Clinical trial results:
A two part randomized, double-blind, parallel-group, placebo-controlled study to evaluate the renal safety, tolerability and pharmacokinetics of LHW090 in patients with moderately impaired renal function on angiotensin receptor blockers

Summary

EudraCT number	2015-004570-15
Trial protocol	DE
Global end of trial date	11 October 2018

Results information

Result version number	v1 (current)
This version publication date	20 October 2019
First version publication date	20 October 2019

Trial information

Trial identification

Sponsor protocol code	CLHW090X2102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02678000
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 6132411111, Novartis.email@novartis.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	11 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Primary Objective for Part 1 was to assess the safety and tolerability of ascending doses of LHW090 in patients with moderate renal impairment to inform design of Part 2. The primary objective for Part 2 was to assess the renal safety of LHW090 in patients with moderate renal impairment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	84
EEA total number of subjects	36

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)	22
From 65 to 84 years	62

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects (N=11) who enrolled in in PART 1 completed the study : LHW090 (N=7) and placebo (N=4). Of all subjects (N=73) in PART 2, a total of 69 subjects completed and 4 subjects discontinued.

Pre-assignment

Screening details:

All subjects (N=11) who enrolled in in PART 1 completed the study : LHW090 (N=7) and placebo (N=4). Of all subjects (N=73) in PART 2, a total of 69 subjects completed and 4 subjects discontinued.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LHW090 (PART 1)

Arm description:

For Part 1, patients will receive 3 doses of LHW090 once daily with escalating doses every 4 days for a total 12 days of treatment.

Arm type	Experimental
Investigational medicinal product name	LHW090
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

LHW090 25 mg, LHW090 50 mg, LHW090 100 mg

Arm title	Placebo (PART 1)

Arm description:

For Part 1, patients will receive matching placebo once daily for 12 days.

Arm type	Placebo
Investigational medicinal product name	Placebo to match LHW090
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Placebo 25 mg, 50 mg, 100 mg

Arm title	LHW090 100mg (PART 2)

Arm description:

For PART 2, patients will receive LWH090 100 mg for 4 weeks

Arm type	Experimental

Investigational medicinal product name	LHW090
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
LHW090 100 mg once daily for 4 weeks

Arm title	LHW090 200mg (PART 2)

Arm description:
For PART 2, patients will receive LWH090 200 mg for 4 weeks

Arm type	Experimental
Investigational medicinal product name	LHW090
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
LHW090 200 mg once daily for 4 weeks

Arm title	Placebo (PART 2)

Arm description:
For Part 2, patients will receive matching placebo once daily for 4 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
Placebo once daily for 4 weeks

Number of subjects in period 1	LHW090 (PART 1)	Placebo (PART 1)	LHW090 100mg (PART 2)
Started	7	4	28
Completed	7	4	25
Not completed	0	0	3
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	2

Number of subjects in period 1	LHW090 200mg (PART 2)	Placebo (PART 2)
Started	27	18
Completed	26	18
Not completed	1	0
Consent withdrawn by subject	-	-
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	LHW090 (PART 1)
Reporting group description:	
For Part 1, patients will receive 3 doses of LHW090 once daily with escalating doses every 4 days for a total 12 days of treatment.	
Reporting group title	Placebo (PART 1)
Reporting group description:	
For Part 1, patients will receive matching placebo once daily for 12 days.	
Reporting group title	LHW090 100mg (PART 2)
Reporting group description:	
For PART 2, patients will receive LWH090 100 mg for 4 weeks	
Reporting group title	LHW090 200mg (PART 2)
Reporting group description:	
For PART 2, patients will receive LWH090 200 mg for 4 weeks	
Reporting group title	Placebo (PART 2)
Reporting group description:	
For Part 2, patients will receive matching placebo once daily for 4 weeks.	

