

Symptom Severity Assessment Using MG-ADL Items and Domains in Active-Treatment Phase: vibrance-mg Phase 2/3 Study of Nipocalimab in Adolescents With Generalized Myasthenia Gravis

Tuan Vu,^{1*} Marie Fitzgibbon,² Ibrahim Turkoz,³ Dan Huang,⁴ Carly J. Paoli,⁵ Jelena Dukovski⁴

¹University of South Florida, Morsani College of Medicine, Tampa, FL, USA; ²Johnson & Johnson, Raritan, NJ, USA; ³Johnson & Johnson, Titusville, NJ, USA;

⁴Johnson & Johnson, Neuss, Germany; ⁵Johnson & Johnson, Horsham, PA, USA

*Presenting author

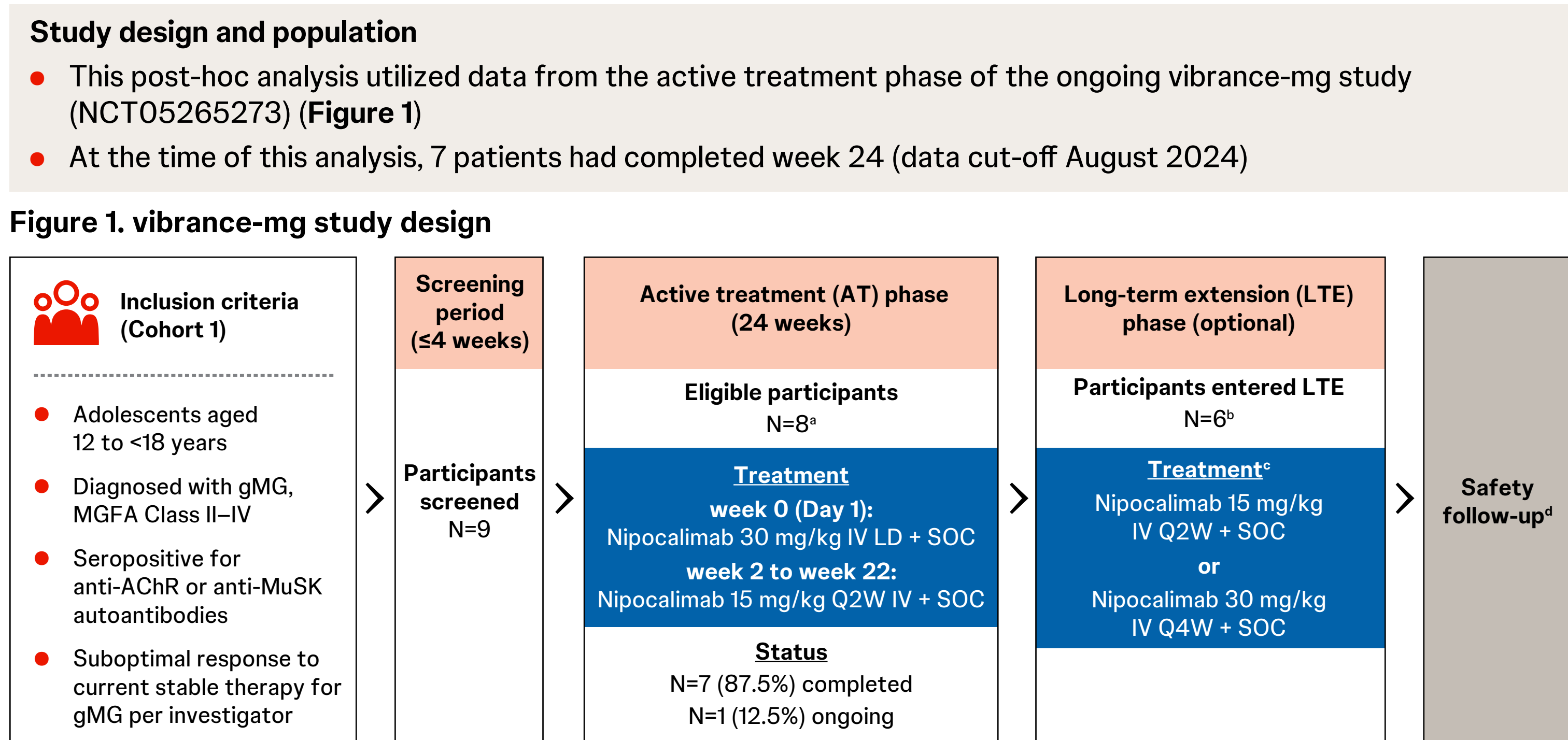
Introduction

- Generalized myasthenia gravis (gMG) is a chronic autoantibody-driven disorder characterized by muscle weakness and fatigue, which can adversely impact daily functioning and quality-of-life^{1,2}
- Nipocalimab is the first neonatal Fc receptor (FcRn) blocker approved for the treatment of gMG in anti-acetylcholine receptor (AChR) or anti-muscle-specific receptor tyrosine kinase (MuSK) antibody-positive adults and adolescents (≥12 years of age) with gMG^{3,4}
- In the pivotal phase 3 Vivacity-MG3 study in adults with gMG, nipocalimab added to standard-of-care (SOC) treatment lowered levels of circulating immunoglobulin G (IgG) and pathogenic IgG autoantibodies and demonstrated sustained disease control⁵
- In the 24-week phase 2/3 vibrance-mg study (NCT05265273) in adolescents (aged 12 to <18 years) with gMG, nipocalimab+SOC demonstrated substantial IgG reduction and sustained disease control with a clinically meaningful reduction in Myasthenia Gravis Activities of Daily Living (MG-ADL) score, a measure of MG symptom severity⁶

Objective

To evaluate the effect of nipocalimab+SOC treatment on MG-ADL items and domains in adolescents with gMG through 24 weeks in the vibrance-mg study

Methods



*One participant failed during the Screening phase. *Out of 7 participants who completed the AT phase, 6 entered the LTE phase. *Four participants switched from Q2W to Q4W at various times and were ongoing in LTE at data cut-off. *Participants who withdraw or discontinue after receiving any amount of study intervention will be required to complete a safety follow-up visit 8 weeks after their last dose. **AChR**=acetylcholine receptor, **AT**=active treatment, **gMG**=generalized myasthenia gravis, **IV**=intravenous, **LD**=loading dose, **LTE**=long-term extension, **MGFA**=Myasthenia Gravis Foundation of America, **MuSK**=muscle-specific receptor tyrosine kinase, **Q2W**=every 2 weeks, **Q4W**=every 4 weeks, **SOC**=standard-of-care.

Analysis

- Baseline floor effects (score=0) distribution was evaluated using item-level frequency distributions
- Mean and median change from baseline for all 4 domains (bulbar, respiratory, limb weakness, ocular) and 8 MG-ADL items were evaluated through week 24. The Wilcoxon signed-rank test was used to assess statistical significance of changes from baseline. The negative change in scores indicate improvement
- Based on items/domains score distributions, those patients with ≥1-point improvement in domains/items were evaluated

MG-ADL items and domains

- The MG-ADL (Figure 2) is an 8-item, clinician-reported assessment based on patient recall of activities of daily living across four muscle function groups of bulbar, respiratory, limb function, and ocular muscles
- The MG-ADL score ranges from 0 to 24; higher scores mean worse symptoms and more difficulty in daily activities
- A change of at least 1-point on MG-ADL items may be meaningful from an individual patient's perspective; for example, a 1-point change in the respiratory domain could be the difference between experiencing shortness of breath or requiring a ventilator

Figure 2: MG-ADL items and domains

Domain function	Item	Score=0	Score=1	Score=2	Score=3
Bulbar	Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal speech, but can be understood	Difficult to understand speech
	Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube
	Swallowing	Normal	Rare episode of choking	Frequent choking necessitating change in diet	Gastric tube
Respiratory	Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence
Limb Function	Brushing teeth or hair	Normal	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions
	Arising from chair	Normal	Mild, sometimes uses arms	Moderate, always uses arms	Severe, required assistance
Ocular	Double vision	Normal	Occurs, but not daily	Daily, but not constant	Constant
	Eyelid droop	Normal	Occurs, but not daily	Daily, but not constant	Constant
		Your Total Score =			

MG-ADL=Myasthenia Gravis-Activities of Daily Living.

Results

Demographics and baseline characteristics

- At baseline (N=8), mean (range) MG-ADL domain scores were higher for ocular and bulbar domains (Table 1)
 - Bulbar 1.31 (0–3)
 - Respiratory 0.25 (0–1)
 - Limb weakness 0.69 (0–3)
 - Ocular 2.13 (1–3)

Table 1. Demographics and baseline characteristics

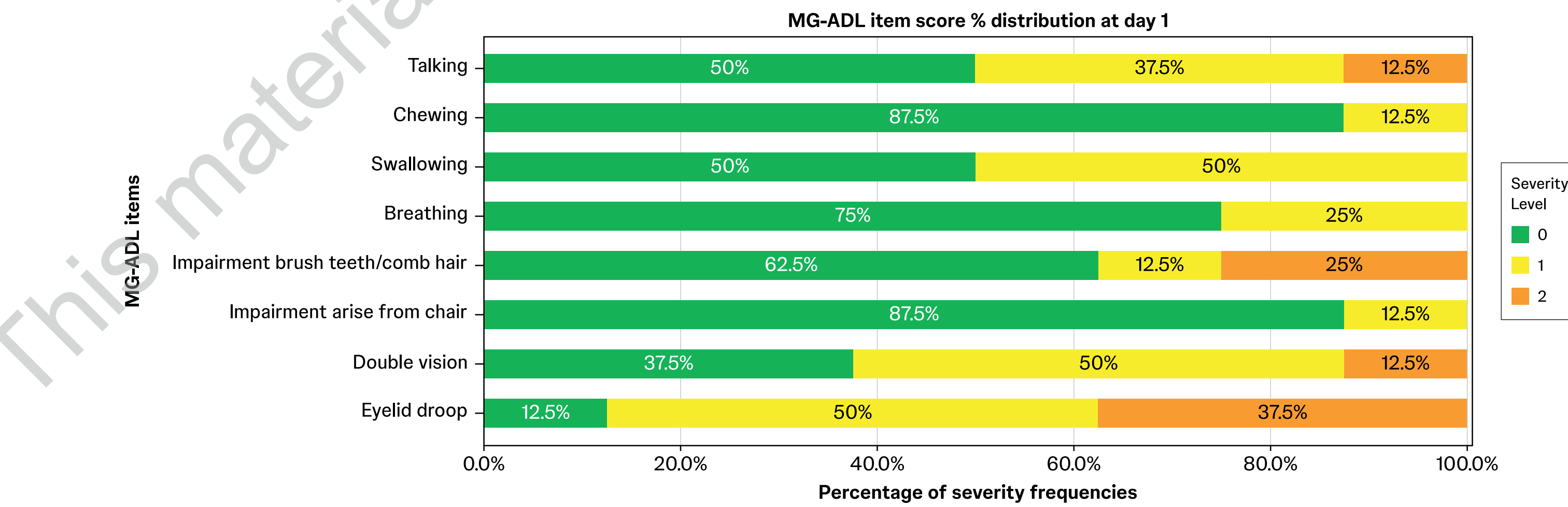
	(N=8)
Demographics	
Age, mean (range), years	13.9 (12–16)
Female, n (%)	7 (87.5)
Race, n (%)	
Asian	5 (62.5)
Black or African American	1 (12.5)
Unknown	2 (25.0)
Ethnicity, n (%)	
Hispanic or Latino	1 (12.5)
Not Hispanic or Latino	6 (75.0)
Unknown	1 (12.5)
Autoantibody type, anti-AChR+, n (%)	8 (100)
Baseline MG-ADL score, median (range)	3.5 (2.5–9.5)
Duration of MG, median (range), years	3.6 (0.8–11.5)
Baseline MG-ADL domain scores, Mean (SD); median (range)	
Bulbar	1.31 (1.13); 1.25 (0.0–3.0)
Respiratory	0.25 (0.38); 0.00 (0.0–1.0)
Limb function	0.69 (1.03); 0.25 (0.0–3.0)
Ocular	2.13 (0.74); 2.25 (1.0–3.0)
Baseline MG-ADL item scores, Mean (SD); median (range)	
Chewing	0.38 (0.44); 0.25 (0.0–1.0)
Eyelid droop	1.31 (0.59); 1.25 (0.5–2.5)
Double vision	0.81 (0.75); 1.00 (0.0–2.0)
Talking	0.50 (0.53); 0.50 (0.0–1.5)
Swallowing	0.44 (0.50); 0.25 (0.0–1.0)
Impairment brush teeth/comb	0.56 (0.73); 0.25 (0.0–2.0)
Breathing	0.25 (0.36); 0.00 (0.0–1.0)
Impairment arise from chair	0.13 (0.35); 0.00 (0.0–1.0)

Note: Baseline values are mean of domain scores and item scores are listed as an average of screening value and day 1 value. **AChR**=acetylcholine receptor, **MG**=myasthenia gravis, **MG-ADL**=Myasthenia Gravis-Activities of Daily Living.

Baseline MG-ADL item analyses

- In 8 participants symptom burden was mainly concentrated in the ocular and bulbar items (Figure 3)
- Every item had at least some participants scoring above 0, and median item scores ranged 0.0–2.5

Figure 3. Baseline MG-ADL item score distribution



Domain score: Mean change and ≥1-point improvement

- At week 24, mean (SD) and median (range) MG-ADL domain scores were: bulbar 0.43 (0.53) and 0.00 (0.0; 1.0), respiratory 0.29 (0.49) and 0.00 (0.0; 1.0), limb weakness 0.43 (1.13) and 0.00 (0.0; 3.0), and ocular 0.57 (0.79) and 0.00 (0.0; 2.0), respectively
- The highest change from baseline (CFB) was observed in the ocular domain (mean [SD] –1.64 [0.80]; median [range] –1.50 [–3.0; –0.5]) followed by bulbar (mean [SD] –0.79 [0.76]; median [range] –0.50 [–2.0; 0.0]), limb weakness (mean [SD] –0.21 [0.40]; median [range] 0.00 [–1.0; 0.0]), and respiratory (mean [SD] 0.07 [0.45]; median [range] 0.00 [–0.5; 1.0]) (Figure 4)
- At week 24, highest (85.7% of patients) ≥1-point improvement was noted in the ocular domain, while 42.9% of patients achieved this in bulbar domain and 14.3% of patients achieved this in limb function (Figure 5)

Figure 4. Mean change from baseline to week 24 in MG-ADL domain scores (n=7)

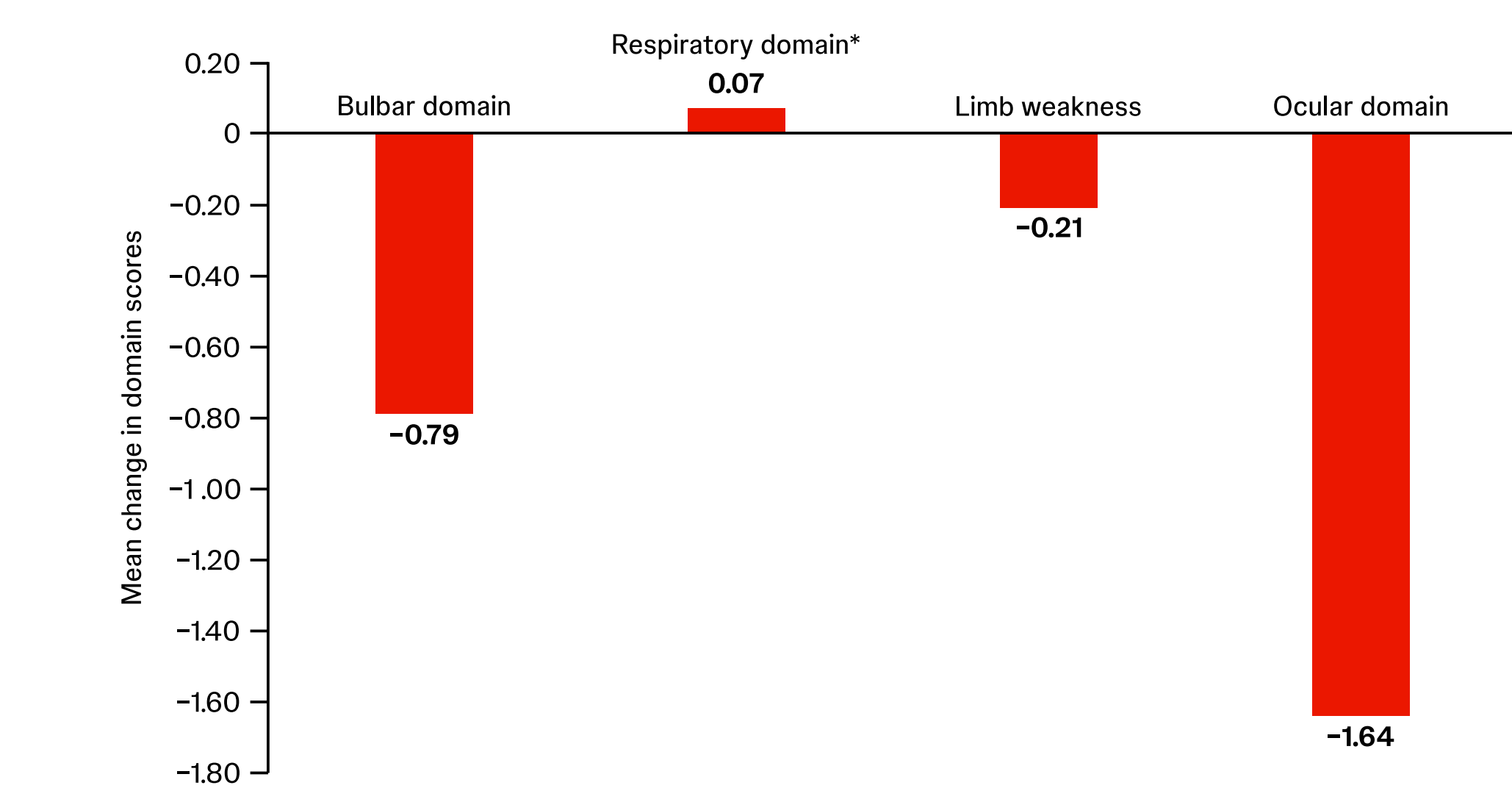
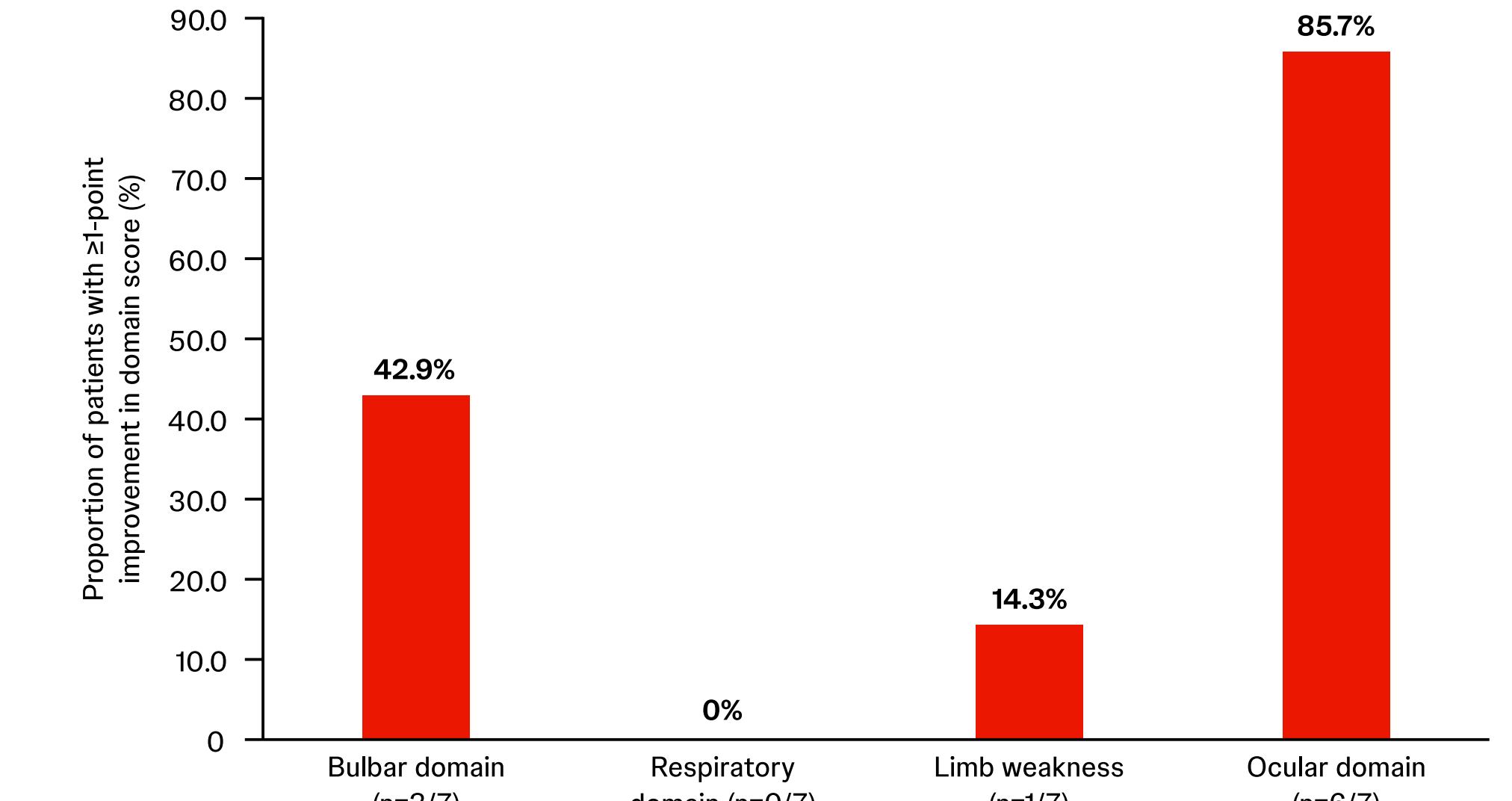


Figure 5. Patients achieving ≥1-point improvement in MG-ADL domain scores



Item score: Mean change and ≥1-point improvement

- At week 24, the mean (SD)/median (range) item scores were highest for eyelid droop 0.29 (0.49)/0.00 (0.0; 1.0), double vision 0.29 (0.49)/0.00 (0.0; 1.0), talking 0.29 (0.49)/0.00 (0.0; 1.0), brush teeth/ comb hair 0.29 (0.76)/0.00 (0.0; 2.0), breathing 0.29 (0.49)/0.00 (0.0; 1.0), followed by swallowing 0.14 (0.38)/0.00 (0.0; 1.0), impair arise from chair 0.14 (0.38)/0.00 (0.0; 1.0), and chewing 0.00 (0.00)/0.00 (0.0; 0.0)
- The highest CFB was observed in the eyelid droop (mean [SD] –1.00 (0.41); median [range] –1.00 [–1.5; –0.5]), followed by double vision (mean [SD] –0.64 (0.63); median [range] –1.00 [–1.5; 0.0]) and chewing (mean [SD] –0.36 (0.48); median [range] 0.00 [–1.0; 0.0]); statistically significant improvements were observed in the ocular domain and eyelid droop item (p=0.016) (Figure 6)
- At week 24, 71.4% of patients achieved a ≥1-point improvement in the eyelid droop item, while 57.1% of patients achieved this in double vision item, and 28.6% of patients achieved for chewing item (Figure 7)

Figure 6. Mean change from baseline to week 24 in MG-ADL item scores (n=7)

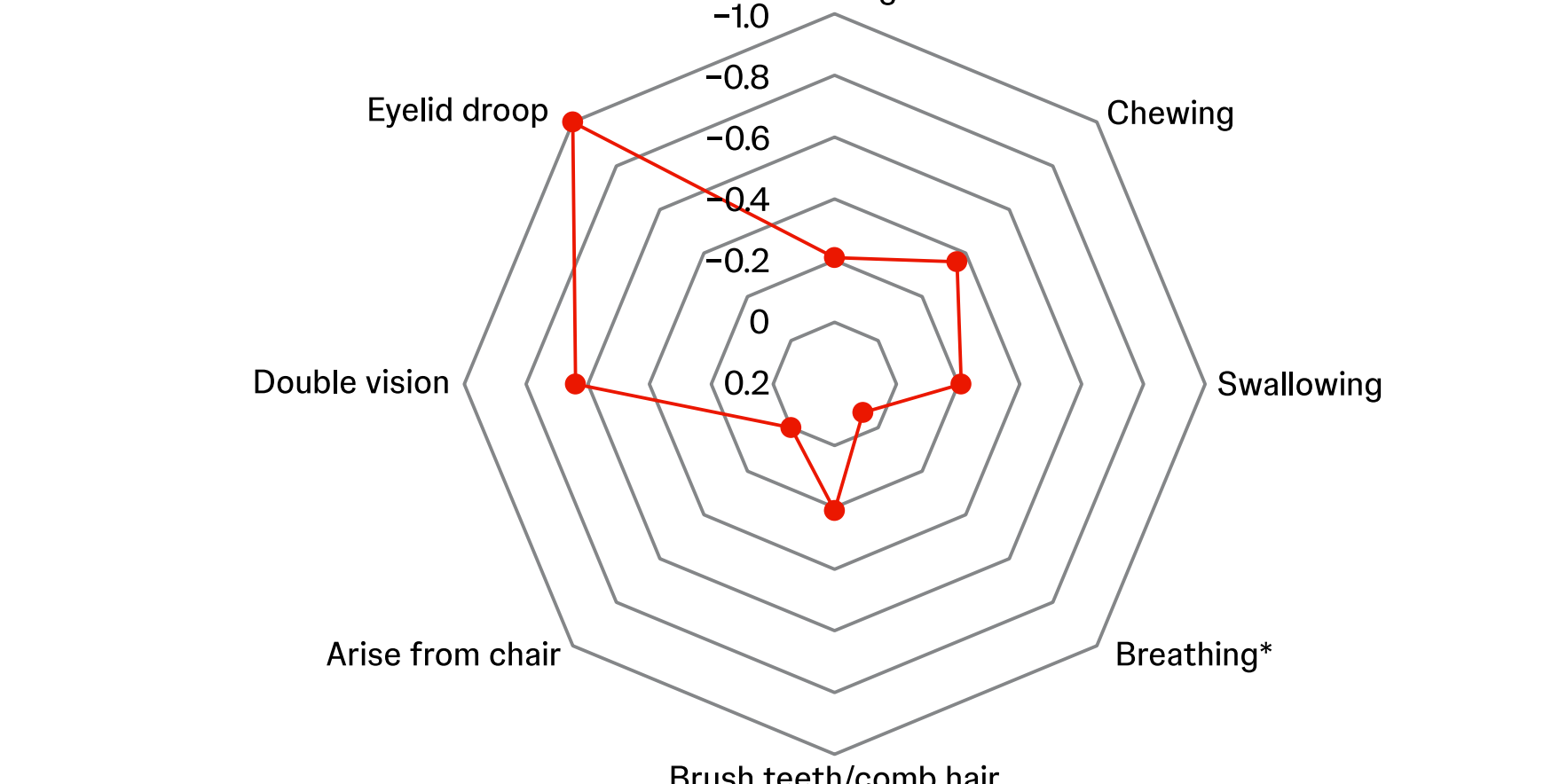


Figure 7. Patients achieving ≥1-point improvement in MG-ADL item domain scores

