Clinical trial results:
A Phase IB/II, open-label, multicenter study of INC280 administered orally in combination with gefitinib in adult patients with EGFR mutated, cMET-amplified non-small cell lung cancer who have progressed after EGFR inhibitor treatment

Summary

EudraCT number	2011-002569-39
Trial protocol	BE IT ES DE NL FR
Global end of trial date	27 May 2020

Results information

Result version number	v2 (current)
This version publication date	20 June 2021
First version publication date	28 March 2021
Version creation reason	• New data added to full data set Description for adverse events updated

Trial information

Trial identification

Sponsor protocol code	CINC280X2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01610336
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
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 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	27 May 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase Ib: To estimate the MTD/RP2D of capmatinib in combination with gefitinib in NSCLC patients with cMET gene dysregulation.
Phase II: To estimate overall clinical activity of capmatinib in combination with gefitinib in NSCLC patients with cMET gene dysregulation.
Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

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	05 April 2012
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	Australia: 2
Country: Number of subjects enrolled	China: 67
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	Korea, Republic of: 36
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Singapore: 8
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 6

Worldwide total number of subjects	161
EEA total number of subjects	28

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)	108
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 31 centers located on: Australia, Belgium, China, France, Germany, Israel, Italy, Japan, Korea, Netherlands, New Zealand, Singapore, Spain, Taiwan and Thailand.

Pre-assignment

Screening details:

All patients must had documented evidence of EGFR mutation. A locally documented result from anytime during the patients treatment cycle was acceptable.. If EGFR mutation status was unknown, patients could be tested for EGFR mutation status centrally.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	INC280 100 mg Cap QD Phase Ib

Arm description:

cap=capsule; QD=once daily

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

INC280 100 mg once daily oral capsule

Arm title	INC280 200 mg Cap QD Phase Ib

Arm description:

cap=capsule; QD=once daily

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

INC280 200 mg once daily oral Capsule

Arm title	INC280 400 mg Cap QD Phase Ib

Arm description:

cap=capsule; QD=once daily

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details: INC280 400 mg once daily oral capsule	

Arm title	INC280 800 mg Cap QD Phase Ib
Arm description: cap=capsule; QD=once daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: INCC280 800 mg once daily oral capsule	
Arm title	INC280 200 mg Cap BID Phase Ib
Arm description: cap=capsule; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: INC280 200 mg twice daily oral capsule	
Arm title	INC280 400 mg Cap BID Phase Ib
Arm description: cap=capsule; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: INC280 400 mg twice daily oral capsule	
Arm title	INC280 600 mg Cap BID Phase Ib
Arm description: cap=capsule; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: INC280 600 mg twice daily oral capsule	
Arm title	INC280 200 mg Tab BID Phase Ib

Arm description: tab=tablet; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: INC280 200 mg twice daily oral tablet	
Arm title	INC280 400 mg Tab BID Phase Ib
Arm description: tab=tablet; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: INC280 400 mg twice daily oral tablet	
Arm title	INC280 400 mg Cap BID Phase II
Arm description: cap=capsule; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: INC280 400 mg twice daily oral capsule	
Arm title	INC280 400 mg Tab BID Phase II
Arm description: tab=tablet; BID=twice daily	
Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: INC280 400 mg twice daily oral tablet	

Number of subjects in period 1	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib
Started	5	7	6
Completed	0	0	0
Not completed	5	7	6
Adverse event, serious fatal	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Protocol Deviation	-	-	-
Progressive Disease	4	6	6
Subject/Guardian decision	1	1	-
Transfer to another trial	-	-	-
Non-Compliance with study treatment	-	-	-

Number of subjects in period 1	INC280 800 mg Cap QD Phase Ib	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib
Started	7	4	12
Completed	0	0	0
Not completed	7	4	12
Adverse event, serious fatal	-	-	1
Physician decision	-	-	-
Adverse event, non-fatal	1	1	1
Protocol Deviation	-	-	-
Progressive Disease	5	3	10
Subject/Guardian decision	1	-	-
Transfer to another trial	-	-	-
Non-Compliance with study treatment	-	-	-

Number of subjects in period 1	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib	INC280 400 mg Tab BID Phase Ib
Started	5	7	8
Completed	0	0	0
Not completed	5	7	8
Adverse event, serious fatal	3	-	-
Physician decision	1	-	-
Adverse event, non-fatal	-	-	2
Protocol Deviation	-	-	-
Progressive Disease	1	6	6
Subject/Guardian decision	-	1	-
Transfer to another trial	-	-	-
Non-Compliance with study treatment	-	-	-

Number of subjects in period 1	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II
Started	53	47
Completed	0	0
Not completed	53	47
Adverse event, serious fatal	1	2
Physician decision	-	-
Adverse event, non-fatal	8	6
Protocol Deviation	1	-
Progressive Disease	40	36
Subject/Guardian decision	2	2
Transfer to another trial	-	1
Non-Compliance with study treatment	1	-

Baseline characteristics

Reporting groups	
Reporting group title	INC280 100 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 200 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 400 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 800 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 200 mg Cap BID Phase Ib
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 400 mg Cap BID Phase Ib
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 600 mg Cap BID Phase Ib
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 200 mg Tab BID Phase Ib
Reporting group description: tab=tablet; BID=twice daily	
Reporting group title	INC280 400 mg Tab BID Phase Ib
Reporting group description: tab=tablet; BID=twice daily	
Reporting group title	INC280 400 mg Cap BID Phase II
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 400 mg Tab BID Phase II
Reporting group description: tab=tablet; BID=twice daily	

Reporting group values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib
Number of subjects	5	7	6
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)	3	3	5
From 65-84 years	2	4	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	57.8	60.4	59.5
standard deviation	± 11.05	± 15.27	± 6.89
Sex: Female, Male Units: participants			
Female	2	5	4
Male	3	2	2
Race/Ethnicity, Customized Units: Subjects			
Russian	0	0	0
Mixed Ethnicity	0	0	0
Not reported	0	0	0
Unknown	0	0	0
Hispanic or Latino	0	0	0
Southeast Asian	1	1	0
Other	0	0	0
East Asian	4	6	6

Reporting group values	INC280 800 mg Cap QD Phase Ib	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib
Number of subjects	7	4	12
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)	7	2	11
From 65-84 years	0	2	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	51.3	64.5	55.9
standard deviation	± 8.88	± 8.89	± 10.81
Sex: Female, Male Units: participants			
Female	5	4	4
Male	2	0	8
Race/Ethnicity, Customized Units: Subjects			
Russian	0	0	0
Mixed Ethnicity	0	0	0
Not reported	0	0	0
Unknown	0	0	0

Hispanic or Latino	0	0	1
Southeast Asian	0	0	0
Other	0	1	2
East Asian	7	3	9

Reporting group values	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib	INC280 400 mg Tab BID Phase Ib
Number of subjects	5	7	8
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	7
From 65-84 years	1	3	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	61.0	60.9	58.4
standard deviation	± 8.46	± 12.86	± 5.01
Sex: Female, Male Units: participants			
Female	2	5	5
Male	3	2	3
Race/Ethnicity, Customized Units: Subjects			
Russian	0	0	0
Mixed Ethnicity	0	0	0
Not reported	0	0	0
Unknown	0	0	0
Hispanic or Latino	0	1	0
Southeast Asian	0	1	1
Other	1	2	0
East Asian	4	3	7

Reporting group values	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II	Total
Number of subjects	53	47	161
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)	35	27	108

From 65-84 years	18	20	53
85 years and over	0	0	0

Age Continuous Units: years			
arithmetic mean	58.6	62.8	
standard deviation	± 10.50	± 9.32	-
Sex: Female, Male Units: participants			
Female	33	19	88
Male	20	28	73
Race/Ethnicity, Customized Units: Subjects			
Russian	0	1	1
Mixed Ethnicity	0	1	1
Not reported	0	2	2
Unknown	0	3	3
Hispanic or Latino	0	5	7
Southeast Asian	0	8	12
Other	0	11	17
East Asian	53	16	118

End points

End points reporting groups

Reporting group title	INC280 100 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 200 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 400 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 800 mg Cap QD Phase Ib
Reporting group description: cap=capsule; QD=once daily	
Reporting group title	INC280 200 mg Cap BID Phase Ib
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 400 mg Cap BID Phase Ib
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 600 mg Cap BID Phase Ib
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 200 mg Tab BID Phase Ib
Reporting group description: tab=tablet; BID=twice daily	
Reporting group title	INC280 400 mg Tab BID Phase Ib
Reporting group description: tab=tablet; BID=twice daily	
Reporting group title	INC280 400 mg Cap BID Phase II
Reporting group description: cap=capsule; BID=twice daily	
Reporting group title	INC280 400 mg Tab BID Phase II
Reporting group description: tab=tablet; BID=twice daily	

Primary: Phase Ib: Frequency of dose limiting toxicities (DLTs)

End point title	Phase Ib: Frequency of dose limiting toxicities (DLTs)[1][2]
End point description: A dose-limiting toxicity (DLT) was defined as an adverse event or abnormal laboratory value assessed as unrelated to disease progression, inter-current illness, or concomitant medications that met certain criteria as defined in the protocol.	
End point type	Primary
End point timeframe: Up to 215 weeks	

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 performed

[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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	5
Units: Participants				
Cough	0	0	0	0
Dizziness	0	0	0	1
Dyspnoea	0	0	0	0

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	1	7
Units: Participants				
Cough	0	0	1	0
Dizziness	0	0	0	0
Dyspnoea	0	0	1	0

End point values	INC280 400 mg Tab BID Phase Ib			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Cough	0			
Dizziness	0			
Dyspnoea	0			

Statistical analyses

No statistical analyses for this end point

Primary: Phase II : Overall Response Rate (ORR)

End point title	Phase II : Overall Response Rate (ORR)[3][4]

End point description:

Overall response rate is defined as the proportion of patients with best overall response (BOR) of

complete response (CR) or partial response (PR), as per RECIST 1.1 (Overall Response (OR) = CR + PR).
Complete Response (CR): Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as
target lesions must have a reduction in short axis to < 10 mm
Partial Response (PR): At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of
diameters.

End point type	Primary

End point timeframe:

Until disease progression, up to 60.8 weeks

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: No statistical analysis was performed

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was performed

End point values	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	47		
Units: Participants	12	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and II: Number of participants with Adverse Events (AEs)

End point title	Phase Ib and II: Number of participants with Adverse Events (AEs)

End point description:

Adverse events were assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0

End point type	Secondary

End point timeframe:

Up to 421 weeks

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	6	7
Units: Participants				
AEs	5	7	6	7
Grade 3/4 AEs	3	4	2	4

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	5	7
Units: Participants				
AEs	4	12	5	7
Grade 3/4 AEs	2	6	4	6

End point values	INC280 400 mg Tab BID Phase Ib	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	53	47	
Units: Participants				
AEs	8	51	47	
Grade 3/4 AEs	4	24	35	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and II: Number of participants with serious adverse events (SAEs)

End point title	Phase Ib and II: Number of participants with serious adverse events (SAEs)

End point description:

Serious adverse events were assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0

End point type	Secondary

End point timeframe:

Up to 421 weeks

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	6	7
Units: Participants	1	2	2	3

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	5	7
Units: Participants	0	4	3	5

End point values	INC280 400 mg Tab BID Phase Ib	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	53	47	
Units: Participants	3	12	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and II: Number of patients with dose reductions of INC280 by dose level

End point title	Phase Ib and II: Number of patients with dose reductions of INC280 by dose level
End point description:	
Number of patients with dose reductions of INC280 by dose level as a measure of tolerability.	
End point type	Secondary
End point timeframe:	
Up to 417 weeks	

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	6	7
Units: Participants				
Without dose reductions	5	6	5	6
Only 1 dose reduction	0	1	0	1
2 dose reductions	0	0	1	0
3 dose reductions	0	0	0	0
>3 dose reductions	0	0	0	0

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	5	7
Units: Participants				
Without dose reductions	1	8	1	5
Only 1 dose reduction	2	2	2	0
2 dose reductions	0	1	1	1
3 dose reductions	1	0	1	0
>3 dose reductions	0	1	0	1

End point values	INC280 400 mg Tab BID Phase Ib	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	53	47	
Units: Participants				
Without dose reductions	5	30	23	
Only 1 dose reduction	1	13	17	
2 dose reductions	1	6	5	
3 dose reductions	0	1	1	
>3 dose reductions	1	3	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and II: Number of patients with dose interruptions of gefitinib by dose level

End point title	Phase Ib and II: Number of patients with dose interruptions of gefitinib by dose level[5]

End point description:

Number of patients with dose interruptions of gefitinib by dose level as a measure of tolerability

End point type	Secondary

End point timeframe:

Up to 417 weeks

Notes:

[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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	6	7
Units: Participants				
Without dose interruptions	5	5	6	4
With only one dose interruption	0	2	0	2
2 dose interruptions	0	0	0	0
3 dose interruptions	0	0	0	1

>3 dose interruptions	0	0	0	0

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	5	7
Units: Participants				
Without dose interruptions	4	6	4	4
With only one dose interruption	0	3	0	0
2 dose interruptions	0	1	0	1
3 dose interruptions	0	2	0	0
>3 dose interruptions	0	0	1	2

End point values	INC280 400 mg Tab BID Phase Ib	INC280 400 mg Tab BID Phase II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	47		
Units: Participants				
Without dose interruptions	4	25		
With only one dose interruption	2	16		
2 dose interruptions	0	4		
3 dose interruptions	1	2		
>3 dose interruptions	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Overall survival (OS)

End point title	Phase II: Overall survival (OS)[6]

End point description:

Overall survival is defined as the time from the start of treatment date to the date of death, due to any cause

End point type	Secondary

End point timeframe:

From date of treatment until death due to any cause, up to 70.2 months

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: No statistical analysis was performed

End point values	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	47		
Units: Months				
median (confidence interval 95%)	12.3 (8.1 to 15.4)	15.2 (11.7 to 20.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Progression free survival (PFS)

End point title	Phase II: Progression free survival (PFS)[7]

End point description:

Progression-free survivalis the time from date of randomization/start of treatment to the date of event defined as the first documented progression or death due to any cause.

End point type	Secondary

End point timeframe:

Up to 60.8 months

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: No statistical analysis was performed

End point values	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	47		
Units: Months				
median (confidence interval 95%)	5.1 (3.6 to 5.6)	5.5 (3.8 to 7.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Duration of response (DoR)

End point title	Phase II: Duration of response (DoR)[8]

End point description:

Duration of overall response (DOR) is defined as the time between the date of first documented response (CR or PR) and the date of first documented disease progression or death due to underlying cancer.

End point type	Secondary

End point timeframe:

Up to 23.2 months

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: No statistical analysis was performed

End point values	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	17		
Units: Months				
median (confidence interval 95%)	5.6 (3.7 to 6.2)	5.6 (3.7 to 7.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: PK parameters AUCtau of INC280 and gefitinib

End point title	Phase I: PK parameters AUCtau of INC280 and gefitinib[9]

End point description:

PK parameters were estimated from each individual plasma concentration-time profile using non-compartmental analysis.
Area under the plasma concentration-time curve (AUC) from time zero to the end of dosing interval at steady state (tau), where tau=24 hours for once daily dosing and tau=12 hours for twice daily dosing

End point type	Secondary

End point timeframe:

Cycle 1 day 15 (pre-dose, 0.5, 1, 2, 4, 6, 8 and 24 hours post dose) (Cycle=28 days)

Notes:

[9] - 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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[10]	7[11]	5[12]	3[13]
Units: hr·ng/mL				
arithmetic mean (standard deviation)				
INC280	4510 (± 1960)	9140 (± 5550)	29200 (± 12700)	30300 (± 19800)
Gefitinib	7690 (± 1400)	8070 (± 2080)	7140 (± 1830)	12800 (± 999)

Notes:

[10] - 4 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.
[11] - 7 subjects analyzed for INC280.
6 subjects analyzed for Gefitinib.
[12] - 5 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.
[13] - 3 subjects analyzed for INC280.
1 subjects analyzed for Gefitinib.

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[14]	10[15]	2[16]	7[17]
Units: hr·ng/mL				
arithmetic mean (standard deviation)				
INC280	9660 (± 5780)	21400 (± 8420)	37300 (± 18800)	13900 (± 4470)
Gefitinib	8440 (± 2360)	8500 (± 5330)	999 (± 999)	7160 (± 2040)

Notes:

[14] - 4 subjects analyzed for INC280.
2 subjects analyzed for Gefitinib.
[15] - 10 subjects analyzed for INC280.
6 subjects analyzed for Gefitinib.
[16] - 2 subjects analyzed for INC280.
0 subjects analyzed for Gefitinib.
[17] - 7 subjects analyzed for INC280.
5 subjects analyzed for Gefitinib.

End point values	INC280 400 mg Tab BID Phase Ib			
Subject group type	Reporting group			
Number of subjects analysed	7[18]			
Units: hr·ng/mL				
arithmetic mean (standard deviation)				
INC280	28700 (± 5460)			
Gefitinib	7820 (± 1130)			

Notes:

[18] - 7 subjects analyzed for INC280.
4 subjects analyzed for Gefitinib.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: PK parameters Cmax of INC280 and gefitinib

End point title	Phase I: PK parameters Cmax of INC280 and gefitinib[19]

End point description:

PK parameters were estimated from each individual plasma concentration-time profile using non-compartmental analysis.
Cmax is the maximum observed plasma concentration of INC280 and gefitinib

End point type	Secondary

End point timeframe:

Cycle 1 day 15 (pre-dose, 0.5, 1, 2, 4, 6, 8 and 24 hours post dose) (Cycle=28 days)

Notes:

[19] - 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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	6	4
Units: ng/mL				
arithmetic mean (standard deviation)				

INC280	826 (± 521)	1490 (± 1430)	4620 (± 3060)	6570 (± 4360)
Gefitinib	417 (± 42.9)	378 (± 85.2)	405 (± 144)	357 (± 225)

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	2	7
Units: ng/mL				
arithmetic mean (standard deviation)				
INC280	1950 (± 985)	4220 (± 2100)	4840 (± 1990)	2550 (± 676)
Gefitinib	480 (± 191)	464 (± 209)	255 (± 158)	479 (± 167)

End point values	INC280 400 mg Tab BID Phase Ib			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: ng/mL				
arithmetic mean (standard deviation)				
INC280	6760 (± 1740)			
Gefitinib	355 (± 74.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: PK parameters Tmax of INC280 and gefitinib

End point title	Phase I: PK parameters Tmax of INC280 and gefitinib[20]

End point description:

PK parameters were estimated from each individual plasma concentration-time profile using non-compartmental analysis.
Tmax is the time to reach maximum plasma concentration of INC280 and gefitinib

End point type	Secondary

End point timeframe:

Cycle 1 day 15 (pre-dose, 0.5, 1, 2, 4, 6, 8 and 24 hours post dose) (Cycle=28 days)

Notes:

[20] - 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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	6	4
Units: Hours				
median (full range (min-max))				
INC280	1.96 (1.50 to 3.92)	2.00 (1.00 to 24.0)	2.00 (1.98 to 6.00)	2.05 (1.92 to 5.97)
Gefitinib	3.92 (0 to 8.00)	6.00 (3.97 to 24.0)	6.02 (2.00 to 8.0)	5.94 (2.10 to 7.28)

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	2	7
Units: Hours				
median (full range (min-max))				
INC280	1.50 (1.00 to 3.98)	2.00 (0.50 to 4.00)	5.00 (4.00 to 6.00)	2.00 (1.00 to 4.00)
Gefitinib	5.00 (4.00 to 8.00)	6.00 (3.97 to 8.00)	11.3 (0 to 22.5)	6.00 (2.00 to 7.50)

End point values	INC280 400 mg Tab BID Phase Ib			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Hours				
median (full range (min-max))				
INC280	1.08 (1.00 to 4.00)			
Gefitinib	6.00 (3.90 to 7.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: PK parameters apparent systemic plasma clearance rate of INC280 and gefitinib

End point title	Phase I: PK parameters apparent systemic plasma clearance rate of INC280 and gefitinib[21]

End point description:

PK parameters were estimated from each individual plasma concentration-time profile using non-compartmental analysis.
Apparent systemic plasma clearance rate of INC280 and gefitinib

End point type	Secondary

End point timeframe:

Cycle 1 day 15 (pre-dose, 0.5, 1, 2, 4, 6, 8 and 24 hours post dose) (Cycle=28 days)

Notes:

[21] - 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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[22]	7[23]	5[24]	3[25]
Units: L/hr				
arithmetic mean (standard deviation)				
INC 280	26.9 (± 15.0)	29.4 (± 15.7)	16.3 (± 7.61)	47.7 (± 49.1)
Gefitinib	33.3 (± 6.78)	32.9 (± 9.65)	36.5 (± 8.41)	19.5 (± 999)

Notes:

[22] - 4 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.
[23] - 7 subjects analyzed for INC280.
6 subjects analyzed for Gefitinib.
[24] - 5 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.
[25] - 3 subjects analyzed for INC280.
1 subjects analyzed for Gefitinib.

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[26]	10[27]	2[28]	7[29]
Units: L/hr				
arithmetic mean (standard deviation)				
INC 280	27.0 (± 14.7)	24.2 (± 18.3)	18.4 (± 9.31)	15.4 (± 3.89)
Gefitinib	30.8 (± 8.61)	41.0 (± 24.1)	999 (± 999)	36.9 (± 8.81)

Notes:

[26] - 4 subjects analyzed for INC280.
2 subjects analyzed for Gefitinib.
[27] - 10 subjects analyzed for INC280.
6 subjects analyzed for Gefitinib.
[28] - 2 subjects analyzed for INC280.
0 subjects analyzed for Gefitinib.
[29] - 7 subjects analyzed for INC280.
5 subjects analyzed for Gefitinib.

End point values	INC280 400 mg Tab BID Phase Ib			
Subject group type	Reporting group			
Number of subjects analysed	7[30]			
Units: L/hr				
arithmetic mean (standard deviation)				
INC 280	14.4 (± 3.10)			
Gefitinib	32.5 (± 4.99)			

Notes:

[30] - 7 subjects analyzed for INC280.
4 subjects analyzed for Gefitinib.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: PK parameters half-life of INC280 and gefitinib

End point title	Phase I: PK parameters half-life of INC280 and gefitinib[31]

End point description:

PK parameters were estimated from each individual plasma concentration-time profile using non-compartmental analysis.
The elimination half-life of INC280 and gefitinib associated with the terminal slope (Lamda_z) of a semi-logarithmic plasma concentration-time curve

End point type	Secondary

End point timeframe:

Cycle 1 day 15 (pre-dose, 0.5, 1, 2, 4, 6, 8 and 24 hours post dose)(Cycle=28 days)

Notes:

[31] - 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: No statistical analysis was performed

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[32]	6[33]	5[34]	3[35]
Units: hours				
arithmetic mean (standard deviation)				
INC280	3.86 (± 0.564)	5.10 (± 2.01)	3.16 (± 0.361)	3.67 (± 0.796)
Gefitinib	18.8 (± 999)	26.9 (± 4.63)	36.3 (± 8.20)	37.8 (± 999)

Notes:

[32] - 4 subjects analyzed for INC280.
1 subjects analyzed for Gefitinib.
[33] - 6 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.
[34] - 5 subjects analyzed for INC280.
2 subjects analyzed for Gefitinib.
[35] - 3 subjects analyzed for INC280.
1 subjects analyzed for Gefitinib.

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[36]	9[37]	0[38]	7[39]
Units: hours				
arithmetic mean (standard deviation)				
INC280	3.19 (± 0.942)	3.01 (± 1.38)	()	3.75 (± 1.94)
Gefitinib	16.3 (± 2.16)	18.7 (± 7.75)	()	17.8 (± 5.08)

Notes:

[36] - 3 subjects analyzed for INC280.
2 subjects analyzed for Gefitinib.
[37] - 9 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.
[38] - No patients analyzed due to insufficient number of blood samples
[39] - 7 subjects analyzed for INC280.
3 subjects analyzed for Gefitinib.

End point values	INC280 400			

	mg Tab BID Phase Ib			
Subject group type	Reporting group			
Number of subjects analysed	6[40]			
Units: hours				
arithmetic mean (standard deviation)				
INC280	3.17 (± 0.783)			
Gefitinib	23.9 (± 999)			

Notes:

[40] - 6 subjects analyzed for INC280.
1 subjects analyzed for Gefitinib.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Phase I: Percentage of change from baseline in C-MET H score at cycle 1 day 15

End point title	Phase I: Percentage of change from baseline in C-MET H score at cycle 1 day 15

End point description:

Inhibition of c-MET signaling by pre- and post- treatment immunohistochemistry of p-c-MET

End point type	Other pre-specified

End point timeframe:

Baseline, Day 15 of cycle 1 (Cycle=28days)

End point values	INC280 100 mg Cap QD Phase Ib	INC280 200 mg Cap QD Phase Ib	INC280 400 mg Cap QD Phase Ib	INC280 800 mg Cap QD Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0[41]	0[42]	0[43]
Units: Percentage				
median (full range (min-max))	-100 (-100 to -100)	(to)	(to)	(to)

Notes:

[41] - No tumor samples were available since tumor biopsy was optional for this study.

[42] - No tumor samples were available since tumor biopsy was optional for this study.

[43] - No tumor samples were available since tumor biopsy was optional for this study.

End point values	INC280 200 mg Cap BID Phase Ib	INC280 400 mg Cap BID Phase Ib	INC280 600 mg Cap BID Phase Ib	INC280 200 mg Tab BID Phase Ib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[44]	3	0[45]	0[46]
Units: Percentage				
median (full range (min-max))	(to)	-100 (-100 to -100)	(to)	(to)

Notes:

[44] - No tumor samples were available since tumor biopsy was optional for this study.

[45] - No tumor samples were available since tumor biopsy was optional for this study.

[46] - No tumor samples were available since tumor biopsy was optional for this study.

End point values	INC280 400 mg Tab BID Phase Ib	INC280 400 mg Cap BID Phase II	INC280 400 mg Tab BID Phase II	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[47]	1	0[48]	
Units: Percentage				
median (full range (min-max))	(to)	-31 (-31 to -31)	(to)	

Notes:

[47] - No tumor samples were available since tumor biopsy was optional for this study.

[48] - No tumor samples were available since tumor biopsy was optional for this study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 8 years.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	100 mg Cap QD (Ph Ib)
Reporting group description: 100 mg Cap QD (Ph Ib)	
Reporting group title	200 mg Cap QD (Ph Ib)
Reporting group description: 200 mg Cap QD (Ph Ib)	
Reporting group title	400 mg Cap QD (Ph Ib)
Reporting group description: 400 mg Cap QD (Ph Ib)	
Reporting group title	800 mg Cap QD (Ph Ib)
Reporting group description: 800 mg Cap QD (Ph Ib)	
Reporting group title	200 mg Cap BID (Ph Ib)
Reporting group description: 200 mg Cap BID (Ph Ib)	
Reporting group title	400 mg Cap BID (Ph Ib)
Reporting group description: 400 mg Cap BID (Ph Ib)	
Reporting group title	600 mg Cap BID (Ph Ib)
Reporting group description: 600 mg Cap BID (Ph Ib)	
Reporting group title	200 mg Tab BID (Ph Ib)
Reporting group description: 200 mg Tab BID (Ph Ib)	
Reporting group title	400 mg Tab BID (Ph Ib)
Reporting group description: 400 mg Tab BID (Ph Ib)	
Reporting group title	400 mg Cap BID (Ph II)
Reporting group description: 400 mg Cap BID (Ph II)	
Reporting group title	400 mg Tab BID (Ph II)
Reporting group description: 400 mg Tab BID (Ph II)	

Serious adverse events	100 mg Cap QD (Ph Ib)	200 mg Cap QD (Ph Ib)	400 mg Cap QD (Ph Ib)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	2 / 6 (33.33%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritumoural oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Femur fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (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
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	800 mg Cap QD (Ph Ib)	200 mg Cap BID (Ph Ib)	400 mg Cap BID (Ph Ib)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	4 / 12 (33.33%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Peritumoural oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Oedema peripheral			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Dyspnoea exertional			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Haemoptysis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Pulmonary embolism			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (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
Respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Bilirubin conjugated increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 pressure decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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

Fibula fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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			
Angina pectoris			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Pericardial effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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

Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 pressure increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Somnolence			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (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
Spinal cord compression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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 and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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			

Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Ileus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Intestinal perforation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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			
Cholecystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Device related infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Erysipelas			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Klebsiella infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Peritonitis bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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

Pneumonia mycoplasmal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Septic shock			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Tracheobronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (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	600 mg Cap BID (Ph Ib)	200 mg Tab BID (Ph Ib)	400 mg Tab BID (Ph Ib)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	5 / 7 (71.43%)	3 / 8 (37.50%)
number of deaths (all causes)	3	0	1
number of deaths resulting from	1	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Peritumoural oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 5 (40.00%)	0 / 7 (0.00%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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 failure			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Bilirubin conjugated increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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 pressure decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Fibula fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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

Hip fracture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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 disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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

Haemorrhage intracranial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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 pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Spinal cord compression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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 and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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

Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Ileus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Intestinal perforation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Erysipelas			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Klebsiella infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Peritonitis bacterial			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia mycoplasmal			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Septic shock			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Tracheobronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (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	400 mg Cap BID (Ph II)	400 mg Tab BID (Ph II)	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 53 (22.64%)	19 / 47 (40.43%)	
number of deaths (all causes)	6	2	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritumoural oedema			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 53 (1.89%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 53 (1.89%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bilirubin conjugated increased			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure decreased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hip fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemorrhage intracranial			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastritis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 53 (7.55%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 0	
Pneumonia mycoplasmal			

subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	100 mg Cap QD (Ph Ib)	200 mg Cap QD (Ph Ib)	400 mg Cap QD (Ph Ib)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	7 / 7 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral vascular disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Chest discomfort			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Generalised oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	1 / 6 (16.67%)
occurrences (all)	1	2	2
Oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Dysphonia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Haemoptysis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Interstitial lung disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	2 / 5 (40.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Bilirubin conjugated increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Crystal urine present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Protein total increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary sediment present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urine analysis abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urine bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urine ketone body present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Urobilinogen urine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tracheal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyskinesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Facial spasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 5 (60.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Dry mouth			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Duodenal ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	3 / 6 (50.00%)
occurrences (all)	3	3	4
Stomatitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	2 / 5 (40.00%)	3 / 7 (42.86%)	2 / 6 (33.33%)
occurrences (all)	3	3	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Dermatosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pruritus			

subjects affected / exposed	3 / 5 (60.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Rash			
subjects affected / exposed	2 / 5 (40.00%)	3 / 7 (42.86%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Rash macular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash vesicular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Haemoglobinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Proteinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	4 / 7 (57.14%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gouty arthritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infected dermal cyst			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	2 / 5 (40.00%)	1 / 7 (14.29%)	2 / 6 (33.33%)
occurrences (all)	2	1	2
Periodontitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	1 / 6 (16.67%)
occurrences (all)	2	2	1
Hyperamylasaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoproteinaemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	800 mg Cap QD (Ph Ib)	200 mg Cap BID (Ph Ib)	400 mg Cap BID (Ph Ib)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	12 / 12 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Peripheral vascular disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Generalised oedema			

subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	4 / 12 (33.33%)
occurrences (all)	1	4	4
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	3 / 12 (25.00%)
occurrences (all)	1	1	3
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	4 / 12 (33.33%)
occurrences (all)	3	1	4
Haemoptysis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Interstitial lung disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 4 (50.00%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
Amylase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	4 / 12 (33.33%)
occurrences (all)	0	1	6
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Bilirubin conjugated increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood albumin decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	5 / 12 (41.67%)
occurrences (all)	0	0	8
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
Blood glucose increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood iron decreased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood phosphorus increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Crystal urine present			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Protein total increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Protein urine present			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Urinary sediment present			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urine analysis abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urine bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Urine ketone body present			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Urobilinogen urine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
White blood cells urine positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tracheal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Wound complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tachycardia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Dyskinesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Facial spasm			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nervous system disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Tremor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 4 (50.00%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Leukopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Tinnitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	3 / 4 (75.00%)	4 / 12 (33.33%)
occurrences (all)	2	4	6
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Duodenal ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Mouth ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	6 / 7 (85.71%)	2 / 4 (50.00%)	1 / 12 (8.33%)
occurrences (all)	7	2	1
Stomatitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	7 / 7 (100.00%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	8	1	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Dermatosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry skin			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Rash			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	4 / 12 (33.33%)
occurrences (all)	2	2	4
Rash macular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash vesicular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Haemoglobinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gouty arthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ligament pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	2 / 4 (50.00%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Muscle tightness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Folliculitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infected dermal cyst			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Paronychia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 4 (50.00%)	4 / 12 (33.33%)
occurrences (all)	0	2	4
Periodontitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 7 (57.14%)	1 / 4 (25.00%)	1 / 12 (8.33%)
occurrences (all)	4	1	1
Hyperamylasaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 7 (28.57%)	3 / 4 (75.00%)	7 / 12 (58.33%)
occurrences (all)	2	4	7
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypochloraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypophosphataemia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoproteinaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	600 mg Cap BID (Ph Ib)	200 mg Tab BID (Ph Ib)	400 mg Tab BID (Ph Ib)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	6 / 7 (85.71%)	7 / 8 (87.50%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Peripheral vascular disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Phlebitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	1 / 8 (12.50%)
occurrences (all)	1	4	1
Chest discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Fatigue			

subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Generalised oedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Oedema peripheral			
subjects affected / exposed	2 / 5 (40.00%)	3 / 7 (42.86%)	2 / 8 (25.00%)
occurrences (all)	2	18	2
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	1 / 8 (12.50%)
occurrences (all)	1	1	2
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	3 / 5 (60.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Dysphonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Interstitial lung disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 7 (42.86%)	1 / 8 (12.50%)
occurrences (all)	1	3	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Blood glucose increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Crystal urine present			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Lipase increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	3	1	0
Neutrophil count decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Protein total increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	2 / 5 (40.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Urinary sediment present			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Urine analysis abnormal			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Urine bilirubin increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Urine ketone body present			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Urobilinogen urine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 8 (25.00%)
occurrences (all)	0	1	3
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tracheal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Cardiac failure congestive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Depressed level of consciousness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Dyskinesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Facial spasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	3 / 8 (37.50%)
occurrences (all)	1	2	3
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nervous system disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Eye irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	1 / 8 (12.50%)
occurrences (all)	0	3	1
Photopsia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	2 / 8 (25.00%)
occurrences (all)	1	2	2
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 8 (25.00%)
occurrences (all)	0	2	3
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	3 / 8 (37.50%)
occurrences (all)	2	2	3
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Duodenal ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	5 / 7 (71.43%)	3 / 8 (37.50%)
occurrences (all)	1	6	4
Stomatitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	3 / 8 (37.50%)
occurrences (all)	1	2	5
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			

subjects affected / exposed	0 / 5 (0.00%)	4 / 7 (57.14%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Dermatosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	3 / 8 (37.50%)
occurrences (all)	1	5	4
Rash macular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash vesicular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemoglobinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gouty arthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Ligament pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Muscle tightness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Neck pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	3 / 7 (42.86%)	1 / 8 (12.50%)
occurrences (all)	0	5	1

Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Eye infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infected dermal cyst			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Paronychia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	3 / 8 (37.50%)
occurrences (all)	0	6	3
Periodontitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Skin infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 5 (60.00%)	3 / 7 (42.86%)	3 / 8 (37.50%)
occurrences (all)	3	4	5
Hyperamylasaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Hypochloraemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	6	0	0
Hypomagnesaemia			

subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	0 / 8 (0.00%)
occurrences (all)	3	2	0
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypoproteinaemia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	400 mg Cap BID (Ph II)	400 mg Tab BID (Ph II)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 53 (92.45%)	47 / 47 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Orthostatic hypotension			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Phlebitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 53 (5.66%)	4 / 47 (8.51%)	
occurrences (all)	3	5	
Chest discomfort			

subjects affected / exposed	1 / 53 (1.89%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Face oedema			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	10 / 53 (18.87%)	17 / 47 (36.17%)	
occurrences (all)	12	22	
Generalised oedema			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	
Influenza like illness			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	8 / 53 (15.09%)	4 / 47 (8.51%)	
occurrences (all)	8	5	
Oedema			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Oedema peripheral			
subjects affected / exposed	15 / 53 (28.30%)	21 / 47 (44.68%)	
occurrences (all)	20	30	
Pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	4	
Pyrexia			
subjects affected / exposed	2 / 53 (3.77%)	4 / 47 (8.51%)	
occurrences (all)	2	6	
Respiratory, thoracic and mediastinal			

disorders				
Aspiration				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Cough				
subjects affected / exposed	14 / 53 (26.42%)	8 / 47 (17.02%)		
occurrences (all)	16	10		
Dysphonia				
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)		
occurrences (all)	1	0		
Dyspnoea				
subjects affected / exposed	3 / 53 (5.66%)	9 / 47 (19.15%)		
occurrences (all)	3	9		
Haemoptysis				
subjects affected / exposed	8 / 53 (15.09%)	2 / 47 (4.26%)		
occurrences (all)	12	2		
Interstitial lung disease				
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)		
occurrences (all)	1	0		
Nasal dryness				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Oropharyngeal pain				
subjects affected / exposed	4 / 53 (7.55%)	0 / 47 (0.00%)		
occurrences (all)	4	0		
Productive cough				
subjects affected / exposed	1 / 53 (1.89%)	4 / 47 (8.51%)		
occurrences (all)	1	4		
Pulmonary embolism				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Rhinorrhoea				

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Tachypnoea			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	7 / 53 (13.21%)	2 / 47 (4.26%)	
occurrences (all)	7	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 53 (24.53%)	5 / 47 (10.64%)	
occurrences (all)	17	7	
Amylase increased			
subjects affected / exposed	7 / 53 (13.21%)	11 / 47 (23.40%)	
occurrences (all)	9	15	
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 53 (18.87%)	7 / 47 (14.89%)	
occurrences (all)	16	9	
Bilirubin conjugated increased			
subjects affected / exposed	5 / 53 (9.43%)	0 / 47 (0.00%)	
occurrences (all)	5	0	
Blood albumin decreased			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 53 (3.77%)	4 / 47 (8.51%)	
occurrences (all)	2	4	
Blood bilirubin increased			

subjects affected / exposed	8 / 53 (15.09%)	4 / 47 (8.51%)		
occurrences (all)	14	6		
Blood creatinine increased				
subjects affected / exposed	9 / 53 (16.98%)	8 / 47 (17.02%)		
occurrences (all)	12	11		
Blood glucose increased				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Blood iron decreased				
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)		
occurrences (all)	1	0		
Blood phosphorus increased				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Crystal urine present				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	3 / 53 (5.66%)	5 / 47 (10.64%)		
occurrences (all)	3	6		
Haemoglobin decreased				
subjects affected / exposed	3 / 53 (5.66%)	0 / 47 (0.00%)		
occurrences (all)	4	0		
Lipase increased				
subjects affected / exposed	5 / 53 (9.43%)	10 / 47 (21.28%)		
occurrences (all)	6	16		
Neutrophil count decreased				
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)		
occurrences (all)	1	0		
Protein total increased				
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)		
occurrences (all)	0	0		
Protein urine present				
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)		
occurrences (all)	4	0		

Urinary sediment present			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Urine analysis abnormal			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Urine bilirubin increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Urine ketone body present			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Urobilinogen urine increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 53 (0.00%)	4 / 47 (8.51%)	
occurrences (all)	0	4	
Weight increased			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	4	
White blood cell count decreased			
subjects affected / exposed	2 / 53 (3.77%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
White blood cells urine positive			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Tracheal haemorrhage			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Wound complication			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Depressed level of consciousness			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	6 / 53 (11.32%)	3 / 47 (6.38%)	
occurrences (all)	8	4	
Dyskinesia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Facial spasm			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	3 / 53 (5.66%)	8 / 47 (17.02%)	
occurrences (all)	4	10	
Hypoaesthesia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Nervous system disorder			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Taste disorder			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 53 (33.96%)	4 / 47 (8.51%)	
occurrences (all)	28	7	
Leukopenia			
subjects affected / exposed	5 / 53 (9.43%)	0 / 47 (0.00%)	
occurrences (all)	13	0	
Neutropenia			
subjects affected / exposed	4 / 53 (7.55%)	0 / 47 (0.00%)	
occurrences (all)	9	0	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Tinnitus			
subjects affected / exposed	1 / 53 (1.89%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Eye irritation			

subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Lacrimation increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Photopsia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Abdominal distension			
subjects affected / exposed	3 / 53 (5.66%)	1 / 47 (2.13%)	
occurrences (all)	3	2	
Abdominal pain			
subjects affected / exposed	1 / 53 (1.89%)	4 / 47 (8.51%)	
occurrences (all)	1	4	
Abdominal pain upper			
subjects affected / exposed	1 / 53 (1.89%)	4 / 47 (8.51%)	
occurrences (all)	1	7	
Constipation			
subjects affected / exposed	5 / 53 (9.43%)	11 / 47 (23.40%)	
occurrences (all)	5	11	
Diarrhoea			
subjects affected / exposed	7 / 53 (13.21%)	15 / 47 (31.91%)	
occurrences (all)	10	23	
Dry mouth			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	

Duodenal ulcer			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	5	
Dysphagia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Gastric ulcer			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Gastritis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Gingival bleeding			
subjects affected / exposed	3 / 53 (5.66%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Mouth ulceration			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	7 / 53 (13.21%)	26 / 47 (55.32%)	
occurrences (all)	11	34	
Stomatitis			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	10 / 53 (18.87%)	10 / 47 (21.28%)	
occurrences (all)	14	13	
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Decubitus ulcer			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 53 (0.00%)	5 / 47 (10.64%)	
occurrences (all)	0	8	
Dermatosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 53 (1.89%)	4 / 47 (8.51%)	
occurrences (all)	1	4	
Pruritus			
subjects affected / exposed	2 / 53 (3.77%)	5 / 47 (10.64%)	
occurrences (all)	2	5	
Rash			
subjects affected / exposed	7 / 53 (13.21%)	15 / 47 (31.91%)	
occurrences (all)	9	19	
Rash macular			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Rash vesicular			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Skin fissures			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Azotaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Haematuria			
subjects affected / exposed	5 / 53 (9.43%)	2 / 47 (4.26%)	
occurrences (all)	9	2	
Haemoglobinuria			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Proteinuria			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences (all)	5	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 53 (1.89%)	3 / 47 (6.38%)	
occurrences (all)	1	4	
Back pain			
subjects affected / exposed	4 / 53 (7.55%)	4 / 47 (8.51%)	
occurrences (all)	4	4	
Bone pain			
subjects affected / exposed	2 / 53 (3.77%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Flank pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Gouty arthritis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Joint swelling			

subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Ligament pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	1 / 53 (1.89%)	3 / 47 (6.38%)	
occurrences (all)	1	4	
Muscle tightness			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 53 (3.77%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Musculoskeletal pain			
subjects affected / exposed	3 / 53 (5.66%)	3 / 47 (6.38%)	
occurrences (all)	3	4	
Myalgia			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Neck pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	1 / 53 (1.89%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Rhabdomyolysis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 53 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	4	

Conjunctivitis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	3	
Cystitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Ear infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Eye infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Folliculitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Infected dermal cyst			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Localised infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	5 / 53 (9.43%)	1 / 47 (2.13%)	
occurrences (all)	14	1	
Paronychia			
subjects affected / exposed	7 / 53 (13.21%)	10 / 47 (21.28%)	
occurrences (all)	7	11	
Periodontitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	

Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Skin infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 53 (3.77%)	4 / 47 (8.51%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	0 / 53 (0.00%)	4 / 47 (8.51%)	
occurrences (all)	0	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	13 / 53 (24.53%)	19 / 47 (40.43%)	
occurrences (all)	19	21	
Hyperamylasaemia			
subjects affected / exposed	8 / 53 (15.09%)	0 / 47 (0.00%)	
occurrences (all)	14	0	
Hyperglycaemia			
subjects affected / exposed	2 / 53 (3.77%)	4 / 47 (8.51%)	
occurrences (all)	4	5	
Hyperkalaemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	
Hypoalbuminaemia			
subjects affected / exposed	23 / 53 (43.40%)	12 / 47 (25.53%)	
occurrences (all)	28	20	
Hypocalcaemia			
subjects affected / exposed	8 / 53 (15.09%)	3 / 47 (6.38%)	
occurrences (all)	13	4	
Hypochloraemia			

subjects affected / exposed	2 / 53 (3.77%)	0 / 47 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			
subjects affected / exposed	7 / 53 (13.21%)	4 / 47 (8.51%)	
occurrences (all)	8	4	
Hypomagnesaemia			
subjects affected / exposed	1 / 53 (1.89%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Hyponatraemia			
subjects affected / exposed	6 / 53 (11.32%)	1 / 47 (2.13%)	
occurrences (all)	11	3	
Hypophosphataemia			
subjects affected / exposed	3 / 53 (5.66%)	1 / 47 (2.13%)	
occurrences (all)	5	2	
Hypoproteinaemia			
subjects affected / exposed	5 / 53 (9.43%)	0 / 47 (0.00%)	
occurrences (all)	5	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2012	The main purpose of Amendment 1 was to further clarify the patient population with EGFR mutation, cMET amplified NSCLC who progressed on prior EGFR TKIs (e.g. gefitinib or erlotinib). Also a bid administration of capmatinib was to be investigated, based on emerging safety, PK, PD and efficacy results.
20 December 2013	The main purpose of Amendment 2 was to introduce the use of capmatinib tablets.
15 July 2014	The main purpose of Amendment 3 was to include additional NSCLC patients (200 in total) in Phase II. These additional NSCLC patients were to be selected based on high cMET dysregulation defined as ≥ 50% of tumor cells with an IHC score of =3+; or an IHC score of =2+ and ≥ 5 gene copies detected by FISH.
24 July 2015	The main purpose of Amendment 4 was to provide a safety update, revised inclusion and exclusion criteria including the molecular pre-screening criteria, and reassess the sample size.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: