OP0041

Treatment of Primary Sjögren's Disease by Blocking FcRn

Clinical and Translational Data From RHO, a Phase 2 Randomized, Placebo Controlled, Double-Blind, Proof-of-Concept Study With Efgartigimod

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We gratefully acknowledge the clinicians and patients involved

Disclosures

Isabelle Peene: Consultant: argenx, BMS

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Joke Deprez: Nothing to declare

Dirk Elewaut: Nothing to declare

Hendrika Bootsma: Nothing to declare

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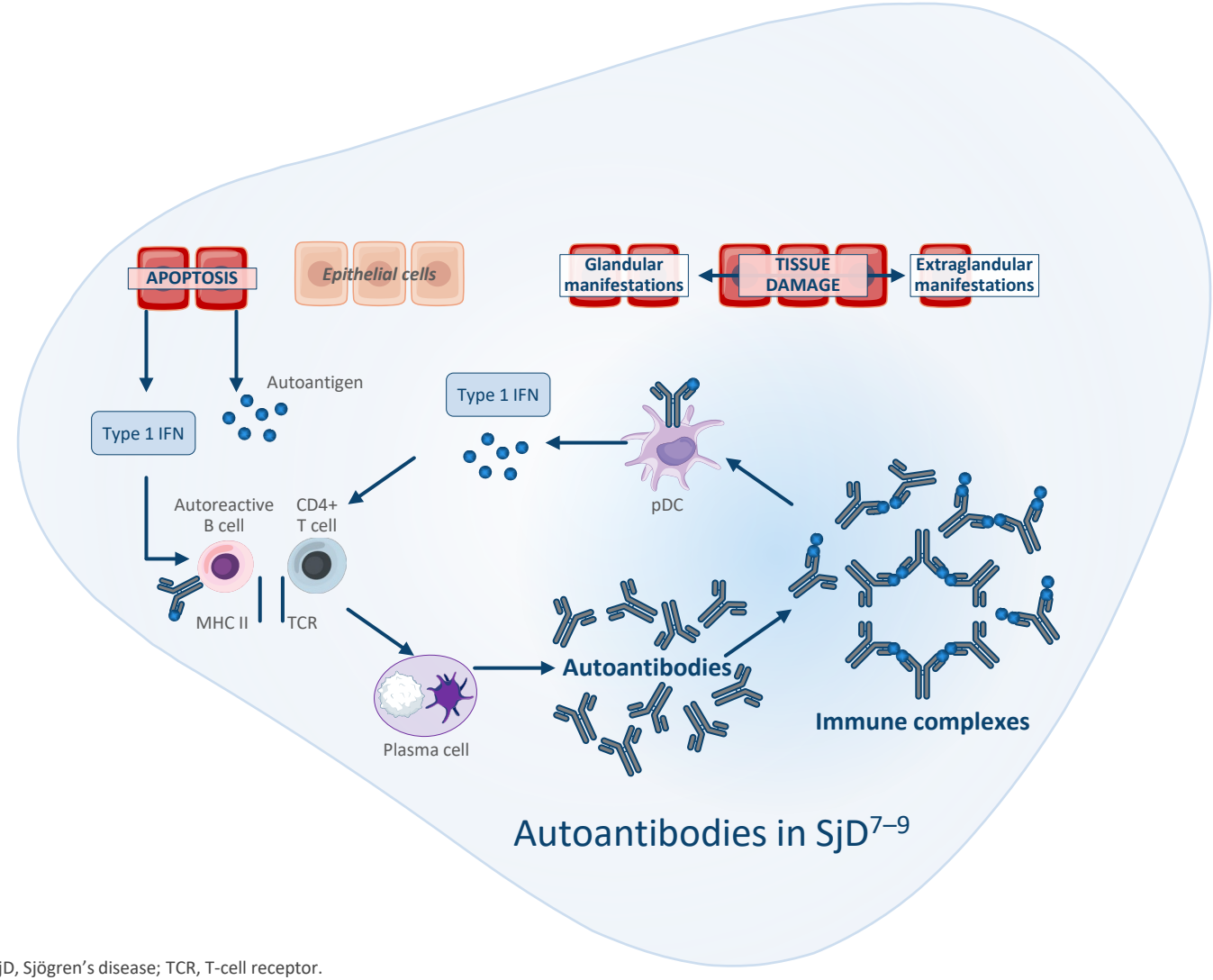
Picture Taking

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

There is an unmet need for effective treatments targeting the complex pathophysiology of SjD

- SjD is a **chronic** and **progressive**, **systemic, autoimmune disease**
- Characterized by **lymphocytic infiltration** and **immune-mediated dysfunction of exocrine glands**, with **possible extraglandular manifestations**[1–4]
- **IgG autoantibodies** targeting **Ro52, Ro60, and La antigens** contribute to **disease pathology**[5,6]



IFN, interferon; IgG, immunoglobulin G; MHC, major histocompatibility complex; pDC, plasmacytoid dendritic cell; SjD, Sjögren's disease; TCR, T-cell receptor.

1. Negrini S, et al. *Clin Exp Med*. 2022;22:9–25. **2.** Roszkowska AM, et al. *Genes (Basel)*. 2021;12:365. **3.** Zhang H, et al. *Medicine (Baltimore)*. 2015;94:e387. **4.** Vílchez-Oya F, et al. *Front Immunol*. 2022;13:1003054. **5.** Kelly AL, et al. *J Clin Med*. 2022;11:5227. **6.** Veenbergen S, et al. *J Transl Autoimmun*. 2022;5:100138. **7.** Mariette X, et al. *N Engl J Med*. 2018;378:931–39. **8.** Nocturne G, et al. *Nat Rev Rheumatol*. 2018;14:133–45. **9.** Pringle S, et al. *Arthritis Rheumatol*. 2019;71:133–42.

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

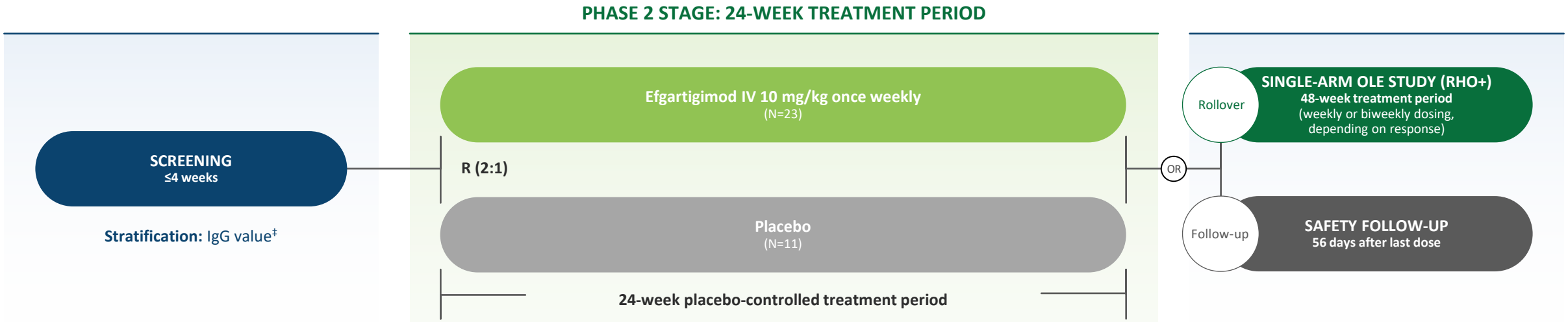
1. **Efgartigimod outcompetes endogenous IgG antibodies and pathogenic autoantibodies for binding to FcRn, due to increased affinity to FcRn**
2. **FcRn-bound efgartigimod, IgG antibodies, and pathogenic autoantibodies escape cellular degradation**
3. **Remaining unbound IgG antibodies, pathogenic autoantibodies,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

FcRn, neonatal Fc receptor; IgG, immunoglobulin G; 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.

RHO

A Randomized, Double-Blinded, Placebo-Controlled, Phase 2, Multicenter Study



Key Inclusion Criteria

Adults with:

- ACR/EULAR 2016 criteria for SjD who met criteria ≤7 years before screening†
- ESSDAI ≥5
- Anti-Ro/SS-A positive
- Presence of residual salivary flow (UWSF rate >0 mL/min and/or SWSF rate >0.10 mL/min)

Study population

34
Patients with SjD*

*3 patients did not meet eligibility criteria and were (i) discontinued within the first weeks after randomization, and (ii) removed from the efficacy analysis. †Patients with secondary Sjögren's syndrome overlap syndromes where another confirmed autoimmune rheumatic or systemic inflammatory condition (eg, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, inflammatory bowel disease) is the primary diagnosis were excluded. ‡> 16.0 g/L or ≤ 16 g/L.

ACR, American College of Rheumatology; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; EULAR, European Alliance of Associations for Rheumatology; IgG, immunoglobulin G; IV, intravenous; OLE, open-label extension; R, randomization; SS-A, anti-Sjögren's syndrome–related antigen; SjD, Sjögren's disease; SWSF, stimulated whole salivary flow; UWSF, unstimulated whole salivary flow.

ClinicalTrials.gov Identifier: NCT05817669. https://clinicaltrials.gov/study/NCT05817669. Accessed April 2025.

RHO — A Randomized, Double-Blinded, Placebo-Controlled, Phase 2, Multicenter Study

OBJECTIVE

To evaluate the efficacy and safety of intravenous efgartigimod in adults with SjD

Primary Endpoint

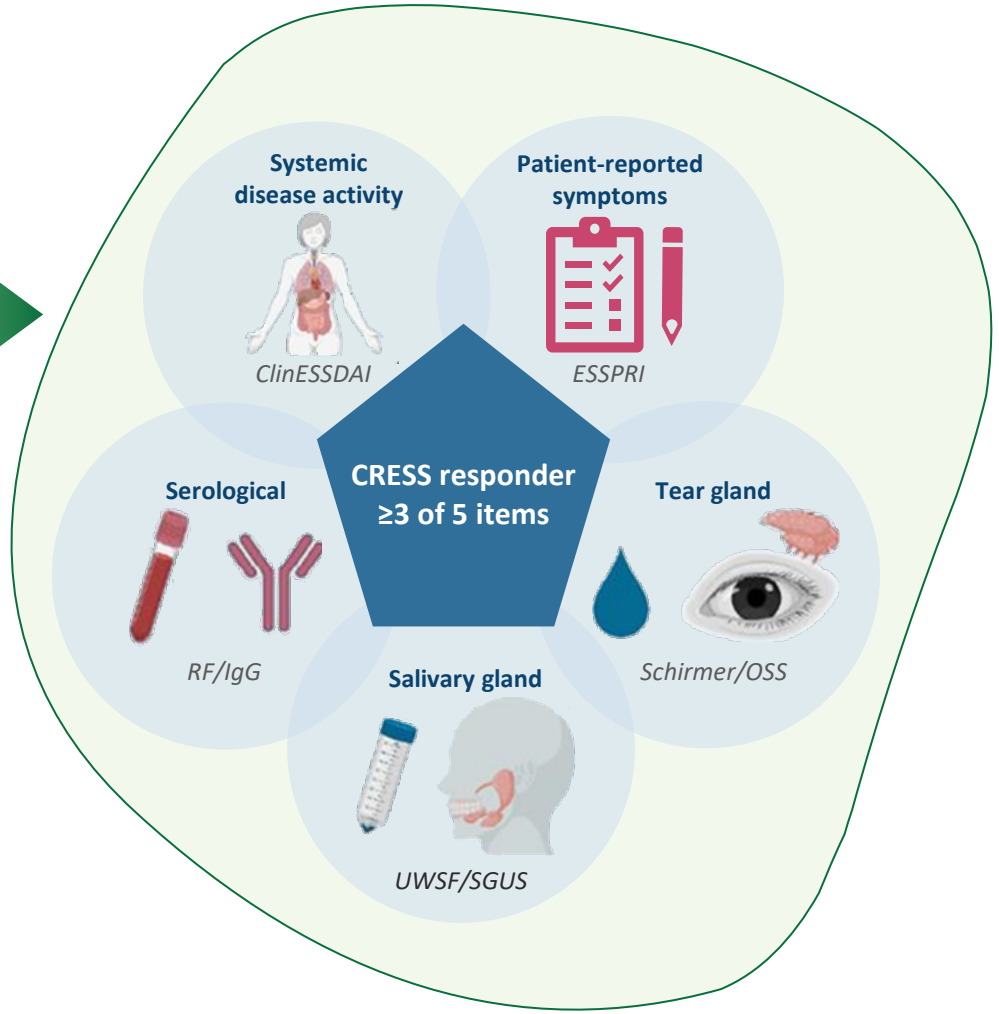
Proportion of responders to the CRESS* (response on ≥3 out of 5 items) at Week 24

Select Secondary Endpoints

- Proportion of responders to cSTAR (score ≥5) at Week 24
- Effect on disease activity (ESSDAI, clinESSDAI, ESSPRI)
- Safety, evaluated by the incidence and severity of AEs

Exploratory

- Exploratory biomarkers to understand the effects of efgartigimod on disease pathology



*CRESS response thresholds: clinESSDAI (score of <5 points); ESSPRI (decrease of ≥1 point or ≥15% from baseline); tear gland function (increase of ≥5 mm from baseline in Schirmer's test or decrease of ≥2 points from baseline in OSS); UWSF/SGUS (increase of ≥25% in UWSF or decrease of ≥25% in the SGUS Hocevar score, or if UWSF was 0 mL/min at baseline, any increase from baseline); RF/IgG (RF decrease of ≥25% from baseline or IgG reduction of ≥10%).

AE, adverse event; clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; cSTAR, candidate Sjögren's Tool for Assessing Response; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; OSS, ocular staining score; RF, rheumatoid factor; SGUS, salivary gland ultrasound; SjD, Sjögren's disease; UWSF, unstimulated whole salivary flow.

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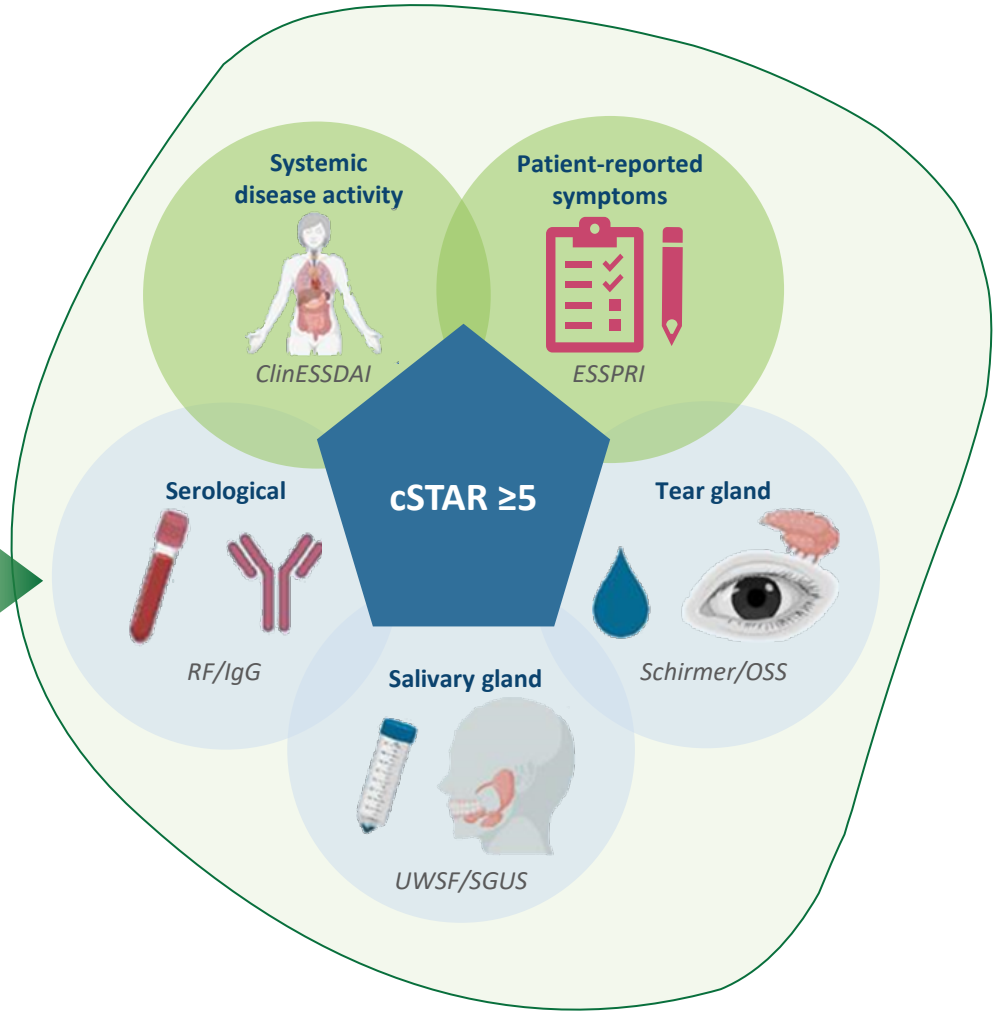

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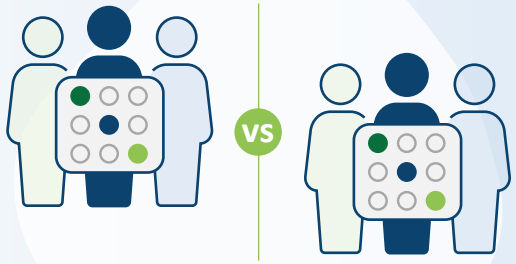
Participant **Demographics** and **Baseline Characteristics**

- **34 patients were randomized** in the study; **3 did not meet eligibility criteria** and were removed from the efficacy analysis
- Participant demographics were **generally comparable** between treatment groups



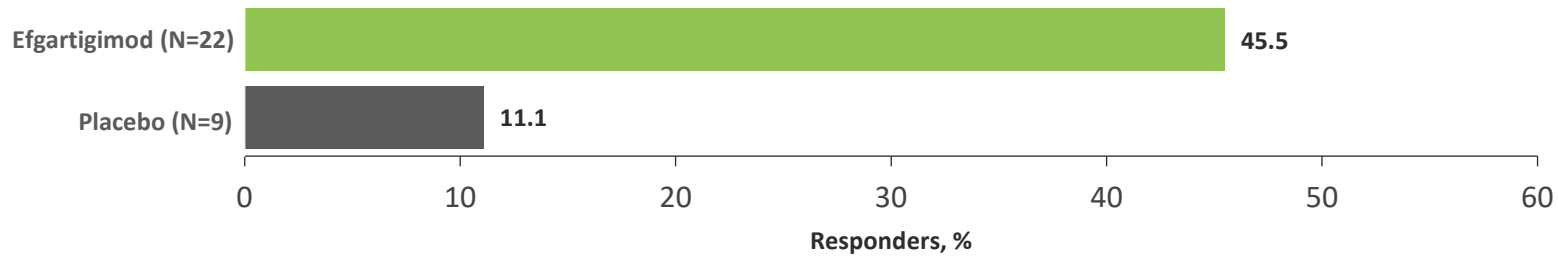
	Efgartigimod (N=23)	**Placebo** (N=11)
Age, years, median (Q1, Q3)	49 (39, 64)	58 (45, 69)
Sex, female, n (%)	22 (95.7)	11 (100.0)
Time since diagnosis, years, median (Q1, Q3)	3 (1, 6)	6 (3, 7)
Race, n (%)		
White	22 (95.7)	11 (100.0)
Unknown	1 (4.3)	0
ESSDAI total score, median (Q1, Q3)	12 (8, 15)	17 (8, 19)
clinESSDAI total score, median (Q1, Q3)	13 (9, 17)	18 (9, 21)
ESSPRI score, median (Q1, Q3)	6.7 (5.8, 7.7)	5.0 (4.7, 6.3)
Schirmer <5 mm/5 min in ≥1 eye, n (%)	18 (78.3)	9 (81.8)
UWSF, mL/min, median (Q1, Q3)	0.12 (0.05, 0.17)	0.10 (0.07, 0.15)
IgG, g/L, median (Q1, Q3)	17.32 (10.91, 22.20)	17.75 (10.77, 18.76)
RF, IU/mL, median (Q1, Q3)	51.0 (21.0, 89.0)	59.0 (37.0, 176.0)

clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; IU, international units; Q, quartile; RF, rheumatoid factor; UWSF, unstimulated whole salivary flow.

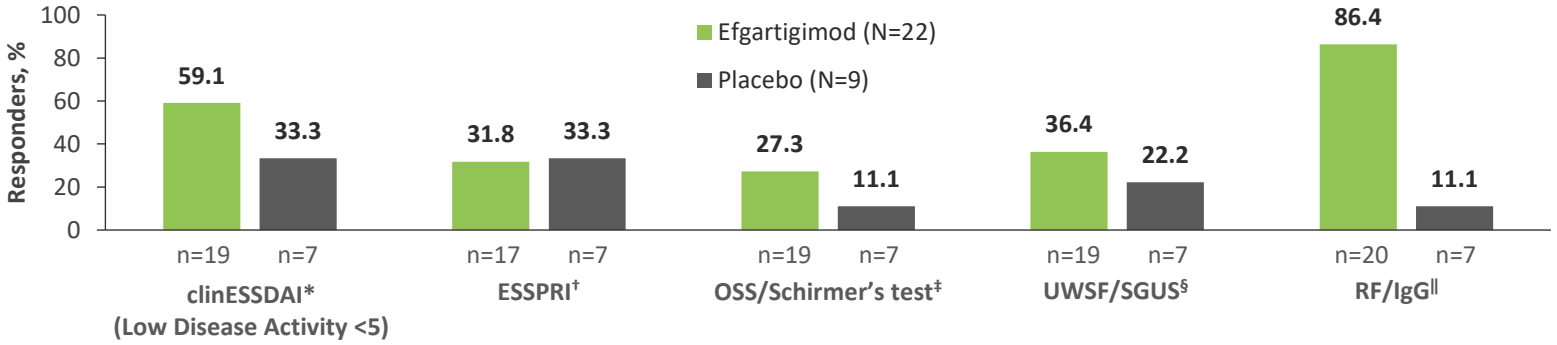
Proportion of **Responders** to Individual CRESS Items at Week 24

- A **numerical difference of 34.4 percentage points** in the proportion of **responders to ≥3 of 5 CRESS items at Week 24 was observed** in this proof-of-concept study
- For 4 of the 5 individual CRESS items, the **proportion of responders was numerically higher with efgartigimod** versus placebo
- **50.0% of efgartigimod-treated participants responded on RF only** (≥25% reduction), compared with 0% in the placebo group

Proportion of CRESS Responders (≥3 of 5 CRESS Items)



Proportion of Responders to Individual CRESS Items at Week 24

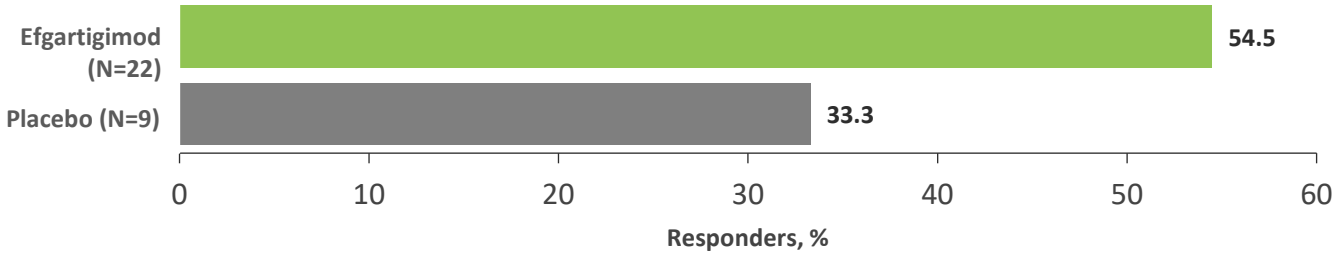


*Total clinESSDAI score <5 points from baseline. †Total ESSPRI score decrease of ≥1 point or ≥15% from baseline. ‡Increase in Schirmer's test ≥5 mm or a decrease in OSS ≥2 points from baseline or stable. §Increase in UWSF ≥25%, or any increase if baseline is 0, or decrease in SGUS ≥25%. ‖Decrease in RF ≥25% or decrease in IgG ≥10%; 50.0% of participants in the efgartigimod group had a ≥25% decrease from baseline in RF compared with 0% in the placebo group.

CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; OSS, ocular staining score; RF, rheumatoid factor; SGUS, salivary gland ultrasound; UWSF, unstimulated whole salivary flow.

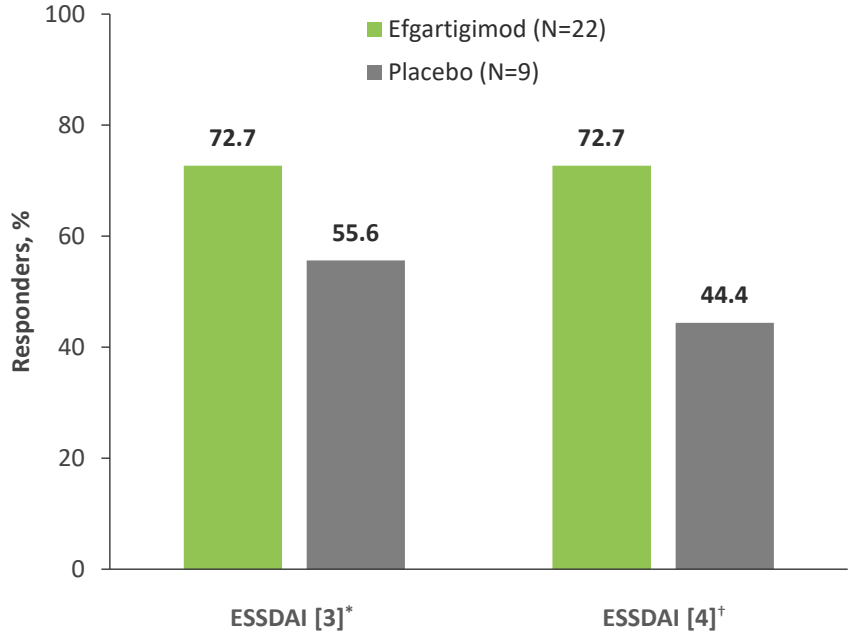
Proportion of **Responders** and Clinically Meaningful ESSDAI **Improvements**

Proportion of cSTAR Responders (≥5 Score)



- Median (Q1, Q3) **change from baseline in the clinESSDAI total scores was –7.0 (–12.0, –3.0) in the efgartigimod group** and –4.0 (–17.0, –3.0) in the placebo group at Week 24

Clinically Meaningful Changes in ESSDAI Response

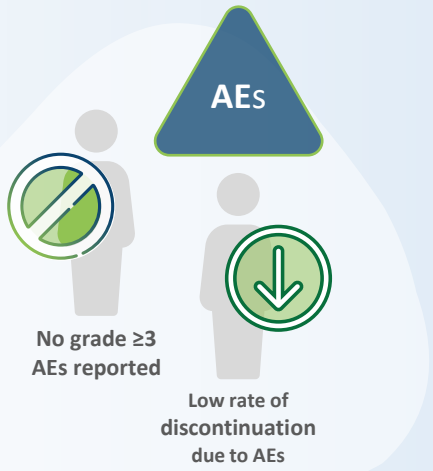


*Defined as improvement of ≥3 points in ESSDAI score at Week 24. †Defined as improvement of ≥4 points in ESSDAI score at Week 24.

clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; cSTAR, candidate Sjögren's Tool for Assessing Response; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index.

Summary of **Safety**

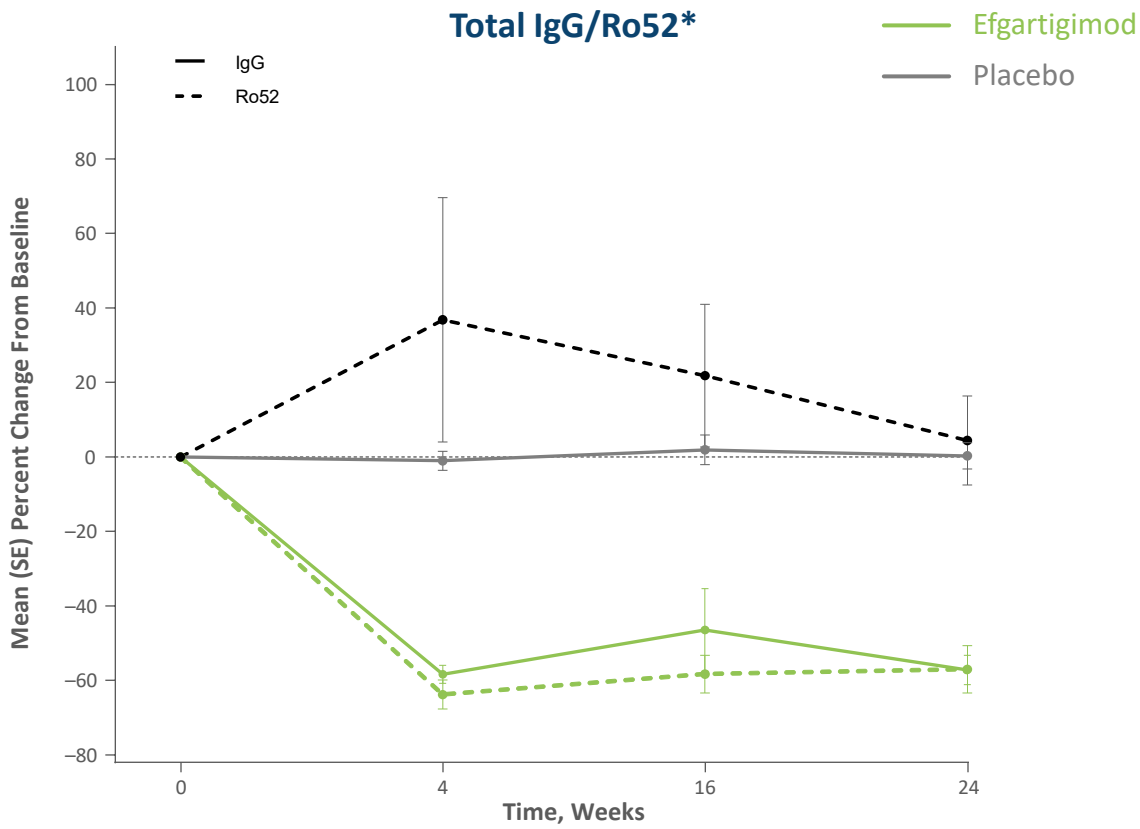
- **Efgartigimod well tolerated**, with **no grade ≥3 AEs reported** and a **low rate of discontinuation** due to AEs

