

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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Background

Sjögren disease (SjD) is a chronic, systemic autoimmune disorder characterized by lymphoid infiltration of exocrine glands and potential systemic manifestations. Prominent symptoms include mucosal dryness, pain, and fatigue. In SjD, aberrant B-cell and plasma-cell activation results in autoantibody production, hypergammaglobulinemia, increased levels of rheumatoid factor, immune complex formation, and increased inflammatory cytokines, which drive disease pathophysiology, systemic complications, and increased lymphoma risk. The cytokines, B-cell activating factor (BAFF), and a proliferation-inducing ligand (APRIL) play a central role in B-cell and plasma-cell differentiation, maturation, and survival. Telitacicept, a novel, fully human transmembrane activator and calcium-modulator and cyclophilin ligand interactor (TACI)-Fc fusion protein, targets and neutralizes BAFF and APRIL, thereby modulating upstream B-cell activity across a broad spectrum of the B-cell lineage and reducing antibody production as well as antibody-independent B-cell pathology. Telitacicept has demonstrated efficacy and safety in phase 2 (NCT04078386) and 3 (NCT05673993) studies conducted in China in participants with primary SjD.

Aim

To present the study design of an international, multicenter, randomized, double-blind, placebo-controlled phase 3 trial of telitacicept 160 mg in adult participants with active primary SjD.

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. Participants must be positive for anti-SSA/Ro antibodies at screening, although anti-SSA/Ro-negative participants may

enroll with a positive salivary gland biopsy ($\leq 10\%$ of study population). Stable low-dose prednisone (≤ 10 mg/day or equivalent), hydroxychloroquine, and up to one additional background immunosuppressant are permitted, provided doses have been stable prior to screening: hydroxychloroquine for ≥ 8 weeks and prednisone/additional immunosuppressant for ≥ 4 weeks.

Results

The trial is currently enrolling and approximately 250 eligible participants will be randomized 1:1 to telitacicept 160 mg or placebo and will receive weekly subcutaneous injections for 48 weeks. The study consists of up to 4 weeks of screening, a 48-week double-blind treatment period, an 8-week safety follow-up, and a planned open-label extension for those who complete the study (Figure 1). The primary endpoint is change from baseline in ESSDAI score at week 48. Secondary endpoints assessed at week 48 include measures of disease activity (eg, proportion of participants achieving ESSDAI response thresholds and change in physician global assessment of disease activity), glandular function (eg, salivary flow and Schirmer's test), and patient-reported outcomes, including change from baseline in the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F), SF-36, and patient global assessment of disease activity. Additional secondary endpoints include composite responder outcomes such as CRESS and STAR. Exploratory endpoints include changes in biomarkers such as autoantibodies, immunoglobulin levels, complement components, immunophenotyping of B-cell subsets, cytokines (BAFF, APRIL), and other serum/plasma proteins. Safety endpoints include incidence of adverse events, vital signs, and clinical laboratory assessments.

Discussion / Conclusion

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.

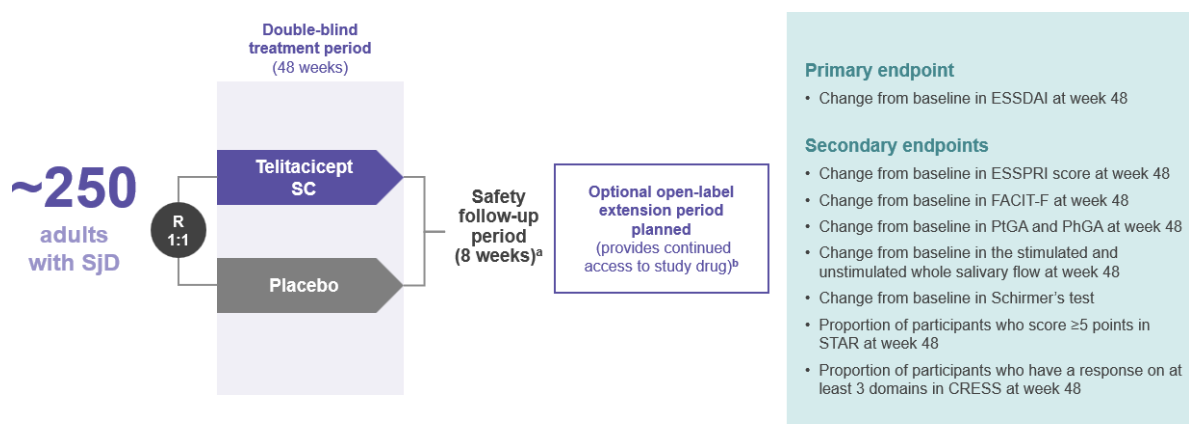
Disclosures:

1. Pierre-Marie Duret has received consulting fees from Vor Biopharma and a research grant from Novartis.
2. Alan N. Baer has received consulting fees from Bristol Myers Squibb.
3. Jacques-Eric Gottenberg has received honoraria from AbbVie, Bristol Myers Squibb, Galapagos, Gilead, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB.
4. Ronald van Vollenhoven has received consultancy and/or speaker fees from AbbVie, AstraZeneca, Biogen, Bristol Myers Squibb, Cabaletta, Galapagos, GSK, Janssen, Kyowa Kirin, Pfizer, RemeGen, Sanofi, UCB, and Vor Biopharma and grant support from

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5. Jeremy Sokolove is an employee of Vor Biopharma Inc. and owns company stock.
6. Xavier Mariette has received consulting fees from Bristol Myers Squibb, GSK, Janssen, Novartis, Pfizer, and Vor Biopharma.

Figure 1. UPSTREAM SjD Study Design



^aParticipants who complete the last dosing will have two follow-up visits at weeks 4 and 8 after the last dose of study medication to perform safety and immunogenicity assessments.

^bFor patients who complete the double-blind treatment period in its entirety and who meet the eligibility criteria for enrollment in the OLE period. Participation in the OLE will be voluntary, and informed consent specific to the extension study will be obtained prior to enrollment.