

**Clinical trial results:****A Phase 2, Multicenter, Double-Blinded, Placebo-Controlled, Multiple-Dose Study to Evaluate Safety, Tolerability, Efficacy, Pharmacokinetics, and Pharmacodynamics of Lumacaftor Monotherapy, and Lumacaftor and Ivacaftor Combination Therapy in Subjects with Cystic Fibrosis, Homozygous or Heterozygous for the F508del-CFTR Mutation**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

**Summary**

EudraCT number	2010-020413-90
Trial protocol	DE BE GB IE
Global end of trial date	29 April 2014

**Results information**

Result version number	v2 (current)
This version publication date	13 July 2016
First version publication date	08 August 2015
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set requires edit to address results section (Secondary Endpoints data , and reporting groups shuffle) affected by system bug which has now been fixed.</li></ul>

**Trial information****Trial identification**

Sponsor protocol code	VX09-809-102
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01225211
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States, 022101862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.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	No

1901/2006 apply to this trial?
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Notes:

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### Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2014
Was the trial ended prematurely?	No

Notes:

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### General information about the trial

Main objective of the trial:

Cohort 1, Cohort 2, and Cohort 3: To evaluate the safety and tolerability when lumacaftor is administered alone or in combination with ivacaftor; To evaluate the effect of lumacaftor administered alone or in combination with ivacaftor on sweat chloride. Cohort 4: To evaluate the safety and tolerability of lumacaftor in combination with ivacaftor; To evaluate the efficacy of lumacaftor in combination with ivacaftor.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 October 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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### Population of trial subjects

#### Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 227
Country: Number of subjects enrolled	Australia: 40
Worldwide total number of subjects	311
EEA total number of subjects	37

Notes:

<b>Subjects enrolled per age group</b>	
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)	311
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants in each cohort are mutually exclusive. A total of 312 participants were randomized of which one participant did not receive any treatment and a total of 311 participants were treated.

### Pre-assignment

Screening details:

Study included 4 cohorts which were studied in sequential manner. For results reporting, combined placebo arm was reported for Cohort 2 and 3 and results for these 2 cohorts are reported collectively.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Cohort 1: Placebo

Arm description:

Participants homozygous (HO) for the F508del-CF transmembrane conductance regulator gene (CFTR) mutation received lumacaftor matched placebo once daily (qd) (Day 1 through Day 14), followed by lumacaftor matched placebo qd in combination with ivacaftor matched placebo every 12 hours (q12h) (Day 15 through Day 21).

Arm type	Placebo
Investigational medicinal product name	Lumacaftor Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo tablet qd as described in reporting group description.

Investigational medicinal product name	Ivacaftor Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo tablet qd as described in reporting group description.

<b>Arm title</b>	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 150 mg q12h
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Arm description:

Participants homozygous for the F508del-CFTR mutation received 200 milligram (mg) of lumacaftor (LUM) qd (Day 1 through Day 14), followed by 200 mg of lumacaftor qd in combination with 150 mg of ivacaftor (IVA) q12h (Day 15 through Day 21).

Arm type	Experimental
Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:	
Lumacaftor tablet qd as described in reporting group description.	
Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ivacaftor tablet qd as described in reporting group description.	
<b>Arm title</b>	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h
Arm description:	
Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd (Day 1 through Day 14), followed by 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).	
Arm type	Experimental
Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Lumacaftor tablet qd as described in reporting group description.	
Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ivacaftor tablet qd as described in reporting group description.	
<b>Arm title</b>	Cohort 2 and 3: Placebo (HO and HE)
Arm description:	
Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 28), followed by lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).	
Arm type	Placebo
Investigational medicinal product name	Lumacaftor Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo tablet qd as described in reporting group description.	
Investigational medicinal product name	Ivacaftor Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo tablet qd as described in reporting group description.	
<b>Arm title</b>	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)
Arm description:	
Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1	

through Day 28), followed by 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Arm type	Experimental
Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lumacaftor tablet qd as described in reporting group description.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor tablet qd as described in reporting group description.

<b>Arm title</b>	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)
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Arm description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 400 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Arm type	Experimental
Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lumacaftor tablet qd as described in reporting group description.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor tablet qd as described in reporting group description.

<b>Arm title</b>	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO&HE)
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Arm description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Arm type	Experimental
Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lumacaftor tablet qd as described in reporting group description.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ivacaftor tablet qd as described in reporting group description.	
<b>Arm title</b>	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)
Arm description:	
Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone q12h (Day 1 through Day 28), followed by 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Arm type	Experimental
Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Lumacaftor tablet qd as described in reporting group description.	
Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ivacaftor tablet qd as described in reporting group description.	
<b>Arm title</b>	Cohort 4: Placebo
Arm description:	
Participants heterozygous for the F508del-CFTR mutation received lumacaftor in combination with ivacaftor matched placebo q12h (Day 1 through Day 56).	
Arm type	Placebo
Investigational medicinal product name	Lumacaftor Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo tablet qd as described in reporting group description.	
Investigational medicinal product name	Ivacaftor Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo tablet qd as described in reporting group description.	
<b>Arm title</b>	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h
Arm description:	
Participants heterozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 1 through Day 56).	
Arm type	Experimental

Investigational medicinal product name	Lumacaftor
Investigational medicinal product code	
Other name	VX-809, LUM
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lumacaftor tablet qd as described in reporting group description.

Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	
Other name	VX-770, IVA
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ivacaftor tablet qd as described in reporting group description.