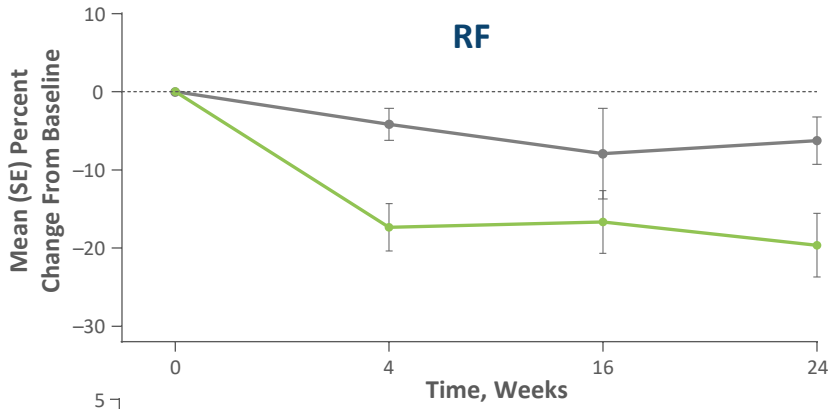


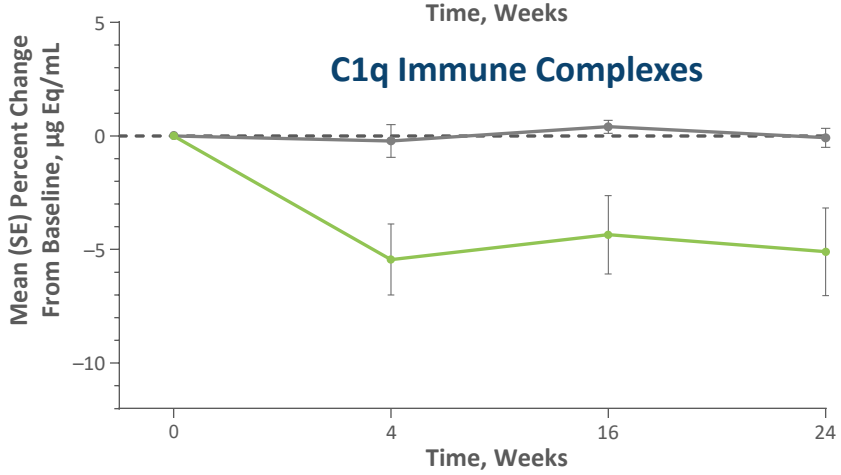
	Efgartigimod (N=23; PYFU=12.62)*		Placebo (N=11; PYFU=5)†	
Number of administrations, median (Q1, Q3)	22 (20, 24)		22 (2, 23)	
	n (%)	**m (ER)**	**n (%)**	**m (ER)**
≥1 AE	20 (87.0)	81 (6.4)	7 (63.6)	23 (4.6)
≥1 SAE‡	1 (4.3)	1 (0.1)	0	0
≥1 Grade ≥3 AE	0	0	0	0
≥1 AE leading to study drug discontinuation	1 (4.3)	1 (0.1)	0	0
≥1 AESI (infection)§	15 (65.2)	25 (2.0)	5 (45.5)	7 (1.4)
≥1 injection- and infusion-related reaction	3 (13.0)	5 (0.4)	1 (9.1)	1 (0.2)
≥1 fatal AE	0	0	0	0
Most common AEs (occurring in >10% of participants)				
Headache	4 (17.4)	6	1 (9.1)	1
Nasopharyngitis	4 (17.4)	5	1 (9.1)	1
Influenza	3 (13.0)	3	0	0
Upper respiratory tract infection	3 (13.0)	3	2 (18.2)	2
Urinary tract infection	3 (13.0)	3	1 (9.1)	1

*18 participants from the efgartigimod arm completed study treatment. †7 participants from the placebo arm completed study treatment. ‡Grade 2 SAE of vasospasm, which the investigator and sponsor considered not related to efgartigimod.
§Efgartigimod treatment leads to reduced IgG levels; as low IgG levels are associated with increased infection risks, events in the MedDRA System Organ Class Infections and Infestations are considered adverse events of special interest in this study.
AE, adverse events; AESI, adverse events of special interest; COVID-19, coronavirus disease 2019; ER, event rate (number of events/PYFU); m, number of events; MedDRA, Medical Dictionary for Regulatory Activities;
N, number of participants; PYFU, participant years of follow-up; SAE, serious adverse event.

Efgartigimod on **Total IgG**, **RF**, and **C1q Immune Complex** Levels Over Time







- A **similar pattern of response** was observed for **anti-Ro60** and **anti-La** autoantibodies

*For anti-Ro52, data only available for a subset of patients.

C1q, complement component 1q; IgG, immunoglobulin G; RF, rheumatoid factor; SE, standard error.

KEY TAKEAWAYS

Results from this proof-of-concept study suggest an **improved outcome with efgartigimod use** compared with placebo for the primary endpoint and secondary endpoints

Efgartigimod was safe and well tolerated, with no new safety signals observed

Treatment with efgartigimod led to a **rapid and sustained reduction in total IgG**, disease-relevant autoantibodies, and RF

The phase 3 UNITY trial (NCT06684847) is currently **underway to assess the efficacy and safety of efgartigimod PH20 SC*** (administered by prefilled syringe) in patients with SjD with clinESSDAI ≥6

*Coformulated with recombinant human hyaluronidase PH20.

clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; IgG, immunoglobulin G; PH20, recombinant human hyaluronidase PH20; RF, rheumatoid factor; SC, subcutaneous; SjD, Sjögren's disease.