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

EPO-612

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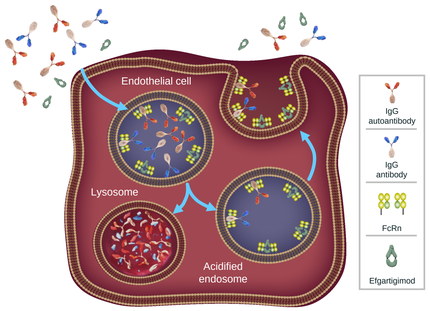
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn

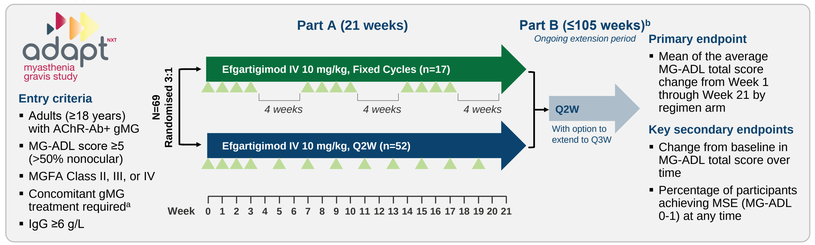


- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as albumin recycling, as well as IgG-dependent phagocytosis and antigen presentation[2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand 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[5-8]

METHODS

ADAPT NXT is a phase 3B, randomised, open-label, parallel-group study designed to evaluate 2 dosing regimens of efgartigimod IV to maximise 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 NSIST's, 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; patients in Fixed Cycle arm will receive another cycle before transitioning to Q2W dosing.

CONCLUSION

- Both Fixed Cycles and Q2W dosing resulted in similar clinically meaningful improvements in MG-ADL scores that were 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 individualise efgartigimod treatment 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 categorisation, n (%)		
5-12	17 (100.0)	39 (75.0)
>12	0	13 (25.0)
Total MG-Qol15r score, mean (SD)	14.3 (5.6)	17.7 (6.1)
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)

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)

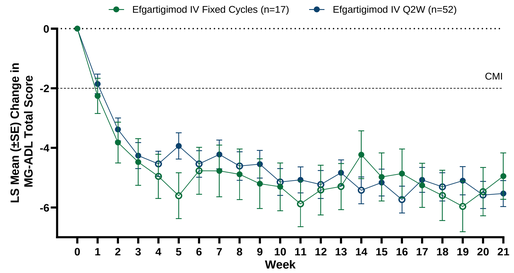
[a]The ANCOVA model includes the treatment arm as a factor and the baseline MG-ADL total score as a covariate.

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

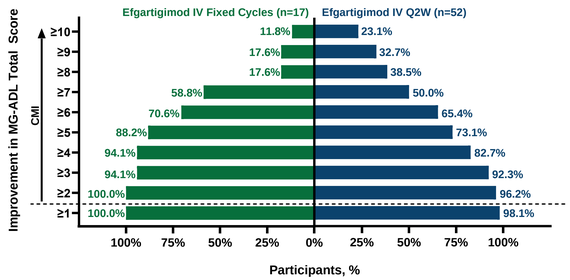


Figure 3. Percentage of Participants Achieving MSE (MG-ADL 0-1; Week 1-21)

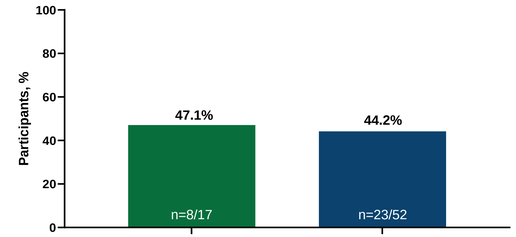


Table 4. Percentage of Participants Achieving MSE (MG-ADL 0-1) by Study Interval[a]

	Efgartigimod IV Fixed Cycles		Efgartigimod IV Q2W	
Interval	n	MSE, n (%)	n	MSE, n (%)
Week 1 – Week 7	17	8 (47.1)	52	14 (26.9)
Week 8 – Week 14	16	7 (43.8)	52	18 (34.6)
Week 15 – Week 21	16	5 (31.3)	49	19 (38.8)
Week 8 – Week 21	16	7 (43.8)	52	22 (42.3)
Week 1 – Week 21	17	8 (47.1)	52	23 (44.2)

[a]A participant is reported as achieving MSE if an MG-ADL score of 0 or 1 was observed at least once during the interval.

ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor autoantibody; AChR-Ab+, acetylcholine receptor autoantibody positive; ANCOVA, analysis of covariance; BL, baseline; CMI, clinically meaningful improvement; ER, event rate; Fc, fragment crystallisable region; FcRn, neonatal Fc receptor; gMG, generalised 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; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; 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.

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