POS0844

Efficacy and Safety of Efgartigimod PH20 Subcutaneous by Prefilled Syringe in Adults With Primary Sjögren's Disease: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial With Open-Label Extension (UNITY)

Isabelle Peene,[1] Xavier Mariette,[2] Dirk Elewaut,[1] Thomas Dörner,[3] Hendrika Bootsma,[4] Matthew Charles Baker,[5] Andrew Kelly,[6] Lana Vandersarren,[6] Edward Bowen,[7] Livia Lai,[7] Julie Jacobs,[6] Paul Meyvisch,[6] Parvin Fardipour,[7] Karen Bureau,[7] Despoina Papadopoulou,[6] Thomas Grader-Beck,[8] Wan-Fai Ng,[9] Simon J. Bowman[10]

[1]Department of Rheumatology, Ghent University Hospital and Unit Molecular Immunology and Inflammation, VIB Center for Inflammation Research, Ghent University, Ghent, Belgium; [2]Université Paris-Saclay, Paris, France, and Department of Rheumatology, Assistance Publique - Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin-Bicêtre, Paris, France; [3]Department of Medicine, Rheumatology and Clinical Immunology, Charité Universitätsmedizin and Deutsches Rheumaforschungszentrum, Berlin, Germany; [4]Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands; [5]Division of Immunology and Rheumatology, Stanford University, Palo Alto, CA, USA; [6]argenx, Ghent, Belgium; [7]IQVIA, Durham, NC, USA; [8]Division of Rheumatology, Johns Hopkins School of Medicine, Baltimore, MD, USA; [9]Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UK, and NIHR Newcastle Biomedical Research Centre, Newcastle upon Tyne NHS Foundation Trust, Newcastle Upon Tyne, Tyne and Wear, UK, and HRB Clinical Research Facility, University College Cork, Cork, Ireland; [10]Rheumatology Department, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

BACKGROUND

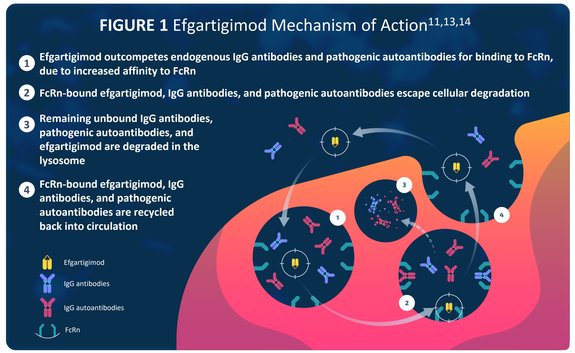
Primary Sjögren's Disease

- pSjD is a chronic, progressive, systemic autoimmune disease characterized by lymphocytic infiltration and immune-mediated dysfunction of the exocrine glands with extraglandular manifestations[1–4]
- The pathology of pSjD involves the production of RF, as well as autoantibodies, including IgG autoantibodies, against Ro52, Ro60, and La antigens[5,6]
- Despite the significant impact on daily function and QoL caused by chronic fatigue, pain, and unbearable dryness, there are no approved systemic, disease-modifying therapies for pSjD that target the underlying pathophysiology[7–9]
- Current treatments focus mainly on symptom management and disease manifestations[1,10]

Efgartigimod

- Efgartigimod is a **human IgG1 antibody Fc fragment** that has been engineered for **increased affinity to FcRn** compared with endogenous IgG and is **uniquely composed of the only part of the IgG antibody that normally binds FcRn**[11,12]

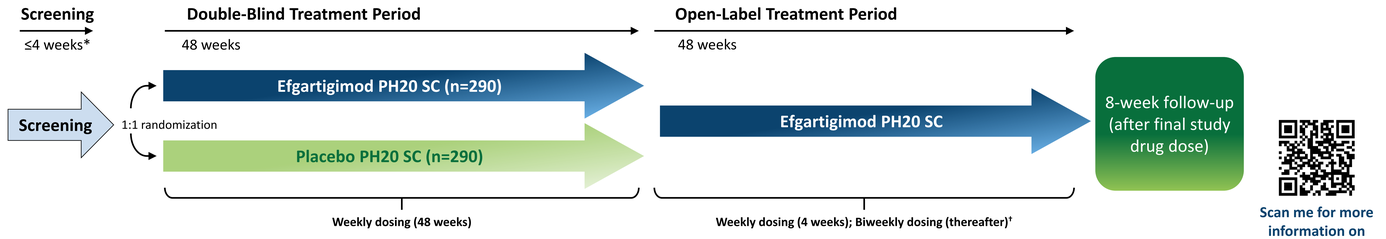
FIGURE 1 Efgartigimod Mechanism of Action[11,13,14]



- By blocking FcRn, **efgartigimod selectively reduces IgG antibodies and pathogenic autoantibodies** (**Figure 1**), and it does so **without:**[11,15–17]
  - Impacting antibody production (including other Ig antibodies) or other parts of the immune system
  - Decreasing albumin levels
  - Increasing LDL cholesterol levels
- **Efgartigimod PH20 SC** is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for **rapid (30–90-second single-injection)** SC administration[18]
- Our hypothesis is that efgartigimod PH20 SC may successfully reduce disease activity and symptoms in patients with pSjD due to reduction in IgG, including disease-specific autoantibodies, thereby targeting the underlying pathogenesis of pSjD
- The UNITY trial (**Figure 2**) will evaluate the efficacy, safety, tolerability, PK, PD, and immunogenicity of efgartigimod PH20 SC compared with placebo PH20 SC in patients with pSjD (clinESSDAI ≥6)

STUDY DESIGN

FIGURE 2 UNITY: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial With OLE to Evaluate the Efficacy, Safety, and Tolerability of Efgartigimod PH20 SC Administered by Prefilled Syringe in Adult Patients With pSjD (NCT06684847)



Scan me for more information on UNITY

*The screening period may be extended to 28 days if additional/repeated tests (eg, clinical laboratory assessments) are required or results are delayed. †Upon disease worsening, participants can switch back to weekly dosing.

STUDY ENDPOINTS

Primary Endpoint

- **Change from baseline in clinESSDAI score at Week 48**

Secondary Endpoints

- Change from baseline in ESSDAI score at Week 48
- Proportion of participants at Week 48:
  - With low disease activity according to clinESSDAI score (<5 points)
  - Who are responders on STAR (≥5 points)
  - With MCII in ESSDAI score (≥3 points)
- Change from baseline in DiSSA at Week 48, including total DiSSA, sicca domain, and joint pain scores
- Change from baseline in clinESSDAI score at Week 24

KEY ELIGIBILITY CRITERIA

Inclusion

- At screening, participants must meet the following criteria:
  - 2016 ACR/EULAR classification criteria for pSjD
  - clinESSDAI ≥6
  - Anti-Ro/SS-A positive at central laboratory
  - Unstimulated residual salivary flow (≥0.01 mL/min)

Exclusion

- Secondary (also referred to as associated) Sjögren's disease, defined as overlap with another autoimmune rheumatic or systemic inflammatory condition as the main diagnosis
- IgG concentration <4 g/L at screening

Scan me for additional eligibility criteria

KEY FEATURES

- Efgartigimod was administered IV during the phase 2 proof-of-concept RHO trial (NCT05817669), whereas the phase 3 UNITY trial utilizes a **prefilled syringe** with efgartigimod PH20 SC for rapid administration and improved treatment convenience
- Efgartigimod PH20 SC has resulted in a mean reduction from baseline in IgG levels of >60%, consistent with previous clinical trials with efgartigimod IV[11,15,19,20]

The primary endpoint was measured utilizing CRESS during the phase 2 proof-of-concept RHO study, whereas the phase 3 UNITY trial utilizes **clinESSDAI**, which is a **reliable and validated tool** for evaluating treatment efficacy in patients with pSjD[21]

The **DiSSA patient diary** was developed and content validated for the UNITY trial to assess pSjD symptom severity

- **DiSSA is a PRO measure and comprises 6 symptoms:**
  - Mouth dryness, eye dryness, exhaustion, pain in joints, difficulty thinking, and genital dryness
- Patients **rate the severity of each symptom** at its worst in the previous 24 hours
  - 11-point Likert scale: 0=none, 10=worst possible

KEY TAKEAWAYS

pSjD is a chronic, progressive, autoimmune rheumatic disease for which there are currently no approved therapies that modify the disease course

Our hypothesis is that efgartigimod PH20 SC may reduce IgG autoantibodies, including disease-specific autoantibodies, thereby potentially targeting the underlying pathogenesis of pSjD

The UNITY phase 3 study will evaluate efgartigimod PH20 SC versus placebo PH20 SC in adult participants with pSjD

The UNITY trial utilizes DiSSA, a new patient diary that patients can use to assess their symptoms

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ABBREVIATIONS

ACR, American College of Rheumatology; (clin)ESSDAI, (clinical) EULAR Sjögren's Syndrome Disease Activity Index; CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; DiSSA, Diary of Sjögren's Symptoms Assessment; EULAR, European Alliance of Associations for Rheumatology; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; IgG(1), immunoglobulin G (1); IV, intravenous; LDL, low-density lipoprotein; MCII, minimal clinically important improvement; OLE, open-label extension; pSjD, primary Sjögren's d isease; PD, pharmacodynamics; PK, pharmacokinetics; PRO, patient-reported outcome; QoL, quality of life; RF, rheumatoid factor; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SS-A, Sjögren's syndrome-related antigen A; STAR, Sjögren's Tool for Assessing Response.

DISCLOSURES AND ACKNOWLEDGMENTS

IP: argenx; **XM**: Bristol-Myers Squibb, GSK, Janssen, Novartis, Otsuka, Pfizer; **DE**: Nothing to disclose; **TD**: argenx, Bristol-Myers Squibb, Janssen, Novartis; **HB**: Nothing to disclose; **MCB**: Nothing to disclose; **AK, LV, JJ, PM, DP**: Employees of argenx; **EB, LL, PF, KB**: Employees of IQVIA; **TGB**: Nothing to disclose; **WFN**: Nothing to disclose; **SJB**: Nothing to disclose.

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