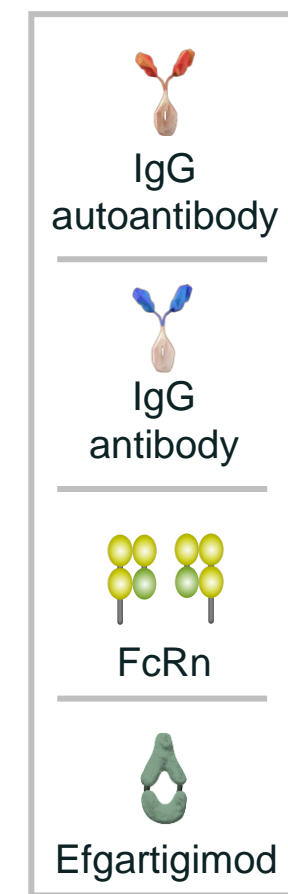
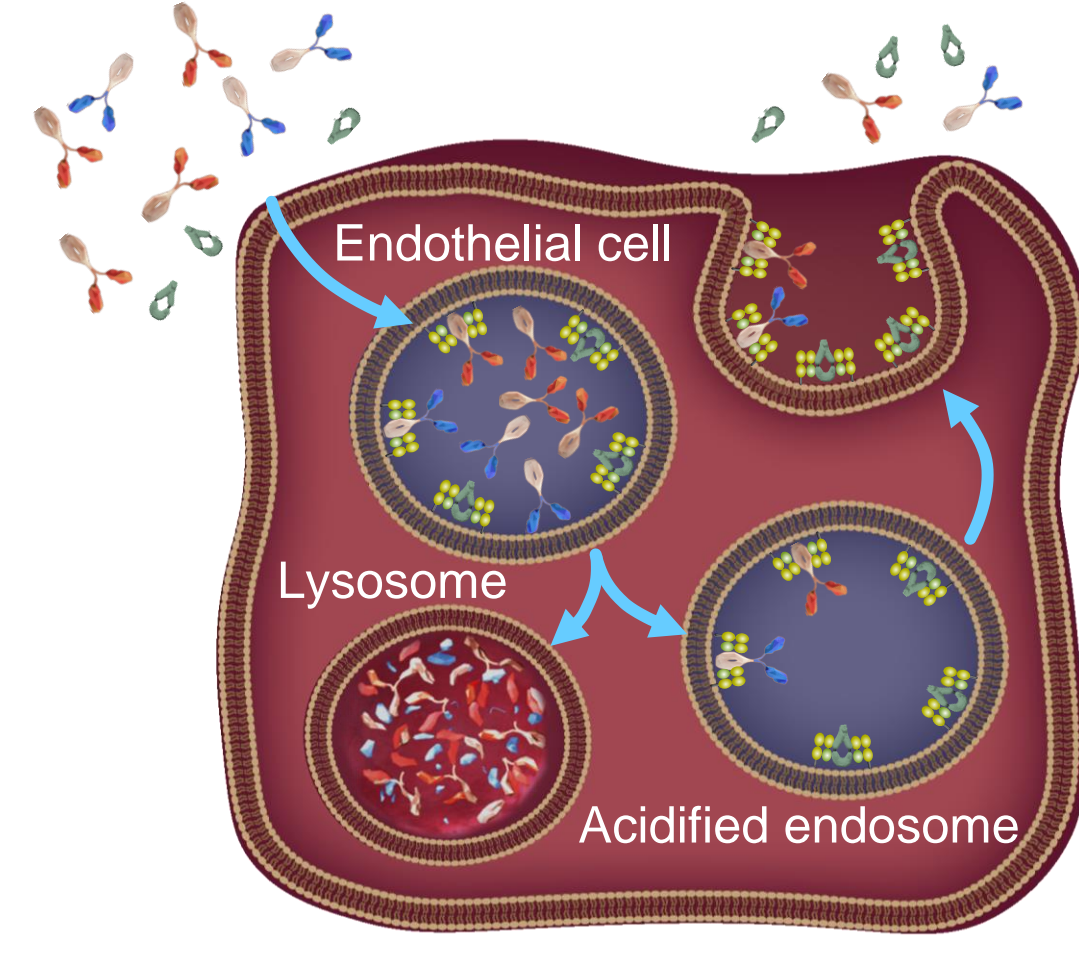




## Background

### Efgartigimod Mechanism of Action



- Approximately 1%-5% of patients with gMG have detectable LRP4 autoantibodies<sup>1</sup>
- FcRn recycles IgG antibodies, including pathogenic IgG autoantibodies, extending their half-lives and maintaining high serum concentrations<sup>2</sup>
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG<sup>3,4</sup>
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, thus reducing IgG levels without directly impacting IgG production<sup>3-6</sup>
  - No impact on levels of IgM, IgA, IgE, or IgD<sup>3,6</sup>
  - No reduction in albumin or increase in cholesterol levels<sup>5-7</sup>
  - Targeted reduction of all IgG subtypes<sup>3,5</sup>
- Since LRP4 autoantibodies are predominantly of the IgG1 or IgG2 subtypes, it is hypothesized that LRP4+ patients with MG could benefit from treatment with efgartigimod<sup>1</sup>

## Conclusions

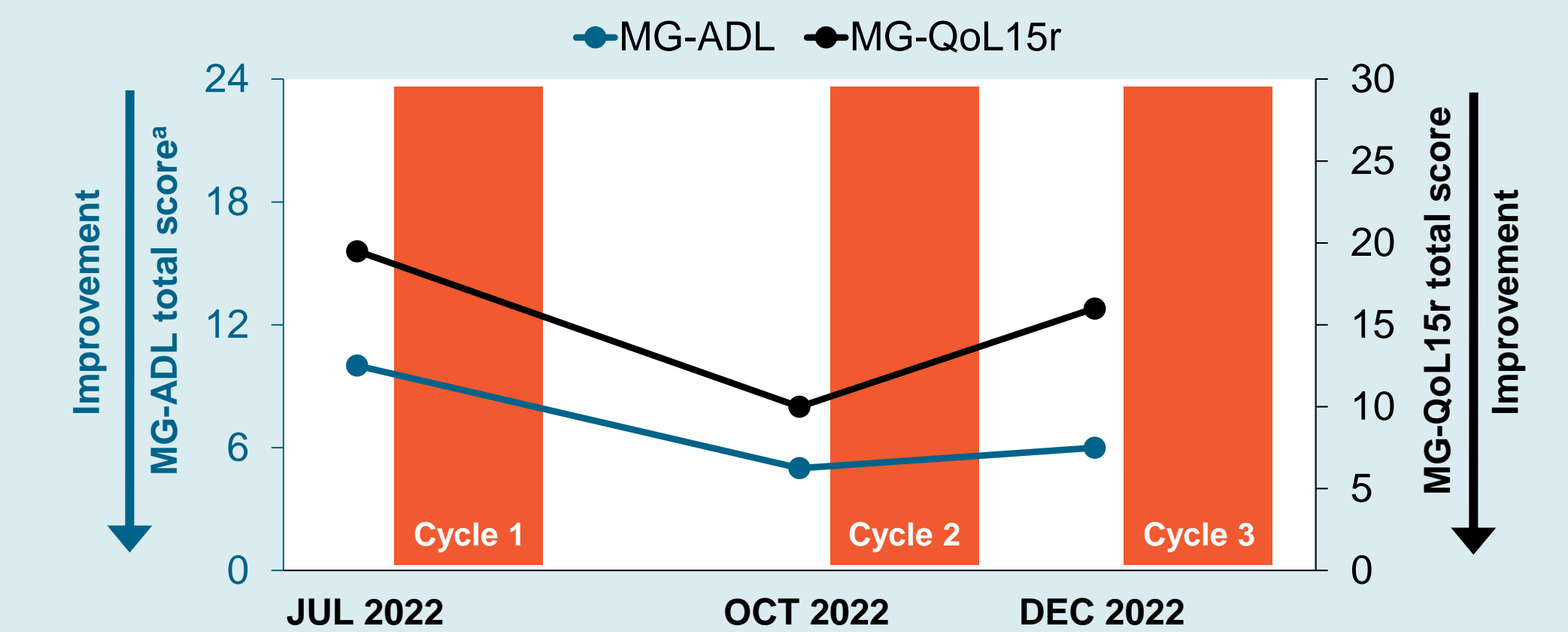
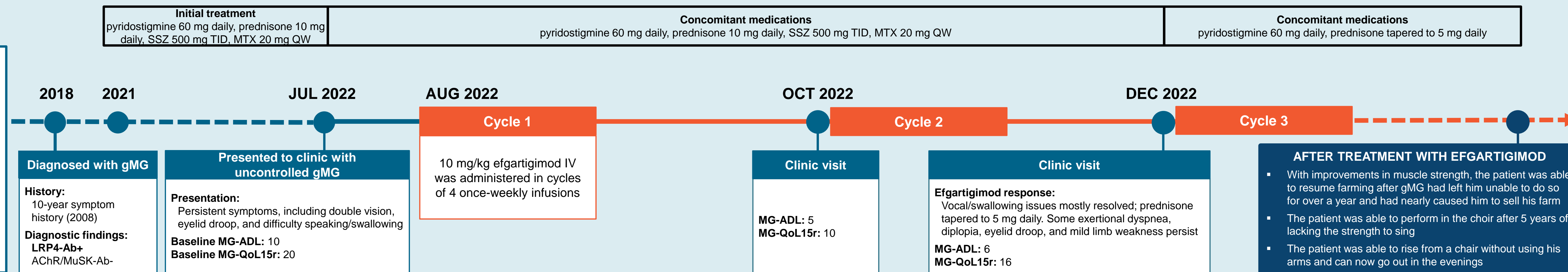
- ≈1%-5% of patients with gMG have detectable LRP4 IgG autoantibodies
- FcRn blockade with efgartigimod provides targeted reduction of all IgG subtypes, including pathogenic autoantibodies
- Two LRP4-Ab+ patients with gMG in our clinic experienced improvements in ADLs and QoL, and 1 patient had reductions in corticosteroid dose (patient 2 did not take any corticosteroids out of concern for AEs) following treatment with efgartigimod
- Efgartigimod was well tolerated in these cases
- While more studies are needed, efgartigimod may be an effective treatment option for patients with LRP4+ gMG

## Patient Cases

### CASE 1: Male Aged 66 Years

#### Presentation:

- Farmer with an active social life, including singing in a church choir
- Diagnosed with gMG in 2018 after a 10-year symptom history, which has since worsened despite treatment
- Symptoms are impacting occupational and social activities
- Medical history notable for stroke (left occipital lobe without motor involvement; March 2022) and rheumatoid arthritis (diagnosed in 2018, shortly after gMG diagnosis)

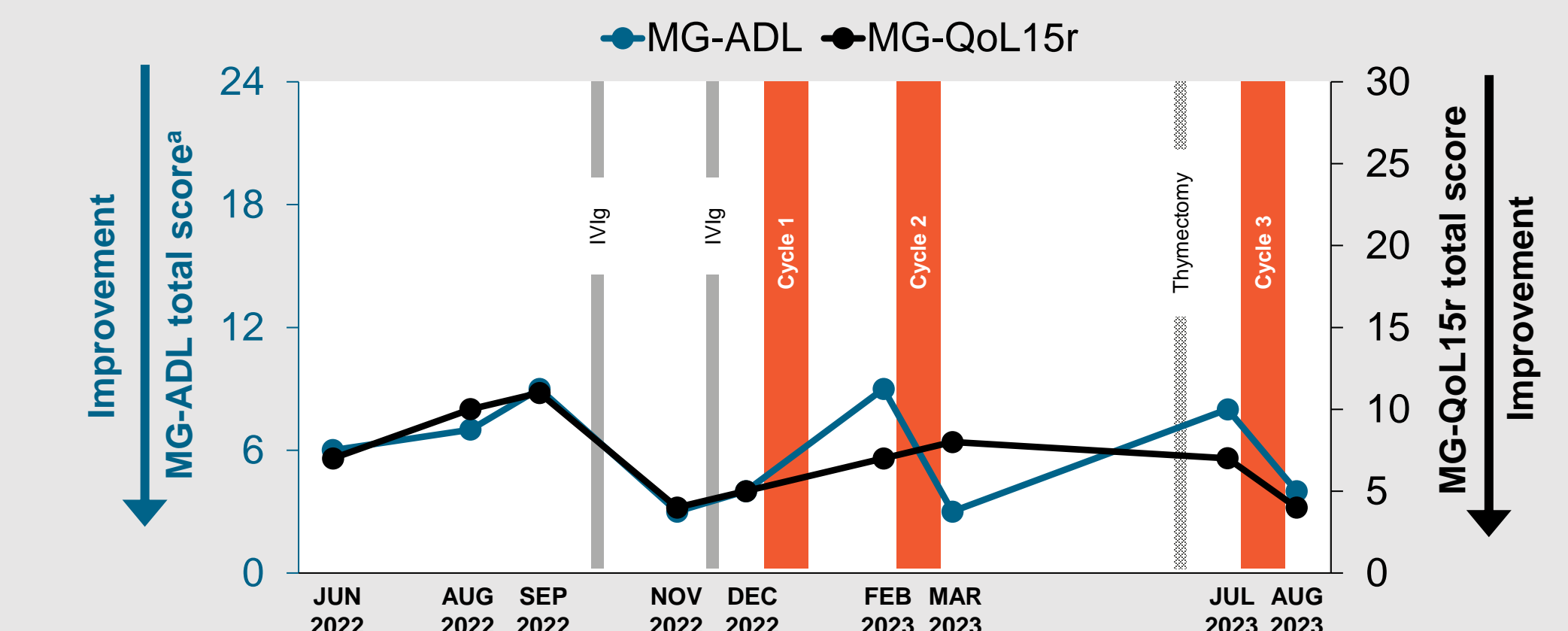
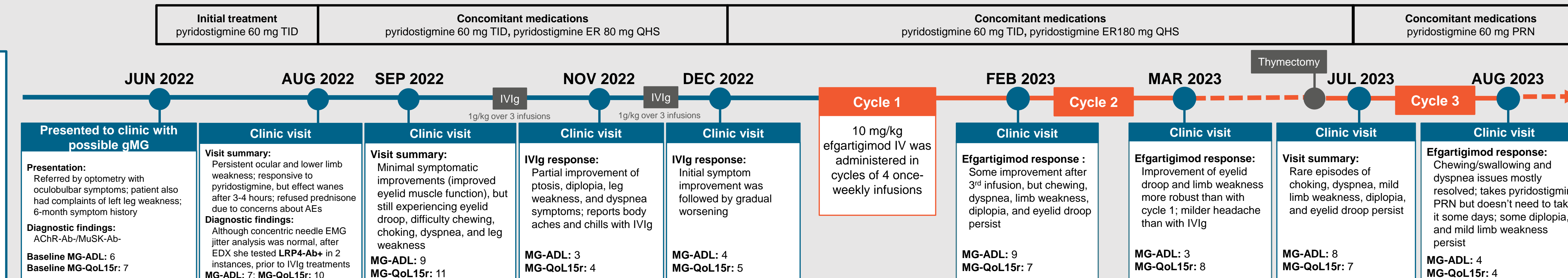


\*Clinically meaningful improvement is defined as a 2-point improvement in MG-ADL score.

### CASE 2: Female Aged 40 Years

#### Presentation:

- Referred from optometrist with suspected gMG due to eye misalignment and eyelid droop
- Noted fatigue while doing chores, difficulty chewing, diplopia, and rare instances of choking
- Neurological examination: Cranial nerves II to XII reveal right upper eyelid ptosis and significant right frontalis muscle weakness
- Medical history notable for migraines with visual aura, ANA+/anti-dsDNA+ without clinical features of lupus



\*Clinically meaningful improvement is defined as a 2-point improvement in MG-ADL score.

**Abbreviations:** AChR-Ab, acetylcholine receptor antibody; ADL, activities of daily living; AE, adverse event; ANA, antinuclear antibody; dsDNA, double-stranded DNA; EDX, electrodiagnostic; EMG, electromyography; ER, extended release; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IV, intravenous; IVIg, intravenous immunoglobulin; LRP4, low-density lipoprotein receptor-related protein 4; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item Scale-Revised; MuSK, muscle-specific kinase; MTX, methotrexate; PRN, by mouth; QD, once daily; QHS, bedtime; QoL, quality of life; QW, once weekly; SSZ, sulfasalazine; TID, 3 times a day.

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