958

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

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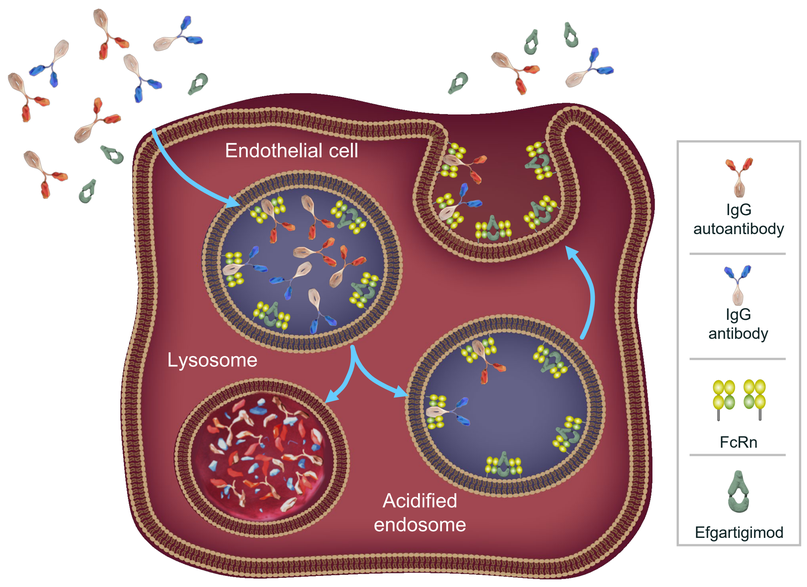
INTRODUCTION

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]
- Blocking FcRn to selectively reduce IgG levels is therefore a rational therapeutic approach in patients with IgG-mediated autoimmune diseases[1,2]
- 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 prevents IgG recycling by blocking IgG antibodies from binding to FcRn, with unbound IgG antibodies being degraded[1,4]

SUMMARY

- **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 individualize efgartigimod treatment for the treatment of gMG**

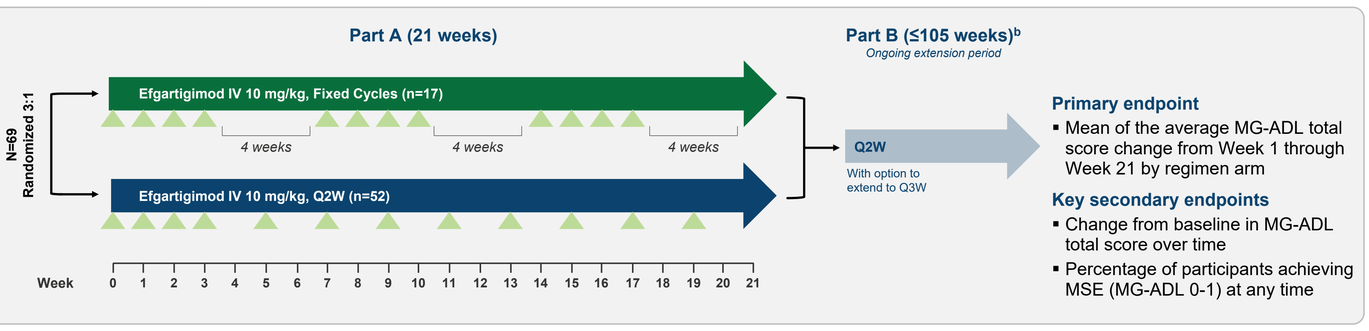
METHODS

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

adapt NXT myasthenia gravis study

Entry criteria
- Adults (≥18 years) with AChR-Ab+ gMG
- MG-ADL score ≥5 (>50% nonocular)
- MGFA Class II, III, or IV
- Concomitant gMG treatment permitted[a]
- IgG ≥6 g/L



Primary endpoint
- Mean of the average MG-ADL total score change from Week 1 through Week 21 by regimen arm

Key secondary endpoints
- Change from baseline in MG-ADL total score over time
- Percentage of participants achieving MSE (MG-ADL 0-1) at any time

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; patients in Fixed Cycle arm will receive another cycle before transitioning to Q2W dosing.

RESULTS

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

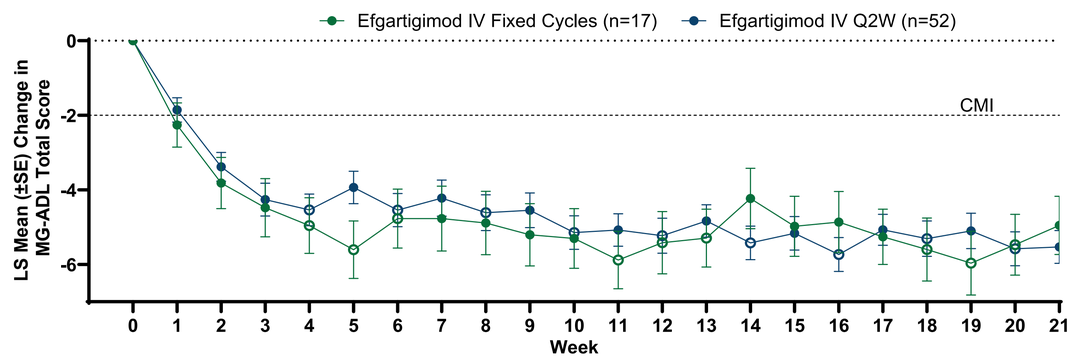
	Efgartigimod IV Fixed Cycles (n=17)	Efgartigimod IV Q2W (n=52)
Age, years, mean (SD)	52.4 (16.1)	57.1 (16.5)
Age ≥65 years, n (%)	5 (29.4)	20 (38.5)
Sex, female, n (%)	9 (52.9)	34 (65.4)
Time since diagnosis, y, mean (SD)	7.4 (6.6)	6.9 (7.3)
MGFA classification at screening, n (%)		
Class II	6 (35.3)	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)
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 Weeks 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.

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.

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

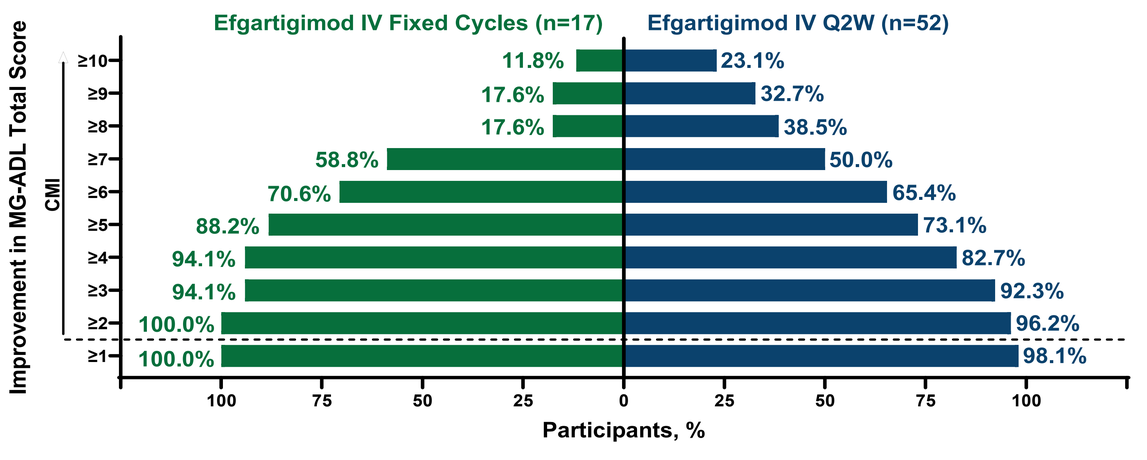


Figure 3. Percentage of Participants Achieving MSE (MG-ADL 0-1; Week 1-21)

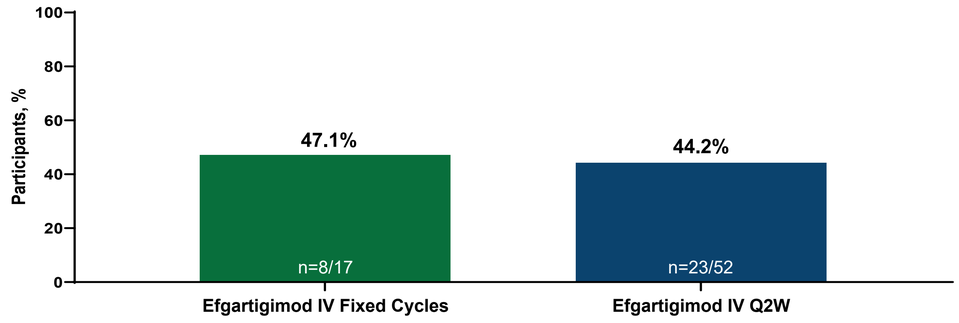


Table 4. Percentage of Participants Achieving MSE (MG-ADL 0-1) by Study Interval[a]

	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 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; 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; Q3W, every third week; TEAE, treatment-emergent adverse event.

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