Long-Term Safety, Tolerability, and Efficacy of Efgartigimod in Patients With Generalized Myasthenia Gravis: Interim Results of the ADAPT+ Study

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Efgartigimod Mechanism of Action: Blocking FcRn

- FcRn recycles IgG, extending its half-life and serum concentration[1]

- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2]

- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling, and promoting lysosomal degradation of IgG, without impacting its production[2-5]
  - Targeted reduction of all IgG subtypes
  - No impact on IgM or IgA
  - No reduction in albumin levels
  - No increase in cholesterol
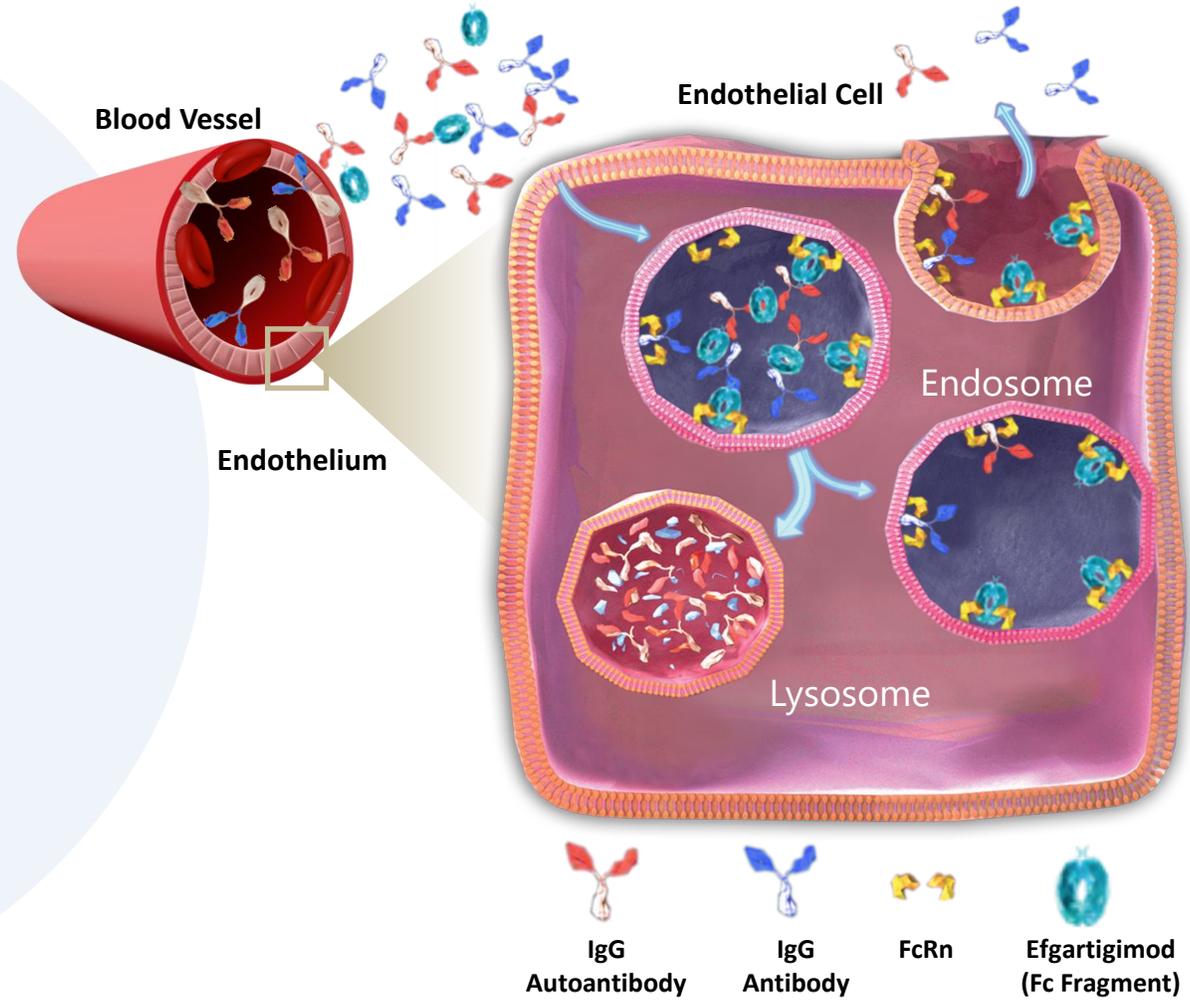
Image adapted from Kang TH, Jung ST.*Exp Mol Med*. 2019;51(11):1-9.

FC, crystallizable fragment; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M.
1. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533-2550. **2.** Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386. **3.** Vaccaro C, et al. *Nat Biotech.* 2005;23(10):1283-1288.
4. Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536. **5.** argenx Data on File, 2022.

ADAPT+ Study Design

ADAPT[1]
(Placebo controlled)

ADAPT+
(Open-label efgartigimod)

2 weeks screening

MGFA Class II, III, IV

AChR-antibody positive or negative

MG-ADL score ≥5[a]

On ≥1 stable gMG treatment[b]

IgG ≥6 g/L

N=167

1:1

26 weeks (max. 3 cycles)

Up to 3 years

Part A (1 y)

Part B (2 y)

Efgartigimod n=84

Placebo n=83

N=151

Efgartigimod

Efgartigimod

≥5 weeks
Between treatment cycles

≥4 weeks
Between treatment cycles

Subsequent treatment cycle(s) if required[c]

Subsequent treatment cycle(s) if required[c]

Arrows indicate treatment periods of 4 infusions at weekly intervals

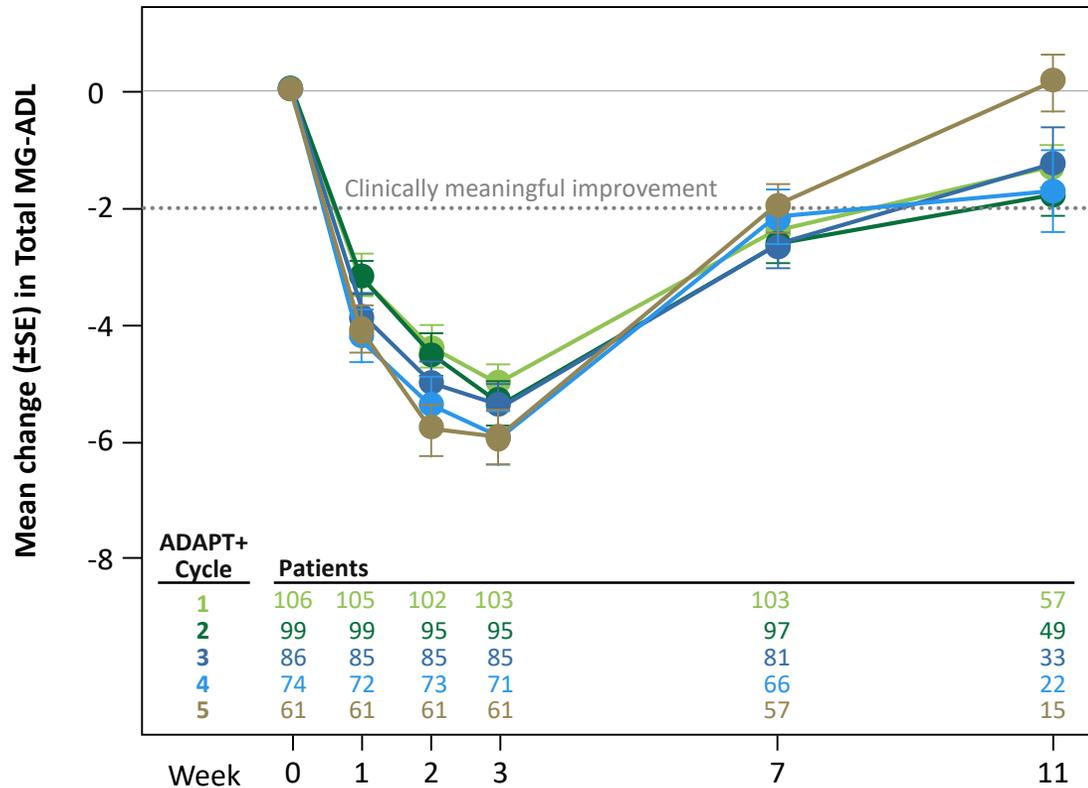**Efgartigimod**
10 mg/kg IV

Placebo

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; Wk, week. Note: Patients requiring rescue therapy discontinued from the study treatment. [a]50% of the score attributed to nonocular items. [b]Acetylcholinesterase inhibitor, steroid +/or nonsteroidal immunosuppressive therapy (for the duration of the trial). [c] Based on clinical evaluation. Patients needed to have an MG-ADL score ≥5 (>50% from nonocular items) and needed to have a reduction in MG-ADL total score <2 points from study/cycle baseline to be eligible to receive a new cycle. **1.** Howard JF Jr, et al. *Lancet Neurol*. 2021;20(7):526-536.

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Efgartigimod Demonstrated Repeatable and Sustained Improvement in Both MG-ADL and QMG Over Multiple Cycles[a] in ADAPT+
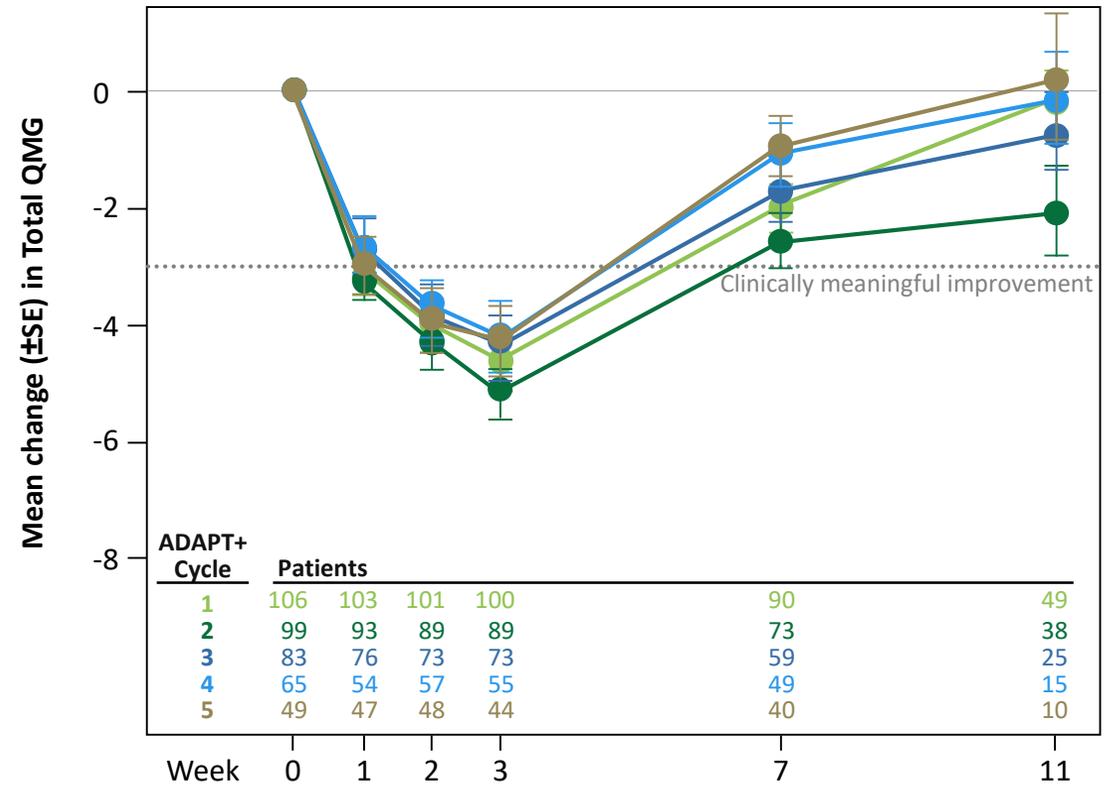
AChR-Ab+ Population

MG-ADL Total Score
Mean Change From Cycle Baseline by Cycle
(Efgartigimod + current TX)

ADAPT+ Cycle	Patients					
1	106	105	102	103	103	57
2	99	99	95	95	97	49
3	86	85	85	85	81	33
4	74	72	73	71	66	22
5	61	61	61	61	57	15

Week: 0 1 2 3 7 11

QMG Total Score
Mean Change From Cycle Baseline by Cycle
(Efgartigimod + current TX)

ADAPT+ Cycle	Patients					
1	106	103	101	100	90	49
2	99	93	89	89	73	38
3	83	76	73	73	59	25
4	65	54	57	55	49	15
5	49	47	48	44	40	10

Week: 0 1 2 3 7 11

AChR-Ab, acetylcholine receptor autoantibody; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; TX, treatment.
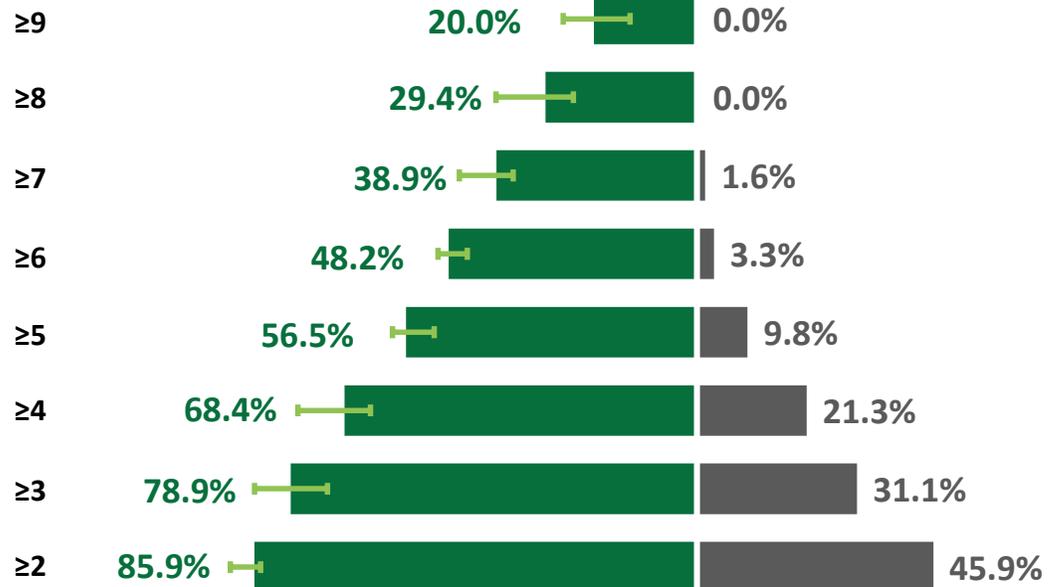[a] Only cycles with data out to week 11 are depicted

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Proportion of Patients With Increasing MG-ADL or QMG Improvement Over Multiple Cycles[a]

AChR-Ab+ Population

Change in MG-ADL Total Score

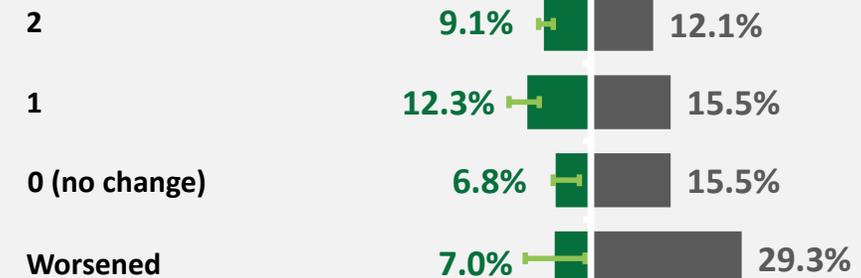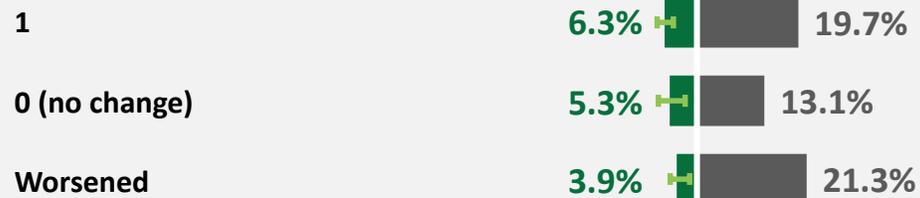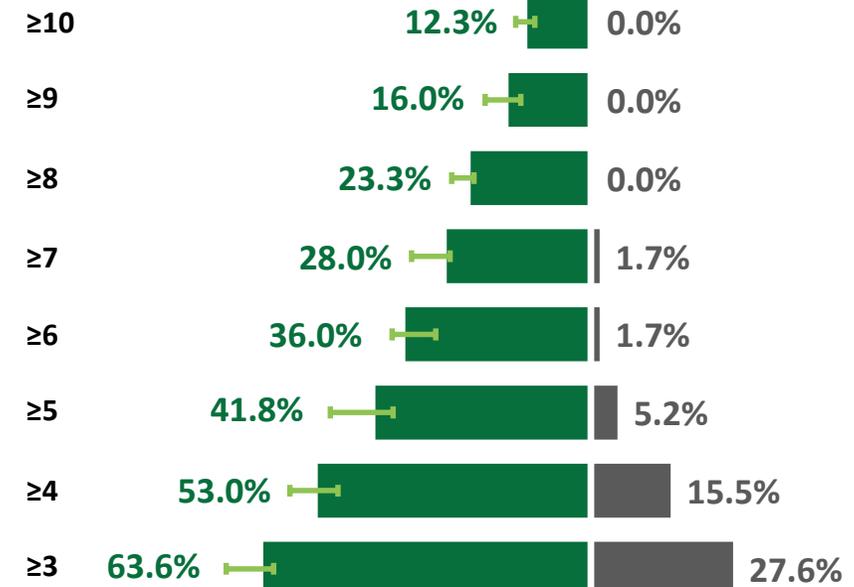|	Efgartigimod (open-label) Week 3 of cycles 1-5[a] in ADAPT+ *median % (range)*	Placebo (phase 3) Week 3 of Cycle 1 in ADAPT %
≥9	20.0%	0.0%
≥8	29.4%	0.0%
≥7	38.9%	1.6%
≥6	48.2%	3.3%
≥5	56.5%	9.8%
≥4	68.4%	21.3%
≥3	78.9%	31.1%
≥2	85.9%	45.9%
1	6.3%	19.7%
0 (no change)	5.3%	13.1%
Worsened	3.9%	21.3%

Change in QMG Total Score

	Efgartigimod (open-label) Week 3 of cycles 1-5[a] in ADAPT+ *median % (range)*	Placebo (phase 3) Week 3 of Cycle 1 in ADAPT %
≥10	12.3%	0.0%
≥9	16.0%	0.0%
≥8	23.3%	0.0%
≥7	28.0%	1.7%
≥6	36.0%	1.7%
≥5	41.8%	5.2%
≥4	53.0%	15.5%
≥3	63.6%	27.6%
2	9.1%	12.1%
1	12.3%	15.5%
0 (no change)	6.8%	15.5%
Worsened	7.0%	29.3%

CMI (cumulative %)

No CMI (Categorical %)

AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.

[a] Only cycles with data out to week 11 are included.

Safety: Summary of AEs
Safety Population

	ADAPT				ADAPT+	
	Placebo (n=83) [34.51 PY]		Efgartigimod (n=84) [34.86 PY]		Efgartigimod (n=139) [138.14 PY]	
	IR/PY	% (n)	IR/PY	% (n)	IR/PY	% (n)
AEs	7.83	84 (70)	7.23	77 (65)	4.06	81 (112)
SAEs	0.29	8 (7)	0.11	5 (4)	0.25	15 (21)
≥1 Infusion-related reaction event	0.26	10 (8)	0.09	4 (3)	0.09	7 (10)
Infection AEs	1.22	37 (31)	1.61	46 (39)	0.84	47 (65)
Discontinued study treatment due to AEs	0.09	4 (3)	0.20	4 (3)	0.07	6 (8)
Severe AEs (grade ≥3)	0.35	10 (8)	0.29	11 (9)	0.41	19 (26)
Death	0	0 (0)	0	0 (0)	0.04	4 (5)
Most frequent AEs						
Nasopharyngitis	0.49	18 (15)	0.34	12 (10)	0.14	11 (15)
Upper respiratory tract infection	0.15	5 (4)	0.32	11 (9)	0.04	4 (5)
Urinary tract infection	0.12	5 (4)	0.26	10 (8)	0.09	7 (10)
Headache	1.13	28 (23)	1.15	29 (24)	0.49	22 (31)
Nausea	0.43	11 (9)	0.20	8 (7)	0.07	5 (7)
Diarrhea	0.41	11 (9)	0.17	7 (6)	0.11	9 (12)

AE, adverse event; IR, incidence rate; MG, myasthenia gravis; PY, patient year; SAE, serious adverse event; URTI, upper respiratory tract infection.

Deaths in ADAPT+: None Related to Efgartigimod per Investigator

Age, y/ Sex	Cause of Death	Days from last dose	Comorbidities/Medical History
72/F	Unknown; preexisting CV disease, autopsy confirmed coronary artery atherosclerosis and cardiomegaly	4	Pulmonary embolism, chronic obstructive pulmonary disease, hypertension, hypokalemia, and colon bladder fistula
79/M	MG crisis and progression of underlying disease/*Escherichia coli* pneumonia	79	Chronic rhinitis, anxiety
66/F	Malignant lung neoplasm (Stage IV)	60	Histoplasmosis, asthma, diabetes mellitus, hypercholesterolemia, macular degeneration, hypertension, squamous cell carcinoma, and bundle branch block
55/M	Acute MI and generalized unspecified atherosclerosis	24	Anemia, subarachnoid hemorrhage, CTO PCI and angioplasty procedures
62/M	Septic shock/ COVID-19 pneumonia	69	Chronic venous insufficiency, arterial hypertension, deep vein thrombosis, rheumatoid arthritis, and paroxysmal atrial fibrillation

CTO PTI, chronic total occlusion percutaneous coronary intervention; CV, cardiovascular; MI, myocardial infarction; MG, myasthenia gravis; PBO, placebo; PI, principal investigator.

Distribution of Efgartigimod Complete Cycles Over 1 Year

AChR-Ab+ population with ≥ 1 year of follow-up in ADAPT/ADAPT+ (N=88)

54.6% of patients received **≤5.5 cycles** per year

Mean: 4.87
Median: 5.21

Patients (%)

Number of cycles per year
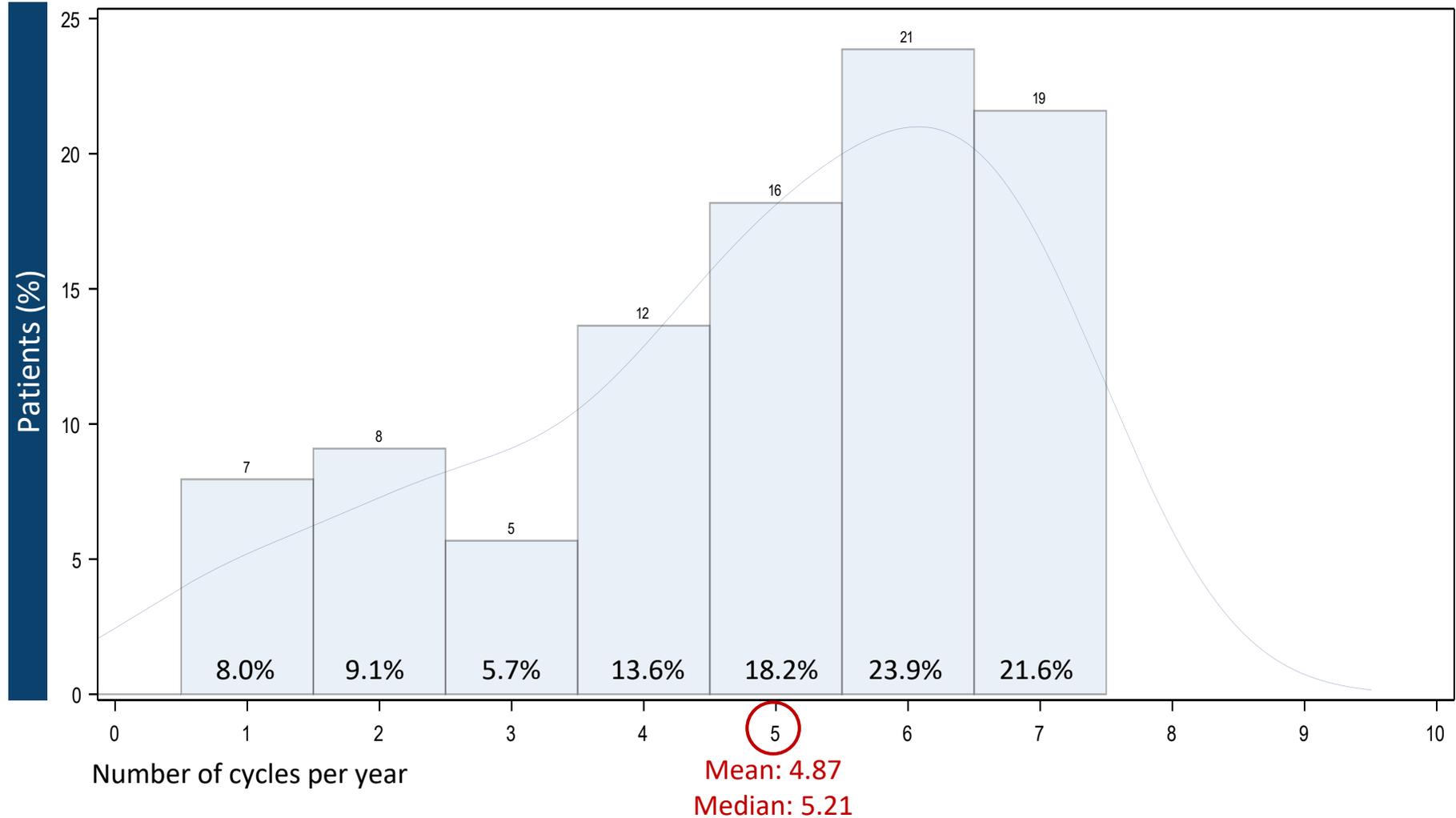
Cycles per year across ADAPT and ADAPT+

AChR-Ab, acetylcholine receptor autoantibody.

Summary

The safety profile observed during long-term treatment with efgartigimod in ADAPT+ mirrored that seen during ADAPT, even while being conducted during the COVID-19 global pandemic

This analysis suggests that long-term treatment with efgartigimod is efficacious, providing consistent and repeatable clinically meaningful improvement in function and strength while remaining well tolerated

ADAPT+ is a planned 3-year study and is currently ongoing

COVID-19, coronavirus disease 2019.