Format: Abstract

Lancet. 2011 Feb 26;377(9767):721-31. doi: 10.1016/S0140-6736(10)61354-2. Epub 2011 Feb 4.

Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial.

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Abstract

BACKGROUND: Systemic lupus erythematosus is a heterogeneous autoimmune disease that is associated with B-cell hyperactivity, autoantibodies, and increased concentrations of B-lymphocyte stimulator (BLyS). The efficacy and safety of the fully human monoclonal antibody belimumab (BLyS-specific inhibitor) was assessed in patients with active systemic lupus erythematosus.

METHODS: Patients (aged ≥18 years) who were seropositive with scores of at least 6 on the Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) were enrolled in a multicentre phase 3 study, which was done in Latin America, Asia-Pacific, and eastern Europe. Patients were randomly assigned by use of a central interactive voice response system in a 1:1:1 ratio to belimumab 1 mg/kg or 10 mg/kg, or placebo by intravenous infusion in 1 h on days 0, 14, and 28, and then every 28 days until 48 weeks, with standard of care. Patients, investigators, study coordinators, and sponsors were masked to treatment assignment. Primary efficacy endpoint was improvement in the Systemic Lupus Erythematosus Responder Index (SRI) at week 52 (reduction ≥4 points in SELENA-SLEDAI score; no new British Isles Lupus Assessment Group [BILAG] A organ domain score and no more than 1 new B organ domain score; and no worsening [<0·3 increase] in Physician's Global Assessment [PGA] score) versus baseline. Method of analysis was by modified intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00424476.

FINDINGS: 867 patients were randomly assigned to belimumab 1 mg/kg (n=289) or 10 mg/kg (n=290), or placebo (n=288). 865 were treated and analysed in the belimumab (1 mg/kg, n=288; 10 mg/kg, n=290) and placebo groups (n=287). Significantly higher SRI rates were noted with belimumab 1 mg/kg (148 [51%], odds ratio 1·55 [95% CI 1·10-2·19]; p=0·0129) and 10 mg/kg (167 [58%], 1·83 [1·30-2·59]; p=0·0006) than with placebo (125 [44%]) at week 52. More patients had their SELENA-SLEDAI score reduced by at least 4 points during 52 weeks with belimumab 1 mg/kg (153 [53%], 1·51 [1·07-2·14]; p=0·0189) and 10 mg/kg (169 [58%], 1·71 [1·21-2·41]; p=0·0024) than with placebo (132 [46%]). More patients given belimumab 1 mg/kg (226 [78%], 1·38 [0·93-2·04];

p=0·1064) and 10 mg/kg (236 [81%], 1·62 [1·09-2·42]; p=0·0181) had no new BILAG A or no more than 1 new B flare than did those in the placebo group (210 [73%]). No worsening in PGA score was noted in more patients with belimumab 1 mg/kg (227 [79%], 1·68 [1·15-2·47]; p=0·0078) and 10 mg/kg (231 [80%], 1·74 [1·18-2·55]; p=0·0048) than with placebo (199 [69%]). Rates of adverse events were similar in the groups given belimumab 1 mg/kg and 10 mg/kg, and placebo: serious infection was reported in 22 (8%), 13 (4%), and 17 (6%) patients, respectively, and severe or serious hypersensitivity reactions on an infusion day were reported in two (<1%), two (<1%), and no patients, respectively. No malignant diseases were reported.

INTERPRETATION: Belimumab has the potential to be the first targeted biological treatment that is approved specifically for systemic lupus erythematosus, providing a new option for the management of this important prototypic autoimmune disease.

FUNDING: Human Genome Sciences and GlaxoSmithKline.

Comment in

BLISS! Lupus learns its lessons. [Lancet. 2011]
Belimumab for systemic lupus erythematosus. [Lancet. 2011]
Belimumab for systemic lupus erythematosus. [Lancet. 2011]
The first biological approved to treat systemic lupus erythematosus. [Immunotherapy. 2011]
A randomized controlled trial of belimumab for the treatment of active systemic lupus erythematosus. [Arch Dermatol. 2012]

PMID: 21296403 DOI: 10.1016/S0140-6736(10)61354-2

[Indexed for MEDLINE]

Publication types, MeSH terms, Substances, Secondary source ID

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