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COVID-19 Vaccination Response in Participants Across Clinical Trials Investigating Efgartigimod in Autoimmune Diseases

Ali A. Habib,[1] Tuan Vu,[2] Francesco Saccà,[3] James F. Howard Jr,[4] John W. Sleasman,[5] Fien Gistelinck,[6] Paul Duncombe,[6] Benjamin Van Hoorick,[6] Sophie Steeland,[6] Renato Mantegazza,[7] Jan L. De Bleecker,[8] Antoine Azar,[9] Kevin Winthrop[10]

[1]Department of Neurology, University of California, Irvine, Orange, California; [2]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, Florida; [3]GENESIS Department, Federico II University of Naples, Naples, Italy; [4]Department of Neurology, The University of North Carolina, Chapel Hill, North Carolina; [5]Duke University School of Medicine, Division of Allergy, Immunology, and Pulmonary Medicine, Durham, North Carolina; [6]argenx, Ghent, Belgium; [7]Emeritus Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [8]Department of Neurology, Ghent University Hospital, Ghent, Belgium; [9]Johns Hopkins University School of Medicine, Division of Allergy and Clinical Immunology, Baltimore, Maryland; [10]Oregon Health and Science University, Division of Infectious Disease, Portland, Oregon

INTRODUCTION

- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared to endogenous IgG, 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 or other parts of the immune system, and does not decrease albumin[1-3]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[4,5]

Efgartigimod Mechanism of Action: Blocking FcRn

1. Efgartigimod and IgG are internalized[1,6]
2. Efgartigimod competes with endogenous IgG for binding to FcRn[1]
3. Unbound IgG enters the lysosomal degradation pathway[1,6]
4. Efgartigimod and fewer IgGs are recycled back into the bloodstream[1]

Some immunosuppressive therapies used in the treatment of autoimmune diseases impair immune response to vaccines[7]

- Some immunosuppressive and B-cell–depleting therapies can reduce immunogenicity of vaccines, including vaccines to SARS-CoV-2[8,9]
- In previous studies, 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[3,10,11]

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, CIDP, ITP, and PV across multiple clinical trials[a]

SARS-CoV-2-IgG-RBD, -S, -N, and -NEUT Titers Measured during gMG, CIDP, ITP, and PV studies at[b,c]:

PreVacc:	≥4 wk post Vacc:	Max EFG PD[d]:	
Prevaccination (last available value prior to vaccination)	≥4 wk after vaccination (at maximum vaccine effect)	**Cyclic dosing:** ~1 wk after 4th efgartigimod administration[e]	**Once-weekly/Q2W dosing:** ≥4 wk after 1st efgartigimod administration (at maximum efgartigimod PD effect)

	gMG				CIDP	ITP	PV	
	ADAPT	ADAPT+	ADAPT-SC	ADAPT-SC+	ADHERE	ADVANCE	ADDRESS	ADDRESS+
Phase	3	3, OLE	3	3, OLE	2	3	3	3, OLE
Dosing	EFG IV 10 mg/kg: ≤3 cycles of 4 once-weekly infusions	EFG IV 10 mg/kg: ≤19 cycles of 4 once-weekly infusions	EFG IV 10 mg/kg or EFG PH20 SC 1000 mg: 1 cycle of 4 once-weekly administrations	EFG PH20 SC 1000 mg: ≤11 cycles of 4 once-weekly injections	EFG PH20 SC 1000 mg: Once-weekly injections	EFG IV 10 mg/kg: 4 once-weekly injections, then once-weekly or Q2W infusions	EFG PH20 SC 1000 mg (2000 mg on days 1 and 8): Once-weekly injections	
Participants	EFG IV: n=84 PBO: n=83	EFG IV: n=145	EFG IV: n=55 EFG PH20 SC: n=55	EFG PH20 SC: n=179	Stage A, EFG PH20 SC: n=322 Stage B, EFG PH20 SC: n=111 PBO: 110	EFG IV: n=86 PBO: n=45	EFG PH20 SC: n=147 PBO: n=75	EFG PH20 SC: n=123 PBO: n=60
Duration	26 weeks	≤3 years	10 weeks	≤3 years	≤12 weeks (Stage A) ≤48 weeks (Stage B)	24 weeks	30 weeks	≤60 weeks

Rollover: ADAPT → ADAPT+; ADAPT-SC → ADAPT-SC+; ADDRESS → ADDRESS+

[a]Not all participants enrolled in these studies 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]One sample was collected if postvaccination time points (≥4 wk post Vacc at maximum vaccine effect and Max EFG PD) coincided with each other. [e]Samples were collected from the first cycle that occurred after the vaccination.

SUMMARY

Participants receiving efgartigimod IV or efgartigimod PH20 SC across multiple indications and dosing schedules mounted antigen-specific IgG responses to 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, regardless of indication or dosing regimen; similar responses were seen with placebo

Additional data on several different vaccines are being retrospectively analyzed from efgartigimod studies across multiple indications

RESULTS

Table 1. Baseline Demographics of Participants in gMG, CIDP, ITP, and PV Studies Receiving COVID-19 Vaccines[a]

Characteristic	gMG (n=71)	CIDP (n=29)	ITP (n=17)	PV (n=31)
Age, y, mean (SD)	49.0 (14.1)	53.3 (13.2)	53.3 (17.1)	50.1 (11.4)
Age category, n (%)				
18-64 y	58 (81.7)	24 (82.8)	13 (76.5)	29 (93.5)
65-74 y	11 (15.5)	4 (13.8)	3 (17.6)	1 (3.2)
≥75 y	2 (2.8)	1 (3.4)	1 (5.9)	1 (3.2)
Sex at birth, n (%)				
Female	47 (66.2)	10 (34.5)	6 (35.3)	15 (48.4)
BMI, (kg/m)				
Mean (SD)	28.6 (7.9)[b]	27.5 (4.6)	27.3 (6.0)	27.5 (4.5)
Range (min; max)	18.0; 64.4	18.6; 36.6	17.5; 41.8	19.5; 41.6
Race, n (%)				
Asian	9 (12.7)	4 (13.8)	2 (11.8)	4 (12.9)
Black or African American	-	-	-	1 (3.2)
White	60 (84.5)	21 (72.4)	15 (88.2)	26 (83.9)
Multiple	2 (2.8)	-	-	-
Not reported	-	4 (13.8)	-	-

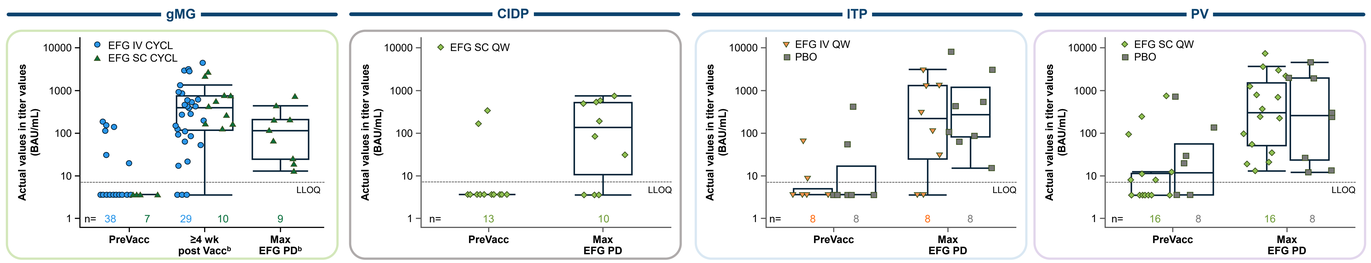
[a]Participant data are included only for those who had a prevaccination titer sample and ≥1 postvaccination titer sample available.
[b]BMI data were unavailable for 2 individuals.

Table 2. First Documented COVID-19 Vaccination Received by Participants in gMG, CIDP, ITP, and PV Studies[a,b]

First COVID-19 Vaccine[d], n (%)	gMG[c]	CIDP[c]	ITP		PV	
	EFG IV/SC (n=45)	EFG SC (n=13)	EFG IV (n=8)	PBO (n=8)	EFG SC (n=16)	PBO (n=8)
Pfizer-BioNTech	33 (73.3)	5 (38.5)	5 (62.5)	3 (37.5)	9 (56.3)	5 (62.5)
Unknown	5 (11.1)	2 (15.4)	1 (12.5)	1 (12.5)	4 (25.0)	-
Spikevax (Moderna)	4 (8.9)	2 (15.4)	-	1 (12.5)	2 (12.5)	1 (12.5)
Janssen	1 (2.2)	2 (15.4)	-	1 (12.5)	1 (6.3)	-
Oxford–AstraZeneca	-	1 (7.7)	1 (12.5)	-	-	1 (12.5)
Sputnik V	2 (4.4)	-	-	-	-	1 (12.5)
Sinovac	-	-	-	2 (25.0)	-	-
Sinopharm	-	1 (7.7)	1 (12.5)	-	-	-

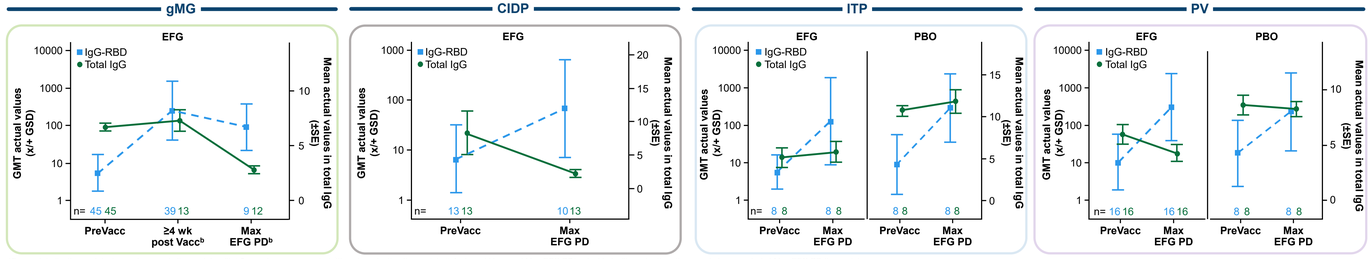
[a]For COVID-19 vaccinations consisting of multiple injections (ie, injections within 45 days of each other), only blood samples before the first injection and after the last injection were selected. [b]Participants who had prevaccination titer sample and ≥1 postvaccination titer sample available. [c]One participant in the gMG group and 4 participants in the CIDP group treated with placebo received their first COVID-19 vaccination during the study but were excluded from this analysis due to low n values in these groups. [d]Participants who received a COVID-19 vaccination before entering the study are excluded from Table 2.

Figure 1. Individual SARS-CoV-2-IgG-RBD Titer Values Box Plots After First Documented Vaccination Across Indications[a]



[a]For each indication and dosing regimen, only time points with ≥5 samples are presented. [b]If postvaccination time points (≥4 weeks post Vacc and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD time point.

Figure 2. GMT Actual SARS-CoV-2-IgG-RBD Values and Mean Actual Total IgG Titer Values After First Documented Vaccination Across Indications[a]



[a]For each indication and dosing regimen, only time points with ≥5 samples are presented. [b]If postvaccination time points (≥4 wk post Vacc and Max EFG PD) coincided with each other, the sample is presented at Max EFG PD time point.

SARS-CoV-2-IgG-S, SARS-CoV-2-IgG-N, and SARS-CoV-2-IgG-NEUT Titer Values Across

- 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]
- SARS-CoV-2-IgG-NEUT titer values increased in response to vaccination, regardless of indication or dosing regimen

ABBREVIATIONS
CIDP, chronic inflammatory demyelinating polyneuropathy; COVID-19, coronavirus disease 2019; EFG, efgartigimod; ELISA, enzyme-linked immunosorbent assay; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; GMT, geometric mean titer; Ig, immunoglobulin; ITP, immune thrombocytopenia; IV, intravenous; LLOQ, lower limit of quantification; MG, myasthenia gravis; mRNA, messenger RNA; -N, nucleocapsid protein; -NEUT, neutralizing antibodies; OLE, open-label extension; PBO, placebo; PD, pharmacodynamic; PreVacc, prevaccination; PV, pemphigus vulgaris; QW, once a week; Q2W, every other week; -RBD, receptor-binding domain of S protein; rHuPh20, recombinant human hyaluronidase PH20; -S, spike protein; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SARS-CoV-2-IgG, severe acute respiratory syndrome coronavirus 2 specific IgG; SC, subcutaneous.

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