

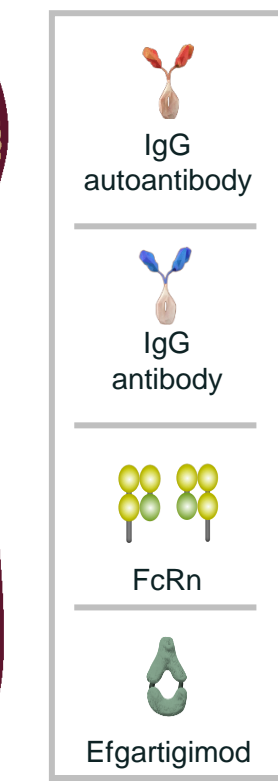
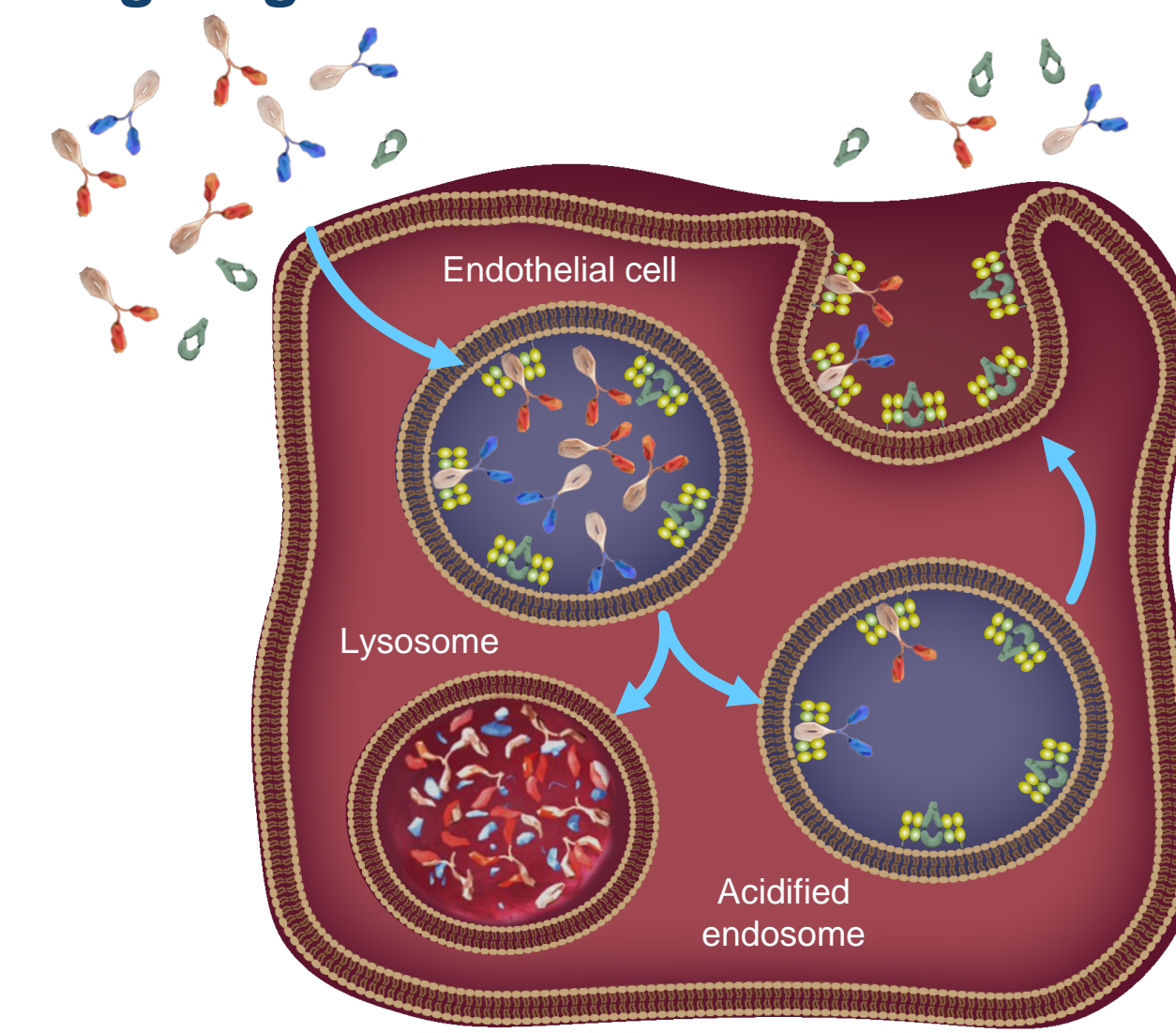
Humoral Immune Response to Polyvalent Pneumococcal Vaccine in Healthy Participants Receiving Efgartigimod

