EPO-210

Achievement of Minimal Symptom Expression in Participants Treated With Efgartigimod in ADAPT+ and ADAPT-SC+

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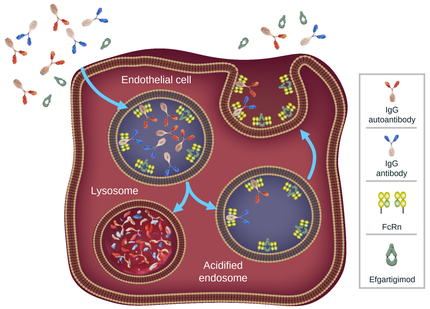
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as albumin recycling, as well as IgG-dependent phagocytosis and antigen presentation[2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[3,4]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, reducing IgG levels without impacting IgG production[3-6]
  - Targeted reduction of all IgG subtypes[3,5]
  - No impact on levels of IgM, IgA, IgE, or IgD[3,6]
  - No reduction in albumin or increase in cholesterol levels[5-8]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[9,10]
- PK/PD modeling and phase 3 data (ADAPT-SC) suggest 4 once-weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[9,11]

METHODS

Efgartigimod IV

ADAPT	ADAPT+
Placebo-Controlled, Randomised, Phase 3 Trial	Long-Term, OLE
Efgartigimod: n=84 Placebo: n=83	Efgartigimod: n=145
Efgartigimod 10 mg/kg IV ≤3 cycles[a,b]	Efgartigimod 10 mg/kg IV ≤19 cycles[a,c]
Study duration: 26 weeks	Study duration: ≤3 years

Efgartigimod PH20 SC

ADAPT SC	ADAPT SC+
Phase 3, Randomised, Noninferiority, PD Trial	Long-Term, OLE
Efgartigimod IV: n=55 Efgartigimod PH20 SC: n=55	Efgartigimod PH20 SC: n=179
Efgartigimod 10 mg/kg IV Efgartigimod PH20 SC 1000 mg 1 cycle[a,d]	Efgartigimod PH20 SC 1000 mg ≤11 cycles[a,e]
Study duration: 10 weeks	Study duration: ≤3 years

[a]Efgartigimod IV and efgartigimod PH20 SC were administered in cycles of 4 once-weekly infusions or injections, respectively. [b]Subsequent cycles could be initiated when the following conditions were met: ≥5 weeks since last treatment, MG-ADL score ≥5 (with >50% from nonocular items), and MG-ADL score within 2 points of baseline. [c]Subsequent cycles could be initiated in Year 1 when the following conditions were met: ≥4 weeks since last treatment, MG-ADL score ≥5 (with >50% from nonocular items), and MG-ADL score within 2 points of baseline. In Years 2 and 3, subsequent cycles can be administered when it has been ≥4 weeks at the investigator's discretion. [d]Participants could not receive treatment in the 7-week follow-up period. [e]≥28 days between the last dose of the previous treatment period and the first dose of the next treatment period and based on the need for treatment as determined by the investigator.

CONCLUSION

- MSE is an important treatment goal in gMG to ensure adequate disease control and improve QoL
- The proportion of participants reaching MSE at any time in 19 cycles of the ADAPT+ OLE was comparable to ADAPT and ADAPT-SC
- More than half of participants reached MSE at any timepoint over 9 cycles during the ADAPT-SC+ OLE
- Participants who reached MSE in ADAPT also improved across multiple disease-specific measures and experienced QoL comparable to the healthy population
- Efgartigimod IV and efgartigimod PH20 SC were well tolerated; adverse events were predominantly mild to moderate and did not increase in frequency during long-term treatment in ADAPT+ or ADAPT-SC+

RESULTS

Table 1. Baseline Demographics and Disease Characteristics for ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+

AChR-Ab+ Population

Placebo — Efgartigimod IV — Efgartigimod PH20 SC

Characteristics	ADAPT (n=64)	ADAPT (n=65)	ADAPT+ (n=111)	ADAPT-SC (n=46)	ADAPT-SC (n=45)	ADAPT-SC+ (n=141)
Age, y, mean (SD)	49.2 (15.5)	44.7 (15.0)	47.1 (15.5)	57.0 (14.8)	51.3 (16.3)	51.0 (15.9)
Sex, n (%)						
Female	40 (62.5)	46 (70.8)	75 (67.6)	26 (56.5)	25 (55.6)	90 (63.8)
Male	24 (37.5)	19 (29.2)	36 (32.4)	20 (43.5)	20 (44.4)	51 (36.2)
Weight, kg, mean (SD)	79.5 (19.5)	81.6 (29.8)	81.4 (25.6)	83.9 (22.8)	77.3 (19.6)	79.1 (20.7)
Time since gMG diagnosis, y, mean (SD)	8.9 (8.2)	9.7 (8.3)	9.7 (7.9)	7.9 (8.9)	6.7 (6.7)	9.1 (8.5)
MGFA class at screening, n (%)						
II	25 (39.1)	28 (43.1)	44 (39.6)	17 (37.0)	25 (55.6)	58 (41.1)
III	36 (56.3)	35 (53.8)	63 (56.8)	27 (58.7)	19 (52.2)	78 (55.3)
IV	3 (4.7)	2 (3.1)	4 (3.6)	2 (4.3)	1 (2.2)	5 (3.5)
Previous thymectomy, n (%)	30 (46.9)	45 (69.2)	68 (61.3)	12 (26.1)	14 (31.1)	59 (41.8)
Total MG-ADL score, mean (SD)	8.6 (2.1)	9.0 (2.5)	9.5 (3.1)	8.3 (2.5)	8.6 (2.6)	7.6 (3.4)
Total QMG score, mean (SD)	15.2 (4.4)	16.0 (5.1)	15.3 (5.7)	15.1 (4.3)	14.4 (4.4)	N/A[a]
Commonly prescribed therapies, n (%)						
NSIST	37 (57.8)	40 (61.5)	67 (60.4)	18 (40.0)	19 (41.3)	67 (47.5)
Steroid	51 (79.7)	46 (70.8)	85 (76.6)	34 (75.6)	29 (63.0)	103 (73.0)

[a]QMG was not collected as part of the ADAPT-SC+ study.

Table 2. Summary of TEAEs

Overall Population

Placebo — Efgartigimod IV — Efgartigimod PH20 SC

	ADAPT (n=83) [34.5 PY]		ADAPT (n=84) [34.9 PY]		ADAPT+ (n=145) [229.0 PY]		ADAPT-SC (n=55) [10.5 PY]		ADAPT-SC (n=55) [10.7 PY]		ADAPT-SC+ (n=179) [193.4 PY]	
	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)	ER[a]	n (%)
TEAEs	7.83	70 (84.3)	7.22	65 (77.4)	3.53	124 (85.5)	7.62	28 (50.9)	12.43	37 (67.3)	8.95	152 (84.9)
Serious TEAEs	0.29	7 (8.4)	0.11	4 (4.8)	0.24	36 (24.8)	0.48	4 (7.3)	0.93	8 (14.5)	0.26	33 (18.4)
Discontinued due to TEAE	0.09	3 (3.6)	0.20	3 (3.6)	0.06	12 (8.3)	0	0	0.19	2 (3.6)	0.03	4 (2.2)

[a]ER was calculated as number of events per total PY of follow-up.

ABBREVIATIONS

AChR-Ab, acetylcholine receptor antibody; ER, event rate; Fc, fragment crystallisable region; FcRn, neonatal Fc receptor; gMG, generalised myasthenia gravis; IgA, immunoglobulin A; IgD, immunoglobulin D; IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M; IV, intravenously; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PD, pharmacodynamic; PY, participant-year; QMG, Quantitative Myasthenia Gravis; QoL, quality of life; SC, subcutaneous; TEAE, treatment-emergent adverse event.

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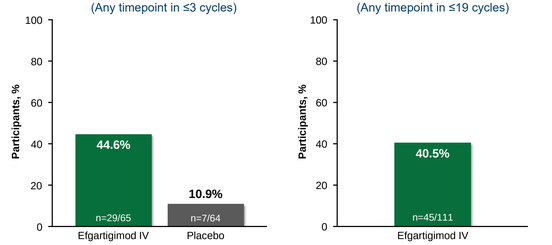
Figure 1. Proportion of Participants With MSE in ADAPT/ADAPT+

AChR-Ab+ Population

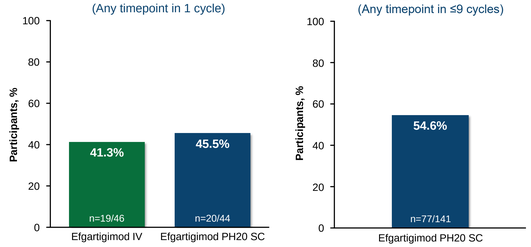


- 21 of 26[b] participants (81%) from the efgartigimod arm who achieved MSE during ADAPT also achieved MSE during ADAPT+
- 8 of 35[b] participants (23%) from the efgartigimod arm who did not achieve MSE in ADAPT achieved MSE during ADAPT+

[a]To limit study visits, sampling in ADAPT+ did not include assessment at week 4 (when maximal pharmacodynamic and clinical effects were observed in ADAPT), and consequently these results may not fully capture the extent of MSE in this population. [b]61 of the 65 AChR-Ab+ participants treated with efgartigimod in ADAPT rolled over into ADAPT+.

Figure 2. Proportion of Participants With MSE in ADAPT-SC/ADAPT-SC+

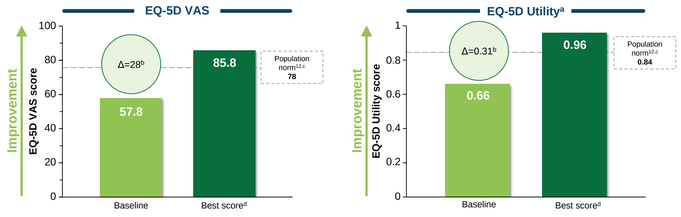
AChR-Ab+ Population



- 28 of 57 (49.1%) AChR-Ab+ participants that rolled over from ADAPT+ achieved MSE in ADAPT-SC+
- 23 of 41 (56.1%) AChR-Ab+ participants from the efgartigimod IV arm of ADAPT-SC achieved MSE in ADAPT-SC+
- 26 of 43 (60.5%) AChR-Ab+ participants from the efgartigimod PH20 SC arm of ADAPT-SC achieved MSE in ADAPT-SC+

Figure 3. Change in HRQoL Outcomes Among Participants Who Achieved MSE in ADAPT (n=29)

AChR-Ab+ Population



[a]EQ-5D utility scores are based on the US value sets. [b]Change (Δ) reported is maximum change from study baseline across postbaseline visits of any treatment cycle of ADAPT. [c]Population normal values were derived from an age-matched cohort with individuals aged 35 to 44 years. [d]Best score is reported as maximal score/change from study baseline across postbaseline visits at any cycle.

Figure 4. Change in QMG and MGC Among Participants Who Achieved MSE in ADAPT (n=29)

AChR-Ab+ Population

[a]Change (Δ) reported is maximum change from study baseline across postbaseline visits of any treatment cycle of ADAPT. [b]Best score is reported as the minimal score/maximal reduction from study baseline across postbaseline visits at any cycle.

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