# Abstract: P1542

# Title: RILIPRUBART (SAR445088) IN COLD AGGLUTININ DISEASE: INTERIM ANALYSIS FROM PART 2 OF A LONG-TERM PHASE 1B TRIAL CONFIRMS ACCEPTABLE EFFICACY AND SAFETY WITH 12-WEEKLY IV ADMINISTRATION

**Abstract Type: Poster Presentation**

**Topic: Enzymopathies, membranopathies and other anemias**


**Background:**

Riliprubart (SAR445088) is a humanized immunoglobulin G4 monoclonal antibody that inhibits the active form of C1s of the classical complement pathway. It is currently in development for the treatment of complement-mediated diseases, including cold agglutinin disease (CAD).

**Aims:**

To evaluate if intravenous (IV) riliprubart 3.5 g every 3 months plus an additional dose on Day 29, derived from a pharmacokinetic/pharmacodynamic (PK/PD) model, is adequate for the Phase 3 study. Here, we present interim safety, efficacy, PK, and PD results from Part 2 of LTS16637, the ongoing long-term Phase 1b study of riliprubart in patients with CAD (NCT04802057).

**Methods:**

Completers of the Phase 1b PDY16370 study and Part 1 of the Phase 1b LTS16637 study (maintenance subcutaneous doses of riliprubart 600 mg every 4 weeks) continued to Part 2 and received the new dose regimen (riliprubart 3.5 g IV every 12 weeks with an additional dose on Day 29). Part 2 interim data were analyzed at the cutoff date when patients were scheduled to have received at least 3 doses.

Analyses included treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events, discontinuations, treatment-emergent antidrug antibodies (ADAs), hemolysis, anemia, CH50, and riliprubart concentration data.

Baseline values for Part 2 were taken pre-dose on Day 1 of the new dose regimen.

**Results:**

Six patients transitioned to Part 2 and received ≥1 dose of riliprubart 3.5 g IV by the cutoff date. Four patients completed the Day 85 visit and received ≥3 doses. All patients were included in PK, PD, and biomarker activity analyses.

Four TEAEs were reported in 4 (66.7%) patients: iron-deficiency anemia, breakthrough hemolysis, fatigue, and acrocyanosis (n=1 [16.7%] each). Three TEAEs were of grade 2 severity. One TEAE of recurrent acrocyanosis (16.7%) was grade 3 and assessed as drug-related by the Investigator, leading to temporary drug interruption. No TEAEs of meningococcal infection, systemic lupus erythematosus, or serious hypersensitivity reaction or anaphylaxis were reported. One patient (16.7%) discontinued the study due to a post-treatment adverse event of Waldenström's macroglobulinemia which was a progression of underlying Waldenström's disease. The event was assessed as not drug-related by the Investigator. All patients tested ADA negative at baseline (PDY16370) and 4 patients with ADA measurement during treatment tested ADA negative (PDY16370, LTS16637 Part 1 and 2).

At Part 2 baseline, mean (standard deviation [SD]) hemoglobin was 11.5 (1.6) g/dL (Figure 1) and mean (SD) bilirubin was 8.41 (4.2) umol/L, below the upper limit of normal. No significant changes were observed up to the last visit before cutoff for 3 of the 4 patients who completed Day 85 IV visit and received ≥3 doses, indicating sustained control of hemolysis and anemia with quarterly IV dosing of riliprubart.

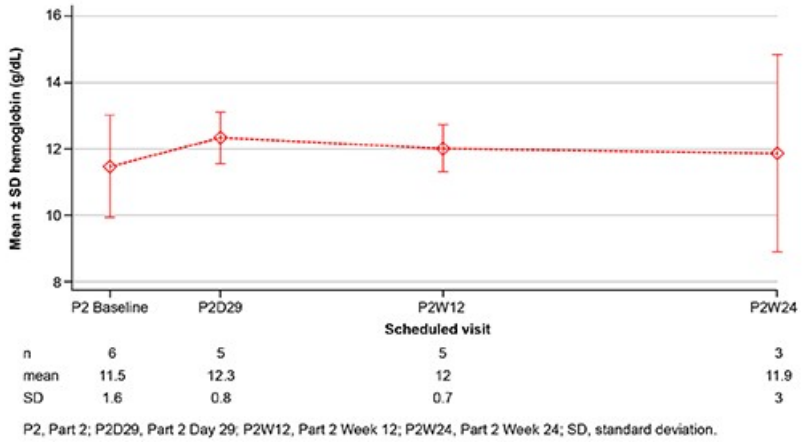
PD data showed the mean CH50 value was above 10 IU/mL in 1 patient and below 10 IU/mL in 5 patients at Part 2 baseline. Post-treatment samples were below 10 IU/mL in all patients.

Concentration-time profiles of riliprubart demonstrated consistency with the 90% prediction interval simulated for a 70 kg CAD patient using a PopPK model. Based on the PopPK modeling and simulation, steady state is anticipated at Week 12 after the third 3.5 g IV infusion. Available PK data validate the PopPK model in predicting riliprubart exposures in CAD patients.

**Summary/Conclusion:**

These safety, efficacy, PK, and PD results support IV administration of 3.5 g of riliprubart every 12 weeks, with an additional IV infusion on Day 29 after the initial dose, for the Phase 3 study.

**Figure 1.** Mean changes in hemoglobin (g/dL) from Part 2 baseline to Part 2 Week 24




P2, Part 2; P2D29, Part 2 Day 29; P2W12, Part 2 Week 12; P2W24, Part 2 Week 24; SD, standard deviation.

**Keywords:** Clinical trial, Phase I, Monoclonal antibody, Autoimmune hemolytic anemia (AIHA)