Clinical trial results:
SB012 for the treatment of active ulcerative colitis (SECURE): a prospective, multi-centre, randomised, double-blind, placebo-controlled phase IIa clinical trial to evaluate the efficacy, pharmacokinetics, tolerability, and safety of SB012 enema administered once daily

Summary

EudraCT number	2013-004599-36
Trial protocol	DE
Global end of trial date	20 June 2017

Results information

Result version number	v1 (current)
This version publication date	25 December 2021
First version publication date	25 December 2021

Trial information

Trial identification

Sponsor protocol code	SB012/01/2013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02129439
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	21 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical trial is to evaluate the efficacy of SB012 enema in subjects with moderate to severe active ulcerative colitis at end of treatment.

Subjects with moderate to severe active ulcerative colitis were randomised to treatment with either SB012 or placebo at a 2:1 ratio, in a multi-centre setting. Subjects were treated as out-patients and self-administered the IMP. The study consisted of a treatment and a follow-up phase.

SB012 is a DNAzyme-based GATA-3 antagonist investigated in a major chronic inflammatory indication (ulcerative colitis). SB012 is enema-applied formulation for the potential treatment of ulcerative colitis

The active principle hgd40 of the investigational medicinal product SB012 belongs to a new class of antisense oligonucleotide therapeutics, the 10-23 DNA(deoxyribonucleic acid)zymes (antisense oligonucleotide). DNAzymes are catalytically active nucleic acids that cleave complementary RNA (ribonucleic acid).

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 June 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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 20 adult subjects both male and female, 18 to 75 years, with active ulcerative colitis were eligible for enrolment into the trial.

Pre-assignment

Screening details:

Adult male and female subjects (18 to 75 years) with active ulcerative colitis 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
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SB012

Arm description:

Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to SB012 enema. Rectal administration of IMPs (placebo enema: 30ml) was performed once daily (preferably at bedtime) by the subjects at home, after completing an instruction and training session at the trial centre on Day 1 (V3) — except for the first (Day 1/V3) and last (Day 29/V8) IMP administration, which were done at the trial centre.

Arm type	Placebo
Investigational medicinal product name	SB012
Investigational medicinal product code	
Other name	hgd40
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

SB012 (active substance: hgd40)

Liquid solution, concentration of 7.5mg/ml hgd40 in 30ml phosphate buffered saline (PBS).

Rectal administration of IMP (enema: plastic rectal tube, 30ml) once daily (preferably at bedtime) by the subject at home except for the first (Day 1/Visit [V] 3) and last (Day 28/V7) IMP administration which were performed at the trial centre in the morning, each.

Arm title	Placebo

Arm description:

Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to placebo enema. Rectal administration of IMPs (placebo enema: 30ml) was performed once daily (preferably at bedtime) by the subjects at home, after completing an instruction and training session at the trial centre on Day 1 (V3) — except for the first (Day 1/V3) and last (Day 29/V8) IMP administration, which were done at the trial centre.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Placebo

Liquid solution

Rectal administration of IMP (enema: plastic rectal tube, 30ml) once daily (preferably at bedtime) by the subject at home except for the first (Day 1/V3) and last (Day 28/V7) IMP administration which were performed at the trial centre in the morning, each.

Number of subjects in period 1	SB012	Placebo
Started	13	7
Completed	12	6
Not completed	1	1
Physician decision	1	-
Adverse event, non-fatal	-	1

Period 2

Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SB012

Arm description:

No treatment was administered during the Follow-up period.
Patients were followed-up by phone call on day 42±3, to assess the Clinical Mayo score#; adverse events/serious adverse events; and concomitant medications.

The Clinical Mayo score represents a subscore of the Total Mayo score and comprises the components stool frequency and rectal bleeding. It ranges from 0 to 6.

Arm type	Experimental
Investigational medicinal product name	SB012
Investigational medicinal product code	
Other name	hgd40
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

No treatment was administered during the Follow-up period.

