FPO

Efficacy and Safety of Efgartigimod PH20 SC in Adult Participants With Active Idiopathic Inflammatory Myopathy

Phase 2 Results From the ALKIVIA Study

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We gratefully acknowledge the clinicians and patients involved

Disclosures

Hector Chinoy: AstraZeneca, Pfizer, PTC Therapeutics, UCB

Sebastian C. Rodriguez-Garcia: Consultant: argenx; Employee: InCa (PPD)

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Picture Taking

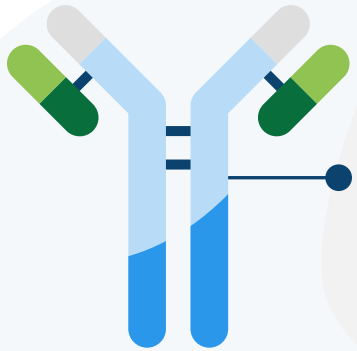
Picture taking **is ALLOWED** during my presentation (including presented slides)

We gratefully acknowledge the clinicians, patient organizations, and scientists who have collaborated on the design of this trial

Study Hypothesis: **IIM Is Driven by Autoantibodies**

Idiopathic inflammatory myopathy (IIM) is characterized by skeletal muscle inflammation and extra-muscular manifestations[1]

- Heterogeneous disease with different subtypes, such as DM, IMNM, and PM, including ASyS[1]
- Persistent impairment of muscle function, leading to difficulties in daily life activities and suboptimal health-related quality of life[1]
- IgG myositis-specific autoantibodies (MSAs) contribute to the pathogenesis of most IIM subtypes[2–4]



Pathogenic IgG autoantibodies (MSAs)[2–4]

DM
anti-Mi-2, anti-TIF-1γ, anti-NXP2, anti-MDA5, anti-SAE

IMNM
anti-SRP, anti-HMGCR

ASyS
anti-aminoacyl-tRNA synthetase MSAs: anti-Jo1, anti-PL-7, anti-PL-12, anti-EJ, anti-OJ, anti-Zo, anti-Ha, anti-Ly, anti-VRS

There is an unmet need for targeted treatment options with a favorable safety profile and corticosteroid-sparing effect, which can provide a sustained response in muscular and extra-muscular manifestations across IIM subtypes

ASyS, anti-synthetase syndrome; DM, dermatomyositis; HMGCR, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase; IgG, immunoglobulin G; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; MDA5, melanoma differentiation-associated protein 5; Mi-2, chromodomain helicase DNA binding protein 4; MSA, myositis-specific antibody; NXP2, nuclear matrix protein 2; PM, polymyositis; SAE, small ubiquitin-like modifier activating enzyme; SRP, signal recognition particle; TIF-1, transcriptional intermediary factor 1; tRNA, transfer ribonucleic acid.

1. Lundberg IE, et al. *Nat Rev Dis Primers*. 2021;7:86. **2.** Musai J, Mammen AL, Pinal-Fernandez I. *Curr Rheumatol Rep*. 2024;26:421–30. **3.** Wischnewski S, et al. *Trends Pharmacol Sci*. 2025;46:249–63. **4.** Wang G, McHugh NJ. *Clin Exp Rheumatol*. 2025;43:364–71.

Efgartigimod Blocks FcRn and Reduces IgG Levels

Efgartigimod

- Human **IgG1** antibody **Fc fragment**
- Engineered for **increased affinity to FcRn**
- Uniquely composed of the **only part of the IgG antibody** that **normally binds FcRn**[1,2]
- **Selectively reduces IgG antibodies** and **pathogenic autoantibodies** without:[1,5–7]
  - Impacting antibody production (including other Ig antibodies) or other parts of the immune system
  - Decreasing albumin levels
  - Increasing LDL cholesterol levels

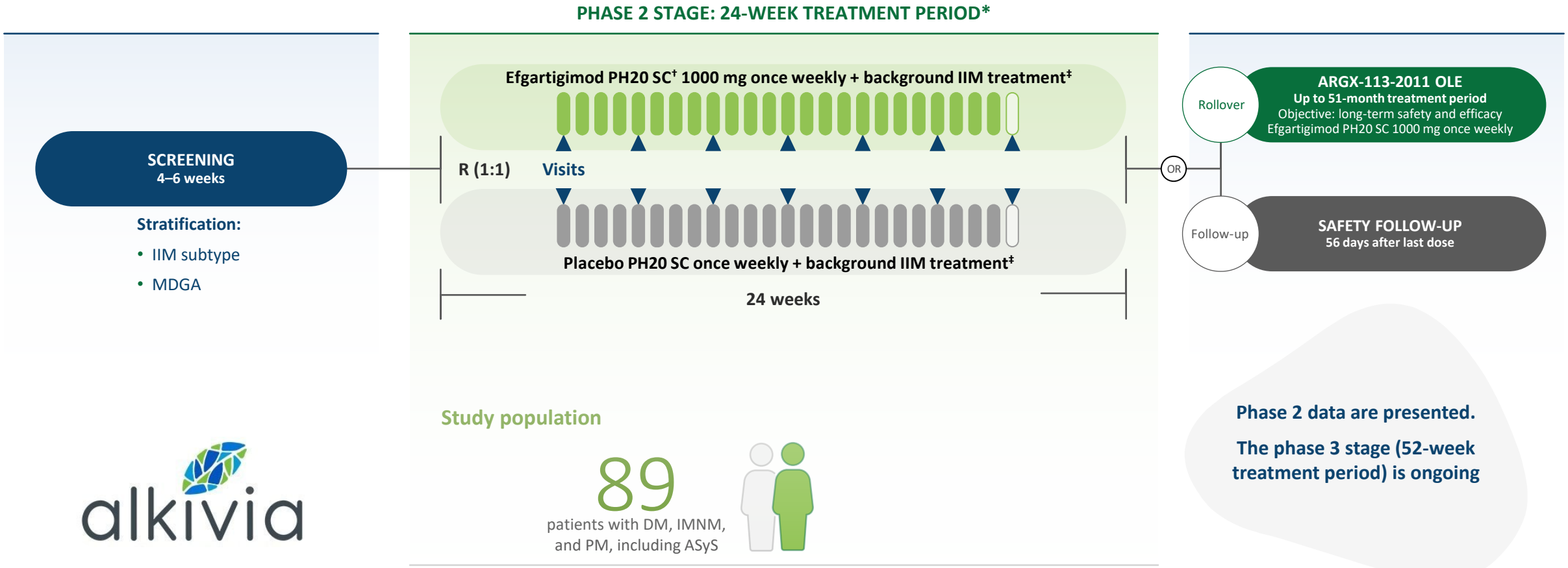
1. **Efgartigimod outcompetes endogenous IgG antibodies and pathogenic autoantibodies for binding to FcRn, due to increased affinity to FcRn**
2. **FcRn-bound efgartigimod, IgG antibodies, and pathogenic autoantibodies escape cellular degradation**
3. **Unbound IgG antibodies, pathogenic autoantibodies, and efgartigimod are degraded in the lysosome**
4. **FcRn-bound efgartigimod and FcRn-bound IgG antibodies/pathogenic autoantibodies are recycled back into circulation**

FcRn, neonatal Fc receptor; LDL, low-density lipoprotein.

1. Ulrichts P, et al. *J Clin Invest*. 2018;128:4372–86. **2.** Vaccaro C, et al. *Nat Biotechnol*. 2005;23:1283–8. **3.** Roopenian DC, Akilesh S. *Nat Rev Immunol*. 2007;7:715–25. **4.** Ward ES, Ober RJ. *Trends Pharmacol Sci*. 2018;39:892–904. **5**. Howard JF, Jr., et al. *Lancet Neurol*. 2021;20:526–36. **6.** Guptill JT, et al. *Autoimmunity*. 2022;55:620–31. **7.** argenx, data on file.

ALKIVIA

A Seamless, Phase 2/3, Randomized, Double-Blinded, Placebo-Controlled, Parallel Group Trial in IIM



Phase 2 data are presented.

The phase 3 stage (52-week treatment period) is ongoing

DM, dermatomyositis; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; MDGA, medical doctor (physician) global assessment; OCS, oral corticosteroids; OLE, open label extension; PH20, recombinant human hyaluronidase PH20; PM, polymyositis; R, randomization; SC, subcutaneous.

*Phase 2 and phase 3 stages are independent cohorts. †Efgartigimod co-formulated with hyaluronidase PH20 for convenient SC administration in <2 minutes. ‡Participants may receive OCS and/or up to 1 antimalarial or immunosuppressant. Permitted treatments include – OCS: cortisol, cortisone, prednisone, prednisolone, triamcinolone, methylprednisolone, dexamethasone, betamethasone; antimalarials: hydroxychloroquine, quinacrine, chloroquine; immunosuppressants: methotrexate, azathioprine, mycophenolate mofetil, mycophenolic acid, tacrolimus, cyclosporine, leflunomide, mizoribine.

ClinicalTrials.gov Identifier: NCT05523167. https://www.clinicaltrials.gov/study/NCT05523167. Accessed May 2025.

Phase 2 **Objectives** and **Endpoints**

OBJECTIVE

To evaluate the efficacy of efgartigimod PH20 SC compared with placebo in IIM, in addition to standard-of-care therapy

Primary Endpoint

Total Improvement Score (TIS), as defined by the 2016 ACR/EULAR myositis response criteria, at Week 24 (Composite endpoint)

KEY Secondary Endpoints

- Proportion of participants with TIS ≥20 and TIS ≥40 at Week 24
- Time to reach TIS ≥20 and TIS ≥40
- Change in MMT8 score, PGA, MDGA

OTHER Secondary Endpoints

- Safety: incidence and severity of TEAEs, AESIs, and SAEs
- Immunogenicity: Prevalence of antidrug antibodies

TIS is a composite endpoint combining 6 Core Set Measures (CSM)

1. MDGA (Medical Doctor (Physician) Global Assessment)
2. PGA (Patient Global Assessment)
3. MMT8 (Manual Muscle Testing-8)
4. HAQ-DI (Health Assessment Questionnaire Disability Index)
5. Muscle enzymes
6. Extra-muscular Global Assessment

Ranges from 0 (worsening or no improvement) to 100

- TIS ≥20 = minimal improvement
- TIS ≥40 = moderate improvement
- TIS ≥60 = major improvement

ACR/EULAR, American College of Rheumatology/ European Alliance of Associations for Rheumatology; AESI, adverse event of special interest; HAQ-DI, Health Assessment Questionnaire Disability Index; IIM, idiopathic inflammatory myopathy; MDGA, medical doctor (physician) global assessment; MMT8, manual muscle testing-8; PGA, Patient Global Assessment; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TIS, total improvement score.

Participant **Demographics** and **Baseline Characteristics**

Demographics	Efgartigimod PH20 SC (N=47)	Placebo PH20 SC (N=42)
Age, years, mean (SD)	58.2 (13.9)	54.7 (12.7)
Sex, female, n (%)	35 (74.5)	33 (78.6)
BMI, kg/m^2, mean (SD)	27.3 (6.3)	27.3 (6.1)
Race, n (%)		
White	32 (71.1)	29 (72.5)
Geographical region, n (%)		
Asia	11 (23.4)	5 (11.9)
Europe	20 (42.6)	23 (54.8)
North America (US and Canada)	16 (34.0)	11 (26.2)
Rest of World	0	3 (7.1)

Disease Characteristics	Efgartigimod PH20 SC (N=47)	Placebo PH20 SC (N=42)
Time since diagnosis, years, median (Q1,Q3)	4.4 (1.8, 7.8)	4.3 (2.0, 7.0)
MDGA category (CRF source), n (%)		
Non-severe [MDGA <5]	17 (36.2)	15 (35.7)
Severe [MDGA ≥5]	30 (63.8)	27 (64.3)
Positive MSA determination, n (%)	40 (85.1)	36 (85.7)
Concurrent IIM therapy at baseline, n (%)		
Non-corticosteroid medication*	36 (76.6)	32 (76.2)
Immunosuppressants	31 (66.0)	31 (73.8)
Antimalarials	5 (10.6)	1 (2.4)
Systemic corticosteroid medication*	38 (80.9)	35 (83.3)
Both non-corticosteroid and corticosteroid medications	27 (57.4)	25 (59.5)

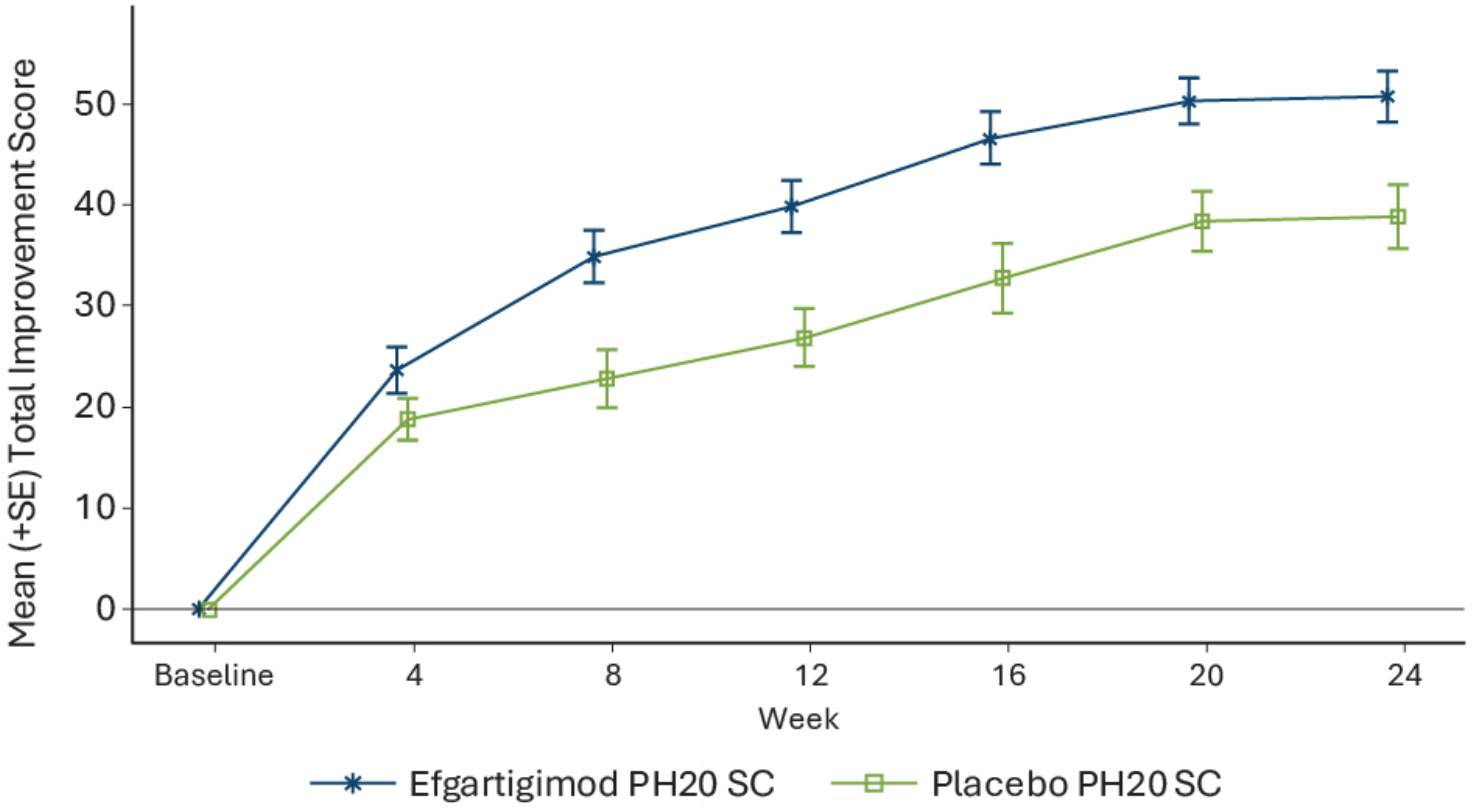
BMI, body mass index; CRF, case report form; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; MDGA, medical doctor (physician) global assessment; MSA, myositis-specific antibodies; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SD, standard deviation; US United States.

*Counts all participants independent of any other concomitant use.

