

Safety and Efficacy of Claseprubart, an Active C1s Inhibitor, in Patients with Generalized Myasthenia Gravis

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Disclosures

This study was sponsored by Dianthus Therapeutics, New York, USA.

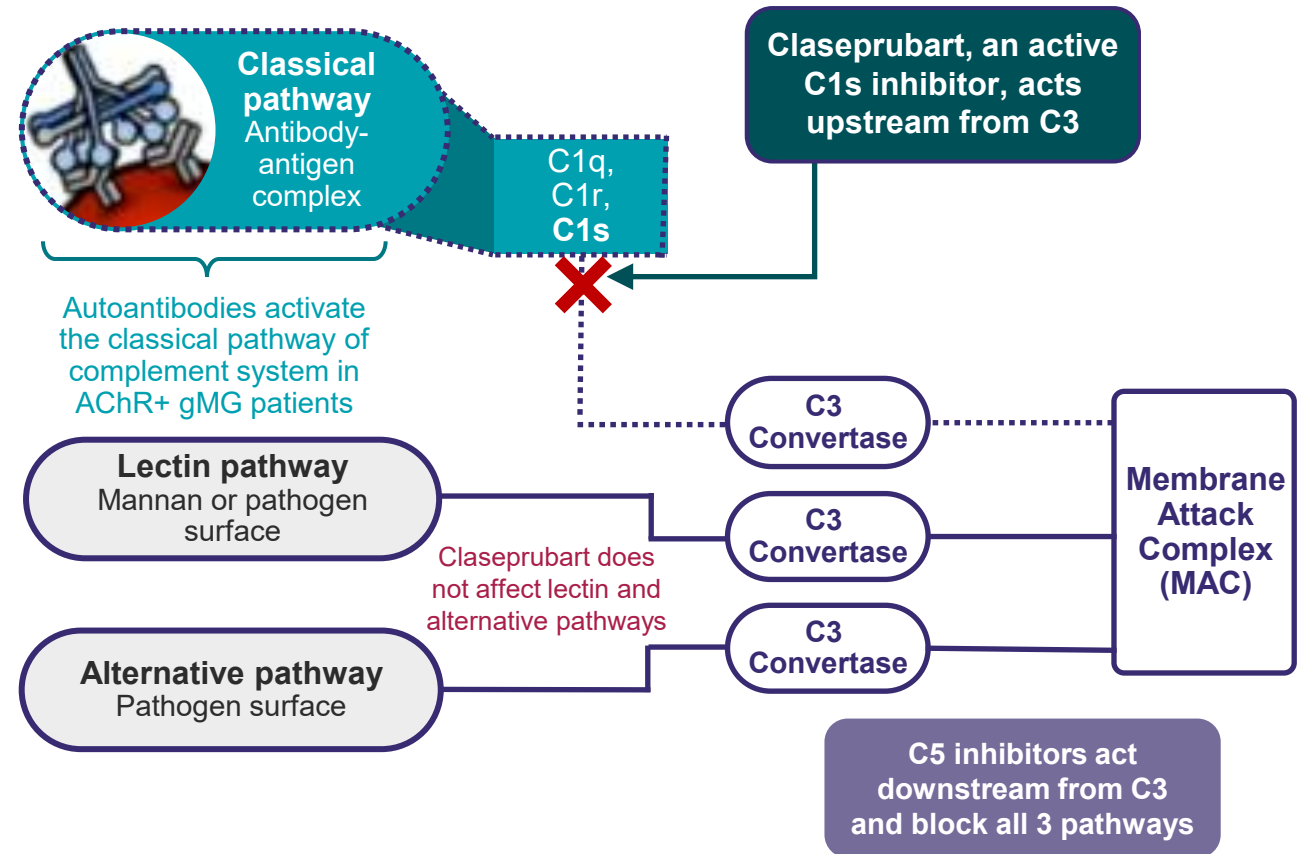
Dr. Vu has served as:

- USF Site Principal Investigator for MG clinical trials sponsored by Alexion/AstraZeneca Rare Disease, Amgen, argenx, Cartesian Therapeutics, COUR, Dianthus Therapeutics, EMD Serono, ImmunAbs, Immunovant, Johnson & Johnson, NMD Pharma, Novartis, Regeneron, Sanofi, VOR, Vertex, and UCB.
- Speaker for Alexion/AstraZeneca Rare Disease, Amgen, argenx, CSL Behring, Novartis, and Johnson & Johnson.
- Advisory board member and/or consultant for Alexion/AstraZeneca Rare Disease, argenx, Amgen, Dianthus Therapeutics, Johnson & Johnson, NMD Pharma, Takeda, and VOR.
- Speaker/presenter in CME events sponsored by AcademicCME, CMEO, PER, PVI, and MedLive.

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Introduction

- **Claseprubart** (DNTH103) targets the classical complement pathway through **active C1s (aC1s)** inhibition.
- **Claseprubart** is the **first aC1s inhibitor** evaluated in **generalized myasthenia gravis (gMG)**.
- Unlike **C5 inhibition**, which blocks **all complement pathways** (classical, lectin, and alternative) downstream, **claseprubart aC1s inhibition specifically targets the classical pathway upstream**, offering a more focused approach, with the potential to reduce the activity of upstream components, including C3a and C3b
- **Claseprubart preserves lectin and alternative complement activity**, which may address MG disease pathology while reducing the risk of severe encapsulated bacterial infections seen with broad C5 inhibition.



MaGic is a global Phase 2 trial in AChR+ gMG patients

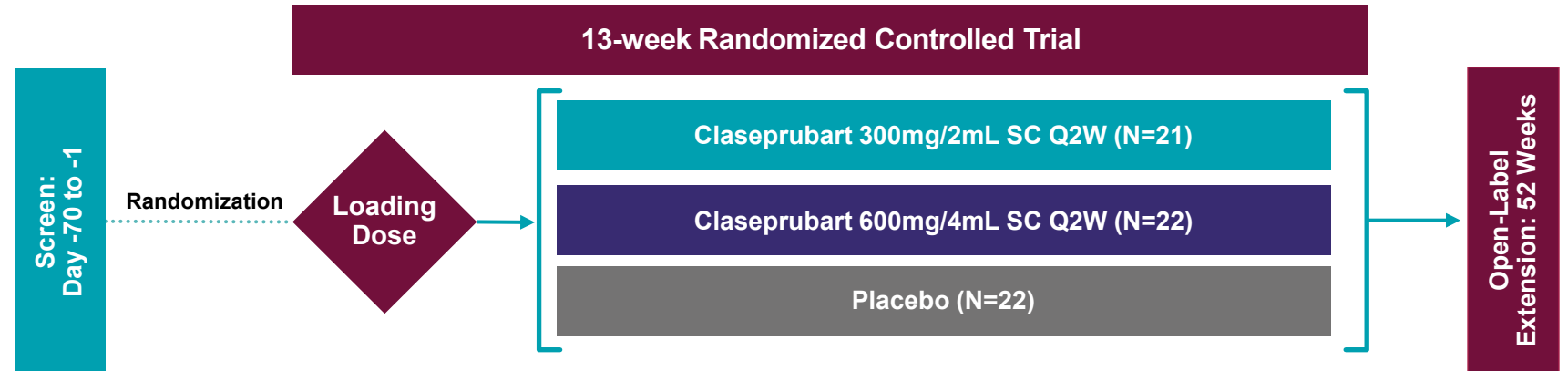
A global, multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety, efficacy, and PK/PD of claseprubart administered subcutaneously following initial loading dose

Highlights

- **Design:** ~60 male and female subjects randomized to receive either claseprubart or placebo for 13 weeks
- **Inclusion:** ≥18 years old with AChR antibody + gMG, must be on an at least one immunosuppressant
- **Dosing:** IV Loading Dose* followed by 300mg/2mL or 600mg/4mL SC Q2W starting Day 7

Endpoints

- **Primary:** Safety
- **Secondary / Exploratory:** Efficacy (MG-ADL, QMG, MSE, MGC, MG-QoL-15r)



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Trial enrollment exceeded target, with 65 participants enrolled

Baseline characteristics were generally well-balanced across treatment arms

	Placebo (N=22)	Claseprubart 300mg Q2W (N=21)	Claseprubart 600mg Q2W (N=22)
Age, mean (SD), years	52.2 (16.5)	57.1 (13.7)	55.3 (12.0)
Male, n (%)	13 (59%)	14 (67%)	10 (45%)
Weight, mean (SD), pounds	195.0 (48.0)	192.5 (35.5)	179.0 (35.4)
Duration of disease, median (range), years	7.7 (0.4–21.2)	3.0 (0.5–22.1)	7.6 (1.0–37.3)
MG-ADL score at baseline, mean (SD)	8.5 (2.9)	8.2 (2.2)	8.4 (2.6)
QMG score at baseline, mean (SD)	14.2 (5.8)	12.2 (2.7)	12.2 (3.6)
MG Composite score at baseline, mean (SD)	15.0 (7.8)	16.3 (4.5)	16.0 (5.3)
MG-QoL-15r score at baseline, mean (SD)	14.3 (7.0)	15.4 (6.6)	14.9 (5.9)
MGFA class at screening, n (%)			
II	7 (32%)	11 (52%)	12 (55%)
III	12 (55%)	10 (48%)	9 (41%)
IVa	3 (14%)	0 (0%)	1 (5%)
Prior thymectomy, n (%)	8 (36%)	6 (29%)	7 (32%)
Baseline corticosteroid use, n (%)	19 (86%)	17 (81%)	20 (91%)
Number of ISTs at baseline, n (%)			
1	11 (50%)	10 (48%)	12 (55%)
>1	11 (50%)	11 (52%)	10 (45%)
FcRn use in prior 24 months, n (%)	0 (0%)	1 (5%)	0 (0%)

Claseprubart was generally well-tolerated

	Placebo (N=22)	Claseprubart 300mg Q2W (n=21)	Claseprubart 600mg Q2W (n=22)
Clinical adverse events (AEs) ¹	11 (50.0%)	13 (61.9%)	15 (68.2%)
Related serious AEs	1 (4.5%)	0 (0%)	0 (0%)
RCT discontinuation due to related AE	0 (0%)	0 (0%)	0 (0%)
Infections	10 (45.5%)	5 (23.8%)	6 (27.3%)
Related serious infections	1 (4.5%)	0 (0%)	0 (0%)
Injection site reactions ²	0 (0%)	2 (9.5%)	2 (9.1%)
Newly positive for anti-nuclear antibodies (ANA) ³	0 (0%)	1 (5.9%)	8 (36.4%)
Myasthenia gravis exacerbations ⁴	2 (9.1%)	2 (9.5%)	2 (9.1%)*
Rashes	0 (0%)	0 (0%)	0 (0%)
Arthralgia	1 (4.5%)	1 (4.8%)	0 (0%)

Comparable clinical safety profile to placebo with remarkably benign administration, no encapsulated bacterial infections and no symptoms indicative of autoimmune activation

1. Excludes events in the investigations System Organ Class (MedDRA). 2. All injection site reactions were mild to moderate. 3. Represents participants who were ANA negative at baseline and tested positive at ≥1:320 at any point during RCT (percentages calculated from n=17 for 300mg arm and n=22 for 600mg arm). An ANA titer of ≥1:320 was an exclusion criterion for the clinical trial protocol. At end of RCT (Week 13), 2 of the 8 patients in 600mg arm tested negative for ANA, 2 of the 8 patients in 600mg arm remained positive but at <1:320. 4. Defined as worsening of disease regardless of receiving rescue treatment. No patients required respiratory intervention and one patient in each arm received rescue treatment for the exacerbation. *One patient had MG worsening attributed to missed Mestinon doses on the first day of claseprubart dosing (Day 1).

Most common adverse events

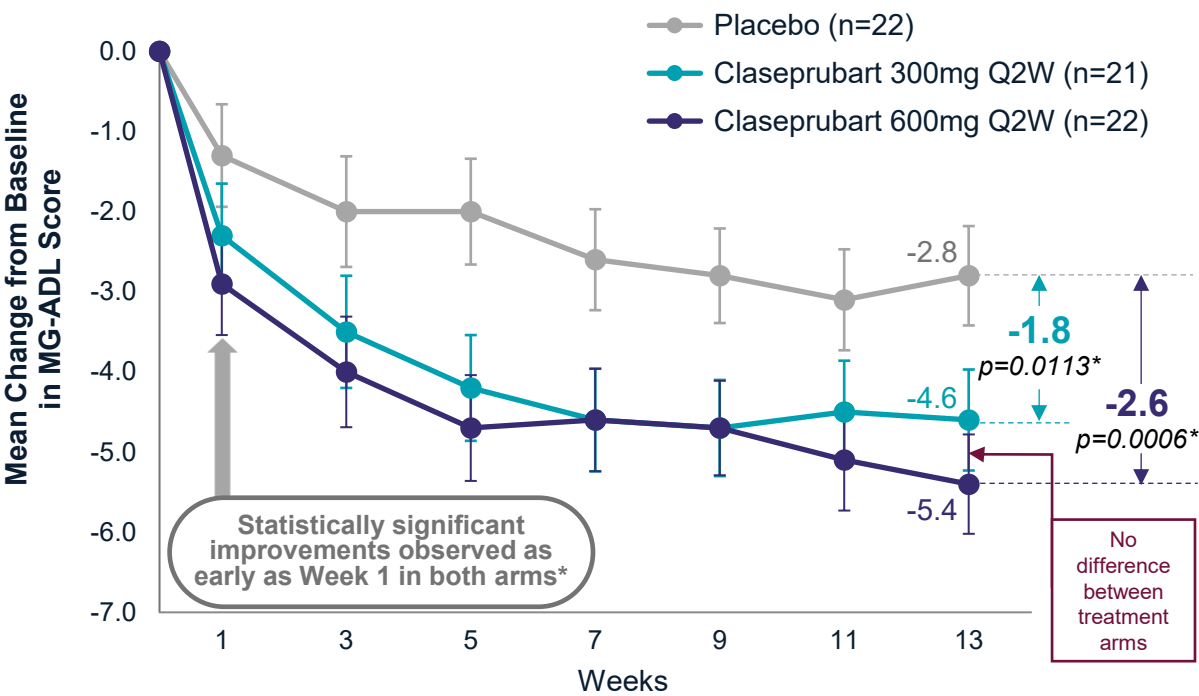
>5% in any treatment arm

	Placebo (N=22)	Claseprubart 300mg Q2W (n=21)	Claseprubart 600mg Q2W (n=22)
Nasopharyngitis	1 (4.5)	3 (14.3%)	3 (13.6)
Lipase increased	0 (0%)	3 (14.3%)	2 (9.1%)
Upper respiratory tract infection	3 (13.6%)	0 (0%)	1 (4.5%)
Sinusitis	2 (9.1%)	0 (0%)	0 (0%)
Headache	2 (9.1%)	0 (0%)	0 (0%)
Diarrhea	2 (9.1%)	0 (0%)	0 (0%)

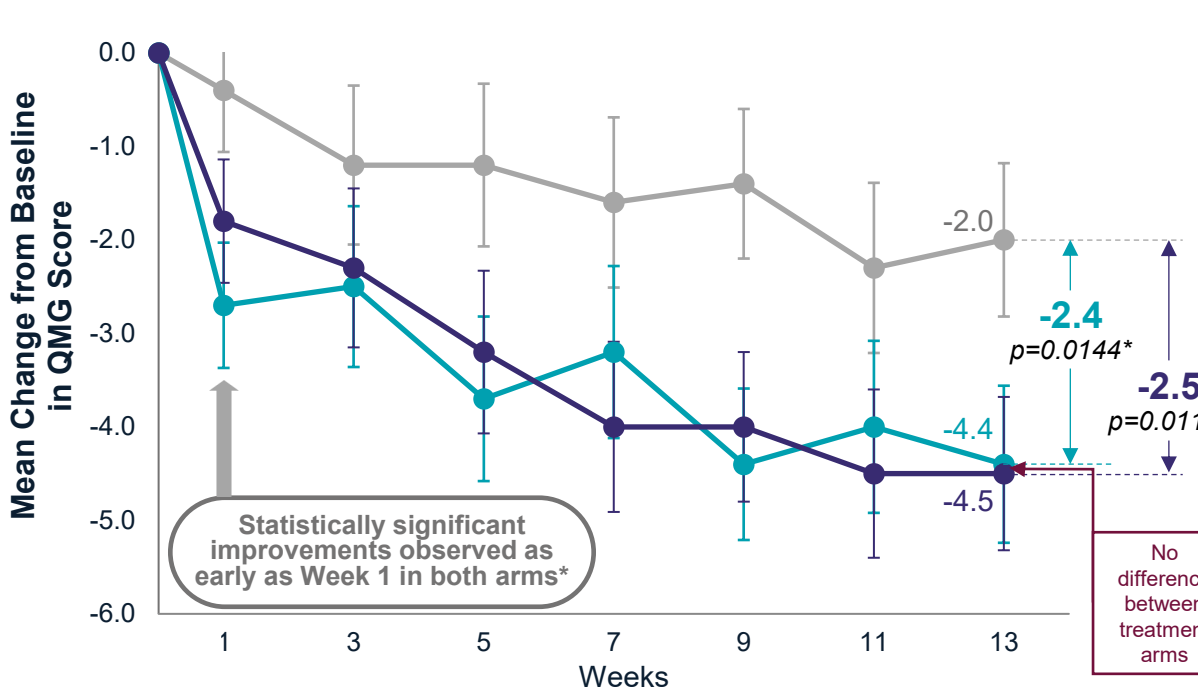
All treatment-related adverse events in both claseprubart arms were mild or moderate in severity.

Claseprubart arms demonstrated rapid, sustained, and clinically meaningful improvements in MG-ADL and QMG scores

Mean Change in MG-ADL Score



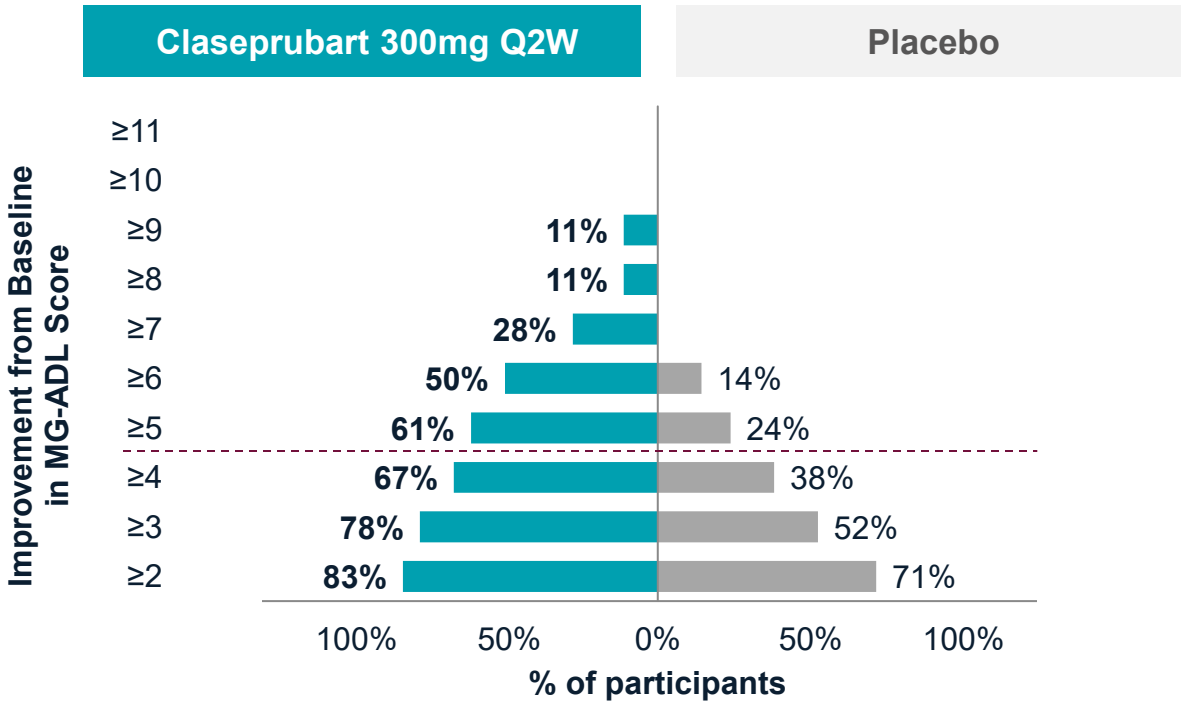
Mean Change in QMG Score



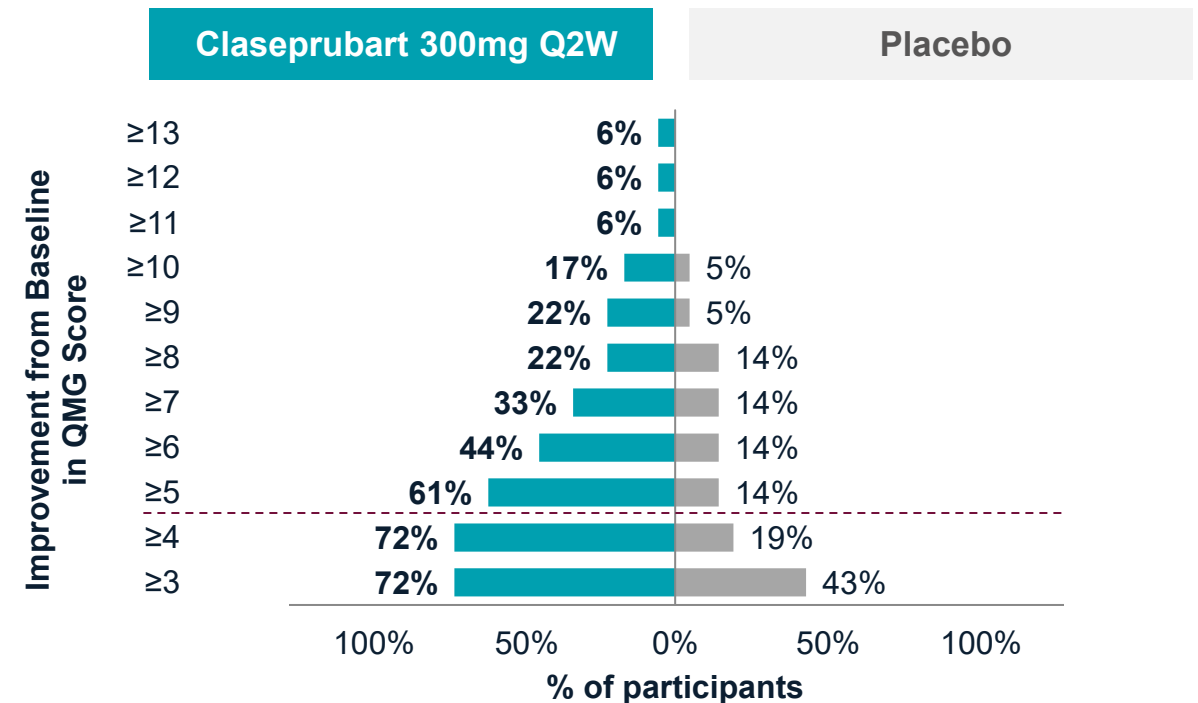
MG-ADL and QMG improvements for patients treated with claseprubart were rapid, sustained, clinically meaningful and statistically significant as early as Week 1

>60% of patients on claseprubart 300mg achieved ≥5 point improvement in MG-ADL and QMG

Improvement in MG-ADL Score at Week 13

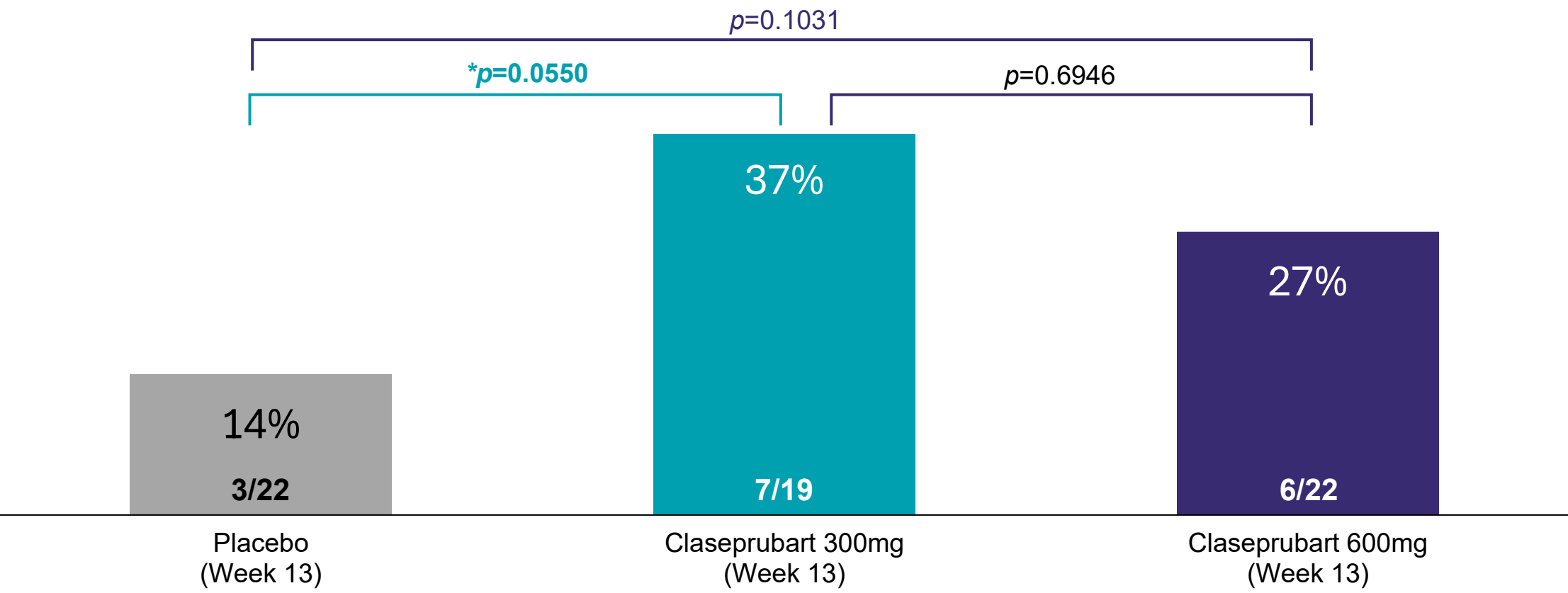


Improvement in QMG Score at Week 13



Patients across both treatment arms achieved robust improvements in MG-ADL and QMG at Week 13

Claseprubart 300mg arm more likely to achieve MG-ADL minimal symptom expression vs. placebo at Week 13



300mg claseprubart-treated patients were more likely to achieve minimal symptom expression; median time to MSE was 3 weeks

Across key efficacy measures, claseprubart delivered clinically meaningful responses

	Placebo	Claseprubart 300mg Q2W		Claseprubart 600mg Q2W	
		Absolute	Placebo-adjusted	Absolute	Placebo-adjusted
MG-ADL mean change from baseline at Week 13	-2.8	-4.6	-1.8 (P=0.0113)*	-5.4	-2.6 (P=0.0006)*
QMG mean change from baseline at Week 13	-2.0	-4.4	-2.4 (P=0.0144)*	-4.5	-2.5 (P=0.0111)*
MSE at Week 13	14%	37%	23% (P=0.0550)*	27%	13% (P=0.1031)
MGC mean change from baseline at Week 13	-3.1	-8.7	-5.6 (P=0.0008)*	-8.6	-5.5 (P=0.0008)*
MG-QoL-15r mean change from baseline at Week 13	-3.9	-6.1	-2.2 (P=0.0414)*	-5.4	-1.5 (P=0.1122)

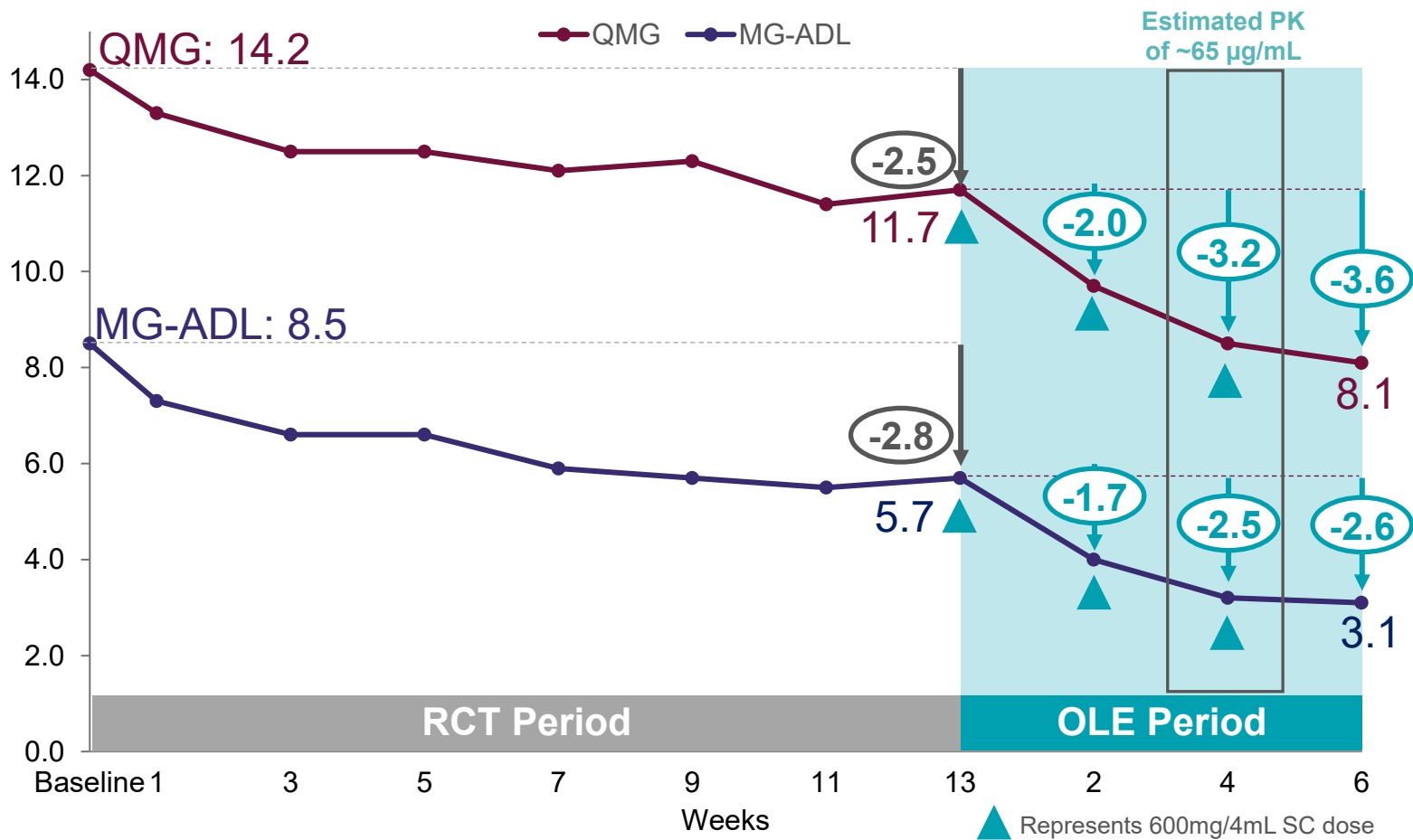
Claseprubart 300mg Q2W treatment arm achieved statistical significance vs. placebo across all five key efficacy measures

*One-sided p-values are presented for comparisons of claseprubart vs placebo, with any p-value below 0.1 considered nominally statistically significant.

OLE data support addition of lower dose of 300mg Q4W in Ph. 3

PK levels approximately half of 300mg Q2W steady state resulted in robust reductions on MG-ADL & QMG

Mean Change in Placebo Patients' MG-ADL and QMG Score from RCT Baseline to OLE Week 6



- PBO Patients Entering OLE Received 600mg/4mL Q2W w/ No Loading Dose**
- PK of ~65 µg/mL at week 4 after only two 600mg/4mL doses is substantially lower than steady state seen with 300mg/2mL dosing of ~100-120 µg/mL
 - Robust reductions in MG-ADL and QMG are achieved by week 4, after just two 600mg/4mL doses and remain stable in subsequent weeks
 - Growing external evidence further supports that lower levels of complement inhibition (<90%) may be sufficient for efficacy in gMG¹

EMERGE is a global Ph. 3 trial evaluating Q4W and Q2W S.C. claseprubart in AChR+ gMG; top-line data 2H'28

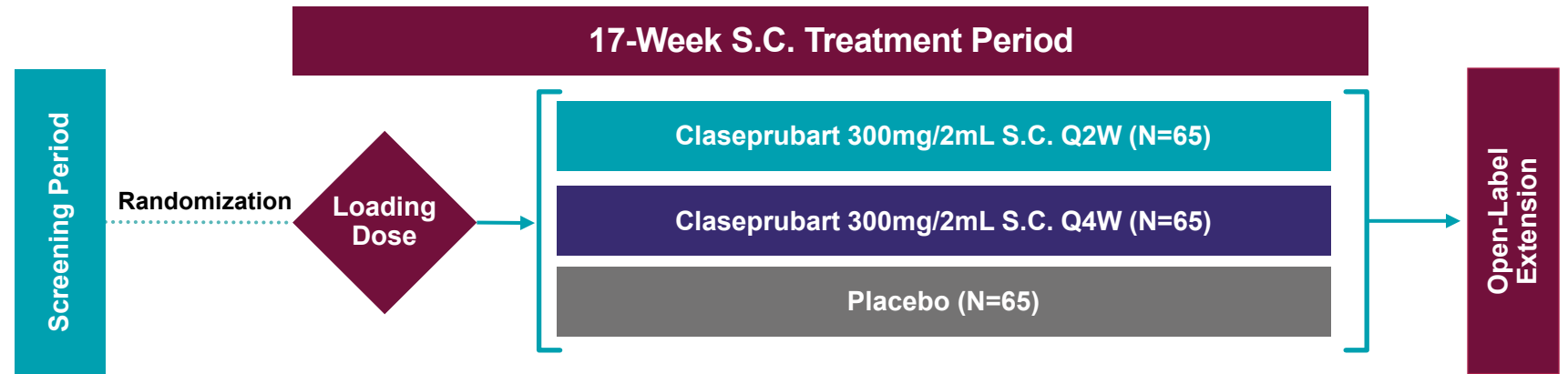
No ANA screening exclusion criteria or routine ANA testing during RCT or OLE, inclusion criteria of MG-ADL of ≥ 6 and QMG of ≥ 10 , and 17-week S.C. treatment period

Highlights

- **Design:** Male and female subjects randomized to receive either claseprubart or placebo for 17 weeks
- **Inclusion:** ≥ 18 years old with AChR antibody + gMG, **MG-ADL of ≥ 6 and QMG of ≥ 10**
- **Dosing:** I.V. Loading Dose followed by 300mg/2mL S.C. Q2W or **Q4W** starting Day 7
- **No ANA screening exclusion criteria or routine ANA testing** during the RCT or OLE

Endpoints

- **Primary:** MG-ADL change from baseline
- **Secondary / Exploratory:** Efficacy (QMG, MSE, MGC, MG-QoL-15r)



Potential to further enhance best-in-class differentiation on efficacy and dosing convenience with QMG screening criteria and 300mg/2mL Q4W dosing

Conclusions

- Claseprubart treatment was well tolerated and resulted in clinically meaningful and statistically significant improvements in the 300 mg arm across key assessments
- The benefit/risk profile of both doses was similar, supporting research focus on the lower dose
- Claseprubart has the potential to deliver meaningful benefit to AChR+ gMG patients via infrequent self administered SC injections and likely reduced risk of encapsulated bacterial infections versus C5 inhibitors
- Claseprubart 300 Q2W and Q4W will be evaluated in an upcoming Phase 3 gMG trial
 - Claseprubart is also advancing in a Phase 3 study for CIDP (CAPTIVATE) and a Phase 2 study for MMN (MOMENTUM).

