Clinical trial results:
A 48-week, phase II, randomized, double-blind, placebo controlled, proof of concept and dose-finding study of three different dose regimens of BI 655066 administered subcutaneously in patients with ankylosing spondylitis

Summary

EudraCT number	2013-003666-13
Trial protocol	ES FI DE IT BE NL
Global end of trial date	26 July 2016

Results information

Result version number	v1 (current)
This version publication date	06 August 2017
First version publication date	06 August 2017

Trial information

Trial identification

Sponsor protocol code	1311.8

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02047110
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.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 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 March 2015
Global end of trial reached?	Yes
Global end of trial date	26 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This trial assessed the efficacy and safety of three subcutaneous doses of BI 655066 in adult patients with ankylosing spondylitis (AS) for clinical proof of concept and dose selection.
The primary objective was to compare the efficacy of BI 655066 with placebo.
The assessment of efficacy was based on the percentage of patients who achieved a clinical response according to the Assessment in SpondyloArthritis international Society 40 (ASAS 40) criteria at Week 12.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Finland: 20
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Hong Kong: 10
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Korea, Republic of: 13
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Taiwan: 55
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	219
EEA total number of subjects	121

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)	216
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial had a DB treatment period up to Week 24, an Escape treatment period up to Week 40, and an open-label-extension (OLE) treatment period that lasted 26 weeks after OLE entry. Each of the treatment periods was followed by a 24- week post-treatment follow-up period.

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subjects) met all inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated

Period 1

Period 1 title	DB treatment period up to Week 24
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Double-blind trial; The patients, investigators, site staff, and the study team were blinded to treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period

Arm type	Placebo
Investigational medicinal product name	matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period

Arm title	BI 655066 18 mg

Arm description:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks

Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks

Arm title	BI 655066 90 mg

Arm description:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Arm title	BI 655066 180 mg
Arm description:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	

Number of subjects in period 1[1]	Placebo	BI 655066 18 mg	BI 655066 90 mg
Started	40	40	39
Completed	35	38	36
Not completed	5	2	3
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	-	-
Other than specified	1	2	3
Lost to follow-up	1	-	-
Protocol deviation	1	-	-

Number of subjects in period 1[1]	BI 655066 180 mg
Started	40
Completed	38
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Other than specified	1
Lost to follow-up	-

Protocol deviation	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one of the trial medication.

Period 2

Period 2 title	DB (Week 12 up to Week 24)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Double-blind trial; The patients, investigators, site staff, and the study team were blinded to treatment allocation. As patients from the previous period continue in this period, hence non-mutually exclusive arms.

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period

Arm type	Placebo
Investigational medicinal product name	matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period

Arm title	BI 655066 18 mg

Arm description:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks

Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks

Arm title	BI 655066 90 mg

Arm description:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Arm title	BI 655066 180 mg
Arm description:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	

Number of subjects in period 2	Placebo	BI 655066 18 mg	BI 655066 90 mg
Started	9	17	13
Completed	9	15	12
Not completed	0	2	1
Consent withdrawn by subject	-	1	-
Other than specified	-	1	1

Number of subjects in period 2	BI 655066 180 mg
Started	12
Completed	12
Not completed	0
Consent withdrawn by subject	-
Other than specified	-

Period 3

Period 3 title	Escape treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Double-blind trial; The patients, investigators, site staff, and the study team were blinded to treatment allocation. As patients from the previous period continue in this period, hence non-mutually exclusive arms.

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 week (At Day1 and at Week 8) up to 2 times during the regular treatment period.
For escape period, the patients who did not achieve Assessment in SpondyloArthritis international Society 20 (ASAS 20) response at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm type	Placebo
Investigational medicinal product name	matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 week (At Day1 and at Week 8) up to 2 times during the regular treatment period.
For escape period, the patients who did not achieve Assessment in SpondyloArthritis international Society 20 (ASAS 20) response at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm title	BI 655066 18 mg

Arm description:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo at week 8, up to 2 times during the regular treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo at week 8, up to 2 times during the regular treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm title	BI 655066 90 mg

Arm description:

Subcutaneous injection of BI 655066 90 mg administered at Day 1 and Week 8, up to 2 times during the treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm type	Experimental

Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 90 mg administered at Day 1 and Week 8, up to 2 times during the treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm title	BI 655066 180 mg

Arm description:

Subcutaneous injection of BI 655066 180 mg administered at Day 1 and Week 8, up to 2 times during the treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 180 mg administered at Day 1 and Week 8, up to 2 times during the treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Number of subjects in period 3	Placebo	BI 655066 18 mg	BI 655066 90 mg
Started	26	21	23
Completed	23	15	20
Not completed	3	6	3
Consent withdrawn by subject	1	2	1
Adverse event, non-fatal	1	2	2
Other than specified	1	2	-

Number of subjects in period 3	BI 655066 180 mg
Started	26
Completed	24
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Other than specified	1

Period 4

Period 4 title	OLE treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

Double-blind trial; The patients, investigators, site staff, and the study team were blinded to treatment allocation. As patients from the previous period continue in this period, hence non-mutually exclusive arms.

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm type	Placebo
Investigational medicinal product name	matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm title	BI 655066 18 mg

Arm description:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm title	BI 655066 90 mg

Arm description:

Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm type	Experimental

Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm title	BI 655066 180 mg

Arm description:

Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Arm type	Experimental
Investigational medicinal product name	BI 655066
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Number of subjects in period 4	Placebo	BI 655066 18 mg	BI 655066 90 mg
Started	4	8	5
Completed	4	8	4
Not completed	0	0	1
Other than specified	-	-	1

Number of subjects in period 4	BI 655066 180 mg
Started	9
Completed	9
Not completed	0
Other than specified	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	BI 655066 18 mg
Reporting group description:	
Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks	
Reporting group title	BI 655066 90 mg
Reporting group description:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	BI 655066 180 mg
Reporting group description:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	

Reporting group values	Placebo	BI 655066 18 mg	BI 655066 90 mg
Number of subjects	40	40	39
Age categorical			
Units: Subjects			

Age Continuous			
Treated set (TS): All patients who received at least 1 dose of trial medication			
Units: years			
arithmetic mean	37.6	38	39.5
standard deviation	± 11	± 11.1	± 10.8
Gender, Male/Female			
Treated set (TS): All patients who received at least 1 dose of trial medication			
Units: Subjects			
Female	15	12	9
Male	25	28	30

Reporting group values	BI 655066 180 mg	Total	
Number of subjects	40	159	
Age categorical			
Units: Subjects			

Age Continuous			
Treated set (TS): All patients who received at least 1 dose of trial medication			
Units: years			
arithmetic mean	40.6		
standard deviation	± 11.9	-	
Gender, Male/Female			
Treated set (TS): All patients who received at least 1 dose of trial medication			
Units: Subjects			

Female	10	46	
Male	30	113	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	BI 655066 18 mg
Reporting group description:	
Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks	
Reporting group title	BI 655066 90 mg
Reporting group description:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	BI 655066 180 mg
Reporting group description:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	Placebo
Reporting group description:	
Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	BI 655066 18 mg
Reporting group description:	
Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks	
Reporting group title	BI 655066 90 mg
Reporting group description:	
Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	BI 655066 180 mg
Reporting group description:	
Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period	
Reporting group title	Placebo
Reporting group description:	
Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 week (At Day1 and at Week 8) up to 2 times during the regular treatment period. For escape period, the patients who did not achieve Assessment in SpondyloArthritis international Society 20 (ASAS 20) response at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)	
Reporting group title	BI 655066 18 mg
Reporting group description:	
Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo at week 8, up to 2 times during the regular treatment period. For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)	
Reporting group title	BI 655066 90 mg
Reporting group description:	
Subcutaneous injection of BI 655066 90 mg administered at Day 1 and Week 8, up to 2 times during the treatment period. For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)	

Reporting group title	BI 655066 180 mg

Reporting group description:

Subcutaneous injection of BI 655066 180 mg administered at Day 1 and Week 8, up to 2 times during the treatment period.
For escape period, the patients who did not achieve ASAS 20 at week 12 received up to 4 additional injections of 180 mg from week 16 (total of 6 injections)

Reporting group title	Placebo

Reporting group description:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Reporting group title	BI 655066 18 mg

Reporting group description:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Reporting group title	BI 655066 90 mg

Reporting group description:

Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Reporting group title	BI 655066 180 mg

Reporting group description:

Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period.
For OLE treatment period, the patient received 4 additional 180 mg treatments

Primary: Percentage of patients who achieved Assessment of Spondyloarthritis International Society (ASAS) 40 improvement criteria at Week 12.

End point title	Percentage of patients who achieved Assessment of Spondyloarthritis International Society (ASAS) 40 improvement criteria at Week 12.

End point description:

ASAS 40 evaluations are based on the following 4 components (also called domains) that include patient' self-assessments on a numerical rating scale (NRS) from 0 to 10 with higher numbers representing a worse disease status: -Global AS disease activity -Inflammation based on the mean of Bath AS Disease Activity Index (BASDAI) questions addressing the level of morning stiffness and duration -Spinal pain based on the mean of 2 questions -Physical function based on the Bath AS Functional Index (BASFI) The ASAS 40 response is defined as an improvement in 3 of 4 components and no worsening in the remaining component; an improvement is defined as a reduction from baseline of ≥40% and an absolute reduction of ≥2 units in each of the 3 components. Full Analysis set (FAS) is the population set for this endpoint. FAS comprised of all randomised patients who received at least 1 dose of trial medication

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[1]	40[2]	39[3]	40[4]
Units: Percentage of participants				
number (not applicable)	17.5	25	20.5	15

Notes:

[1] - FAS

[2] - FAS

[3] - FAS

[4] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

To control the type I error rate, the primary endpoint was tested in a hierarchical fixed sequence approach. The proportion of patients achieving ASAS 40 response at Week 12 was pairwise compared in the following sequence: BI 655066 180 mg vs. placebo (1.) and BI 655066 90 mg vs. placebo (2.). The significance level was 5% (1-sided). The comparison BI 655066 18 mg vs. placebo was not included in the formal testing sequence; an exploratory p-value was provided.

Comparison groups	Placebo v BI 655066 18 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.2652 [6]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	7.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.1
upper limit	26.6

Notes:

[5] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper-Pearson method. Difference calculated as "BI 655066 18 mg minus Placebo".

[6] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the primary endpoint, ASAS 40 response at Week 12, between treatment groups.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

To control the type I error rate, the primary endpoint was tested in a hierarchical fixed sequence approach. The proportion of patients achieving ASAS 40 response at Week 12 was pairwise compared in the following sequence: BI 655066 180 mg vs. placebo (1.) and BI 655066 90 mg vs. placebo (2.). The significance level was 5% (1-sided). The comparison BI 655066 18 mg vs. placebo was not included in the formal testing sequence; an exploratory p-value was provided.

Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.4129 [8]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	3

Confidence interval	
level	90 %
sides	2-sided
lower limit	-15.9
upper limit	20.8

Notes:

[7] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 90 mg minus Placebo".
[8] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the primary endpoint, ASAS 40 response at Week 12, between treatment groups.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

To control the type I error rate, the primary endpoint was tested in a hierarchical fixed sequence approach. The proportion of patients achieving ASAS 40 response at Week 12 was pairwise compared in the following sequence: BI 655066 180 mg vs. placebo (1.) and BI 655066 90 mg vs. placebo (2.). The significance level was 5% (1-sided). The comparison BI 655066 18 mg vs. placebo was not included in the formal testing sequence; an exploratory p-value was provided.

Comparison groups	Placebo v BI 655066 180 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.4243 [10]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	-2.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.8
upper limit	17

Notes:

[9] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 180 mg minus Placebo".
[10] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the primary endpoint, ASAS 40 response at Week 12, between treatment groups

Secondary: Change from baseline to Week 12 in disease activity assessed by the Ankylosing Spondylitis Disease Activity Score (ASDAS).

End point title	Change from baseline to Week 12 in disease activity assessed by the Ankylosing Spondylitis Disease Activity Score (ASDAS).

End point description:

This is the key secondary endpoint. ASDAS score is calculated with a formula integrating C-reactive serum protein (CRP) level [milligram per Litre (mg/L)] in serum and 4 variables of patients' assessments based on NRS: back pain based on BASDAI question 2; duration of morning stiffness based on BASDAI question 6; global AS disease activity; peripheral joint pain/swelling based on BASDAI question 3.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[11]	40[12]	39[13]	40[14]
Units: Unit on scale				
median (inter-quartile range (Q1-Q3))	-0.2 (-0.9 to 0.2)	-0.7 (-1.3 to -0.2)	-0.6 (-1 to 0.1)	-0.7 (-1.1 to -0.3)

Notes:

[11] - FAS

[12] - FAS

[13] - FAS

[14] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v BI 655066 18 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.0229 [16]
Method	Wilcoxon rank−sum test
Parameter estimate	Median estimate by Hodges−Lehmann method
Point estimate	-0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.7
upper limit	-0.1

Notes:

[15] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Moses method. Difference calculated as "BI 655066 18 mg minus Placebo".
[16] - One sided p-value from Wilcoxon rank−sum test

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.1038 [18]
Method	Wilcoxon rank−sum test
Parameter estimate	Median estimate by Hodges−Lehmann method
Point estimate	-0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.6
upper limit	0.1

Notes:

[17] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Moses method. Difference calculated as "BI 655066 90 mg minus Placebo".
[18] - One sided p-value from Wilcoxon rank−sum test

Statistical analysis title	Statistical analysis 3

Comparison groups	Placebo v BI 655066 180 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.0101 [20]
Method	Wilcoxon rank−sum test
Parameter estimate	Median estimate by Hodges−Lehmann method
Point estimate	-0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.7
upper limit	-0.1

Notes:

[19] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Moses method. Difference calculated as "BI 655066 180 mg minus Placebo".
[20] - One sided p-value from Wilcoxon rank−sum test

Secondary: Percentage of patients who achieved ASAS 5/6 improvement criteria at Week 12

End point title	Percentage of patients who achieved ASAS 5/6 improvement criteria at Week 12

End point description:

The ASAS 5/6 evaluation is based on 6 components: -Global AS disease activity -Inflammation based on the mean of BASDAI questions addressing the level-of morning stiffness and duration -Spinal pain -Physical function based on the Bath AS Functional Index (BASFI) -Spinal mobility assessment (lateral lumbar flexion), corresponding to one out of 5 measurements of Bath Ankylosing Spondylitis Metrology Index (BASMI) -Serum CRP levels The ASAS 5/6 response is defined as an improvement in any 5 of the 6 components and no worsening in the remaining component. A reduction from baseline of ≥20% is defined as an improvement according to the ASAS criteria.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[21]	40[22]	39[23]	40[24]
Units: Percentage of participants				
number (not applicable)	5	20	23.1	17.5

Notes:

[21] - FAS

[22] - FAS

[23] - FAS

[24] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v BI 655066 18 mg

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.0238 [26]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.6
upper limit	33.8

Notes:

[25] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper-Pearson method. Difference calculated as "BI 655066 18 mg minus Placebo".
[26] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 12, between treatment groups.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.012 [28]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	18.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.8
upper limit	35.3

Notes:

[27] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 90 mg minus Placebo".
[28] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 12, between treatment groups.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v BI 655066 180 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.0465 [30]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	12.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.1
upper limit	31.4

Notes:

[29] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 180 mg minus Placebo".
[30] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 12, between treatment groups

Secondary: Percentage of patients who achieved partial remission according to the ASAS criteria at Week 12

End point title	Percentage of patients who achieved partial remission according to the ASAS criteria at Week 12

End point description:

Percentage of patients who achieved partial remission according to the ASAS criteria at Week 12 is presented

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[31]	40[32]	39[33]	40[34]
Units: Percentage of participants				
number (not applicable)	2.5	2.5	2.6	10

Notes:

[31] - FAS

[32] - FAS

[33] - FAS

[34] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

p-values are not presented as they were not meaningful; 3 treatment groups had only a single patient with partial remission.

Comparison groups	Placebo v BI 655066 18 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[35]
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-19.4
upper limit	19.4

Notes:

[35] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper-Pearson method. Difference calculated as "BI 655066 18 mg minus Placebo".

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

p-values are not presented as they were not meaningful; 3 treatment groups had only a single patient with partial remission.

Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[36]
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.3
upper limit	18.3

Notes:

[36] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 90 mg minus Placebo".

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

p-values are not presented as they were not meaningful; 3 treatment groups had only a single patient with partial remission.

Comparison groups	Placebo v BI 655066 180 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[37]
Parameter estimate	Risk difference (RD)
Point estimate	7.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.1
upper limit	26.6

Notes:

[37] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 180 mg minus Placebo".

Secondary: Percentage of patients who achieved ASAS 20 improvement criteria at Week 12

End point title	Percentage of patients who achieved ASAS 20 improvement criteria at Week 12

End point description:

ASAS 20 evaluations are based on the following 4 components (also called domains) that include patient' self-assessments on a numerical rating scale (NRS) from 0 to 10 with higher numbers representing a worse disease status: -Global AS disease activity -Inflammation based on the mean of Bath AS Disease Activity Index (BASDAI) questions addressing the level of morning stiffness and duration -Spinal pain based on the mean of 2 questions -Physical function based on the Bath AS Functional Index (BASFI) The ASAS 20 response is defined as an improvement in 3 of 4 components and no worsening in the remaining component; an improvement is defined as a reduction from baseline of ≥20% and an absolute reduction of ≥1 units in each of the 3 components.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[38]	40[39]	39[40]	40[41]
Units: Percentage of participants				
number (not applicable)	20	45	33.3	32.5

Notes:

[38] - FAS

[39] - FAS

[40] - FAS

[41] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v BI 655066 18 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.0092 [43]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	25
Confidence interval	
level	90 %
sides	2-sided
lower limit	5.5
upper limit	43.1

Notes:

[42] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper-Pearson method. Difference calculated as "BI 655066 18 mg minus Placebo".

[43] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 12, between treatment groups.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	= 0.1243 [45]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	13.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.9
upper limit	30.5

Notes:

[44] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 90 mg minus Placebo".
[45] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 12, between treatment groups.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v BI 655066 180 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[46]
P-value	= 0.1198 [47]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	12.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.1
upper limit	31.4

Notes:

[46] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 180 mg minus Placebo".
[47] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 12, between treatment groups

Secondary: Change from baseline to Week 12 in disease activity assessed by BASDAI

End point title	Change from baseline to Week 12 in disease activity assessed by BASDAI

End point description:

BASDAI assesses the AS disease activity of a patient within the last week based on 6 questions on a NRS (1 to 10) How would you describe the overall level of 1] fatigue/tiredness you have experienced? 2] AS neck, back or hip pain you have had? 3] pain/swelling in joints other than neck, back or hips you have had? 4] discomfort you have had from any areas tender to touch or pressure? 5] morning stiffness you have had from the time you wake up? How long does your 6] morning stiffness last from the time you wake up? A score of 10 means very severe disease activity for each of the BASDAI questions 1, 2, 3, 4 and 5. BASDAI question 6 addresses the stiffness duration. A NRS of 0 means 0 h; a NRS of 10 mean ≥2 h. The BASDAI was computed in the following way: the sum of the values of question 1 to 4 was calculated and the mean of questions 5 and 6 was added. This value was divided by 5.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[48]	40[49]	39[50]	40[51]
Units: Unit on scale				
median (inter-quartile range (Q1-Q3))	-0.6 (-2.8 to -0.1)	-1.2 (-2.8 to -0.4)	-0.8 (-2.1 to 1)	-1 (-2 to -0.2)

Notes:

[48] - FAS

[49] - FAS
[50] - FAS
[51] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v BI 655066 18 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[52]
P-value	= 0.1241 [53]
Method	Wilcoxon rank−sum test
Parameter estimate	Median estimate by Hodges−Lehmann method
Point estimate	-0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1
upper limit	0.2

Notes:

[52] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Moses method. Difference calculated as "BI 655066 18 mg minus Placebo".
[53] - One sided p-value from Wilcoxon rank−sum test

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[54]
P-value	= 0.3033 [55]
Method	Wilcoxon rank−sum test
Parameter estimate	Median estimate by Hodges−Lehmann method
Point estimate	0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.5
upper limit	1

Notes:

[54] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Moses method. Difference calculated as "BI 655066 90 mg minus Placebo".
[55] - One sided p-value from Wilcoxon rank−sum test

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v BI 655066 180 mg

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[56]
P-value	= 0.3203 [57]
Method	Wilcoxon rank−sum test
Parameter estimate	Median estimate by Hodges−Lehmann method
Point estimate	-0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.8
upper limit	0.4

Notes:

[56] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Moses method. Difference calculated as "BI 655066 180 mg minus Placebo".
[57] - One sided p-value from Wilcoxon rank−sum test

Secondary: Percentage of patients who achieved ASAS 40 improvement criteria at Week 24

End point title	Percentage of patients who achieved ASAS 40 improvement criteria at Week 24

End point description:

Percentage of patients who achieved ASAS 40 improvement criteria at Week 24 is presented

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	BI 655066 18 mg	BI 655066 90 mg	BI 655066 180 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[58]	40[59]	39[60]	40[61]
Units: Percentage of participants				
number (not applicable)	15	22.5	23.1	12.5

Notes:

[58] - FAS

[59] - FAS

[60] - FAS

[61] - FAS

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v BI 655066 18 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[62]
P-value	= 0.2639 [63]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	7.5

Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.1
upper limit	26.6

Notes:

[62] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper-Pearson method. Difference calculated as "BI 655066 18 mg minus Placebo".
[63] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 24, between treatment groups.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v BI 655066 90 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[64]
P-value	= 0.2691 [65]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	8.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.9
upper limit	25.7

Notes:

[64] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 90 mg minus Placebo".
[65] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 24, between treatment groups.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v BI 655066 180 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[66]
P-value	= 0.4174 [67]
Method	Suissa-Shuster unconditional exact test
Parameter estimate	Risk difference (RD)
Point estimate	-2.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.8
upper limit	17

Notes:

[66] - The confidence interval for the difference in proportion between the treatment groups was obtained by the Clopper- Pearson method. Difference calculated as "BI 655066 180 mg minus Placebo".
[67] - The Suissa-Shuster unconditional exact test was used to test the difference in the proportion of patients achieving the endpoint at Week 24, between treatment groups

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events reported during the DB, the Escape, and the OLE treatment period; up to 50 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subcutaneous injection of Placebo (solution for injection matching BI 655066, 1 mL pre-filled syringe) administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period. Patients in this group did not receive active treatment.

Reporting group title	BI 655066 18 mg

Reporting group description:

Subcutaneous injection of BI 655066 18 mg administered at Day 1 only, followed by placebo every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks.

Reporting group title	BI 655066 90 mg

Reporting group description:

Subcutaneous injection of BI 655066 90 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period

Reporting group title	BI 655066 180 mg

Reporting group description:

Subcutaneous injection of BI 655066 180 mg administered every 8 weeks (At Day1 and at Weeks 8, 16, and 24) up to 4 times during the regular treatment period

Reporting group title	Escape Low

Reporting group description:

Patients who received BI 655066 180 mg in the Escape treatment period and who were randomized to either Placebo or BI 655066 18 mg at Day 1 of the DB treatment period

Reporting group title	Escape High

Reporting group description:

Patients who received BI 655066 180 mg in the Escape treatment period and who were randomized to either BI 655066 90 mg or BI 655066 180 mg at Day 1 of the DB treatment period

Reporting group title	Escape

Reporting group description:

Patients who received escape treatments of BI 655066 180 mg regardless of the initial randomization group

Reporting group title	Open label Extension (OLE)

Reporting group description:

Patients who received 180 mg BI 655066 (administered subcutaneously) every 8 weeks in OLE treatment period

Reporting group title	BI 655066 High

Reporting group description:

Patients who received at least one BI 655066 90 mg or 180 mg treatment during the entire trial

Reporting group title	BI 655066 Total

Reporting group description:

Patients who received at least one BI 655066 treatment at any dose level

Reporting group title	Total_all

Reporting group description:

All randomised patients

Serious adverse events	Placebo	BI 655066 18 mg	BI 655066 90 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arthralgia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site cellulitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BI 655066 180 mg	Escape Low	Escape High
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 40 (5.00%)	1 / 47 (2.13%)	2 / 48 (4.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 40 (0.00%)	1 / 47 (2.13%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			

subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site cellulitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Escape	Open label Extension (OLE)	BI 655066 High
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 95 (3.16%)	1 / 26 (3.85%)	9 / 138 (6.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	0 / 138 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 26 (3.85%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site cellulitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	1 / 138 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BI 655066 Total	Total_all	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 149 (6.04%)	10 / 159 (6.29%)	

number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 149 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitis			

subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site cellulitis			
subjects affected / exposed	1 / 149 (0.67%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	BI 655066 18 mg	BI 655066 90 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 40 (52.50%)	21 / 40 (52.50%)	22 / 39 (56.41%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	3
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 40 (7.50%)	1 / 40 (2.50%)	2 / 39 (5.13%)
occurrences (all)	5	1	2
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	3 / 40 (7.50%)	5 / 40 (12.50%)	3 / 39 (7.69%)
occurrences (all)	3	5	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 40 (5.00%)	2 / 40 (5.00%)	1 / 39 (2.56%)
occurrences (all)	2	2	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	1 / 39 (2.56%)
occurrences (all)	0	2	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	1	0	2
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	2 / 40 (5.00%)	1 / 40 (2.50%)	1 / 39 (2.56%)
occurrences (all)	4	1	1
Arthralgia			
subjects affected / exposed	4 / 40 (10.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	4	0	3
Back pain			
subjects affected / exposed	3 / 40 (7.50%)	3 / 40 (7.50%)	2 / 39 (5.13%)
occurrences (all)	3	3	2
Plantar fasciitis			

subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	1 / 39 (2.56%)
occurrences (all)	1	2	1
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	1 / 39 (2.56%)
occurrences (all)	1	1	1
Influenza			
subjects affected / exposed	1 / 40 (2.50%)	2 / 40 (5.00%)	2 / 39 (5.13%)
occurrences (all)	1	2	2
Nasopharyngitis			
subjects affected / exposed	4 / 40 (10.00%)	7 / 40 (17.50%)	7 / 39 (17.95%)
occurrences (all)	5	8	7
Sinusitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	3 / 39 (7.69%)
occurrences (all)	1	0	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	1 / 39 (2.56%)
occurrences (all)	0	3	1
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2

Non-serious adverse events	BI 655066 180 mg	Escape Low	Escape High
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 40 (55.00%)	10 / 47 (21.28%)	17 / 48 (35.42%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural			

complications			
Wound			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	3 / 48 (6.25%)
occurrences (all)	1	0	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	4 / 40 (10.00%)	2 / 47 (4.26%)	1 / 48 (2.08%)
occurrences (all)	4	2	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 40 (10.00%)	1 / 47 (2.13%)	1 / 48 (2.08%)
occurrences (all)	4	1	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	3 / 40 (7.50%)	1 / 47 (2.13%)	1 / 48 (2.08%)
occurrences (all)	3	1	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	2 / 48 (4.17%)
occurrences (all)	1	0	2
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	1 / 40 (2.50%)	1 / 47 (2.13%)	5 / 48 (10.42%)
occurrences (all)	1	1	5
Arthralgia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1

Back pain			
subjects affected / exposed	2 / 40 (5.00%)	2 / 47 (4.26%)	1 / 48 (2.08%)
occurrences (all)	2	2	1
Plantar fasciitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 47 (2.13%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 40 (7.50%)	1 / 47 (2.13%)	1 / 48 (2.08%)
occurrences (all)	3	2	1
Gastroenteritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 47 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	2 / 40 (5.00%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 40 (12.50%)	5 / 47 (10.64%)	5 / 48 (10.42%)
occurrences (all)	5	5	5
Sinusitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)	1 / 47 (2.13%)	1 / 48 (2.08%)
occurrences (all)	2	1	1
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 47 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Escape	Open label Extension (OLE)	BI 655066 High
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 95 (28.42%)	11 / 26 (42.31%)	85 / 138 (61.59%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	3 / 138 (2.17%)
occurrences (all)	1	0	4

Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	5 / 138 (3.62%)
occurrences (all)	0	0	5
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	3 / 95 (3.16%)	0 / 26 (0.00%)	5 / 138 (3.62%)
occurrences (all)	3	0	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	4 / 138 (2.90%)
occurrences (all)	1	0	4
Headache			
subjects affected / exposed	3 / 95 (3.16%)	0 / 26 (0.00%)	14 / 138 (10.14%)
occurrences (all)	3	0	14
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 95 (2.11%)	0 / 26 (0.00%)	9 / 138 (6.52%)
occurrences (all)	2	0	9
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	3 / 138 (2.17%)
occurrences (all)	1	0	3
Diarrhoea			
subjects affected / exposed	2 / 95 (2.11%)	0 / 26 (0.00%)	8 / 138 (5.80%)
occurrences (all)	2	0	8
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 95 (2.11%)	2 / 26 (7.69%)	7 / 138 (5.07%)
occurrences (all)	2	2	7
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	3 / 138 (2.17%)
occurrences (all)	1	0	3
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			

subjects affected / exposed	6 / 95 (6.32%)	1 / 26 (3.85%)	8 / 138 (5.80%)
occurrences (all)	6	1	10
Arthralgia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 26 (0.00%)	6 / 138 (4.35%)
occurrences (all)	1	0	7
Back pain			
subjects affected / exposed	3 / 95 (3.16%)	0 / 26 (0.00%)	10 / 138 (7.25%)
occurrences (all)	3	0	10
Plantar fasciitis			
subjects affected / exposed	1 / 95 (1.05%)	2 / 26 (7.69%)	3 / 138 (2.17%)
occurrences (all)	1	2	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 95 (2.11%)	0 / 26 (0.00%)	8 / 138 (5.80%)
occurrences (all)	3	0	10
Gastroenteritis			
subjects affected / exposed	1 / 95 (1.05%)	2 / 26 (7.69%)	4 / 138 (2.90%)
occurrences (all)	1	2	4
Influenza			
subjects affected / exposed	0 / 95 (0.00%)	2 / 26 (7.69%)	6 / 138 (4.35%)
occurrences (all)	0	2	7
Nasopharyngitis			
subjects affected / exposed	10 / 95 (10.53%)	2 / 26 (7.69%)	30 / 138 (21.74%)
occurrences (all)	10	4	36
Sinusitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 26 (0.00%)	5 / 138 (3.62%)
occurrences (all)	0	0	5
Upper respiratory tract infection			
subjects affected / exposed	2 / 95 (2.11%)	2 / 26 (7.69%)	8 / 138 (5.80%)
occurrences (all)	2	2	10
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 26 (3.85%)	3 / 138 (2.17%)
occurrences (all)	0	1	4

Non-serious adverse events	BI 655066 Total	Total_all	
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	91 / 149 (61.07%)	99 / 159 (62.26%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 149 (2.01%)	3 / 159 (1.89%)	
occurrences (all)	4	4	
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 149 (3.36%)	7 / 159 (4.40%)	
occurrences (all)	5	9	
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	6 / 149 (4.03%)	6 / 159 (3.77%)	
occurrences (all)	6	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 149 (2.68%)	4 / 159 (2.52%)	
occurrences (all)	4	4	
Headache			
subjects affected / exposed	15 / 149 (10.07%)	17 / 159 (10.69%)	
occurrences (all)	15	17	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 149 (7.38%)	11 / 159 (6.92%)	
occurrences (all)	11	11	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 149 (2.01%)	3 / 159 (1.89%)	
occurrences (all)	3	3	
Diarrhoea			
subjects affected / exposed	8 / 149 (5.37%)	8 / 159 (5.03%)	
occurrences (all)	8	8	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	7 / 149 (4.70%)	7 / 159 (4.40%)	
occurrences (all)	7	7	
Renal and urinary disorders			

Renal colic			
subjects affected / exposed	3 / 149 (2.01%)	3 / 159 (1.89%)	
occurrences (all)	3	3	
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	9 / 149 (6.04%)	11 / 159 (6.92%)	
occurrences (all)	11	15	
Arthralgia			
subjects affected / exposed	6 / 149 (4.03%)	8 / 159 (5.03%)	
occurrences (all)	7	9	
Back pain			
subjects affected / exposed	12 / 149 (8.05%)	12 / 159 (7.55%)	
occurrences (all)	12	12	
Plantar fasciitis			
subjects affected / exposed	3 / 149 (2.01%)	3 / 159 (1.89%)	
occurrences (all)	3	3	
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 149 (5.37%)	8 / 159 (5.03%)	
occurrences (all)	10	10	
Gastroenteritis			
subjects affected / exposed	5 / 149 (3.36%)	6 / 159 (3.77%)	
occurrences (all)	5	6	
Influenza			
subjects affected / exposed	7 / 149 (4.70%)	8 / 159 (5.03%)	
occurrences (all)	8	9	
Nasopharyngitis			
subjects affected / exposed	32 / 149 (21.48%)	33 / 159 (20.75%)	
occurrences (all)	38	39	
Sinusitis			
subjects affected / exposed	5 / 149 (3.36%)	5 / 159 (3.14%)	
occurrences (all)	5	5	
Upper respiratory tract infection			
subjects affected / exposed	8 / 149 (5.37%)	8 / 159 (5.03%)	
occurrences (all)	10	10	
Metabolism and nutrition disorders			

Hypercholesterolaemia subjects affected / exposed occurrences (all)	3 / 149 (2.01%) 4	3 / 159 (1.89%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2014	3 exclusion criteria were clarified; Criterion No. 3 clarified that patients were to be excluded if they participated in trials that tested any biological immune-modulating agent; Criterion No. 10 confirmed that patients with a latent or active tuberculosis infection were to be excluded from the trial. It was specified under which conditions patients could be included if their infection had been adequately treated. Criterion No. 15 was changed to make clear that drug abuse was an exclusion criterion, however, a positive drug screening result due to consumption of prescribed drugs was not. Amendment included 4 changes to clarify the definition, the timing, and the purpose of MRI assessments. MRI assessments at Week 12 were performed only for patients who entered the Escape period. MRI assessments were also performed for patients who discontinued treatment prematurely and who were at least 8 weeks under treatment because for these patients the MRI assessments were performed as their final assessment. The time windows for MRI assessments were modified to increase operational flexibility.The blinding procedure was updated to harmonise it across the project.The evaluation of the safety parameter 'local tolerability' by the investigator was specified.The administration site of the s.c. injection was to be assessed with regard to 'swelling', 'induration', 'heat', 'redness', 'pain', or 'other findings'.The time window for the assignment of adverse events after the last treatment was changed from 16 to 15 weeks to align with the project standard.Adverse events that occurred 15 weeks after the last treatment were to be assigned to the on-treatment period.Section 4.1.5.1 describing blinding and unblinding procedures of the trial was clarified.The specification of the unconditional exact test was deleted to harmonise the statistical model for the binary endpoint on project level.TCM was replaced. Several editorial changes were made and typographical errors were
18 June 2014	The following inclusion criterion was deleted from the CTP: 'Serum level of CRP at screening >ULN according to the range of the central lab used in the trial'. This change was implemented, because of challenges in patient recruitment and a significant proportion of patients with a limited elevation of CRP levels.
08 April 2015	In this non-substantial amendment, few changes to the text were made to align the protocol with the terminology of the clinical trial protocol template, to harmonise it with the information presented in the flow charts, and to reconcile the terminology across the entire protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The hierarchical testing p-values are exploratory in nature, due to the study design, as the primary endpoint of study failed to meet the desired objective.

Notes: