Humoral Immune Response to Polyvalent Pneumococcal Vaccine in Healthy Participants Receiving Efgartigimod

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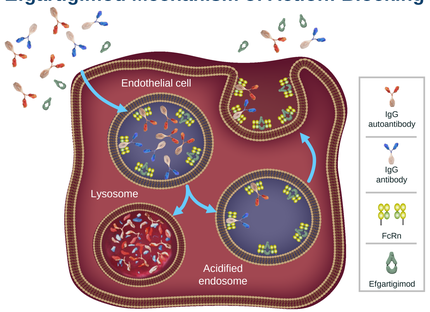
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[2,3]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, reducing IgG levels without impacting IgG production[2-5]
  - Targeted reduction of all IgG subtypes[2,4]
  - No impact on levels of IgM, IgA, IgE, or IgD[2,5]
  - No reduction in albumin or increase in cholesterol levels[4-6]

- In participants with gMG, efgartigimod treatment in ADAPT, ADAPT-SC, and their OLE studies (ADAPT+ and ADAPT-SC+) resulted in consistent and repeatable improvements in efficacy outcomes (eg, MG-ADL, QMG)[4,7-9]
- While some immunosuppressive therapies used in the management of gMG have been shown to blunt responses to vaccines, preliminary studies have suggested that efgartigimod does not prevent responses to either T-cell–independent or –dependent vaccines[10-13]
- The aim of this study was to evaluate whether efgartigimod affects T-cell–independent humoral immune responses to a pneumococcal vaccine (PNEUMOVAX 23) to provide additional clarity on administering vaccinations to patients (including those with gMG) receiving efgartigimod

RESULTS

Table 1. Baseline Demographics
Safety Analysis Set

	EFG-1 (n=12)	EFG-2 (n=12)	Placebo (n=12)
Age, y, mean (SD)	46 (22)	47 (20)	61 (19)
Sex, n (%)			
Female	10 (83.3)	6 (50.0)	6 (50.0)
Male	2 (16.7)	6 (50.0)	6 (50.0)
Race, n (%)			
White	12 (100)	11 (91.7)	11 (91.7)
White and Asian	0	0	1 (8.3)
Black or African	0	1 (8.3)	0

Table 2. Summary of TEAEs
Safety Analysis Set

- No grade ≥3 TEAEs, treatment-emergent SAEs, or deaths were reported

	EFG-1 (n=12)		EFG-2 (n=12)		Placebo (n=12)	
	Events	n (%)	Events	n (%)	Events	n (%)
TEAEs	25	10 (83.3)	35	10 (83.3)	24	10 (83.3)
Related TEAEs	2[a]	2 (16.7)	0	0	0	0
Discontinued due to TEAEs	2[b]	2 (16.7)	0	0	0	0

[a]The 2 TEAEs were grade 1 erythema and grade 2 herpes zoster. [b]TEAEs were COVID-19, which required discontinuation per study protocol.

ABBREVIATIONS
AE, adverse event; BMI, body mass index; EFG, efgartigimod; ELISPOT, enzyme-linked immunosorbent spot; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; LLOQ, lower limit of quantification; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event; TEAE, treatment-emergent adverse event; VAX, vaccination with PNEUMOVAX 23.

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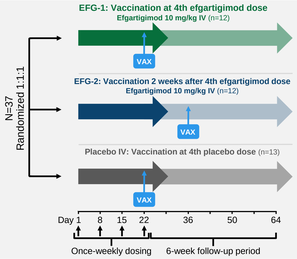
METHODS

A randomized, open-label, placebo-controlled, parallel-group study evaluated immune response to PNEUMOVAX 23 in healthy participants receiving efgartigimod

- PNEUMOVAX 23 is a T-cell–independent, 23-valent pneumococcal polysaccharide vaccine indicated to prevent pneumococcal disease caused by the 23 serotypes[a] contained in the vaccine

Entry criteria
- Healthy adult participants
- BMI between 18 kg/m^2 and 30 kg/m^2
- Total IgG >6 g/L
- No live or live-attenuated vaccines <4 weeks before screening
- No pneumococcal vaccination in the past 10 years
- No documented pneumococcal infection in the past 5 years



Primary endpoints
- Variation in the immune response assessed by comparing pneumococcal capsular polysaccharide titers before and after administration of PNEUMOVAX 23 among study arms

Key secondary endpoint
- Incidence and severity of AEs

Key exploratory endpoints
- Antigen-specific B-cell response before and after PNEUMOVAX 23
- Functional antibody titers before and after PNEUMOVAX 23 administration

[a]Serotypes include 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F.

SUMMARY

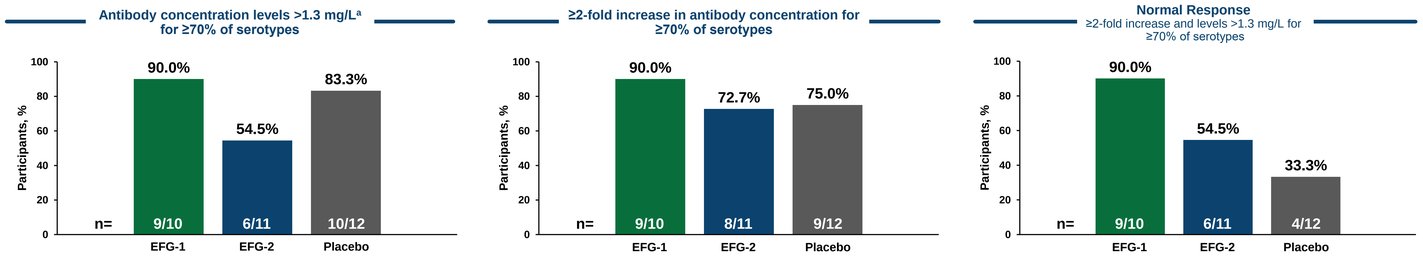
Regardless of vaccination timing (during or after efgartigimod administration), participants were able to mount effective humoral immune responses to a T-cell–independent vaccine

Efgartigimod exhibited a favorable safety profile in a small sample of healthy participants, consistent with previous studies in participants with autoimmune diseases[4,15]

Studies on vaccine response in efgartigimod-treated participants with IgG-mediated autoimmune diseases are ongoing

RESULTS

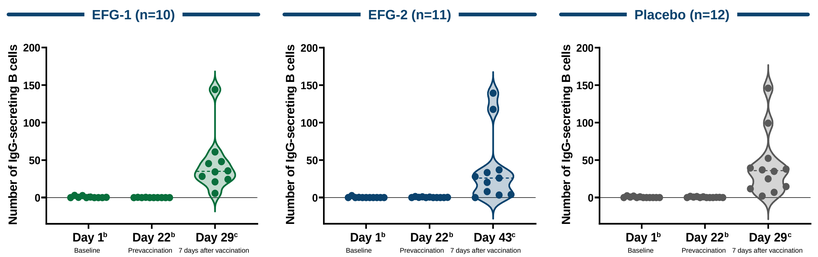
Figure 1. Summary of Participants With Response to Pneumococcal Capsular Polysaccharide Vaccine (Serotypes Combined) 4 Weeks After Vaccination



- Overall, a consistent IgG response for all 23 serotypes was observed after vaccination
- Considerable variability was observed across individual participants and individual serotypes

[a]A level of 1.3 mg/L has been suggested as the threshold for a protective titer.[14]

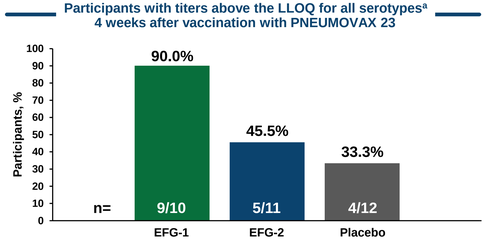
Figure 2. Antigen-Specific IgG-Secreting Plasma B-Cell Response[a] at Baseline, Prevaccination, and 7 Days After Vaccination



[a]The number of antigen-specific IgG-secreting plasma B cells was measured in peripheral blood mononuclear cell samples using a single-color B-cell ELISPOT assay. [b]Absolute values with derived number of cells <0 were set to 0. [c]Dashed line indicates the median.

Figure 3. Functional Antibody Titers: Opsonization Titers After Vaccination With PNEUMOVAX 23

- Geometric mean opsonization titers increased after vaccination with PNEUMOVAX 23 for 8 serotypes[a] in all arms
- Similar to the pneumococcal capsular polysaccharide titers, variability occurred between serotypes and participants



[a]Serotypes included 1, 4, 5, 6B, 7F, 14, 19A, and 23F, which are the most prevalent pneumococcus serotypes.

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