\u201cA Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Belimumab plus Standard of Care versus Placebo plus Standard of Care in Adult Subjects with Active Lupus Nephritis\u201d (protocol HGS1006-C1121)

Published: 20-07-2015
Last updated: 19-04-2024

* To evaluate the efficacy of belimumab in combination with standard of care in adult subjects with lupus nephritis Class III, IV, or V using the 2003 ISN/RPS criteria. * To assess the safety and tolerability of belimumab plus standard of care...

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

Summary

ID

NL-OMON47929

Source
ToetsingOnline

Brief title
BLISS-LN

Condition

- Autoimmune disorders
- Renal disorders (excl nephropathies)

Synonym
lupus nephritis, Systemic lupus erythematosus (SLE) nephritis

Research involving
Human

Sponsors and support

Primary sponsor: Human Genome Sciences, Inc. (a wholly owned subsidiary of GSK PLC)
Source(s) of monetary or material Support: Sponsor: HGSI/GSK

Intervention

Keyword: belimumab, lupus nefritis, phase 3

Outcome measures

Primary outcome

- Number of participants with Primary Efficacy Renal Response (PERR) at Week

104

Secondary outcome

- Complete Renal Response (CRR) at Week 104 (see definition under Ordinal Renal

Response).

- PERR at Week 52.

- Time to Death or Renal-related Event defined as any of the following: i) end

stage renal disease (ESRD), ii) doubling of serum creatinine, iii) renal

worsening as evidenced by increased proteinuria and/or impaired renal function,

or iv) renal disease-related treatment failure

- Ordinal Renal Response (ORR; complete, partial or no reponse) at Week 104

defined as follows:

- Complete Renal Response (CRR): Estimated glomerular filtration rate (GFR) is

no more than 10% below the pre-flare value or within normal range AND Urinary

protein:creatinine ratio <0.5 AND no receipt of prohibited (rescue) therapy

resulting in treatment failure (see Section 5.5 and Section 5.6)

- Partial Renal Response (PRR): Estimated GFR no more than 10% below the

baseline value or within normal range AND * 50% decrease in the urine protein:

creatinine ratio with one of the following: a urine protein:creatinine ratio of

< 1.0, if the baseline ratio was * 3.0 OR a urine protein:creatinine ratio of <

3.0, if the baseline ratio was > 3.0 AND No receipt of prohibited (rescue)

therapy resulting in treatment failure (see Section 5.5 and Section 5.6).

- No Renal Response (NRR): Not meeting criteria for either CRR or PRR.

Study description

Background summary

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by autoantibody production and abnormal B lymphocyte function (Pisetsky, 2001). The etiology of SLE is unknown, although genetics, sex hormones, and environmental conditions are thought to play a role (Kotzin, 1996; Pisetsky, 1998; Sobel et al, 1999). This disease is more common in women (~90% of patients) than men (NWHIC, 2003) and more prevalent in African-Americans than Caucasians (OMHRC, 2001; NWHIC, 2003). In the United States (US) the reported prevalence is 100,000 to 500,000 patients with some estimates of 1 million as the incidence increased 2-3 fold between 1950 and 1979. In the European Union (EU), prevalence rates have been reported ranging from 25 to 39 cases per 100,000 persons (Jimenez et al, 2003). In community-based studies among Asians, the prevalence (per 100,000) of SLE ranged from 3.2 to 70.4 (Thumboo and Wee, 2006). The disease onset is generally between the ages of 20 and 40. Patients with SLE have about a 3-fold greater risk of mortality than the general population. Approximately 70% of SLE patients survive 20 years from time of diagnosis (Houssiau et al, 2004). SLE can lead to arthritis, kidney failure, heart and lung inflammation, central nervous system (CNS) changes, vasculitis, severe skin rash, and blood dyscrasias such as anemia, leukopenia, and thrombocytopenia. The manifestations of SLE vary from patient to patient and it may take many years to render the proper diagnosis. The American College of Rheumatology (ACR) criteria that define a diagnosis of this heterogeneous disease require 4 of 11 criteria that

include SLE-associated signs or symptoms, lab abnormalities, and the presence of specific anti-nuclear autoantibodies (Tan et al, 1982). Approximately 35% of all adult patients with SLE develop clinically significant lupus nephritis and despite improvements in both diagnosis and treatment over the last few decades it remains an indicator of poor prognosis (Gordon et al, 2009; Waldman and Appel, 2006). Manifestations of lupus nephritis include proteinuria, elevations in serum creatinine, and the presence of urinary sediment. Alongside these clinical manifestations, morphological changes can be observed in renal biopsy specimens. In 1975 the World Health Organization (WHO) proposed a classification system for renal biopsies in SLE which was continually revised by them up until 1995. In 2004 updated criteria jointly developed by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) were published (Weening et al, 2004). Within the 5 overall classes, Classes I and II reflect disease restricted to mesangial abnormalities. Classes III and IV represent either focal (< 50% glomeruli involved - Class III) or diffuse (\u2265 50% glomeruli involved - Class IV) segmental or global glomerulonephritis. Class V represents membranous disease with Class VI representing advanced sclerosis. Classes I and II are rarely accompanied by clinical manifestations and there is no activity in Class VI only damage, so therapy has traditionally focused on Classes III-V. Belimumab (BENLYSTA\u2122) administered intravenously (IV) is approved in the US, Canada, and EU for the treatment of adult patients with active autoantibody-positive SLE who are receiving standard therapy; patients with severe active lupus nephritis and severe active CNS lupus were excluded, as were patients receiving other biologics and IV cyclophosphamide (refer to specific country labeling for additional information regarding the approved indication). Approval of IV belimumab for SLE is being sought in other regions of the world.

Study objective

* To evaluate the efficacy of belimumab in combination with standard of care in adult subjects with lupus nephritis Class III, IV, or V using the 2003 ISN/RPS criteria. * To assess the safety and tolerability of belimumab plus standard of care versus placebo plus standard of care in adult subjects with lupus nephritis Class III, IV, or V using the 2003 ISN/RPS criteria.

Study design

This is a Phase 3, multi-center, multi-national, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of IV belimumab 10 mg/kg plus standard of care compared to placebo plus standard of care in adult subjects with active lupus nephritis. Subjects who meet the eligibility criteria during screening will be randomized to 1 of 2 treatment groups in a 1:1 ratio: 10 mg/kg belimumab plus standard of care or placebo plus standard of care. The randomization of all eligible subjects will be stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus CYC vs HDCS plus MMF)

and race (black race vs other). Subjects will be dosed with study agent on Days 0 (baseline), 14, 28, and then every 28 days thereafter through 100 weeks with a final evaluation for the double-blind treatment period at 104 weeks. At least 400 and up to approximately 464 lupus nephritis subjects will be randomized with a target of at least 200 and up to approximately 232 subjects in each treatment group (belimumab or placebo). All subjects will receive background therapy consisting of one of the following standard of care regimens: \u2022 High Dose Corticosteroids (HDCS) + Cyclophosphamide (CYC) for induction therapy followed by Azathioprine (AZA) for maintenance therapy OR \u2022 HDCS + Mycophenolate Mofetil (MMF) for induction followed by MMF for maintenance therapy The standard of care medications are described in Section 5.5.1. Renal response will be measured as complete, partial, or no response based on study defined criteria (see Section 8.5). Week 104 renal response will be defined by a response at Week 100 that is confirmed by a repeat measurement at Week 104. Likewise, complete renal response at Week 104 will be defined by a complete renal response at Week 100 that is confirmed by a repeat measurement at Week 104. All subjects who discontinue treatment with study agent during the double-blind period (for reasons other than withdrawal of consent) should return for all scheduled visits through Week 104. In the event that a subject withdraws consent from the study, an attempt should be made to obtain consent to collect follow-up safety data (at an exit visit approximately 4 weeks after the last dose of study agent as well as a follow-up visit approximately 8 weeks after the last dose of study agent) and to obtain survival status at Week 104. Any subject that withdraws consent for use and disclosure of research-related health information will be considered withdrawn from the study and will not be followed for mortality. Subjects who receive treatment with study agent through Week 100 and complete Week 104 assessments in the double-blind period may enter into a 6-month open-label extension. The Week 104 visit of the double-blind period will serve as the Day 0 visit for subjects entering the 6-month open-label extension. In the open-label extension, all subjects will receive 10 mg/kg belimumab every 28 days until Week 24, with a final evaluation at Week 28 (4 weeks after the last dose). The first dose on the open-label extension will be given at the Week 104 visit of the double-blind period following the completion of all Week 104 assessments. Subjects participating in the open-label extension will continue to be monitored for efficacy and safety as per the study calendar (see Table 6-3). Subjects who complete the 104-week double-blind period, but do not enter the open-label extension will be required to return for an additional follow up visit 8 weeks after the last dose of study agent. All subjects who enter the open-label extension period and withdraw early will return for an Exit visit approximately 4 weeks after their last dose of study agent as well as a follow-up visit approximately 8 weeks after the last dose of study agent. At the end of the 6-month open-label extension period, subjects who wish to continue treatment may do so by being prescribed commercially available belimumab. If belimumab is not commercially available in a subject\u2019s country of participation, the subject may continue to receive belimumab under a separate continuation protocol if permissible according to local regulations. A separate informed consent will

need to be provided for the continuation protocol. The 8 week follow-up visit is not required for subjects entering the continuation protocol.

Intervention

In treatment phase the subjects will receive either belimumab or placebo through IV at 28 of the 37 visits (inclusive 1 follow up visit). In the open label phase all subjects will receive belimumab through IV at 6 of the 8 visits (inclusive 1 follow up visit). More details can be found in Annex 3 of the patient information sheet.

Study burden and risks

Belimumab administered by IV infusion is indicated for reducing disease activity in adult patients with active autoantibody positive SLE who are receiving standard therapy. The benefit/risk profile of belimumab for SLE remains favorable. Identified risks include hypersensitivity/infusion reactions and infections. Potential risks (i.e., based on pharmacology but no association identified to date) include progressive multifocal leukoencephalopathy (PML), malignancies, immunogenicity, effects on immunizations (including interactions with live vaccine), and psychiatric events including depression and suicidality. The most common AEs reported in the primary safety population of adults with SLE were associated with hypersensitivity/infusion related reactions, non opportunistic infections, and symptoms consistent with SLE. The majority of reports of infusion-related and hypersensitivity reactions were non-serious and include symptoms such as nausea, vomiting, diarrhea, chills, fever, rash, urticaria, pruritus, headache, dizziness, and dyspnea. However, infusion and hypersensitivity reactions can be severe and fatal. Infections were commonly reported events with belimumab and are expected due to the mechanism of action of belimumab and the SLE patient population. In the post-marketing setting with IV belimumab, delayed onset of symptoms of acute hypersensitivity reactions as well as recurrence of clinically significant reactions after initial appropriate treatment has been observed. Subjects will remain at the clinic for 3 hours following the first 2 infusions for observation. Should symptoms of acute hypersensitivity occur, an extended period of monitoring may be appropriate, based on clinical judgment. Subjects should be made aware of the potential risk for severe or lifethreatening hypersensitivity reactions, the signs and symptoms of such reactions, the potential for delayed onset or recurrence of symptoms, and the importance of immediately seeking medical attention should they occur. Belimumab should be administered by a healthcare professional prepared to treat hypersensitivity reactions including anaphylaxis. An Independent Data Monitoring Committee (IDMC) reviews unblinded safety data for this Phase 3 study on an ongoing basis until the data are locked and analyzed through Week 104. At all times the sites and sponsor will remain blinded to treatment allocation. Events to be monitored during the safety review include, at a minimum, all serious adverse events

(including deaths, serious psychiatric events, and serious infections), Grade 3 and Grade 4 laboratory abnormalities, opportunistic infections (serious and nonserious), malignancies, and hypersensitivity/ anaphylactic reactions during the double-blind and open-label extension portions of the study. Investigators (and IRBs/IECs, as appropriate,) will be notified of the outcome of each IDMC meeting. Benefit Assessment The primary data supporting efficacy of belimumab were the Phase 3 trials (C1056 and C1057) in which 1,684 subjects including those patients with renal manifestations were treated for up to 52 weeks (C1057) or 76 weeks (C1056) (Belimumab IB, Section 5.3.1.2). Belimumab produced significant improvements in the SLE Responder Index as well as in individual component SELENA-SLEDAI score in both studies. Pooled analyses demonstrated steroid sparing, delay in median time to first flare, and decreased risk of severe flares over 52 weeks. In a post hoc analysis of the pooled data in subjects with renal involvement at baseline, there were favorable trends of greater reduction in proteinuria, hematuria, pyuria, and lower renal flare rate with belimumab. These preliminary findings in patients with renal involvement support that belimumab may provide potential benefit to these patients (Dooley et al, 2013). Clinical trial data for belimumab since approval continue to show efficacy in the treatment of SLE through decreased SLE flares and decreased disease activity across multiple organ systems (Belimumab IB, Section 5.3.1.3; Dooley et al, 2013). Overall Benefit:Risk Conclusion The safety profile of belimumab remains consistent with that known at approval and is consistent with expected events based on the mechanism of action and the disease under study. Appropriate risk mitigation measures are in place; rare and long-term risks will be further evaluated via the large safety study and registry, ongoing and future studies, and routine pharmacovigilance. Review of safety data is conducted on a continual basis in order to identify new safety signals which may arise from clinical trial and/or post-marketing reports. The benefit: risk profile of belimumab for SLE continues to be favorable. In addition, the preliminary evidence suggests that patients with lupus nephritis may potentially benefit from belimumab.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Males or females at least 18 years of age.2. Have a clinical diagnosis of systemic lupus erythematosus (SLE) according to the American College of Rheumatology (ACR) criteria (Appendix 1).3. Have active, biopsy-proven proliferative lupus nephritis Class III or IV [excluding Class III(C), IV-S(C), and IV-G(C)] either with or without the presence of Class V, or pure Class V membranous using the 2003 ISN/RPS criteria (Appendix 2); the biopsy must be performed in the 6 months prior to the screening visit or during the screening period. The local biopsy report will be used to confirm subject eligibility. A tissue sample from the renal biopsy used to qualify the subject for randomization needs to be sent to a central reading center after Day 0 (baseline).4. Have unequivocally positive anti-nuclear antibody (ANA) test results defined as an ANA titer \u2265 1:80 (based on Hep-2 immunofluorescence assay or equivalence by enzyme immunoassay assay), and/or a positive anti-dsDNA (\u2265 30 IU/mL based on ELISA assay) serum antibody test at the screening visit based on the study\u2019s central laboratory results.5. Have documentation of active renal disease at screening requiring induction therapy with high dose corticosteroids (HDCS) with either intravenous (IV) cyclophosphamide (CYC) or mycophenolate mofetil (MMF) or other oral forms of mycophenolate. The following factors will be used to define active renal disease at screening: \u2022 Urinary protein:creatinine ratio of \u2265 1.0 AND \uf02d Active urinary sediment as defined by at least 1 of the following (in absence of menses and genitourinary tract infection). \uf02d - > 5 red blood cell (RBC)/high power field (hpf) or above the laboratory reference range. \uf02d - > 5 white blood cell (WBC)/hpf or above the laboratory reference range. \uf02d - Presence of cellular casts (RBC or WBC). \uf02d - Subjects

without active urinary sediment are eligible if they meet at least 1 of the following criteria:\uf02d *Have a confirmatory biopsy performed within 3 months prior to the screening visit or during the screening period meeting the criteria outlined in Inclusion Criterion 3. \uf02d *Have proteinuria \u2265 3.5 grams/day (or urinary protein:creatinine ratio\u2265 3.5).6. Have active renal disease defined as above which requires induction therapy with high dose corticosteroids (HDCS) with either intravenous (IV) cyclophosphamide (CYC) or mycophenolate mofetil (MMF) or other oral forms of mycophenolate:Induction therapy may begin before Screening but should be initiated within 60 days prior to or on Day 0 (baseline). Initiation of induction is when both HDCS and either MMF or CYC have been started.The study recommended doses for induction therapy are as follows, adjustments may be made for tolerability issues (refer to Section 5.5.1 Standard of Care Medication for details):- MMF 1-3g/day orally or Mycophenolate sodium 720 - 2160 mg/day orally - corticosteroids: 0-3 IV pulses of methylprednisolone 500 -1000 mg/pulse followed by oral prednisone 0.5-1.0 mg/kg/day with total daily dose up to 60 mg/day (or equivalence)- CYC 500 mg by IV infusion every 2 weeks (\uf0b1 3 days) for 6 infusionsSubjects who have been on MMF for SLE including lupus renal disease may be eligible if they have received, or will receive, the following induction therapy within 60 days prior to or on Day 0:- initiation of HDCS with MMF dose increase to reach the target dose for induction in the subject (if the subject did not previously fail MMF induction based on the investigator\u2019s opinion), OR- initiation of HDCS with discontinuation of MMF and initiation of CYC.Note: It is recommended that subject eligibility should be discussed with the Medical Monitor if a subject initiated but did not complete an induction therapy within 6 months prior to the initiation of current induction therapy for the study.7. A female subject is eligible to enter the study if she is: \u2022 Not pregnant or nursing; \u2022 Of non-childbearing potential (ie, women who had a hysterectomy, are postmenopausal which is defined as 1 year without menses, have both ovaries surgically removed, or have current documented tubal ligation or any other permanent female sterilization procedure); or \u2022 Of childbearing potential (ie, women with functional ovaries and no documented impairment of oviductal or uterine function that would cause sterility). This category includes women with oligomenorrhoea [even severe], women who are perimenopausal, or have just begun to menstruate. These women must have a negative serum pregnancy test at screening, and agree to 1 of the following:\uf02d *Complete abstinence from intercourse from 2 weeks prior to administration of the 1st dose of study agent until 16 weeks after the last dose of study agent; or \uf02d *Consistent and correct use of 1 of the following acceptable methods of birth control for 1 month prior to the start of the study agent, during study, and for 16 weeks after the last dose of study agent:\u25e6 Implants of levonorgestrel or etonogestrel; \u25e6 Ethinyl estradiol/Etonogestrel vaginal ring; \u25e6 Injectable progesterone; \u25e6 Any intrauterine device (IUD) with a documented failure rate of less than 1% per year; \u25e6 Oral contraceptives (either combined or progesterone only); \u25e6 Double barrier method: condom and occlusive cap (diaphragm or cervical/vault caps) with spermidical foam/gel/film/cream/suppository; \u25e6 Transdermal contraceptive patch; \u25e6

Male partner sterilisation with documentation of azoospermia prior to the female subject\u2019s entry into the study, and this male is the sole partner for that subject. The documentation on male sterility can come from the site personnel\u2019s review of subject\u2019s medical records, medical examination and/or semen analysis, or medical history interview provided by her or her partner.Note: If stricter female or male contraception requirements are specified in the country-specific label for induction and/or maintenance standard of care medications, they must be followed.8. Have the ability to understand the requirements of the study, provide written informed consent (including consent for the use and disclosure of research-related health information), and comply with the study protocol procedures (including required study visits).

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Exclusion criteria

1. Subjects who have previously failed both CYC and MMF (or other forms of mycophenolate) induction therapies based on the investigator\u2019s opinion. If a subject has failed only 1 of the 2 therapies for induction, they may be eligible for study inclusion if the other induction therapy is initiated within 60 days prior to or on Day 0 (ie, a subject who failed MMF is eligible if newly initiating induction therapy with CYC or a subject who failed CYC is eligible if newly initiating induction therapy with MMF).2. Subjects who received an induction therapy with CYC within 3 months prior to the planned initiation of the current induction for the study.3. Subjects who receive CYC whose pre-induction leukocyte count is Grade 3 or 4 based on the Adverse Event Severity Grading Tables (Appendix 7).4. Known hypersensitivity or contraindication to any drug products or any component of these drug products

they plan to receive (eg, CYC, MMF, azathioprine (AZA), corticosteroids).5. Have a history of an anaphylactic reaction to parenteral administration of contrast agents, human or murine proteins or monoclonal antibodies.6. Have received treatment with belimumab within 364 days of baseline (Day 0).7. Received any of the following within 364 days of baseline (Day 0): Nitrogen mustard Chlorambucil Vincristine Procarbazine Etoposide Abatacept Treatment with any B cell targeted therapy (eg, rituximab, other anti-CD20 agents, anti-CD22 [epratuzumab], anti-CD52 [alemtuzumab], BLyS-receptor fusion protein [BR3], TACI-Fc, or LY2127399 [anti-BAFF]) A biologic investigational agent (eg, abetimus sodium, anti-CD40L antibody [BG9588/ IDEC-131]). Investigational agent applies to any drug not approved for sale in the country in which it is being used. Treatment with interleukin-6 targeted therapy (e.g., tocilizumab, sirukumab).8. Received any of the following within 90 days of baseline (Day 0): Anti-TNF therapy (eg, adalimumab, etanercept, infliximab, certolizumab, golimumab pegol) Interleukin-1 receptor antagonist (anakinra). Intravenous immunoglobulin (IVIG). Plasmapheresis.9. Received a non-biological investigational agent within 60 days of baseline (Day 0).10. Received a live vaccine within 30 days of baseline (Day 0).11. Have severe active central nervous system (CNS) lupus (including seizures, psychosis, organic brain syndrome, cerebrovascular accident [CVA], cerebritis, or CNS vasculitis) requiring therapeutic intervention within 60 days of baseline (Day 0). 12. Have a history of a major organ transplant (eg, heart, lung, kidney, liver) or hematopoietic stem cell/marrow transplant or are due to receive transplantation.13. Subjects who have been on dialysis within 364 days of baseline (Day 0).14. An estimated glomerular filtration rate < 30 mL/min/1.73m\262 at the screening visit (using the simplified Modification of Diet in Renal Disease [MDRD] equation).15. Have clinical evidence of significant unstable or uncontrolled acute or chronic diseases not due to SLE (ie, cardiovascular, pulmonary, hematologic, gastrointestinal, hepatic, renal, neurological, malignancy, or infectious diseases) which, in the opinion of the principal investigator, could confound the results of the study or put the subject at undue risk.16. Have a planned surgical procedure or a history of any other medical disease (eg, cardiopulmonary), laboratory abnormality, or condition (eg, poor venous access) that, in the opinion of the principal investigator, makes the subject unsuitable for the study.17. Have a history of malignant neoplasm within the last 5 years, except for adequately treated cancers of the skin (basal or squamous cell) or carcinoma in situ of the uterine cervix.18. Have acute or chronic infection requiring management, as follows: \uf02d Currently on any suppressive therapy for a chronic infection (such as tuberculosis, pneumocystis, cytomegalovirus, herpes simplex virus, herpes zoster, or atypical mycobacteria). \uf02d Hospitalization for treatment of infection within 60 days of baseline (Day 0). \uf02d Have had infection requiring treatment with parenteral (IV or IM) antibiotics (antibacterials, antivirals, anti-fungals, or anti-parasitic agents) within 60 days of baseline (Day 0).19. Have current drug or alcohol abuse or dependence, or a history of drug or alcohol abuse or dependence within 364 days prior to baseline (Day 0).20. Have a historically positive test or test positive at screening for HIV

antibody.21. Hepatitis B: Serologic evidence of Hepatitis B (HB) infection based on the results of testing for HBsAg, anti-HBc and anti-HBs as follows: \uf02d Patients positive for HBsAg are excluded. \uf02d Patients negative for HBsAg but positive for Anti-HBc, regardless of Anti-HBs antibody status, will require clarification of their status by testing for HBV DNAo if HBV DNA positive, patients will be excluded from participation o if HBV DNA negative, patients will be eligible to enrol. NOTE: For those subjects randomised, additional ongoing assessment during the study is required (see Section 6.7.5).22. Hepatitis C: Positive test for Hepatitis C antibody confirmed on a subsequent blood sample by RNA-PCR assay. Subjects who are positive for Hepatitis C antibody and negative when the Hepatitis C RNA-PCR assay is performed on a subsequent sample will be eligible to participate. Subjects who are positive for Hepatitis C antibody and have a positive result for the HCV when the Hepatitis C RNA-PCR assay is performed on the subsequent sample will not be eligible to participate. Subjects in China with positive test for Hepatitis C antibody will be excluded without confirmatory Hepatitis C RNA-PCR testing.23. Have an IgA deficiency (IgA level < 10 mg/dL).24. Have a Grade 3 or greater laboratory abnormality (including serum IgG level) based on the Adverse Event Severity Grading Tables (Appendix 7) except for the following that are allowed: \uf02d Urinalysis (eg, proteinuria) \uf02d Hematuria \uf02d Pyuria \uf02d Casts \uf02d Hypoalbuminemia due to lupus nephritis \uf02d Stable Grade 3 prothrombin time (PT) secondary to warfarin treatment. \uf02d Stable Grade 3 partial thromboplastin time (PTT) due to lupus anticoagulant and not related to liver disease or anti-coagulant therapy. \uf02d Stable Grade 3 gamma glutamyl transferase (GGT) elevation due to lupus hepatitis, and not related to alcoholic liver disease, uncontrolled diabetes or viral hepatitis. If present, any abnormalities in the ALT and/or AST must be \u2264 Grade 2. \uf02d Stable Grade 3 reduction in hemoglobin levels due to SLE \uf02d Stable Grade 3 neutropenia or stable Grade 3 white blood cell count [with the exception of subjects receiving CYC who will be excluded if WBC is Grade 3 or 4 per Exclusion Criterion 3]. Note that WBC count should be obtained immediately prior to starting induction therapy. If immediate pre-induction WBC is not available, a WBC count obtained within 28 days prior to induction may be used. \uf02d Hyperuricemia or blood urea nitrogen (BUN) elevation due to lupus nephritis or SLE.25. Subjects who have evidence of serious suicide risk including any history of suicidal behavior in the last 6 months and/or any suicidal ideation of type 4 or 5 on the Columbia- Suicide Severity Rating Scale (C-SSRS) (Appendix 8) in the last 2 months or who, in the investigator\'s opinion, pose a significant suicide risk.].Klasse_10;
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Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-02-2016
Enrollment:	12
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:	20-07-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	23-09-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	24-09-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-04-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-05-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-06-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-03-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2011\u20100045-NL
ClinicalTrials.gov	NCT01639339
CCMO	NL53821.056.15