

Telitacicept as a Novel BAFF/APRIL-Targeted Therapy for Sjögren's Disease

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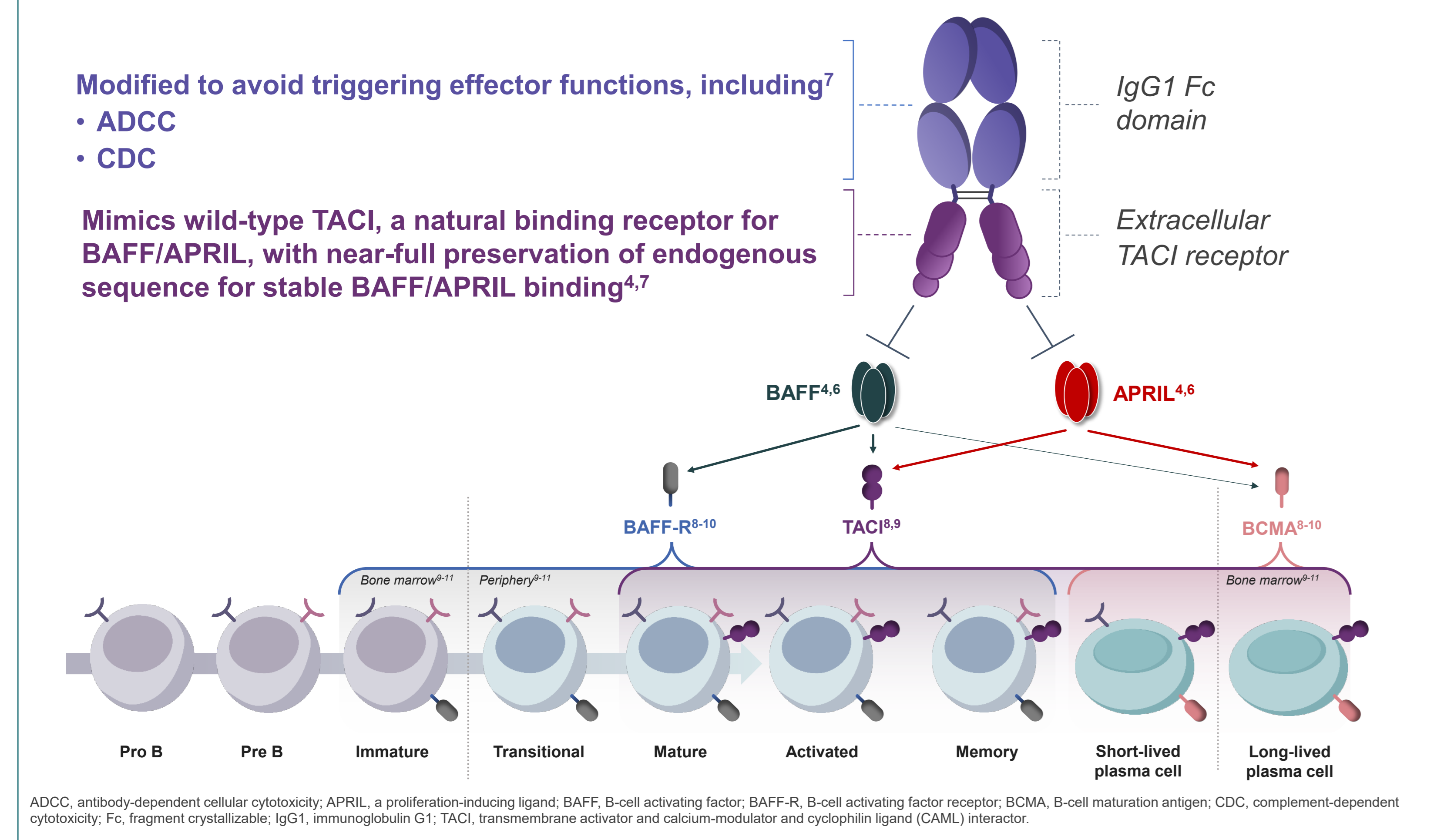
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BACKGROUND

- Sjögren disease (SjD) is a systemic autoimmune disease in which autoreactive B cells target and damage the epithelial cells of exocrine glands¹⁻⁴
- Lymphocytic infiltration of exocrine glands such as salivary and lacrimal glands results in the predominant characterizations of xerostomia, keratoconjunctivitis sicca, and fatigue; approximately 30% of patients develop additional systemic manifestations¹⁻⁵
- Pathologic B-cell and plasma cell activation contributes to SjD pathogenesis and drives tissue injury by promoting autoantibody production, immune complex formation, and antibody-independent mechanisms such as T-cell activation and cytokine production, ultimately leading to disease progression, systemic complications, and increased risk of lymphoma¹⁻³
- Current therapies for SjD largely remain symptomatic or are associated with non-selective immunosuppression, representing a high unmet need for innovative and effective treatment options^{1,4}
- Telitacicept is a novel, fully human, TACI-Fc fusion protein that targets B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL)^{4,6,7}
- Through this novel dual inhibition mechanism, telitacicept modulates upstream B-cell development and survival, which ultimately may reduce pathogenic autoantibodies implicated in autoimmune disease, including SjD (Figure 1)^{4,6,7}

Figure 1. Telitacicept is a Fusion Protein Based on the Human TACI Receptor Designed to Target BAFF and APRIL



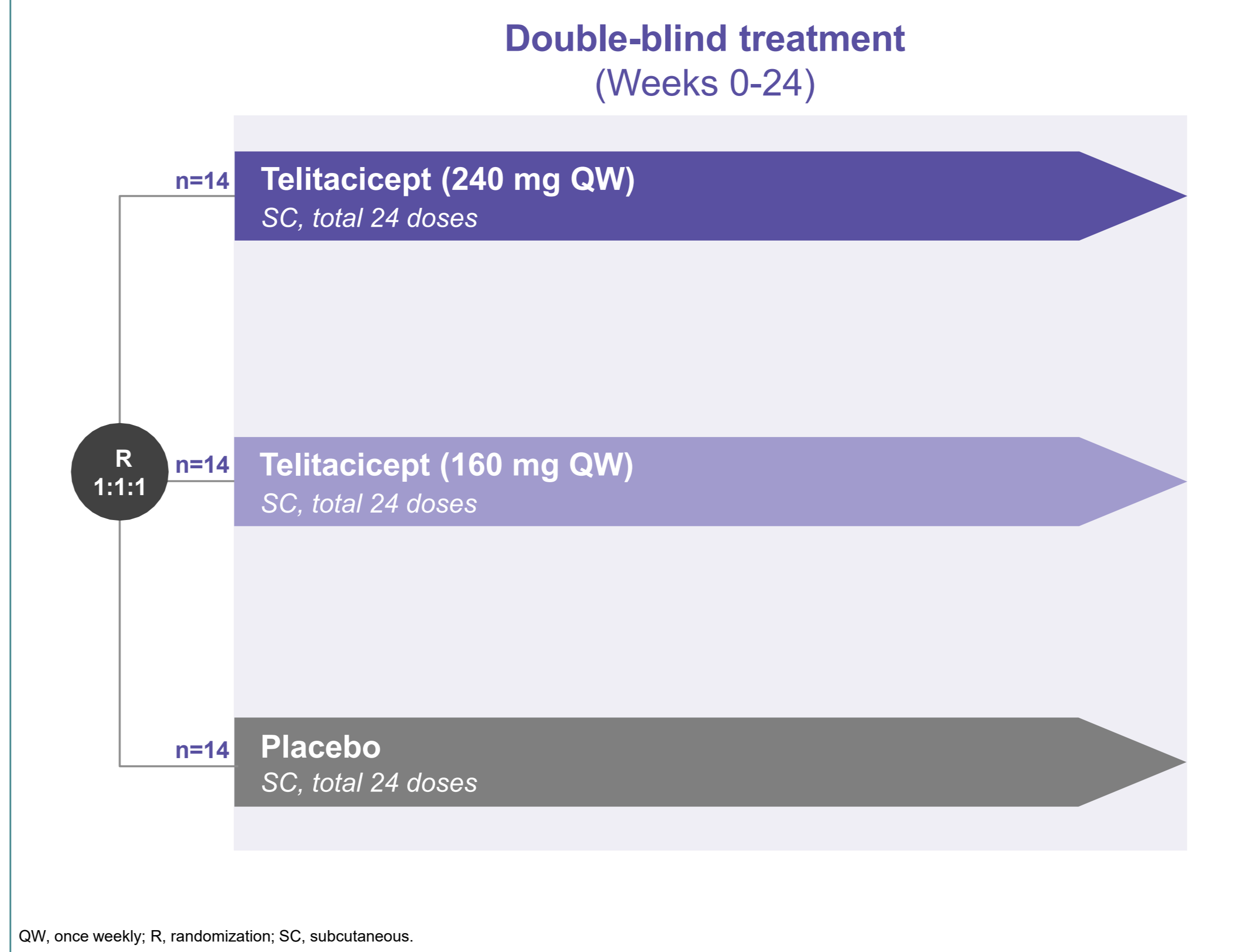
- Data from phase 2 (NCT04078386) and phase 3 (NCT05673993) studies of telitacicept conducted in China and sponsored by RemeGen Co., Ltd. showed efficacy and safety in adults with primary SjD¹²⁻¹⁵
- Here, we present the pharmacodynamic findings from a phase 2 study of telitacicept in adults with primary SjD conducted in China

METHODS

Study Design

- Eligible participants were randomly assigned (1:1:1) to receive subcutaneous telitacicept (240 mg), subcutaneous telitacicept (160 mg), or placebo for 24 weeks, once weekly (Figure 2)
- Eligibility criteria included participants with primary SjD who fulfilled the 2016 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) classification criteria for SjD, were aged 18-65 years, had anti-Sjögren's syndrome-related antigen A (SSA) antibody positivity, and a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score of ≥ 5 points
- Participants were not permitted to receive concomitant treatment for SjD except hydroxychloroquine if stable for >12 weeks before randomization

Figure 2. Study Design



Endpoints

- The primary endpoint was the change from baseline in the ESSDAI score at week 24
- Biomarkers included immunoglobulin G (IgG), IgA, IgM, C3, C4, CD19+ B cells, CD4+ T cells, and CD8+ T cells
- Safety assessments included the incidence and severity of adverse events (AEs)

RESULTS

Efficacy

- Telitacicept was associated with reductions in serum IgG, IgA, and IgM, and CD19+ B-cell counts compared with placebo (Figure 3)
- At week 24, IgG levels reduced from 19.6 to 15.6 g/L, IgA from 3.0 to 1.5 g/L, and IgM from 1.2 to 0.5 g/L, while circulating CD19+ B-cell counts decreased from 157.8 to 81.7 cells/ μ L in participants treated with telitacicept 160 mg (Table 1)
- The primary endpoint of change from baseline in ESSDAI score at week 24 was met with statistical significance, and the efficacy of telitacicept was replicated across multiple endpoints in a phase 3 randomized controlled study conducted in China with 380 participants with similar changes in pharmacodynamics

Figure 3. Pharmacodynamic Parameters: Change From Baseline in Immunoglobulins and CD19+ B Cells

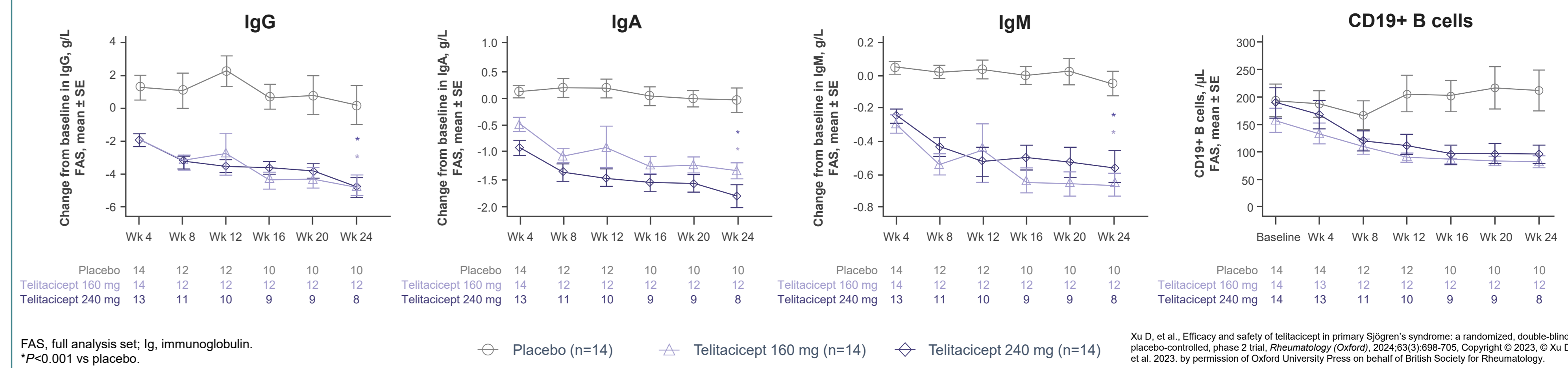


Table 1. Mean Change in Immunoglobulins and CD19+ B-Cell Counts at Week 24 Compared With Baseline

Mean (SD)	Placebo		Telitacicept 160 mg	
	Baseline	Week 24	Baseline	Week 24
IgG, g/L	16.3 (4.6)	16.9 (6.3)	19.6 (6.1)	15.6 (5.4)*
IgA, g/L	3.5 (1.6)	3.7 (1.7)	3.0 (1.2)	1.5 (0.6)*
IgM, g/L	1.3 (0.7)	1.0 (0.7)	1.2 (0.4)	0.5 (0.3)*
CD19+ B cells, μ L	193.7 (112.5)	211.6 (118.0)	157.8 (83.2)	81.7 (35.3)

Ig, immunoglobulin. *Statistically significant compared with placebo (P<0.001).

Safety

- Telitacicept showed a generally well-tolerated safety profile in participants with primary SjD, with most AEs being mild or moderate in severity (Table 2)
- No deaths or serious AEs occurred in the telitacicept treatment groups

Table 2. Selected Adverse Events That Occurred in ≥ 2 Participants in Any Group

System organ class preferred term, n (%)	Placebo (n=14)	Telitacicept 160 mg (n=14)
Adverse events	13 (92.9)	12 (85.7)
Adverse reactions	9 (64.3)	9 (64.3)
Infections and infestations	8 (57.1)	9 (64.3)
General disorders and administration site conditions	0 (0)	7 (50.0)*

CTCAE, Common Terminology Criteria for Adverse Events. *Included 6 instances of injection site reactions (CTCAE grade 1-2). *Statistically significant compared with placebo (P<0.05).

CONCLUSIONS

- BAFF/APRIL inhibition may provide meaningful clinical benefit in SjD while largely preserving overall B-cell and Ig compartments, consistent with selective modulation of pathogenic B-cell populations
- A global, multicenter, randomized, double-blind, placebo-controlled phase 3 study evaluating the efficacy and safety of telitacicept in adult participants with active primary SjD is currently recruiting (NCT07404865; UPSTREAM SjD)
- Results from a global adult primary SjD population will further characterize the efficacy and safety of telitacicept

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