A Multi-center, Randomized Parallel Group, Placebo-Controlled Double-Blind Trial to Evaluate the Safety, Efficacy, and Pharmacokinetics of Belimumab, a Human Monoclonal Anti-BLyS Antibody, Plus Standard Therapy in Pediatric Patients with Systemic Lupus Erythematosus (SLE) (BEL114055)

Published: 02-07-2012
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Primary: safety and tolerability of belimumab in a pediatric population (5-17 y) with SLE.Secondary: PK, efficacy, quality of life.

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON44106

Source
ToetsingOnline

Brief title
BEL114055

Condition

- Autoimmune disorders

Synonym

systemic lupus erythematosus; SLE

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline BV
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: belimumab, children, safety, SLE

Outcome measures

Primary outcome

Safety and tolerability.

Secondary outcome

PK, efficacy (main: >=4 point reduction from baseline in SELENA SLEDAI score, No worsening (increase of < 0.30 points from baseline) in Physician*s Global Assessment, No new BILAG A organ domain score or 2 new BILAG B organ domain scores compared with baseline) and quality of life.

Study description

Background summary

Recent and past studies consistently show that adult and pediatric SLE patients have increased serum BLyS levels. In SLE, the elevation of BLyS may contribute to the persistence of B-cell subsets that produce pathogenic auto-antibodies or promote inflammation that would otherwise be subject to down regulation. Thus a therapeutic strategy that involves an antagonist to BLyS may have therapeutic benefit in SLE. Belimumab is a BLyS specific inhibitor and has been registered for the treatment of adults with active SLE.
In general, pediatric SLE patients have more severe disease and thus higher disease activity index on average than adults. Adult SLE subjects who presented with more active disease performed better with belimumab. It is theorized based on this, that belimumab will have a beneficial effect in the pediatric SLE

population.
The aim of the present study is to generate data on the effects of belimumab in children with active SLE.

Study objective

Primary: safety and tolerability of belimumab in a pediatric population (5-17 y) with SLE.
Secondary: PK, efficacy, quality of life.

Study design

Multi-center, Randomized Parallel Group, Placebo-Controlled Double-Blind Trial.
Part A: comparison between belimumab and placebo. Cohort 1 (12 subjects 12-17 y, belimumab:placebo=5:1) No further inclusion until PK is known. Thereafter cohort 2 starts (similar to cohort 1, but 5-11 y) as well as cohort 3 (subjects 12-17 y, randomization 1:1). When PK and safety of cohort 2 is known: inclusion of additional subjects 5-11 y in cohort 3.
Starting dose belimumab 10 mg/kg i.v. infusion (minimal duration 1 h), First 3 infusions every 2 weeks, thereafter every 4 weeks. Duration 48 weeks. Existing anti-SLE treatment will be continued.
Part B: long-term open-label follow-up study for those who have completed part A. All subjects treated with belimumab. Duration up to 10 y.
Part C: follow-up for those who did not complete part A. No study treatment. Duration up to 10 y.
Approx. 100 patients.
Interim-analyses, see protocol page 81.
IDMC, see protocol page 91.

Intervention

Treatment with belimumab or (in part A) placebo.

Study burden and risks

Risk: adverse events of study treatment.
Burden: Study visits part A-B: every 2 weeks (3x), thereafter every 4 weeks. Part C; every month (3x), yearly thereafter. Duration part A: approx. 1 year. Part B and C: up to 10 years.
Belimumab infusions (or placebo in part A) every 2 weeks (3x) and thereafter every 4 weeks. Duration at least 1 h.
Physical examination every 4 weeks.
Blood tests every 4 weeks, up to 10 ml/visit. 4x serial PK, 3 samples in 2-4 h.
Urine tests every visit.
ECG during screening.

Completion questionnaires (incl. suicidal thoughts).
Optional pharmacogenetic research (saliva).

Contacts

Public
GlaxoSmithKline BV

Huis ter Heideweg 62
Zeist 3705 LZ
NL
Scientific
GlaxoSmithKline BV

Huis ter Heideweg 62
Zeist 3705 LZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• 5 to 17 years of age
• Have or have had in series, 4 or more of the ACR 11 criteria for the classification of SLE.
• Active SLE disease defined as a SELENA SLEDAI score >= 6 at screening.
• Unequivocally positive autoantibody test results defined as an ANA titre >= 1:80 and/or a positive anti-dsDNA (>= 30 IU/mL) serum antibody test from 2 independent time points. See protocol page 29 for details.
• On a stable SLE treatment regimen. See protocol page 29 for details.

• Sexually active females: adequate method of contraception. See protocol page 30 for details.

Exclusion criteria

• Treatment with belimumab any time.
• Any B-cell targeted therapy, Abatacept or biologic investigational agent during the last year.
• 3 or more courses of systemic corticosteroids for concomitant conditions in the last year.
• Forbidden treatments within the last 30/60/90 days; see protocol pages 32-33for details.
• Active central nervous system lupus requiring therapeutic intervention within last 60 days.
• eGFR as calculated by Schwartz Formula <30 ml/min
• Subjects >= 12 years who have evidence of serious suicide risk. See protocol page 33 for details.
• Pregnancy or breastfeeding

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2012
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Benlysta
Generic name:	belimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-07-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-11-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-01-2014
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-09-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	06-01-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2011-000368-88-NL
CCMO	NL40462.078.12