DG, AS, RHJ,** and **DH:** argenx. **RM:** Alexion, argenx, Ra, BioMarin, Catalyst, UCB, Teva, Merck, Roche, and Biogen.
The ADAPT NXT trial was funded by argenx. Medical writing and editorial support for this presentation was provided by PRECISION Value & Health and funded by argenx.

Presented at the American Academy of Neurology (AAN) Annual Meeting; April 13-18, 2024; Denver, Colorado