Number of subjects in period 1	Cohort 1: Placebo	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 150 mg q12h	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h
Started	21	20	21
Completed	21	20	20
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	1
Unspecified	-	-	-

Number of subjects in period 1	Cohort 2 and 3: Placebo (HO and HE)	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)
Started	27	23	21
Completed	27	23	21
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Unspecified	-	-	-

Number of subjects in period 1	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO&HE)	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)	Cohort 4: Placebo
Started	42	11	63
Completed	41	11	62
Not completed	1	0	1
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	-	-	-
Unspecified	-	-	-



<b>Number of subjects in period 1</b>	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h
Started	62
Completed	57
Not completed	5
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Unspecified	1

## Baseline characteristics

### Reporting groups

Reporting group title	Cohort 1: Placebo
Reporting group description: Participants homozygous (HO) for the F508del-CF transmembrane conductance regulator gene (CFTR) mutation received lumacaftor matched placebo once daily (qd) (Day 1 through Day 14), followed by lumacaftor matched placebo qd in combination with ivacaftor matched placebo every 12 hours (q12h) (Day 15 through Day 21).	
Reporting group title	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 150 mg q12h
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 200 milligram (mg) of lumacaftor (LUM) qd (Day 1 through Day 14), followed by 200 mg of lumacaftor qd in combination with 150 mg of ivacaftor (IVA) q12h (Day 15 through Day 21).	
Reporting group title	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd (Day 1 through Day 14), followed by 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).	
Reporting group title	Cohort 2 and 3: Placebo (HO and HE)
Reporting group description: Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 28), followed by lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).	
Reporting group title	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 400 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO&HE)
Reporting group description: Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone q12h (Day 1 through Day 28), followed by 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 4: Placebo
Reporting group description: Participants heterozygous for the F508del-CFTR mutation received lumacaftor in combination with ivacaftor matched placebo q12h (Day 1 through Day 56).	
Reporting group title	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h
Reporting group description: Participants heterozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 1 through Day 56).	

Reporting group values	Cohort 1: Placebo	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 150 mg q12h	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h
Number of subjects	21	20	21
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	21	20	21
>=65 years	0	0	0
Gender categorical Units: Subjects			
Female	10	8	13
Male	11	12	8

Reporting group values	Cohort 2 and 3: Placebo (HO and HE)	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)
Number of subjects	27	23	21
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	27	23	21
>=65 years	0	0	0
Gender categorical Units: Subjects			
Female	9	11	9
Male	18	12	12

Reporting group values	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO&HE)	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)	Cohort 4: Placebo
Number of subjects	42	11	63
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	42	11	63
>=65 years	0	0	0
Gender categorical Units: Subjects			
Female	19	5	31
Male	23	6	32

Reporting group values	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h	Total	
Number of subjects	62	311	
Age categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	62	311	

>=65 years	0	0	
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Gender categorical			
Units: Subjects			
Female	29	144	
Male	33	167	

## End points

### End points reporting groups

Reporting group title	Cohort 1: Placebo
Reporting group description: Participants homozygous (HO) for the F508del-CF transmembrane conductance regulator gene (CFTR) mutation received lumacaftor matched placebo once daily (qd) (Day 1 through Day 14), followed by lumacaftor matched placebo qd in combination with ivacaftor matched placebo every 12 hours (q12h) (Day 15 through Day 21).	
Reporting group title	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 150 mg q12h
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 200 milligram (mg) of lumacaftor (LUM) qd (Day 1 through Day 14), followed by 200 mg of lumacaftor qd in combination with 150 mg of ivacaftor (IVA) q12h (Day 15 through Day 21).	
Reporting group title	Cohort 1: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd (Day 1 through Day 14), followed by 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).	
Reporting group title	Cohort 2 and 3: Placebo (HO and HE)
Reporting group description: Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 28), followed by lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).	
Reporting group title	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 400 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO&HE)
Reporting group description: Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)
Reporting group description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone q12h (Day 1 through Day 28), followed by 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Reporting group title	Cohort 4: Placebo
Reporting group description: Participants heterozygous for the F508del-CFTR mutation received lumacaftor in combination with ivacaftor matched placebo q12h (Day 1 through Day 56).	
Reporting group title	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h
Reporting group description: Participants heterozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 1 through Day 56).	

Subject analysis set title	Cohort 1: Placebo – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd in combination with ivacaftor matched placebo q12h (Day 15 through Day 21).	
Subject analysis set title	Cohort 1: LUM 200 mg qd – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 14).	
Subject analysis set title	Cohort 1: Placebo – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 14).	
Subject analysis set title	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 150 mg of ivacaftor q12h (Day 15 through Day 21).	
Subject analysis set title	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).	
Subject analysis set title	Cohort 2 and 3: Placebo (HO and HE) – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 28).	
Subject analysis set title	Cohort 2: LUM 200 mg qd – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 28).	
Subject analysis set title	Cohort 2: LUM 400 mg qd – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone qd (Day 1 through Day 28).	
Subject analysis set title	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 3: LUM 400 mg q12h – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone q12h (Day 1 through Day 28).	
Subject analysis set title	Cohort 2: LUM 600 mg qd – Period 1
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28).	

Subject analysis set title	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO&HE) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h
Subject analysis set type	Full analysis
Subject analysis set description: Participants heterozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 1 through Day 56).	
Subject analysis set title	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 150 mg of ivacaftor q12h (Day 15 through Day 21).	
Subject analysis set title	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).	
Subject analysis set title	Cohort 1: Placebo – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd in combination with ivacaftor matched placebo q12h (Day 15 through Day 21).	
Subject analysis set title	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2
Subject analysis set type	Full analysis
Subject analysis set description: Participants heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).	
Subject analysis set title	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 1: Placebo – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 14).

Subject analysis set title	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2: LUM 200 mg qd – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 28).

Subject analysis set title	Cohort 1: LUM 200 mg qd – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 14).

Subject analysis set title	Cohort 2: LUM 400 mg qd – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone qd (Day 1 through Day 28).

Subject analysis set title	Cohort 2: LUM 600 mg qd (HO) – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28).

Subject analysis set title	Cohort 2: LUM 600 mg qd (HE) – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28).

Subject analysis set title	Cohort 2 and 3: Placebo (HO and HE) – Period 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 28).

Subject analysis set title	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2
Subject analysis set type	Full analysis



Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).

Subject analysis set title	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HE)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants heterozygous (HE) for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HO)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA 250 mg q12h (HE)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants heterozygous (HE) for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28), followed by 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Subject analysis set title	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).

**Primary: Cohort 1: Safety and Tolerability Based on Adverse Events (AEs)**

End point title	Cohort 1: Safety and Tolerability Based on Adverse Events (AEs) <sup>[1]</sup>
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End point description:

AE: any untoward medical occurrence during study; irrespective of relationship with treatment, including any newly occurring event or previous condition that has increased in severity/frequency after informed consent. SAE: medical event or condition, which falls into any of the following categories, regardless of its relationship to study drug: death, life threatening adverse experience, in-patient hospitalization/prolongation of hospitalization, persistent/significant disability or incapacity, congenital anomaly/birth defect, important medical event. AE that started at/after initial dosing of study drug, or increased in severity after initial dosing of study drug is considered treatment-emergent. Results are reported separately for monotherapy period (Period 1: Day 1 to Day 14) and combination therapy period (Period 2: Day 15 to Day 21). Analysis was performed on Cohort 1 Safety Set, which included all participants who received at least 1 dose of study drug in Cohort 1.

End point type	Primary
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End point timeframe:

Cohort 1: Day 1 up to 28 days after last dose (Last dose = Day 21)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned for this endpoint.

End point values	Cohort 1: Placebo – Period 2	Cohort 1: LUM 200 mg qd – Period 1	Cohort 1: Placebo – Period 1	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	41	21	20
Units: participants				
number (not applicable)				
Participants with any AEs	15	29	12	14
Participants with SAEs	0	0	0	0

End point values	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: participants				
number (not applicable)				
Participants with any AEs	12			
Participants with SAEs	0			

**Statistical analyses**

No statistical analyses for this end point

**Primary: Cohort 2 and 3: Safety and Tolerability Based on Adverse Events (AEs)**

End point title	Cohort 2 and 3: Safety and Tolerability Based on Adverse
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## End point description:

Detailed description is provided in Outcome Measure 1. Results are reported separately for monotherapy period (Period 1: Day 1 to Day 28) and combination therapy period (Period 2: Day 29 to Day 56). Analysis was performed on Cohort 2 and 3 Safety Set, which included all participants who received at least 1 dose of study drug in Cohort 2 or 3.

## End point type

Primary

## End point timeframe:

Cohort 2 and 3: Day 1 up to 28 days after last dose (Last dose = Day 56)

## Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned for this endpoint.

End point values	Cohort 2 and 3: Placebo (HO and HE) – Period 1	Cohort 2: LUM 200 mg qd – Period 1	Cohort 2: LUM 400 mg qd – Period 1	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	23	21	27
Units: participants				
number (not applicable)				
Participants with any AEs	23	18	18	20
Participants with SAEs	1	2	0	4

End point values	Cohort 3: LUM 400 mg q12h – Period 1	Cohort 2: LUM 600 mg qd – Period 1	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	42	21	20
Units: participants				
number (not applicable)				
Participants with any AEs	7	37	12	15
Participants with SAEs	2	3	0	1

End point values	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO&HE) – Period 2	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	11		
Units: participants				
number (not applicable)				
Participants with any AEs	26	10		
Participants with SAEs	4	1		

## Statistical analyses

No statistical analyses for this end point

### Primary: Cohort 4: Safety and Tolerability Assessed by Number of Participants With AEs and SAEs

End point title	Cohort 4: Safety and Tolerability Assessed by Number of Participants With AEs and SAEs <sup>[3]</sup> <sup>[4]</sup>
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End point description:

AEs and SAEs are defined in Outcome Measure 1. Analysis was performed on Cohort 4 Safety Set, which included all participants who received at least 1 dose of study drug in Cohort 4.

End point type	Primary
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End point timeframe:

Cohort 4: Day 1 up to 28 days after last dose (Last dose = Day 56)

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 planned for this endpoint.

[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: Only arms related to the specified cohort are reported.

<b>End point values</b>	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	63	62		
Units: participants				
number (not applicable)				
Participants with any AEs	53	52		
Participants with SAEs	5	9		

## Statistical analyses

No statistical analyses for this end point

### Primary: Cohort 1: Absolute Change from Day 14 in Sweat Chloride at Day 21

End point title	Cohort 1: Absolute Change from Day 14 in Sweat Chloride at Day 21
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End point description:

Analysis was performed on Cohort 1 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 1. Results are reported for combination therapy period (Period 2: Day 15 to Day 21).

End point type	Primary
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End point timeframe:

Cohort 1: Day 14, Day 21

End point values	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2	Cohort 1: Placebo – Period 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	14	17	
Units: millimole per liter (mmol/L)				
least squares mean (confidence interval 95%)	-2.131 (-5.381 to 1.119)	-9.128 (- 12.893 to - 5.362)	0.548 (-2.955 to 4.052)	

### Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Cohort 1: Placebo – Period 2 v Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.267
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.679
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.484
upper limit	2.125

Statistical analysis title	Statistical Analysis 2
Comparison groups	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2 v Cohort 1: Placebo – Period 2
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-9.676

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.801
upper limit	-4.551

### Primary: Cohort 2 And 3: Absolute Change from Day 28 in Sweat Chloride at Day 56

End point title	Cohort 2 And 3: Absolute Change from Day 28 in Sweat Chloride at Day 56
End point description:	
Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3. Results are reported for combination therapy period (Period 2: Day 29 to Day 56).	
End point type	Primary
End point timeframe:	
Cohort 2 and 3: Day 28, Day 56	

<b>End point values</b>	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	19	17	9
Units: mmol/L				
least squares mean (confidence interval 95%)	0.321 (-4.208 to 4.849)	-1.043 (-5.8 to 3.714)	-1.24 (-6.287 to 3.807)	-2.154 (-9.177 to 4.87)

<b>End point values</b>	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2 and 3: Placebo (HO and HE) – Period 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	24		
Units: mmol/L				
least squares mean (confidence interval 95%)	-2.9 (-7.542 to 1.743)	1.627 (-2.661 to 5.915)		

### Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Comparison groups	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2 v Cohort 2 and 3: Placebo (HO and HE) – Period 2

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.68
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-1.306
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.565
upper limit	4.953

<b>Statistical analysis title</b>	Statistical Analysis 2
Comparison groups	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2 v Cohort 2 and 3: Placebo (HO and HE) – Period 2
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.409
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.053
upper limit	3.712

<b>Statistical analysis title</b>	Statistical Analysis 3
Comparison groups	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2 v Cohort 2 and 3: Placebo (HO and HE) – Period 2
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.161
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-4.526
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.888
upper limit	1.835

<b>Statistical analysis title</b>	Statistical Analysis 4
Comparison groups	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2 v Cohort 2 and 3: Placebo (HO and HE) – Period 2
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.396
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.867
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.543
upper limit	3.81

<b>Statistical analysis title</b>	Statistical Analysis 5
Comparison groups	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2 v Cohort 2 and 3: Placebo (HO and HE) – Period 2
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.365
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-3.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.028
upper limit	4.467

### **Primary: Cohort 4: Absolute Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) at Day 56**

End point title	Cohort 4: Absolute Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (ppFEV1) at Day 56 <sup>[5]</sup>
End point description:	
FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. ppFEV1 (predicted for age, gender, and height) was calculated using the Hankinson method. Analysis was performed on Cohort 4 Full Analysis Set, which included all randomized participants who received any amount of study drug in Cohort 4.	
End point type	Primary
End point timeframe:	
Cohort 4: Baseline, Day 56	

#### **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: Only arms related to the specified cohort are reported.



<b>End point values</b>	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	55		
Units: percent predicted of FEV1				
least squares mean (standard error)	-1.23 (± 0.801)	-0.62 (± 0.829)		

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Comparison groups	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h v Cohort 4: Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5978
Method	Mixed Model Repeated Measure (MMRM)
Parameter estimate	LS Mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	2.86

## Secondary: Cohort 1: Absolute Change from Baseline in Sweat Chloride at Day 14

End point title	Cohort 1: Absolute Change from Baseline in Sweat Chloride at Day 14
End point description:	
Analysis was performed on Cohort 1 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 1. Results are reported for monotherapy period (Period 1: Day 1 to Day 14).	
End point type	Secondary
End point timeframe:	
Cohort 1: Baseline, Day 14	

<b>End point values</b>	Cohort 1: Placebo – Period 1	Cohort 1: LUM 200 mg qd – Period 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	36		
Units: mmol/L				
least squares mean (confidence interval 95%)	-1.668 (-5.606 to 2.271)	-4.442 (-7.141 to -1.742)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2 And 3: Absolute Change from Baseline in Sweat Chloride at Day 14

End point title	Cohort 2 And 3: Absolute Change from Baseline in Sweat Chloride at Day 14
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End point description:

Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3. Results are reported for monotherapy period (Period 1: Day 1 to Day 28).

End point type	Secondary
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End point timeframe:

Cohort 2: Baseline, Day 14

End point values	Cohort 3: LUM 400 mg q12h – Period 1	Cohort 2: LUM 200 mg qd – Period 1	Cohort 2: LUM 400 mg qd – Period 1	Cohort 2: LUM 600 mg qd (HO) – Period 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	19	17	21
Units: mmol/L				
least squares mean (confidence interval 95%)	-9.179 (-15.47 to -2.888)	-6.49 (-11.226 to -1.755)	-5.901 (-10.91 to -0.892)	-9.442 (- 13.953 to - 4.931)

End point values	Cohort 2: LUM 600 mg qd (HE) – Period 1	Cohort 2 and 3: Placebo (HO and HE) – Period 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	25		
Units: mmol/L				
least squares mean (confidence interval 95%)	-3.137 (-8.167 to 1.893)	0.048 (-4.162 to 4.258)		

## Statistical analyses

No statistical analyses for this end point

**Secondary: Cohort 4: Absolute Change from Baseline in Sweat Chloride at Day 56**

End point title	Cohort 4: Absolute Change from Baseline in Sweat Chloride at Day 56 <sup>[6]</sup>
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End point description:

Analysis was performed on Cohort 4 Full Analysis Set, which included all randomized participants who received any amount of study drug in Cohort 4.

End point type	Secondary
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End point timeframe:

Cohort 4: Baseline, Day 56

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: Only arms related to the specified cohort are reported.

<b>End point values</b>	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	54		
Units: mmol/L				
least squares mean (standard error)	-0.78 (± 1.23)	-11.82 (± 1.281)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Cohort 1: Absolute Change From Day 14 in FEV1 at Day 21**

End point title	Cohort 1: Absolute Change From Day 14 in FEV1 at Day 21
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End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. Analysis was performed on Cohort 1 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 1. Results are reported for combination therapy period (Period 2: Day 15 to Day 21).

End point type	Secondary
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End point timeframe:

Cohort 1: Day 14, Day 21

<b>End point values</b>	Cohort 1: Placebo – Period 2	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21	20	18	
Units: liters				
least squares mean (confidence interval 95%)	-0.046 (-0.138 to 0.047)	0.128 (0.03 to 0.225)	0.015 (-0.094 to 0.124)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 1: Absolute Change From Day 14 in ppFEV1 at Day 21

End point title	Cohort 1: Absolute Change From Day 14 in ppFEV1 at Day 21
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End point description:

FEV1 and ppFEV1 are defined in sixth primary endpoint. Analysis was performed on Cohort 1 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 1. Results are reported for combination therapy period (Period 2: Day 15 to Day 21).

End point type	Secondary
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End point timeframe:

Cohort 1: Day 14, Day 21

End point values	Cohort 1: Placebo – Period 2	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21	20	18	
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)	-1.44 (-3.89 to 1.01)	3.46 (0.87 to 6.05)	0.63 (-2.2 to 3.46)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 2 and 3: Absolute Change From Day 28 in ppFEV1 at Day 56

End point title	Cohort 2 and 3: Absolute Change From Day 28 in ppFEV1 at Day 56
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End point description:

FEV1 and ppFEV1 are defined in sixth primary endpoint. Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3. Results are reported for combination therapy period (Period 2: Day 29 to Day 56).

End point type	Secondary
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End point timeframe:

Cohort 2 and 3: Day 28, Day 56

End point values	Cohort 2 and 3: Placebo (HO and HE) – Period 2	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	21	20	10
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)	-1.57 (-4.24 to 1.09)	1.96 (-0.84 to 4.76)	1.99 (-0.87 to 4.84)	6.09 (2.02 to 10.16)

End point values	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	20		
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)	2.29 (-0.82 to 5.39)	6.15 (3.27 to 9.02)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2 and 3: Relative Change From Day 28 in ppFEV1 at Day 56

End point title	Cohort 2 and 3: Relative Change From Day 28 in ppFEV1 at Day 56
End point description:	
FEV1 and ppFEV1 are defined in sixth primary endpoint. Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3. Results are reported for combination therapy period (Period 2: Day 29 to Day 56).	
End point type	Secondary
End point timeframe:	
Cohort 2 and 3: Day 28, Day 56	

End point values	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	20	10	17
Units: percent change				
least squares mean (confidence interval 95%)	3.13 (-1.29 to 7.54)	2.98 (-1.52 to 7.48)	8.24 (1.83 to 14.65)	4.3 (-0.59 to 9.19)

<b>End point values</b>	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2 and 3: Placebo (HO and HE) – Period 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	24		
Units: percent change				
least squares mean (confidence interval 95%)	9.7 (5.17 to 14.23)	-2.05 (-6.25 to 2.15)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2 and 3: Absolute Change From Baseline in ppFEV1 at Day 28 and 56

End point title	Cohort 2 and 3: Absolute Change From Baseline in ppFEV1 at Day 28 and 56 <sup>[7]</sup>
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End point description:

FEV1 and ppFEV1 are defined in sixth primary endpoint. Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3.

End point type	Secondary
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End point timeframe:

Cohort 2 and 3: Baseline, Day 28 and 56

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: Only arms related to the specified cohort are reported.

<b>End point values</b>	Cohort 2 and 3: Placebo (HO and HE)	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	23	21	11
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
Day 28: (n= 27, 21, 20, 11, 20, 18)	-0.03 (-2.68 to 2.62)	0.21 (-2.77 to 3.19)	-1.35 (-4.39 to 1.69)	-4.52 (-8.65 to -0.39)
Day 56: (n= 24, 21, 20, 10, 20, 17)	-2.02 (-4.97 to 0.93)	1.82 (-1.28 to 4.91)	0.64 (-2.52 to 3.8)	2.16 (-2.34 to 6.66)

<b>End point values</b>	Cohort 2: LUM 600 mg	Cohort 2: LUM 600 mg		
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	qd/LUM 600 mg qd+IVA 250 mg q12h (HO)	qd/LUM 600 mg qd+IVA 250 mg q12h (HE)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	21		
Units: percent predicted of FEV1				
least squares mean (confidence interval 95%)				
Day 28: (n= 27, 21, 20, 11, 20, 18)	-2.62 (-5.67 to 0.42)	-3.82 (-7.03 to -0.61)		
Day 56: (n= 24, 21, 20, 10, 20, 17)	3.59 (0.41 to 6.77)	-1.68 (-5.12 to 1.75)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2 and 3: Relative Change From Baseline in FEV1 at Day 28 and 56

End point title	Cohort 2 and 3: Relative Change From Baseline in FEV1 at Day 28 and 56 <sup>[8]</sup>
End point description: FEV1 and ppFEV1 are defined in Outcome Measure 6. Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3.	
End point type	Secondary
End point timeframe: Cohort 2 and 3: Baseline, Day 28 and 56	
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: Only arms related to the specified cohort are reported.	

End point values	Cohort 2 and 3: Placebo (HO and HE)	Cohort 2: LUM 200 mg qd/LUM 200 mg qd+IVA 250 mg q12h (HO)	Cohort 2: LUM 400 mg qd/LUM 400 mg qd+IVA 250 mg q12h (HO)	Cohort 3: LUM 400 mg q12h/LUM 400 mg q12h+IVA 250 mg q12h (HO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	23	21	11
Units: percent change				
least squares mean (confidence interval 95%)				
Day 28: (n= 27, 21, 20, 11, 20, 18)	1.89 (-2.12 to 5.9)	0.24 (-4.27 to 4.75)	-1.15 (-5.75 to 3.45)	-6.39 (-12.65 to -0.14)
Day 56: (n= 24, 21, 20, 10, 20, 17)	-2.42 (-6.91 to 2.08)	2.51 (-2.21 to 7.23)	1.72 (-3.09 to 6.53)	2.96 (-3.9 to 9.81)

End point values	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA	Cohort 2: LUM 600 mg qd/LUM 600 mg qd+IVA		
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	250 mg q12h (HO)	250 mg q12h (HE)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	21		
Units: percent change				
least squares mean (confidence interval 95%)				
Day 28: (n= 27, 21, 20, 11, 20, 18)	-3.13 (-7.74 to 1.48)	-5.46 (-10.32 to -0.6)		
Day 56: (n= 24, 21, 20, 10, 20, 17)	5.55 (0.7 to 10.39)	-2.34 (-7.57 to 2.89)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 4: Relative Change From Baseline in Percent Predicted FEV1 at Day 56

End point title	Cohort 4: Relative Change From Baseline in Percent Predicted FEV1 at Day 56 <sup>[9]</sup>
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End point description:

FEV1 and ppFEV1 are defined in sixth primary outcome. Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3.

End point type	Secondary
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End point timeframe:

Cohort 4: Baseline, Day 56

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: Only arms related to the specified cohort are reported.

End point values	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	55		
Units: percent change				
least squares mean (standard error)	-2.2 (± 1.373)	-0.69 (± 1.423)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 2 and 3: Absolute Change From Day 28 in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score at Day 56

End point title	Cohort 2 and 3: Absolute Change From Day 28 in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score at Day 56
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**End point description:**

The CFQ-R is a validated patient-reported outcome measuring health-related quality of life for subjects with cystic fibrosis. Respiratory domain assessed respiratory symptoms (for example, coughing, congestion, wheezing), score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life. Analysis was performed on Cohort 2 and 3 Full Analysis Set, which included all randomized participants who received at least 1 dose of study drug in Cohort 2 or 3. Results are reported for combination therapy period (Period 2: Day 29 to Day 56).

End point type	Secondary
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**End point timeframe:**

Cohort 2 and 3: Day 28, Day 56
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End point values	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HE) – Period 2	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO) – Period 2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	20	17	20
Units: units on a scale				
least squares mean (confidence interval 95%)	3.3 (-3.6 to 10.1)	7.9 (0.8 to 14.9)	5.5 (-2.1 to 13.1)	8.9 (1.9 to 15.9)

End point values	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2	Cohort 2 and 3: Placebo (HO and HE) – Period 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	25		
Units: units on a scale				
least squares mean (confidence interval 95%)	11.2 (1.3 to 21.1)	-8.6 (-14.9 to -2.2)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Cohort 4: Absolute Change From Baseline in CFQ-R Respiratory Domain Score at Day 56**

End point title	Cohort 4: Absolute Change From Baseline in CFQ-R Respiratory Domain Score at Day 56 <sup>[10]</sup>
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**End point description:**

CFQ-R respiratory domain is defined in previous endpoint. Analysis was performed on Cohort 4 Full Analysis Set, which included all randomized participants who received any amount of study drug in Cohort 4.

End point type	Secondary
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**End point timeframe:**

Cohort 4: Baseline, Day 56
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Notes:

[10] - 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: Only arms related to the specified cohort are reported.

End point values	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	55		
Units: units on a scale				
least squares mean (standard error)	-0.82 (± 1.802)	5.66 (± 1.864)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 4: Absolute Change From Baseline in Body Mass Index (BMI) at Day 56

End point title	Cohort 4: Absolute Change From Baseline in Body Mass Index (BMI) at Day 56 <sup>[11]</sup>
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End point description:

BMI was defined as weight in kilogram (kg) divided by height\*height in square meter (m<sup>2</sup>). Analysis was performed on Cohort 4 Full Analysis Set, which included all randomized participants who received any amount of study drug in Cohort 4.

End point type	Secondary
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End point timeframe:

Cohort 4: Baseline, Day 56

Notes:

[11] - 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: Only arms related to the specified cohort are reported.

End point values	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: kg/m <sup>2</sup>				
least squares mean (standard error)	0.08 (± 0.075)	-0.04 (± 0.077)		

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Cohort 4: Absolute Change From Baseline in Weight at Day 56**

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End point title	Cohort 4: Absolute Change From Baseline in Weight at Day
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End point description:

Analysis was performed on Cohort 4 Full Analysis Set, which included all randomized participants who received any amount of study drug in Cohort 4.

End point type	Secondary
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End point timeframe:

Cohort 4: Baseline, Day 56

Notes:

[12] - 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: Only arms related to the specified cohort are reported.

End point values	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: kg				
least squares mean (standard error)	0.16 (± 0.211)	-0.11 (± 0.216)		

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Cohort 1: Day 1 up to 28 days after last dose (Last dose = Day 21); Cohort 2 and 3: Day 1 up to 28 days after last dose (Last dose = Day 56); Cohort 4: Day 1 up to 28 days after last dose (Last dose = Day 56)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

### Reporting groups

Reporting group title	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 150 mg of ivacaftor q12h (Day 15 through Day 21).

Reporting group title	Cohort 1: LUM 200 mg qd – Period 1
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 14).

Reporting group title	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 15 through Day 21).

Reporting group title	Cohort 1: Placebo – Period 1
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 14).

Reporting group title	Cohort 1: Placebo – Period 2
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd in combination with ivacaftor matched placebo q12h (Day 15 through Day 21).

Reporting group title	Cohort 2: LUM 200 mg qd – Period 1
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor alone qd (Day 1 through Day 28).

Reporting group title	Cohort 2: LUM 400 mg qd – Period 1
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone qd (Day 1 through Day 28).

Reporting group title	Cohort 2: LUM 600 mg qd – Period 1
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Reporting group description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor alone qd (Day 1 through Day 28).

Reporting group title	Cohort 3: LUM 400 mg q12h – Period 1
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor alone q12h (Day 1 through Day 28).

Reporting group title	Cohort 2 and 3: Placebo (HO and HE) – Period 1
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Reporting group description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo qd (Day 1 through Day 28).

Reporting group title	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 200 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Reporting group title	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Reporting group title	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO&HE) – Period 2
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Reporting group description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received 600 mg of lumacaftor qd in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Reporting group title	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2
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Reporting group description:

Participants homozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 29 through Day 56).

Reporting group title	Cohort 2 and 3: Placebo (HO and HE) – Period 2
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Reporting group description:

Participants homozygous or heterozygous for the F508del-CFTR mutation received lumacaftor matched placebo in combination with ivacaftor matched placebo q12h (Day 29 through Day 56).

Reporting group title	Cohort 4: Placebo
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Reporting group description:

Participants heterozygous for the F508del-CFTR mutation received lumacaftor in combination with ivacaftor matched placebo q12h (Day 1 through Day 56).

Reporting group title	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h
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Reporting group description:

Participants heterozygous for the F508del-CFTR mutation received 400 mg of lumacaftor q12h in combination with 250 mg of ivacaftor q12h (Day 1 through Day 56).

