Efficacy and Safety of Intravenous Efgartigimod in Adults With Primary Immune Thrombocytopenia: Results of ADVANCE IV, a Phase 3, Multicenter, Double-blinded, Placebo-controlled, Randomized Clinical Trial

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Presented at the 64th Annual American Society of Hematology (ASH) Annual Meeting; December 10–13, 2022; New Orleans, LA, USA.

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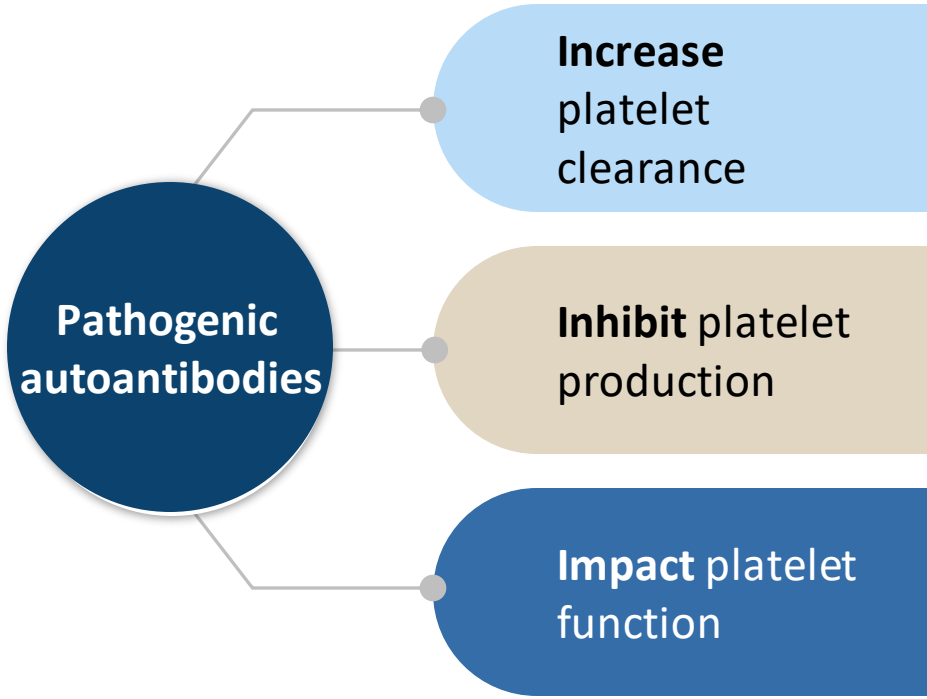
Primary Immune Thrombocytopenia (ITP)

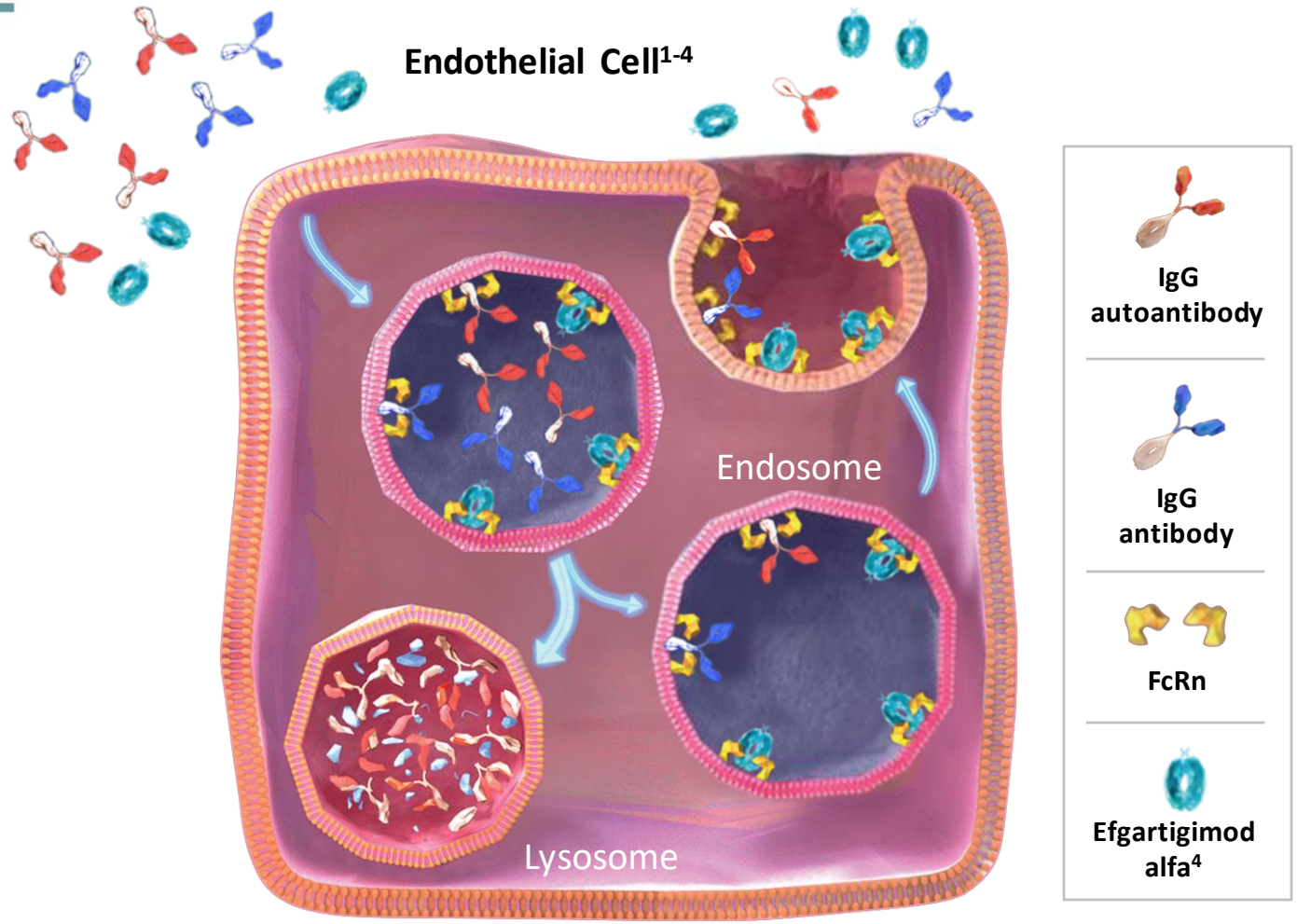
- ITP is an acquired autoimmune disorder characterized by a reduction in platelet count, which can result in[1-4]:
  - Increased risk of bleeding
  - Fatigue
  - Decreased quality of life
- IgG autoantibodies, detected in most patients, target glycoproteins expressed on platelets and megakaryocytes[5-8]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



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

1. Hill QA, Newland AC. *Br J Haematol*. 2015;170:141–149. 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;95:178–187. 6. He R, et al. *Blood.* 1994;83:1024–1032. 7. van Leeuwen EF, et al. *Blood.* 1982;59:23–26. 8. McMillan R, et al. *Blood*. 1987;70:1040–1045. 9. Trotter P, Hill QA. *Patient Relat Outcome Meas*. 2018;9:369–384. 10. McMillan, et al. *Am J Hematol*. 2008;83:150–154. 11. Mathias, et al. *Health Qual Life Outcomes*. 2008;6:13.

Efgartigimod Competitively Inhibits FcRn

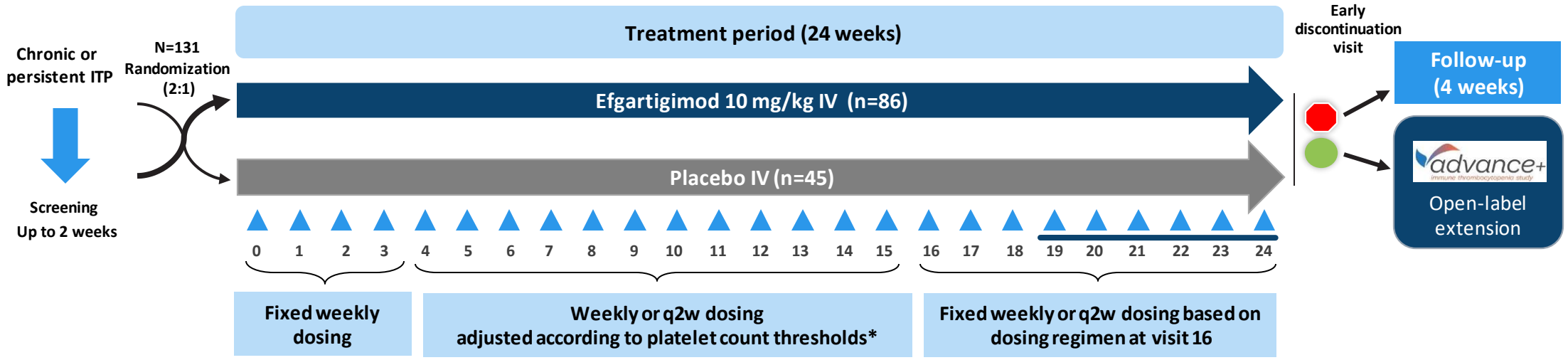


FcRn = neonatal Fc receptor; IgG = immunoglobulin G.

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(10):1283-1288. 3. Ulrichts P, et al. *J Clin Invest*. 2018;128(10):4372-4386. 4. Wolfe G, et al. *J Neurol Sci*. 2021;430:118074. doi:10.1016/j.jns.2021.118074.

ADVANCE IV (NCT04188379): Study Design

Phase 3, Multicenter, Double-blinded, Placebo-controlled, Randomized Clinical Trial

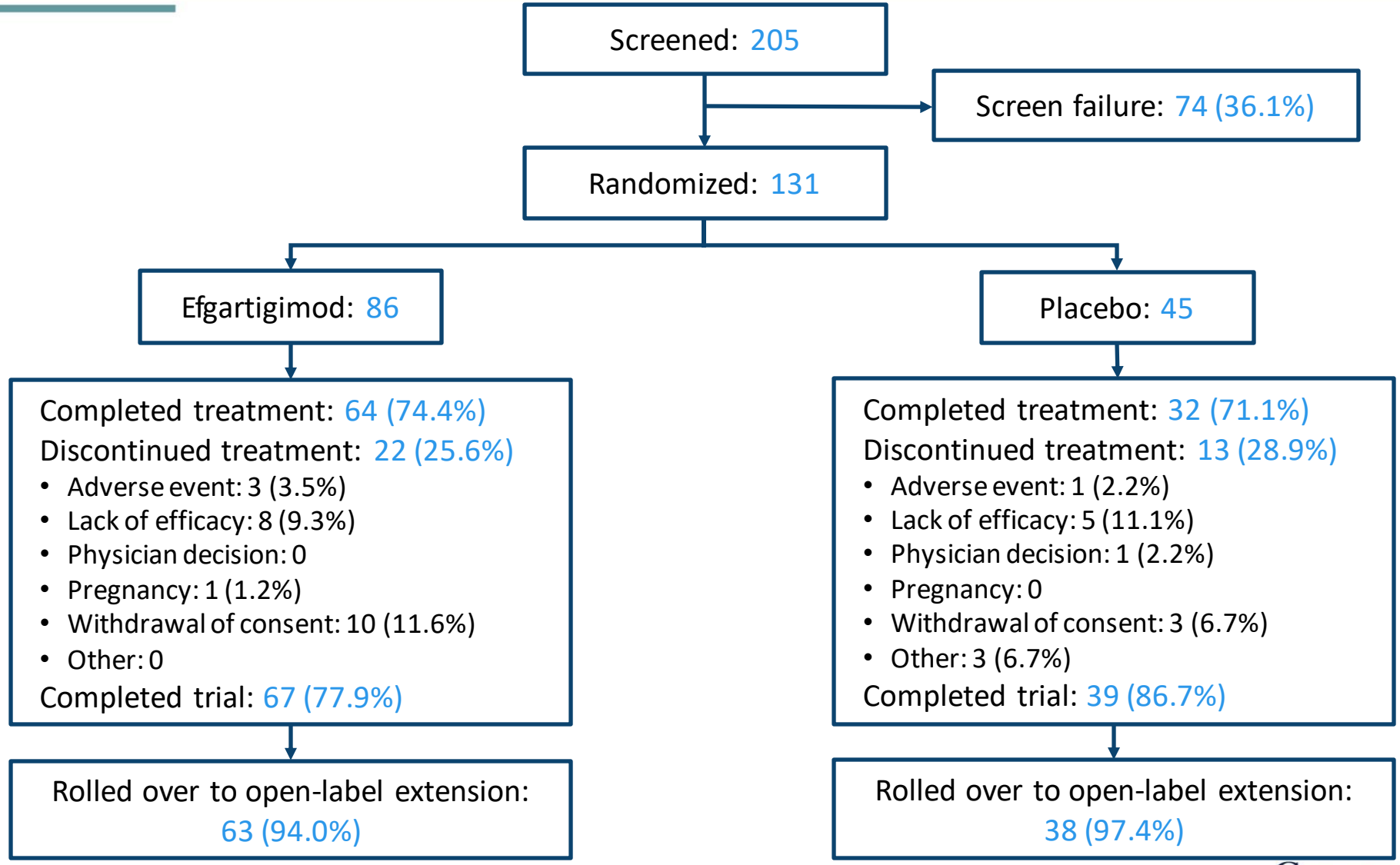


Eligibility criteria

- Age ≥18 years
- Chronic or persistent ITP: Diagnosis supported by a response to a prior ITP therapy
- 2 platelet counts of <30×10^9/L during screening
- At least 2 prior ITP treatments or 1 prior and 1 concurrent treatment
- Concurrent ITP therapy† permitted at stable dose and frequency at study entry and throughout study

*q2w if ≥100×10^9/L for 3 of 4 visits or ≥100×10^9/L for 3 consecutive visits; weekly if <100×10^9/L on 2 consecutive visits, <30×10^9/L at 1 visit or rescue therapy received.
†Concurrent oral corticosteroids, oral immunosuppressants, dapsone, danazol, fostamatinib, and oral thrombopoietin receptor agonists (not romiplostim).
q2w = every other week; ITP = immune thrombocytopenia; IV = intravenously.

Participants Were Randomized 2:1 and Most Completed Treatment



Baseline Characteristics Indicate the Majority of Participants Had Multiple Prior Therapies and Long-standing ITP

	Efgartigimod* (n=86)	Placebo* (n=45)
Age, mean, years (SD)	46.9 (16.6)	51.7 (17.9)
Female, n (%)	47 (54.7)	24 (53.3)
Time since diagnosis, mean, years (SD)	10.3 (12.1)	11.1 (13.1)
Patients with chronic / persistent ITP, n	78 / 8	40 / 5
Platelet count, 10^9/L mean (SD)	17.3 (10.2)	14.2 (9.2)
Patients with history of splenectomy, n (%)	32 (37.2)	17 (37.8)
World Health Organization (WHO) bleeding score, n (%)		
No bleeding	44 (51.2)	16 (35.6)
Grade 1	38 (44.2)	25 (55.6)
≥Grade 2	4 (4.7)	4 (8.9)
Patients with ≥3 prior ITP therapies, n (%)	59 (68.6)	29 (64.4)
Concurrent ITP therapy types at baseline, n (%)		
Corticosteroids	22 (25.6)	12 (26.7)
Oral TPO-RA	20 (23.3)	9 (20.0)
Other immunosuppressants	8 (9.3)	6 (13.3)
None	43 (50.0)	23 (51.1)

[a]Safety Analysis Set.

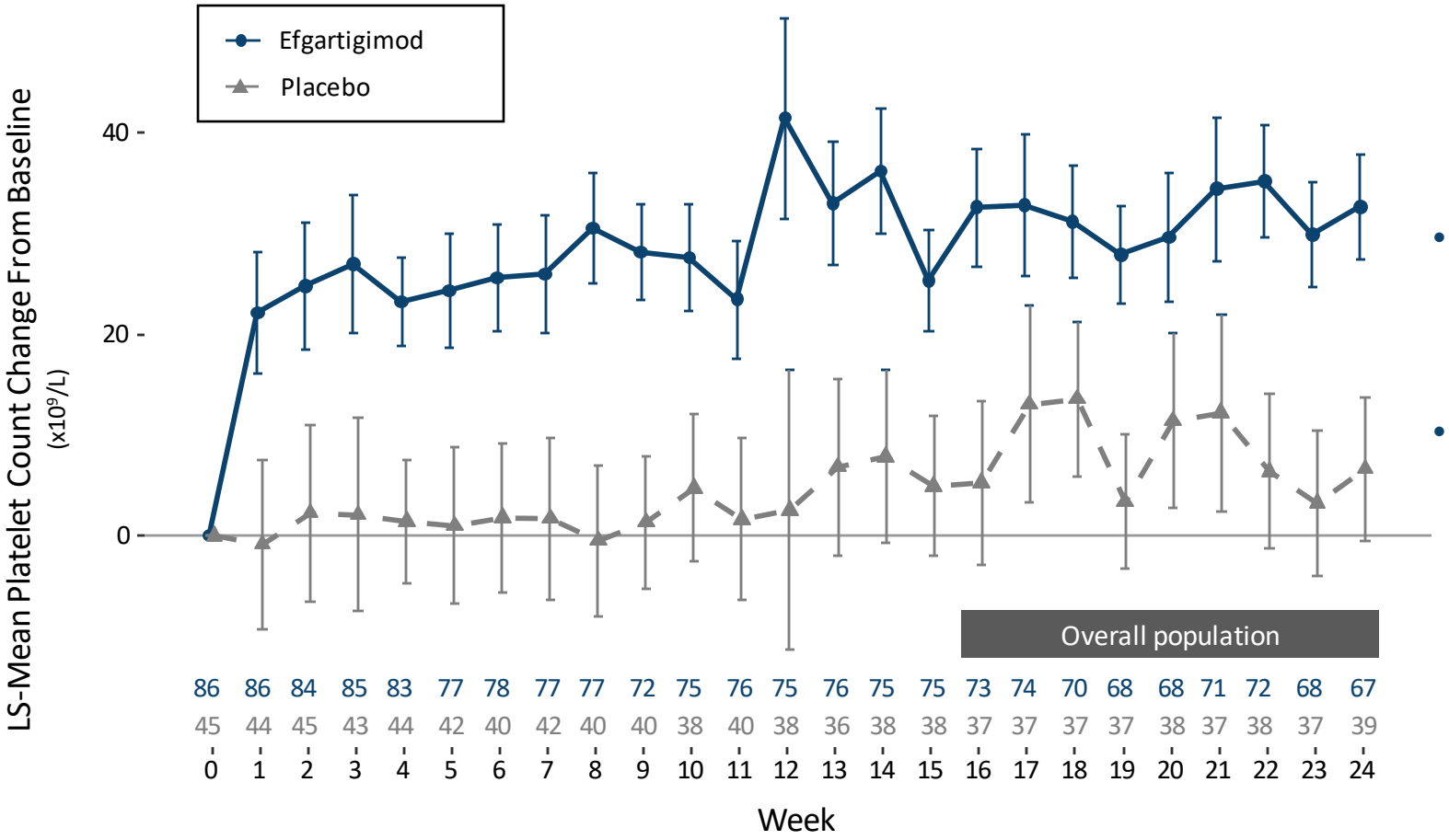
ITP = immune thrombocytopenia; SD = standard deviation; TPO-RA = thrombopoietin receptor agonists; WHO = World Health Organization.

