Clinical trial results:
A phase IIa, single-centre, randomised, vehicle-controlled, double-blind trial for assessment of efficacy, safety and tolerability of the topical formulation SB011 containing a human GATA-3 specific DNAzyme and of systemic absorption of hgd40 following application to lesional skin in patients with atopic eczema

Summary

EudraCT number	2013-001091-38
Trial protocol	DE
Global end of trial date	03 November 2016

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	SB011/02/2013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sterna biologicals GmbH & Co KG
Sponsor organisation address	Bismarckstraße 7, Marburg, Germany, 35037
Public contact	Clinical Trial Manager, Sterna biologicals GmbH & Co KG, clinicaltrials@sterna-biologicals.com
Scientific contact	Clinical Trial Manager, Sterna biologicals GmbH & Co KG, clinicaltrials@sterna-biologicals.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate efficacy of the topical formulation SB011 containing 2% hgd40 on skin lesions by clinical assessment of skin condition in patients with mild to moderate atopic eczema.

For each patient, 2 preferably disseminated and contralateral, comparable skin lesions (treatment areas each 50 cm²) located on the arms, legs, chest, stomach, or neck were examined. All patients received both treatments at the same time i.e. formulation SB011 containing hgd40 and placebo. The test areas were treated for 14 consecutive days and one single last application on Day 15 (overall 29 treatments).

The investigational product SB011 contains the DNAzyme hgd40 (new class of antisense oligonucleotide therapeutics), which targets the mRNA of the transcription factor GATA-3. GATA-3 is the key regulatory factor of T helper cells 2 (Th2)-driven immune responses. The formulation SB011 - containing hgd40 - represents a novel therapy for patients with atopic dermatitis (AD).

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the currently valid Declaration of Helsinki, and are consistent with ICH-GCP (January 1997) and applicable regulatory requirements.

All laboratory tests and procedures used during the study are well established and validated. Adverse events were monitored from the time of signing the informed consent to the end of the study (or study discontinuation).

Background therapy: -

Evidence for comparator:

Abbreviations and special terms used in this entry:

AD=Atopic dermatitis
Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.
AE=Adverse event
hgd40=Human GATA-3-specific DNAzyme
IMP=Investigational medicinal product
SAE=Serious adverse event
SCORAD=SCORing atopic dermatitis (a clinical tool for assessing the severity (i.e., extent, intensity) of AD); SCORAD evaluates the severity of the atopic lesions based on affected body area and intensity of plaque characteristics
SES=Safety evaluation set
TEWL=Transepidermal water loss
Th2=T helper cells 2
W/O/W=Water/Oil/Water (a continuous aqueous phase emulsions inside which droplets of oil contain a secondary aqueous phase i.e. double emulsion

Actual start date of recruitment	17 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrolled into this trial were adults with confirmed diagnosis of atopic dermatitis (AD), as defined by Hanifin and Rajka*, and with a SCORAD score between 20 and 50 (representing mild to moderate atopic dermatitis).

*Diagnostic features of atopic dermatitis. Hanifin JM, Rajka G. Acta Derm Venereol Suppl (Stockh) 1980; 92:44–7

Pre-assignment

Screening details:

Overall, 25 adult male and female subjects (20 to 52-years-old) with atopic dermatitis (AD), were eligible for enrolment into the trial. Subjects were screened according to inclusion and exclusion criteria. Written informed consent was obtained from patients prior to participation in the study.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The IMPs were blinded and supplied by the manufacturer as patient-specifically packaged kits. The treatment test field areas were numbered as 1 and 2. Each kit contained 6 tubes of IMP 1 and 6 tubes of IMP 2. The IMPs 1 and 2 were randomly assigned the codes A and B. For each random number/patient the IMP coded A was applied on test field 1 and the IMP coded B was applied on test field 2. The comparison of the IMPs was performed intraindividually.

Arms

Arm title	SB011 and Placebo

Arm description:

All patients performed treatment with formulation SB011 containing hgd40 and placebo. Treatment was performed on 2 test areas preferably disseminated and contralateral, comparable lesional treatment areas (each 50 cm²), located on the arms, legs, chest, stomach, or neck.

Arm type	Experimental
Investigational medicinal product name	SB011
Investigational medicinal product code	
Other name	hgd40
Pharmaceutical forms	Cutaneous suspension
Routes of administration	Topical

Dosage and administration details:

SB011
Topical multiple water/oil/water (W/O/W) formulation of SB011, containing 2% hgd40 in total; daily dosage was approximately 10 mg hgd40 (total dosage: approximately 145 mg hgd40).

Topical application of approximately 5 mg/cm² W/O/W formulation per treatment area (50 cm²) twice daily on 14 consecutive days and one single last application at the site on Day 15.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous emulsion
Routes of administration	Topical

Dosage and administration details:

Placebo
Active ingredient-free vehicle; Water/Oil/Water emulsion.

Topical application of approximately 5 mg/cm² W/O/W formulation per treatment area (50 cm²) twice daily on 14 consecutive days and one single last application at the site on Day 15.

Number of subjects in period 1	SB011 and Placebo
Started	25
Completed	23
Not completed	2
Physician decision	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	25	25	
Age categorical Units: Subjects			
Adults (18-64 years)	25	25	
Age continuous Units: years arithmetic mean standard deviation	 30.8 ± 10.2	 -	
Gender categorical Units: Subjects			
Female Male	14 11	14 11	
Race Units: Subjects			
Caucasian	25	25	
Body mass index Units: kg/m^2 arithmetic mean full range (min-max)	 24.1 19.6 to 29.3	 -	
SCORAD			
SCORAD* is a clinical tool for assessing the severity (i.e., extent, intensity) of atopic dermatitis. SCORAD was assessed at screening and on Day 1 (baseline) by the investigator. The intensity of each of the criteria erythema, edema/papulation, oozing/crusts, excoriations, lichenification and dryness were graded according to the following 4 point scale: 0=absent; 1=mild; 2=moderate; 3=severe. *SCORAD=SCORing atopic dermatitis			
Units: score arithmetic mean full range (min-max)	 44.5 38.5 to 49.7	 -	

End points

End points reporting groups

Reporting group title	SB011 and Placebo

Reporting group description:

All patients performed treatment with formulation SB011 containing hgd40 and placebo. Treatment was performed on 2 test areas preferably disseminated and contralateral, comparable lesional treatment areas (each 50 cm²), located on the arms, legs, chest, stomach, or neck.

Subject analysis set title	SB011
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The evaluation of efficacy was performed for the valid cases set (VCS), which is equivalent to the intention-to-treat analysis set. The VCS included all randomised patients without any major protocol violation, i.e. violations that would interfere with the primary analysis, as shown below.

Major protocol violation:
• Violation of inclusion criteria;
• Application of any interfering concomitant medication;
• Application of less than 60 % or more than 145% of the full planned IMP amount (7.25 g), i.e. less than 4.35 g or more than 10.51 g, of any of the two IMPs;
• Missing values of the modified local SCORAD (primary variable) on Day 15.

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The evaluation of efficacy was performed for the valid cases set (VCS), which is equivalent to the intention-to-treat analysis set. The VCS included all randomised patients without any major protocol violation, i.e. violations that would interfere with the primary analysis, as shown below.

Major protocol violation:
• Violation of inclusion criteria;
• Application of any interfering concomitant medication;
• Application of less than 60 % or more than 145% of the full planned IMP amount (7.25 g), i.e. less than 4.35 g or more than 10.51 g, of any of the two IMPs;
• Missing values of the modified local SCORAD (primary variable) on Day 15.

Primary: 1_Modified local SCORAD on Day 15 -- Change from baseline

End point title	1_Modified local SCORAD on Day 15 -- Change from baseline

End point description:

The modified local SCORAD* intensity scale represents one part of the SCORAD index, which is a severity scoring system for AD.
The intensity part includes the following local intensity criteria: erythema, edema/papulation, oozing/crusts, excoriations, and lichenification.

The intensity of each of the criteria was graded according to the 4 point scale: 0=absent; 1=mild; 2=moderate, 3=severe. The modified local SCORAD was calculated as the sum of the 5 individual scores (for the local symptoms specified above).

In this study, the severity of the lesions was assessed by the investigator at every visit.
The comparison of the IMPs was performed intra-individually.

*SCORAD=SCORing atopic dermatitis is a clinical tool for assessing the severity (i.e., extent, intensity) of AD

End point type	Primary

End point timeframe:

Baseline (before treatment), Day 15.

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[1]	22[2]		
Units: score				
arithmetic mean (standard deviation)	-2.6 (± 2.2)	-2.5 (± 1.8)		

Notes:

[1] - Valid cases set

[2] - Valid cases set

Statistical analyses

Statistical analysis title	SCORAD - Change from baseline Day 15

Statistical analysis description:

There was no subdivision into treatment groups. The same patients were treated with both the SB011 and placebo - applying the treatment at different, prespecifies body sites - on the same day.

The total number of subjects in this analysis shown below (N=44) is not correct; this is due to a known innate error of the EudraCT database system). The correct number of patients in this analysis is N=22.

Comparison groups	SB011 v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.8829
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.6

Notes:

[3] - The statistical evaluation was an exploratory.

Secondary: 2_Modified local SCORAD on Days 3, 5, 8, 12 -- Change from baseline

End point title	2_Modified local SCORAD on Days 3, 5, 8, 12 -- Change from baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline (before treatment), Days 3, 5, 8, 12

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[4]	22[5]		
Units: score				
arithmetic mean (standard deviation)				
Day 3	-0.8 (± 1.4)	-0.9 (± 0.9)		
Day 5	-1.9 (± 1.5)	-1.9 (± 1.4)		
Day 8	-2.5 (± 1.7)	-2.0 (± 1.6)		
Day 12	-2.5 (± 1.8)	-2.1 (± 2.0)		

Notes:

[4] - Valid cases set

[5] - Valid cases set

Statistical analyses

No statistical analyses for this end point

Secondary: 3_Modified local SCORAD on Days 1, 3, 5, 8, 12, 15

End point title	3_Modified local SCORAD on Days 1, 3, 5, 8, 12, 15

End point description:

End point type	Secondary

End point timeframe:

Baseline (before treatment), Days 1, 3, 5, 8, 12, 15

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[6]	22[7]		
Units: score				
arithmetic mean (standard deviation)				
Day 1	7.7 (± 0.8)	7.5 (± 0.7)		
Day 3	6.9 (± 1.8)	6.6 (± 1.0)		
Day 5	5.9 (± 1.7)	5.6 (± 1.5)		
Day 8	5.2 (± 1.6)	5.5 (± 1.8)		
Day 12	5.2 (± 1.8)	5.4 (± 2.1)		
Day 15	5.1 (± 2.2)	5.0 (± 1.9)		

Notes:

[6] - Valid cases set

[7] - Valid cases set

Statistical analyses

No statistical analyses for this end point

Secondary: 4_Transepidermal water loss (TEWL) -- on Days 3, 5, 8, 12, 15 -- -- Change from baseline

End point title	4_Transepidermal water loss (TEWL) -- on Days 3, 5, 8, 12, 15 -- -- Change from baseline

End point description:

Measurement of TEWL (evaporimetry) is a widely used non-invasive method for evaluation of skin impairment.

TEWL, expressed in grams per square cm and per hour, is used to study the water barrier function of the human skin. The more perfect the skin protective coat, the higher the water content and the lower the TEWL.

In this study, TEWL was measured using a Tewameter (TM 300, Courage & Khazaka, either attached to an MPA9 central unit and a PC with the appropriate software or as a stand-alone device) after acclimatisation of the patient for 30 minutes.

End point type	Secondary

End point timeframe:

Baseline (before treatment), Days 3, 5, 8, 12, 15

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[8]	22[9]		
Units: g/m²h				
arithmetic mean (full range (min-max))				
Day 3	-2.020 (-18.07 to 19.19)	-0.931 (-23.31 to 24.02)		
Day 5	-3.303 (-32.67 to 18.41)	-3.176 (-22.28 to 24.60)		
Day 8	-3.553 (-21.84 to 15.81)	-4.225 (-22.91 to 14.37)		
Day 12	-2.573 (-37.08 to 25.48)	-0.701 (-15.61 to 20.72)		
Day 15	-2.290 (-23.96 to 40.14)	2.312 (-20.43 to 48.76)		

Notes:

[8] - Valid cases set

[9] - Valid cases set

Statistical analyses

No statistical analyses for this end point

Secondary: 5_Transepidermal water loss (TEWL) -- on Days 1, 3, 5, 8, 12, 15

End point title	5_Transepidermal water loss (TEWL) -- on Days 1, 3, 5, 8, 12, 15

End point description:

Measurement of TEWL (evaporimetry) is a widely used non-invasive method for evaluation of skin impairment.

TEWL, expressed in grams per square cm and per hour, is used to study the water barrier function of the human skin. The more perfect the skin protective coat, the higher the water content and the lower the TEWL.

In this study, TEWL was measured using a Tewameter (TM 300, Courage & Khazaka, either attached to an MPA9 central unit and a PC with the appropriate software or as a stand-alone device) after acclimatisation of the patient for 30 minutes.

End point type	Secondary

End point timeframe:

Baseline (before treatment), Days 1, 3, 5, 8, 12, 15

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[10]	22[11]		
Units: g/m²h				
arithmetic mean (standard deviation)				
Day 1	30.643 (± 13.798)	29.142 (± 11.096)		
Day 3	28.622 (± 13.812)	28.211 (± 12.149)		
Day 5	27.340 (± 12.247)	25.966 (± 11.817)		
Day 8	27.090 (± 11.054)	24.917 (± 10.323)		
Day 12	28.070 (± 11.320)	28.440 (± 13.549)		
Day 15	28.353 (± 15.034)	31.454 (± 16.794)		

Notes:

[10] - Valid cases set

[11] - Valid cases set

Statistical analyses

No statistical analyses for this end point

Secondary: 6_Subjective assessment of pruritus -- on Days 1, 3, 5, 8, 12, 15

End point title	6_Subjective assessment of pruritus -- on Days 1, 3, 5, 8, 12, 15

End point description:

Severity of pruritus (itching) during the last 24 hours was assessed in each test area by asking the patients and recording the score of a 10-point scale ranging from: "no itching" (score 1) to "worst possible itching" (score 10).

End point type	Secondary

End point timeframe:

Baseline (before treatment), Days 1, 3, 5, 8, 12, 15

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[12]	22[13]		
Units: score				
arithmetic mean (standard deviation)				
Day 1	5.2 (± 1.7)	5.4 (± 1.6)		
Day 3	4.4 (± 1.7)	4.2 (± 1.8)		

Day 5	3.4 (± 1.5)	3.9 (± 1.9)		
Day 8	3.4 (± 1.4)	3.4 (± 1.6)		
Day 12	3.6 (± 1.8)	3.6 (± 2.0)		
Day 15	3.7 (± 1.9)	3.6 (± 2.0)		

Notes:

[12] - Valid cases set

[13] - Valid cases set

Statistical analyses

No statistical analyses for this end point

Secondary: 7_Subjective efficacy assessment on Days 3, 5, 8, 12, 15

End point title	7_Subjective efficacy assessment on Days 3, 5, 8, 12, 15

End point description:

Efficacy of the IMPs was assessed in each test area by asking the patients to use the following 5-point rating score scale: 0=No activity; 1=Poor; 2=Fair; 3=Good; 4=Excellent.

End point type	Secondary

End point timeframe:

Baseline (before treatment), Days 3, 5, 8, 12, 15

Baseline(Day 1)=Last observation collected prior to application of first dose of study drug.

End point values	SB011	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[14]	22[15]		
Units: score				
arithmetic mean (standard deviation)				
Day 3	1.6 (± 1.1)	1.7 (± 1.1)		
Day 5	1.7 (± 0.9)	1.8 (± 1.0)		
Day 8	1.9 (± 1.1)	2.1 (± 1.2)		
Day 12	1.8 (± 1.2)	2.0 (± 1.1)		
Day 15	2.0 (± 1.2)	2.1 (± 1.2)		

Notes:

[14] - Valid cases set

[15] - Valid cases set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were monitored throughout the study: from the time of signing the informed consent form until end of study visit or up to study discontinuation.

Adverse event reporting additional description:

The safety evaluation set (SES) included all patients who received any IMP at least once; all safety and pharmacokinetic analyses were based on the SES.

Skin area fields, treated with the SB011 (test) and placebo, were assessed and reported separately.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.5

Reporting groups

Reporting group title	SB011
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	SB011	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SB011	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 25 (44.00%)	10 / 25 (40.00%)	
Skin and subcutaneous tissue disorders			
Burning sensation			
subjects affected / exposed	8 / 25 (32.00%)	8 / 25 (32.00%)	
occurrences (all)	12	12	
Pustule			
subjects affected / exposed	1 / 25 (4.00%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			

Tension pain subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 25 (4.00%) 1	
Infections and infestations Biopsy wound infection subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	2 / 25 (8.00%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2014	Amendment 03 to the original clinical trial protocol was necessary because the inclusion criterion No. 3 was partly changed; Body weight according to a Body Mass Index (BMI) ≥18.0 and ≤29.0 kg/m².
01 June 2016	Amendment 05 was necessary because the in- and exclusion criteria were changed to facilitate recruitment; restriction by Body Mass index (BMI) was deleted. Patients with a resting heart rate <50 and >100 bpm, systolic blood pressure <90 and >150 mmHg, diastolic blood pressure <50 and >95 mmHg, on condition that the patient does not present any clinical symptoms of hypotension. Patients smoking ≤10 cigarettes/day.
30 June 2016	Amendment 07 to clinical trial protocol was necessary because the deputy investigator has changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported