BEconneCTD-ILD

BEconneCTD-ILD (BElimumab for conneCtive Tissue Disease ILD)

A study of the efficacy and safety of belimumab in adults with interstitial lung disease (ILD) associated with connective tissue disease (CTD)

This document provides an overview of the BEconneCTD-ILD Study and outlines key points to help guide your discussions with potential participants.

Background

- B cells have been reported to play a central role in the pathogenesis of ILD, and B-cell depletion has been shown to improve lung function in patients with CTD-ILD.[1,2]
- Belimumab is a monoclonal antibody that has been shown to inhibit the survival of B cells and reduce differentiation into IgG-producing plasma cells. It is believed that belimumab will lead to reduced inflammation and fibrosis across multiple organ systems.
- Based on its mechanism of action, proven efficacy in patients with lupus,* as well as its established safety profile, belimumab is expected to improve/stabilize lung function decline, slow ILD progression, and have a positive effect on symptoms such as dyspnea, cough, and fatigue.

*Benlysta™ (belimumab) is indicated for patients aged ≥5 with active systemic lupus erythematosus or active lupus nephritis who are receiving standard therapy.

Key inclusion criteria

- 18 years of age or older
- Documented diagnosis of rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), idiopathic inflammatory myopathy (IIM; including polymyositis, dermatomyositis, antisynthetase syndrome), Sjogren's syndrome (pSS), or mixed connective tissue disease (MCTD). NOTE: patients with overlap syndrome (including SSc overlap) are permitted if their primary diagnosis is RA, SLE, IIM, pSS, or MCTD.
- Diagnosis of ILD on high-resolution CT with disease extent of ≥10% of the whole lung, as confirmed by central reader at screening. NOTE: the 10% extent of ILD includes the combined assessment of reticulation/fibrosis and ground glass opacity.
- Evidence of ILD progression in the previous 24 months defined as at least one of the following criteria:
  - → ≥10% relative decline in FVC, OR
  - → ≥5 to <10% relative decline in FVC combined with worsening of respiratory symptoms, OR
  - → ≥5 to <10% relative decline in FVC combined with radiological evidence of ILD (combined assessment of reticulation/fibrosis and ground glass opacity) progression as assessed by the investigator comparing the screening scan and a previous scan done within 24 months prior to screening, OR
  - → Relative decline in DLCO (corrected for haemoglobin) ≥10% combined with radiological evidence of ILD (combined assessment of reticulation/fibrosis and ground glass opacity) progression as assessed by the investigator comparing the screening scan and a previous scan done within 24 months prior to screening.
- Must be currently receiving stable standard therapy to manage ILD and/or underlying CTD, or to have failed or failed to tolerate first-line standard therapy

Key exclusion criteria

- Diagnosis of ILD other than CTD-ILD
- Primary diagnosis of systemic sclerosis
- Dependence on continuous oxygen supplementation

Primary objective

The primary study objective is to demonstrate superiority of belimumab + standard therapy over a placebo + standard therapy in reducing the decline in lung volume at Week 52.

Study schedule overview

<table>
<tr><th>Screening Period (up to 6 weeks)</th><th>Study Treatment Period (52 weeks)</th><th colspan="2">Long-Term Extension Study</th></tr>
<tr><td rowspan="3">1 or more clinic visits to check eligibility</td><td rowspan="3">Belimumab or a placebo by SC injection once weekly</td><td colspan="2">Open-label belimumab for at least 52 weeks</td></tr>
<tr><td>OR</td><td>Safety Follow-up</td></tr>
<tr><td colspan="2">1 visit 8 weeks after final dose</td></tr>
</table>

Participants will be trained to self-inject the study drug at home. The first 2 injections (Day 1 and Day 8) will be done at the study site under the supervision of the study doctor/staff.

Participants will be provided with an electronic device (eDiary) to record injections, acknowledge receipt of the study drug, and to report pregnancy test results (if applicable). The eDiary will be reviewed at study visits.

Imaging will include high-resolution CT scans on Day 1 and Week 52. Lung-function tests (spirometry and gas transfer) will be performed at each visit (except Day 8).

Questionnaires will be completed at the start of each visit (except Day 8). Topics include general and mental health, disease severity, and symptoms.

Blood samples will be taken at each study visit to monitor the participant's health and for research purposes (pharmacokinetics, immunoglobulins, autoantibodies, serum biomarkers, and others).

Electrocardiograms will be performed about every 3 months.

Scan the code or visit [studywebsite.com].

[QR]

CT = computed tomography; DLCO = diffusion lung capacity for carbon monoxide; FVC = forced vital capacity; IgG = immunoglobulin; SC = subcutaneous; SSc = systemic sclerosis.

References:
1. Bagnato G, Harari S. *Eur Respir Rev.* 2015;24(135):102-114. doi:10.1183/09059180.00003214
2. Maher TM, Tudor VA, Saunders P, et al. *Lancet Respir Med.* 2023;11(1):45-54. doi:10.1016/S2213-2600(22)00359-9