68

Evaluation of Cardiovascular Comorbidity Burden in Patients With Generalized Myasthenia Gravis Treated With Efgartigimod

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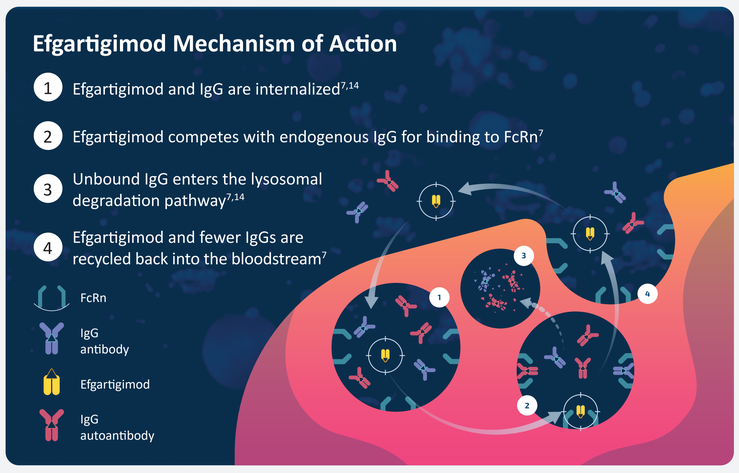
INTRODUCTION

- MG is a rare, chronic, and severe autoimmune disease associated with pathogenic autoantibodies directed against the NMJ[1-3]
- CV comorbidities can be common in patients with MG and may be exacerbated by MG treatments, emphasizing the importance of HCP awareness of CV risk when considering MG treatment options[4,5]
  - For example, dyslipidemia (a known risk factor for CV diseases) can occur in 1 of 4 patients with MG and may impact MG treatment and management strategies[6]
- Efgartigimod is a human IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared with endogenous IgG and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[7,8]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production or other parts of the immune system, and does not decrease albumin or increase cholesterol levels [7-11]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[12,13]
- Albumin has a role in modulating cholesterol transport and vascular function, which can influence lipid levels and CV disease[11]



METHODS

OBJECTIVE

- To assess frequency of CV risk factors in pooled participants with gMG receiving intravenous efgartigimod or subcutaneous efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20)
- To assess CV-related AEs and impact on LDL levels in participants with gMG receiving intravenous efgartigimod compared with placebo

	ADAPT	ADAPT-SC	ADAPT NXT
Phase	3	3	3b
Dosing	EFG IV 10 mg/kg	EFG IV 10 mg/kg or EFG PH20 SC 1000 mg	EFG IV 10 mg/kg
Participants	EFG IV: n=84 PBO: n=83	EFG IV: n=55 EFG PH20 SC: n=55	EFG IV: N=69
Study duration	26 weeks	10 weeks	126 weeks

ANALYSIS STRATEGY

- To assess baseline CV risk factors and CV comorbidities, participants from ADAPT, ADAPT-SC, and ADAPT NXT were pooled and divided by the presence and absence of CV risk factors at baseline[a]
- To understand the impact of efgartigimod treatment, data from ADAPT were used to compare efgartigimod and placebo groups

[a]Preferred terms for CV risk factors included: atrial fibrillation, VTE (DVT/PE), diabetes, metabolic syndrome, hypertension, CKD, and obstructive sleep apnea. CV comorbidities included: coronary heart disease, aortic atherosclerosis, thoracic/abdominal aortic aneurysm, MI, acute coronary syndrome, angina pectoris, ischemic heart disease, heart failure, cerebrovascular disease, transient ischemic attack, PAD, and obesity (BMI >30).

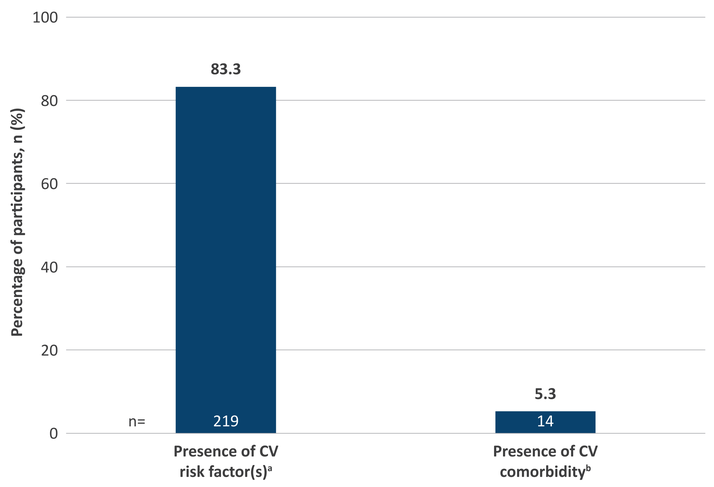
RESULTS

TABLE 1. Baseline Demographics and Disease Characteristics Among Pooled Participants by Baseline CV Risk[a]

	CV risk at baseline (n=219)	No CV risk at baseline (n=44)
Age, years, mean (SD)	55.2 (14.7)	34.2 (8.8)
Age category, years, n (%)		
Age 18-<65	153 (69.9)	44 (100.0)
Age ≥65	66 (30.1)	0
Sex at birth, female, n (%)	132 (60.3)	39 (88.6)
Race, n (%)		
American Indian or Alaska Native	2 (0.9)	0
Asian	15 (6.8)	3 (7.0)
Black or African American	5 (2.3)	0
Multiple	1 (0.5)	1 (2.3)
White	195 (89.0)	39 (90.7)
Other	1 (0.5)	0
BMI, kg/m^2, mean (SD)	29.8 (7.2)	22.8 (3.0)
Corticosteroid therapy, n (%)	144 (65.8)	29 (65.9)
Time since diagnosis, years, mean (SD)	7.9 (8.3)	8.6 (6.6)
Prior thymectomy, n (%)	80 (36.5)	28 (63.6)
MGFA classification at screening, n (%)		
Class II	91 (41.6)	17 (38.6)
Class III	120 (54.8)	25 (56.8)
Class IV	8 (3.7)	2 (4.5)
Total MG-ADL score, mean (SD)	9.1 (2.8)	8.9 (2.8)

[a]Denominator for the percentage calculations was the total number of participants per treatment in the safety analysis set, excluding missing value.

FIGURE 1. Frequency of CV Risk and CV Comorbidity at Baseline Among Pooled Participants (N=263)



[a]CV risk was defined as having ≥1 of the following: ≥1 CV risk factor terms in medical history; baseline BMI >30; ≥1 baseline laboratory measure was high for total cholesterol, LDL, triglyceride, HgA1C, BUN, or creatinine; or HDL was low. [b]CV comorbidity was defined as participants with ≥1 CV morbidity terms in their medical history.

FIGURE 2. Frequency of CV Risk and CV Comorbidity at Baseline Among Participants in ADAPT (N=167)

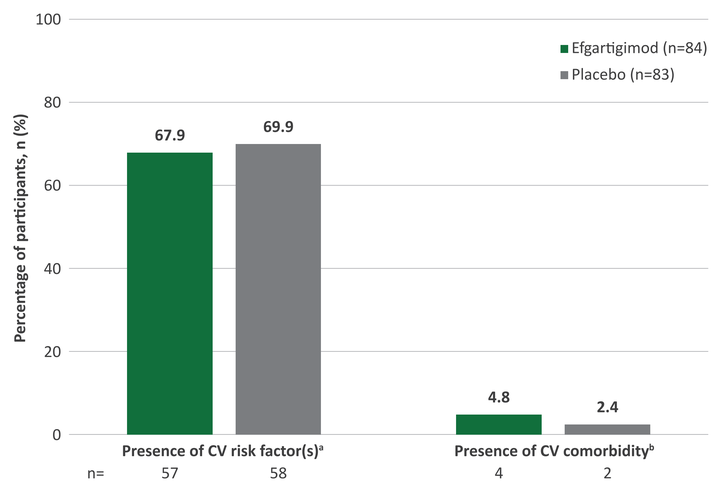


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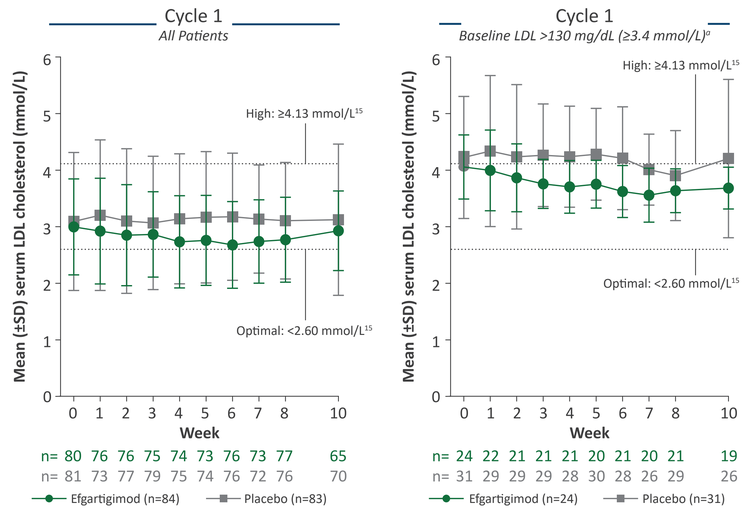
TABLE 2. CV-Related TEAEs by MedDRA System Organ Class and Preferred Term by CV Risk at Baseline in ADAPT[a]

System Organ Class Preferred Term	CV risk at baseline						No CV risk at baseline					
	Efgartigimod (n=57)			Placebo (n=58)			Efgartigimod (n=27)			Placebo (n=25)		
	n	%	m	n	%	m	n	%	m	n	%	m
Any TEAE	50	87.7	196	50	86.2	207	15	55.6	56	20	80.0	63
Cardiac disorders	0	-	-	3	5.2	4	2	7.4	2	1	4.0	1
Angina pectoris	0	-	-	1	1.7	1	0	-	-	0	-	-
Atrial fibrillation	0	-	-	2	3.4	2	0	-	-	0	-	-
Cyanosis	0	-	-	0	-	-	1	3.7	1	0	-	-
Mitral valve prolapse	0	-	-	0	-	-	1	3.7	1	0	-	-
Myocardial ischemia	0	-	-	0	-	-	0	-	-	1	4.0	1
Tachycardia	0	-	-	1	1.7	1	0	-	-	0	-	-
Vascular disorders	7	12.3	9	4	6.9	4	0	-	-	2	8.0	2
Hematoma	1	1.8	1	0	-	-	0	-	-	0	-	-
Hot flush	1	1.8	2	0	-	-	0	-	-	0	-	-
Hypertension	3	5.3	4	4	6.9	4	0	-	-	2	8.0	2
Orthostatic hypotension	1	1.8	1	0	-	-	0	-	-	0	-	-
Varicose vein	1	1.8	1	0	-	-	0	-	-	0	-	-

[a]The denominator for the percentage calculations is the total number of participants per treatment in the safety analysis set, excluding missing value.

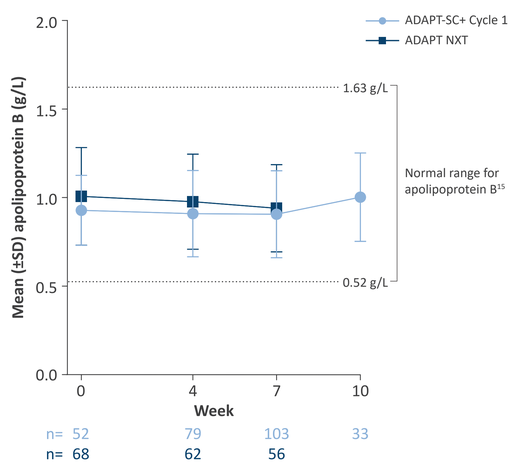
- Distribution of CV-related TEAEs was similar between efgartigimod and placebo groups irrespective of the presence or absence of CV risk factors at baseline
- Edema events were not observed during the ADAPT study

FIGURE 3. Change in LDL Levels Over Time in Cycle 1 of ADAPT



[a]3.4 mmol/L is the lower threshold for borderline high LDL cholesterol in people who do not have coronary artery disease and high LDL cholesterol in people with coronary artery disease or other atherosclerosis.[16]

FIGURE 4. Apolipoprotein B Levels Over Time in ADAPT-SC+ and ADAPT NXT[a]



[a]Participants in ADAPT-SC+ were enrolled from both ADAPT-SC and ADAPT+ (open-label extension of ADAPT) trials.

SUMMARY

- >80% of participants with gMG have at least 1 CV risk factor
- In ADAPT, there were no notable differences in CV-related TEAEs between efgartigimod and placebo irrespective of the presence or absence of CV risk factors at baseline
- Efgartigimod treatment did not increase LDL levels irrespective of baseline LDL levels and did not increase apolipoprotein B levels (a more accurate marker of CV risk)
- Careful assessment of CV risk factors and comorbidities, such as hyperlipidemia, is important when making MG treatment decisions

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ABBREVIATIONS

AE, adverse event; **BUN**, blood urea nitrogen; **CKD**, chronic kidney disease; **CV**, cardiovascular; **DVT**, deep vein thrombosis; **EFG**, efgartigimod alfa-fcab; **Fc**, fragment crystallizable region; **FcRn**, neonatal Fc receptor; **gMG**, generalized myasthenia gravis; **HCP**, healthcare provider; **HDL**, high-density lipoprotein; **HgA1C**, glycosylated hemoglobin A1C; **IgG**, immunoglobulin G; **IV**, intravenous; **LDL**, low-density lipoprotein; **MedDRA**, Medical Dictionary for Regulatory Activities; **MG**, myasthenia gravis; **MG-ADL**, Myasthenia Gravis Activities of Daily Living; **MGFA**, Myasthenia Gravis Foundation of America; **NMJ**, neuromuscular junction; **MI**, myocardial infarction; **PAD**, peripheral arterial disease; **PBO**, placebo; **PE**, pulmonary embolism; **SC**, subcutaneous; **TEAE**, treatment-emergent adverse event; **VTE**, venous thromboembolism.

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