Antoine Azar,¹ John W. Sleasman,² Fien M. Verhamme,³ Kevin Winthrop⁴
¹Johns Hopkins University, Division of Allergy and Clinical Immunology, Baltimore, Maryland; ²Duke University School of Medicine, Division of Allergy and Immunology, Durham, North Carolina; ³argenx, Ghent, Belgium; ⁴Oregon Health and Science University, Division of Infectious Disease, Portland, Oregon



INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG to extend its half-life and maintain its high serum concentration¹
- 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 production²⁻⁵
 - 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 levels⁴⁻⁶

- 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 vaccines¹⁰⁻¹³
- 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

^aThe 2 TEAEs were grade 1 erythema and grade 2 herpes zoster. ^bTEAEs were COVID-19, which required discontinuation per study protocol.

ABBREVIATIONS

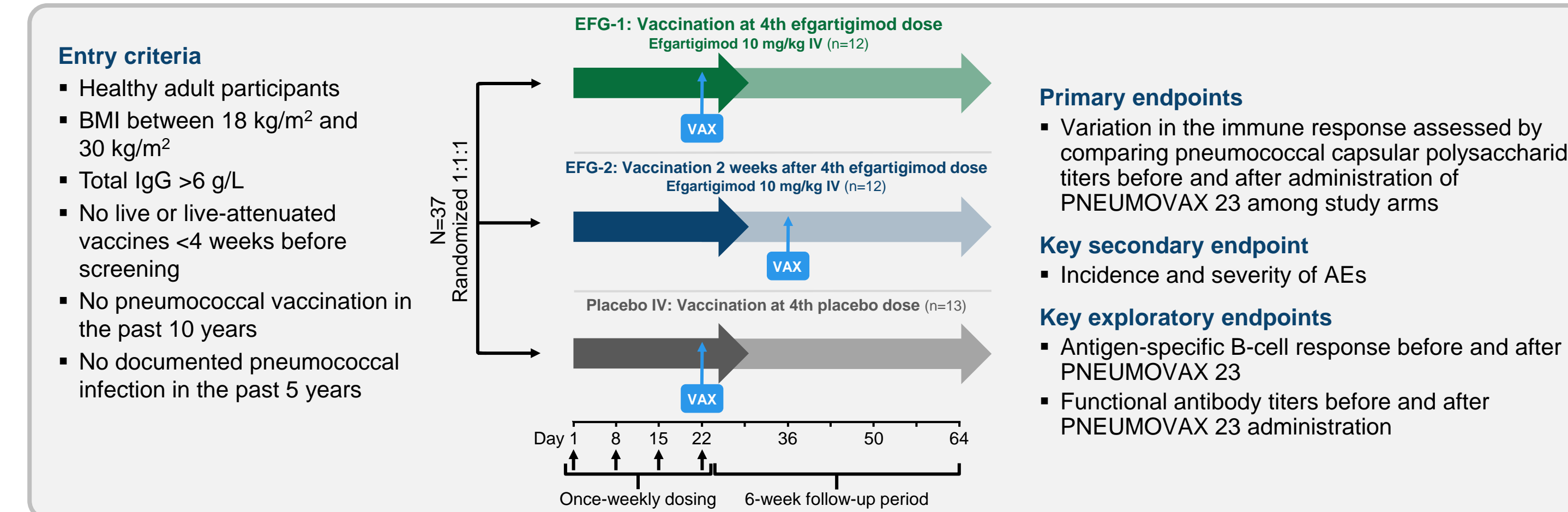
AE, adverse event; BMI, body mass index; EFG, efgartigimod; ELISPOT, enzyme-linked immunosorbent spot; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; LLOQ, lower limit of quantification; MG-ADL, Myasthenia Gravis Activities of Daily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

ACKNOWLEDGMENTS AND DISCLOSURES: The authors gratefully acknowledge the trial participants and investigators. AA has received research support from X4 and Grifols and is a consultant for Grifols, Takeda, Pfizer, Janssen, and argenx. JWS receives research and salary support from the National Institutes of Health, Collective, Enzyvant, and the Jeffrey Modell Foundation and is a consultant for argenx. FMV is an employee of argenx. KW has received research support from Bristol Myers Squibb and Pfizer and consulting honoraria from Pfizer, AbbVie, UCB, Eli Lilly, Galapagos, GSK, Roche, Gilead, Bristol Myers Squibb, Regeneron, Sanofi, AstraZeneca, and Novartis. This trial was funded by argenx. Medical writing and editorial support for this presentation was provided by PRECISION Value & Health and funded by argenx.

