Clinical Study Report

Study title:	Efficacy of BELImumab for therapy-resistant SKIN manifestations in patients with lupus erythematosus (LE): A phase III, multicenter, randomized, double-blind, placebo-controlled trial
Shorttitle:	BELI-SKIN
Sponsor´s Protocol Code	DER-201701
EudraCT No.:	2017-003051-35
Sponsor:	Rheinische Friedrich-Wilhelm-University of Bonn, represented by the Faculty of Medicine of the University of Bonn, represented by the Dean of the Medical Faculty, Venusberg- Campus 1, D-53127 Bonn, Germany
Investigational product	Trade Name: Benlysta® Substance: Belimumab Manufacturer: GlaxoSmithKline (GSK) Dose: 200 mg weekly Mode of application: subcutaneous injection Duration of treatment: 24 weeks Open-label extension: optional 24 weeks treatment with belimumab
Indication:	Lupus erythematosus (LE)
Brief description (design, comparison, duration, dose and population):	prospective, phase III, multicenter, randomized, double-blind, placebo-controlled for the first 24 weeks followed by an optional open-label extension for 24 weeks
Phase of study:	III
Study initiation date (FPI):	04.02.2019
Study completion/early termination date (LPO):	LPFV: 31.10.2022; LPO: 17.01.2024
Date of Report	09.04.2025
Version of Report:	1

Prof. Dr. med. Jörg Wenzel

(Principal/coordinating investigator/ Sponsor delegated person)

Department of Dermatology and Allergology
University Hospital Bonn
Venusberg- Campus 1, 53127 Bonn

Tel: +49 - 228 287 15370
Fax: +49 – 228 287 14333
Email: joerg.wenzel@ukbonn.de

Signatures Clinical Study Report

By their signature, the authors confirm that they agree to the content of this Clinical Study Report. The clinical trial reported on has been conducted in compliance with the Declaration of Helsinki, the ICH-GCP guidelines, and the national laws and regulations.

Sponsor/Sponsor Delegated Person (SDP):

Prof. Dr. Jörg Wenzel
(SDP)

11 Apr. 2025
Date

Signature

Principal Investigator

Prof. Dr. Jörg Wenzel
(LKP)

11 Apr. 2025
Date

Signature

Responsible Biometrician:

Dr. Robert Németh
(Statistician)

09-Apr-2025
Date

Signature

Synopsis

<table>
<tr><td>Sponsor:</td><td>Rheinische Friedrich-Wilhelm-University of Bonn,
represented by the Faculty of Medicine of the University of Bonn,
represented by the Dean of the Medical Faculty,
Venusberg- Campus 1, D-53127 Bonn, Germany</td></tr>
<tr><td>Investigational product (IMP):</td><td>Trade Name: Benlysta®
Substance: Belimumab
Manufacturer: GlaxoSmithKline (GSK)</td></tr>
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Route of administration: subcutaneous injection
Batch numbers:
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Open-label extension: optional 24 weeks treatment with belimumab</td></tr>
<tr><td>Reference therapy:</td><td>Matching Placebo</td></tr>
<tr><td>Reference therapy (dose, route of administration, batch number):</td><td>Dose: 200 mg weekly
Route of administration: subcutaneous injection
Duration of Treatment: 24 weeks</td></tr>
</table>

Study title:	Efficacy of BELImumab for therapy-resistant SKIN manifestations in patients with lupus erythematosus (LE): A phase III, multicenter, randomized, double-blind, placebo-controlled, 24-week trial
Trial history:	

Protocol-Version	Modifikation
V1 to V2	Update Protocol and Synopsis: Synopsis, section 7.5: Trial time schedule was adjusted Sections 2.2, 2.3, 2.5 and 10.1.4: To provide a better overview visit names SC01-05 were added Section 5.4.1: Updated due to new IB Version (v14) per authority request Section 8.6: More information regarding randomization were added per authority request Sections 13.3.3 and 13.3.5: More information regarding the Type I error were added per authority request
V2 to V3	Update Protocol and Synopsis: Synopsis, section 8.3 and 9.15.6: Exclusion criteria were adapted and added as well as excluded concomitant medications were specified per ethics request. Synopsis and section 8.3: Indication specific exclusion criteria: thresholds for liver parameters were added Synopsis and section 7.5: Time Schedule was updated Section 13.3.6: CSSRS was added Section 10.3.10 and Appendix 3: Process of image transferring was changed
V3 to V4	Update Protocol and Synopsis: Sections 2.1, 2.2, 2.3, 2.5 and 10.1.5: A safety Follow up visit was added Synopsis, section 6.4 and 13.3.2: Secondary Endpoints were added Synopsis and section 7.5: Trial time schedule was adjusted Synopsis, section 8.2 and 8.3: Inclusion criteria and Exclusion criteria were adapted for more clarification Synopsis and 8.3.1: Special precautions for Intravenous Cyclophosphamide as concomitant medication were separated Section 9.15.3: Section was updated for more clarification Section 10.3.1: Information for SLab and ALab was updated Section 10.3.5: Section was updated Section 10.3.9: Description of SELENA-SLEDAI was updated for more clarification Section 12.4: The documentation and reporting period of AEs was corrected Section 12.5 and 16.2.2: Notification process for safety information was adjusted

	V3 to V4	Section 16.2.2: PML and Occurrence of suicidal behavior were added as reasons for trial termination by Investigator Section 18.12.2: Wording for reimbursement of subjects was clarified Appendix 1: Detailed information for subcutaneous self-dosing instructions replaced to accompanying scientific program Appendix 2 and 3: Removed because more skin biopsy and photo documentation procedure in separate manual. Whole protocol: change from IV to SC injection was corrected Update ICF
	V4 to V5	Update Protocol and Synopsis: Synopsis and section 8.2: For clarification, former inclusion criteria 5 (removed in amendment 3) was reinserted as a crossed-out text and marked as 'no longer applicable after amendment 3' Sections 2.1 and 2.2: new row was added to clarify the 24h urine collection procedure Section 2.1: Instruction for separate PIC for open label phase was added Section 5.4.1: Information on suicidality was updated due to a DIL from GSK (26.02.2019) and moved from section 10.3 to section 5.4.1 to improve consistency Synopsis and sections 8.3 and 9.15.6: "intravenous cyclophosphamide" was added as excluded concomitant medication, "Special precautions for Intra-venous Cyclophosphamide as concomitant medication" was removed Synopsis and sections 8.2 and 8.3 and 9.15.3 and 9.15.6: "oral cyclophosphamide" was removed from the list of permitted standard medication and added to the list of excluded concomitant medication Synopsis and sections 8.3 and 9.15.3: Details on the use of topical therapies were added for clarification Synopsis and sections 8.2 and 9.15.3: dispone was added to the list of permitted concomitant medication Synopsis and section 8.3: Exclusion criterion nr. 18 was specified Section 10.3.1: Instruction for enhanced IgG-monitoring in case of IV cyclophosphamide was removed due to exclusion of IV Cyclophosphamide as concomitant medication Synopsis and section 8.3: "Patients with neutrophils <1.5X109/L" was added as exclusion criterion Section 10.3.1: CH 50 was removed from RLAB in order to conform with amendment 3; IgG-serum level was transferred from SLAB to RLAB due to new stopping criterion, Histone was removed from ALAB Section 10.3.3: Specification for rare cases was added Section 10.3.10: Details for photodocumentation were added

	V4 to V5	Section 12.1.2: “Fatal events” were added to the list of “Adverse events of special interest” due to DIL from GSK (26.02.2019) Section 16.2.2: New termination criteria were added: “Neutrophils <1X109/L”, “Life threatening infection”, “IgG < 400mg/dL if associated with serious infection”, “Treatment will be held and medical monitor contacted for IgG < 250 mg/dL” Section 9.8: Procedure for missed injection was detailed for clarification Section 9.9.1: Administration instructions: Requirement of 3hours of supervision was reduced from first two visits to first visit according to updated information from GSK for subcutaneous injections. Requirement for 3hours of supervision at first injection of open label phase was added for clarification. Section 10.3.5: 24hour urine: clarification Section 5.4.1: Updated due to new IB-version (IB-Nr. 15, may 2019) Section 5.4.2: Updated due to DIL from GSK (26.02.2019) Section 9.8: Updated for clarification
	V5 to V6	Update Protocol: Section 5.4: updated regading the changes of IB V16 Sections 10.1.2 and 10.1.4 minor corrections to comply with amendment 4 Protocol Approval Signature: New responsible biometrician Update-IB and ICF
	V6 to V7	Update Protocol: Sections 1 and 7.5: time schedule updated Section 9.8 procedure in case of dosage interruption updated for clarification
	V7 to V8	Trial Site deregistration and add new trial Site , Update Synopsis and Protocol 7.3: Number of trial sites Update-IB
Coordinating investigator:	Prof. Dr. med. Jörg Wenzel	
Trial site:	University Hospital Bonn AöR, Venusberg-Campus 1 (former: Sigmund-Freud-Str. 25), 53127 Bonn Email: joerg.wenzel@ukbonn.de University Hospital Münster Klinik für Dermatologie und Venerologie Von Esmarchstr. 58, 48149 Münster Email: jan.ehrchen@ukmuenster.de Charité - Universitätsmedizin Berlin Klinik für Dermatologie, Venerologie und Allergologie Luisenstr.2, 10117 Berlin Email: margitta.worm@charite.de	