Efficacy Endpoints: Primary and All Platelet-related Secondary Endpoints Were Met*

Endpoint†	Efgartigimod	Placebo	*P*-value
Primary endpoint			
Proportion with sustained platelet count response, n/N (%)‡ ≥50×10^9/L in ≥4/6 visits during weeks 19-24, in the absence of intercurrent events†	17/78 (21.8%)	2/40 (5.0%)	**0.0316**
Key secondary endpoints			
Number of cumulative weeks of disease control, Mean (SD)‡ Number of weeks with platelet counts ≥ 50 x 10^9/L	6.1 (7.66)	1.5 (3.23)	**0.0009**
Sustained platelet count response, n/N (%)§ ≥ 50x10^9/L in ≥4/6 visits during weeks 19-24	22/86 (25.6%)	3/45 (6.7%)	**0.0108**
Number of visits with a WHO Bleeding Score ≥ 1, Mean (SD)§	6.2 (6.39)	8.3 (8.01)	0.8287
Durable sustained platelet count response, n/N (%)§ ≥ 50x10^9/L in ≥6/8 visits during weeks 17-24	19/86 (22.1%)	3/45 (6.7%)	0.0265

*All endpoints were statistically tested in a fixed sequence to maintain an overall statistical significance level or alpha value of 5%. Although endpoints were subjected to a hierarchical testing procedure, nominal *p*-values are always less than 0.05 for platelet-based endpoints.
†Analyzed on Full Analysis Set.
‡Chronic population.
§Chronic + persistent population.
SD = standard deviation; WHO = World Health Organization.

Efgartigimod Demonstrated Early Sustained Increases in Platelet Counts*



- **33 (38.4%) of efgartigimod** treated participants compared to **5 (11.1%) placebo** reached a platelet count of $30X10^9$ platelets at week 1
- **Sustained platelet count response** achieved in **90%** (9/10) of participants who switched from weekly to every other week dosing

*Analyzed on Full Analysis Set.
LS = least squares.

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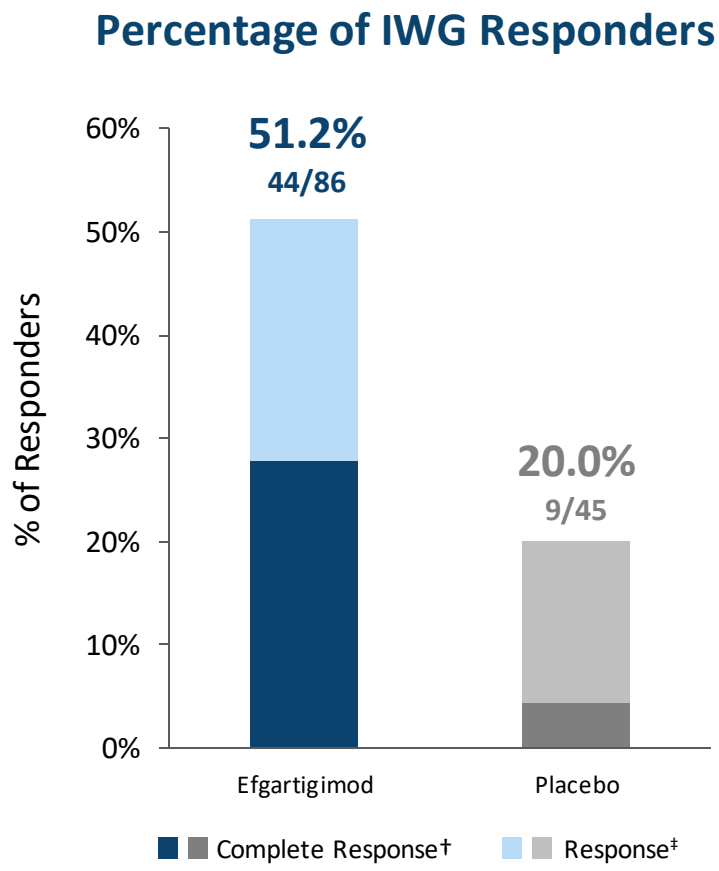
Efgartigimod Resulted in Higher Responses than Placebo on Analysis of IWG Response Criteria, Consistent with Previous Platelet Response Results

Criterion*	Efgartigimod (n=86) n (%)	Placebo (n=45) n (%)	Difference in response (95% CI)
IWG complete response†	24 (27.9)	2 (4.4)	23.5 (10.3; 35.0)
IWG response‡	44 (51.2)	9 (20.0)	31.2 (13.8; 46.0)
IWG initial response§	27 (31.4)	3 (6.7)	24.7 (10.3; 37.0)

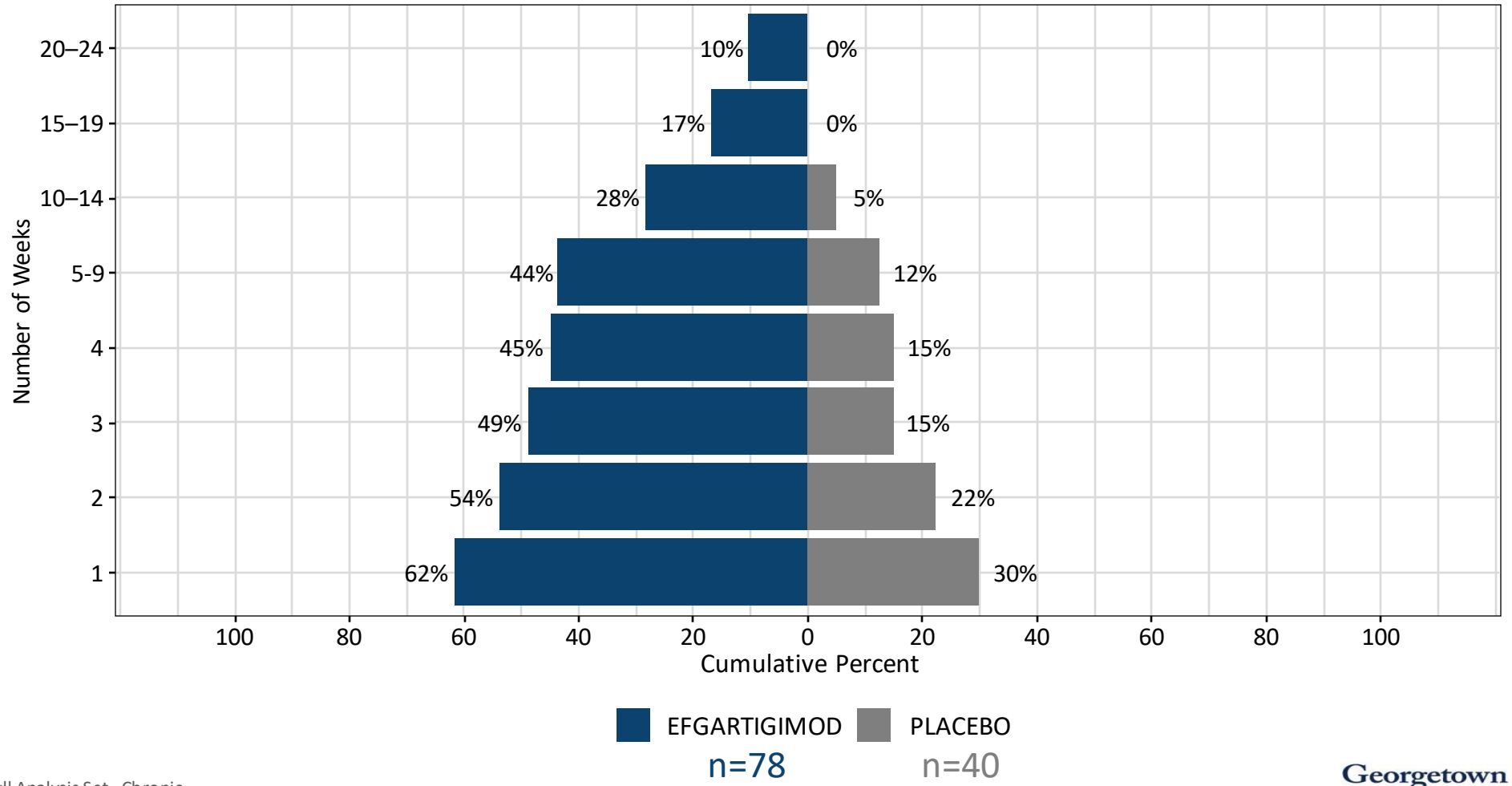
Based on analysis of IWG response criteria, which incorporate the absence of bleeding events, results were clinically meaningful



*Pre-defined analyses, Full Analysis Set.
†platelet counts of at least 100×10^9/L and the absence of bleeding events (WHO Grading = 0) for at least 2 separate, consecutive analysis visits which were at least 7 days apart.
‡platelet counts of at least 30×10^9/L and a 2-fold increase of platelet count from baseline and the absence of bleeding events (WHO Grading = 0) for at least 2 separate, consecutive analysis visits which were at least 7 days apart.
§platelet counts of at least 30×10^9/L and a 2-fold increase of platelet count from baseline at analysis visit 5.
CI = confidence interval; IWG = International Working Group; WHO = World Health Organization.

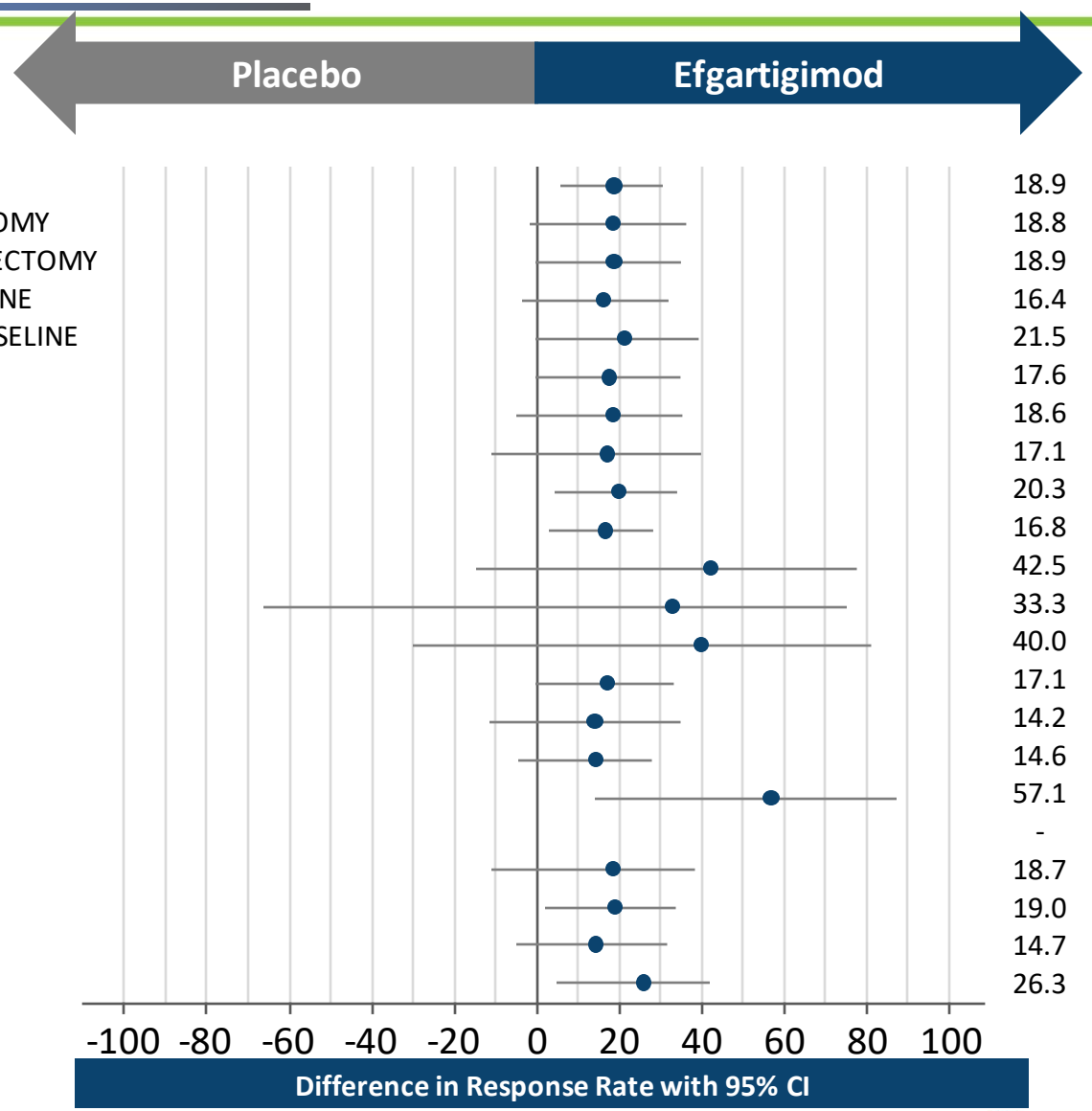
Efgartigimod-treated Participants Experienced Substantially More Weeks With Disease Control*

Extent of Disease Control (≥50×10^9/L): Cumulative Number of Weeks of Disease Control



*Analyzed on Full Analysis Set - Chronic

Sustained Platelet Count Response by Subgroup Analysis Favored Efgartigimod*

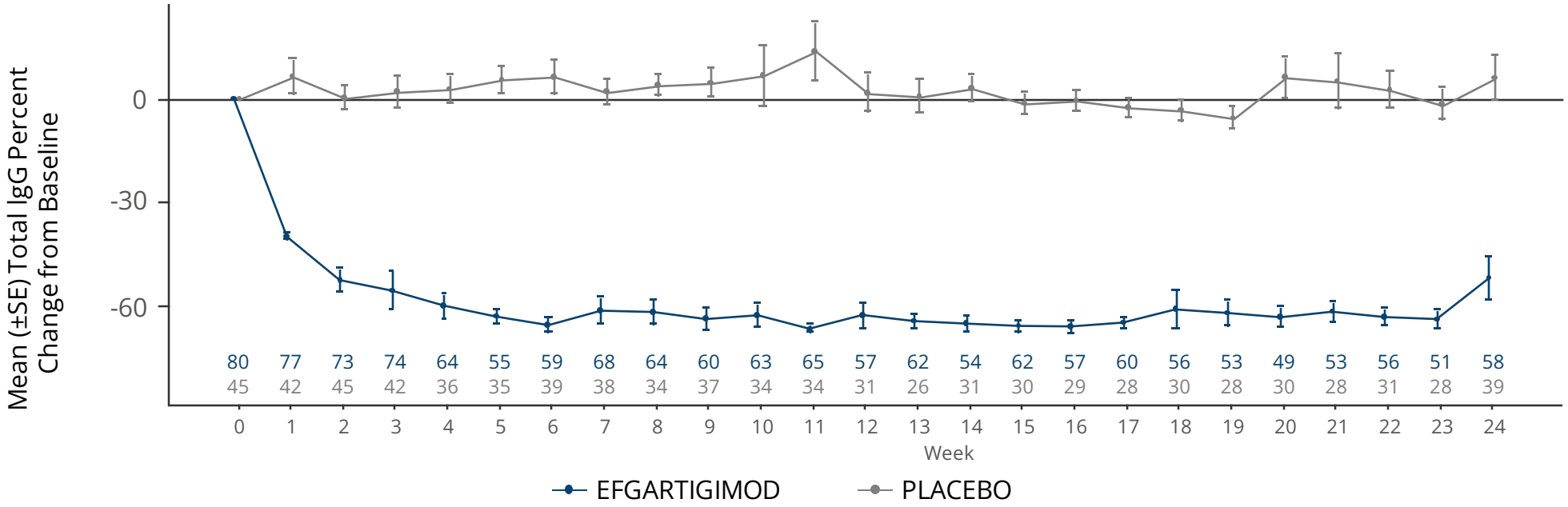


All Patients	OVERALL	18.9	(5.3, 30.7)
Splenectomy History	HISTORY OF SPLENECTOMY	18.8	(-1.9, 35.8)
	NO HISTORY OF SPLENECTOMY	18.9	(-1.0, 35.2)
Baseline ITP Therapies	ITP THERAPY AT BASELINE	16.4	(-4.0, 32.0)
	NO ITP THERAPY AT BASELINE	21.5	(0.1, 39.6)
Baseline Platelet Count	<15x10^9/L	17.6	(-0.8, 34.8)
	≥15x10^9/L	18.6	(-5.0, 35.4)
Prior ITP Therapies	<3	17.1	(-11.1, 39.9)
	≥3	20.3	(4.4, 33.9)
Time Since Diagnosis	CHRONIC ITP	16.8	(3.1, 28.5)
	PERSISTENT ITP	42.5	(-14.6, 77.4)
Region	UNITED STATES	33.3	(-65.9, 75.5)
	JAPAN	40.0	(-30.3, 81.1)
	EU/EEA/EFTA	17.1	(0.7, 33.5)
	REST OF THE WORLD	14.2	(-11.5, 35.0)
Age Group	18 - <65 YEARS	14.6	(-4.5, 27.9)
	65 - <75 YEARS	57.1	(14.0, 87.1)
	≥75 YEARS	-	-
Prior Rituximab	YES	18.7	(-11.0, 38.4)
	NO	19.0	(1.9, 34.1)
Prior TPO-RA	YES	14.7	(-5.1, 31.5)
	NO	26.3	(4.6, 42.1)

*Full Analysis Set. CI = confidence interval; EEA = European Economic Area; EFTA = European Free Trade Union; EU = European Union; ITP = immune thrombocytopenia; TPO-RA= thrombopoietin receptor agonists.

Efgartigimod Resulted in Targeted Reduction of IgG Levels*

Mean % Change from Baseline in Total IgG Levels over Time*†



- **Mean IgG levels decreased steadily over the first 4 weeks of treatment, which was sustained across time and corresponded with platelet count responses**
  - **After the initial decrease in IgG, mean maximum reductions from baseline remained >60% throughout the trial**

*Full Analysis Set. †Errors bars are standard errors around the least squares (LS) means.
IgG = immunoglobulin G; SE = standard error.

Efgartigimod Was Well-Tolerated in Patients With ITP and Consistent With Other Efgartigimod Studies[1-5]

	Efgartigimod (n=86)	Placebo (n=45)
Patients with event, n (%)		
≥1 TEAE	80 (93.0)	43 (95.6)
≥1 serious TEAE	7 (8.1)	7 (15.6)
≥1 TEAE leading to discontinuation of study drug	4 (4.7)	1 (2.2)
≥1 treatment-related TEAE according to PI	15 (17.4)	10 (22.2)
≥1 serious treatment-related TEAE according to PI	0	0
AESI: Any bleeding event	61 (70.9)	39 (86.7)
AESI: Any infection event	25 (29.1)	10 (22.2)
Infusion-related reaction event	10 (11.6)	5 (11.1)
Most common TEAEs, n (%)		
Asthenia	6 (7.0)	0 (0.0)
Fatigue	4 (4.7)	1 (2.2)
Headache	14 (16.3)	6 (13.3)
Petechiae	13 (15.1)	12 (26.7)
Hypertension	5 (5.8)	0 (0.0)
Nausea	5 (5.8)	2 (4.4)
Haematuria	14 (16.3)	7 (15.6)
Purpura	7 (8.1)	4 (8.9)

AESI = adverse event of special interest (defined per protocol); ITP = immune thrombocytopenia; PI = principal investigator; TEAE = treatment-emergent adverse event.

1. Howard JF Jr, et al. *Neurology*. 2019;92(23):e2661-e2673. 2. Howard JF Jr, et al. *Lancet Neurol*. 2021;20(7):526-536. 3. Newland AC, et al. *Am J Hematol*. 2020;95:178-187. 4. Goebeler M, et al. *Br J Dermatol*. 2021. doi:10.1111/bjd.20782.

Efgartigimod Phase 3 (ADVANCE) IV Study Conclusions

The benefits of targeting FcRn and lowering total IgG levels were demonstrated by clinically and statistically significant improvements in platelet counts compared with placebo

Efgartigimod was well-tolerated and most adverse events were mild to moderate with no new safety signals

The results of the study support both weekly and every-other-week administration, allowing for adjustments based on platelet counts

Over 90% of participants who completed ADVANCE IV enrolled in the open-label extension (ADVANCE+; NCT04225156)

FcRn = neonatal Fc receptor; IgG = immunoglobulin G; IV = intravenous.

Acknowledgements

- We thank the patients who participated in this study and their caregivers, the physicians and nurses who care for them, the staff at study sites, and the staff involved in data collection and analyses
- This study was funded by argenx
- Medical writing support was provided by Danielle Colas-Zelin, PhD, of Eloquent Scientific Solutions, and funded by argenx