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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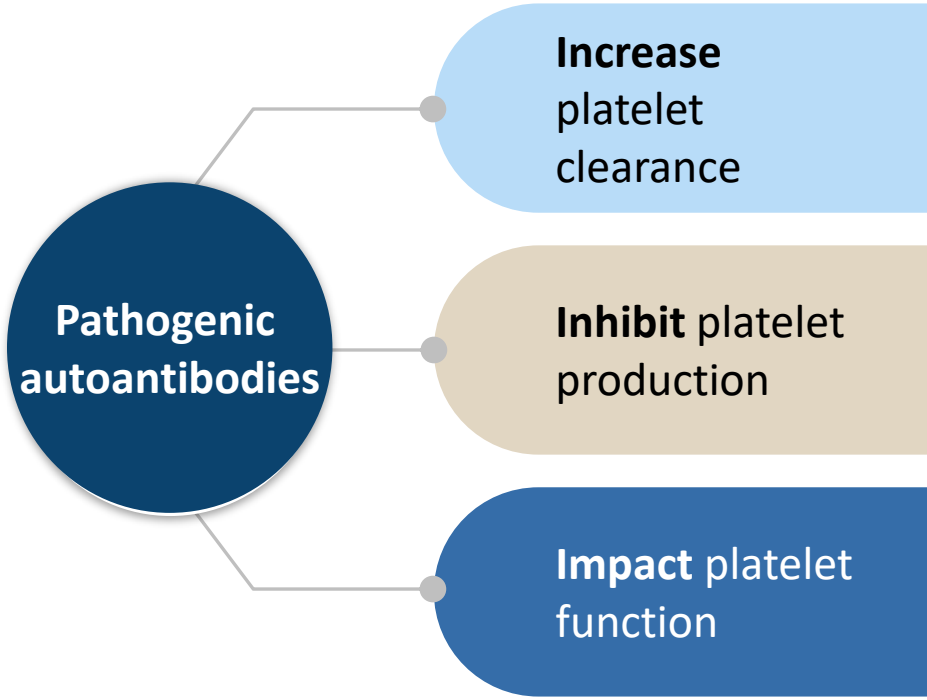
Primary Immune Thrombocytopenia (ITP)

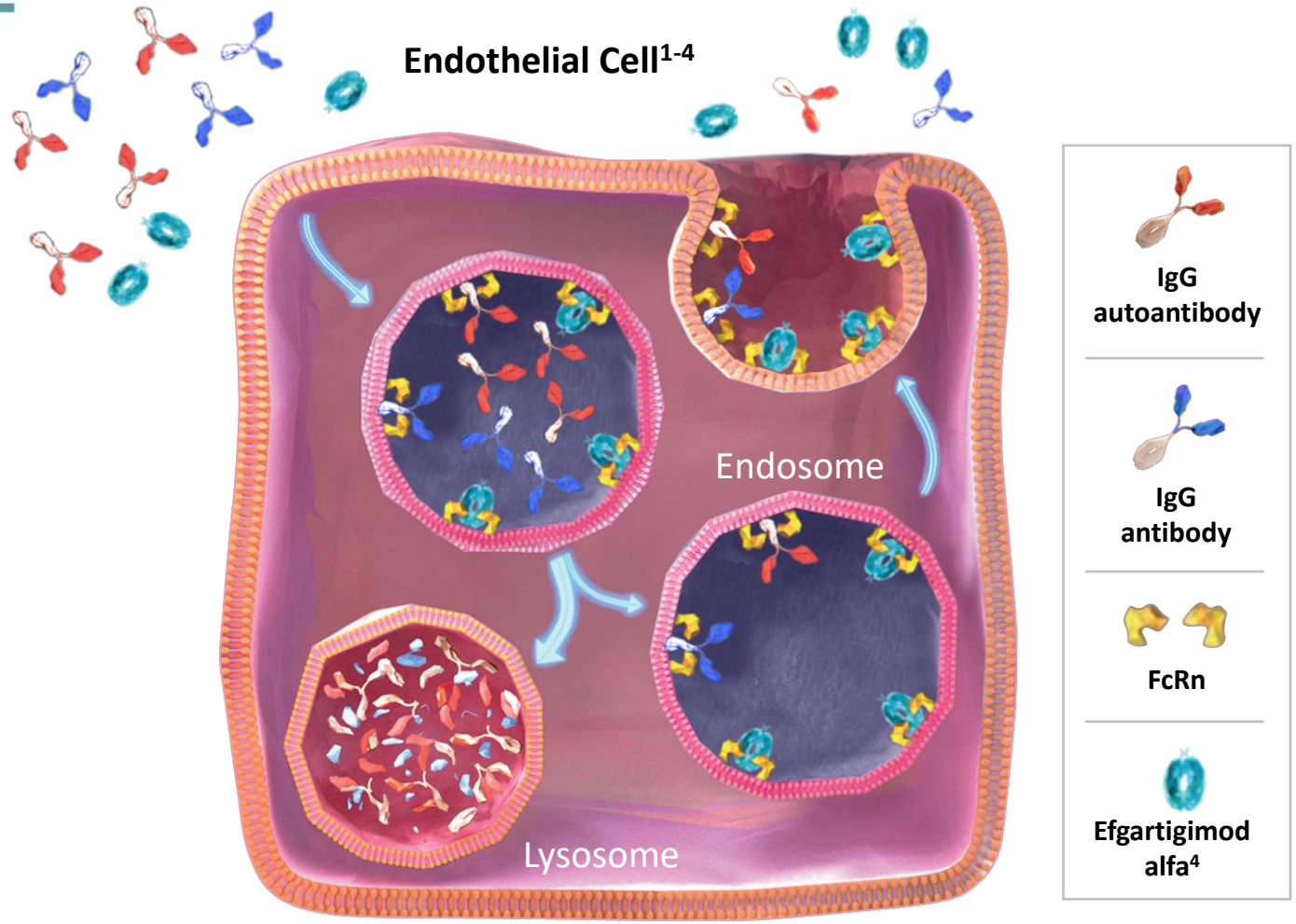
- ITP is an acquired autoimmune disorder characterized by a reduction in platelet count, which can result in[1-4]:
  - Increased risk of bleeding
  - Fatigue
  - Decreased quality of life
- IgG autoantibodies, detected in most patients, target glycoproteins expressed on platelets and megakaryocytes[5-8]
- 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

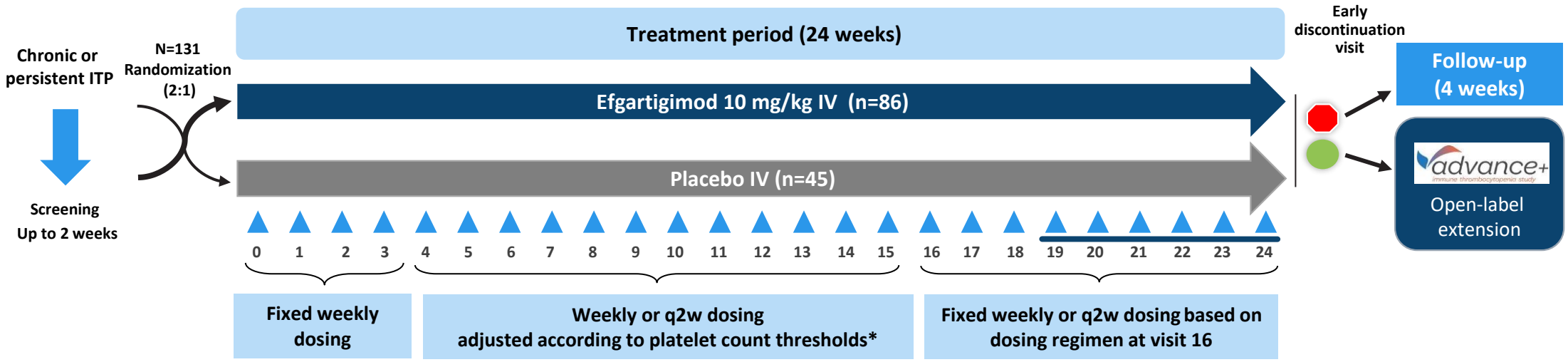


FcRn = neonatal Fc receptor; IgG = immunoglobulin G.

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

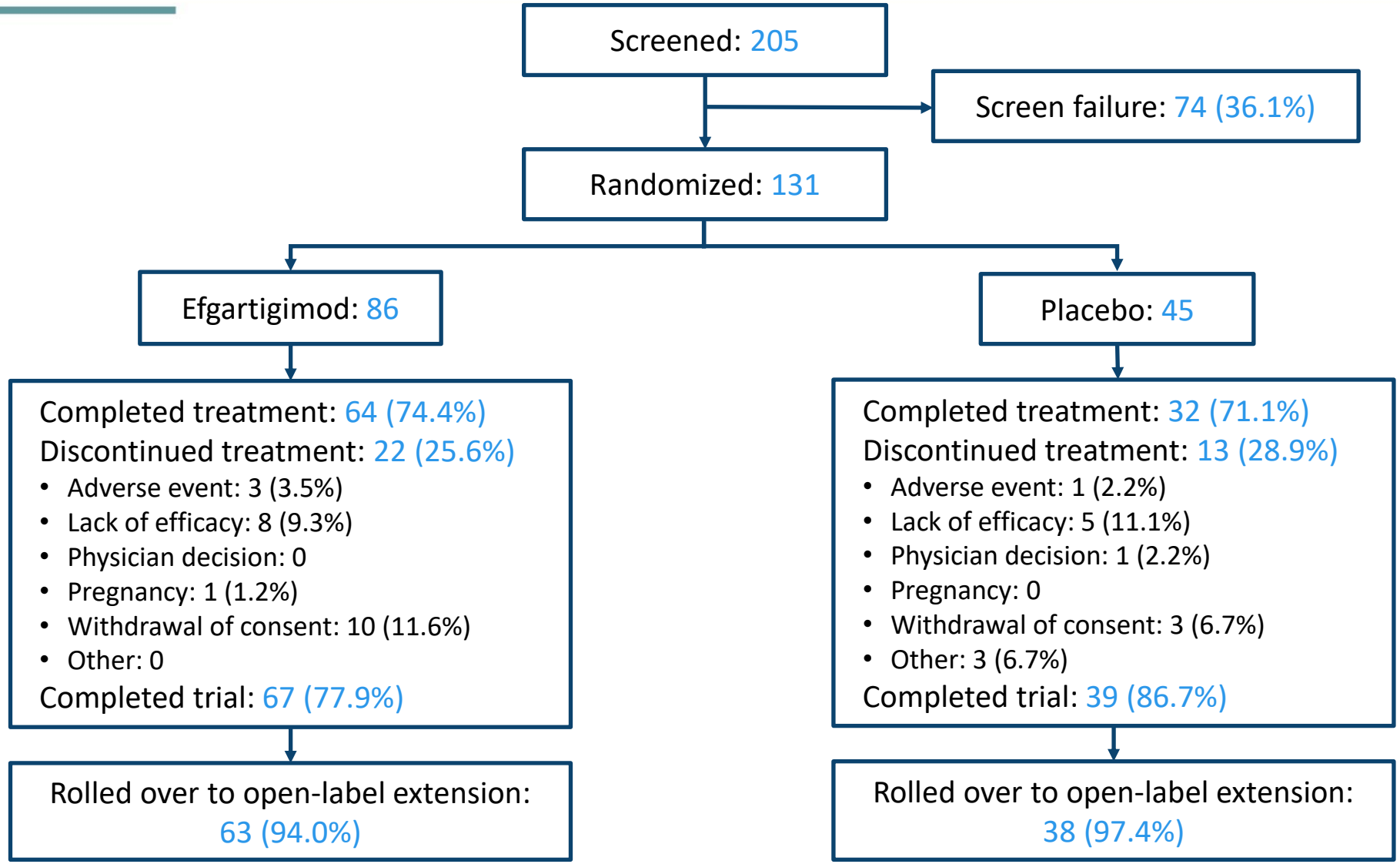


Eligibility criteria

- 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)

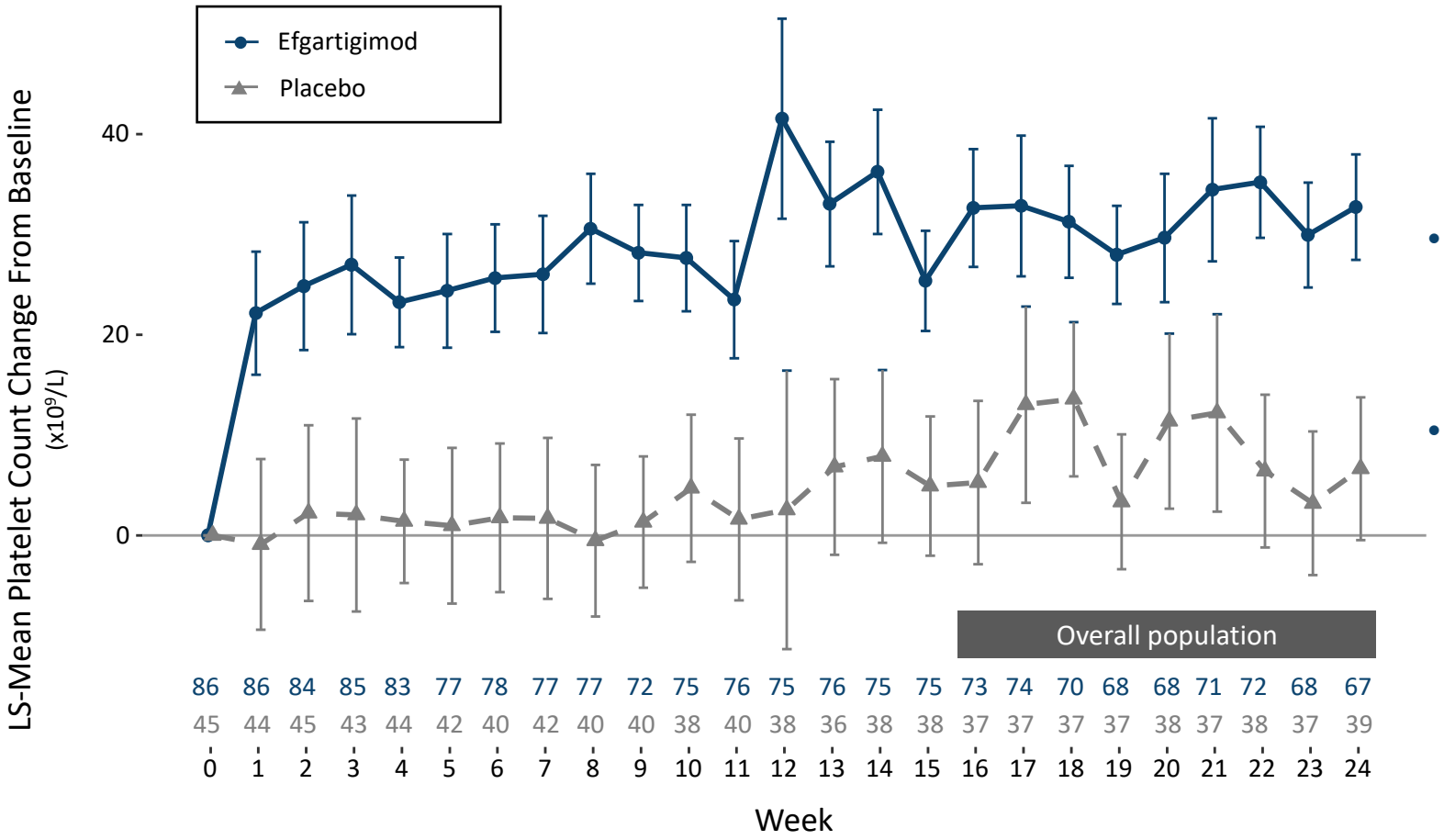
[a]Safety Analysis Set.
ITP = immune thrombocytopenia; SD = standard deviation; TPO-RA = thrombopoietin receptor agonists; WHO = World Health Organization.

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*



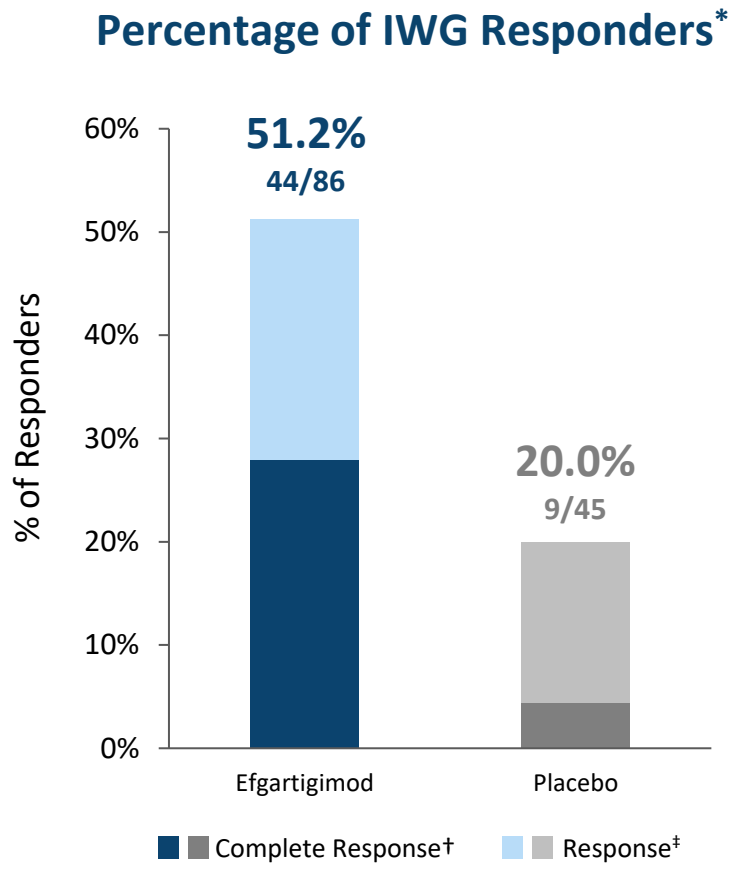
- **33 (38.4%) of efgartigimod** treated participants compared to **5 (11.1%) placebo** reached a platelet count of $30X10^9$ platelets at week 1
- **Sustained platelet count response** achieved in **90%** (9/10) of participants who switched from weekly to every other week dosing

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

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)

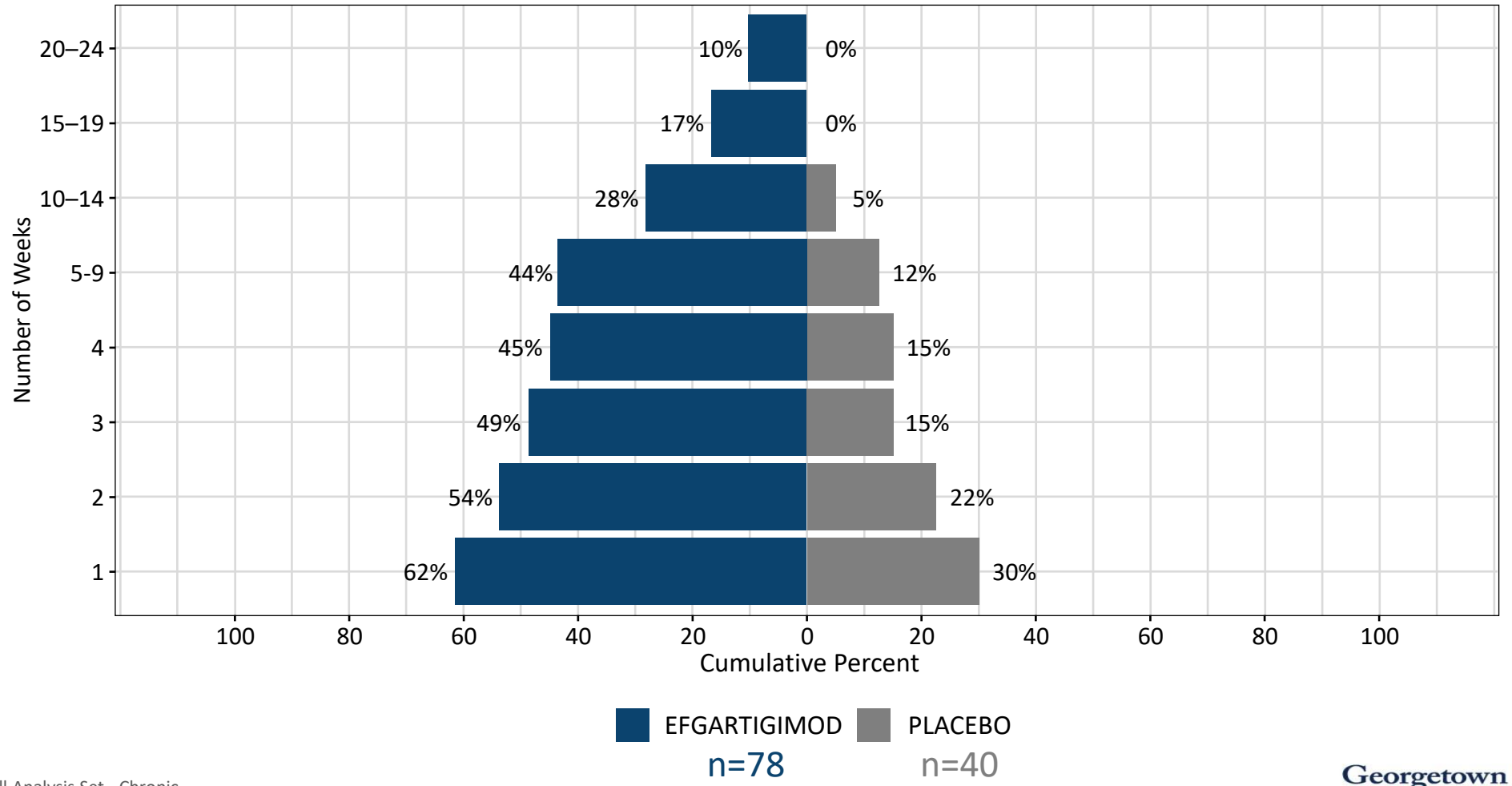
Based on analysis of IWG response criteria, which incorporate the absence of bleeding events, results were clinically meaningful



*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.

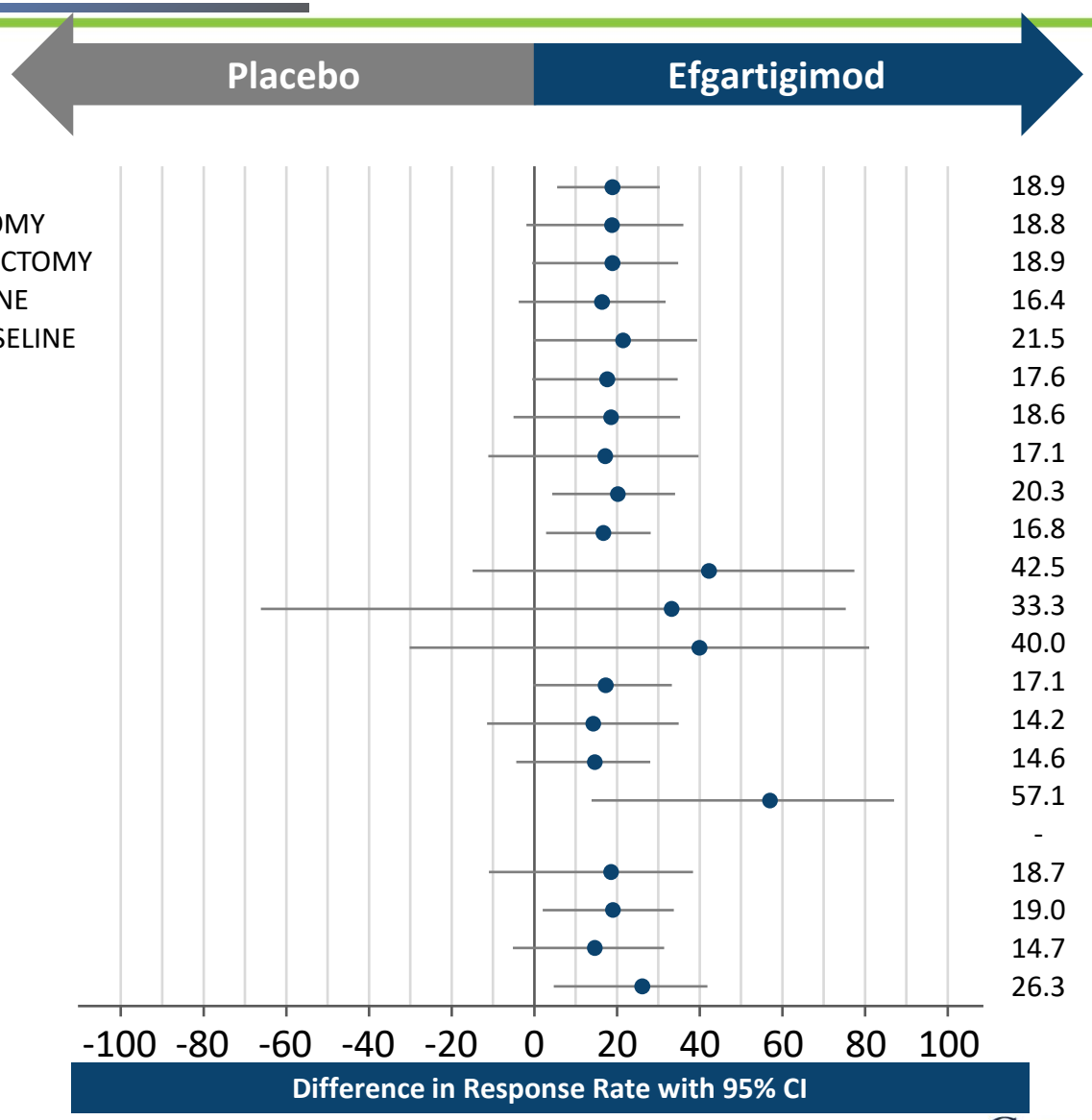
Efgartigimod-treated Participants Experienced Substantially More Weeks With Disease Control*