	University Hospital Leipzig AöR Klinik für Dermatologie, Venerologie und Allergologie Philipp-Rosenthal-Straße 23, 04103 Leipzig Email: jan.simon@medizin.uni-leipzig.de University Hospital Erlangen Hautklinik Ulmenweg 18, 91054 Erlangen Email: michael.sticherling@uk-erlangen.de University Hospital Schleswig-Holstein, Campus Lübeck Klinik für Dermatologie, Allergologie und Venerologie Ratzeburger Allee 160, 23538 Lübeck Email: artem.vorobyev@uksh.de University Hospital Schleswig-Holstein, Campus Kiel Abteilung für Dermatologie, Allergologie und Venerologie Arnold-Heller-Straße 3, 24105 Kiel Email: sgerdes@dermatology.uni-kiel.de University Hospital Düsseldorf Klinik für Dermatologie Moorenstr. 5, 40225 Düsseldorf Email: Stephan.Meller@med.uni-duesseldorf.de Technical University Munich Klinik und Poliklinik für Dermatologie und Allergologie am Biederstein Biedersteinerstrasse 29, 80802 München Email: Felix.Lauffer@mri.tum.de
Indication studied:	Lupus erythematosus (LE)
Main criteria for inclusion:	Inclusion criteria: 1. At least 18 years of age 2. Patients with a clinically and histologically confirmed diagnosis of LE-specific skin lesions 3. Patients with active skin manifestations at time of enrolment 4. Patients who meet at least two of the American College of Rheumatology (ACR) criteria for SLE (≥ 2 criteria) (Patients with cutaneous forms of LE without systemic involvement who meet all inclusion criteria may be included) 5. Patients with positive ANA (titre ≥ 1:80, at least once within the last 3 years *(no longer applicable after amendment 3*) 6. Total RCLASI skin activity score of ≥ 6

	7. Patients receiving stable standard therapy for at least 30 days prior to day 0; corticosteroids may have been added as new medication or dose adjusted up to 30 days prior to day 0; new LE therapy, other than corticosteroids, were not added within 60 days prior to day 0; permitted medications for stable standard therapy alone or in combination included: o Systemic prednisone or its equivalent up to 40 mg/day and/or class I, II, or III topical corticoster-oids up to 2 times a day (lesional application only) o antimalarials including hydroxychloroquine, chloroquine or quinacrine o non-steroidal anti-inflammatory agents (NSAID) o immunosuppressive or immunomodulatory agents including methotrexate, azathioprine, dap-sone, leflunomide, mycophenolate (including mycophenolate mofetil, mycophenolate mofetil hy-drochloride, and mycophenolate sodium), calcineurin inhibitors (eg, tacrolimus, cyclosporine), si-rolimus, 6-mercaptopurine or thalidomide and/or topical calcineurin inhibitors (e.g., tacrolimus, pimecrolimus) up to 2 times a day (lesional application only) o Please note: Topical corticosteroids (class I, II, or III up to 2 times a day with lesional application only) or topical calcineurin inhibitors (such as tacrolimus or pimecrolimus, up to 2 times a day with lesional application only) as the only Standard of Care medication is exclusively permitted in lo-calized CLE disease (in accordance with the EADV s2k guideline4). For severe and widespread skin manifestations, a purely topical therapy is not sufficient as SOC. 8. Subjects with the ability to follow study instructions and likely to attend and complete all required visits 9. Written informed consent of the subject <u>General Exclusion criteria:</u> 1. Subjects not able to give consent 2. Subject without legal capacity who is unable to understand the nature, scope, significance and conse-quences of this clinical trial 3. Known history of hypersensitivity to B-lymphocyte-targeted drugs (including rituximab), the investiga-tional drug or to drugs with a similar chemical structure 4. Simultaneous participation in another investigational clinical trial or participation in any clinical trial involving administration of an

	investigational medicinal product/biological agent within 60 days prior to clinical trial beginning 5. Subjects with a physical or psychiatric condition which at the investigator's discretion may put the subject at risk, may confound the trial results, or may interfere with the subject's participation in this clinical trial 6. Known or persistent abuse of medication, drugs or alcohol within 365 days prior to day 0 <u>Exclusion criteria regarding special restrictions for females:</u> 7. Current or planned pregnancy or nursing women 8. Females of childbearing potential, who are not using and not willing to use medically reliable methods of contraception for the entire study duration (such as oral, injectable, or implantable contraceptives, or intrauterine contraceptive devices) unless they are surgically sterilized / hysterectomized or there are any other criteria considered sufficiently reliable by the investigator in individual cases. <u>Indication specific exclusion criteria:</u> 9. Patients with a history of malignant neoplasm within the last 5 years with the exception of basal cell or squamous cell carcinoma of the skin treated with local resection only or carcinoma in situ of the uterine cervix treated locally and with no evidence of metastatic disease for 3 years 10. Patients with evidence of serious suicide risk including any history of suicidal behavior in the last 6 months and/or any suicidal ideation ≥ 4 on the CSSRS ideation scale in the last 2 months or who in the investigator's judgment, pose a significant suicide risk 11. Patients who have required high-dose prednisone (>100 mg/day) or its equivalent within 90 days prior to day 0 12. Severe lupus kidney disease (proteinuria >6 g/24 hour or equivalent using spot urine protein to creat-inine ratio, or serum creatinine >2.5 mg/dL), active nephritis or have required hemodialysis or high-dose prednisone (>100 mg/day) within 90 days prior to day 0 13. Active central nervous system (CNS) lupus, including seizures, psychosis, organic brain syndrome, cerebrovascular accident, cerebritis or CNS vasculitis, that required therapeutic intervention within 60 days prior to day 0

	14. History of a major organ transplant (eg, heart, kidney, liver) or hematopoietic stem cell/marrow trans-plant 15. Previous treatment with intravenous Ig (IVIG) up to 3 months before enrolment 16. Previous treatment with belimumab or any investigational biologic agent within 1 year before enrolment or an investigational non biologic agent within 60 days prior to enrolment 17. Treatment with immunomodulating drugs for other reasons than LE within 60 days prior to day 0 18. Active inflammatory skin disease other than LE-specific or LE-non-specific manifestations 19. Patients previously hypersensitive to B-lymphocyte-targeted drug (including rituximab) or belimumab
Brief description (design, comparison, duration, dose and population):	Multicenter, national, prospective, double-blind, placebo-controlled, randomized, 2 arm parallelgroup, clinical trial. The efficacy assessment phase of the trial (24 weeks) is followed by an optional open-label extension for additional 168 days
Phase of study:	III
Study initiation date (FPI):	04.02.2019
Study completion/early termination date (LPO):	LPFV: 31.10.2022 LPO: 17.01.2024
Date of Report	09.04.2025
Version of Report:	1
Objectives:	<u>Primary Objective:</u> To evaluate the efficacy of belimumab for therapy-resistant LE-specific skin manifestations of LE patients in addition to Standard of Care (SOC) therapy <u>Secondary Objective:</u> To assess whether the administration of belimumab in active, therapy-resistant skin manifestations of LE-patients under Standard of Care (SOC) therapy is associated with reduced concurrent medication. To assess whether the administration of belimumab in active, therapy-resistant skin manifestations of LE-patients under Standard of Care (SOC) therapy is associated with a reduction of inflammatory parameters in skin lesions and serum.

Endpoint(s):	<u>Primary Endpoint:</u> Differences in relative change from baseline of the mean Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI) activity score after 24 weeks (V8) between placebo and active treatment arm <u>Secondary Endpoints:</u> • Change to baseline in the RCLASI activity score after 7, 28, 56, 84, 112, 140 and 168 days of treatment in both arms • Change to baseline in the RCLASI skin activity score after 7, 28, 56, 84,112,140 and 168 days of treatment in both arms • Change to baseline in the RCLASI alopecia activity score after 7, 28, 56, 84, 112, 140 and 168 days of treatment in both arms • Change to baseline in the RCLASI mucous membrane lesions activity score after 7, 28, 56, 84, 112, 140 and 168 days of treatment in both arms • Change to baseline in the SELENA-SLEDAI score after 56 and 168 days of treatment in both arms • Change in consumption of concurrent medication after 7, 28, 56, 84, 112, 140 and 168 days of treatment in both arms • Change in CSSRS scores after 7, 28, 56, 84,112,140 and 168 days of treatment in both arms • Change to baseline in Dermatology Life Quality Index (DLQI) score and Beck Depression Inventory II (BDI-II) score after 56 and 168 days of treatment in both arms • Change of lesional histological inflammation score (V0 vs V8) • Change of lesional MxA expression (IFN-score; V0 vs V8) • Change in gene expression profile (serum; V0 vs. V8) • Occurrence of any adverse event (including changes in laboratory test parameters) • Change to baseline in the RCLASI total activity score, skin activity, alopecia activity, and mucous membrane lesions activity score at VOL-1, VOL-2, VOL-3, and Safety FU in both arms • Change to baseline in the SELENA-SLEDAI score, DLQI score, CSSRS scores, and BDI-II score at VOL-1, VOL-2, and VOL-3 in both arms • Change in consumption of concurrent medication at VOL-1, VOL-2, and VOL-3 in both arms
Number of patients:	Planned: 70 (35 per treatment arm)

	Analyzed: 70 (ITT), 69 (SAF), 61 (PP)
Statistical methods:	**Primary endpoint** The primary outcome, the relative change of RCLASI activity score after day 168 (week 24) from baseline, was compared between the treatment groups with a two-sided Mann-Whitney-Wilcoxon test at a level of 5% overall and stratified by Lupus subtype (van Elteren test). Primary analysis collective was the ITT population, which includes all randomized patients. For this analysis, patients were assigned to the treatment to which they were randomized. Missing values of the primary analysis were replaced by the last observation carried forward (LOCF) method. As sensitivity analysis, the primary analysis was repeated with those patients who completed the trial without relevant protocol violations (PP-population). **Secondary endpoints** Descriptive tables containing mean, standard deviation, minimum, median and maximum of the secondary outcome values at each time point and separated for the treatment arms were provided. In addition, mixed linear models were used to compare the course of the repeatedly measured secondary outcome variables over time between the treatment groups. For each measurement time the difference of the secondary measurements between the treatment groups were estimated with two-sided 95% confidence limits.

Abstract/ Summary – Conclusions:

The BeliSkin study, in which belimumab was used in patients with cutaneous lupus erythematosus, was conducted as a multicenter study in Germany between 2017 and 2023. A total of 70 patients were randomized in the study, of whom 61 were included in the PP population.

When comparing the treatment effect in the overall collective (ITT population) between baseline and V8, there was no significant difference. However, the per-protocol analysis showed a significant treatment success in the verum group with regard to the relative treatment response of the RCLASI-Activity score in the MMRM analysis. Furthermore, there was a significant improvement in quality of life (measured with the DLQI). Regarding the reported side effects, there was no relevant difference between the therapy group and the placebo group.

I. Introduction/ Background

Belimumab is an antibody that targets BLYS/BAFF and reduces B-cell activation. The drug is approved for the treatment of systemic lupus erythematosus (SLE), but not for the treatment of cutaneous lupus erythematosus (CLE). In the literature, there are case reports and smaller case series suggesting the efficacy of belimumab in CLE. However, randomized double-blind controlled studies on the efficacy of belimumab in CLE are not yet available. The aim of this study was to close this gap. The study was conducted as a multicenter study in Germany, with a total of 70 patients included.

Working Hypotheses/ Endpoints:

1. Belimumab therapy significantly reduces disease activity in patients with CLE, measured using the RCLASI-A, within six months.
2. Belimumab therapy significantly improves the quality of life of patients with CLE, measured using the DLQI, within six months.
3. Belimumab therapy significantly improves the depressive mood of patients with CLE, measured using the BDI-II, within six months.
4. Belimumab therapy is reflected in gene expression profiles in whole blood by downregulating the LE-typical immune activation of the innate and adaptive immune system. This should particularly affect B-cell immune pathways.

II. Results

Description of the study group and procedure for evaluating the study:

Overview of the patients included (N=70)

A total of 70 patients were included in the study. As planned, there was randomization into two study arms of equal size, each with 35 patients. Of these, a total of 62 patients completed the study, one patient ended the study due to side effects, two patients withdrew their informed consent and five patients ended the study for other, primarily personal reasons. Number of patients completing the blinded treatment period were comparable in both arms (Belimumab n=30 (85.7%), Placebo n=32 (91.4%)). A total of 69 patients (Belimumab n=34, Placebo=35) were actually treated.

Descriptive statistics for demographic parameters

Age distribution and body size:

Age distribution and height were comparable in both studies: mean age in the verum group was 48.6 years, in the placebo group 49.9 years in the ITT population. Mean height in the belimumab group was 168.7 cm, in the placebo group 170.5 cm (see Appendix) in the ITT population.

Ethnicity and gender:

67 of the 70 patients were of Caucasian ethnicity. A total of 52 women and 18 men took part (see Appendix).

Compliance of patients during the study

Overall the treatment compliance was good with 91% and 80% of relative frequencies of subjects with a compliance assessment of “good” in the placebo and belimumab groups, respectively (see Appendix).

Safety profile: Observed Treatment-Emergent Adverse Events (TEAE) in the study:

Overall, the study drug was well tolerated and there was no relevant difference between the verum group and the placebo group with regard to adverse events (incidence rates were 88.2 and 88.6% in the verum and placebo groups, respectively). Specific side effects associated with the administration of the study drug were slightly more common in the belimumab group (38.2% versus 17.1% in the placebo group). In total, 3 SAEs were observed in the study (double-blind phase): one case of renal failure with deterioration of the general condition in the verum group, which was associated with the underlying disease. Furthermore, gastritis and an ocular vein occlusion were observed in the placebo group, both with hospitalization.

Analysis of the primary endpoint (RCLASI-Activity Overall Score):

Comparison of the RCLASI-Activity overall score between baseline and end of study (V8).

There was no significant difference between the control and verum group in the non-parametric analyses stratified by Lupus subtype (ITT p=0.81, PP p=0.35). However, one lupus subtype (ACLE) is undermanned in the study groups. An additional repeated measure analysis (MMRM) comparing the course of the repeatedly measured outcome variable over time between the treatment groups using Lupus subtype, center, treatment, visit and treatment*visit interaction as fixed effect and the baseline value as covariate showed no significant difference between the control and verum group in the ITT analysis, but a significant treatment success in the verum group (p=0.0476) in the per-protocol analysis with an estimated mean difference of 19% (SE=9.6%).

DLQI (Dermatology Life Quality Index)

The DLQI is a questionnaire for the quality of life of dermatological patients. It comprises a total of ten questions that allow a basic assessment of the patient's quality of life. The following classifications have been established: (0-1: no impairment of quality of life, 2-5: minor impairment, 6-10: moderate impairment, 11-20: severe impairment, 21-30: very severe impairment)

Development of DLQI over the course of the study (PP-population):

In both study arms, patients showed a moderate impairment of quality of life compared to the initial basal value, which was slightly higher in the belimumab group than in the placebo group. In the belimumab group, the mean DLQI score improved by 3 score points to the end of study. In the placebo group, there was only a slight improvement during the study (of 1 score point).

Changes in the secondary endpoint DLQI:

The subsequent analyses showed a significant improvement in the DLQI value over the course of the study in the verum group (ITT Population, V0 vs V8: p=0.012; PP-population, V0 vs V8: p=0.004). In the placebo group, there was no significant improvement in the DLQI during the double-blind study phase (ITT Population, V0 vs V8: p=0.093, PP-population, V0 vs V8: p=0.15). Here, the quality of life only improved significantly in the open-label phase (V0 vs V-OL-3: p<0.001).

Analyses of the BDI-II (Beck Depression Inventory-II)

The BDI-II is a self-assessment instrument for measuring the severity of depression. The BDI-II consists of 21 questions (items) that cover various symptoms of depression. These include emotional, cognitive, motivational and physical aspects. The total score ranges from 0 to 63, with higher scores indicating a more severe depression. (0-13: no or minimal depression, 14-19: mild depression, 20-28: moderate depression, 29-63: severe depression).
Overall, both groups showed low to moderate depressive stress, which tended to improve slightly over the course of the study and also in the open label phase, without this difference being significant (see Appendix).

Analyses of the secondary endpoint SELENA-SLEDAI:

SELENA-SLEDAI stands for Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index. It is a standardized instrument for the assessment of disease activity in systemic lupus erythematosus (SLE). This instrument was used in the study to classify the systemic activity of the included patients with cutaneous lupus erythematosus. The SELENA-SLEDAI assesses 24 parameters covering different organ systems and symptoms. The scores are summed to obtain an overall score (0 points: No disease activity, 1-5 points: Low disease activity, 6-12 points: Moderate disease activity, ≥13 points: High disease activity).

The evaluation of the SELENA-SLEDAI scores showed an average low systemic activity which did not change significantly in the groups during the course of the study (see Appendix).

Publication

in preparation

Appendix – Analyses results

DISPOSITION

Table: Disposition
Population: ITT

	Belimumab N= 35	Placebo N= 35	Overall N= 70
Number of subjects randomized	35 (100.0%)	35 (100.0%)	70 (100.0%)
Number of subjects in ITT	35 (100.0%)	35 (100.0%)	70 (100.0%)
Number of subjects in PP	29 (82.9%)	32 (91.4%)	61 (87.1%)
Number of subjects in SAF	34 (97.1%)	35 (100.0%)	69 (98.6%)
Number of subjects completing the study (ITT)	30 (85.7%)	32 (91.4%)	62 (88.6%)
Number of subjects withdrawn from the study	5 (14.3%)	3 (8.6%)	8 (11.4%)
Reason for premature discontinuation:			
AE/SAE	1 (2.9%)	0 (0.0%)	1 (1.4%)
Other reasons	2 (5.7%)	3 (8.6%)	5 (7.1%)
Withdrawn informed consent	2 (5.7%)	0 (0.0%)	2 (2.9%)

Note: Percentage based on number of randomized patients.

DEMOGRAHICS

Table: Descriptive statistics for the demographic parameters
Population: ITT

Parameter	Treatment	N	Mean	SD	Min.	1. Quartile	Median	3. Quartile	Max.
Age (years)	Belimumab	35	48.63	14.06	24.00	37.00	49.00	57.00	83.00
	Placebo	35	49.94	12.34	28.00	40.00	49.00	60.00	73.00
Height (cm)	Belimumab	35	168.66	7.31	157.00	162.00	168.00	175.00	183.00
	Placebo	35	170.46	7.31	157.00	165.00	170.00	176.00	185.00

Parameter	Treatment		N (%)
Ethnic group	Belimumab	Caucasian	33 (94.3%)
		Other	2 (5.7%)
	Placebo	Caucasian	34 (97.1%)
		Other	1 (2.9%)
Sex	Belimumab	Female	29 (82.9%)
		Male	6 (17.1%)
	Placebo	Female	23 (65.7%)
		Male	12 (34.3%)

Table: Descriptive statistics for the demographic parameters
Population: PP

Parameter	Treatment	N	Mean	SD	Min.	1. Quartile	Median	3. Quartile	Max.
Age (years)	Belimumab	29	48.97	12.73	25.00	39.00	49.00	57.00	71.00
	Placebo	32	49.19	12.31	28.00	39.50	49.00	59.50	73.00
Height (cm)	Belimumab	29	168.31	7.05	157.00	162.00	168.00	173.00	183.00
	Placebo	32	170.25	7.48	157.00	164.50	169.50	176.50	185.00

Parameter	Treatment		N (%)
Ethnic group	Belimumab	Caucasian	28 (96.6%)
		Other	1 (3.4%)
	Placebo	Caucasian	31 (96.9%)
		Other	1 (3.1%)
Sex	Belimumab	Female	25 (86.2%)
		Male	4 (13.8%)
	Placebo	Female	22 (68.8%)
		Male	10 (31.3%)

COMPLIANCE

Table: Descriptive statistics for compliance and exposure data
Population: ITT

Parameter	Treatment	N	Mean	SD	Min.	1. Quartile	Median	3. Quartile	Max.
Compliance[%]	Belimumab	34	89.22	22.80	33.33	91.67	100.00	100.00	108.33
	Placebo	35	95.60	16.36	37.50	100.00	100.00	100.00	112.50
Number of subcutaneous injection	Belimumab	34	21.41	5.47	8.00	22.00	24.00	24.00	26.00
	Placebo	35	22.94	3.93	9.00	24.00	24.00	24.00	27.00

Frequency table for compliance category
Population: ITT

Parameter	Treatment		N (%)
Compliance category	Belimumab	.	1 (2.9%)
		good	28 (80.0%)
		moderate	2 (5.7%)
		poor	4 (11.4%)
	Placebo	good	32 (91.4%)
		moderate	1 (2.9%)
		poor	2 (5.7%)

PRIMARY ENDPOINT - RCLASI

Table: Comparison of the relative RCLASI change at V8 - Mann-Whitney-Wilcoxon test stratified by Lupus subtype (van Elteren test)
Population: ITT

The NPAR1WAY Procedure

dummy=1 param=Overall score

Stratum Information

Stratum	*strat*	*N Obs*
1	ACLE	2
2	CCLE	39
3	LET	8
4	SCLE	19

Stratified Wilcoxon (Van Elteren) Test for relchange

Classified by r_trtarm

N Obs	*N Strata*	*Statistic*	*Expected*	*Std Dev*	*Z*	*Pr < Z*	*Pr > |Z|*
65	3	15.7	16.00	1.136715	-0.2299	0.4091	0.8182

Table: Comparison of the relative RCLASI change at V8 - Mann-Whitney-Wilcoxon test stratified by Lupus subtype (van Elteren test)
Population: PP

The NPAR1WAY Procedure

dummy=1 param=Overall score

Stratum Information

Stratum	*strat*	*N Obs*
1	ACLE	2
2	CCLE	35
3	LET	6
4	SCLE	18

Stratified Wilcoxon (Van Elteren) Test for relchange

Classified by r_trtarm

N Obs	*N Strata*	*Statistic*	*Expected*	*Std Dev*	*Z*	*Pr < Z*	*Pr > |Z|*
58	3	12.5	13.50	1.068363	-0.9346	0.1750	0.3500

Table: Comparison of the relative changes by means of a repeated measure mixed model with center and lupus subtype as fixed effects
Population: ITT

The Mixed Procedure

*F Test for visnum*r_trtarm Least Squares Means Slice*

Slice	Num DF	Den DF	F Value	Pr > F
visnum 8	1	206	1.71	0.1930

*Simple Differences of visnum*r_trtarm Least Squares Means*

Slice	Randomisation Treatment Arm	Randomisation Treatment Arm	Estimate	Standard Error	DF	t Value	Pr > |t|
visnum 8	Arm A - Belimumab	Arm B - Placebo	-0.1138	0.08715	206	-1.31	0.1930

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|
Relchange at visit 8	0.1138	0.08715	206	1.31	0.1930

Table: Comparison of the relative changes by means of a repeated measure mixed model with center and lupus subtype as fixed effects
Population: PP

The Mixed Procedure

*F Test for visnum*r_trtarm Least Squares Means Slice*

Slice	Num DF	Den DF	F Value	Pr > F
visnum 8	1	175.5	3.98	0.0476

*Simple Differences of visnum*r_trtarm Least Squares Means*

Slice	Randomisation Treatment Arm	Randomisation Treatment Arm	Estimate	Standard Error	DF	t Value	Pr > |t|
visnum 8	Arm A - Belimumab	Arm B - Placebo	-0.1910	0.09575	175.5	-1.99	0.0476

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|
Relchange at visit 8	0.1910	0.09575	176	1.99	0.0476

SECONDARY ENDPOINTS - Selena-Sledai Score, BDI-II and DLQI

Descriptive statistics for the Selena-Sledai Score - Observed values
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
Selena-Sledai	Belimumab	Visit 1 (Baseline, Day 0)	33	4.27	8.69	0.00	2.00	50.00	(1.231 ; 7.314)	<.001
		Visit 4 (Day 56)	32	3.78	7.02	0.00	2.00	40.00	(1.288 ; 6.275)	<.001
		Visit 8 (Day 168)	34	4.65	7.89	0.00	2.00	40.00	(1.928 ; 7.366)	<.001
		Visit OL-2 (Day 224)	28	8.21	15.58	0.00	2.00	70.00	(2.297 ; 14.132)	<.001
		Visit OL-3 (Day 336)	27	4.48	6.56	0.00	2.00	30.00	(1.945 ; 7.018)	<.001
	Placebo	Visit 1 (Baseline, Day 0)	35	2.06	1.78	0.00	2.00	8.00	(1.452 ; 2.662)	<.001
		Visit 4 (Day 56)	33	1.85	2.72	0.00	2.00	14.00	(0.898 ; 2.799)	<.001
		Visit 8 (Day 168)	34	2.24	1.95	0.00	2.00	8.00	(1.562 ; 2.909)	<.001
		Visit OL-2 (Day 224)	31	2.26	2.05	0.00	2.00	8.00	(1.519 ; 2.998)	<.001
		Visit OL-3 (Day 336)	27	1.96	1.85	0.00	2.00	6.00	(1.248 ; 2.678)	<.001

Descriptive statistics for the Selena-Sledai Score – Absolute change from baseline
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
Selena-Sledai	Belimumab	Visit 4 (Day 56)	31	-0.58	11.66	-50.00	0.00	36.00	(-4.791 ; 3.629)	0.812
		Visit 8 (Day 168)	33	-0.70	9.68	-50.00	0.00	16.00	(-4.082 ; 2.688)	0.780
		Visit OL-2 (Day 224)	27	4.04	14.31	-4.00	0.00	68.00	(-1.498 ; 9.572)	0.337
		Visit OL-3 (Day 336)	26	1.54	7.18	-8.00	0.00	28.00	(-1.293 ; 4.370)	0.730
	Placebo	Visit 4 (Day 56)	33	-0.27	2.61	-4.00	0.00	12.00	(-1.187 ; 0.641)	0.094
		Visit 8 (Day 168)	34	0.18	2.28	-4.00	0.00	6.00	(-0.608 ; 0.961)	0.723
		Visit OL-2 (Day 224)	31	0.13	2.63	-6.00	0.00	8.00	(-0.820 ; 1.078)	0.952
		Visit OL-3 (Day 336)	27	-0.19	2.39	-6.00	0.00	4.00	(-1.108 ; 0.738)	0.710

Descriptive statistics for the Selena-Sledai Score – Relative change from baseline
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
Selena-Sledai	Belimumab	Visit 4 (Day 56)	25	0.23	1.88	-1.00	0.00	9.00	(-0.522 ; 0.989)	0.656
		Visit 8 (Day 168)	26	0.04	0.91	-1.00	0.00	4.00	(-0.322 ; 0.396)	0.563
		Visit OL-2 (Day 224)	21	2.24	7.68	-1.00	0.00	34.00	(-1.130 ; 5.603)	0.557
		Visit OL-3 (Day 336)	20	0.67	3.31	-1.00	0.00	14.00	(-0.815 ; 2.162)	0.846
	Placebo	Visit 4 (Day 56)	25	-0.08	1.38	-1.00	0.00	6.00	(-0.635 ; 0.475)	0.093
		Visit 8 (Day 168)	25	0.11	0.95	-1.00	0.00	3.00	(-0.270 ; 0.497)	0.599
		Visit OL-2 (Day 224)	23	0.02	0.78	-1.00	0.00	2.00	(-0.303 ; 0.347)	1.000
		Visit OL-3 (Day 336)	20	-0.06	0.83	-1.00	0.00	2.00	(-0.438 ; 0.313)	0.672

Descriptive statistics for the Selena-Sledai Score - Observed values
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
Selena-Sledai	Belimumab	Visit 1 (Baseline, Day 0)	28	4.21	9.18	0.00	2.00	50.00	(0.728 ; 7.700)	<.001
		Visit 4 (Day 56)	29	3.93	7.34	0.00	2.00	40.00	(1.193 ; 6.669)	<.001
		Visit 8 (Day 168)	29	4.55	7.78	0.00	2.00	40.00	(1.648 ; 7.455)	<.001
		Visit OL-2 (Day 224)	27	7.70	15.64	0.00	2.00	70.00	(1.656 ; 13.751)	<.001
		Visit OL-3 (Day 336)	26	4.38	6.67	0.00	2.00	30.00	(1.756 ; 7.013)	<.001
	Placebo	Visit 1 (Baseline, Day 0)	32	2.06	1.87	0.00	2.00	8.00	(1.400 ; 2.725)	<.001
		Visit 4 (Day 56)	31	1.87	2.78	0.00	2.00	14.00	(0.868 ; 2.874)	<.001
		Visit 8 (Day 168)	32	2.31	1.97	0.00	2.00	8.00	(1.611 ; 3.014)	<.001
		Visit OL-2 (Day 224)	31	2.26	2.05	0.00	2.00	8.00	(1.519 ; 2.998)	<.001
		Visit OL-3 (Day 336)	27	1.96	1.85	0.00	2.00	6.00	(1.248 ; 2.678)	<.001

Descriptive statistics for the Selena-Sledai Score – Absolute change from baseline
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
Selena-Sledai	Belimumab	Visit 4 (Day 56)	28	-0.14	12.13	-50.00	0.00	36.00	(-4.751 ; 4.465)	0.755
		Visit 8 (Day 168)	28	-0.93	10.41	-50.00	0.00	16.00	(-4.881 ; 3.023)	0.906
		Visit OL-2 (Day 224)	26	3.92	14.58	-4.00	0.00	68.00	(-1.824 ; 9.670)	0.571
		Visit OL-3 (Day 336)	25	1.92	7.06	-4.00	0.00	28.00	(-0.917 ; 4.757)	0.526
	Placebo	Visit 4 (Day 56)	31	-0.26	2.67	-4.00	0.00	12.00	(-1.222 ; 0.706)	0.135
		Visit 8 (Day 168)	32	0.25	2.31	-4.00	0.00	6.00	(-0.572 ; 1.072)	0.629
		Visit OL-2 (Day 224)	31	0.13	2.63	-6.00	0.00	8.00	(-0.820 ; 1.078)	0.952
		Visit OL-3 (Day 336)	27	-0.19	2.39	-6.00	0.00	4.00	(-1.108 ; 0.738)	0.710

Descriptive statistics for the Selena-Sledai Score – Relative change from baseline
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
Selena-Sledai	Belimumab	Visit 4 (Day 56)	22	0.34	1.98	-1.00	0.00	9.00	(-0.506 ; 1.188)	0.977
		Visit 8 (Day 168)	22	0.07	0.96	-1.00	0.00	4.00	(-0.344 ; 0.481)	0.875
		Visit OL-2 (Day 224)	20	2.33	7.87	-1.00	0.00	34.00	(-1.209 ; 5.859)	0.500
		Visit OL-3 (Day 336)	19	0.74	3.39	-1.00	0.00	14.00	(-0.827 ; 2.300)	1.000
	Placebo	Visit 4 (Day 56)	23	-0.07	1.42	-1.00	0.00	6.00	(-0.662 ; 0.532)	0.139
		Visit 8 (Day 168)	23	0.17	0.97	-1.00	0.00	3.00	(-0.238 ; 0.572)	0.455
		Visit OL-2 (Day 224)	23	0.02	0.78	-1.00	0.00	2.00	(-0.303 ; 0.347)	1.000
		Visit OL-3 (Day 336)	20	-0.06	0.83	-1.00	0.00	2.00	(-0.438 ; 0.313)	0.672

Descriptive statistics for questionnaire DLQI - Observed values
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
DLQII	Belimumab	Visit 1 (Baseline, Day 0)	33	9.52	5.75	1.00	10.00	22.00	(7.503 ; 11.527)	<.001
		Visit 4 (Day 56)	32	7.13	4.90	0.00	7.00	20.00	(5.385 ; 8.865)	<.001
		Visit 8 (Day 168)	34	6.62	5.43	0.00	5.50	20.00	(4.747 ; 8.488)	<.001
		Visit OL-2 (Day 224)	28	7.04	6.26	0.00	5.50	23.00	(4.660 ; 9.412)	<.001
		Visit OL-3 (Day 336)	27	7.07	5.74	0.00	7.00	19.00	(4.853 ; 9.296)	<.001
	Placebo	Visit 1 (Baseline, Day 0)	35	6.77	5.82	0.00	5.00	19.00	(4.796 ; 8.747)	<.001
		Visit 4 (Day 56)	34	5.35	5.63	0.00	3.50	23.00	(3.411 ; 7.295)	<.001
		Visit 8 (Day 168)	34	5.62	5.74	0.00	3.50	18.00	(3.639 ; 7.597)	<.001
		Visit OL-2 (Day 224)	31	5.19	4.80	0.00	3.00	16.00	(3.462 ; 6.926)	<.001
		Visit OL-3 (Day 336)	28	4.54	4.45	0.00	2.50	13.00	(2.845 ; 6.226)	<.001

Descriptive statistics for questionnaire DLQI – Absolute change from baseline
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
DLQI	Belimumab	Visit 4 (Day 56)	31	-2.81	4.94	-12.00	-2.00	7.00	(-4.588 ; -1.025)	0.004
		Visit 8 (Day 168)	33	-2.94	6.32	-15.00	-1.00	14.00	(-5.150 ; -0.729)	0.012
		Visit OL-2 (Day 224)	27	-2.96	5.72	-15.00	-2.00	11.00	(-5.176 ; -0.750)	0.008
		Visit OL-3 (Day 336)	26	-3.04	4.70	-10.00	-3.00	9.00	(-4.892 ; -1.185)	0.003
	Placebo	Visit 4 (Day 56)	34	-1.50	3.31	-13.00	-1.00	4.00	(-2.642 ; -0.358)	0.007
		Visit 8 (Day 168)	34	-1.21	4.45	-12.00	-1.00	9.00	(-2.740 ; 0.328)	0.093
		Visit OL-2 (Day 224)	31	-2.13	3.32	-11.00	-3.00	5.00	(-3.329 ; -0.929)	0.001
		Visit OL-3 (Day 336)	28	-2.96	3.78	-14.00	-2.50	5.00	(-4.398 ; -1.530)	<.001

Descriptive statistics for questionnaire DLQI – Relative change from baseline
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
DLQII	Belimumab	Visit 4 (Day 56)	31	-0.20	0.57	-1.00	-0.36	1.75	(-0.410 ; 0.002)	0.012
		Visit 8 (Day 168)	33	-0.15	0.84	-1.00	-0.33	3.50	(-0.442 ; 0.146)	0.027
		Visit OL-2 (Day 224)	27	-0.28	0.69	-1.00	-0.50	2.00	(-0.543 ; -0.011)	0.015
		Visit OL-3 (Day 336)	26	-0.34	0.52	-1.00	-0.46	0.90	(-0.549 ; -0.138)	0.002
	Placebo	Visit 4 (Day 56)	33	-0.24	0.56	-1.00	-0.22	1.00	(-0.433 ; -0.042)	0.016
		Visit 8 (Day 168)	33	0.01	1.15	-1.00	-0.13	5.00	(-0.397 ; 0.410)	0.241
		Visit OL-2 (Day 224)	31	-0.10	0.95	-1.00	-0.28	3.00	(-0.441 ; 0.245)	0.030
		Visit OL-3 (Day 336)	28	-0.35	0.72	-1.00	-0.46	2.00	(-0.625 ; -0.079)	0.001

Descriptive statistics for questionnaire DLQI - Observed values
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
DLQI	Belimumab	Visit 1 (Baseline, Day 0)	28	9.82	5.92	1.00	10.00	22.00	(7.573 ; 12.070)	<.001
		Visit 4 (Day 56)	29	7.00	4.95	0.00	7.00	20.00	(5.153 ; 8.847)	<.001
		Visit 8 (Day 168)	29	6.38	5.35	0.00	5.00	20.00	(4.384 ; 8.375)	<.001
		Visit OL-2 (Day 224)	27	6.93	6.35	0.00	5.00	23.00	(4.471 ; 9.381)	<.001
		Visit OL-3 (Day 336)	26	7.08	5.86	0.00	7.00	19.00	(4.768 ; 9.386)	<.001
	Placebo	Visit 1 (Baseline, Day 0)	32	7.09	5.96	0.00	5.00	19.00	(4.975 ; 9.213)	<.001
		Visit 4 (Day 56)	32	5.59	5.71	0.00	4.50	23.00	(3.564 ; 7.623)	<.001
		Visit 8 (Day 168)	32	5.97	5.74	0.00	4.00	18.00	(3.930 ; 8.007)	<.001
		Visit OL-2 (Day 224)	31	5.19	4.80	0.00	3.00	16.00	(3.462 ; 6.926)	<.001
		Visit OL-3 (Day 336)	28	4.54	4.45	0.00	2.50	13.00	(2.845 ; 6.226)	<.001

Descriptive statistics for questionnaire DLQI – Absolute change from baseline
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
DLQI	Belimumab	Visit 4 (Day 56)	28	-2.86	4.75	-12.00	-2.50	7.00	(-4.661 ; -1.053)	0.004
		Visit 8 (Day 168)	28	-3.50	5.62	-15.00	-3.00	6.00	(-5.635 ; -1.365)	0.004
		Visit OL-2 (Day 224)	26	-2.88	5.82	-15.00	-2.00	11.00	(-5.178 ; -0.591)	0.013
		Visit OL-3 (Day 336)	25	-2.84	4.69	-10.00	-3.00	9.00	(-4.724 ; -0.956)	0.005
	Placebo	Visit 4 (Day 56)	32	-1.50	3.42	-13.00	-1.00	4.00	(-2.714 ; -0.286)	0.013
		Visit 8 (Day 168)	32	-1.13	4.56	-12.00	-1.00	9.00	(-2.746 ; 0.496)	0.154
		Visit OL-2 (Day 224)	31	-2.13	3.32	-11.00	-3.00	5.00	(-3.329 ; -0.929)	0.001
		Visit OL-3 (Day 336)	28	-2.96	3.78	-14.00	-2.50	5.00	(-4.398 ; -1.530)	<.001

Descriptive statistics for questionnaire DLQI – Relative change from baseline
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
DLQI	Belimumab	Visit 4 (Day 56)	28	-0.21	0.58	-1.00	-0.37	1.75	(-0.434 ; 0.006)	0.012
		Visit 8 (Day 168)	28	-0.28	0.55	-1.00	-0.39	1.00	(-0.483 ; -0.067)	0.009
		Visit OL-2 (Day 224)	26	-0.27	0.70	-1.00	-0.50	2.00	(-0.551 ; 0.002)	0.020
		Visit OL-3 (Day 336)	25	-0.34	0.53	-1.00	-0.42	0.90	(-0.549 ; -0.122)	0.004
	Placebo	Visit 4 (Day 56)	31	-0.21	0.56	-1.00	-0.21	1.00	(-0.409 ; -0.006)	0.040
		Visit 8 (Day 168)	31	0.07	1.16	-1.00	-0.11	5.00	(-0.347 ; 0.490)	0.433
		Visit OL-2 (Day 224)	31	-0.10	0.95	-1.00	-0.28	3.00	(-0.441 ; 0.245)	0.030
		Visit OL-3 (Day 336)	28	-0.35	0.72	-1.00	-0.46	2.00	(-0.625 ; -0.079)	0.001

Descriptive statistics for questionnaire BDI-II - Observed values
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
BDI-II	Belimumab	Visit 0 (Screening/Randomization)	35	6.86	5.83	0.00	6.00	19.00	(4.878 ; 8.836)	<.001
		Visit 4 (Day 56)	32	6.34	5.88	0.00	4.50	18.00	(4.254 ; 8.434)	<.001
		Visit 8 (Day 168)	34	5.53	5.00	0.00	5.00	21.00	(3.805 ; 7.254)	<.001
		Visit OL-2 (Day 224)	28	5.32	5.58	0.00	4.00	21.00	(3.200 ; 7.442)	<.001
		Visit OL-3 (Day 336)	27	5.67	6.23	0.00	4.00	20.00	(3.256 ; 8.077)	<.001
	Placebo	Visit 0 (Screening/Randomization)	35	5.51	5.77	0.00	4.00	21.00	(3.555 ; 7.473)	<.001
		Visit 4 (Day 56)	34	4.85	5.02	0.00	4.00	15.00	(3.124 ; 6.582)	<.001
		Visit 8 (Day 168)	34	4.74	5.79	0.00	3.00	23.00	(2.741 ; 6.729)	<.001
		Visit OL-2 (Day 224)	31	4.90	5.57	0.00	3.00	21.00	(2.893 ; 6.914)	<.001
		Visit OL-3 (Day 336)	28	4.18	4.90	0.00	2.00	17.00	(2.318 ; 6.039)	<.001

Descriptive statistics for questionnaire BDI-II – Absolute change from baseline
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
BDI-II	Belimumab	Visit 4 (Day 56)	32	-0.81	5.44	-14.00	0.00	8.00	(-2.744 ; 1.119)	0.614
		Visit 8 (Day 168)	34	-1.44	5.31	-19.00	0.00	6.00	(-3.271 ; 0.389)	0.159
		Visit OL-2 (Day 224)	28	-1.96	4.22	-15.00	-1.50	4.00	(-3.567 ; -0.361)	0.010
		Visit OL-3 (Day 336)	27	-1.81	5.53	-16.00	-2.00	8.00	(-3.955 ; 0.325)	0.167
	Placebo	Visit 4 (Day 56)	34	-0.62	3.68	-10.00	0.00	8.00	(-1.885 ; 0.649)	0.223
		Visit 8 (Day 168)	34	-0.76	4.13	-15.00	0.00	9.00	(-2.190 ; 0.660)	0.246
		Visit OL-2 (Day 224)	31	-0.81	3.69	-10.00	0.00	10.00	(-2.139 ; 0.526)	0.123
		Visit OL-3 (Day 336)	28	-1.64	4.34	-13.00	-1.00	6.00	(-3.291 ; 0.005)	0.052

Descriptive statistics for questionnaire BDI-II – Relative change from baseline
Population: ITT

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
BDI-II	Belimumab	Visit 4 (Day 56)	26	0.20	1.42	-1.00	0.03	6.00	(-0.354 ; 0.762)	0.979
		Visit 8 (Day 168)	28	0.10	1.08	-1.00	-0.18	4.00	(-0.308 ; 0.515)	0.873
		Visit OL-2 (Day 224)	22	-0.27	0.70	-1.00	-0.48	2.00	(-0.567 ; 0.032)	0.027
		Visit OL-3 (Day 336)	21	-0.16	0.94	-1.00	-0.38	3.00	(-0.574 ; 0.252)	0.158
	Placebo	Visit 4 (Day 56)	24	-0.02	1.10	-1.00	-0.23	4.00	(-0.473 ; 0.426)	0.095
		Visit 8 (Day 168)	24	-0.09	0.81	-1.00	-0.26	2.00	(-0.423 ; 0.240)	0.251
		Visit OL-2 (Day 224)	22	0.06	0.99	-1.00	-0.24	2.50	(-0.363 ; 0.486)	0.404
		Visit OL-3 (Day 336)	20	-0.07	0.99	-1.00	-0.29	3.00	(-0.519 ; 0.371)	0.178

Descriptive statistics for questionnaire BDI-II - Observed values
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
BDI-II	Belimumab	Visit 0 (Screening/Randomization)	29	6.90	5.92	0.00	7.00	19.00	(4.688 ; 9.105)	<.001
		Visit 4 (Day 56)	29	6.07	5.98	0.00	4.00	18.00	(3.839 ; 8.299)	<.001
		Visit 8 (Day 168)	29	5.10	5.06	0.00	4.00	21.00	(3.215 ; 6.991)	<.001
		Visit OL-2 (Day 224)	27	5.41	5.67	0.00	4.00	21.00	(3.214 ; 7.601)	<.001
		Visit OL-3 (Day 336)	26	5.69	6.35	0.00	4.00	20.00	(3.188 ; 8.197)	<.001
	Placebo	Visit 0 (Screening/Randomization)	32	5.53	6.02	0.00	3.50	21.00	(3.394 ; 7.668)	<.001
		Visit 4 (Day 56)	32	4.94	5.12	0.00	4.00	15.00	(3.117 ; 6.758)	<.001
		Visit 8 (Day 168)	32	4.91	5.90	0.00	3.00	23.00	(2.809 ; 7.004)	<.001
		Visit OL-2 (Day 224)	31	4.90	5.57	0.00	3.00	21.00	(2.893 ; 6.914)	<.001
		Visit OL-3 (Day 336)	28	4.18	4.90	0.00	2.00	17.00	(2.318 ; 6.039)	<.001

Descriptive statistics for questionnaire BDI-II – Absolute change from baseline
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
BDI-II	Belimumab	Visit 4 (Day 56)	29	-0.83	5.51	-14.00	0.00	8.00	(-2.884 ; 1.229)	0.697
		Visit 8 (Day 168)	29	-1.79	5.47	-19.00	0.00	6.00	(-3.833 ; 0.247)	0.101
		Visit OL-2 (Day 224)	27	-1.85	4.26	-15.00	-1.00	4.00	(-3.499 ; -0.205)	0.020
		Visit OL-3 (Day 336)	26	-1.77	5.64	-16.00	-1.00	8.00	(-3.991 ; 0.453)	0.192
	Placebo	Visit 4 (Day 56)	32	-0.59	3.78	-10.00	0.00	8.00	(-1.938 ; 0.750)	0.290
		Visit 8 (Day 168)	32	-0.63	4.23	-15.00	0.00	9.00	(-2.126 ; 0.876)	0.415
		Visit OL-2 (Day 224)	31	-0.81	3.69	-10.00	0.00	10.00	(-2.139 ; 0.526)	0.123
		Visit OL-3 (Day 336)	28	-1.64	4.34	-13.00	-1.00	6.00	(-3.291 ; 0.005)	0.052

Descriptive statistics for questionnaire BDI-II – Relative change from baseline
Population: PP

Parameter	Treatment	Visit	N	Mean	SD	Min.	Median	Max.	95% CI#	Signed rank test#
BDI-II	Belimumab	Visit 4 (Day 56)	23	0.18	1.45	-1.00	0.06	6.00	(-0.432 ; 0.783)	0.937
		Visit 8 (Day 168)	23	0.06	1.15	-1.00	-0.22	4.00	(-0.427 ; 0.541)	0.488
		Visit OL-2 (Day 224)	21	-0.25	0.71	-1.00	-0.45	2.00	(-0.563 ; 0.062)	0.039
		Visit OL-3 (Day 336)	20	-0.15	0.96	-1.00	-0.38	3.00	(-0.584 ; 0.283)	0.199
	Placebo	Visit 4 (Day 56)	22	0.00	1.14	-1.00	-0.23	4.00	(-0.483 ; 0.492)	0.141
		Visit 8 (Day 168)	22	-0.04	0.82	-1.00	-0.20	2.00	(-0.385 ; 0.315)	0.425
		Visit OL-2 (Day 224)	22	0.06	0.99	-1.00	-0.24	2.50	(-0.363 ; 0.486)	0.404
		Visit OL-3 (Day 336)	20	-0.07	0.99	-1.00	-0.29	3.00	(-0.519 ; 0.371)	0.178

SAFETY - AEs

Overview of TEAEs in double blind phase
Population: SAF

Number of treated subjects - n (%)	Belimumab N= 34	Placebo N= 35	p-Value*
with any TEAE	30 (88.2%)	31 (88.6%)	0.9652
with TEAE related to investigational product	13 (38.2%)	6 (17.1%)	0.0626
with severe TEAE	3 (8.8%)	1 (2.9%)	0.2890
with SAE	1 (2.9%)	2 (5.7%)	0.5723

Note: Calculation of percentages based on number of patients in Safety population
*by Chi-Square test. If any category has a cell count less than 5, then the Fisher exact test will be used

Incidence of TEAEs in Double-Blind Treatment Period by SOC and PT
Population: SAF

System Organ Class	Preferred term	Belimumab N= 34	Placebo N= 35	P-Value* (Chi-Square/Fisher Exact)
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	Total	10 (29.4%)	5 (14.3%)	0.1278
	Brustkorbschmerz	0 (0.0%)	1 (2.9%)	1.0000
	Durst	1 (2.9%)	0 (0.0%)	0.4928
	Ermuedung	0 (0.0%)	4 (11.4%)	0.1142
	Fieber	1 (2.9%)	0 (0.0%)	0.4928
	Gefuehl anomal	1 (2.9%)	0 (0.0%)	0.4928
	Generelle Verschlechterung des physischen Gesundheitszustandes	1 (2.9%)	0 (0.0%)	0.4928
	Gesichtsschmerzen	1 (2.9%)	0 (0.0%)	0.4928
	Haematom an der Applikationsstelle	1 (2.9%)	0 (0.0%)	0.4928
	Periphere Schwellung	2 (5.9%)	0 (0.0%)	0.2391
	Raumforderung an der Injektionsstelle	1 (2.9%)	0 (0.0%)	0.4928
	Schmerzen versursacht durch Medizinprodukt	1 (2.9%)	0 (0.0%)	0.4928
	Ulkus	1 (2.9%)	0 (0.0%)	0.4928
	Unwohlsein	1 (2.9%)	0 (0.0%)	0.4928
Augenerkrankungen	Total	3 (8.8%)	1 (2.9%)	0.3565
	Augenvenenthrombose	0 (0.0%)	1 (2.9%)	1.0000
	Blepharospasmus	1 (2.9%)	0 (0.0%)	0.4928
	Sehen verschwommen	1 (2.9%)	0 (0.0%)	0.4928

	Sehverschlechterung	1 (2.9%)	0 (0.0%)	0.4928
Chirurgische und medizinische Eingriffe	Total	0 (0.0%)	1 (2.9%)	1.0000
	Zahnextraktion	0 (0.0%)	1 (2.9%)	1.0000
Erkrankungen der Atemwege, des Brustraums und Mediastinums	Total	4 (11.8%)	2 (5.7%)	0.4283
	Anomalie der Nasenmuschel	1 (2.9%)	0 (0.0%)	0.4928
	Asthma	1 (2.9%)	0 (0.0%)	0.4928
	Dysphonie	1 (2.9%)	0 (0.0%)	0.4928
	Dyspnoe	0 (0.0%)	1 (2.9%)	1.0000

System Organ Class	Preferred term	Belimumab N= 34	Placebo N= 35	P-Value* (Chi-Square/Fisher Exact)
Erkrankungen der Atemwege, des Brustraums und Mediastinums	Total	4 (11.8%)	2 (5.7%)	0.4283
	Anomalie der Nasenmuschel	1 (2.9%)	0 (0.0%)	0.4928
	Asthma	1 (2.9%)	0 (0.0%)	0.4928
	Dysphonie	1 (2.9%)	0 (0.0%)	0.4928
	Dyspnoe	0 (0.0%)	1 (2.9%)	1.0000
	Epistaxis	0 (0.0%)	1 (2.9%)	1.0000
	Husten	1 (2.9%)	0 (0.0%)	0.4928
Erkrankungen der Geschlechtsorgane und der Brustdruese	Total	0 (0.0%)	3 (8.6%)	0.2391
	Menstruationsbeschwerden	0 (0.0%)	2 (5.7%)	0.4928
	Vulvovaginale Trockenheit	0 (0.0%)	1 (2.9%)	1.0000
Erkrankungen der Haut und des Unterhautgewebes	Total	7 (20.6%)	6 (17.1%)	0.7144
	Ausschlag mit Juckreiz	0 (0.0%)	1 (2.9%)	1.0000

	Erythem	1 (2.9%)	0 (0.0%)	0.4928
	Handekzem	1 (2.9%)	0 (0.0%)	0.4928
	Hautstruktur anomal	0 (0.0%)	1 (2.9%)	1.0000
	Hautzyste	0 (0.0%)	1 (2.9%)	1.0000
	Hyperkeratose	1 (2.9%)	0 (0.0%)	0.4928
	Lupus erythematodes integumentalis	0 (0.0%)	1 (2.9%)	1.0000
	Medikamentenausschlag	1 (2.9%)	0 (0.0%)	0.4928
	Naechtliche Schweissausbrueche	1 (2.9%)	0 (0.0%)	0.4928
	Petechien	2 (5.9%)	0 (0.0%)	0.2391
	Pruritus	1 (2.9%)	1 (2.9%)	1.0000
	Subakuter kutaner Lupus erythematodes	0 (0.0%)	1 (2.9%)	1.0000
	Urtikaria	0 (0.0%)	1 (2.9%)	1.0000
Erkrankungen der Nieren und Harnwege	Total	1 (2.9%)	0 (0.0%)	0.4928
	Akute Nierenschaedigung	1 (2.9%)	0 (0.0%)	0.4928
Erkrankungen des Blutes und des Lymphsystems	Total	2 (5.9%)	2 (5.7%)	1.0000
	Eisenmangelanaemie	1 (2.9%)	0 (0.0%)	0.4928
	Leukopenie	0 (0.0%)	1 (2.9%)	1.0000
	Lymphadenopathie	0 (0.0%)	1 (2.9%)	1.0000
	Lymphopenie	1 (2.9%)	0 (0.0%)	0.4928

System Organ Class	Preferred term	Belimumab N= 34	Placebo N= 35	P-Value* (Chi-Square/Fisher Exact)
	Thrombozytopenie	0 (0.0%)	1 (2.9%)	1.0000
Erkrankungen des Gastrointestinaltrakts	Total	6 (17.6%)	6 (17.1%)	0.9559
	Abdominale Beschwerden	1 (2.9%)	2 (5.7%)	1.0000
	Abdominalschmerz	0 (0.0%)	1 (2.9%)	1.0000
	Bauch aufgetrieben	1 (2.9%)	0 (0.0%)	0.4928
	Cheilitis	1 (2.9%)	0 (0.0%)	0.4928
	Darmobstruktion	1 (2.9%)	0 (0.0%)	0.4928
	Dysphagie	1 (2.9%)	0 (0.0%)	0.4928
	Erbrechen	0 (0.0%)	1 (2.9%)	1.0000
	Gastritis	0 (0.0%)	1 (2.9%)	1.0000
	Loser Zahn	0 (0.0%)	1 (2.9%)	1.0000
	Nahrungsmittelvergiftung	0 (0.0%)	1 (2.9%)	1.0000
	Uebelkeit	1 (2.9%)	2 (5.7%)	1.0000
Erkrankungen des Nervensystems	Total	8 (23.5%)	8 (22.9%)	0.9473
	Geschmacksstoerung	1 (2.9%)	0 (0.0%)	0.4928
	Kopfschmerz	4 (11.8%)	5 (14.3%)	1.0000
	Kubitaltunnelsyndrom	0 (0.0%)	1 (2.9%)	1.0000
	Migraene	2 (5.9%)	1 (2.9%)	0.6139
	Polyneuropathie	1 (2.9%)	0 (0.0%)	0.4928
	Schwindelgefuehl	1 (2.9%)	1 (2.9%)	1.0000

Erkrankungen des Ohrs und des Labyrinths	Total	1 (2.9%)	0 (0.0%)	0.4928
	Ohrschmerzen	1 (2.9%)	0 (0.0%)	0.4928
Gefaesserkrankungen	Total	2 (5.9%)	3 (8.6%)	1.0000
	Haematom	1 (2.9%)	0 (0.0%)	0.4928
	Hypertonie	1 (2.9%)	2 (5.7%)	1.0000
	Kreislaufkollaps	0 (0.0%)	1 (2.9%)	1.0000

System Organ Class	Preferred term	Belimumab N= 34	Placebo N= 35	P-Value* (Chi-Square/Fisher Exact)
Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)	Total	1 (2.9%)	0 (0.0%)	0.4928
	Basalzellkarzinom	1 (2.9%)	0 (0.0%)	0.4928
Infektionen und parasitaere Erkrankungen	Total	13 (38.2%)	12 (34.3%)	0.7329
	Bronchitis	2 (5.9%)	0 (0.0%)	0.2391
	Candida-Infektion	1 (2.9%)	0 (0.0%)	0.4928
	Coronavirus-Infektion	7 (20.6%)	4 (11.4%)	0.3420
	Gastroenteritis	0 (0.0%)	1 (2.9%)	1.0000
	Harnwegsinfektion	2 (5.9%)	3 (8.6%)	1.0000
	Konjunktivitis	1 (2.9%)	0 (0.0%)	0.4928
	Nasopharyngitis	4 (11.8%)	7 (20.0%)	0.5130
	Oraler Herpes	1 (2.9%)	0 (0.0%)	0.4928
	Pulpitis dentalis	0 (0.0%)	2 (5.7%)	0.4928
	Sinusitis	0 (0.0%)	1 (2.9%)	1.0000
	Subkutaner Abszess	1 (2.9%)	0 (0.0%)	0.4928

	Vulvovaginale Pilzinfektion	0 (0.0%)	1 (2.9%)	1.0000
	Zystitis	1 (2.9%)	0 (0.0%)	0.4928
Kongenitale, familiaere und genetische Erkrankungen	Total	0 (0.0%)	1 (2.9%)	1.0000
	Phimose	0 (0.0%)	1 (2.9%)	1.0000
Leber- und Gallenerkrankungen	Total	0 (0.0%)	1 (2.9%)	1.0000
	Akute Hepatitis	0 (0.0%)	1 (2.9%)	1.0000
Psychiatrische Erkrankungen	Total	3 (8.8%)	2 (5.7%)	0.6733
	Alptraum	0 (0.0%)	1 (2.9%)	1.0000
	Depressive Verstimmung	1 (2.9%)	1 (2.9%)	1.0000
	Einschlafstoerung	1 (2.9%)	0 (0.0%)	0.4928
	Schlaflosigkeit	0 (0.0%)	1 (2.9%)	1.0000
	Suizidgedanken	1 (2.9%)	0 (0.0%)	0.4928

System Organ Class	Preferred term	Belimumab N= 34	Placebo N= 35	P-Value* (Chi-Square/Fisher Exact)
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	Total	7 (20.6%)	9 (25.7%)	0.6140
	Arthralgie	2 (5.9%)	5 (14.3%)	0.4283
	Bandscheibenprotrusion	0 (0.0%)	1 (2.9%)	1.0000
	Gelenkschwellung	1 (2.9%)	1 (2.9%)	1.0000
	Knochenschmerzen	0 (0.0%)	1 (2.9%)	1.0000
	Myalgie	0 (0.0%)	2 (5.7%)	0.4928
	Plantare Fasciitis	1 (2.9%)	0 (0.0%)	0.4928
	Rheumatoide Arthritis	1 (2.9%)	0 (0.0%)	0.4928

	Rueckenschmerzen	0 (0.0%)	2 (5.7%)	0.4928
	Schmerz in einer Extremitaet	2 (5.9%)	1 (2.9%)	0.6139
Stoffwechsel- und Ernaehrungsstoerungen	Total	4 (11.8%)	1 (2.9%)	0.1981
	Appetit vermindert	1 (2.9%)	0 (0.0%)	0.4928
	Hyperurikaemie	1 (2.9%)	0 (0.0%)	0.4928
	Hypokaliaemie	1 (2.9%)	0 (0.0%)	0.4928
	Hyponatriaemie	0 (0.0%)	1 (2.9%)	1.0000
	Vitamin B12-Mangel	1 (2.9%)	0 (0.0%)	0.4928
Untersuchungen	Total	5 (14.7%)	7 (20.0%)	0.5619
	Alaninaminotransferase anomal	0 (0.0%)	1 (2.9%)	1.0000
	Blutdruck erhoeht	0 (0.0%)	2 (5.7%)	0.4928
	C-reaktives Protein erhoeht	0 (0.0%)	1 (2.9%)	1.0000
	Folat im Blut erniedrigt	1 (2.9%)	0 (0.0%)	0.4928
	Gewicht erhoeht	1 (2.9%)	1 (2.9%)	1.0000
	Herzgeraeusch	0 (0.0%)	1 (2.9%)	1.0000
	Leberenzym erhoeht	1 (2.9%)	0 (0.0%)	0.4928
	Lipase erhoeht	1 (2.9%)	0 (0.0%)	0.4928
	Natrium im Blut erniedrigt	1 (2.9%)	0 (0.0%)	0.4928
	Protein im Urin	0 (0.0%)	1 (2.9%)	1.0000
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	Total	1 (2.9%)	4 (11.4%)	0.3565
	Meniskusverletzung	0 (0.0%)	1 (2.9%)	1.0000
	Quetschung einer Extremitaet	0 (0.0%)	1 (2.9%)	1.0000

	Sonnenbrand	1 (2.9%)	0 (0.0%)	0.4928
	Sturz	0 (0.0%)	1 (2.9%)	1.0000
	Wunde	0 (0.0%)	2 (5.7%)	0.4928

Note: Calculation of percentages based on number of patients in SP
Note: A patient with more than one TEAE within a PT was counted once in PT
*If any category has a cell count less than 5, then the Fisher exact test will be used