Clinical trial results:
Phase II long-term extension study to assess the safety, tolerability, and efficacy of BI 730357 in patients with moderate-to-severe plaque psoriasis

Summary

EudraCT number	2018-003487-31
Trial protocol	DE
Global end of trial date	27 July 2021

Results information

Result version number	v1 (current)
This version publication date	09 August 2022
First version publication date	09 August 2022

Trial information

Trial identification

Sponsor protocol code	1407-0005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03835481
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	Boehringer Ingelheim, Call Centre, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Centre, Boehringer Ingelheim, 001 18002430127, 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	08 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2021
Global end of trial reached?	Yes
Global end of trial date	27 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess long-term safety, tolerability, and efficacy of BI 730357 in patients with moderate-to-severe chronic plaque psoriasis.

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	29 March 2019
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	Canada: 40
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	United States: 100
Worldwide total number of subjects	165
EEA total number of subjects	25

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	137
From 65 to 84 years	28

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Long-term extension trial in patients with psoriasis who completed the preceding trial 1407-0030. Patients rolling over from part 1 remained on their blinded treatment until the open label period started at week 13 (dose group 25-200 mg). Patients rolling over from part 2 were assigned at visit 1 to receive open label treatment with 400 mg BI.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial.
Only subjects which met all inclusion and none of the exclusion criteria were included in the trial.
Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Patients entering the extension trial will remain on their blinded BI 730357 dose treatment from the preceding trial until the open label period of 1407-0005 begins at Visit 2.

Arms

Are arms mutually exclusive?	Yes
Arm title	25 mg BI 730357

Arm description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Arm title	50 mg BI 730357

Arm description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open-label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Arm type	Experimental
Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Arm title	100 mg BI 730357

Arm description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Arm title	200 mg BI 730357

Arm description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram

(mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Arm title	400 mg BI 730357

Arm description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Arm type	Experimental
Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Number of subjects in period 1	25 mg BI 730357	50 mg BI 730357	100 mg BI 730357
Started	2	20	16
Completed	2	18	15
Not completed	0	2	1
Consent withdrawn by subject	-	-	1
Other not stated below	-	-	-
Lost to follow-up	-	-	-
Termination of treatment by sponsor	-	-	-
Protocol deviation	-	2	-

Number of subjects in period 1	200 mg BI 730357	400 mg BI 730357

Started	49	78
Completed	46	37
Not completed	3	41
Consent withdrawn by subject	-	5
Other not stated below	1	1
Lost to follow-up	1	-
Termination of treatment by sponsor	-	35
Protocol deviation	1	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open label period.

Arms

Are arms mutually exclusive?	Yes
Arm title	100 mg BI 730357

Arm description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Arm type	Experimental
Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At day 1 of week 13 (visit 2) patients were assigned to 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Arm title	200 mg BI 730357

Arm description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Arm type	Experimental

Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At day 1 of week 13 (visit 2) patients were assigned to 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Arm title	400 mg BI 730357

Arm description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Arm type	Experimental
Investigational medicinal product name	BI 730357
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Number of subjects in period 2	100 mg BI 730357	200 mg BI 730357	400 mg BI 730357
Started	35	46	37
Completed	0	0	0
Not completed	35	46	37
Consent withdrawn by subject	7	9	1
Adverse event, non-fatal	1	1	-
Termination of treatment by sponsor	23	31	35
Lost to follow-up	4	3	-
Other not stated above	-	1	1
Covid-19 related, not due to Adverse event	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	25 mg BI 730357
Reporting group description:	
Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.	
Reporting group title	50 mg BI 730357
Reporting group description:	
Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open-label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.	
Reporting group title	100 mg BI 730357
Reporting group description:	
Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.	
Reporting group title	200 mg BI 730357
Reporting group description:	
Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).	
Reporting group title	400 mg BI 730357
Reporting group description:	
Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.	

Reporting group values	25 mg BI 730357	50 mg BI 730357	100 mg BI 730357
Number of subjects	2	20	16
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	15	9
From 65-84 years	0	5	7
85 years and over	0	0	0

Age Continuous			
Units: Years			
arithmetic mean	41.0	47.2	58.1
standard deviation	± 2.8	± 18.3	± 13.5
Sex: Female, Male			
Units: Participants			
Female	0	8	7
Male	2	12	9
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	3	1
White	1	17	13
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	6	2
Not Hispanic or Latino	1	14	14
Unknown or Not Reported	0	0	0

Reporting group values	200 mg BI 730357	400 mg BI 730357	Total
Number of subjects	49	78	165
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	69	137
From 65-84 years	7	9	28
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	49.9	44.5	
standard deviation	± 13.3	± 13.3	-
Sex: Female, Male			
Units: Participants			
Female	12	22	49
Male	37	56	116
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	6	7	15
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	1	6	12
White	42	64	137
More than one race	0	0	0
Unknown or Not Reported	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12	23	44
Not Hispanic or Latino	37	55	121
Unknown or Not Reported	0	0	0

Subject analysis sets

Subject analysis set title	25 mg BI - 100 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	25 mg BI - 100 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Subject analysis set title	50 mg BI - 100 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	50 mg BI - 100 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Subject analysis set title	100 mg BI - 100 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	100 mg BI - 100 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 mg BI 730357

and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Subject analysis set title	200 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to the 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	400 mg BI - 400 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial. Patients in this group are those part 2 patients who have received treatment for more than 12 weeks.

Reporting group values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI
Number of subjects	1	1	5
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Years			
arithmetic mean	1	0	3
standard deviation	±	±	±
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			

Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			

Reporting group values	50 mg BI - 100 mg BI - 200 mg BI	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI
Number of subjects	13	6	9
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Years			
arithmetic mean	8	3	6
standard deviation	±	±	±
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			

Reporting group values	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI	
Number of subjects	46	37	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	 28 ±	 ±	
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	25 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Reporting group title	50 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open-label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Reporting group title	100 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Reporting group title	200 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Reporting group title	400 mg BI 730357

Reporting group description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Reporting group title	100 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2) or received an optional up-titration to 200 mg BI 730357.

Reporting group title	200 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Reporting group title	400 mg BI 730357

Reporting group description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Subject analysis set title	25 mg BI - 100 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	25 mg BI - 100 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Subject analysis set title	50 mg BI - 100 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	50 mg BI - 100 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Subject analysis set title	100 mg BI - 100 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	100 mg BI - 100 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Subject analysis set title	200 mg BI - 200 mg BI
Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to the 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Subject analysis set title	400 mg BI - 400 mg BI

Subject analysis set type	Per protocol

Subject analysis set description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial. Patients in this group are those part 2 patients who have received treatment for more than 12 weeks.

Primary: Number of participants with treatment emergent adverse events (TEAEs)

End point title	Number of participants with treatment emergent adverse events (TEAEs)[1]

End point description:

Number of participants with treatment emergent adverse events (TEAEs).
For dose groups 25 mg - 200 mg BI, TEAEs are reported seperately for period 1 and period 2.
Period 1: All patients who started in period 1 are reported by starting dose (25, 50, 100 and 200 mg).
Period 2: Only patients who participated in period 2 are reported by dose sequence group.
For dose group 400 mg BI, TEAEs are reported overall (period 1 + period 2).
Number of participants with TEAEs is reported.
Treated Set: All patients who received at least one dose in the extension trial.

End point type	Primary

End point timeframe:

For part 1 patients in period 1: Up to 117 days. For part 1 patients in period 2: From week 13 onwards, up to 692 days. For part 2 patients (period 1 + 2): Up to 802 days.

Notes:

[1] - 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: No statistical analysis have been conducted for the primary endpoint

End point values	25 mg BI 730357	50 mg BI 730357	100 mg BI 730357	200 mg BI 730357
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	20	16	49
Units: Participants	0	6	6	10

End point values	400 mg BI 730357	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	78	1	1	5
Units: Participants	14	1	0	3

End point values	50 mg BI - 100 mg BI - 200 mg BI	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	6	9	46
Units: Participants	8	3	6	28

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Psoriasis Area and Severity Index (PASI)50/PASI75/PASI90/PASI100 response at week 24

End point title	Number of participants with Psoriasis Area and Severity Index (PASI)50/PASI75/PASI90/PASI100 response at week 24

End point description:

Number of participants with PASI50/75/90/100 response, where PASI50/75/90/100 is 50%/75%/90%/100% reduction in PASI score.
The PASI score is an established measure of clinical efficacy for psoriasis medications, which provides a numeric scoring for patients overall psoriasis disease state, ranging from 0 to 72, with a lower score indicating a better outcome. It is a linear combination of percent of surface area of skin that is affected and the severity of erythema, infiltration, and desquamation over four body regions. The endpoint is based on the percent reduction from baseline, summarized as a dichotomous outcome based on achieving over an X% reduction (or PASI X), where X is 50, 75, 90 and 100.
The percent reduction from baseline is calculated by % PASI reduction from baseline = ((PASI at baseline - PASI at Visit X) / PASI at baseline) *100, at all visits with PASI collected.
Treated Set. Results are reported by dose-sequence group.

End point type	Secondary

End point timeframe:

At baseline and at week 24.

End point values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI	50 mg BI - 100 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	4	13
Units: Participants				
PASI50	0	1	4	12
PASI75	0	1	3	9
PASI90	0	1	1	4
PASI100	9	1	1	2

End point values	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	45	16
Units: Participants				
PASI50	2	8	33	9
PASI75	2	3	23	6
PASI90	0	2	10	5
PASI100	0	0	3	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Static Physician Global Assessment (sPGA) clear or almost clear response at week 24

End point title	Number of participants with Static Physician Global Assessment (sPGA) clear or almost clear response at week 24

End point description:

Number of participants with sPGA clear or almost clear response at week 24. The sPGA is a 5 point score based on the physician's assessment of the average thickness, erythema, and scaling of all psoriatic lesions. The score ranges from 0 - 4, with a lower score indicating a better outcome.
0= clear (no signs of psoriasis),
1= almost clear;
2= mild;
3= moderate;
4 = severe (e.g. deep dark red coloration).
Treated Set. Results are reported by dose-sequence group. Only participants with non-missing results are reported.

End point type	Secondary

End point timeframe:

At week 24.

End point values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI	50 mg BI - 100 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	4	13
Units: Participants	0	1	2	5

End point values	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	45	16
Units: Participants	1	3	18	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Static Physician Global Assessment (sPGA) clear response at week 24

End point title	Number of participants with Static Physician Global Assessment (sPGA) clear response at week 24

End point description:

Number of participants with sPGA clear response at week 24. The sPGA is a 5 point score based on the physician's assessment of the average thickness, erythema, and scaling of all psoriatic lesions. The score ranges from 0 - 4, with a lower score indicating a better outcome.
0= clear (No signs of psoriasis),
1= almost clear;
2= mild;
3= moderate;
4 = severe (e.g. deep dark red coloration).

Treated Set. Results are reported by dose sequence group. Only participants with non-missing results are reported.

End point type	Secondary

End point timeframe:

At week 24.

End point values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI	50 mg BI - 100 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	4	13
Units: Participants	0	1	1	2

End point values	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	45	16
Units: Participants	0	0	3	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Psoriasis Area and Severity Index (PASI)50/PASI75/PASI90 or PASI100 response at any time and loss of PASI

End point title	Number of participants with Psoriasis Area and Severity Index (PASI)50/PASI75/PASI90 or PASI100 response at any time and loss of PASI response[2]

End point description:

The time-to-loss analysis of PASI response was not performed because the analysis would not provide any statistically valid estimates of the parameter due to the premature ending of the trial. Instead, the number of participants with PASI50/75/90/100 response at any time and loss of response at the last efficacy assessment is reported.
PASI50/75/90/100 is 50%/75%/90%/100% reduction in PASI score. PASI score is a measure of clinical efficacy for psoriasis medications, which ranges from 0 to 72, with a lower score indicating a better outcome.
A patient was a PASI responder if he or she achieved a response at any time from enrollment to 7 days (Residual effect period (REP)) after last dosing date.
A patient with the event of loss of response was a responder that lost their PASI response at the last efficacy assessment regardless if it was done within 7 days (REP) after the last dosing date or not.
Treated Set.

End point type	Secondary

End point timeframe:

Up to 802 days.

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results are reported per starting dose (50, 100, 200 and 400 mg) for patients who participated only in period 1, and per dose-sequence group for patients who participated in period 1 and

period 2.

End point values	50 mg BI 730357	100 mg BI 730357	200 mg BI 730357	400 mg BI 730357
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	3	41
Units: Participants				
PASI50 Responders	0	1	2	23
PASI50 Loss of Response	0	0	1	1
PASI75 Responders	0	1	0	12
PASI75 Loss of Response	0	0	0	1
PASI90 Responders	0	1	0	2
PASI90 Loss of Response	0	0	0	0
PASI100 Responders	0	1	0	1
PASI100 Loss of Response	0	0	0	0

End point values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI	50 mg BI - 100 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	5	13
Units: Participants				
PASI50 Responders	1	1	5	13
PASI50 Loss of Response	0	0	0	1
PASI75 Responders	1	1	4	12
PASI75 Loss of Response	1	0	1	2
PASI90 Responders	0	1	2	5
PASI90 Loss of Response	0	0	0	2
PASI100 Responders	0	1	2	4
PASI100 Loss of Response	0	0	1	3

End point values	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	46	37
Units: Participants				
PASI50 Responders	6	9	46	30
PASI50 Loss of Response	5	3	11	4
PASI75 Responders	3	6	32	21
PASI75 Loss of Response	2	1	12	5
PASI90 Responders	0	3	21	10
PASI90 Loss of Response	0	1	12	2
PASI100 Responders	0	1	12	4
PASI100 Loss of Response	0	0	7	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Static Physician's Global Assessment (sPGA) clear or almost clear response at any time and loss of sPGA clear or almost clear response

End point title	Number of participants with Static Physician's Global Assessment (sPGA) clear or almost clear response at any time and loss of sPGA clear or almost clear response[3]

End point description:

The time-to-loss analysis of PASI response was not performed because the analysis would not provide any statistically valid estimates of the parameter due to the premature ending of the trial. Instead, the number of participants with sPGA clear or almost clear response at any time, and loss of response at the last efficacy assessment is reported.
The sPGA is based on the physician's assessment of average thickness, erythema and scaling of all psoriatic lesions. It ranges from 0 to 4, with 0=clear (best outcome), 1=almost clear, 2=mild, 3=moderate and 4=severe (worst outcome).
A patient was an sPGA responder if he or she achieved a response at any time from enrolment to 7 days (residual effect period (REP)) after last dosing date. A patient with the event of loss of response was a responder that lost their sPGA response at the last efficacy assessment regardless if it was done within 7 days (REP) after the last dosing date or not.
Treated Set.

End point type	Secondary

End point timeframe:

Up to 802 days.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results are reported per starting dose (50, 100, 200 and 400 mg) for patients who participated only in period 1, and per dose-sequence group for patients who participated in period 1 and period 2.

End point values	50 mg BI 730357	100 mg BI 730357	200 mg BI 730357	400 mg BI 730357
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	3	41
Units: Participants				
Resonders	0	1	0	13
Loss of response	0	0	0	2

End point values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI	50 mg BI - 100 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	5	13
Units: Participants				
Resonders	0	1	3	9

Loss of response	0	0	1	4

End point values	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	46	37
Units: Participants				
Resonders	3	6	32	17
Loss of response	3	2	18	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Static Physician’s Global Assessment (sPGA) clear response at any time and loss of sPGA clear response

End point title	Number of participants with Static Physician’s Global Assessment (sPGA) clear response at any time and loss of sPGA clear response[4]

End point description:

The time-to-loss analysis of PASI response was not performed because the analysis would not provide any statistically valid estimates of the parameter due to the premature ending of the trial. Instead, the number of participants with sPGA clear response at any time, and loss of response at the last efficacy assessment is reported.
The sPGA is based on the physician’s assessment of the average thickness, erythema, and scaling of all psoriatic lesions. It ranges from 0 to 4, with 0=clear (best outcome), 1=almost clear, 2=mild, 3=moderate and 4=severe (worst outcome).
A patient was a sPGA responder if he or she achieved a response at any time from enrolment to 7 days (residual effect period (REP)) after last dosing date.
A patient with the event of loss of response was a responder that lost their sPGA response at the last efficacy assessment regardless if it was done within 7 days (REP) after the last dosing date or not.
Treated Set.

End point type	Secondary

End point timeframe:

Up to 802 days.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results are reported per starting dose (50, 100, 200 and 400 mg) for patients who participated only in period 1, and per dose-sequence group for patients who participated in period 1 and period 2.

End point values	50 mg BI 730357	100 mg BI 730357	200 mg BI 730357	400 mg BI 730357
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	3	41
Units: Participants				
Resonders	0	1	0	1
Loss of response	0	0	0	0

End point values	25 mg BI - 100 mg BI	25 mg BI - 100 mg BI - 200 mg BI	50 mg BI - 100 mg BI	50 mg BI - 100 mg BI - 200 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	5	13
Units: Participants				
Resonders	0	1	2	4
Loss of response	0	0	1	3

End point values	100 mg BI - 100 mg BI	100 mg BI - 100 mg BI - 200 mg BI	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	9	46	37
Units: Participants				
Resonders	0	1	12	4
Loss of response	0	0	7	1

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Period 1: From start of treatment until end of period 1 plus 7 days of residual effect period, up to 117 days.
Period 1 and Period 2: From start of treatment until end of period 2, plus 7 days of residual effect period, up to 802 days.

Adverse event reporting additional description:

Treated Set (TS): All patients who received at least one dose of treatment in the extension trial. Adverse events are reported per starting dose (50, 100, 200 and 400 mg) for patients who participated only in period 1, and per dose-sequence group for patients who participated in period 1 and period 2.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	50 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 milligram (mg) BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Reporting group title	50 mg BI - 100 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Reporting group title	100 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 milligram (mg) BI 730357 and 3 film-coated tablet of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1).

Reporting group title	25 mg BI - 100 mg BI - 200 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Reporting group title	25 mg BI - 100 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 25 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Reporting group title	400 mg BI 730357

Reporting group description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial.

Reporting group title	200 mg BI 730357

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for

the initial 12 week double-blind treatment period (period 1).

Reporting group title	200 mg BI - 200 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 2 film-coated tablets of 100 milligram (mg) BI 730357 and 2 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were assigned to the 200 mg BI 730357 open label dose, receiving 2 film-coated tablets of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Reporting group title	400 mg BI - 400 mg BI

Reporting group description:

Patients entering from part 2 of 1407-0030 were administered open label treatment of 4 film-coated tablets of 100 milligram (mg) BI730357 orally once daily (QD) under fed conditions throughout the trial. Patients in this group are those part 2 patients who have received treatment for more than 12 weeks.

Reporting group title	50 mg BI - 100 mg BI - 200 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 50 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Reporting group title	100 mg BI - 100 mg BI - 200 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily and were up-titrated to 200 mg BI 730357 once daily until end of study (period 2).

Reporting group title	100 mg BI - 100 mg BI

Reporting group description:

Patients entering from part 1 of 1407-0030 were administered 1 film-coated tablet of 100 mg BI 730357 and 3 film-coated tablets of placebo orally once daily (q.d.) under fasted conditions for the initial 12 week double-blind treatment period (period 1). At day 1 of week 13 (visit 2) patients were reassigned to the 100 mg BI 730357 open label dose, receiving 1 film-coated tablet of 100 mg BI 730357 orally administered once daily until end of study (period 2).

Serious adverse events	50 mg BI 730357	50 mg BI - 100 mg BI	100 mg BI 730357
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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
Squamous cell carcinoma of skin			

subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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			
Erysipelas			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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
Pyelonephritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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
Urosepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (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	25 mg BI - 100 mg BI - 200 mg BI	25 mg BI - 100 mg BI	400 mg BI 730357
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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			
Erysipelas			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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
Pyelonephritis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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
Urosepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (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	200 mg BI 730357	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	2 / 46 (4.35%)	0 / 37 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (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
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (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
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (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
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (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
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (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
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (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

Serious adverse events	50 mg BI - 100 mg BI - 200 mg BI	100 mg BI - 100 mg BI - 200 mg BI	100 mg BI - 100 mg BI
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	2 / 9 (22.22%)	2 / 6 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 13 (0.00%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tendon rupture			

subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (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			
Erysipelas			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (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
Urosepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (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

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

Non-serious adverse events	50 mg BI 730357	50 mg BI - 100 mg BI	100 mg BI 730357
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	3 / 5 (60.00%)	1 / 1 (100.00%)
Investigations			

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Liver function test increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Cervical radiculopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			

subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hepatitis E			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	1 / 1 (100.00%)
occurrences (all)	0	1	1
Tinea cruris			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Wound infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 5 (20.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 5 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	25 mg BI - 100 mg BI - 200 mg BI	25 mg BI - 100 mg BI	400 mg BI 730357
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	2 / 41 (4.88%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Cervical radiculopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Psoriasis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hepatitis E			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Tinea cruris			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Sinusitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	200 mg BI 730357	200 mg BI - 200 mg BI	400 mg BI - 400 mg BI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	24 / 46 (52.17%)	5 / 37 (13.51%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Alanine aminotransferase increased			

subjects affected / exposed	1 / 3 (33.33%)	1 / 46 (2.17%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Blood potassium increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Liver function test increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Cervical radiculopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	1 / 37 (2.70%)
occurrences (all)	0	3	1
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	0 / 37 (0.00%)
occurrences (all)	0	4	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Rhinitis allergic			

subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 46 (4.35%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 46 (4.35%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Hepatitis E			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Tinea cruris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 46 (4.35%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Tinea pedis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 46 (2.17%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0

Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 46 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	3 / 46 (6.52%)	0 / 37 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	50 mg BI - 100 mg BI - 200 mg BI	100 mg BI - 100 mg BI - 200 mg BI	100 mg BI - 100 mg BI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)	7 / 9 (77.78%)	3 / 6 (50.00%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cervical radiculopathy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Urticaria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatitis E			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Tinea cruris			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Tinea pedis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Wound infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	0 / 13 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 May 2019	The requirement for contraception in male study participants and use of a barrier method was removed following new nonclinical data, which showed no genotoxicity or suspected human teratogenicity/fetotoxicity at therapeutic systemic exposure levels. The benefit-risk assessment was updated to include the information that no drug-drug interactions of CYP3A4 substrates and BI 730357 as a perpetrator were to be expected. The adverse event of special interest (AESI) "Mycobacterium tuberculosis" was replaced by "all mycobacterial infections" to include and cover a more complete picture of opportunistic infections in the definition. The residual effect period was reduced from 28 days to 7 days.
04 June 2019	No changes were made to the content of the CTP. The amendment was a technical update due to errors in the signature process of Version 2.0.
06 October 2020	Part 2 was added to align with the addition of Part 2 to trial 1407-0030 and to allow those patients to roll over to this trial. Additional safety information was included to ensure the safety of patients who had been in the placebo arm of 1407-0030. The original patient population was described as Part 1. Patients in Part 1 on the 100 mg dose were permitted to up-titrate to a 200 mg dose because data from 1407-0030 indicated that 100 mg was sub-optimal. Guidance was provided to investigators to manage visit disruptions due to Covid-19. Remote source data verification (SDV) was permitted in certain circumstances, and patient status could be monitored flexibly during the Covid-19 pandemic if in-person visits were not possible. AEs consistent with gastric intolerance or gastritis were designated as AESIs to reflect the latest results from drug-drug interaction and toxicology trials. Candidiasis was removed as an exclusion criterion and was no longer considered a safety concern. Urinalysis variables were updated to correspond to current central laboratory standard tests and reporting. The wording of the primary endpoint was revised because the definition of 'an endpoint' should be at individual level at one particular time point, and to make the wording consistent across the project.

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 trial was ended prematurely by the sponsor as a precautionary measure following nonclinical findings. As a consequence, primary and secondary endpoints were limited to descriptive outcome measures. The recruitment was completed as planned.

Notes: