Clinical trial results:
A Phase Ib/II study of the ALK inhibitor ceritinib in combination with the CDK4/6 inhibitor LEE011 in patients with ALK-positive Non-Small Cell Lung Cancer

Summary

EudraCT number	2014-003032-39
Trial protocol	ES FR IT
Global end of trial date	26 September 2018

Results information

Result version number	v1 (current)
This version publication date	11 October 2019
First version publication date	11 October 2019

Trial information

Trial identification

Sponsor protocol code	CLEE011X2110C

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 41 613241111, 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	03 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2018
Global end of trial reached?	Yes
Global end of trial date	26 September 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objectives were, in the Phase Ib part, to estimate the maximum tolerated doses (MTD(s)) and/or recommended Phase 2 doses (RP2D(s)) and schedule of ribociclib in combination with ceritinib in ALKpositive NSCLC patients.

And in the Phase II part: To assess preliminary anti-tumor activity of the ribociclib and ceritinib combination

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	14 May 2015
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	France: 1
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Taiwan: 8
Worldwide total number of subjects	27
EEA total number of subjects	18

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	22
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Phase II was not initiated & enrollment in Phase Ib was terminated early based on changes in treatment landscape for ALK+ NSCLC. The RP2D was identified on 19-Apr-2017 based on additional safety data. Recruitment halt & early termination were not a result of any safety concerns. Patients that moved to a rollover protocol were considered completed

Pre-assignment

Screening details:

27 patients were enrolled between 14-May-2015 (FPFV) and 26-Sep-2018 (LPLV) in the dose escalation phase, and all discontinued study treatment. Primary reason for discontinuation was Progressive Disease (PD) (14 patients, 51.9%). Other reasons for discontinuations included moved to rollover protocol due to early termination and AEs

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ribociclib 100 mg + Ceritinib 300 mg

Arm description:

LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use

Arm type	Experimental
Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CAPSULE

Arm title	Ribociclib 100 mg + Ceritinib 450 mg

Arm description:

LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use

Arm type	Experimental
Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CAPSULE

Arm title	Ribociclib 200 mg + Ceritinib 300 mg

Arm description:

LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use

Arm type	Experimental

Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
CAPSULE

Arm title	Ribociclib 200 mg + Ceritinib 450 mg

Arm description:
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use

Arm type	Experimental
Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
CAPSULE

Arm title	Ribociclib 300 mg + Ceritinib 450 mg

Arm description:
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use

Arm type	Experimental
Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
CAPSULE

Number of subjects in period 1	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg
Started	4	7	4
Completed	0	0	0
Not completed	4	7	4
Adverse event, serious fatal	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	2	-
Progressive disease	4	2	2
Moved to rollover protocol	-	2	1
Protocol deviation	-	1	1

Number of subjects in period 1	Ribociclib 200 mg + Ceritinib 450 mg	Ribociclib 300 mg + Ceritinib 450 mg
Started	7	5
Completed	0	0
Not completed	7	5

Adverse event, serious fatal	1	-
Physician decision	-	1
Adverse event, non-fatal	1	-
Progressive disease	3	3
Moved to rollover protocol	2	1
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Ribociclib 100 mg + Ceritinib 300 mg
Reporting group description:	
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 100 mg + Ceritinib 450 mg
Reporting group description:	
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 200 mg + Ceritinib 300 mg
Reporting group description:	
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 200 mg + Ceritinib 450 mg
Reporting group description:	
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 300 mg + Ceritinib 450 mg
Reporting group description:	
LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	

Reporting group values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg
Number of subjects	4	7	4
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)	4	4	4
From 65-84 years	0	3	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	52.75	62.43	53.00
standard deviation	± 8.655	± 12.501	± 14.652
Gender categorical			
Units: Subjects			
Female	1	4	4
Male	3	3	0

Reporting group values	Ribociclib 200 mg + Ceritinib 450 mg	Ribociclib 300 mg + Ceritinib 450 mg	Total
Number of subjects	7	5	27
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)	6	4	22
From 65-84 years	1	1	5
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	47.57	57.00	
standard deviation	± 12.882	± 14.000	-
Gender categorical			
Units: Subjects			
Female	4	3	16
Male	3	2	11

End points

End points reporting groups

Reporting group title	Ribociclib 100 mg + Ceritinib 300 mg
Reporting group description: LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 100 mg + Ceritinib 450 mg
Reporting group description: LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 200 mg + Ceritinib 300 mg
Reporting group description: LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 200 mg + Ceritinib 450 mg
Reporting group description: LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	
Reporting group title	Ribociclib 300 mg + Ceritinib 450 mg
Reporting group description: LEE011 capsule for oral use (ribociclib) and Ceritinib for oral use	

Primary: Incidence rate of dose limiting toxicities (DLTs) during the first cycle of treatment (Phase Ib)

End point title	Incidence rate of dose limiting toxicities (DLTs) during the first cycle of treatment (Phase Ib)[1]
End point description: Maximum Tolerated Dose(s) (MTD(s)) and/or recommended phase 2 dose (RP2D(s)) and schedule of LEE011 in combination with ceritinib in ALK-positive non-small cell lung cancer (NSCLC) patients. Cycle = 28 days	
End point type	Primary
End point timeframe: Day 28	

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 was planned for phase Ib. This study did not move into Phase II.

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: participants	0	1	0	0

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Exposure to LEE011 and ceritinib (Phase Ib)

End point title	Exposure to LEE011 and ceritinib (Phase Ib)[2]

End point description:

Duration of exposure to study treatment by treatment group in Phase Ib (Safety Set)

End point type	Primary

End point timeframe:

Up to 36 months

Notes:

[2] - 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 was planned for phase Ib. This study did not move into Phase II.

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: months				
arithmetic mean (standard deviation)	30.90 (± 5.797)	13.43 (± 10.769)	14.63 (± 12.962)	8.49 (± 7.445)

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: months				
arithmetic mean (standard deviation)	7.04 (± 5.356)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) as per RECIST v1.1

End point title	Overall Response Rate (ORR) as per RECIST v1.1

End point description:

Preliminary anti-tumor activity of the LEE011 and ceritinib combination

End point type	Secondary

End point timeframe:
Up to 24 months

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: participants				
Complete Response (CR)	1	0	0	0
Partial Response (PR)	2	2	2	2
Stable Disease (SD)	1	3	1	3
Progressive Disease (PD)	0	0	0	0
Unknown (UNK)	0	2	1	2
Overall Response Rate (ORR: CR+PR)	3	2	2	2
Disease Control Rate (DCR: CR+PR+SD)	4	5	3	5

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: participants				
Complete Response (CR)	0			
Partial Response (PR)	1			
Stable Disease (SD)	3			
Progressive Disease (PD)	1			
Unknown (UNK)	0			
Overall Response Rate (ORR: CR+PR)	1			
Disease Control Rate (DCR: CR+PR+SD)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameters of LEE011 and ceritinib

End point title	PK parameters of LEE011 and ceritinib

End point description:
Characterization of the PK of LEE011 and ceritinib

End point type	Secondary

End point timeframe:
Up to 6 months

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: participants				
number (not applicable)	4	7	4	7

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: participants				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of dose interruptions and dose reductions phase Ib

End point title	Frequency of dose interruptions and dose reductions phase Ib

End point description:

Characterization of tolerability Number of patients requiring dose reductions, interruptions of ceritinib, by treatment group in Phase Ib

End point type	Secondary

End point timeframe:

Up to 24 months

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: participants				
0 dose reductions	3	4	4	5
1 dose reduction	1	2	0	1
2 dose reductions	0	0	0	1
>=3 dose reductions	0	1	0	0

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: participants				
0 dose reductions	2			
1 dose reduction	3			
2 dose reductions	0			
>=3 dose reductions	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS) per RECIST v1.1 - Phase Ib

End point title	Progression free survival (PFS) per RECIST v1.1 - Phase Ib
End point description: Preliminary measures of anti-tumor activity of LEE011 and ceritinib combination	
End point type	Secondary
End point timeframe: median number of day 28 (min-max)	

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: days				
median (full range (min-max))	845.5 (653 to 1171)	167.0 (1 to 813)	460.5 (1 to 765)	113.0 (1 to 588)

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: days				
median (full range (min-max))	168.0 (48 to 416)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

Preliminary measure of anti-tumor activity of LEE011 and ceritinib combination

End point type	Secondary

End point timeframe:

Up to 24 months

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: median number of days (min-max)				
median (full range (min-max))	706.0 (248 to 868)	84.5 (1 to 763)	413.5 (111 to 716)	254.0 (58 to 460)

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: median number of days (min-max)				
median (full range (min-max))	113.0 (113 to 113)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response (TTR) - Phase Ib

End point title	Time to response (TTR) - Phase Ib

End point description:

Preliminary measures of anti-tumor activity of LEE011 and ceritinib combination

End point type	Secondary

End point timeframe:

Up to 24 months

End point values	Ribociclib 100 mg + Ceritinib 300 mg	Ribociclib 100 mg + Ceritinib 450 mg	Ribociclib 200 mg + Ceritinib 300 mg	Ribociclib 200 mg + Ceritinib 450 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	7
Units: median number of days (min-max)				
median (full range (min-max))	62.0 (57 to 924)	53.0 (27 to 56)	53.5 (50 to 57)	52.0 (52 to 335)

End point values	Ribociclib 300 mg + Ceritinib 450 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: median number of days (min-max)				
median (full range (min-max))	56.0 (56 to 56)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AE timeframe: Adverse events were collected from first dose of study treatment until end of study treatment plus 28 days post treatment, up to maximum duration of 24 months	
Adverse event reporting additional description:	
Any sign or symptom that occurs during the study treatment plus the 28 days post treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	LEE011 100mg +@CERITINIB 300mg
Reporting group description:	
LEE011 100mg +@CERITINIB 300mg	
Reporting group title	LEE011 100mg +@CERITINIB 450mg
Reporting group description:	
LEE011 100mg +@CERITINIB 450mg	
Reporting group title	LEE011 200mg +@CERITINIB 300mg
Reporting group description:	
LEE011 200mg +@CERITINIB 300mg	
Reporting group title	LEE011 200mg +@CERITINIB 450mg
Reporting group description:	
LEE011 200mg +@CERITINIB 450mg	
Reporting group title	LEE011 300mg +@CERITINIB 450mg
Reporting group description:	
LEE011 300mg +@CERITINIB 450mg	
Reporting group title	All patients
Reporting group description:	
All patients	

Serious adverse events	LEE011 100mg +@CERITINIB 300mg	LEE011 100mg +@CERITINIB 450mg	LEE011 200mg +@CERITINIB 300mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Amylase increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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			
Acute coronary syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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

Intracranial mass			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (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
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Respiratory failure			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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
Lymphangitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (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	LEE011 200mg +@CERITINIB 450mg	LEE011 300mg +@CERITINIB 450mg	All patients
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	4 / 5 (80.00%)	9 / 27 (33.33%)
number of deaths (all causes)	1	1	3
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial mass			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Lymphopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	2 / 27 (7.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Interstitial lung disease			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infections and infestations			
Influenza			

subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
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	LEE011 100mg +@CERITINIB 300mg	LEE011 100mg +@CERITINIB 450mg	LEE011 200mg +@CERITINIB 300mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	7 / 7 (100.00%)	4 / 4 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 4 (100.00%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	6	0	3
Chills			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	4 / 7 (57.14%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Feeling jittery			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Non-cardiac chest pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	2 / 4 (50.00%)
occurrences (all)	2	1	2
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	4	1	1
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation delayed			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Penile erythema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Polymenorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 4 (25.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Dysphonia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	4	1	0

Dyspnoea			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Haemoptysis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Sneezing			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sputum increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sputum retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	2 / 4 (50.00%)
occurrences (all)	1	1	2
Mood altered			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	4 / 7 (57.14%)	1 / 4 (25.00%)
occurrences (all)	3	5	1
Amylase increased			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	4 / 7 (57.14%)	1 / 4 (25.00%)
occurrences (all)	3	10	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	3	1
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood creatine increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 7 (28.57%)	1 / 4 (25.00%)
occurrences (all)	1	2	4
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Lipase increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	2	2	1
Monocyte count decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	3 / 7 (42.86%)	0 / 4 (0.00%)
occurrences (all)	0	8	0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Ligament sprain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Balance disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dizziness			

subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Speech disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Anaemia macrocytic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1

Neutropenia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	8	1	1
Pancytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Macular oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 7 (42.86%)	1 / 4 (25.00%)
occurrences (all)	0	3	1
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Constipation			

subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	4 / 4 (100.00%)	5 / 7 (71.43%)	4 / 4 (100.00%)
occurrences (all)	13	6	7
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Duodenal ulcer			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Gingival swelling			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	3 / 7 (42.86%)	3 / 4 (75.00%)
occurrences (all)	0	4	3
Stomatitis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Toothache			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	5 / 7 (71.43%)	2 / 4 (50.00%)
occurrences (all)	2	37	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	3 / 4 (75.00%)	2 / 7 (28.57%)	1 / 4 (25.00%)
occurrences (all)	3	3	2
Skin exfoliation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Renal failure			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	3	1	1
Bone pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Muscle contracture			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Neck pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Trigger finger			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Cystitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Helicobacter infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	2 / 4 (50.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	3 / 7 (42.86%)	1 / 4 (25.00%)
occurrences (all)	0	3	1
Diabetes mellitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Steroid diabetes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	LEE011 200mg +@CERITINIB 450mg	LEE011 300mg +@CERITINIB 450mg	All patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	5 / 5 (100.00%)	27 / 27 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 5 (20.00%)	9 / 27 (33.33%)
occurrences (all)	2	2	13
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	4 / 27 (14.81%)
occurrences (all)	0	0	4
Feeling jittery			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	6 / 27 (22.22%)
occurrences (all)	0	1	6
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	5 / 27 (18.52%)
occurrences (all)	0	0	6
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	2	2
Reproductive system and breast disorders			
Menstruation delayed			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Penile erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2

Polymenorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	2 / 7 (28.57%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	3	0	3
Cough			
subjects affected / exposed	2 / 7 (28.57%)	1 / 5 (20.00%)	6 / 27 (22.22%)
occurrences (all)	3	1	8
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	5
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	4 / 27 (14.81%)
occurrences (all)	0	1	4
Haemoptysis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	3
Rhinorrhoea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	4 / 27 (14.81%)
occurrences (all)	1	1	4
Sneezing			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Sputum increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Sputum retention			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Wheezing			

subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	5 / 27 (18.52%)
occurrences (all)	1	0	5
Mood altered			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 7 (42.86%)	3 / 5 (60.00%)	12 / 27 (44.44%)
occurrences (all)	9	4	22
Amylase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	3 / 27 (11.11%)
occurrences (all)	2	1	4
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 7 (42.86%)	3 / 5 (60.00%)	12 / 27 (44.44%)
occurrences (all)	6	4	24
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	4
Blood bilirubin increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Blood creatine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 7 (28.57%)	1 / 5 (20.00%)	4 / 27 (14.81%)
occurrences (all)	2	1	4
Blood creatinine increased			
subjects affected / exposed	3 / 7 (42.86%)	2 / 5 (40.00%)	9 / 27 (33.33%)
occurrences (all)	6	3	16
Blood thyroid stimulating hormone decreased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 5 (0.00%)	5 / 27 (18.52%)
occurrences (all)	2	0	5
Lipase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	4 / 27 (14.81%)
occurrences (all)	2	0	7
Monocyte count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Neutrophil count decreased			
subjects affected / exposed	4 / 7 (57.14%)	4 / 5 (80.00%)	11 / 27 (40.74%)
occurrences (all)	5	16	29
Platelet count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	3
White blood cell count decreased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	3 / 27 (11.11%)
occurrences (all)	2	8	14
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Balance disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	4 / 27 (14.81%)
occurrences (all)	1	1	4
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	2 / 7 (28.57%)	2 / 5 (40.00%)	7 / 27 (25.93%)
occurrences (all)	2	2	7
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Seizure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	2	2
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Speech disorder			

subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	3 / 27 (11.11%)
occurrences (all)	1	1	3
Anaemia macrocytic			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	2 / 27 (7.41%)
occurrences (all)	0	2	3
Neutropenia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 5 (0.00%)	7 / 27 (25.93%)
occurrences (all)	7	0	17
Pancytopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Tinnitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2
Vertigo			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Eye disorders			

Blepharitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Macular oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	5 / 27 (18.52%)
occurrences (all)	2	0	6
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	2	0	3
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	2	0	3
Diarrhoea			
subjects affected / exposed	6 / 7 (85.71%)	4 / 5 (80.00%)	23 / 27 (85.19%)
occurrences (all)	16	4	46
Dry mouth			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Duodenal ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 5 (40.00%)	4 / 27 (14.81%)
occurrences (all)	2	2	5
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Gingival swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	2 / 5 (40.00%)	9 / 27 (33.33%)
occurrences (all)	1	4	12
Stomatitis			
subjects affected / exposed	2 / 7 (28.57%)	0 / 5 (0.00%)	4 / 27 (14.81%)
occurrences (all)	2	0	4
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	4 / 7 (57.14%)	4 / 5 (80.00%)	17 / 27 (62.96%)
occurrences (all)	15	6	65
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Night sweats			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1

Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 5 (20.00%)	3 / 27 (11.11%)
occurrences (all)	1	1	3
Rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	7 / 27 (25.93%)
occurrences (all)	0	3	11
Skin exfoliation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2
Renal failure			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	5 / 27 (18.52%)
occurrences (all)	0	1	6
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Muscle contracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1

Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	3
Musculoskeletal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Trigger finger			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Escherichia urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Helicobacter infection			

subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	4
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	2 / 5 (40.00%)	9 / 27 (33.33%)
occurrences (all)	3	3	10
Diabetes mellitus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	3
Hyperkalaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1

Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	3
Hypoalbuminaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Steroid diabetes			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported