

UPSTREAM SjD: A Global Phase 3 Study to Evaluate the Efficacy and Safety of Telitacicept in Patients With Primary Sjögren Disease

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Sjögren disease (SjD) is a chronic autoimmune disorder characterized by abnormal B-cell activation, lymphocytic infiltration of exocrine glands, and systemic inflammation. B-cell hyperactivity leads to pathogenic autoantibody production, hypergammaglobulinemia, elevated rheumatoid factor, circulating immune complexes, and increased inflammatory cytokines. B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are key cytokines that promote B-cell and plasma-cell differentiation, maturation, and survival. Telitacicept is a novel, fully human transmembrane activator and calcium-modulator and cyclophilin ligand interactor (TACI)-Fc fusion protein that neutralizes BAFF and APRIL, thereby modulating B-cell and plasma-cell function, reducing both antibody production and antibody-independent B-cell pathology. Telitacicept has shown efficacy and was generally well tolerated in phase 2 (NCT04078386) and 3 (NCT05673993) studies conducted in China in participants with primary SjD. Here, the study design of an international, multicenter, randomized, double-blind, placebo-controlled phase 3 trial of telitacicept in adult participants with active primary SjD is presented (NCT07404865).

Methods

Participants aged 18 to 75 years meeting 2016 American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) criteria with a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥ 5 are eligible. Anti-SSA/Ro positivity is required, though up to 10% may enroll with a positive salivary gland biopsy instead. Stable background therapy is allowed: hydroxychloroquine for ≥ 8 weeks and low dose-prednisone (≤ 10 mg/day or equivalent) or one immunosuppressant for ≥ 4 weeks before screening.

Results

Approximately 250 eligible participants will be randomized 1:1 to weekly subcutaneous telitacicept 160 mg or placebo for 48 weeks. The study includes a 4-week screening period, a

48-week double-blind treatment period, a planned open-label extension, and an 8-week safety follow-up upon study completion (Figure 1). The primary endpoint is change from baseline in ESSDAI score at week 48. Secondary endpoints focus on measures of disease activity, including the proportion of participants achieving prespecified ESSDAI response thresholds, changes in physician global assessment of disease activity (PhGA), and glandular function (eg, salivary flow and Schirmer's test). Patient-reported outcomes include change from baseline in the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), and patient global assessment of disease activity (PtGA). Safety will also be assessed.

Conclusions

Results from this study will expand on the phase 2 and 3 evidence generated in China by evaluating the efficacy of BAFF/APRIL inhibition with telitacicept in a global primary SjD population.

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10. Himanshu Patel: Is an employee of Vor Biopharma Inc. and owns company stock.
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Figure 1. UPSTREAM SjD Study Design