Arm title	Placebo

Arm description:

No treatment was administered during the Follow-up period.
Patients were followed-up by phone call on day 42±3, to assess the Clinical Mayo score#; adverse events/serious adverse events; and concomitant medications.

The Clinical Mayo score represents a subscore of the Total Mayo score and comprises the components stool frequency and rectal bleeding. It ranges from 0 to 6.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

No treatment was administered during the Follow-up period.

Number of subjects in period 2	SB012	Placebo
Started	12	6
Completed	8	2
Not completed	4	4
Physician decision	3	2
Consent withdrawn by subject	1	-
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	SB012
Reporting group description:	
Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to SB012 enema. Rectal administration of IMPs (placebo enema: 30ml) was performed once daily (preferably at bedtime) by the subjects at home, after completing an instruction and training session at the trial centre on Day 1 (V3) — except for the first (Day 1/V3) and last (Day 29/V8) IMP administration, which were done at the trial centre.	
Reporting group title	Placebo
Reporting group description:	
Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to placebo enema. Rectal administration of IMPs (placebo enema: 30ml) was performed once daily (preferably at bedtime) by the subjects at home, after completing an instruction and training session at the trial centre on Day 1 (V3) — except for the first (Day 1/V3) and last (Day 29/V8) IMP administration, which were done at the trial centre.	

Reporting group values	SB012	Placebo	Total
Number of subjects	13	7	20
Age categorical Units: Subjects			
Adults (18-64 years)	13	7	20
Age continuous Units: years			
arithmetic mean	36.5	35.0	
standard deviation	± 13.1	± 12.4	-
Gender categorical Units: Subjects			
Female	7	1	8
Male	6	6	12
Race Units: Subjects			
Caucasian	12	7	19
Mixed (Black American-Caucasian)	1	0	1
Glucorticoid use at baseline Units: Subjects			
Yes	7	1	8
No	6	6	12
Body mass index Units: kg/m^2			
arithmetic mean	24.29	24.50	
full range (min-max)	19.5 to 28.9	20.0 to 29.0	-
Duration of colitis ulcerosa Units: year			
arithmetic mean	8.10	6.63	
standard deviation	± 8.00	± 3.21	-

End points

End points reporting groups

Reporting group title	SB012

Reporting group description:

Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to SB012 enema. Rectal administration of IMPs (placebo enema: 30ml) was performed once daily (preferably at bedtime) by the subjects at home, after completing an instruction and training session at the trial centre on Day 1 (V3) — except for the first (Day 1/V3) and last (Day 29/V8) IMP administration, which were done at the trial centre.

Reporting group title	Placebo

Reporting group description:

Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to placebo enema. Rectal administration of IMPs (placebo enema: 30ml) was performed once daily (preferably at bedtime) by the subjects at home, after completing an instruction and training session at the trial centre on Day 1 (V3) — except for the first (Day 1/V3) and last (Day 29/V8) IMP administration, which were done at the trial centre.

Reporting group title	SB012

Reporting group description:

No treatment was administered during the Follow-up period.
Patients were followed-up by phone call on day 42±3, to assess the Clinical Mayo score#; adverse events/serious adverse events; and concomitant medications.

The Clinical Mayo score represents a subscore of the Total Mayo score and comprises the components stool frequency and rectal bleeding. It ranges from 0 to 6.

Reporting group title	Placebo

Reporting group description:

No treatment was administered during the Follow-up period.
Patients were followed-up by phone call on day 42±3, to assess the Clinical Mayo score#; adverse events/serious adverse events; and concomitant medications.

The Clinical Mayo score represents a subscore of the Total Mayo score and comprises the components stool frequency and rectal bleeding. It ranges from 0 to 6.

Primary: 1_Total Mayo score -- After 4 weeks -- Change from baseline

End point title	1_Total Mayo score -- After 4 weeks -- Change from baseline

End point description:

Change from baseline

Change in Total Mayo score# after 4 weeks of treatment (Week 4, Day 28) compared with baseline value in the active treatment group (SB012) and in the Placebo group.

The Total Mayo score is a 13-point ordinal scale for the assessment of concurrent severity of ulcerative colitis. It comprises of four components: stool frequency, rectal bleeding, endoscopic findings, and physician’s global assessment of disease severity. Each component has four grades ranging from 0 to 3. The Total Mayo score ranges from 0 to 12, with 12 representing the most severe disease (disease severity scores: 0-2=Remission, 3-5=Mild, 6-10=Moderate, 11-12=Severe)

End point type	Primary

End point timeframe:

Baseline (pre treatment), after treatment at week 4 (Day 28).

Baseline=Last observation collected prior to application of first dose of IMP

End point values	SB012	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[1]	6[2]		
Units: score				
arithmetic mean (standard deviation)	-1.8 (± 1.6)	-1.0 (± 1.3)		

Notes:

[1] - Per protocol set

[2] - Per protocol set

Statistical analyses

Statistical analysis title	Treatment effect -- Between groups
Comparison groups	SB012 v Placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2864 [3]
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimate
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1

Notes:

[3] - Two-sided exact Wilcoxon signed-rank test

Primary: 2_Total Mayo score -- After 4 weeks -- Actual values

End point title	2_Total Mayo score -- After 4 weeks -- Actual values[4]

End point description:

Actual values

Total Mayo score after 4 weeks of treatment (Week 4, Day 28) in the active treatment group (SB012) and in the Placebo group.

Details regarding the Total Mayo score are presented in the description for end point 1.

End point type	Primary

End point timeframe:

Baseline (pre treatment), after treatment at week 4 (Day 28).

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical evaluation for the actual Total Mayo score results was not performed.
Please refer to the statistical analysis shown for end point 1 (Total Mayo score -- Change from baseline).

End point values	SB012	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[5]	6[6]		
Units: score				
arithmetic mean (standard deviation)	6.5 (± 2.6)	9.0 (± 1.3)		

Notes:

[5] - Per protocol set

[6] - Per protocol set

Statistical analyses

No statistical analyses for this end point

Secondary: 3_Total Mayo score -- After 8 weeks -- Change from baseline

End point title	3_Total Mayo score -- After 8 weeks -- Change from baseline

End point description:

Change in Total Mayo score# 8 weeks after start of treatment (week 8, Day 56, end of study) compared with baseline value in the active treatment group (SB012) and in the Placebo group

Details regarding the Total Mayo score are presented in the description for end point 1.
For secondary efficacy end points, the analyses were performed descriptively.

End point type	Secondary

End point timeframe:

Baseline (pre treatment), after treatment at week 8 (Day 56).

Baseline=Last observation collected prior to application of first dose of IMP

End point values	SB012	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[7]	2[8]		
Units: score				
arithmetic mean (standard deviation)	-3.0 (± 1.6)	-1.5 (± 2.1)		

Notes:

[7] - Per protocol set

[8] - Per protocol set

Statistical analyses

No statistical analyses for this end point

Secondary: 4_Total Mayo score -- After 8 weeks -- Actual values

End point title	4_Total Mayo score -- After 8 weeks -- Actual values

End point description:

Actual values

Total Mayo score after 8 weeks of treatment (Week 8, Day 56) in the active treatment group (SB012) and in the Placebo group.

Details regarding the Total Mayo score are presented in the description for end point 1.

End point type	Secondary

End point timeframe:

Baseline (pre treatment), after treatment at week 8 (Day 56).

End point values	SB012	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[9]	2[10]		
Units: score				
arithmetic mean (standard deviation)	5.0 (± 3.5)	9.0 (± 1.4)		

Notes:

[9] - Per protocol set

[10] - Per protocol set

Statistical analyses

No statistical analyses for this end point

Secondary: 5_Endoscopic Mayo score -- After 4 weeks -- Change from baseline

End point title	5_Endoscopic Mayo score -- After 4 weeks -- Change from baseline

End point description:

Change in Endoscopic Mayo score# 4 weeks (Day 28) after start of treatment compared with baseline value in the active treatment group (SB012) vs. Placebo.

Results show the number of subjects achieving an Endoscopic Mayo score change from baseline of -1, 0, or 1.

The Endoscopic Mayo score represents a subscore of the Total Mayo score and consists of the endoscopic findings. It ranges from 0 to 3 (0 = normal or inactive disease, 1=Mild disease [erythema, decreased vascular pattern, mild friability], 2=Moderate disease [marked erythema, absent vascular pattern, friability, erosions], 3=Severe disease [spontaneous bleeding, ulceration]).

Secondary efficacy analyses were performed descriptively.

End point type	Secondary

End point timeframe:

Baseline (pre treatment), after treatment at week 4 (Day 28).

Baseline=Last observation collected prior to application of first dose of IMP

End point values	SB012	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[11]	6[12]		
Units: subjects				
Change from baseline of -1	2	1		
Change from baseline of 0	10	5		
Change from baseline of 1	1	0		
Missing	0	0		

Notes:

[11] - Per protocol set

[12] - Per protocol set

Statistical analyses

No statistical analyses for this end point

Secondary: 6_Endoscopic Mayo score -- After 8 weeks -- Change from baseline

End point title	6_Endoscopic Mayo score -- After 8 weeks -- Change from baseline

End point description:

Change in Endoscopic Mayo score* 8 weeks (Day 56) after start of treatment compared with baseline value in the active treatment group (SB012) vs. Placebo.

Results show the number of subjects achieving an Endoscopic Mayo score change from baseline of -1, 0, or 1.

* The Endoscopic Mayo score represents a subscore of the Total Mayo score and consists of the endoscopic findings. It ranges from 0 to 3 (0 = normal or inactive disease, 1=Mild disease [erythema, decreased vascular pattern, mild friability], 2=Moderate disease [marked erythema, absent vascular pattern, friability, erosions], 3=Severe disease [spontaneous bleeding, ulceration]).

Secondary efficacy analyses were performed descriptively.

End point type	Secondary

End point timeframe:

Baseline (pre treatment), after treatment at week 8 (Day 56).

Baseline=Last observation collected prior to application of first dose of IMP

End point values	SB012	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[13]	2[14]		
Units: subjects				
Change from baseline of -1	4	1		
Change from baseline of 0	3	1		
Change from baseline of 1	0	0		
Missing	6	4		

Notes:

[13] - Per protocol set

[14] - Per protocol set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study: from the time when the informed consent form was signed until end of study visit (V10, Day 56±3 days), or up to study discontinuation visit.

Adverse event reporting additional description:

An AE was any untoward medical occurrence in a subject using the investigational medicinal product (IMP) and which did not necessarily have a causal relationship with this treatment.
TEAEs were regarded as "treatment emergent" AEs, if not seen before treatment or, if already present before treatment, worsened after start of treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	SB012

Reporting group description:

Subjects exposed once daily over a 4-week treatment period (28 consecutive days) to SB012 enema.

Reporting group title	Placebo

Reporting group description:

Subjects were exposed once daily over a 4-week treatment period (28 consecutive days) to placebo enema.

Serious adverse events	SB012	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SB012	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 13 (76.92%)	5 / 7 (71.43%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 13 (23.08%)	3 / 7 (42.86%)	
occurrences (all)	4	3	
Tension headache			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Malaise			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	3 / 13 (23.08%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
General physical health deterioration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Colitis ulcerative			
subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Diarrhoea			
subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	
occurrences (all)	3	0	

Dyspepsia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2015	Protocol amendment 3 was submitted to the leading EC as clinical trial protocol version 3.0 because the following changes were instituted: inclusion of a second trial centre to facilitate timely enrolment of subjects, change of the trial design from single- to multi-centre, and a more precise description of the subject replacement procedure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported