74

Sustained Clinical Efficacy and Long-Term Safety of Intravenous Efgartigimod for Generalized Myasthenia Gravis: Part B of ADAPT NXT

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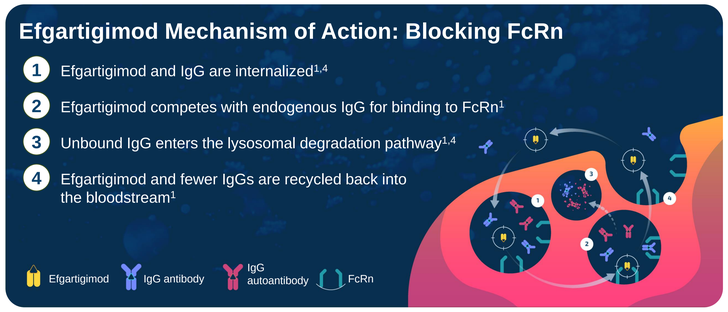
INTRODUCTION

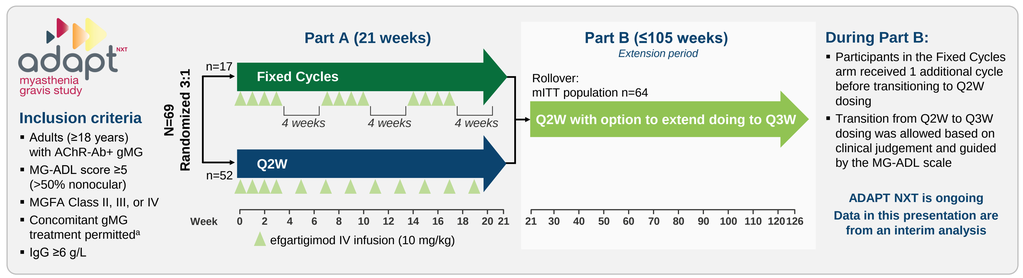
- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared to endogenous IgG, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[1]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production or other parts of the immune system, and does not decrease albumin[1-3]



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

- In Part A, both study arms initially received 1 cycle of 4 once-weekly infusions. Subsequently, the Fixed Cycles arm received 2 additional cycles of 4 once-weekly infusions (with 4 weeks between cycles), and the Q2W arm received infusions once every other week
- In Part B, participants transitioned to or continued Q2W infusions, with the option to extend dosing to every third week (Q3W)



Inclusion 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

During Part B:

- Participants in the Fixed Cycles arm received 1 additional cycle before transitioning to Q2W dosing
- Transition from Q2W to Q3W dosing was allowed based on clinical judgement and guided by the MG-ADL scale

ADAPT NXT is ongoing

Data in this presentation are from an interim analysis

[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.

SUMMARY

- **Clinical improvements were observed as early as Week 1 in both groups and were sustained through 126 weeks**
- **During Part B, the majority of participants had sustained improvements in MG-ADL total score, with 64.1% achieving improvements of ≥3 points at ≥75% of their analysis visits**
- **56.5% of participants achieved MSE during ADAPT NXT, including 51.6% who achieved MSE during Part B**
- **Efgartigimod was well tolerated across dosing regimens and throughout the duration of the study period**
- **ADAPT NXT provides data on further options to individualize efgartigimod dosing for the treatment of gMG**

RESULTS

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

	Efgartigimod IV (N=69)
Age, years, mean (SD)	55.9 (16.4)
Age ≥65 years, n (%)	25 (36.2)
Sex, female, n (%)	43 (62.3)
Time since diagnosis, y, mean (SD)	7.0 (7.1)
MGFA classification at screening, n (%)	
Class II	23 (33.3)
Class III	44 (63.8)
Class IV	2 (2.9)
Total MG-ADL score, mean (SD)	9.4 (3.2)
Total MG-ADL categorization, n (%)	
5-12	56 (81.2)
>12	13 (18.8)
Total MG-QoL15r score, mean (SD)	16.9 (6.1)
Baseline MG therapy, n (%)	
Any steroid	40 (58.0)
Any NSIST	27 (39.1)
Any AChEI	61 (88.4)
AChEI only	17 (24.6)

Table 2. Summary of TEAEs[a]
Safety Analysis Set

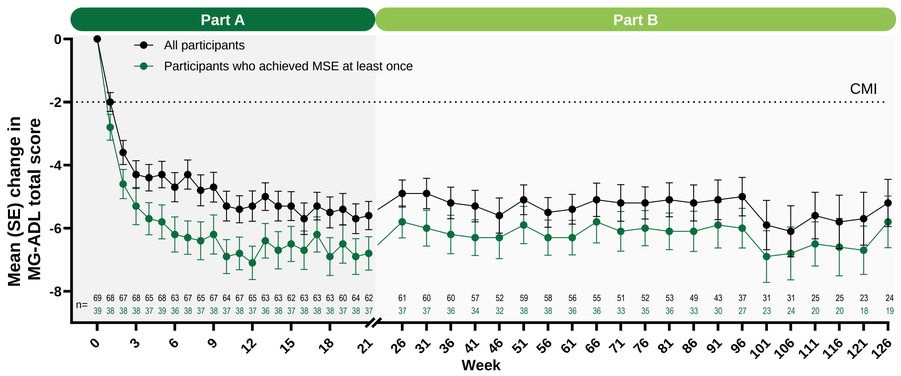
	Efgartigimod IV (N=69, PYFU 134.7)	
	n (%)	ER[b]
TEAE	67 (97.1)	6.0
Serious TEAE	27 (39.1)	0.4
Grade ≥3 TEAE	28 (40.6)	0.5
Fatal TEAE[c]	1 (1.4)	0.01
Discontinued due to TEAEs	5 (7.2)	0.04
Most frequent TEAEs[d]		
COVID-19[e]	28 (40.6)	0.2
Headache	15 (21.7)	0.3
Upper respiratory tract infection	14 (20.3)	0.2
Bronchitis	14 (20.3)	0.2
Myasthenia gravis	14 (20.3)	0.1
Arthralgia	13 (18.8)	0.1
Nasopharyngitis	12 (17.4)	0.1
Back pain	11 (15.9)	0.1
Influenza	11 (15.9)	0.1
Diarrhea	10 (14.5)	0.1
Nausea	9 (13.0)	0.2
Cough	9 (13.0)	0.1
Pyrexia	9 (13.0)	0.1
Urinary tract infection	8 (11.6)	0.1
Fatigue	7 (10.1)	0.1
Myalgia	7 (10.1)	0.1
Dyspnea	7 (10.1)	0.1

[a]TEAE data from Part A and Part B combined. [b]ER was calculated as number of events/PYFU. [c]The fatal TEAE was unexpected but considered unrelated to efgartigimod treatment. [d]Reported by ≥10% of total participants. [e]High frequency of COVID-19 TEAEs are attributable to the study occurring during the COVID-19 pandemic.

Figure 1. Mean Change in MG-ADL Total Score From Baseline (Week 1-126)

Part A Results

- Participants in the Fixed Cycles and Q2W dosing arms demonstrated rapid, clinically meaningful average improvements from baseline in MG-ADL total scores, with **no statistically significant difference detected between dosing arms**[a]
- LS mean of average change from baseline in MG-ADL score during weeks 1-21 (95% CI):
  - Fixed Cycles: -5.13 (-6.50; -3.77)
  - Q2W: -4.61 (-5.38; -3.85)
  - LS mean difference: -0.52 (-2.10; 1.07)

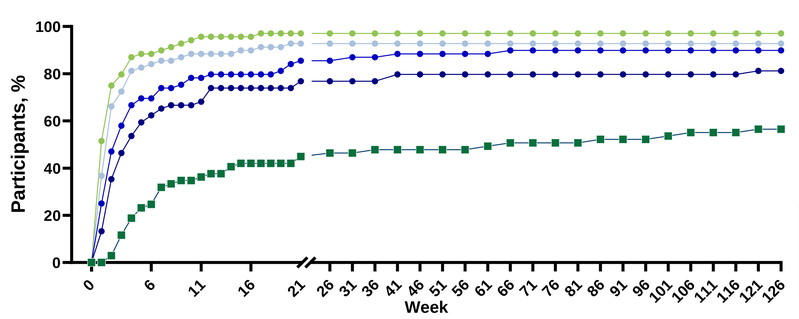


During Part B:

- Participants who maintained clinical improvement had the option to transition from Q2W to Q3W dosing, based on clinical judgement and guided by the MG-ADL scale
  - 57.8% (37/64) transitioned to Q3W dosing, 59.5% (22/37) of these participants remained on Q3W dosing
  - Average treatment duration on Q3W was 382 days (at week 126)
- 57.8% (37/64) of participants were taking steroids[b] at baseline
  - 32.4% (12/37) decreased steroid dose (including 52.9% [9/17] of those with baseline dose >20 mg/d[c])
  - 13.5% (5/37) increased steroid dose (all had final dose ≤20 mg/d[c])
- 11.1% (3/27) not taking steroids at baseline initiated steroids

[a]The ANCOVA model used for statistical analysis included treatment arm as a factor and baseline MG-ADL total score as a covariate to account for any differences in baseline MG-ADL scores. [b]Restricted to oral steroids indicated for treatment of MG. [c]Dosing of different steroids was standardized to prednisone equivalent mg doses for analysis.

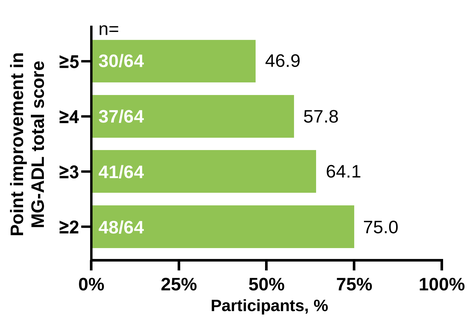
Figure 2. Cumulative Percentage of Participants Achieving MSE (MG-ADL 0-1) or CMI at Any Time in ADAPT NXT[a]



- 56.5% (39/69) of participants achieved MSE at any point during the study
- 51.6% (32/62)[b] achieved MSE during Part B

[a]The denominator is the number of participants in the mITT analysis population during Part A (n=69). [b]2 participants were excluded because they received IVIg during Part A.

Figure 3. Percentage of Participants Achieving Sustained CMI (≥75% of Visits) in MG-ADL Scores During Part B



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; IgG, immunoglobulin G; 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 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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