Long-term Safety and Efficacy of Efgartigimod in Patients With Primary Immune Thrombocytopenia: Interim Results of the ADVANCE+ Study

S302

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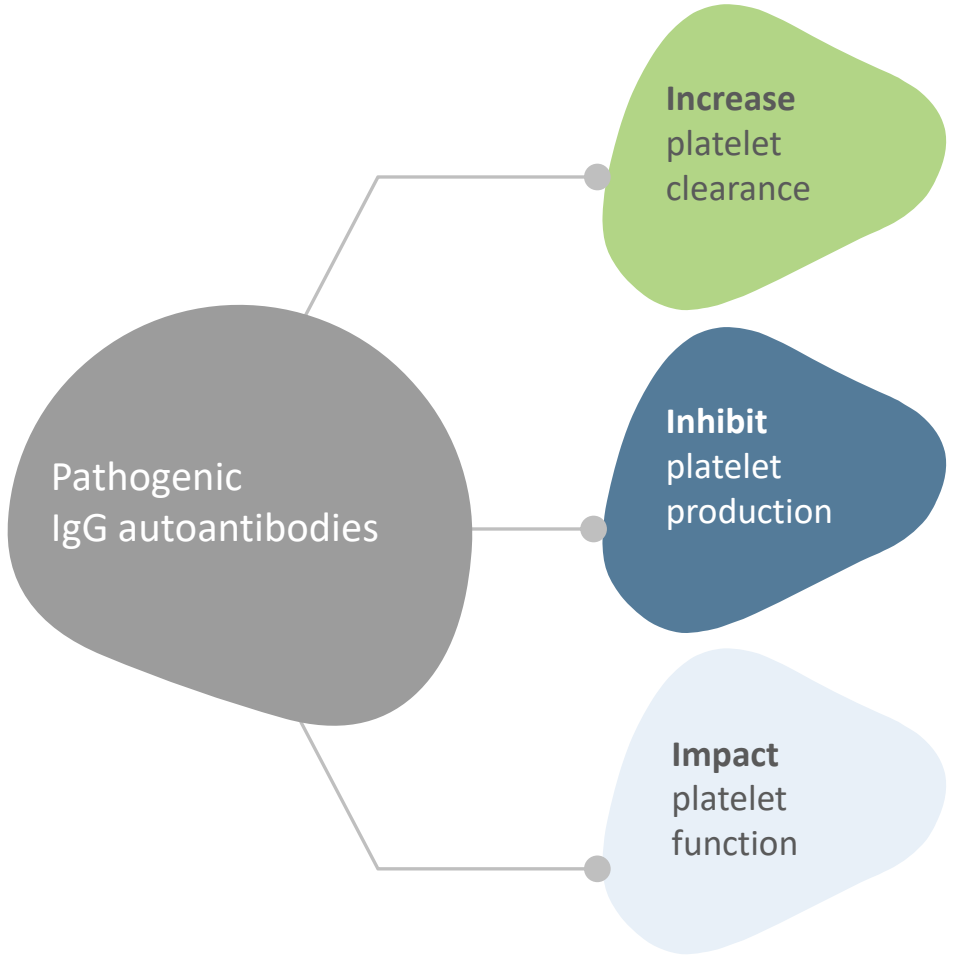
Primary ITP

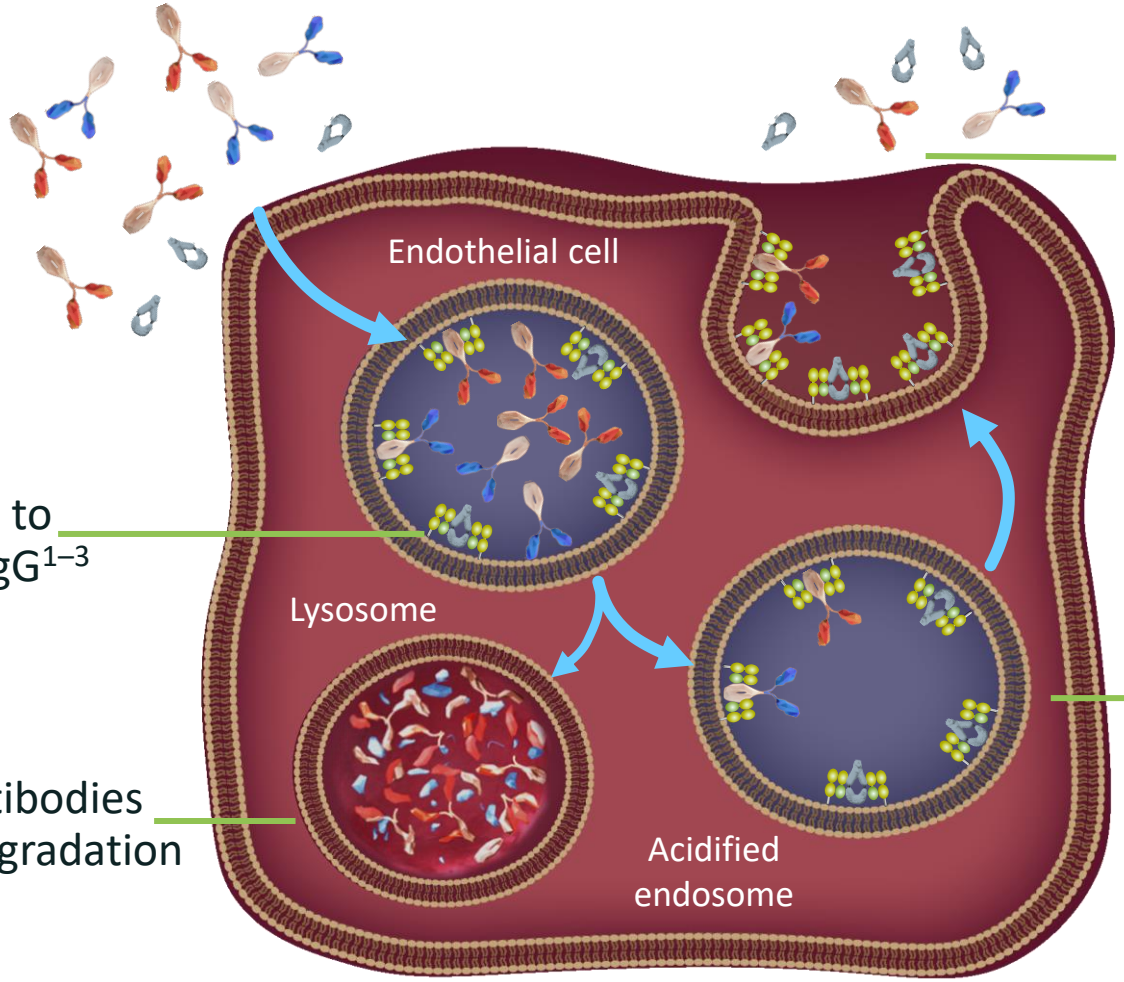
- ITP is an acquired autoimmune disorder characterized by a reduction in platelet count, which can result in[1–4]:
  - Increased risk of bleeding
  - Fatigue
  - Decreased quality of life
- IgG autoantibodies, detected in most patients, target glycoproteins expressed on platelets and megakaryocytes[5–8]
- Current treatment options can be associated with comorbidities, unsatisfactory efficacy and duration of effect, and limited impact on QoL measures[9–11]



IgG, immunoglobulin G; ITP, immune thrombocytopenia; QoL, quality of life.

1. Hill QA, Newland AC. *Br J Haematol*. 2015;170:141–9. **2.** Zufferey A, et al. *J Clin Med*. 2017;6:16. **3.** Kashiwagi H, Tomiyama Y. *Int J Hematol*. 2013;98:24–33. **4.** Swinkels M, et al. *Front Immunol*. 2018;30:880. **5.** Newland AC, et al. *Am J Hematol*. 2020;95:178–87. **6.** He R, et al. *Blood*. 1994;83:1024–32. **7.** van Leeuwen EF, et al. *Blood*. 1982;59:23–26. **8.** McMillan R, et al. *Blood*. 1987;70:1040–5. **9.** Trotter P, Hill QA. *Patient Relat Outcome Meas*. 2018;9:369–84. **10.** McMillan, et al. *Am J Hematol*. 2008;83:150–4. **11.** Mathias, et al. *Health Qual Life Outcomes*. 2008;6:13.

Efgartigimod Competitively Inhibits FcRn



Efgartigimod alfa and fewer IgG (auto)antibodies are recycled back into the bloodstream[3]

Efgartigimod alfa binds to FcRn competing with IgG[1–3]

FcRn-bound complexes are rescued from cellular degradation pathways[2,3]

Unbound IgG (auto)antibodies enter the lysosomal degradation pathway[2,3]

IgG autoantibody

IgG antibody

FcRn

Efgartigimod alfa[4]

FcRn, neonatal Fc receptor; IgG, immunoglobulin G.

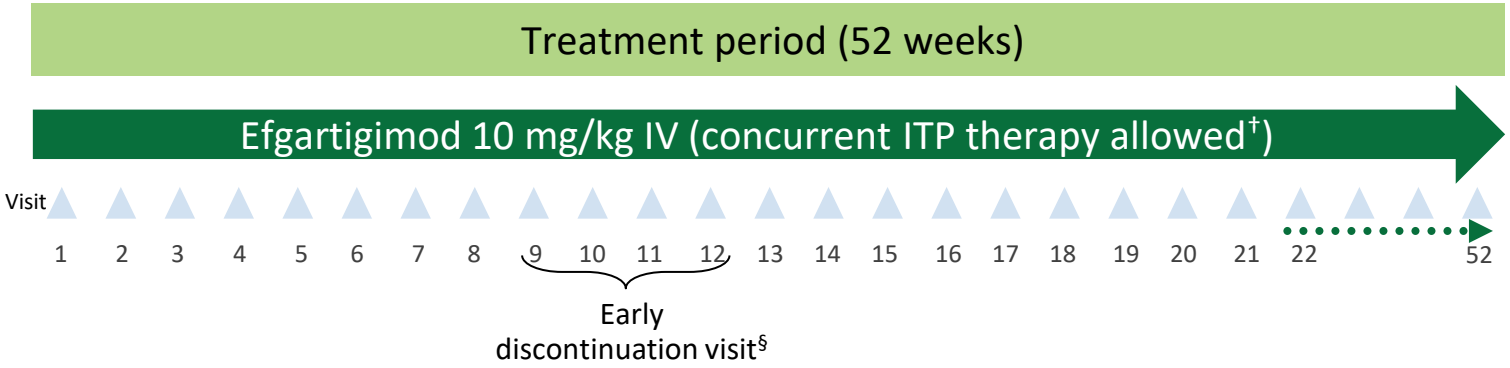
1. VYVGART. Prescribing information. argenx; 2021. Accessed December 17, 2021. https://www.argenx.com/product/vyvgart-prescribing-information.pdf. **2.** Vaccaro C, et al. *Nat Biotech*. 2005;23:1283–8. **3.** Ulrichts P, et al. *J Clin Invest*. 2018;128:4372–86. **4.** Wolfe G, et al. *J Neurol Sci*. 2021;430:118074. Image adapted from Kang TH, Jung ST. Boosting therapeutic potency of antibodies by taming Fc domain functions. *Exp Mol Med*. 2019;51:1–9 and distributed under the terms of the Creative Commons CC-BY license (https://creativecommons.org/licenses/by/4.0/).

ADVANCE+ (NCT04225156): Study Design

Phase 3, Multicenter, Open-label, Long-term Extension Trial ADVANCE+

≥18 years

101 patients with ITP

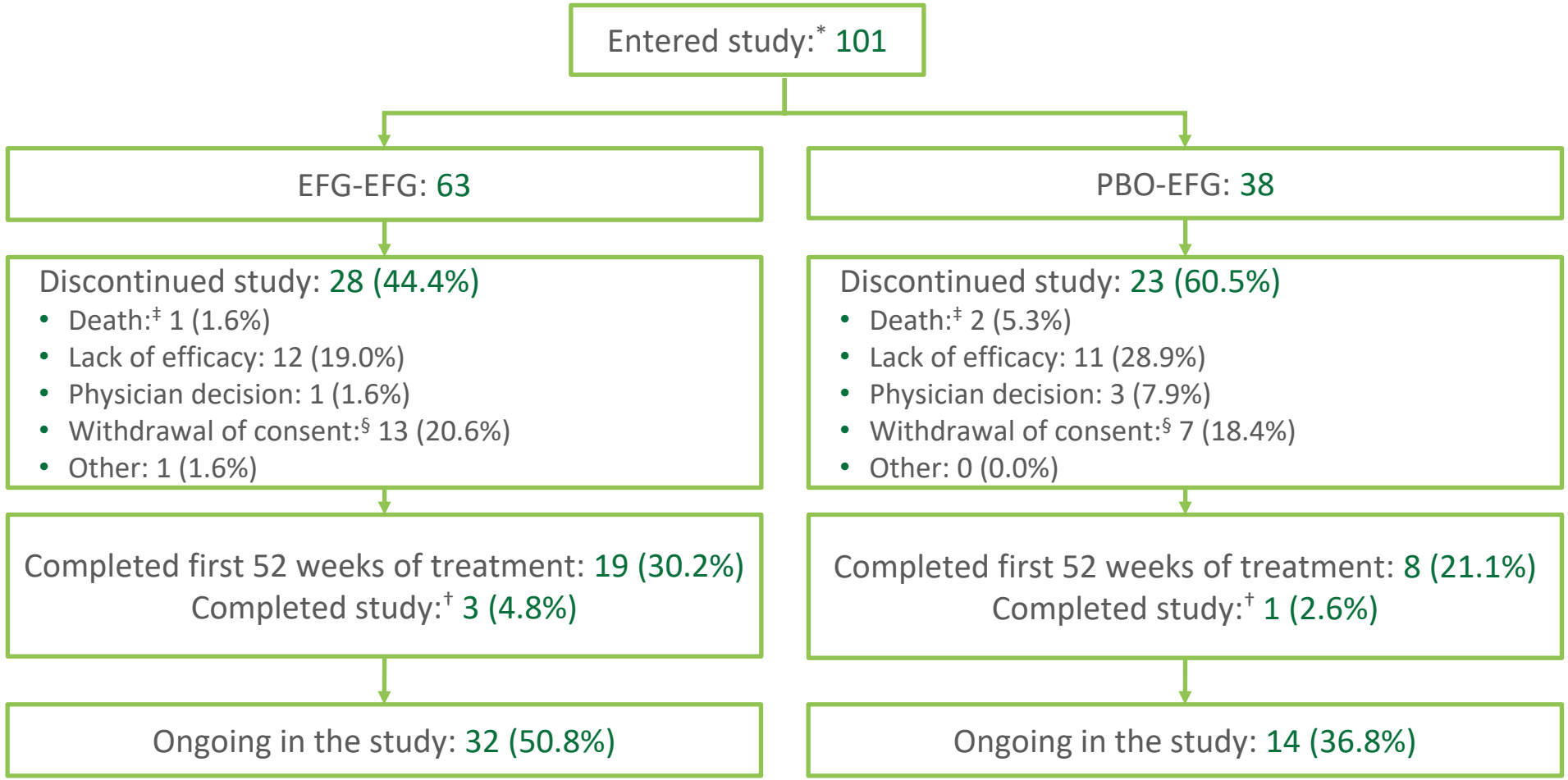


- Dosing frequency will continue as in the ADVANCE study, either once weekly or once every other week (dependent on platelet count response)
- A change in dosing frequency is permitted starting from Visit 1 (baseline)

Primary endpoint	**Long-term safety of efgartigimod in adult participants with primary ITP** • Frequency and severity of AEs • Vital signs and laboratory assessments
Secondary endpoints	• Extent of disease control • Platelet count response • Incidence and severity of the WHO-classified bleeding events • Total IgG • Reduction in concurrent ITP therapy

AE, adverse event; IgG, immunoglobulin G; ITP, immune thrombocytopenia; IV, intravenous; WHO, World Health Organization.
*Such as anti-CD20 therapy, romiplostim, monoclonal antibodies, Fc fusion proteins, or live/live-attenuated vaccines. †Concurrent ITP therapy may be reduced or stopped at the investigator's discretion when platelet count is >100×10^9/L. ‡Extendable up to 3 additional 52-week periods; dosing frequency will continue according to the previous 52-week treatment period (ie, once weekly or once every other week). §Participants who have an insufficient response by Visit 12 will exit the study. An insufficient response is defined as a platelet count of <30×10^9/L in all the last 4 visits between Visit 9 and Visit 12 (both visits inclusive).

Many Participants in ADVANCE+ Are Still Ongoing



EFG, efgartigimod; PBO, placebo.

*Cut-off data as of September 28, 2022. †Participants have completed all treatment and follow-up visits as of the data cut-off date. ‡The investigator did not consider any adverse events leading to death related to efgartigimod.

§Not related to a treatment-emergent adverse event.

EFG-EFG: Participants who received efgartigimod in ADVANCE and continued to receive efgartigimod in ADVANCE+. PBO-EFG: Participants who received a placebo in ADVANCE and who received efgartigimod in ADVANCE+.

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Approximately 30% of Participants Received Once Every-Other-Week Dosing of Efgartigimod

	EFG-EFG (N=63)	PBO-EFG (N=38)	Total (N=101)
Number of administrations			
Mean (SD)	27.7 (18.87)	25.2 (19.07)	26.8 (18.89)
Median (min, max)	24.0 (3, 71)	14.0 (3, 64)	23.0 (3, 71)
Received once every-other-week dosing at any time			
n (%)	22 (34.9)	9 (23.7)	31 (30.7)
Cumulative duration of once every-other-week dosing, weeks			
Mean (SD)	12.3 (8.24)	7.3 (3.32)	10.8 (7.46)
Median (min, max)	15.0 (2, 24)	8.0 (4, 12)	10.0 (2, 24)
Any concurrent ITP therapy, n (%)	**30 (47.6)**	**20 (52.6)**	**50 (49.5)**
Corticosteroids	14 (22.2)	13 (34.2)	27 (26.7)
Danazol	2 (3.2)	1 (2.6)	3 (3.0)
IVIg, anti-D	2 (3.2)*	1 (2.6)*	3 (3.0)
Other immunosuppressants	7 (11.1)	7 (18.4)	14 (13.9)
TPO-RAs	13 (20.6)	9 (23.7)	22 (21.8)

anti-D, anti-D immunoglobulin; EFG, efgartigimod; IVIg, intravenous immunoglobulin; ITP, immune thrombocytopenia; PBO, placebo; TPO-RA, thrombopoietin receptor agonist.
*Participants who had prohibited medications classified as continued concurrent ITP therapies.

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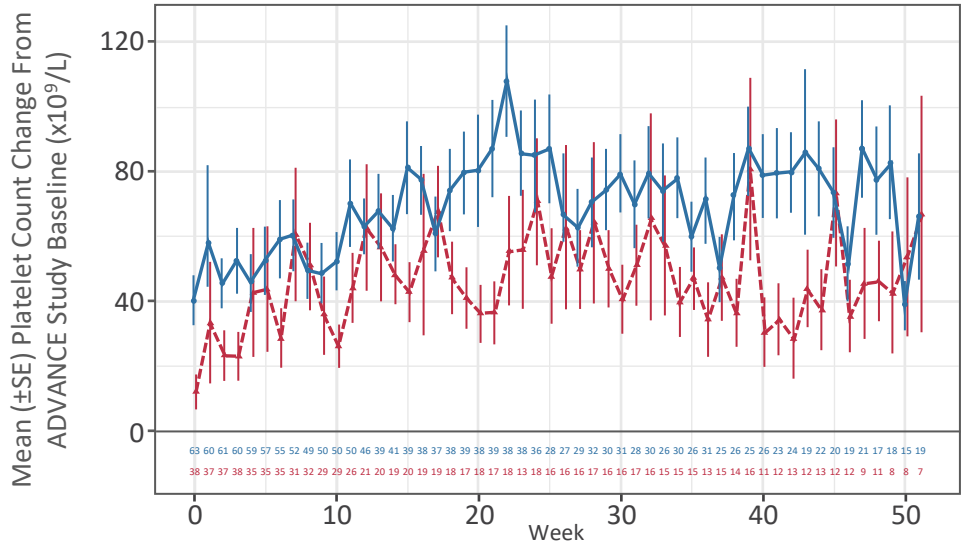
Efgartigimod Administration Rapidly Increased Platelet Levels and Generally Maintained Throughout the Study Period

	EFG-EFG (N=63)	PBO-EFG (N=38)	Total (N=101)
Number of cumulative weeks of disease control, mean (SE) Number of weeks with platelet counts ≥50×10^9/L	45.1 (4.99)	29.3 (5.79)	39.2 (3.86)
Sustained platelet count response, n/N (%) ≥50×10^9/L in ≥4/6 visits during Weeks 13–18	21/63 (33.3)	9/38 (23.7)	30/101 (29.7)
Sustained platelet count response, n/N (%) ≥50×10^9/L in ≥4/6 visits during Weeks 19–24	23/63 (36.5)	10/38 (26.3)	33/101 (32.7)
Overall platelet count responders, n (%) ≥50×10^9/L in ≥4 occasions at any time during the first 52-week treatment period	21 (44.7)	11 (36.7)	32 (41.6)

Mean (±SE) Change From Baseline Over Time in Platelet Count



Of the 77 participants in the total group†, 62 (80.5%) had ≥1 WHO-classified bleeding event (grade 1 or 2)

Of the 41 evaluable participants receiving concurrent therapy‡ at baseline:

- 4 (9.8%) reduced concurrent ITP therapy during the first 52-week treatment period.
  - EFG-EFG: 1 (4.0%)
  - PBO-EFG: 3 (18.8%)

EFG, efgartigimod; ITP, immune thrombocytopenia; NCI, National Cancer Institute; PBO, placebo; SE, standard error; TPO-RA, thrombopoietin receptor agonist; WHO, World Health Organization.
†Only participants who reached Week 51 or discontinued during the first 52-week treatment period were considered. ‡Defined as a decrease in either the dose and/or frequency of at least 1 concurrent ITP therapy without an increase of any concurrent ITP therapies (except TPO-RAs and fostamatinib) during the first 52-week treatment period from study baseline.

Most AEs Were Mild or Moderate in Severity

	EFG-EFG (N=63)			PBO-EFG (N=38)			Total (N=101)		
	n (%)	No. of events	PYFU	n (%)	No. of events	PYFU	n (%)	No. of events	PYFU
≥1 AE	57 (90.5)	324	7.10	36 (94.7)	241	10.25	93 (92.1)	565	8.18
≥1 SAE	8 (12.7)	12	0.26	4 (10.5)	9	0.38	12 (11.9)	21	0.30
≥1 fatal AE	1 (1.6)	1	0.02	2 (5.3)	2	0.09	3 (3.0)	3	0.04
≥1 AESI (bleeding)	43 (68.3)	154	3.38	33 (86.8)	139	5.91	76 (75.2)	293	4.24
≥1 AESI (infections)	22 (34.9)	40	0.88	12 (31.6)	13	0.55	34 (33.7)	53	0.77
Most commonly reported AEs (≥10% of participants)									
COVID-19	14 (22.2)	15		6 (15.8)	6		20 (19.8)	21	
Blood urine present	24 (38.1)	46		18 (47.4)	29		42 (41.6)	75	
Petechiae	11 (17.5)	15		6 (15.8)	16		17 (16.8)	31	

Infections were mostly mild or moderate in severity and occurred in 34 (33.7%) participants

- 58.8% of participants with an infection experienced COVID-19*
- Other infections included influenza, nasopharyngitis, upper respiratory tract infection, urinary tract infection, pulpitis dental, and rhinitis

3 deaths occurred during the study

- 1 participant in the EFG-EFG group died from femur fracture[†] and 2 in the PBO-EFG group died from pulmonary fibrosis[‡] and cerebral hemorrhage[§]
- None of the AEs leading to death were considered related to EFG by the investigator

AE, adverse event; AESI, adverse event of special interest; EFG, efgartigimod; No., number; PBO, placebo; PYFU, event rates per participants years of follow-up; SAE, serious adverse event.
*1 grade 3 infection of COVID-19 pneumonia occurred in 1 participant in the EFG-EFG group; it was not considered by the investigator to be related to efgartigimod. [†]Received 5 EFG doses in ADVANCE and 2 EFG doses in ADVANCE+. [‡]Received 41 EFG doses in ADVANCE+. [§]Received 58 doses of EFG in ADVANCE+.

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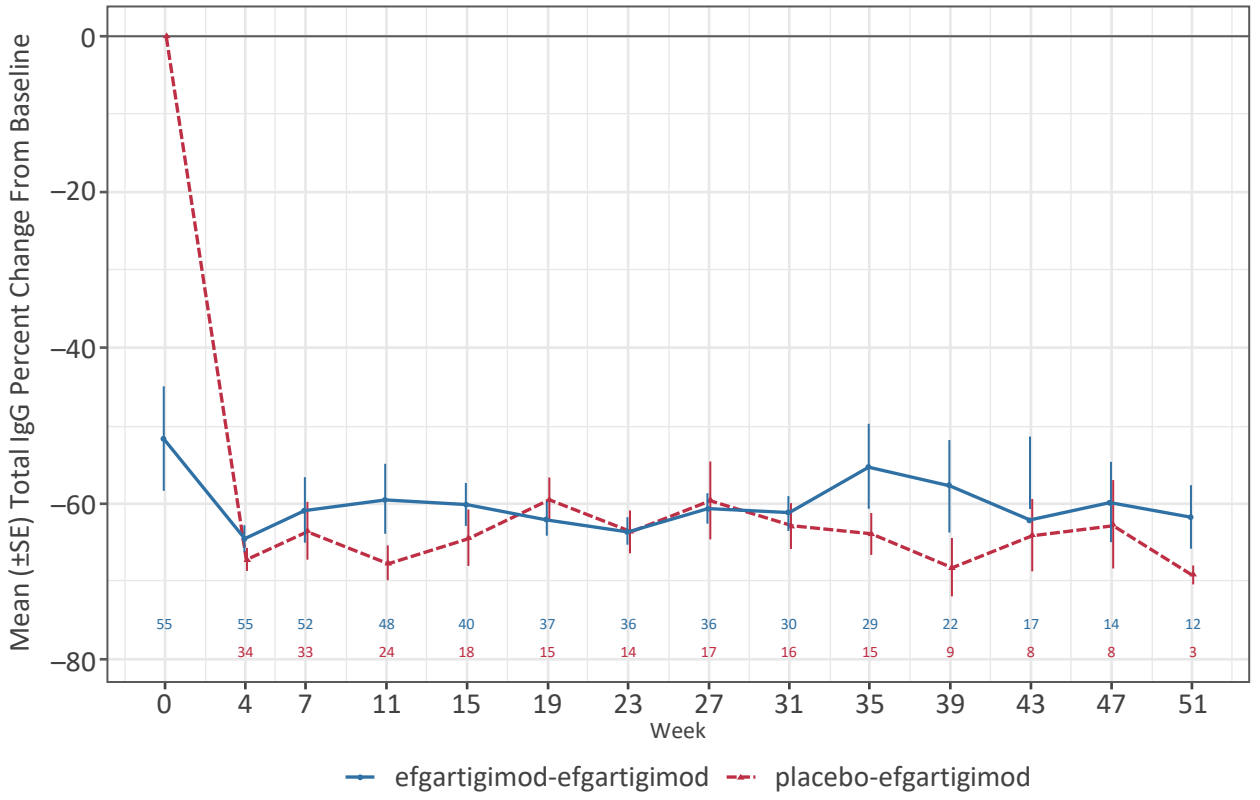
Efgartigimod Administration Resulted in a Sustained Reduction of Total Serum IgG Levels

- Mean reduction in total IgG levels from their respective baselines was approximately 60% in both groups
  - PBO-EGF group: Mean reduction in total IgG levels from the ADVANCE+ baseline was approximately 60% from Week 4 through Week 51
  - EFG-EFG group: Mean IgG reduction maintained similar to the antecedent ADVANCE study (~60%)

Mean (±SE) Percent Change From Baseline in Total IgG Levels (Safety Analysis Set)*



IgG, immunoglobulin G; EFG, efgartigimod; PBO, placebo; SE, standard error.
*For participants who received efgartigimod in the ADVANCE study (efgartigimod-efgartigimod group), baseline total IgG levels from ADVANCE were used. For participants who received placebo in the ADVANCE study (placebo-efgartigimod group), baseline total IgG levels from ADVANCE+ were used.

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Efgartigimod Phase 3 ADVANCE+ Study Conclusions

- Long-term continued efgartigimod treatment in participants with long-standing ITP, including those who have received multiple prior therapies, was well tolerated and not associated with an increased exposure-adjusted risk for infection
- Sustained reductions in total IgG levels and platelet count increases were also observed, indicating no loss of response over time
- Participants who switched from placebo to efgartigimod had early and sustained platelet count increases, which generally mirrored participants who received efgartigimod in ADVANCE including the ability to switch dosing regimen based on response

IgG, immunoglobulin G; ITP, immune thrombocytopenia.

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