Poster #194

Effect of Obesity on Efficacy and Safety in the AChR-Ab+ Patient Population of the ADAPT Trial of Efgartigimod for Generalized Myasthenia Gravis

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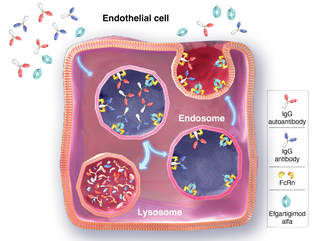
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG, extending its half-life and maintaining its serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting lysosomal degradation of IgG[2-5]
  - Targeted reduction of all IgG subclasses
  - No impact on immunoglobulins M or A
  - No change in albumin or cholesterol
  - No impact on IgG production or ability to mount an immune response

Although efgartigimod has been shown to effectively reduce IgG antibodies in clinical studies in adults,[2,5] limited data exist to assess the impact of weight and BMI[6-8]

- In the phase 3 trial (ADAPT, NCT03669588; 129 AChR-Ab+ patients) IV infusion of efgartigimod demonstrated efficacy compared with placebo and was generally well tolerated[2]:
  - MG-ADL responders in cycle 1: 68% efgartigimod vs 30% placebo (*P*<.0001)
  - QMG responders in cycle 1: 63% efgartigimod vs 14% placebo (*P*<.0001)
- Weight gain is a frequent comorbidity in patients with gMG and is worsened by corticosteroid use.[6-8] Higher BMI is generally associated with increased disease activity[6]

METHODS

ADAPT was a 26-week, global, multicenter, randomized, double-blind, placebo-controlled, phase 3 trial evaluating the safety and efficacy of efgartigimod in patients with gMG[3]

- Post hoc analysis of the ADAPT trial examined the effect of weight and BMI on safety and efficacy

adapt myasthenia gravis study

ADAPT:
Patients randomized 1:1 to receive cycles of 4 infusions at weekly intervals of 10 mg/kg[d] IV efgartigimod or placebo[4]

Inclusion criteria
- MGFA class II, III, IV
- AChR-Ab seropositive or seronegative
- MG-ADL score ≥5 (>50% nonocular)
- On ≥1 stable gMG treatment[a]
- IgG ≥6 g/L

Efgartigimod n=84
1:1
Placebo n=83
26 weeks (≤3 cycles[b])

Initiation of new treatment cycle:
- ≥5 weeks between cycles
- MG-ADL score ≥5[c]
- MG-ADL score within 2 points of baseline

Efficacy
- MG-ADL and QMG response, defined by a ≥2- and ≥3-point improvement respectively, sustained for 4 consecutive weeks and occurring by week 4 of the cycle

Safety
- Incidence and severity of AEs

Note: Beige lines within arrows indicate day of efgartigimod infusion.
[a]Acetylcholinesterase inhibitor, steroid +/or NSIST. Patients could not change concomitant therapies in ADAPT or during dosing in Part A of ADAPT+. Patients could change concomitant therapies between doses in Part A and at any time in Part B of ADAPT+. [b]A cycle had a minimum duration of 8 weeks. [c]With >50% from nonocular items. [d]Max dose capped at 1200 mg (120 kg).

SUMMARY

- **In the ADAPT trial, efgartigimod was effective for the treatment of anti-AChR-Ab+ gMG regardless of weight or BMI despite the maximum efgartigimod dose of 1200 mg**
- **Efgartigimod was well tolerated regardless of weight or BMI**
- **These data add to the existing evidence that efgartigimod is well tolerated and effective for a broad population of patients with anti AChR-Ab+ gMG, including patients with high BMI**

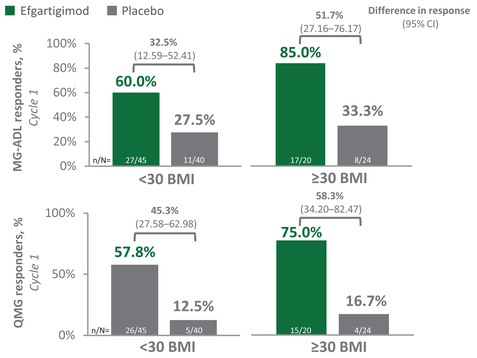
RESULTS

Table 1. Baseline Characteristics[a]
AChR-Ab+ Patients

	Efgartigimod		Placebo		All AChR-Ab+	
Characteristic[b]	<30 BMI N=45	≥30 BMI N=20	<30 BMI N=40	≥30 BMI N=24	EFG N=65	PBO N=64
Age, y	41.4 (14.3)	52.2 (14.1)	45.2 (14.5)	55.8 (15.2)	44.7 (15.0)	49.2 (15.5)
Female, n (%)	37 (82.2)	9 (45.0)	29 (72.5)	11 (45.8)	46 (70.8)	40 (62.5)
Region, n (%)						
US	5 (11.1)	10 (50.0)	3 (7.5)	5 (20.8)	15 (23.1)	8 (12.5)
Japan	6 (13.3)	0	4 (10.0)	0	6 (9.2)	4 (6.3)
Rest of world	34 (75.6)	10 (50.0)	33 (82.5)	16 (66.7)	44 (67.7)	49 (76.6)
Thymectomy, n (%)	34 (75.6)	11 (55.0)	22 (55.0)	8 (33.3)	45 (69.2)	30 (46.9)
Concomitant medications						
Steroids, n(%)	35 (77.8)	11 (55.0)	34 (85.0)	17 (70.8)	46 (70.8)	51 (79.7)
Steroid dose[c], mean (SD) mg	19.2 (11.2)	11.3 (7.7)	18.7 (12.8)	17.1 (8.9)	17.3 (10.9)	18.2 (11.6)
NSISTs, n(%)	30 (66.7)	10 (50.0)	26 (65.0)	11 (45.8)	40 (61.5)	37 (57.8)
Baseline MG-ADL, mean (SD)	8.5 (2.3)	10.2 (2.6)	8.5 (2.1)	8.7 (2.2)	9.0 (2.5)	8.6 (2.1)
Baseline QMG, mean (SD)	15.8 (5.2)	16.7 (5.0)	15.7 (4.6)	14.4 (3.9)	16.0 (5.1)	15.2 (4.4)
Baseline MG-QoL 15r, mean (SD)	14.8 (6.4)	17.9 (5.5)	16.6 (6.0)	16.6 (4.6)	15.7 (6.3)	16.6 (5.5)
Weight, kg (SD)	68.1 (13.2)	112.0 (34.5)	67.7 (11.6)	99.2 (13.1)	81.6 (29.8)	79.5 (19.5)

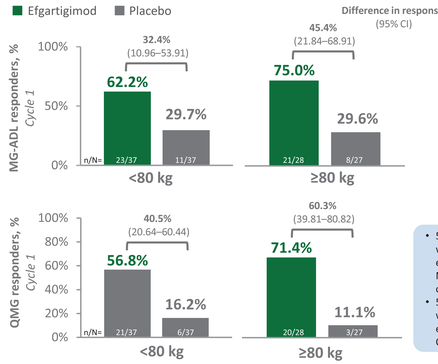
[a]The denominator for the percentage calculations is the total number of participants per treatment in the safety analysis set, excluding missing values.
[b]Characteristic reported as mean (SD) unless otherwise specified. [c]Average daily prednisone equivalent dose.

Figure 1. Proportion of MG-ADL and QMG Responders by BMI[a]
AChR-Ab+ Patients, Cycle 1



[a]MG-ADL and QMG response, defined by a ≥2- and ≥3-point improvement respectively, sustained for 4 consecutive weeks and occurring by week 4 of the cycle.

Figure 2. Proportion of MG-ADL and QMG Responders by Weight
AChR-Ab+ Patients, Cycle 1



- 5 of 6 patients who weighed ≥120 kg in the efgartigimod arm were MG-ADL responders in cycle 1
- 5 of 6 patients who weighed ≥120 kg in the efgartigimod arm were QMG responders in cycle 1

Table 2. AEs Summary[a]
AChR-Ab+ Patients

	Efgartigimod		Placebo		All AChR-Ab+	
Treatment-Emergent AE	<30 BMI N=45	≥30 BMI N=20	<30 BMI N=40	≥30 BMI N=24	EFG N=65	PBO N=64
AEs, n (%)	30 (66.7)	19 (95.0)	31 (77.5)	23 (95.8)	49 (75.4)	54 (84.4)
SAEs, n (%)	2 (4.4)	1 (5.0)	3 (7.5)	3 (12.5)	3 (4.6)	6 (9.4)
≥1 IRR event, n (%)	2 (4.4)	0	3 (7.5)	2 (8.3)	2 (3.1)	5 (7.8)
Infection AEs, n (%)	19 (42.2)	10 (50.0)	15 (37.5)	7 (29.2)	29 (44.6)	22 (34.4)
Discontinued due to AEs, n (%)	1 (2.2)	1 (5.0)	1 (2.5)	2 (8.3)	2 (3.1)	3 (4.7)
Most frequent AEs (≥10%), n (%)						
Nasopharyngitis	6 (13.3)	3 (15.0)	8 (20.0)	3 (12.5)	9 (13.8)	11 (17.2)
URTI	5 (11.1)	4 (20.0)	2 (5.0)	0	9 (13.8)	2 (3.1)
UTI	4 (8.9)	1 (5.0)	0	3 (12.5)	5 (7.7)	3 (4.7)
Headache	13 (28.9)	4 (20.0)	10 (25.0)	7 (29.2)	17 (26.2)	17 (26.6)
Nausea	3 (6.7)	2 (10.0)	2 (5.0)	4 (16.7)	5 (7.7)	6 (9.4)
Diarrhea	4 (8.9)	1 (5.0)	5 (12.5)	3 (12.5)	5 (7.7)	8 (12.5)

[a]The denominator for the percentage calculations is the total number of subjects per treatment in the safety analysis set, excluding missing values.

ABBREVIATIONS
AChR-Ab+, acetylcholine receptor antibody seropositive; AE, adverse event; BMI, body mass index; EFG, efgartigimod; FcRn; neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IRR, infusion-related reaction; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL 15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; NSIST, nonsteroidal immunosuppressive therapy; PBO, placebo; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection.

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