Reporting group values	LHW090 (PART 1)	Placebo (PART 1)	LHW090 100mg (PART 2)
Number of subjects	7	4	28
Age categorical Units: Subjects			
Adults (18-64 years)	1	1	3
From 65-84 years	6	3	25
Age Continuous Units: years			
arithmetic mean	68.3	67.5	71.0
standard deviation	± 3.64	± 16.01	± 9.18
Sex: Female, Male Units: Subjects			
Female	1	3	8
Male	6	1	20
Race (NIH/OMB) Units: Subjects			
Black or African American	1	1	1
White	6	3	27

Reporting group values	LHW090 200mg (PART 2)	Placebo (PART 2)	Total
Number of subjects	27	18	84
Age categorical Units: Subjects			
Adults (18-64 years)	10	7	22
From 65-84 years	17	11	62
Age Continuous Units: years			
arithmetic mean	69.0	65.3	

standard deviation	± 8.82	± 11.58	-

Sex: Female, Male Units: Subjects			
Female	10	9	31
Male	17	9	53
Race (NIH/OMB) Units: Subjects			
Black or African American	3	0	6
White	24	18	78

End points

End points reporting groups

Reporting group title	LHW090 (PART 1)
Reporting group description:	
For Part 1, patients will receive 3 doses of LHW090 once daily with escalating doses every 4 days for a total 12 days of treatment.	
Reporting group title	Placebo (PART 1)
Reporting group description:	
For Part 1, patients will receive matching placebo once daily for 12 days.	
Reporting group title	LHW090 100mg (PART 2)
Reporting group description:	
For PART 2, patients will receive LWH090 100 mg for 4 weeks	
Reporting group title	LHW090 200mg (PART 2)
Reporting group description:	
For PART 2, patients will receive LWH090 200 mg for 4 weeks	
Reporting group title	Placebo (PART 2)
Reporting group description:	
For Part 2, patients will receive matching placebo once daily for 4 weeks.	
Subject analysis set title	LHW090 25 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 25 mg once daily with escalating doses every 4 days for a total 12 days of treatment.	
Subject analysis set title	LHW090 50 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 50 mg once daily with escalating doses every 4 days for a total 12 days of treatment.	
Subject analysis set title	LHW090 100 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 100 mg once daily with escalating doses every 4 days for a total 12 days of treatment.	
Subject analysis set title	LHW090/LHV527 25 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 25 mg once daily with escalating doses every 4 days for a total 12 days of treatment. (PK draw with active metabolite, LHV527)	
Subject analysis set title	LHW090/LHV527 50 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 50 mg once daily with escalating doses every 4 days for a total 12 days of treatment. (PK draw with active metabolite, LHV527)	
Subject analysis set title	LHW090/LHV527 100 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 100 mg once daily with escalating doses every 4 days for a total 12 days of treatment. (PK draw with active metabolite, LHV527)	
Subject analysis set title	LHW090 100 mg (PART 1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
For Part 1, patients will receive 3 doses of LHW090 100 mg once daily with escalating doses every 4	

days for a total 12 days of treatment

Subject analysis set title	LHW090 100 mg (PART 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

For PART 2, patients will receive LWH090 100 mg once daily for 4 weeks

Subject analysis set title	LHW090/LHV527 100 mg (PART 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

For PART 2, patients will receive LWH090 100 mg once daily for 4 weeks. (PK draw with active metabolite, LHV527)

Subject analysis set title	LHW090/LHV527 200 mg (PART 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

For PART 2, patients will receive LWH090 200 mg once daily for 4 weeks. (PK draw with active metabolite, LHV527)

Primary: Number of patients with reported adverse events receiving escalating doses of LHW090 (Part 1)

End point title	Number of patients with reported adverse events receiving escalating doses of LHW090 (Part 1)[1][2]

End point description:

Any sign or symptom that occurs during the study treatment plus the 30 days post treatment. For LHW090, incidence of AEs by primary organ class presented

End point type	Primary

End point timeframe:

Adverse events were collected from first dose of study treatment until end of study treatment, (12 days dosing period + 9 days follow up (PART 1) plus 30 days post treatment, up to maximum duration of approximately 20 months

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: Statistical Analysis was not planned

[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: Statistical Analysis was not planned

End point values	Placebo (PART 1)	LHW090 25 mg (PART 1)	LHW090 50 mg (PART 1)	LHW090 100 mg (PART 1)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	7	7	7
Units: Count of Participants				
Number of patients with at least one AE	2	1	0	1
Gastrointestinal disorders	2	1	1	1
Skin and subcutaneous tissue disorders	2	0	0	1
General disorders & administration site conditions	1	0	0	0
Musculoskeletal and connective tissue disorders	1	0	0	0
Nervous system disorders	1	0	0	0
Psychiatric disorders	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of LHW090/LHV527 (active metabolite) in plasma: area under the plasma concentration-time curve from time zero time 't' where t is a defined time point after administration (AUC0-t) (PART 1)

End point title	Pharmacokinetics of LHW090/LHV527 (active metabolite) in plasma: area under the plasma concentration-time curve from time zero time 't' where t is a defined time point after administration (AUC0-t) (PART 1)[3]

End point description:

The area under the plasma concentration-time curve from time zero to 24 hours. Area Under the Curve (AUC0-t) after 4 days dosing will be reported for PART 1. LHW090 and LHV527 (its active metabolite)

End point type	Primary

End point timeframe:

Within 60 minutes prior to dosing, post dose +/- 10 min from greater or equal to 1 hr to 24 hrs.

Notes:

[3] - 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: Statistical Analysis was not planned

End point values	LHW090 25 mg (PART 1)	LHW090 50 mg (PART 1)	LHW090 100 mg (PART 1)	LHW090/LHV527 25 mg (PART 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7	6
Units: h*ng/mL				
arithmetic mean (standard deviation)	3750 (± 815)	7150 (± 1480)	13900 (± 2180)	19200 (± 3990)

End point values	LHW090/LHV527 50 mg (PART 1)	LHW090/LHV527 100 mg (PART 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: h*ng/mL				
arithmetic mean (standard deviation)	36500 (± 5720)	68800 (± 11800)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients who developed a renal event (PART 2)

End point title	Number of patients who developed a renal event (PART 2)[4][5]

End point description:

Patients who developed a renal event will be reported (defined as a ≥0.3 mg/dL increase in serum creatinine from baseline within 24-48 hours post dose)

End point type	Primary

End point timeframe:

Baseline, within 24 to 48 hours of post-dose weekly for up to 8 weeks

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical Analysis was not planned

[5] - 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: Statistical Analysis was not planned

End point values	LHW090 100mg (PART 2)	LHW090 200mg (PART 2)	Placebo (PART 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	18	
Units: Participants	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax : Pharmacokinetics of LHW090/LHV527 (active metabolite) in plasma: observed maximum plasma concentration following administration of LHW090 (PART 1/PART 2)

End point title	Cmax : Pharmacokinetics of LHW090/LHV527 (active metabolite) in plasma: observed maximum plasma concentration following administration of LHW090 (PART 1/PART 2)[6]

End point description:

The observed maximum plasma (or serum or blood) concentration following drug administration for PART 1 and PART 2

End point type	Secondary

End point timeframe:

PART 1: within 60 minutes prior to dosing, post dose +/- 10 min from greater or equal to 1 hr to 24 hrs.
PART 2: within 60 min +/- 10 min from greater or equal to 1 hr to 8 hours after 4 weeks dosing.

Notes:

[6] - 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: Statistical Analysis was not planned

End point values	LHW090 100mg (PART 2)	LHW090 200mg (PART 2)	LHW090 25 mg (PART 1)	LHW090 50 mg (PART 1)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	7	7
Units: ng / mL				
arithmetic mean (standard deviation)				
PK Value for LHW090	4470 (± 1690)	7530 (± 3750)	1160 (± 589)	2000 (± 1020)
PK Value for LHW090/LHV527(active metabolite)	6200 (± 1560)	10300 (± 1440)	1690 (± 338)	3070 (± 682)

End point values	LHW090 100 mg (PART 1)			

Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng / mL				
arithmetic mean (standard deviation)				
PK Value for LHW090 PK Value for LHW090/LHV527(active metabolite)	4230 (± 1400) 5100 (± 734)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-t: Pharmacokinetics of LHW090/LHV527 (active metabolite)in plasma: area under the plasma concentration-time curve from time zero time 't' where t is a defined time point after administration (PART 2)

End point title	AUC0-t: Pharmacokinetics of LHW090/LHV527 (active metabolite)in plasma: area under the plasma concentration-time curve from time zero time 't' where t is a defined time point after administration (PART 2)[7]

End point description:

The area under the plasma concentration-time curve from time zero to 24 hours

End point type	Secondary

End point timeframe:

PART 2: within60 min +/- 10 min from greater or equal to 1 hr to 8 hours after 4 weeks dosing.

