A multicenter, open-label, non-randomized, Phase 1b/2 study to evaluate the safety, pharmacokinetics, and efficacy of subcutaneous isatuximab in adults with warm autoimmune hemolytic anemia

Short title: wAIHA Isatuximab study

Principal investigator: Liesbeth Oosten

Sponsor: Sanofi

EudraCT nr. (if applicable): 2020-003880-24

Patient population:

Required no. of patients (if applicable): 17-23

Type of study:

Phase 1b/2 open-label, non-randomized, multicenter study

Study objectives:

Primary objectives:

Part A: To evaluate the safety and tolerability of subcutaneous injections of isatuximab in adults with wAIHA.

Part B: To evaluate the efficacy of the selected dose in adults with wAIHA.

Subject eligibility criteria:

Inclusion criteria (selection):

- Males and females with a confirmed diagnosis of primary wAIHA or systemic lupus erythematosus (SLE)-associated wAIHA (without other SLE-related manifestations apart from cutaneous and musculoskeletal manifestations) who meet the following criteria:
  - Hemoglobin level <10 g/dL at Screening.
  - Hemolysis (haptoglobin ≤40 mg/dL and total bilirubin above the upper limit of normal).
  - Positive direct antiglobulin test (DAT) (IgG or IgG + complement C3d pattern or IgM warm autoantibodies [positive dual DAT]).
- Participants who have previously failed to maintain a sustained response after treatment with corticosteroids (corticosteroid-refractory or corticosteroid-dependent primary wAIHA). For Part A but not Part B this must have included anti-CD20 monoclonal antibody treatment.

- Eastern Cooperative Oncology Group (ECOG) performance status Grade 2 or lower.

Exclusion criteria (selection):

- Secondary wAIHA from any cause including drugs, lymphoproliferative disorders, infectious or autoimmune disease (SLE without other SLE-related manifestations apart from cutaneous and musculoskeletal manifestations is allowed), or active hematologic malignancies. Participants with positive antinuclear antibodies but without a definitive diagnosis of an autoimmune disease are allowed.
- Serum gammaglobulin levels <3 g/L.
- Concurrent treatment with corticosteroids or iron supplementation unless on a stable dose prior to enrollment for ≥ 30 days.
- Concurrent treatment with erythropoietin unless on a stable dose prior to enrollment for ≥ 3 months.

Status:

Active

Participating sites:

Leiden University Medical Center

Contact for more information:

Dr. Liesbeth Oosten, l.e.m.oosten@lumc.nl

Summary (optional):

Warm autoimmune hemolytic anemia (wAIHA) is a disease defined by the aberrant production of autoantibodies directed against red blood cells. The primary antibody-producing cell of the body is the plasma cell, which has a life span of months to years and is hypothesized to be responsible for the persistence of autoantibody production in individuals with refractory wAIHA. Plasma cells express a high density of CD38, and the anti-CD38 monoclonal antibody isatuximab is expected to deplete these antibody-producing cells, which are not targeted by glucocorticoids, antiproliferatives, or B-cell depletion by anti-CD20 therapy. This study will assess isatuximab in participants with wAIHA who have failed to respond to prior therapy. The first part of this study will assess safety and determine the isatuximab dose for patients with wAIHA, and the second part of the study will assess efficacy. All participants will receive isatuximab subcutaneously. The screening period is up to 28 days, followed by a treatment period of 42 days (6 weeks) for Cohort 1 or 84 days (12 weeks) for the other participants in the trial. All participants will be followed for at least 24 weeks from the first isatuximab dose. The total length of the study, including screening, is 28 weeks.