Long-term Safety and Efficacy of Efgartigimod in Japanese Patients With gMG: ADAPT+ Final Analysis

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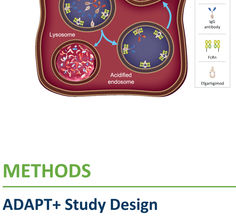
INTRODUCTION

Mechanism of Action of Efgartigimod: Blocking FcRn



- FcRn recycles IgG, extends the half-life of IgG, and maintains IgG serum concentration[1]
- A natural ligand of FcRn, efgartigimod is a human IgG1 Fc fragment, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, prevent IgG recycling, and promote its lysosomal degradation, without directly affecting its production[2,6]
- Efgartigimod provides:
  - Targeted reduction of all IgG subtypes
  - No impact on IgM, IgA, IgE, and IgD
  - No reduction in albumin levels
  - No increase in cholesterol

SUMMARY

Efgartigimod treatment resulted in consistent and repeatable improvements in MG-ADL in patients with AChR-Ab+ and AChR-Ab- gMG

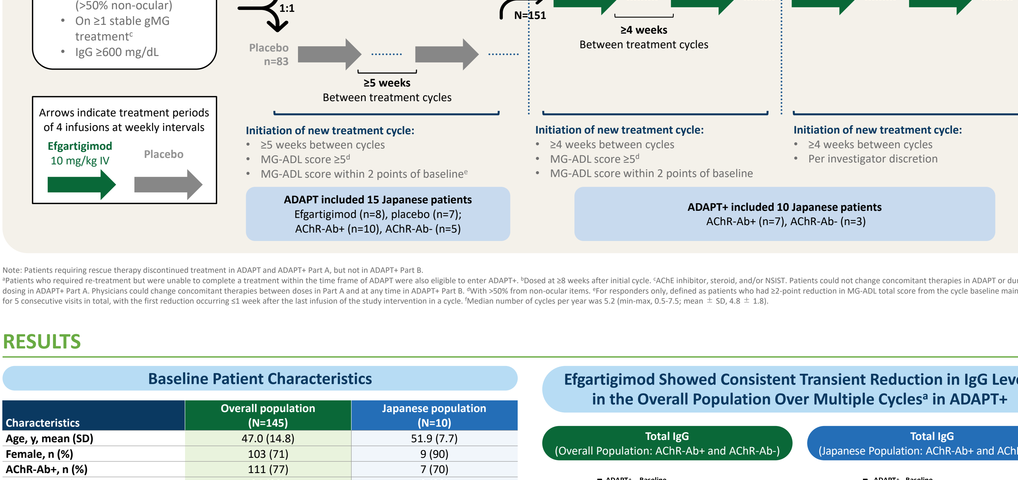
Repeated treatment cycles of efgartigimod were well tolerated; most AEs were mild or moderate in severity, and rates of AEs, including infections, did not increase with additional cycles of treatment

There were no clear trends between infection rates and IgG levels; infection rate did not appear to increase with low IgG levels

The final analysis of ADAPT+ demonstrated long-term efficacy and safety of repeated cycles of efgartigimod in both non-Japanese and Japanese patients with gMG

METHODS

ADAPT+ Study Design



Note: Patients requiring rescue therapy discontinued treatment in ADAPT and ADAPT+ Part A, but not in ADAPT+ Part B.
[a]Patients who required re-treatment but were unable to complete a treatment within the time frame of ADAPT were also eligible to enter ADAPT+. [b]Dosed at ≥8 weeks after initial cycle. [c]AChE inhibitor, steroid, and/or NSIST. Patients could not change concomitant therapies in ADAPT or during dosing in ADAPT+ Part A. Physicians could change concomitant therapies between doses in Part A and at any time in ADAPT+ Part B. [d]With >50% from non-ocular items. [e]For responders only, defined as patients who had ≥2-point reduction in MG-ADL total score from the cycle baseline maintained for 5 consecutive visits in total, with the first reduction occurring ≤1 week after the last infusion of the study intervention in a cycle. [f]Median number of cycles per year was 5.2 (min-max, 0.5-7.5; mean ± SD, 4.8 ± 1.8).

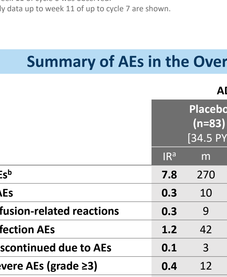
RESULTS

Baseline Patient Characteristics

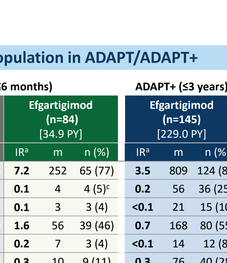
Characteristics	Overall population (N=145)	Japanese population (N=10)
Age, y, mean (SD)	47.0 (14.8)	51.9 (7.7)
Female, n (%)	103 (71)	9 (90)
AChR-Ab+, n (%)	111 (77)	7 (70)
AChR-Ab-, n (%)	34 (23)	3 (30)
MuSK-Ab+, n (%)	4 (3)	0
MuSK-Ab-, n (%)	30 (21)	3 (30)
Time since diagnosis, y, mean (SD)	9.7 (8.2)	12.7 (8.7)
MG-ADL score, mean (SD)	9.8 (3.2)	9.6 (2.2)
QMG score, mean (SD)	15.4 (5.7)	12.9 (6.1)
MG composite score, mean (SD)	18.5 (5.8)	14.9 (7.1)
MG-QoL15r score, mean (SD)	16.3 (6.2)	15.3 (6.5)
MGFA class at screening, n (%)		
Class II	55 (38)	7 (70)
Class III	86 (59)	3 (30)
Class IV	4 (3)	0
Previous thymectomy, n (%)	85 (59)	6 (60)
Baseline gMG therapies, n (%)		
Any NSIST	89 (61)	7 (70)
Steroids	111 (77)	8 (80)
AChE inhibitors	122 (84)	4 (40)

Efgartigimod Showed Consistent Transient Reduction in IgG Levels in the Overall Population Over Multiple Cycles[a] in ADAPT+

Total IgG (Overall Population: AChR-Ab+ and AChR-Ab-)



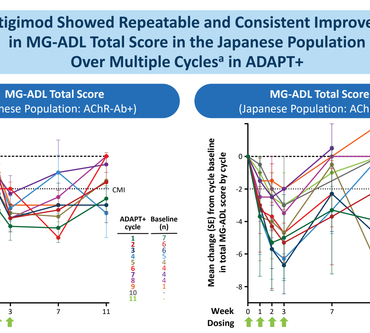
Total IgG (Japanese Population: AChR-Ab+ and AChR-Ab-)



Note: No SE was calculated when the patient number was n=1. For the overall population, due to the small patient number (n=6), a large SE in week 11 of cycle 6 was observed.
[a]Only data up to week 11 of up to cycle 7 are shown.

Efgartigimod Showed Repeatable and Consistent Improvement in MG-ADL Total Score in the Overall Population Over Multiple Cycles[a] in ADAPT+

MG-ADL Total Score (Overall Population: AChR-Ab+ and AChR-Ab-)



[a]Only data up to week 11 of up to cycle 11 are shown.

Efgartigimod Showed Repeatable and Consistent Improvement in MG-ADL Total Score in the Japanese Population Over Multiple Cycles[a] in ADAPT+

MG-ADL Total Score (Japanese Population: AChR-Ab+)

MG-ADL Total Score (Japanese Population: AChR-Ab-)

Note: No SE was calculated when the patient number was n=1.
[a]Only data up to week 11 of up to cycle 11 are shown.

