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

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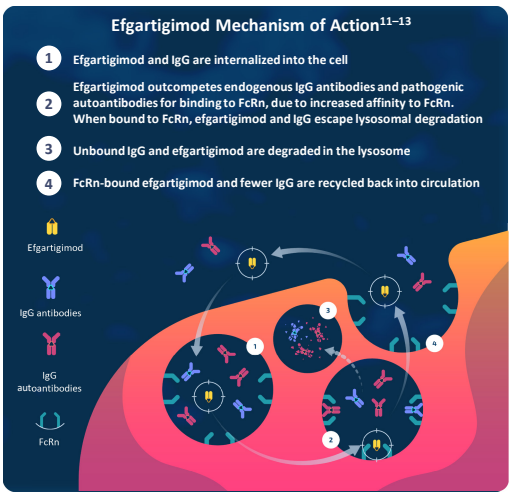
BACKGROUND | METHODS

- gMG is a rare, antibody-mediated, neuromuscular disorder leading to a failure of neuromuscular junction transmission, characterized by fluctuating weakness in ocular, facial, bulbar, axial, and limb muscles.[1–3] The majority of patients (~85%) have autoantibodies against the AChR[3]

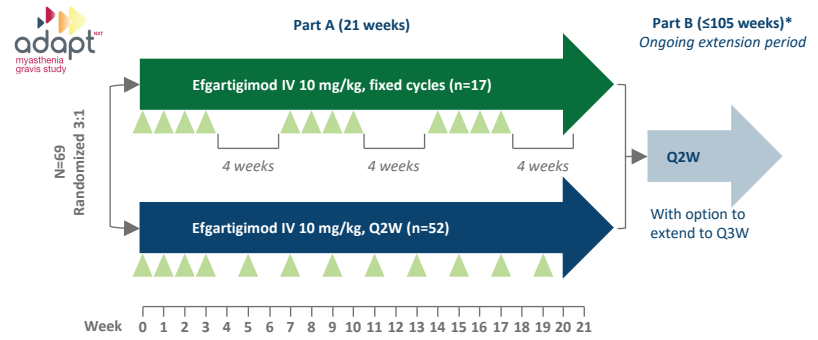
Efgartigimod

- FcRn recycles IgG, extending its half-life and maintaining serum concentrations of both IgG and pathogenic IgG autoantibodies[4]
- Efgartigimod is a human IgG1 Fc fragment engineered to bind to the FcRn receptor on endothelial cells, leading to increased degradation of IgG (including pathological IgG) in the lysosome[5]
- Efgartigimod was approved for the treatment of anti-AChR antibody-positive gMG in 2021[5,6] and is typically dosed with 4 once-weekly infusions, with subsequent cycles administered according to individualized response[7]
- Individualized cyclic administration of efgartigimod IV (10 mg/kg) demonstrated safety and efficacy in randomized, double-blinded, placebo-controlled trials in patients with gMG[5,8]
- Efgartigimod is approved to treat AChR+ gMG patients in the United States, as an add-on to standard therapy to treat adult patients with AChR+ gMG in Europe, and in patients with or without AChR antibodies with insufficient response to steroids or NSISTs in Japan[7,9,10]



- ADAPT NXT is a phase 3b, randomized, open-label, parallel-group study designed to evaluate two dosing regimens of efgartigimod IV and to maximize/maintain clinical benefit in participants with gMG (**Figure 1**)

FIGURE 1 ADAPT-NXT Study Design (NCT4980495)



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

Inclusion criteria
- Adults (≥18 years) with AChR-Ab+ gMG
- MG-ADL score ≥5 (>50% nonocular symptoms)
- MGFA class II, III, or IV
- Concomitant gMG treatment required†

Exclusion criteria
- IgG <6 g/L
- Use of IVIg/SCIg, eculizumab, any other IMP, monoclonal antibody, or rituximab within, respectively, 14 days, 1 month, 3 months or 5 half-lives, 5 half-lives, or 6 months of screening
- History of malignancy
- Received a thymectomy <3 months before screening
- Active infection

*All participants entering Part B will be transitioned to Q2W with the option to extend to Q3W dosing; patients in the fixed cycles arm will receive another cycle before transitioning to Q2W dosing. Green triangles indicate efgartigimod infusion. †Including NSISTs, corticosteroids, and/or AChEis. If receiving corticosteroids and/or NSISTs, must be on a stable dose for ≥1 month prior to screening.

OBJECTIVE | RESULTS

Objective

To evaluate the efficacy, safety, and tolerability of efgartigimod IV (10 mg/kg) in a fixed cycle (4 infusions once weekly with a 4-week break between cycles) or continuous dosing schedule (Q2W)

Clinical Efficacy Was Observed Consistently Across Both Dosing Regimens of Efgartigimod IV

- Baseline demographics and characteristics were similar between treatment arms (**Table 1**)
- Clinical efficacy of efgartigimod in the change in MG-ADL Total Score was similar between treatment arms (**Table 2**)

Clinical Efficacy Was Observed Consistently Across Both Dosing Regimens of Efgartigimod IV

- Both fixed cycles and Q2W dosing resulted in similar CMI in MG -ADL scores that were observed as early as Week 1 and maintained through Week 21 (**Figures 2 and 3**)
- Achievement of MSE was consistent across dosing regimens (**Figure 4 and Table 3**)
- Efgartigimod IV was well tolerated; an increased incidence of TEAEs was not observed with the continuous dosing (**Table 4**)

TABLE 1 Baseline Demographics and Characteristics

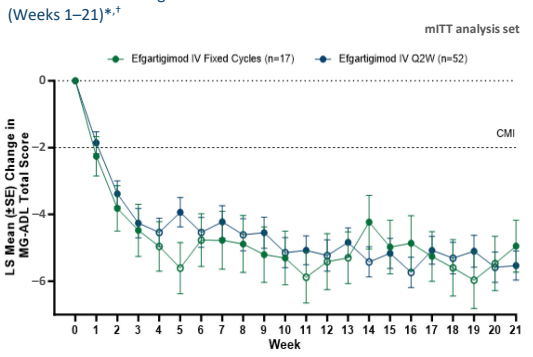
Safety analysis set	Efgartigimod IV Fixed Cycles (n=17)	Efgartigimod IV Q2W (n=52)
Age, years, mean (SD)	52.4 (16.1)	57.1 (16.5)
Age ≥65 years, n (%)	5 (29.4)	20 (38.5)
Sex, female, n (%)	9 (52.9)	34 (65.4)
Time since diagnosis, years, mean (SD)	7.4 (6.6)	6.9 (7.3)
MGFA classification at screening, n (%)		
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 score categorization, n (%)		
5–12	17 (100)	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 Primary Endpoint: Mean of the Average MG-ADL Total Score Change From Baseline (Weeks 1–21)*

mITT analysis set	Efgartigimod IV Fixed Cycles n	Efgartigimod IV Fixed Cycles LS mean (95% CI)	Efgartigimod IV Q2W n	Efgartigimod IV Q2W LS mean (95% CI)	Efgartigimod IV Fixed Cycles vs Q2W LS estimate (95% CI)
Average change from baseline in MG-ADL total score*	17	−5.13 (−6.499, −3.767)	52	−4.61 (−5.383, −3.845)	−0.52 (−2.104, 1.067)

*ANCOVA, including treatment arm as a factor and baseline MG-ADL total score as a covariate, was performed.

FIGURE 2 Mean Changes From Baseline in MG-ADL Total Score (Weeks 1–21)*,†



*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. †A mixed model for repeated measures, with treatment, visit, and treatment by visit interaction as fixed effects, and baseline total MG-ADL score as covariate, was performed.

FIGURE 3 Proportion of Participants With Increasing MG-ADL Thresholds (Weeks 1–21)

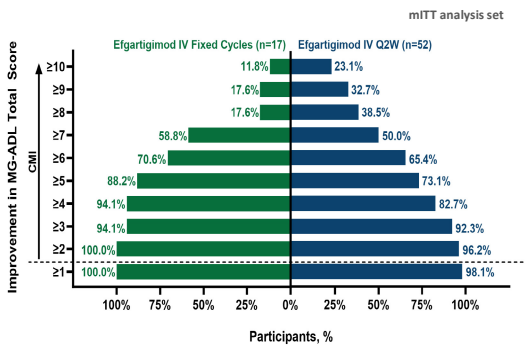


FIGURE 4 Percentage of Participants Achieving MSE (MG-ADL 0–1; Weeks 1–21)

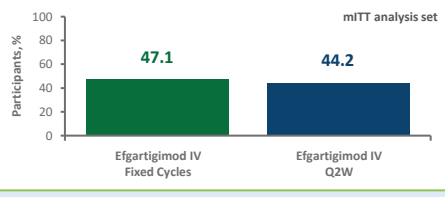


TABLE 3 Percentage of Participants Achieving MSE* (MG-ADL 0–1) by Study Interval

mITT analysis set	Efgartigimod IV Fixed Cycles n	Efgartigimod IV Fixed Cycles MSE, n (%)	Efgartigimod IV Q2W n	Efgartigimod IV Q2W MSE, n (%)
Interval	17	8 (47.1)	52	14 (26.9)
Baseline – 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 participant was reported as achieving MSE if an MG-ADL score of 0 or 1 was observed at least once during the interval.

TABLE 4 Summary of Safety

Safety analysis set	Efgartigimod IV Fixed Cycles (n=17) [PYFU=6.9] n	%	ER†	Efgartigimod IV Q2W (n=52) [PYFU=20.9] n	%	ER†	Total Efgartigimod IV Population (N=69) [PYFU=27.8] n	%	ER†
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 AE	0	-	-	1	1.9	<0.1	1	1.4	<0.1
Most frequent TEAEs									
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 infection	2	11.8	0.4	5	9.6	0.4	7	10.1	0.4

*TEAEs were reported by ≥10% of total participants. †ER was calculated as number of events/PYFU.

KEY TAKEAWAYS

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

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ABBREVIATIONS

AChEI, acetylcholinesterase inhibitor; **AChR,** acetylcholine receptor; **AChR-Ab+,** acetylcholine receptor antibody-positive; **AE,** adverse event; **ANCOVA,** analysis of covariance; **CI,** confidence interval; CMI, clinically meaningful improvement; **ER,** event rate; **FcRn,** neonatal Fc receptor; **gMG,** generalized myasthenia gravis; **Ig,** immunoglobulin; **IMP,** investigational medicinal product; **IV,** intravenous; **IVIg,** intravenous immunoglobulin; **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 intention-to-treat; **MSE,** minimal symptom expression; **NSIST,** nonsteroidal immunosuppressive therapy; **PYFU,** participant-years of follow-up; **Q2W,** every 2 weeks; **Q3W,** every 3 weeks; **SCIg,** subcutaneous immunoglobulin; **SD,** standard deviation; **SE,** standard error; **TEAE,** treatment-emergent adverse event.

DISCLOSURES AND ACKNOWLEDGMENTS

AAH: Alexion, Amgen, argenx, Genentech, Regeneron, Sanofi, UCB; **MG:** Sanofi, Dianthus, Kedrion; **KGC:** Amicus, Alnylam, argenx, Biogen, CSL Behring, Ipsen, Janssen, Lupin, Pfizer, Roche, Sanofi-Genzyme, UCB, Vertex; **KGG:** Alexion, Amgen, argenx, UCB, Xeris; **VB:** Bionevia, CSL Behring, Grifols, Octapharma, Shire, UCB; **YH:** No disclosures to report; **GS:** Alexion, argenx, Biogen, Immunovant, UCB; **EC-V:** Alexion, argenx, Janssen, UCB; **EB, JG, DG, LL, RHJ, MP, DM:** Employees: argenx; **RM:** Alexion, argenx, Biogen, BioMarin, Catalyst, Merck, Roche, Teva, UCB; **AM:** Alexion, argenx, Axunio, Grifols, Hormosan, Janssen, Merck, Novartis, Octapharma, UCB; **AS:** argenx, Takeda, UCB; **SA:** Alexion, argenx, Biogen, Janssen, LFB, Pfizer, Sanofi, UCB.

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