Efgartigimod PH20 SC Led to **Significant Clinical Improvement** as Measured by TIS

- Least-squares mean TIS at Week 24 was **statistically significantly higher in the efgartigimod PH20 SC arm** than the placebo PH20 SC arm (50.45 *vs.* 35.65, 2-sided *P*=0.0004)

- The **efgartigimod PH20 SC arm demonstrated a significant improvement** compared with the placebo PH20 SC arm in mean TIS over time

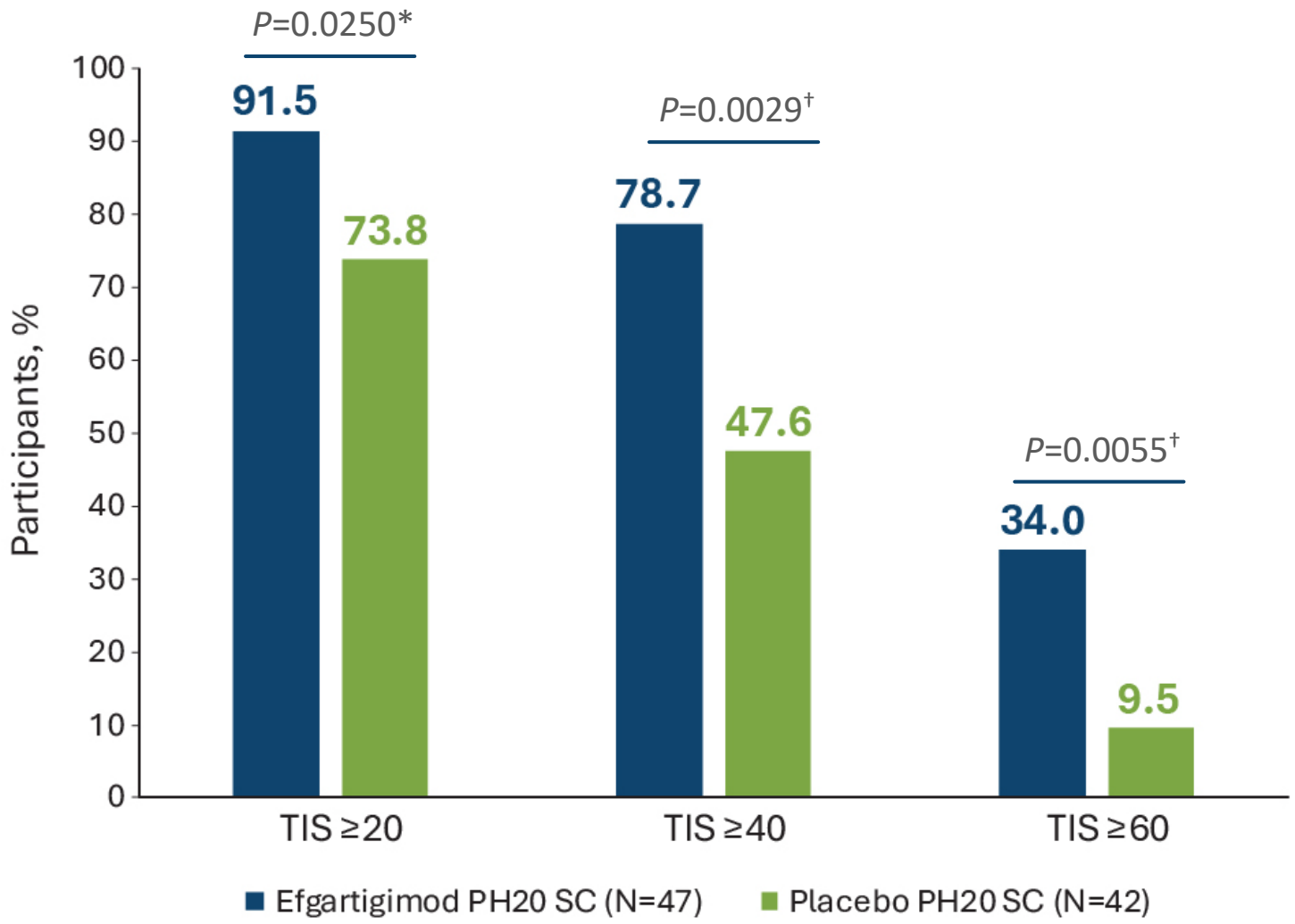


n (mean):						
Efgartigimod PH20 SC: 47	44 (23.64)	45 (35.00)	44 (39.83)	45 (46.72)	42 (50.24)	41 (50.67)
Placebo PH20 SC: 42	42 (18.81)	40 (22.81)	37 (26.89)	36 (32.71)	36 (38.33)	36 (38.96)

PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SE, standard error; TIS, Total Improvement Score.

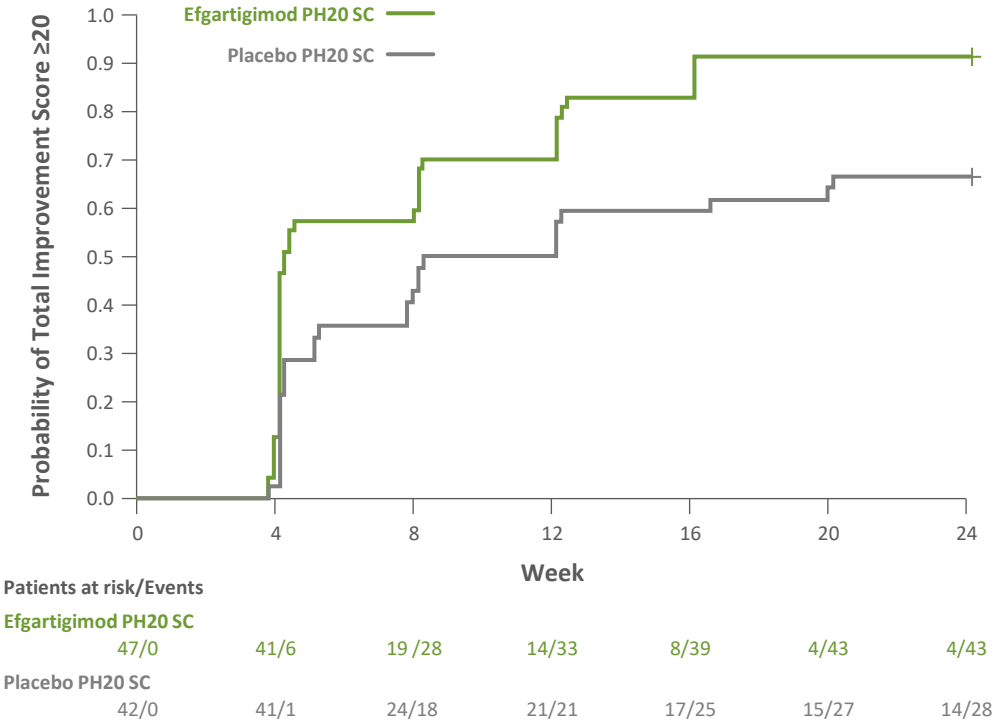
Proportion of Participants With TIS ≥20, ≥40, and ≥60 at Week 24

- A **significant proportion** of participants in the **efgartigimod PH20 SC arm** had a **mild (TIS ≥20), moderate (TIS ≥40), or major (TIS ≥60) clinical improvement** at Week 24 compared with the placebo PH20 SC arm



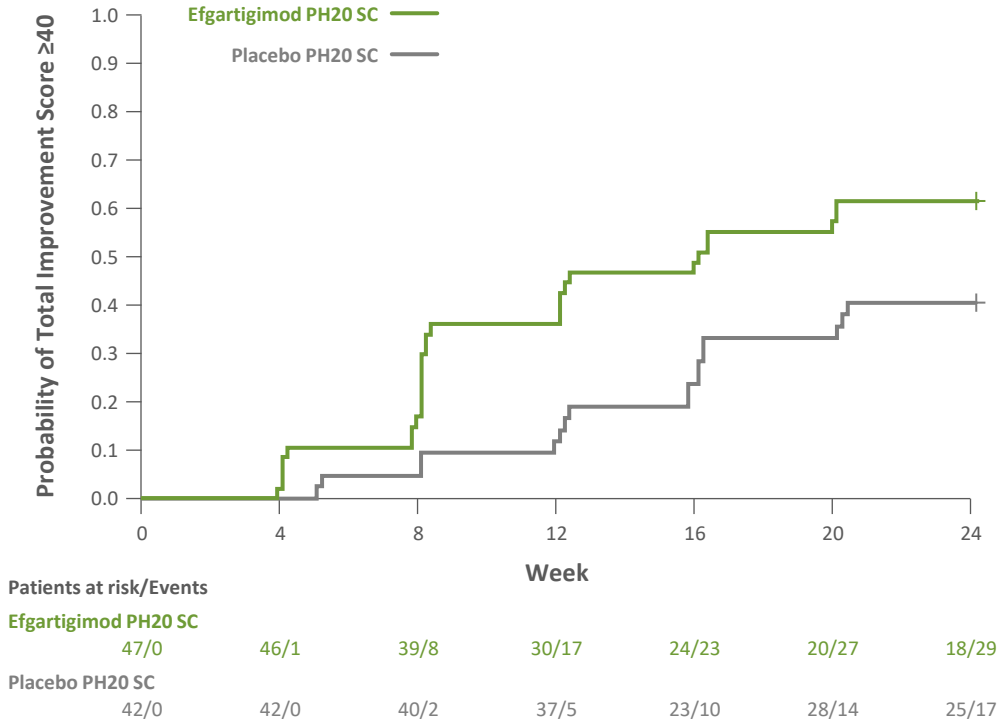
*Statistical significance met in endpoint's preplanned supplemental analysis.†Statistical significance met in endpoint's primary and preplanned supplemental analysis.
PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; TIS, Total Improvement Score.

Median Time to First TIS ≥20 and ≥40



Median time to TIS ≥20 was significantly shorter following treatment with efgartigimod PH20 SC *vs.* placebo PH20 SC

(30 days *vs.* 72 days; *P*=0.0020)



Median time to TIS ≥40 was significantly shorter following treatment with efgartigimod PH20 SC *vs.* placebo PH20 SC

(113 days *vs.* not estimable, *P*=0.0293)

PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; TIS, Total Improvement Score.

Summary of **Safety**

	Efgartigimod PH20 SC (N=47; PYFU=22)			Placebo PH20 SC (N=42; PYFU=18)		
	n (%)	m	ER	n (%)	m	ER
≥1 AE	41 (87.2)	320	14.7	37 (88.1)	168	9.2
≥1 SAE	8 (17.0)	11	0.5	9 (21.4)	10	0.5
≥1 Grade ≥3 AE	7 (14.9)	10	0.5	12 (28.6)	13	0.7
≥1 AE leading to study drug discontinuation	3 (6.4)	3	0.1	4 (9.5)	4	0.2
≥1 AESI (infection)	20 (42.6)	24	1.1	20 (47.6)	31	1.7
≥1 injection site reaction	21 (44.7)	155	7.1	9 (21.4)	41	2.2
≥1 fatal AE	2 (4.3)*	2	<0.1	0	0	0
Most common AEs (occurring in >10% of participants)						
COVID-19	4 (8.5)	4	0.2	5 (11.9)	5	0.3
Diarrhea	6 (12.8)	9	0.4	2 (4.8)	2	0.1
Injection site bruising	5 (10.6)	7	0.3	4 (9.5)	9	0.5
Injection site erythema	11 (23.4)	36	1.6	2 (4.8)	8	0.4
Injection site pain	3 (6.4)	25	1.1	5 (11.9)	14	0.8
Injection site rash	8 (17.0)	41	1.9	0	0	0
Injection site reaction	5 (10.6)	8	0.4	1 (2.4)	5	0.3
Urinary tract infection	1 (2.1)	1	<0.1	5 (11.9)	6	0.3

Participants treated with efgartigimod PH20 SC demonstrated a mean maximum IgG reduction of 72% from baseline

ER is calculated as number of events divided by PYFU.

*Both deaths (road traffic accident and septic shock) were considered unrelated to the study drug.

AE, adverse event; AESI, adverse event of special interest; ER, event rate; IgG, immunoglobulin G; m, number of events; PH20, recombinant human hyaluronidase PH20; PYFU, participant-years of follow-up; SAE, serious AE; SC, subcutaneous.

KEY TAKEAWAYS

Efgartigimod PH20 SC + background IIM treatment

led to significant improvement over

placebo PH20 SC + background IIM treatment in TIS

and key secondary endpoints, with good safety and tolerability

The results demonstrate the mechanistic relevance of FcRn inhibition in IIM, suggesting **potential pathogenicity of autoantibodies in IIM**

These findings support further **evaluation of efgartigimod PH20 SC in IIM** in the ongoing phase 3 part of the study

FcRN, neonatal fragment crystallizable receptor; IIM, idiopathic inflammatory myopathy; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; TIS, Total Improvement Score.