Poster #133

Response to Coronavirus 2019 Vaccination in Patients Receiving Efgartigimod

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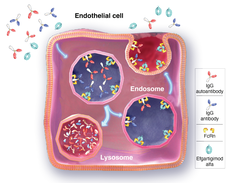
INTRODUCTION

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[2-5]
  - 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

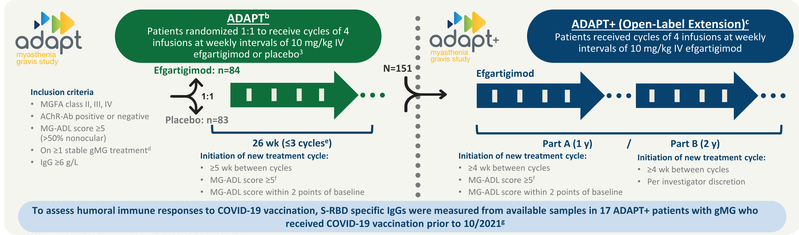
Immunosuppressive therapies used in the treatment of gMG may increase susceptibility to infections and impair immune response to vaccines[6-7]

- Previous gMG treatments have the potential to[6,8-9]:
  - Increase risk of infection
  - Reduce therapeutic antibody response
  - Impair cellular immune responses to vaccination
- Glucocorticoids and B-cell–depleting therapies (including MMF) have been shown to substantially reduce immunogenicity of mRNA vaccines to SARS-CoV-2[7]

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]

- Vaccinations, including inactivated or live-attenuated viruses, were permitted if immunizations were given ≥ 48 hours prior to or 48 hours after administration of efgartigimod



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]The ADAPT study was started on August 22, 2018, and was completed on April 6, 2020. [c]The ADAPT+ study was started on March 1, 2019 and current data cutoff was January 31, 2022. [d]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+. [e]≤3 cycles dosed at ≥8 weeks after initial cycle. [f]With >50% from nonocular items. [g]RBD IgGs specific for SARS-CoV-2 S-protein were assessed using a S-plex Luminex Assay (performed at Q2 Solutions, Morrisville, NC).

SUMMARY

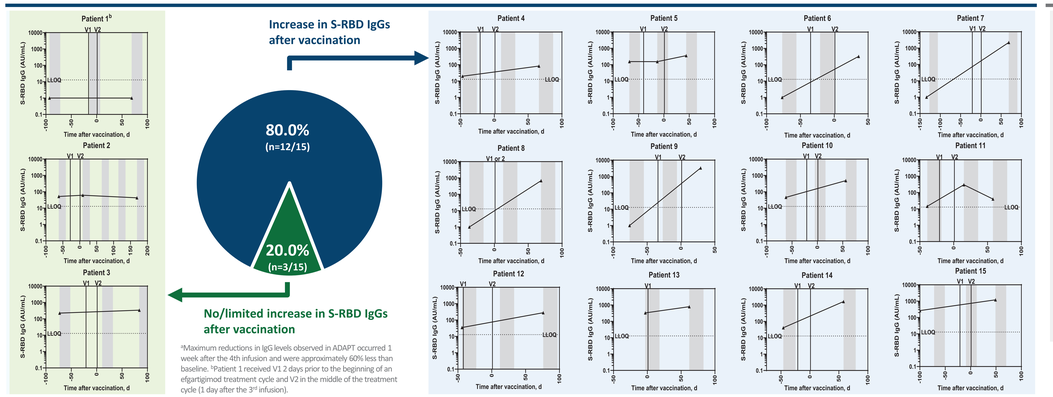
- **COVID-19 immunization resulted in antigen-specific IgG responses in most patients receiving efgartigimod**
- **These preliminary data suggest efgartigimod treatment does not preclude effective humoral immune response to COVID-19 vaccination**
- **Impact of concomitant immunosuppressive therapies warrants additional investigation**
- **Vaccination data are being collected from patients enrolled in current and future studies with efgartigimod**

RESULTS

Table 1. Characteristics of Patients in ADAPT+ Receiving COVID-19 Vaccines

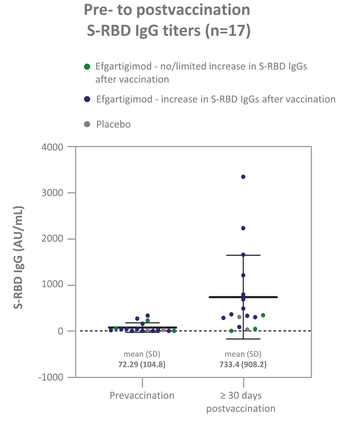
Patient #	Sex at birth, age, y	BMI, kg/m²	Immunosuppressive therapy	ADAPT+ treatment group	Relevant medical history	COVID-19 vaccine received
1	F, 60	47.9	MMF, 1500 mg BID	Efgartigimod	Hypercholesterolemia, depression, lumbar radiculopathy	BNT162b2 (Pfizer-BioNTech)
2	M, 76	34.5	Prednisone, 2 mg QD MMF, 1000 mg BID	Efgartigimod	Hypertension, coronary artery disease, hyperlipidemia, type 2 diabetes, chronic kidney disease, depression, anemia	mRNA-1273 (Moderna)
3	M, 54	47.3	Prednisone, 15 mg QD	Efgartigimod	Hypertension	BNT162b2 (Pfizer-BioNTech)
4	M, 65	35.6	None reported	Efgartigimod	Hyperlipidemia	BNT162b2 (Pfizer-BioNTech)
5	M, 48	23.9	Prednisolone, 3 mg QD MMF, 500 mg, 5x/d	Efgartigimod	None reported	BNT162b2 (Pfizer-BioNTech)
6	F, 47	32.0	Methylprednisolone, 4 mg QD MMF, 500 mg BID	Placebo-Efgartigimod	None reported	BNT162b2 (Pfizer-BioNTech)
7	F, 20	32.8	None reported	Placebo-Efgartigimod	Hashimoto, anemia, vitamin D deficiency	BNT162b2 (Pfizer-BioNTech)
8	M, 55	27.2	Prednisone, 25 mg QD Cyclosporine, 100 mg BID	Efgartigimod	Hypertension, type 2 diabetes	BNT162b2 (Pfizer-BioNTech)
9	F, 44	27.1	Azathioprine, 50 mg BID Methylprednisolone, 8 mg QD	Placebo-Efgartigimod	Asthma, vitamin D deficiency	BNT162b2 (Pfizer-BioNTech)
10	F, 43	18.9	Azathioprine, 100 mg QD Prednisone, 60 mg QOD	Efgartigimod	None reported	BNT162b2 (Pfizer-BioNTech)
11	F, 79	24.1	Prednisolone, 12.5 mg QOD	Placebo-Efgartigimod	Diabetes, depression, hypercholesterolemia, hypertension, polymyalgia rheumatica, urticaria, anemia	BNT162b2 (Pfizer-BioNTech)
12	M, 55	32.3	Azathioprine, 100 mg QD	Efgartigimod	Hypertension	BNT162b2 (Pfizer-BioNTech)
13	M, 54	33.3	None reported	Placebo-Efgartigimod	Prediabetes, chronic obstructive pulmonary disease, asthma, high cholesterol	Ad26.COV2.S (J&J)
14	F, 66	37.8	Methylprednisolone, 8 mg QOD	Placebo-Efgartigimod	Hypertension, elevated blood glucose, obesity	Unknown
15	F, 31	26.4	Azathioprine, 50 mg QD	Efgartigimod	Depression, corticosteroid hypersensitivity	BNT162b2 (Pfizer-BioNTech)
16	M, 71	26.0	None reported	Never treated in ADAPT+, Placebo in ADAPT	None reported	BNT162b2 (Pfizer-BioNTech)
17	F, 62	ND (104 kg)	Azathioprine, 50 mg BID Prednisolone, 15 mg QOD	Efgartigimod, but no treatment during COVID-19 vaccination	Diabetes, hypertension	AZD1222 (AstraZeneca)

Figure 1. Individual Response to COVID-19 Vaccination in ADAPT+



[a]Maximum reductions in IgG levels observed in ADAPT occurred 1 week after the 4th infusion and were approximately 60% less than baseline. [b]Patient 1 received V1 2 days prior to the beginning of an efgartigimod treatment cycle and V2 in the middle of the treatment cycle (1 day after the 3rd infusion).

Figure 2. Summary of Response to COVID-19 Vaccination in ADAPT+



ABBREVIATIONS:
AChR-Ab, acetylcholine receptor antibody; BID, twice daily; BMI, body mass index; COVID-19, coronavirus disease 2019; F, female; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; LLOQ, lower limit of quantification; M, male; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MMF, mycophenolate mofetil; mRNA, messenger RNA; QD, once daily; QOD, every other day; RBD, spike protein receptor–binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; S-RBD, spike protein receptor–binding domain; V, vaccination dose.

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