Notes:

[7] - 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: Statistical Analysis was not planned

End point values	LHW090 100mg (PART 2)	LHW090 200mg (PART 2)	LHW090/LHV527 100 mg (PART 2)	LHW090/LHV527 200 mg (PART 2)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	23	26	22	25
Units: h* ng/mL				
arithmetic mean (standard deviation)	21500 (± 6810)	42900 (± 2700)	96700 (± 32800)	181000 (± 51100)

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax: Pharmacokinetics of LHW090/LHV527 in plasma: time to reach the maximum concentration after administration of LHW090 (PART 1/PART 2)

End point title	Tmax: Pharmacokinetics of LHW090/LHV527 in plasma: time to reach the maximum concentration after administration of LHW090 (PART 1/PART 2)[8]

End point description:

The time to reach the maximum concentration after drug administration

End point type	Secondary

End point timeframe:

Part 1: within 60 minutes prior to dosing, post dose +/- 10 min from greater or equal to 1 hr to 24 hrs. Part2: within60 min +/- 10 min from greater or equal to 1 hr to 8 hours after 4 weeks dosing.

Notes:

[8] - 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: Statistical Analysis was not planned

End point values	LHW090 100mg (PART 2)	LHW090 200mg (PART 2)	LHW090 25 mg (PART 1)	LHW090 50 mg (PART 1)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	7	7
Units: hour (hr)				
median (full range (min-max))				
PK Value for LHW090	2.00 (1.00 to 4.00)	2.50 (1.00 to 12.0)	2.00 (1.00 to 3.00)	1.02 (1.00 to 3.00)
PK Value for LHW090/LHV527(active metabolite)	3.00 (2.00 to 8.00)	4.00 (3.00 to 12.0)	3.58 (2.00 to 12.0)	4.00 (2.00 to 12.0)

End point values	LHW090 100 mg (PART 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: hour (hr)				
median (full range (min-max))				
PK Value for LHW090	1.00 (1.00 to 4.00)			
PK Value for LHW090/LHV527(active metabolite)	4.00 (2.00 to 8.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	PART 1 LHW090 25 mg
Reporting group description:	
PART 1 LHW090 25 mg	
Reporting group title	PART 1 LHW090 50 mg
Reporting group description:	
PART 1 LHW090 50 mg	
Reporting group title	PART 1 LHW090 100 mg
Reporting group description:	
PART 1 LHW090 100 mg	
Reporting group title	PART 1 Placebo
Reporting group description:	
PART 1 Placebo	
Reporting group title	PART 2 LHW090 100 mg
Reporting group description:	
PART 2 LHW090 100 mg	
Reporting group title	PART 2 LHW090 200 mg
Reporting group description:	
PART 2 LHW090 200 mg	
Reporting group title	PART 2 Placebo
Reporting group description:	
PART 2 Placebo	

Serious adverse events	PART 1 LHW090 25 mg	PART 1 LHW090 50 mg	PART 1 LHW090 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (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
Skin laceration			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (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	PART 1 Placebo	PART 2 LHW090 100 mg	PART 2 LHW090 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	3 / 28 (10.71%)	0 / 27 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (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
Skin laceration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (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	PART 2 Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			

Radius fracture			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin laceration			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PART 1 LHW090 25 mg	PART 1 LHW090 50 mg	PART 1 LHW090 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	1 / 7 (14.29%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infusion site haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Apathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Lacrimation increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Drug eruption			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pruritus generalised			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	PART 1 Placebo	PART 2 LHW090 100 mg	PART 2 LHW090 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	13 / 28 (46.43%)	16 / 27 (59.26%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	2 / 28 (7.14%)	2 / 27 (7.41%)
occurrences (all)	0	2	2

General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	2 / 28 (7.14%)	1 / 27 (3.70%)
occurrences (all)	0	2	1
Infusion site haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Nasal pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	4 / 27 (14.81%)
occurrences (all)	0	0	5

Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Apathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Blood pressure decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	1 / 4 (25.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0

Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Lacrimation increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 28 (7.14%)	4 / 27 (14.81%)
occurrences (all)	0	2	5
Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Drug eruption			

subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	6 / 28 (21.43%)	1 / 27 (3.70%)
occurrences (all)	0	11	1
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Rash macular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Gastrointestinal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Lactose intolerance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	PART 2 Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 18 (50.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

Hypotension			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Infusion site haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Xerosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nasal dryness			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		

Nasal pruritus subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Apathy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Sleep disorder subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Blood pressure decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Lacrimation increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Faeces discoloured			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Alopecia			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Drug eruption			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Pruritus generalised			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Rash macular			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Muscle spasms			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Lactose intolerance			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 August 2017	Amendment Version 04

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported