Poster #193

Safety and Tolerability of Efgartigimod in Patients With Generalized Myasthenia Gravis: Analysis of Infection Risk and Hematological Changes During ADAPT and ADAPT+

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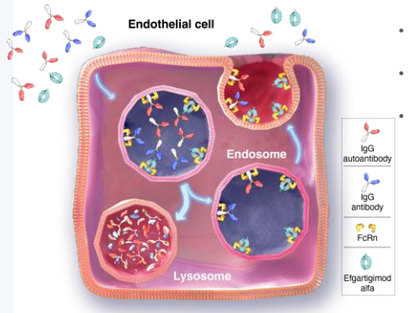
INTRODUCTION

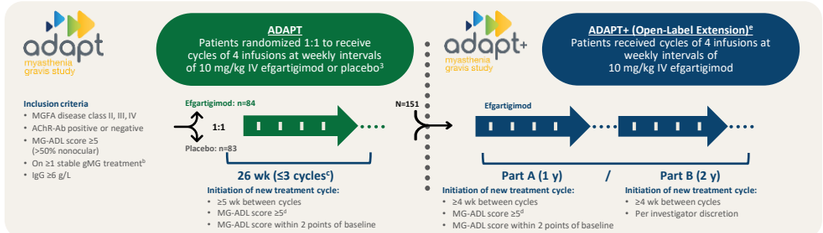
Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG, extending its half-life and maintaining its serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting lysosomal degradation of IgG[2-6]
  - Targeted reduction of all IgG subclasses
  - No impact on immunoglobulins M or A
  - No reduction in albumin levels
  - No increase in cholesterol
  - No impact on IgG production or ability to mount an immune response

METHODS

ADAPT was a 26-week, global, multicenter, randomized, double-blind, placebo-controlled, phase 3 trial evaluating efgartigimod in patients with gMG. Participants who completed ADAPT were eligible to be rolled over to ADAPT+[3,a]



Note: Beige rectangles within arrows indicate day of efgartigimod infusion.
[a]Participants who required retreatment but were unable to complete a treatment cycle within the time frame of ADAPT were also eligible to be rolled over to ADAPT+. [b]Acetylcholinesterase inhibitor, steroid +/or nonsteroidal immunosuppressive therapy. 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]Up to 3 cycles dosed at ≥8 weeks after initial cycle. [d]With >50% from nonocular items. [e]ADAPT+ data depicted in this poster are from the February 2022 cutoff date.

SUMMARY

- No new safety signals were observed during long-term follow-up compared with the 26-week placebo-controlled period
- Incidence of infections did not increase over time with repeated cycles of efgartigimod treatment
- Infection rates in patients with ≥1 treatment-emergent hematologic abnormality (≥ grade 1) were similar between efgartigimod and placebo
- No change in white blood cell counts over time with efgartigimod vs. placebo; single occurrences of decreased counts were incidental, inconsistent over time, and not temporally related to infections
- This analysis suggests that long-term efgartigimod treatment is well tolerated in patients with gMG
- The ADAPT+ study is currently ongoing

RESULTS

Table 1. Summary of AEs
Safety Population

	ADAPT						ADAPT+		
	Placebo (n=83) [34.51 PY]			Efgartigimod (n=84) [34.86 PY]			Efgartigimod (n=145) [217.55 PY]		
	IR[a]	m	n (%)	IR[a]	m	n (%)	IR[a]	m	n (%)
AEs[b]	**7.8**	270	70 (84)	**7.2**	252	65 (77)	**3.6**	783	123 (85)
SAEs	**0.3**	10	7 (8)	**0.1**	4	4 (5)[c]	**0.2**	52	34 (23)[c]
≥1 Infusion-related reaction event	**0.3**	9	8 (10)	**0.1**	3	3 (4)	**0.1**	21	15 (10)
Infection AEs	**1.2**	42	31 (37)	**1.6**	56	39 (46)	**0.8**	164	80 (55)
Discontinued due to AEs	**0.1**	3	3 (4)	**0.2**	7	3 (4)	**0.1**	14	12 (8)
Severe AEs (grade ≥3)	**0.4**	12	8 (10)	**0.3**	10	9 (11)	**0.3**	72	38 (26)
Death[d]	–	0	0 (0)	–	0	0 (0)	**<0.1**	5	5 (3)
Most frequent AEs									
Nasopharyngitis	**0.5**	17	15 (18)	**0.3**	12	10 (12)	**0.1**	24	20 (14)
URTI	**0.2**	5	4 (5)	**0.3**	11	9 (11)	**<0.1**	7	6 (4)
UTI	**0.1**	4	4 (5)	**0.3**	9	8 (10)	**0.1**	18	13 (9)
Headache	**1.1**	39	23 (28)	**1.2**	40	24 (29)	**0.5**	98	36 (25)
Nausea	**0.4**	15	9 (11)	**0.2**	7	7 (8)	**0.1**	13	9 (6)
Diarrhea	**0.4**	14	9 (11)	**0.2**	6	6 (7)	**0.1**	19	14 (10)
COVID-19[e]	–	0	0 (0)	–	0	0 (0)	**0.1**	23	22 (15)

[a]IR was calculated as number of events per total PYs of follow-up. [b]AEs were predominantly mild or moderate. [c]Only 1 SAE was considered treatment related per investigator. [d]None of the deaths in ADAPT+ were deemed related to efgartigimod administration per the principal investigator. [e]Includes all preferred terms of COVID-19, COVID-19 pneumonia, Coronavirus infection, SARS-COV-2 test positive.

Table 2. Infections Occurring in ≥5% of Patients in ADAPT and/or More Frequently[a] in Patients Treated With Efgartigimod vs Placebo, *Safety Population*

	ADAPT		ADAPT+			
	Placebo (n=83) [34.51 PY]		Efgartigimod (n=84) [34.86 PY]		Efgartigimod (n=145) [217.55 PY]	
SOC	IR[b]	n (%)	IR[b]	n (%)	IR[b]	n (%)
Infections and Infestations	**1.2**	31 (37.3)	**1.6**	39 (46.4)	**0.8**	80 (55.2)
Bronchitis	**0.1**	2 (2.4)	**0.2**	5 (6.0)	**<0.1**	4 (2.8)[f]
Nasopharyngitis	**0.5**	15 (18.1)	**0.3**	10 (11.9)[g]	**0.1**	20 (13.8)
URTI	**0.1**	4 (4.8)	**0.3**	9 (10.7)	**<0.1**	6 (4.1)
COVID-19[c]	–	0 (0)	–	0 (0)	**0.1**	22 (15)[g]
UTI	**0.1**	4 (4.8)[d]	**0.3**	8 (9.5)	**0.1**	13 (9.0)[h]
Gastroenteritis	–	0 (0)	**<0.1**	1 (1.2)	**<0.1**	2 (1.4)
Herpes zoster	–	0 (0)	–	0 (0)	**<0.1**	7 (4.8)
Oral herpes	–	0 (0)	**<0.1**	1 (1.2)	**<0.1**	3 (2.1)

[a]Occurring in ≥3 patients in the total efgartigimod group (ADAPT+) compared to placebo group (ADAPT). [b]IR was calculated as number of events per total PYs of follow-up. [c]Includes all preferred terms of COVID-19, COVID-19 pneumonia, Coronavirus infection, SARS-COV-2 test positive. [d]1 event was severe. [e]1 event was severe. [f]1 event was severe. [g]4 events were severe, 5 were serious, and 2 led to treatment discontinuation. [h]2 events were severe, and 1 was serious.

Figure 1. Infections in Patients With ≥1 Treatment-Emergent Hematologic Abnormality (≥ Grade 1) During ADAPT, *Safety Population*

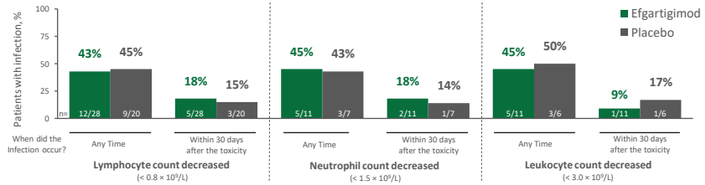
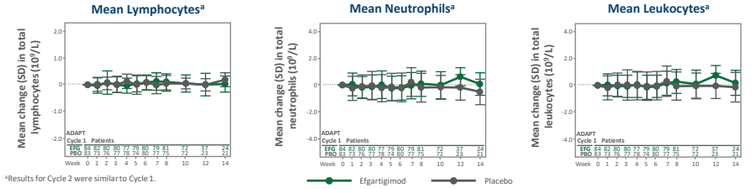
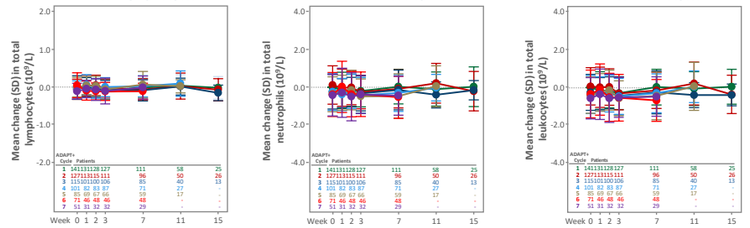


Figure 2. Mean White Blood Cell Change From Study Baseline Over Time in ADAPT (Cycle 1)
Safety Population



[a]Results for Cycle 2 were similar to Cycle 1.

Figure 3. Mean White Blood Cell Change From Study Baseline Over Time in ADAPT+ (Cycles 1–7)
Safety Population



ABBREVIATIONS
AChR-Ab, acetylcholine receptor antibody; AE, adverse event; COVID-19, coronavirus disease 2019; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IR, incidence rate per year of patient follow-up; IV, intravenous; m, number of events; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; PY, patient year; SAE, serious adverse event; SARS-COV-2, severe acute respiratory syndrome coronavirus 2; SOC, system organ class; URTI, upper respiratory tract infection; UTI, urinary tract infection.

REFERENCES
1. Sesarman A, et al. *Cell Mol Life Sci*. 2010;67(15):2533-2550. **2.** Ulrichts P, et al. *J Clin Invest*. 2018;128(10):4372-4386. **3.** Howard JF Jr, et al. *Lancet Neurol*. 2021;20(7):526-536. **4.** Vaccaro C, et al. *Nat Biotech*. 2005;23(10):1283-1288. **5.** Nixon AE, et al. *Front Immunol*. 2015;6:176. **6.** Wolfe GI, et al. *J Neurol Sci*. 2021;430:118074.

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