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*

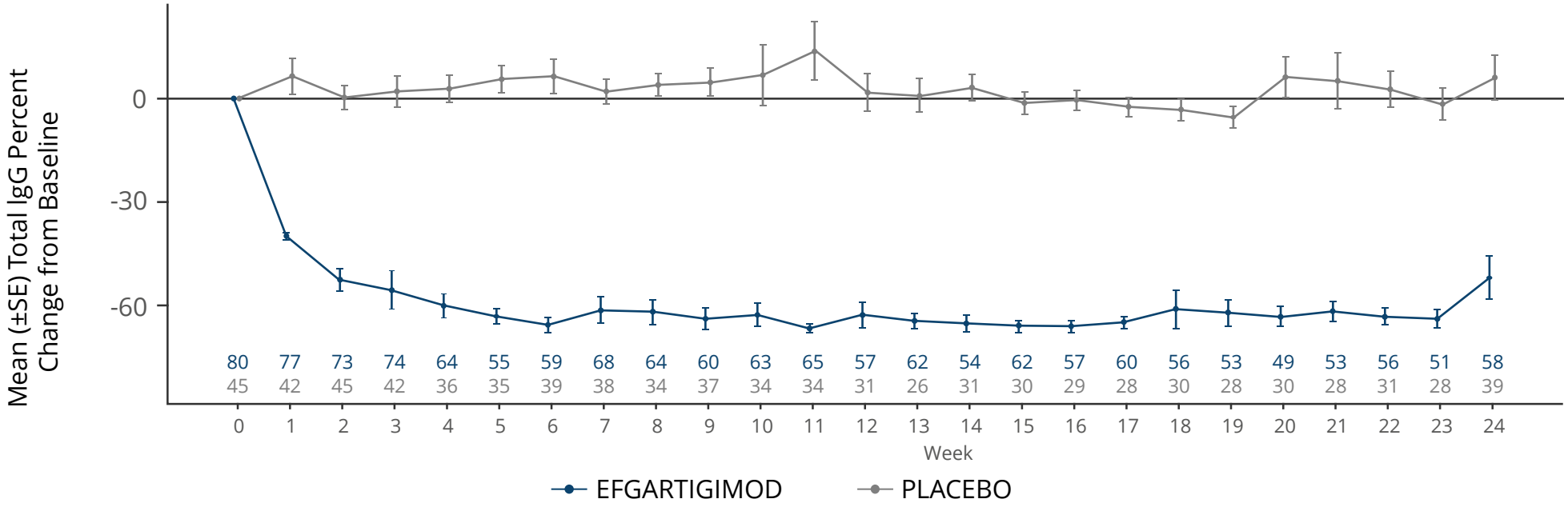


All Patients	OVERALL	18.9	(5.3, 30.7)
Splenectomy History	HISTORY OF SPLENECTOMY	18.8	(-1.9, 35.8)
	NO HISTORY OF SPLENECTOMY	18.9	(-1.0, 35.2)
Baseline ITP Therapies	ITP THERAPY AT BASELINE	16.4	(-4.0, 32.0)
	NO ITP THERAPY AT BASELINE	21.5	(0.1, 39.6)
Baseline Platelet Count	<15x10^9/L	17.6	(-0.8, 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

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