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

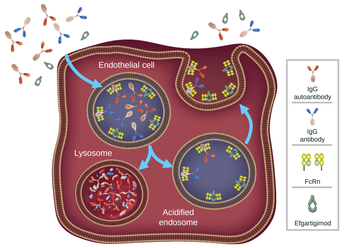
EPO-061

Sophie Steeland,[1] Francesco Saccà,[2] James F. Howard Jr,[3] John W. Sleasman,[4] Fien Gistelinck,[1] Paul Duncombe,[1] Benjamin Van Hoorick,[1] Renato Mantegazza,[5] Jan L. De Bleecker,[6] Antoine Azar,[7] Kevin Winthrop[8]

[1]argenx, Ghent, Belgium; [2]GENESIS Department, Federico II University of Naples, Naples, Italy; [3]Department of Neurology, The University of North Carolina, Chapel Hill, North Carolina, USA; [4]Duke University School of Medicine, Division of Allergy, Immunology, and Pulmonary Medicine, Durham, North Carolina, USA; [5]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [6]Department of Neurology, Ghent University Hospital, Ghent, Belgium; [7]Johns Hopkins University School of Medicine, Division of Allergy and Clinical Immunology, Baltimore, Maryland, USA; [8]Oregon Health and Science University, Division of Infectious Disease, Portland, Oregon, USA

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[3-8]
  - 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[5-7]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[8,9]
  - 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[8,10]

Some immunosuppressive therapies used in the treatment of gMG may increase susceptibility to infections and impair immune response to vaccines[11]

Glucocorticoids, mycophenolate mofetil, and B-cell–depleting therapies can substantially reduce immunogenicity of mRNA vaccines to SARS-CoV-2[12,13]

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**

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**

Rollover

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**

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-d]:

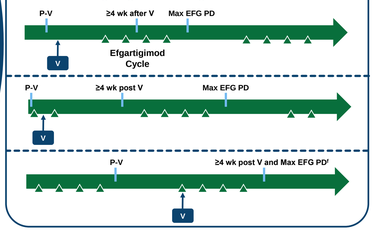
Measured at

- **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) [e,f]

Vaccine numbers

- **V1-V3:** First, second, and third vaccines[d]

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]Inactivated, non-live, or non-live-attenuated vaccines were permitted ≥48 hours prior to or 48 hours after efgartigimod administration. [c]SARS-CoV-2-IgG-RBD, -S, and -N antibodies were assessed using an ELISA assay. [d]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. [e]Samples were collected from the first cycle that occurred after the vaccination. [f]One sample was collected if postvaccination time points (≥4 weeks after V and Max EFG PD) coincided with each other.

CONCLUSION

Participants receiving efgartigimod IV or efgartigimod PH20 SC mounted antigen-specific IgG responses to each COVID-19 immunisation, 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 of 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)

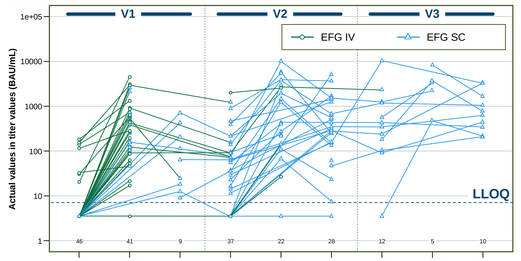
[a]Participant data are included only for those who had a prevaccination titer sample and ≥1 postvaccination titer sample available.

Table 3. Concomitant MG Therapies[a]

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

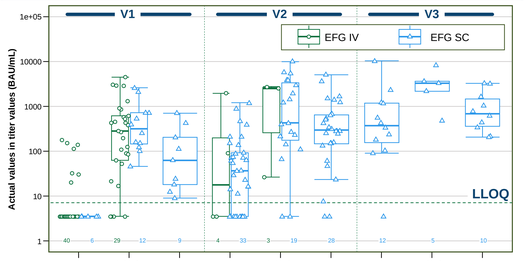
[a]Participant data are included only for those who had a prevaccination titer sample and ≥1 postvaccination titer sample available.

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



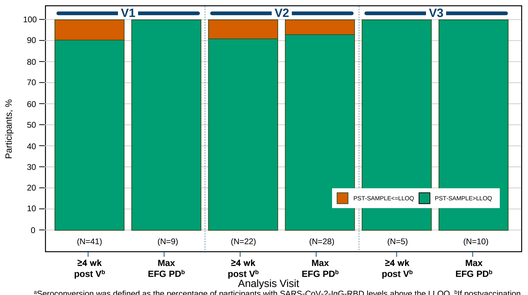
[a]If postvaccination timepoints (≥4 weeks after V and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD timepoint.

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



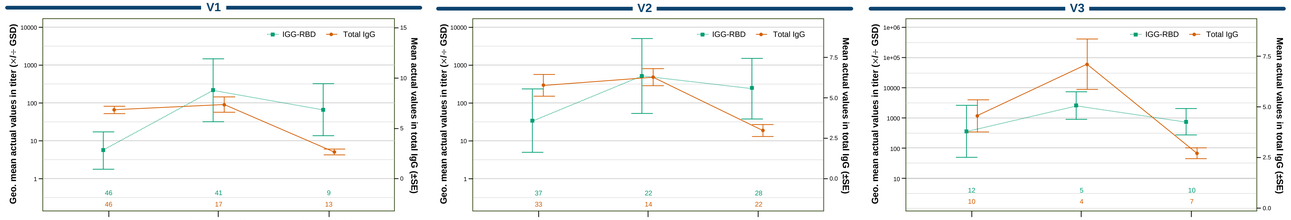
[a]If postvaccination timepoints (≥4 weeks after V and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD timepoint.

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. Geometric Mean Actual SARS-CoV-2-IgG-RBD Titer Values and Mean Actual Total IgG Values Over Time (Combined ADAPT+/ADAPT-SC+)



[a]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 and SARS-CoV-2-IgG-N Titer Values

- 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)[14]

ABBREVIATIONS

AChEi, acetylcholinesterase inhibitor; BMI, body mass index; COVID-19, coronavirus disease 2019; ELISA, enzyme-linked immunosorbent assay; EFG, efgartigimod; Fc, fragment crystallisable region; FcRn, neonatal Fc receptor; gMG, generalised 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.

REFERENCES

1. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533-2550. **2.** Pyzik M, et al. *Nat Rev Immunol.* 2023;23(7):415-432. **3.** Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386. **4.** Vaccaro C, et al. *Nat Biotechnol.* 2005;23(10):1283-1288. **5.** Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536. **6.** Nixon AE, et al. *Front Immunol.* 2015;6:176. **7.** Ward ES, et al. *Front Immunol.* 2022;13:892534. **8.** Study ARGX-113-2001 (ADAPT-SC) Clinical Trial Protocol v2.0, 02 Jul 2021. **9.** Locke KW, et al. *Drug Deliv.* 2019;26(1):98-106. **10.** Behr M, et al. Poster presented at: the Muscular Dystrophy Association (MDA) Clinical & Scientific Conference; March 19–22, 2023; Dallas, TX, USA. **11.** Patel SY, et al. *Front Immunol.* 2019;10(33):1-22. **12.** Deepak P, et al. *Ann Intern Med.* 2021 Nov;174(11):1572-1585. **13.** Zecca E, et al. *Viruses.* 2022;14(8):1766. **14.** Interim Guidelines for COVID-19 Antibody Testing. CDC. Updated December 16, 2022. Accessed June 20, 2024. https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing/antibody-tests-guidelines.html.

ACKNOWLEDGMENTS AND DISCLOSURES: The authors gratefully acknowledge the ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+ trial participants and investigators.

SS, FG, PD, and **BVH:** argenx. **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 Tolerantia AB. **JWS:** National Institutes of Health, Collective, Enzyvant, Jeffrey Modell Foundation, and 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 10th Congress of the European Academy of Neurology (EAN); June 29-July 2, 2024; Helsinki, Finland