METHODS

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

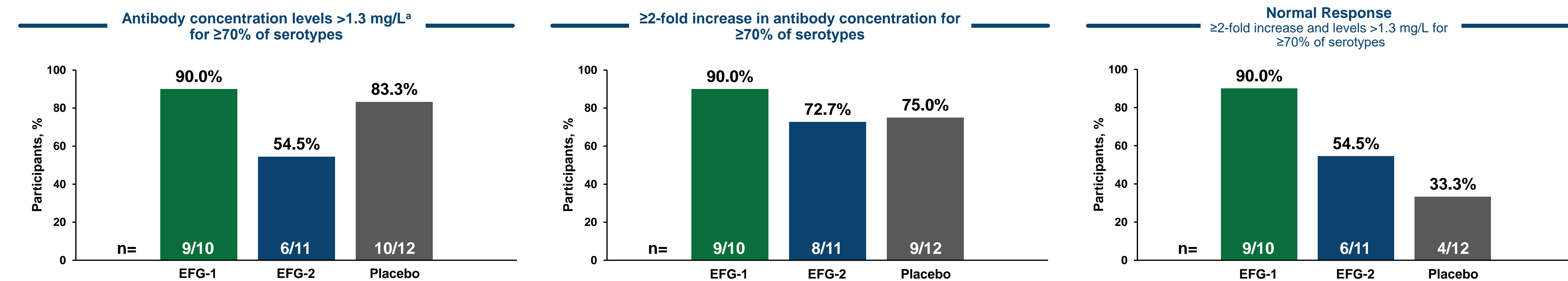
- PNEUMOVAX 23 is a T-cell-independent, 23-valent pneumococcal polysaccharide vaccine indicated to prevent pneumococcal disease caused by the 23 serotypes^a contained in the vaccine



^aSerotypes 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.

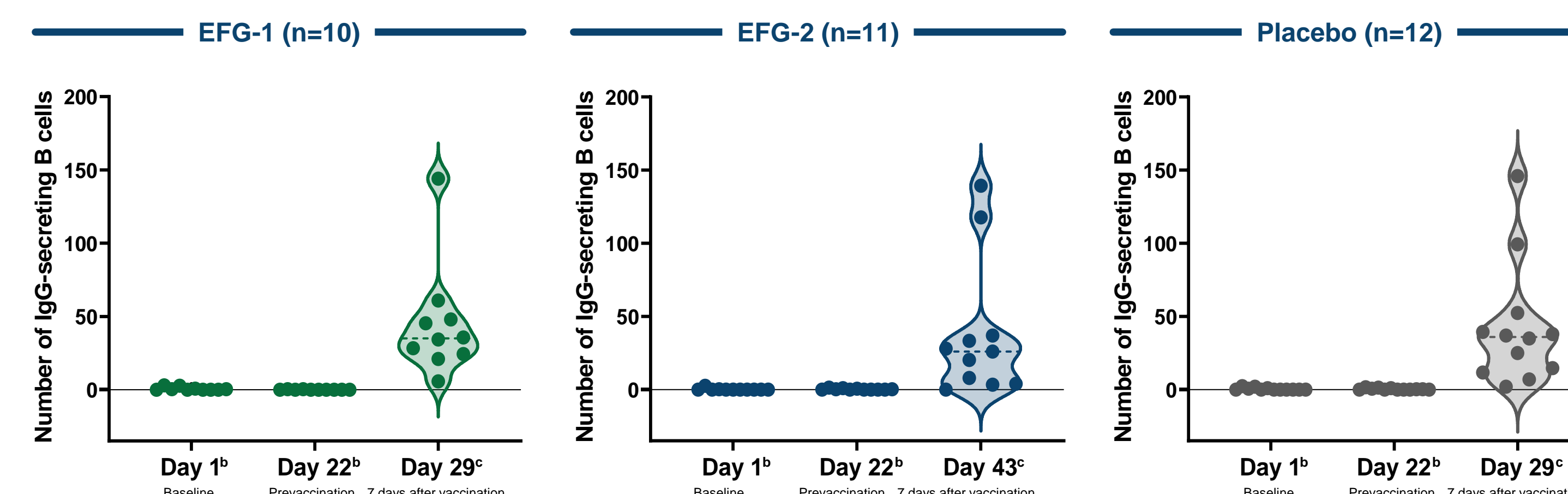
RESULTS

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



^aA 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, Prevacination, and 7 Days After Vaccination



^aThe 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. ^bAbsolute values with derived number of cells <0 were set to 0. ^cDashed line indicates the median.

REFERENCES

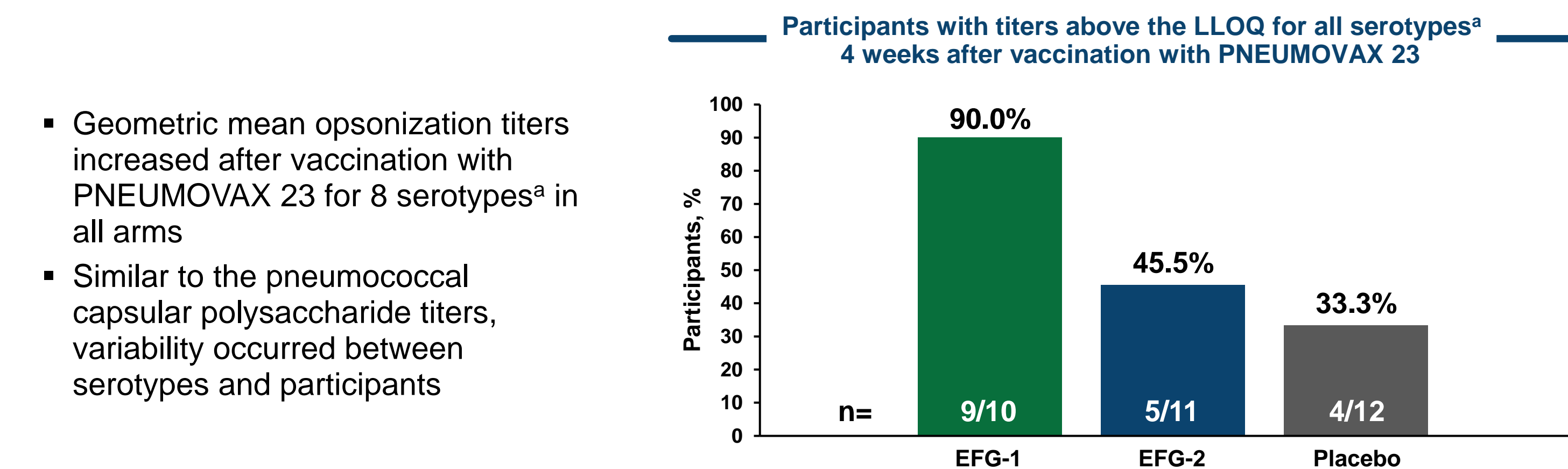
1. Sesarman A, et al. *Cell Mol Life Sci*. 2010;67(15):2533-2550. 2. Ulrichs P, et al. *J Clin Invest*. 2018;128(10):4372-4386. 3. Vaccaro C, et al. *Nat Biotechnol*. 2005;23(10):1283-1288. 4. Howard JF Jr, et al. *Lancet Neurol*. 2021;20(7):526-536. 5. Nixon AE, et al. *Front Immunol*. 2015;6:176. 6. Ward ES, et al. *Front Immunol*. 2022;13:892534. 7. Kaprielian R, et al. Poster presented at: Ottawa International Conference on Neuromuscular Disease and Biology; September 7-9, 2023; Ottawa, Ontario. 8. Howard JF Jr, et al. Poster presented at: AAN (American Academy of Neurology) Annual Meeting; April 22-27, 2023; Boston, Massachusetts. 9. Behr M, et al. Poster presented at: MDA (Muscular Dystrophy Association) Clinical and Scientific Conference; March 19-22, 2023; Dallas, Texas. 10. Gupta JT, et al. *Autoimmunity*. 2022;55(8):620-631. 11. Howard JF Jr, et al. Poster presented at: AANEM (American Association of Neuromuscular & Electrodiagnostic Medicine) annual meeting; September 21-24, 2022; Nashville, Tennessee. 12. Casey J, et al. Poster presented at: ANA (American Neurological Association) Annual Meeting; October 22-25, 2022; Chicago, Illinois. 13. Patel SY, et al. *Front Immunol*. 2019;10:33. 14. Bonilla FA, et al. *J Allergy Clin Immunol*. 2015;136(5):1186-1205. 15. Bri V, et al. Poster presented at: CNSF (Canadian Neurological Sciences Foundation) Congress; June 6-9, 2023; Montreal, Quebec.

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

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

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



^aSerotypes included 1, 4, 5, 6B, 7F, 14, 19A, and 23F, which are the most prevalent pneumococcus serotypes.

