Efficacy of Efgartigimod Treatment in Patients With Anti-Acetylcholine Receptor Antibody Negative Myasthenia Gravis: Clinical Trial and Real-World Data

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Disclosures

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Introduction: Clinical Challenges in the Management of AChR-Ab– gMG

Patients with AChR-Ab– gMG are heterogenous and difficult to diagnose[1]

These patients have high unmet clinical need and have historically been excluded from clinical trials[1]

ADAPT/ADAPT+ were the first clinical trials to include AChR-Ab– patients[2]

Here we present data on experience with efgartigimod in AChR-Ab– patients during ADAPT/ADAPT+ and in preliminary real-world experience

AChR-Ab, acetylcholine receptor autoantibody; gMG, generalized myasthenia gravis.

1. Gilhus NE, Verschuuren JJ. *Lancet Neurology*. 2015;14(10):1023-1036. **2.** Howard JF Jr, et al. *Lancet Neurol*. 2021;20(7):526-536.

ADAPT and ADAPT+ Study Design

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

Open-Label Extension (ADAPT+)[d]
Patients received cycles of 4 infusions at weekly intervals of 10 mg/kg IV efgartigimod

Entry Criteria

MGFA Class II/III/IV

MG-ADL score ≥5[a]

On ≥1 stable gMG treatment[b]

IgG ≥6 g/L

AChR-Ab positive
or
AChR-Ab negative[c]

- Undetectable AChR-Ab by radioimmunoassay
- ≥1 of the following diagnostic criteria:
  1. Abnormal electrodiagnostic testing
  2. Positive edrophonium chloride test
  3. Demonstrated improvement with AChEI

N=167
1:1

26 wk (≤3 cycles)

Efgartigimod
AChR-Ab–: n=19
AChR-Ab+: n=65
MuSK: n=3

Placebo
AChR-Ab–: n=19
AChR-Ab+: n=64
MuSK: n=3

26 wk (≤3 cycles)

Initiation of new treatment cycle
- ≥5 wk between cycles
- MG-ADL score ≥5[a]
- MG-ADL score within 2 points of baseline

N=151

≤3 y

AChR-Ab–: n=16
AChR-Ab+: n=61
MuSK: n=2

AChR-Ab–: n=18
AChR-Ab+: n=50
MuSK: n=2

Part A (1 y) / Part B (2 y)

Initiation of new treatment cycle
- ≥4 wk between cycles
- MG-ADL score ≥5[a]
- MG-ADL score within 2 points of baseline

Initiation of new treatment cycle
- ≥4 wk between cycles
- Per investigator discretion

Note: Beige rectangles within arrows indicate day of efgartigimod infusion.
AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor autoantibody; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific kinase. [a]With >50% from nonocular items. [b]Acetylcholinesterase inhibitor, steroid +/or nonsteroidal immunosuppressive therapy (for the duration of the trial). 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+. [c]Analyses were not powered for AChR-Ab– subgroup. [d]Data cutoff Jan 31, 2022.

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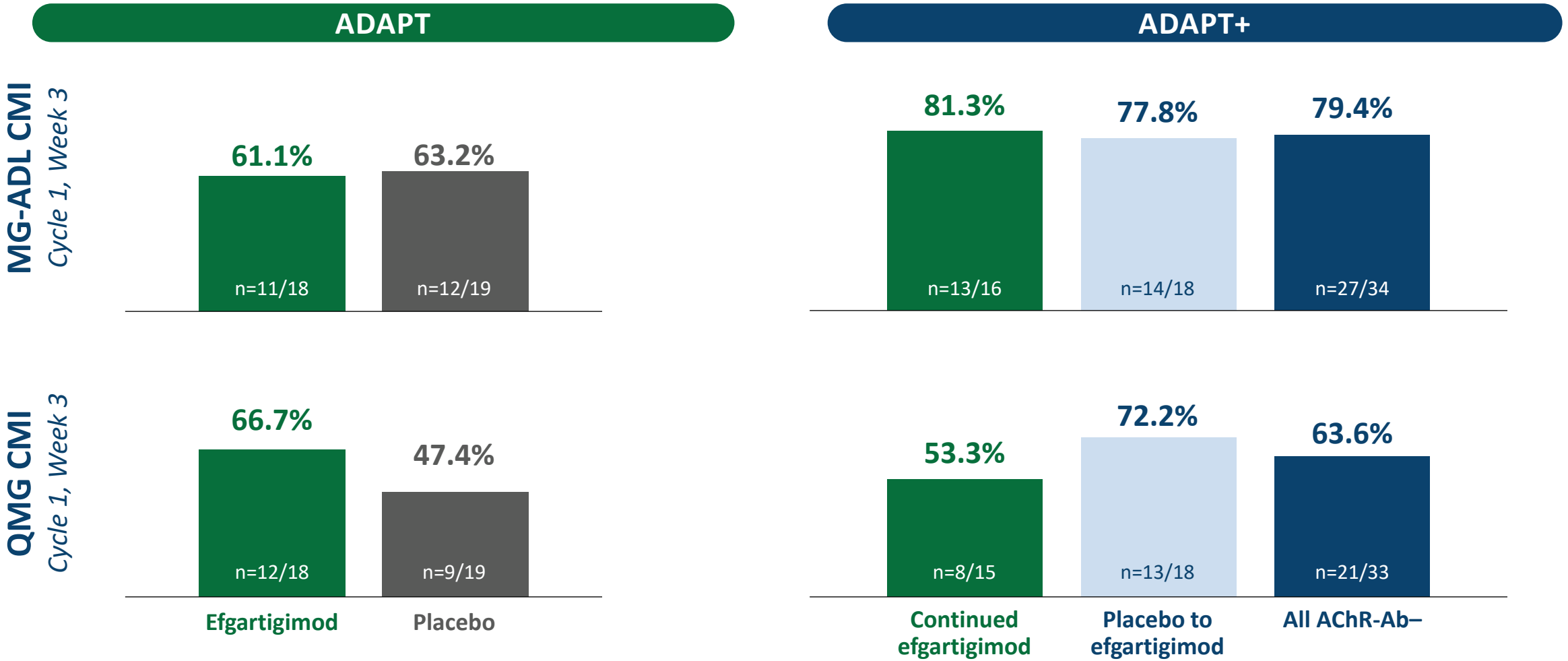
Efficacy of Efgartigimod in AChR-Ab– Patients: Clinical Trial Experience

Proportion of AChR-Ab– Patients With CMI in ADAPT and ADAPT+[a]



AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.
[a]CMI defined as ≥2-point improvement in MG-ADL and ≥3-point improvement in QMG.

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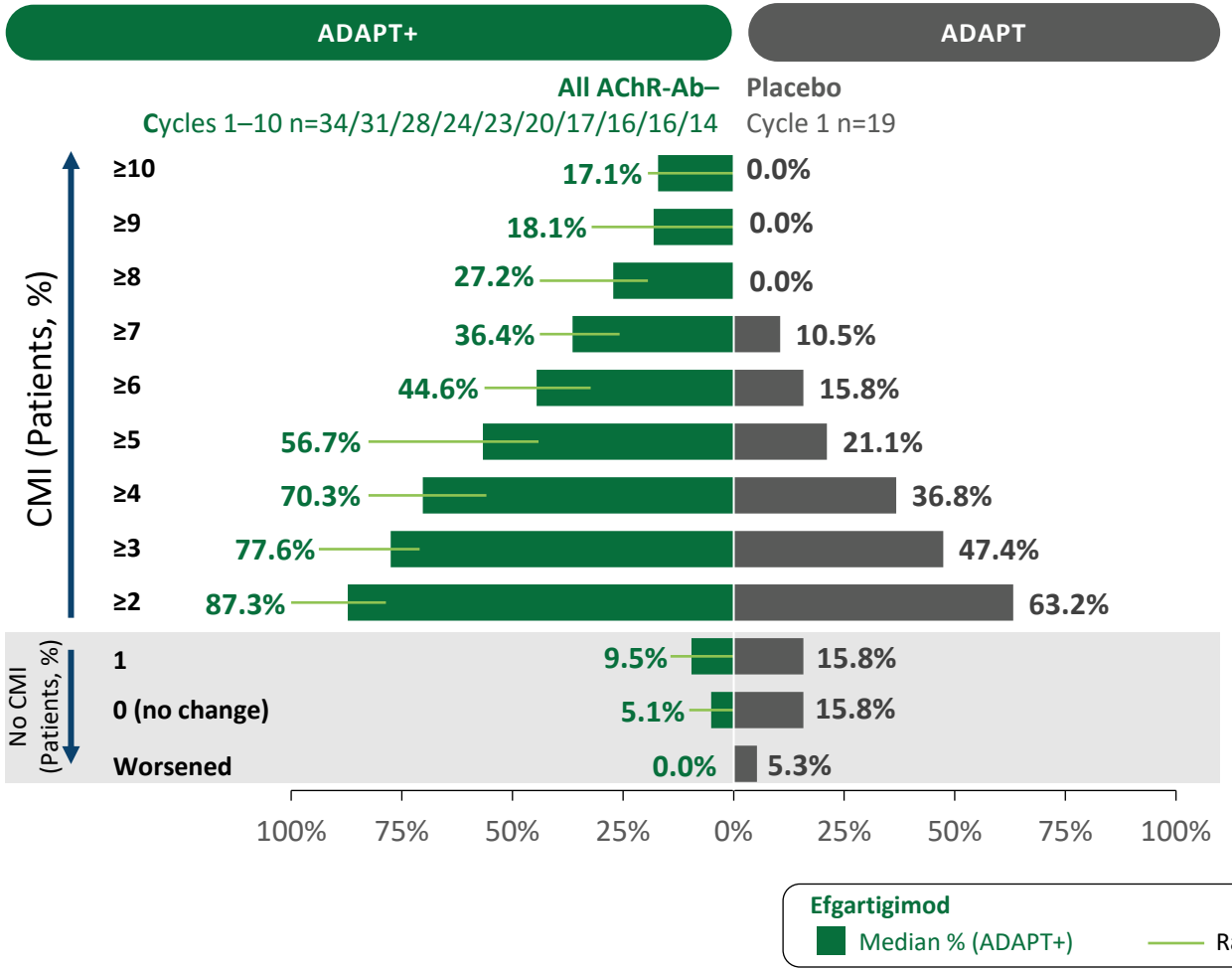
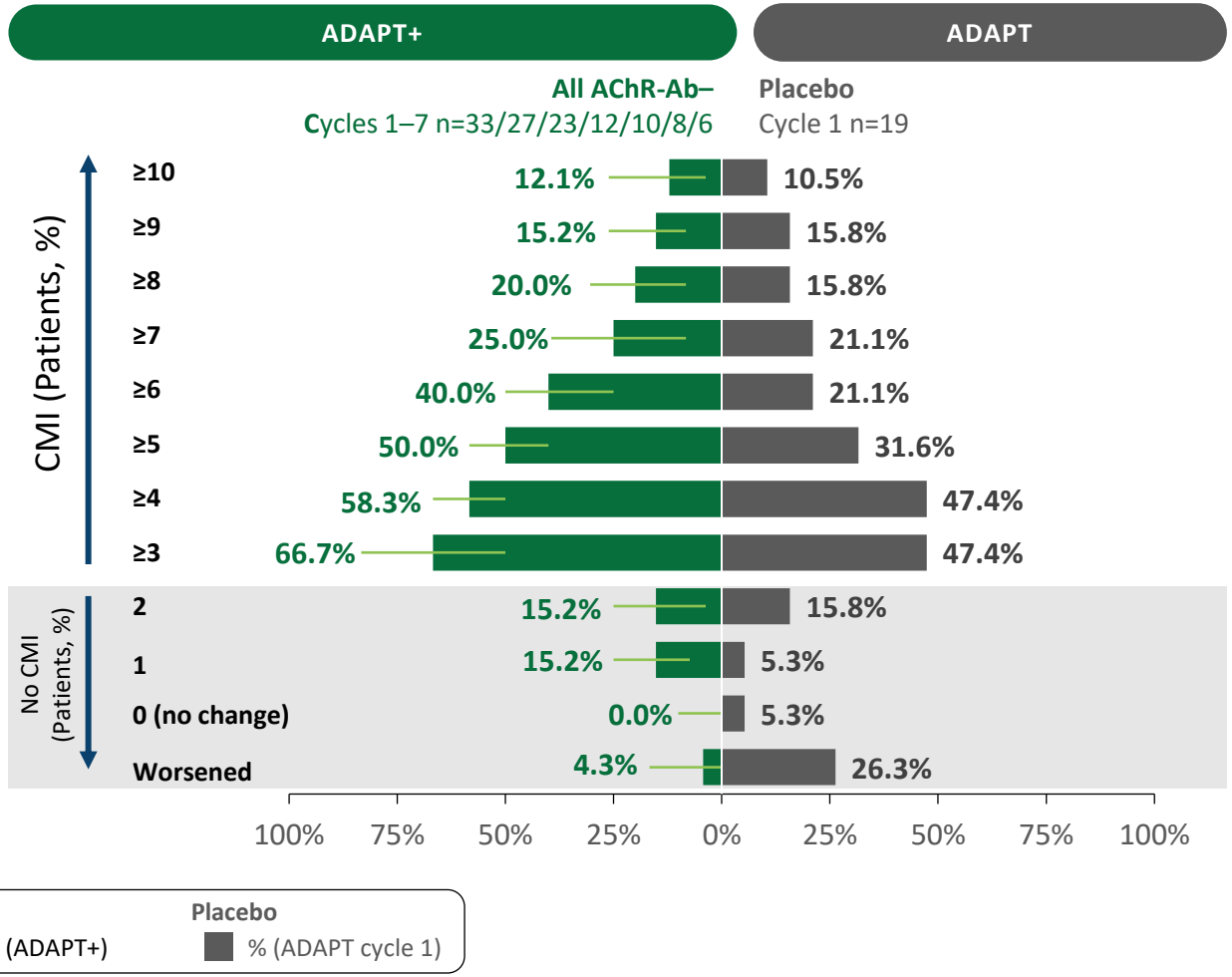
Efficacy of Efgartigimod in AChR-Ab– Patients: Clinical Trial Experience

Proportion of AChR-Ab– Patients With Increasing Improvement in MG-ADL and QMG Scores of Cycles in ADAPT+ (Week 3[a,b])

Change in MG-ADL Total Score



Change in QMG Total Score



Efgartigimod: Median % (ADAPT+); Range (ADAPT+) — Placebo: % (ADAPT cycle 1)

AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.
[a]Cycles with data out to week 11 were included. [b]Study limitation: results do not preclude survivor bias.

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Preliminary Real-World Experience: Clinical Characteristics

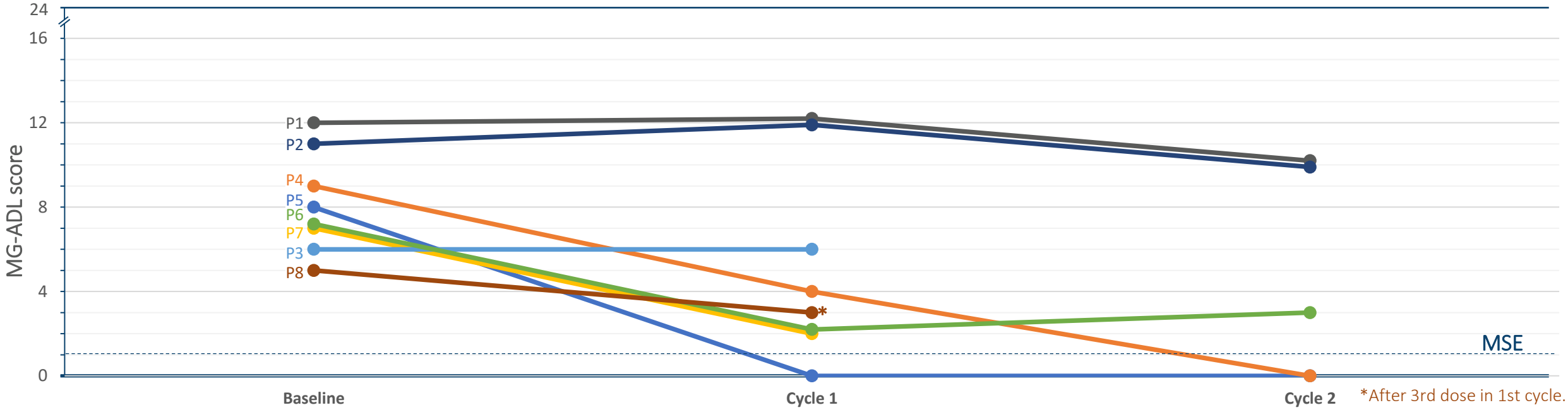
	Patients (n=8)
Age, y (SD)	62.4 (9.6)
Sex at birth, female, n (%)	5 (62.5)
Time since diagnosis, y (SD)	12.9 (15.2)
Total MG-ADL score, Mean (SD)	8.1 (2.4)
MGFA classification at screening, n (%)	
Class II	5 (62.5)
Class III	2 (25.0)
Class IV	1 (12.5)
Antibody status, n (%)	
Anti-AChR–	1 (12.5)
Anti-AChR–/MuSK–	1 (12.5)
Anti-AChR–/MuSK–/LRP4–	6 (75.0)
Diagnostic confirmation, n (%)	
Response to AChEI	5 (62.5)
Single-fiber EMG	3 (37.5)
RNS	2 (25.0)
Rest test (neuro-ophthalmology)	2 (25.0)

	Patients (n=8)
Prior therapy, n (%)	
AChEI	2 (25.0)
Corticosteroids	7 (87.5)
NSIST	5 (62.5)
Rituximab	1 (12.5)
Plasma exchange	3 (37.5)
IVIg	3 (37.5)
Baseline therapy, n (%)	
AChEI	4 (50.0)
Corticosteroids	7 (87.5)
NSIST	4 (50.0)
Rituximab	1 (12.5)

Cases identified by authors from the following centers: CoxHealth Springfield (Springfield, MO, USA), Kettering Health and Dayton Center for Neurological Disorders (Dayton, OH, USA), Ohio University (Athens, OH, USA), University of North Carolina (Chapel Hill, NC, USA), and Yale School of Medicine (New Haven, CT, USA).

AChEI, acetylcholinesterase inhibitor; AChR, acetylcholine receptor; EMG, electromyography; gMG, generalized myasthenia gravis; IVIg, intravenous immunoglobulin; LRP4, lipoprotein-related protein 4; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific kinase; NSIST, nonsteroidal immunosuppressive therapy; RNS, repetitive nerve stimulation.

Preliminary Real-World Experience: Course After Starting Efgartigimod



	Current Non responders (<2 point MG-ADL improvement)			Current Responders (>2 point MG-ADL improvement)				
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
# cycles received	2	2	1	2	2	2	1	ongoing
Time between cycles, weeks	8	8	N/A	4	4	8	N/A	N/A
Changes to concomitant medication	None	None	None	Discontinued steroids, reduced AChEI dosage by 50%	None	Tapering off steroids	No pulsed rituximab	None
AEs experienced	Sinus infection after 1st infusion delayed second dose by 1 wk	None	None	None	None	None	None	None

Cases identified by authors from the following centers: CoxHealth Springfield (Springfield, MO, USA), Kettering Health and Dayton Center for Neurological Disorders (Dayton, OH, USA), Ohio University (Athens, OH, USA), University of North Carolina (Chapel Hill, NC, USA), Yale School of Medicine (New Haven, CT, USA). AChEI, acetylcholinesterase inhibitor; AE, adverse event; MG-ADL, Myasthenia Gravis Activities of Daily Living; MSE, minimal symptom expression; N/A, not applicable.

ADAPT is the first gMG trial to include AChR-Ab– patients

In ADAPT/ADAPT+ similar proportions of AChR-Ab– and AChR-Ab+ patients responded to efgartigimod, but there was a notable placebo response (ADAPT was not powered to detect an efficacy signal in this subgroup)

Preliminary real-world experience is largely consistent with ADAPT/ADAPT+, with 5/8 (62.5%) responding to initial cycles of efgartigimod, and a mean improvement in MG-ADL of 3.9 (range: 0-9) points

Efgartigimod is well tolerated in both clinical trial and clinical practice settings

Additional studies and real-world experience assessing the efficacy of efgartigimod in AChR-Ab– patients are warranted

AChR-Ab, acetylcholine receptor autoantibody; gMG, generalized myasthenia gravis.

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