A Multi-Center, Open-Label Trial to Evaluate the Pharmacokinetics, Safety, and Pharmacodynamics of Subcutaneously Administered Belimumab, a Human Monoclonal Anti-BLyS Antibody, Plus Standard Therapy in Pediatric Participants with Systemic Lupus Erythematosus (SLE)

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

Summary

ID

NL-OMON52524

Source
ToetsingOnline

Brief title
Open label study of Sc Belimumab in Pediatric Participants with SLE

Condition

- Autoimmune disorders

Synonym
SLE, systemic lupus erythematosus

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Belimumab, Children, Safety, SLE

Outcome measures

Primary outcome

• Observed belimumab concentrations at Week 12.

• Steady-state PK parameters: Cavg (AUC), Cmax, Cmin (based on population PK estimates).

Secondary outcome

• Incidence of adverse events, serious adverse events and adverse events of special interest through Week 52.

• Change from baseline in biomarkers (C3/C4, anti-dsDNA, B cell subsets, and immunoglobulins) at Weeks 12 and 52.

• Percent of subjects with a >= 4 point reduction from baseline in SELENA SLEDAI at Weeks 12 and 52.

Study description

Background summary

The purpose of this study is to evaluate the pharmacokinetics (PK), safety, and

pharmacodynamics (PD) of repeat doses of 200 mg belimumab administered subcutaneously (SC) in pediatric participants 5 to 17 years of age with systemic lupus erythematosus (SLE) on a background of standard of care therapy. This bridging PK study is part of an extrapolation strategy to support the use of SC belimumab in pediatric SLE patients, based on the completed adult SLE study with SC belimumab and the pediatric SLE study with IV belimumab, and is a component of a post-approval commitment to EMA (EMA-000520-PIP02-13-M01) and FDA (postmarketing requirement 3239-1 under BLA 761043)

Study objective

The primary objective is to characterize the PK profile of belimumab 200 mg SC in pediatric SLE participants.
The secondary objectives are to evaluate the safety and tolerability of belimumab 200 mg SC in pediatric SLE participants and to characterize the pharmacodynamic profile of SC belimumab 200 mg SC in pediatric SLE participants. Another objective is to characterize the impact on disease activity of belimumab 200 mg SC in pediatric SLE participants.

Study design

This is a single arm, multi-center open-label study to evaluate the PK, safety, and PD of SC belimumab plus background standard therapy in approximately 24 pediatric participants ages 5 to 17 years of age and weighing at least 5 kg with active SLE. The study will include:
• Part A: Open-label, 12-week treatment phase.
• Part B: Optional 40-week open-label continuation phase for any participant who completes Part A.
• Post-treatment follow-up assessments at 8 and 16 weeks after the last dose of SC belimumab.
• Optional Access Extension Phase: Optional post-Week 52 extension phase exclusively for eligible participants who complete Part B (e.g., participants from countries where the IV formulation is not approved for pediatric use; or participants in whom IV Benlysta is not suitable due to medical reasons or significant logistical challenges).

Intervention

The total maximum duration of study participation for each participant is 73 weeks (screening:5 weeks, treatment: up to 52 weeks [12 weeks Part A plus 40 weeks extension phase] and follow-up: 16 weeks).
Cohort 1 will include participants >50 kg body weight, Cohort 2 will include participants <30 to <50 kg body weight and Cohort 3 will include participants <30 kg body weight at baseline. In Part A Cohort 1 will receive weekly doses of belimumab 200 mg SC, Cohort 2 will receive belimumab 200 mg SC every 10 days and Cohort 3 will receive belimumab 200 mg SC every 2 weeks.

In Part B, the dosing frequency may change according to pre-defined criteria based on changes in body weight of the participant.
The optional access extension phase is to provide a mechanism for continued access to belimumab SC from Week 52 onwards. The duration of this optional access extension phase will depend on age of the participants and the conditions for eligibility. During the access extension phase, the dosing frequency may change based on changes in body weight of the participant. Participants who are
enrolled into the optional access extension phase will be withdrawn from treatment if they reach the age of 18 years, if Belimumab SC or IV becomes licensed and commercially available for pediatric use in the Netherlands.

Study burden and risks

The study is using belimumab SC in the pediatric population, thereby allowing patients the potential to administer their medication at home, and decreasing the burden of visits to an infusion center.
Risk: Adverse events of the study medication.Overall, the positive benefit/risk profile of IV belimumab in the BEL114055 pediatric SLE population appears consistent with that of adult IV and SC study populations.
Burden:
Screening period: one (cohort 1&2) or two (cohort 3) visits to the clinic including • blood (27 ml) and urine collection, • pregnancy test (if appropriate), • lupus disease activity assessment, • general health status evaluation incl. physical examination and ECG, • training in use auto-injector.
Part A 12 weeks treatment: 6 visits to the clinic over a 12-week period including • blood (all visits, often 7 or 20 ml per visit and at day 1 21 ml) and urine (most visits) collection for safety testing, measuring the quantity of belimumab in the blood and/or evaluation of the effects of belimumab, • pregnancy test (all visits, if appropriate), general health status evaluation incl. physical examination (all visits), • lupus disease activity assessment (once at the beginning and once at the end). Depending on weight: weekly, every 10 days or bi-weekly injections (1 ml using auto-injector) and completion of injection diary.
Part B optional 40 weeks treatment: 7 visits to the clinic over a 40-week period including • blood (all visits, often 7 or 20 ml per visit) and urine (most visits) collection for safety testing, measuring the quantity of belimumab in the blood and/or evaluation of the effects of belimumab, • pregnancy test (all visits, if appropriate), general health status evaluation incl. physical examination (all visits), • lupus disease activity assessment (once at the end). Depending on weight: weekly, every 10 days or bi-weekly injections and completion of injection diary.
8 weeks post treatment visit to the clinic: • blood (20 ml) and urine collection, • pregnancy test (if appropriate), • general health status evaluation incl. physical examination
16 weeks post treatment phone call from the clinic: • pregnancy test (if appropriate), • general health status evaluation

In the optional extension phase, after the week 52 visit, participants will return to the clinic every 12 weeks for weight measurement, pregnancy test (if applicable), and finally general health status evaluation. At the 8- and 16-week follow-up visits, SAEs and the results of home urine pregnancy test will be collected by phone (if applicable). The 8-week and 16-week follow-up may be performed at a clinic visit, per local requirement.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

For parts A and B of the study
1. Participants between 5 and 17 years of age inclusive, at the time of Day 1.
2. SLE according to the ACR criteria (at least 4/11 criteria). (Appendix 9 of

the protocol)
3. Screening SLEDAI-2K score >=6 (total score). (Appendix 10 of the protocol.)
4. Have unequivocally documented positive autoantibody test results. See protocol page 48 for details.
5. Stable SLE treatment regimen consisting of any of the following medications (alone or in combination) for a period of at least 30 days prior to Day 1: corticosteroids, immunosuppressants, anti-malarials, NSAIDs. See protocol page 48-49 for details.
6. Body weight >=15 kg.
7. Male and/or female participants. Female participant of childbearing potential who agrees to follow the contraceptive guidance in appendix 4 of the protocol during the treatment period and for at least 16 weeks after the last dose of belimumab.
8. Participant signs and dates a written age appropriate assent form/ informed consent form and the parent(s) or legal guardian provides written informed consent for minors between 5 and 16 year old.

Optional Access Extension
1. Male or female participants who complete Week 52 visit of the 200908 study.
2. Age <18 years at completion of Week 52.
3. Documented evidence of clinical benefit in 200908 study per investigator*s judgement.
4. Able to comply with clinic visits and required assessments.
5. Intravenous (IV) Benlysta not currently licensed for the pediatric use in the participant*s country; OR documented evidence of the rationale for IV Benlysta not being suitable for this participant requiring continued treatment with belimumab SC.
6. Participant eligibility agreed with the Medical Monitor prior to enrolling the participant into the optional access extension phase.
7. Participant signs and dates a written age appropriate assent form specific for the access extension phase and the parent or legal guardian (or emancipated minor), provides written informed consent specific to the access extension.

Exclusion criteria

For parts A + B of the study
1. eGFR of less than 30 mL/min
2. Acute severe nephritis defined as significant renal disease. See protocol page 50 for details.
3. History of a major organ transplant or hematopoetic stem cell/marrow transplant.
4. Clinical evidence of significant, unstable or uncontrolled, acute or chronic diseases not due to SLE. See protocol page 50 for details.
5. Planned surgical procedure or a history of any other medical disease , laboratory abnormality, or condition that, in the opinion of the investigator,

makes the participant unsuitable for the study.
6. History of malignant neoplasm within the last 5 years.
7. Evidence of serious suicide risk including any history of suicidal behavior in the last 6 months, or who in the investigator*s opinion, pose a significant suicide risk.
8. History of a primary immunodeficiency.
9. IgA deficiency (IgA level <10 mg/dL).
10. Acute or chronic infections requiring management, See protocol page 44 for details.
11. Grade 3 or greater laboratory abnormality (Page 51 and Appendix 2, Section 10.2.1 of the protocol).
12. History of an anaphylactic reaction to parenteral administration of contrast agents, human or murine proteins or monoclonal antibodies,or to any of the excipients of the study drug
13. Ever received treatment with belimumab (BENLYSTA).
14. Received any of the following within 364 days of Day 1: - Treatment with any B-cell targeted therapy, - Abatacept, - Any biologic investigational agent. See protocol page 51/60 for details.
15. 3 or more courses of systemic corticosteroids for concomitant conditions within 90 days of Day 1
16. Received any of the following within 90 days of Day 1: - Anti-TNF therapy, - Interleukin-1 receptor antagonist, - IV immunoglobulin, - Plasmapheresis.
17. Received any of the following within 30 days of Day 1: - IV cyclophosphamide, - A non-biologic investigational agent, - Any new immunosuppressive/immunomodulatory agent, - High dose prednisone or equivalent (>1.5 mg/kg/day) or any i.m.or i.v. steroid injection.
18. Have received a live or live-attenuated vaccine within 30 days of Day 1.
19. Have active CNS lupus requiring therapeutic intervention within 60 days of Day 1.
20. Have required renal replacement therapy within 90 days of Day 1 or are currently on renal replacement therapy.
21. Participation in an interventional clinical study either concurrently or within 6 months of screening. Participation in an observational study may be permitted.
22/23/24. Positive HIV, hepatitis B or C test. See protocol p 45 for details
25. Have current drug or alcohol abuse or dependence, or a history of drug or alcohol abuse or dependence within 364 days prior to Day 1.
26. Are unable or unlikely, in the opinion of the investigator, to administer belimumab by SC injection and have no reliable source to administer the injection.
27. Children in Care. See protocol page 53 for details.
- Pregnancy/breastfeeding

Optional Access Extension
1. Female participant has positive urine pregnancy test at Week 52 visit.
2. Female participant wishes to become pregnant at or within 4 months of Week 52 visit.

3. Participant has experienced any change in his/her medical history that, per the investigator*s judgement, continued administration of belimumab therapy would be contraindicated.
4. Participant received a live vaccine within 30 days prior to Week 52

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-04-2021
Enrollment:	2
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	29-10-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	29-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-08-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2022
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-04-2022
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
EudraCT	EUCTR2018-004645-16-NL
CCMO	NL71295.078.19
Other	www.gsk-clinicalstudyregister.com; 200908

Study results

Date completed:	12-10-2022
Results posted:	21-06-2023

First publication
06-06-2023