Cadenza Study

A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of BIVV009 in Patients with Primary Cold Agglutinin Disease Without a Recent History of Blood Transfusion

Short title: Cadenza

Sponsor: Bioverativ USA

EudraCT nr. (if applicable):2017-003539-12

Required no. of patients (if applicable): 40

Type of study:

This is a randomized, double-blind, placebo-controlled, multicenter study in patients with primary cold agglutinin disease (CAgD) without a recent history of blood transfusion. Eligible patients will receive study drug (BIVV009 or placebo) and undergo safety and efficacy assessments for 6 months (26 weeks) during Part A.
Following completion of the initial 6-month treatment period (Part A), patients will roll into the open-label long-term safety and durability of response extension phase (Part B) during which they will receive BIVV009.
For the purpose of marketing authorization application, an interim analysis of safety and efficacy data will be performed after all patients have completed the double-blind treatment period (Part A). The Part B open-label extension study will run for approximately 1 year following last patient out (LPO) under Part A.

Study objectives:

The primary objective to determine whether BIVV009 administration results in a ≥ 1.5 g/dL increase in hemoglobin (Hgb) levels and avoidance of transfusion in patients with primary CAgD without a recent history of blood transfusion. The purpose of the open label Part B is to evaluate the long-term safety and tolerability of sutimlimab in participants with primary CAD.

Subject eligibility criteria:

Key Inclusion criteria:

All patients must meet all the following inclusion criteria to be enrolled:
1. Adult male and female patients ≥ 18 years of age at Screening
2. Body weight of ≥ 39 kg at Screening
3. Confirmed diagnosis of primary CAgD based on the following criteria: a. Chronic hemolysis,
b. Polyspecific direct antiglobulin test (DAT) positive,
c. Monospecific DAT strongly positive for C3d,
d. Cold agglutinin titer ≥ 64 at 4oC,
e. IgG DAT ≤ 1+, and
f. No overt malignant disease
4. Hemoglobin level ≤ 10.0 g/dL
5. Bilirubin level above the normal reference range

Key Exclusion criteria:

Patients who meet any of the following criteria will be excluded from the study:
1. Cold agglutinin syndrome secondary to infection, rheumatologic disease, or active hematologic malignancy
2. History of 1 or more blood transfusions within 6 months of enrollment.

4. Clinical diagnosis of systemic lupus erythematosus (SLE); or other autoimmune disorders with anti-nuclear antibodies at Screening
5. Positive hepatitis panel (including hepatitis B surface antigen and/or hepatitis C virus antibody) prior to or at Screening
6. Positive human immunodeficiency virus (HIV) antibody at Screening
7. Treatment with rituximab monotherapy within 3 months or rituximab combination therapies (eg, with bendamustine, fludarabine, ibrutinib, or cytotoxic drugs) within 6 months prior to enrollment
12. Concurrent treatment with other experimental drugs or participation in another clinical trial with any investigational drug within 30 days or 5 half-lives, whichever is greater, prior to treatment start

Participating sites:

Academisch Medisch Centrum, open
Leids Universitair Medisch Centrum, open

Contact for more information:

Academisch Medisch Centrum
Principal Investigator Dr. J.M.I. Vos, hemat.trial@amsterdamumc.nl

Leids Universitair Medisch Centrum
Principal Investigator Dr. L.E.M. Oosten, l.e.m.oosten@lumc.nl