Summary of AEs in the Overall Population in ADAPT/ADAPT+

	ADAPT (≤6 months)						ADAPT+ (≤3 years)		
	Placebo (n=83) [34.5 PY]			Efgartigimod (n=84) [34.9 PY]			Efgartigimod (n=145) [229.0 PY]		
	IR[a]	m	n (%)	IR[a]	m	n (%)	IR[a]	m	n (%)
AEs[b]	**7.8**	270	70 (84)	**7.2**	252	65 (77)	**3.5**	809	124 (86)
SAEs	**0.3**	10	7 (8)	**0.1**	4	4 (5)[c]	**0.2**	56	36 (25)[c]
Infusion-related reactions	**0.3**	9	8 (10)	**0.1**	3	3 (4)	**<0.1**	21	15 (10)
Infection AEs	**1.2**	42	31 (37)	**1.6**	56	39 (46)	**0.7**	168	80 (55)
Discontinued due to AEs	**0.1**	3	3 (4)	**0.2**	7	3 (4)	**<0.1**	14	12 (8)
Severe AEs (grade ≥3)	**0.4**	12	8 (10)	**0.3**	10	9 (11)	**0.3**	76	40 (28)
Death[d]	-	0	0	-	0	0	**<0.05**	5	5 (3)
Most frequent AEs									
Nasopharyngitis	**0.5**	17	15 (18)	**0.3**	12	10 (12)	**0.1**	24	20 (14)
URTI	**0.2**	5	4 (5)	**0.3**	11	9 (11)	**<0.05**	7	6 (4)
UTI	**0.1**	4	4 (5)	**0.3**	9	8 (10)	**<0.1**	19	13 (9)
Headache	**1.1**	39	23 (28)	**1.2**	40	24 (29)	**0.4**	103	36 (25)
Nausea	**0.4**	15	9 (11)	**0.2**	7	7 (8)	**<0.1**	13	9 (6)
Diarrhea	**0.4**	14	9 (11)	**0.2**	6	6 (7)	**<0.1**	19	14 (10)
COVID-19[e]	-	0	0	-	0	0	**0.1**	24	23 (16)[f]

[a]IR was calculated as number of events per total PYs of follow-up. [b]AEs were predominantly mild or moderate. [c]Only 1 SAE was considered treatment related per the investigator. [d]None of the deaths in ADAPT+ were related to efgartigimod administration per the principal investigator. [e]Includes all preferred terms of COVID-19, COVID-19 pneumonia, coronavirus infection, and SARS-CoV-2 test positive. [f]Among patients reporting COVID-19 during ADAPT+, 83% had not received prior vaccination.

Summary of AEs by IgG Level in the Overall Population in ADAPT+

	Nadir[a] IgG level in cycle, mg/dL				
	≤250	>250 to ≤350	>350 to ≤450	>450	All
Number of cycles with IgG measured	185	258	124	173	740
AEs,[b] n (%)	70 (38)	101 (39)	34 (27)	54 (31)	259 (35)
Infection AEs, n (%)	23 (12)	34 (13)	11 (9)	19 (11)	87 (12)
SAEs, n (%)	2 (1)	9 (3)	4 (3)	9 (5)	24 (3)
Discontinued study treatment due to AE, n (%)	0	4 (2)	2 (2)	3 (2)	9 (1)

[a]Cycle nadir is defined as the lowest IgG level for a patient in a cycle. AEs in cycles where IgG level was assessed were included; of a total of 1125 patient cycles, 740 patient-cycles had IgG data available. [b]Reported within 56 days after the start of treatment.

ABBREVIATIONS
Ab, antibody; AChE, acetylcholinesterase; AChR, acetylcholine receptor; AE, adverse event; CMI, clinically meaningful improvement; COVID-19, coronavirus disease 2019; Fc, crystallizable fragment; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgA, immunoglobulin A; IgD, immunoglobulin D; IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M; IR, incidence rate; IV, intravenous; m, number of events; max, maximum; 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; min, minimum; MuSK, muscle-specific kinase; NSIST, nonsteroidal immunosuppressive therapy; PY, patient-year; QMG, quantitative myasthenia gravis; SAE, serious adverse event; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; SE, standard error; URTI, upper respiratory tract infection; UTI, urinary tract infection.

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adapt+ myasthenia gravis study

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