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COVID-19 Vaccination Response in Participants Receiving Efgartigimod IV or Efgartigimod PH20 SC in ADAPT+ or ADAPT-SC+

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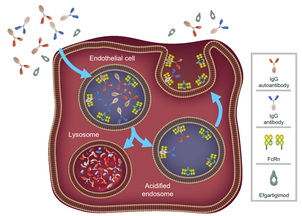
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG antibodies and albumin. This recycling and salvage from lysosomal degradation results in IgG antibodies having the longest half-life and being the most abundant of all immunoglobulins in the plasma[1-3]
- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[1]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production, albumin levels, or other parts of the immune system[1,4,5]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[6,7]
  - PK/PD modeling and phase 3 data (ADAPT-SC) have demonstrated 4 once-weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[6,8]

Some immunosuppressive therapies used in the treatment of gMG may increase susceptibility to infections and impair immune response to vaccines[9]

- Glucocorticoids, mycophenolate mofetil, and B-cell–depleting therapies can substantially reduce immunogenicity of mRNA vaccines to SARS-CoV-2[10,11]
- In previous studies of participants with IgG-mediated autoimmune diseases efgartigimod did not impair generation of IgG responses to antigenic challenges, and levels of both naturally- and vaccine-induced protective antibody titers closely followed total IgG reduction kinetics[5]

METHODS

OBJECTIVE Assess the effects of efgartigimod IV and efgartigimod PH20 SC treatment on humoral immune responses to COVID-19 vaccination in participants with gMG during ADAPT+ and ADAPT-SC+[a]

ADAPT
- Phase 3, Randomised, Placebo-Controlled Trial
- Efgartigimod: n=84
- Placebo: n=83
- Efgartigimod 10 mg/kg IV ≤3 cycles of 4 once-weekly infusions
- Study duration: 26 weeks

Rollover

ADAPT+
- Long-Term, Open-Label Extension
- Efgartigimod: n=145
- Efgartigimod 10 mg/kg IV ≤19 cycles of 4 once-weekly infusions
- Study duration: ≤3 years

ADAPT-SC
- Phase 3, Randomised, Noninferiority, PD Trial
- Efgartigimod IV: n=55
- Efgartigimod PH20 SC: n=55
- Efgartigimod 10 mg/kg IV
- Efgartigimod PH20 SC 1000 mg
- 1 cycle of 4 once-weekly administrations
- Study duration: 10 weeks

Rollover

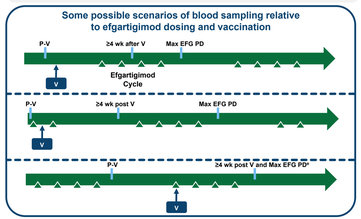
ADAPT-SC+
- Long-Term, Open-Label Extension
- Efgartigimod PH20 SC: n=179
- Efgartigimod PH20 SC 1000 mg ≤11 cycles 4 once-weekly injections
- Study duration: ≤3 years
- Study is currently ongoing

Rollover

SARS-CoV-2-IgG-RBD, -S, and -N Titers[b,c]:
Measured at
- P-V: Prevaccination (last available value prior to vaccination)
- ≥4 wk after V: ≥4 wk after vaccination (at maximum vaccine effect)
- Max EFG PD: ~1 wk after 4th efgartigimod infusion (at maximum efgartigimod PD effect)[d,e]

Vaccine numbers
- V1-V3: First, second, and third vaccines

Some possible scenarios of blood sampling relative to efgartigimod dosing and vaccination



[a]Not all participants enrolled in the ADAPT+ or ADAPT-SC+ received vaccines targeting COVID-19. [b]SARS-CoV-2-IgG-RBD, -S, and -N antibodies were assessed using an ELISA assay. [c]For COVID-19 vaccinations consisting of multiple injections (ie, injections within 45 days of each other), only blood samples before the first injection and after the last injection were selected. [d]Samples were collected from the first cycle that occurred after the vaccination. [e]One sample was collected if postvaccination time points (≥4 weeks after V at maximum vaccine effect and Max EFG PD) coincided with each other.

SUMMARY

Participants receiving efgartigimod IV or efgartigimod PH20 SC mounted antigen-specific IgG responses to each COVID-19 immunization, even when total IgG levels were maximally reduced

Effective humoral immune response to COVID-19 vaccination was not precluded by efgartigimod IV or efgartigimod PH20 SC treatment

Seroconversion was observed for the majority of samples examined in the first through third vaccines received by the participants in ADAPT+ and ADAPT-SC+

RESULTS

Table 1. Baseline Demographics of Participants in ADAPT+/ADAPT-SC+ Receiving COVID-19 Vaccines[a]

Characteristic	Participants (N=68)
Age, y, mean (SD)	49.0 (14.2)
Age category, n (%)	
18-64 y	55 (80.9)
65-74 y	11 (16.2)
≥75 y	2 (2.9)
Sex at birth, n (%)	
Female	44 (64.7)
Male	24 (35.3)
BMI,[b] (kg/m), mean (SD)	28.6 (8.0)
Race, n (%)	
Asian	9 (13.2)
White	57 (83.8)
Multiple	2 (2.9)

[a]Participant data are included only for those who had a prevaccination titer sample and ≥1 postvaccination titer sample available. [b]BMI data were unavailable for 2 individuals.

Table 2. COVID-19 Vaccine Received by Participants in ADAPT+/ADAPT-SC+[a]

COVID-19 Vaccine, n (%)	Participants (N=68)
Oxford–AstraZeneca	1 (1.5)
Janssen	1 (1.5)
Spikevax (Moderna)	12 (17.6)
Sputnik V	3 (4.4)
Pfizer-BioNTech	48 (70.6)
Unknown	7 (10.3)

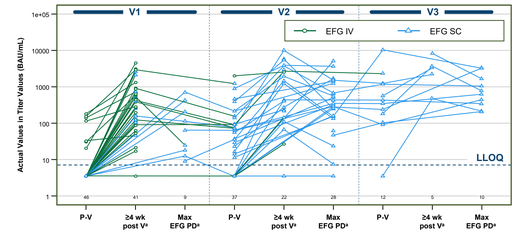
[a]Participants who had a prevaccination titer sample and ≥1 postvaccination titer sample available.

Table 3. Concomitant MG Therapies[a]

Therapy, n (%)	Participants (N=68)
AChEi	56 (82.4)
NSISTs	42 (61.8)
Steroids	45 (66.2)

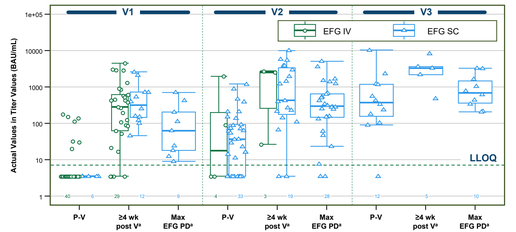
[a]Participant data are included only for those who had a prevaccination titer sample and ≥1 postvaccination titer sample available.

Figure 1. Individual Trend of Actual SARS-CoV-2-IgG-RBD Titer Values Over Time (Combined ADAPT+/ADAPT-SC+)



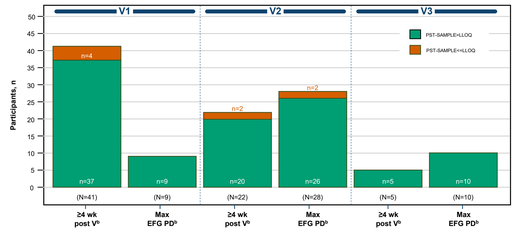
[a]If postvaccination timepoints (≥4 weeks after V and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD timepoint.

Figure 2. Individual SARS-CoV-2-IgG-RBD Titer Values With Boxplots Over Time (Combined ADAPT+/ADAPT-SC+)



[a]If postvaccination timepoints (≥4 weeks after V and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD timepoint.

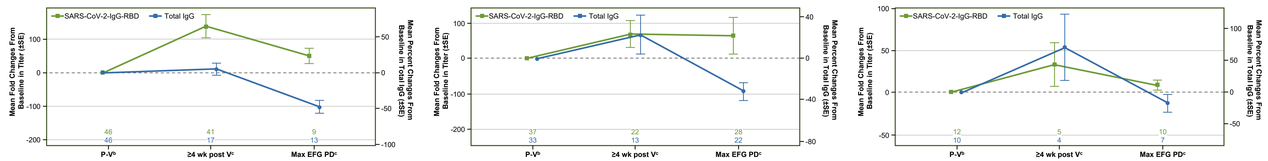
Figure 3. Seroconversion[a] of SARS-CoV-2-IgG-RBD Over Time (Combined ADAPT+/ADAPT-SC+)



[a]Seroconversion was defined as the percentage of participants with SARS-CoV-2-IgG-RBD levels above the LLOQ. [b]If postvaccination timepoints (≥4 weeks after V and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD timepoint.

Figure 4. Mean Fold Changes in SARS-CoV-2-IgG-RBD Titer Values and Mean Percent Changes in Total IgG Values Over Time (Combined ADAPT+/ADAPT-SC+)[a]

SARS-CoV-2-IgG-S and SARS-CoV-2-IgG-N Titer Values



[a]Mean fold change from baseline was imputed with a "1" and the mean percent changes from baseline with a "0" at P-V. [b]Includes all participants with baseline values available. [c]If postvaccination timepoints (≥4 wk post V and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD timepoint.

- SARS-CoV-2-IgG-S titer values showed a similar trend in response to vaccination as SARS-CoV-2-IgG-RBD titer values
- There was no effect of vaccination on SARS-CoV-2-N titer values (positive SARS-CoV-2-N titer values indicate a previous/resolving COVID-19 infection)[12]

ABBREVIATIONS
AChEi, acetylcholinesterase inhibitor; BMI, body mass index; COVID-19, coronavirus disease 2019; ELISA, enzyme-linked immunosorbent assay; EFG, efgartigimod; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IV, intravenous; LLOQ; lower limit of quantification; MG, myasthenia gravis; mRNA, messenger RNA; -N, nucleocapsid protein; NSIST, nonsteroidal immunosuppressive therapy; PD, pharmacodynamic; PK, pharmacokinetic; P-V, prevaccination; -RBD, receptor-binding domain of S protein; rHuPh20, recombinant human hyaluronidase PH20; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; -S, spike protein; SARS-CoV-2-IgG, severe acute respiratory syndrome coronavirus 2 specific IgG; SC, subcutaneous; V, vaccination; V1, first vaccination; V2, second vaccination; V3, third vaccination.

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ACKNOWLEDGMENTS AND DISCLOSURES: The authors gratefully acknowledge the ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+ trial participants and investigators.
TV: Alexion, argenx, CSL Behring, Allergan/AbbVie, AstraZeneca, Ra/UCB, Horizon, Regeneron, Janssen/Momenta, Immunovant, Cartesian Therapeutics, and Sanofi. **FS:** Alexion, Biogen, Mylan, Novartis, Roche, Sanofi, Teva, Almirall, argenx, Avexis, Forward, Lexeo, Merck, Novartis, Pomona, Takeda, and Prilenia. **JFH:** Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, UCB Pharma AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix, CheckRare CME, F. Hoffmann-LaRoche, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron, Sanofi, Zai Labs, and Tolerancia AB. **JWS:** National Institutes of Health, Cellective, Enzyvant, Jeffrey Modell Foundation, and argenx. **SS, FG, PD,** and **BVH:** argenx. **RM:** Alexion, argenx, Ra, Biomarin, Catalyst, UCB, TEVA, Merck, Roche, and Biogen. **JLDB:** argenx, Alexion, CSL, UCB, Alnylam, Janssen, and Sanofi. **AA:** X4, Grifols, Takeda, Pfizer, Janssen, and argenx. **KW:** Bristol Myers Squibb, Pfizer, AbbVie, UCB, Eli Lilly, Galapagos, GSK, Roche, Gilead, Regeneron, Sanofi, AstraZeneca, and Novartis. The ADAPT+ and ADAPT-SC+ trials were funded by argenx. Medical writing and editorial support for this presentation were provided by Precision AQ and funded by argenx.

Presented at the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) Annual Meeting; October 15-18, 2024; Savannah, Georgia