<b>Serious adverse events</b>	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2	Cohort 1: LUM 200 mg qd – Period 1	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Spirometry abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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 CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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
Congenital, familial and genetic			

disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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			
Haemoptysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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
DYSпноEA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (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

<b>Serious adverse events</b>	Cohort 1: Placebo – Period 1	Cohort 1: Placebo – Period 2	Cohort 2: LUM 200 mg qd – Period 1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	2 / 23 (8.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Spirometry abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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 CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (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

<b>Serious adverse events</b>	Cohort 2: LUM 400 mg qd – Period 1	Cohort 2: LUM 600 mg qd – Period 1	Cohort 3: LUM 400 mg q12h – Period 1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	3 / 42 (7.14%)	2 / 11 (18.18%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Spirometry abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (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 CREATINE PHOSPHOKINASE INCREASED			



subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (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
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (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			
Haemoptysis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (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
DYSпноEA			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (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
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (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			
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (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
<b>PNEUMONIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (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

<b>Serious adverse events</b>	Cohort 2 and 3: Placebo (HO and HE) – Period 1	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
<b>Investigations</b>			
<b>Spirometry abnormal</b>			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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
<b>BLOOD CREATINE PHOSPHOKINASE INCREASED</b>			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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
<b>Congenital, familial and genetic disorders</b>			
<b>CYSTIC FIBROSIS LUNG</b>			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Immune system disorders</b>			
<b>HYPERSENSITIVITY</b>			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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
<b>Respiratory, thoracic and mediastinal disorders</b>			

Haemoptysis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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
DYSпноEA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (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	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO&HE) – Period 2	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 38 (10.53%)	1 / 11 (9.09%)	4 / 27 (14.81%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			

Spirometry abnormal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (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 CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	3 / 38 (7.89%)	1 / 11 (9.09%)	4 / 27 (14.81%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (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			
Haemoptysis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSпноEA			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	0 / 27 (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
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (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
<b>PNEUMONIA</b>			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (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

<b>Serious adverse events</b>	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h	
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	5 / 63 (7.94%)	9 / 62 (14.52%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
<b>Investigations</b>			
Spirometry abnormal			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>BLOOD CREATINE PHOSPHOKINASE INCREASED</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Congenital, familial and genetic disorders</b>			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Immune system disorders</b>			

HYPERSENSITIVITY			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSпноEA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (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			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	3 / 63 (4.76%)	7 / 62 (11.29%)	
occurrences causally related to treatment / all	0 / 4	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

<b>Non-serious adverse events</b>	Cohort 1: LUM 200 mg qd+IVA 150 mg q12h – Period 2	Cohort 1: LUM 200 mg qd – Period 1	Cohort 1: LUM 200 mg qd+IVA 250 mg q12h – Period 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)	29 / 41 (70.73%)	12 / 20 (60.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	1 / 20 (5.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
PYREXIA			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
PAIN			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
APPLICATION SITE PRURITUS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
CATHETER SITE HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
CATHETER SITE PAIN			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
CHEST DISCOMFORT			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
CHILLS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
FEELING HOT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

INJECTION SITE HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 41 (2.44%) 1	0 / 20 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Exercise tolerance decreased subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Vessel puncture site bruise subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
NON-CARDIAC CHEST PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
APPLICATION SITE IRRITATION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
FEELING OF BODY TEMPERATURE CHANGE subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
INFLUENZA LIKE ILLNESS subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Reproductive system and breast disorders MENSTRUATION DELAYED subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 41 (2.44%) 1	0 / 20 (0.00%) 0
BREAST TENDERNESS			



subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MENORRHAGIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MENSTRUAL DISORDER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	4 / 20 (20.00%)	6 / 41 (14.63%)	1 / 20 (5.00%)
occurrences (all)	5	6	1
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 20 (5.00%)	3 / 41 (7.32%)	0 / 20 (0.00%)
occurrences (all)	1	3	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	2 / 41 (4.88%)	2 / 20 (10.00%)
occurrences (all)	1	2	2
NASAL CONGESTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	3 / 20 (15.00%)
occurrences (all)	1	0	3
RHINORRHOEA			

subjects affected / exposed	1 / 20 (5.00%)	2 / 41 (4.88%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
DYSPNOEA			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
RALES			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
WHEEZING			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
LUNG HYPERINFLATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
BRONCHIAL SECRETION RETENTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
HYPOVENTILATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INCREASED VISCOSITY OF BRONCHIAL SECRETION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
NASAL MUCOSAL DISORDER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
NASAL OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

PROLONGED EXPIRATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RHONCHI			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
SINUS CONGESTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SINUS DISORDER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
SNEEZING			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
HAEMOPTYSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PLEURITIC PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SPUTUM DISCOLOURED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
OBSTRUCTIVE AIRWAYS DISORDER			

subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
BRONCHOSPASM			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPHONIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASAL INFLAMMATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PAINFUL RESPIRATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PULMONARY CONGESTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SPUTUM INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HICCUPS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASAL DRYNESS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL OEDEMA			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
PLEURISY			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
PULMONARY PAIN			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
INSOMNIA			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	1 / 20 (5.00%) 1
MOOD SWINGS			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
DEPRESSED MOOD			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Abnormal dreams			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Investigations			
BLOOD GLUCOSE INCREASED			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 41 (2.44%) 1	1 / 20 (5.00%) 1
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 41 (2.44%) 1	0 / 20 (0.00%) 0
GLUCOSE URINE PRESENT			
subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 41 (0.00%) 0	1 / 20 (5.00%) 1
LIVER FUNCTION TEST ABNORMAL			

subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	2 / 20 (10.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
PULMONARY FUNCTION TEST DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
BLOOD IMMUNOGLOBULIN E INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
BLOOD SODIUM DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
BLOOD URINE PRESENT			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sputum abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood immunoglobulin G increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Protein total increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BACTERIA URINE IDENTIFIED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD PHOSPHORUS DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
CULTURE THROAT POSITIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM QT PROLONGED			



subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FUNGUS SPUTUM TEST POSITIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PROTEIN URINE PRESENT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
URINE KETONE BODY PRESENT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
EXCORIATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
JOINT SPRAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			

subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
JOINT INJURY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SUNBURN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
VERTEBRAL INJURY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Animal bite			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ARTHROPOD BITE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic			

disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	2 / 20 (10.00%)	2 / 41 (4.88%)	1 / 20 (5.00%)
occurrences (all)	2	2	1
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
SINUS HEADACHE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
MIGRAINE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
TREMOR			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
TUNNEL VISION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
HEADACHE			
subjects affected / exposed	0 / 20 (0.00%)	4 / 41 (9.76%)	1 / 20 (5.00%)
occurrences (all)	0	4	1
NEURALGIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PRESYNCOPE			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
LETHARGY			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
DYSGEUSIA			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Blood and lymphatic system disorders			
LYMPHADENOPATHY			
subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Eosinophilia			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Increased tendency to bruise			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Leukopenia			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
EAR DISCOMFORT			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
EAR DISORDER			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
TINNITUS			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Vertigo			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Eye disorders			
EYELID OEDEMA			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
CONJUNCTIVITIS (EYE)			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
VISION BLURRED			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 41 (2.44%) 1	1 / 20 (5.00%) 1
ABDOMINAL PAIN UPPER			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	3 / 41 (7.32%) 3	0 / 20 (0.00%) 0
ABDOMINAL DISCOMFORT			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
ABDOMINAL PAIN			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 41 (2.44%) 2	0 / 20 (0.00%) 0
NAUSEA			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 41 (4.88%) 2	1 / 20 (5.00%) 1
VOMITING			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	1 / 20 (5.00%) 1
ABDOMINAL DISTENSION			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 41 (2.44%) 1	0 / 20 (0.00%) 0
ABDOMINAL PAIN LOWER			

subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
CONSTIPATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DISTAL ILEAL OBSTRUCTION SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DRY MOUTH			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FAECAL VOLUME INCREASED			

subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
LIP SWELLING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
POST-TUSSIVE VOMITING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
STEATORRHOEA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
RASH MACULAR			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
RASH PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
ACNE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
DERMATITIS CONTACT			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
HYPOAESTHESIA FACIAL			

subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
RASH FOLLICULAR			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
URTICARIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dermatitis atopic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ALOPECIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ECCHYMOSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			



PYURIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chromaturia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSURIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
MYALGIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Clubbing			

subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
COSTOCHONDRITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MEDIAL TIBIAL STRESS SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
TORTICOLLIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
VIRAL INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

RHINITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
BACTERIAL DISEASE CARRIER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
CANDIDIASIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
ORAL HERPES			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Kidney infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			

subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FUNGAL INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HERPES SIMPLEX			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
LARYNGITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
VIRAL RASH			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	1 / 41 (2.44%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
DEHYDRATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Decreased appetite subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
ANOREXIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
HYPERCALCAEMIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0
HYPERGLYCAEMIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 41 (0.00%) 0	0 / 20 (0.00%) 0

<b>Non-serious adverse events</b>	Cohort 1: Placebo – Period 1	Cohort 1: Placebo – Period 2	Cohort 2: LUM 200 mg qd – Period 1
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 21 (57.14%)	15 / 21 (71.43%)	17 / 23 (73.91%)
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	3 / 21 (14.29%) 3	0 / 23 (0.00%) 0
PYREXIA subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
PAIN subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
APPLICATION SITE PRURITUS subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
CATHETER SITE HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0

CATHETER SITE PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
FEELING HOT			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
INJECTION SITE HAEMORRHAGE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
APPLICATION SITE IRRITATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
FEELING OF BODY TEMPERATURE CHANGE			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>INFLUENZA LIKE ILLNESS</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>Immune system disorders</b>			
Seasonal allergy			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>Reproductive system and breast disorders</b>			
<b>MENSTRUATION DELAYED</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>BREAST TENDERNESS</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
<b>MENOMETRORRHAGIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>MENORRHAGIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>MENSTRUAL DISORDER</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
<b>Dysmenorrhoea</b>			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
<b>Vulvovaginal burning sensation</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>Vulvovaginal discomfort</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
<b>Respiratory, thoracic and mediastinal disorders</b>			



COUGH			
subjects affected / exposed	1 / 21 (4.76%)	4 / 21 (19.05%)	3 / 23 (13.04%)
occurrences (all)	1	4	3
PRODUCTIVE COUGH			
subjects affected / exposed	2 / 21 (9.52%)	3 / 21 (14.29%)	2 / 23 (8.70%)
occurrences (all)	2	3	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	2 / 23 (8.70%)
occurrences (all)	0	2	2
NASAL CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
RHINORRHOEA			
subjects affected / exposed	2 / 21 (9.52%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
DYSPNOEA			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
RALES			
subjects affected / exposed	0 / 21 (0.00%)	3 / 21 (14.29%)	0 / 23 (0.00%)
occurrences (all)	0	4	0
RESPIRATION ABNORMAL			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
WHEEZING			
subjects affected / exposed	2 / 21 (9.52%)	2 / 21 (9.52%)	0 / 23 (0.00%)
occurrences (all)	2	2	0
LUNG HYPERINFLATION			
subjects affected / exposed	0 / 21 (0.00%)	3 / 21 (14.29%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL SECRETION RETENTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

HYPOVENTILATION			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
INCREASED VISCOSITY OF BRONCHIAL SECRETION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NASAL MUCOSAL DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NASAL OEDEMA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PROLONGED EXPIRATION			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
RHONCHI			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
SINUS DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
SNEEZING			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HAEMOPTYSIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	4 / 23 (17.39%)
occurrences (all)	0	0	4
PLEURITIC PAIN			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
SPUTUM DISCOLOURED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
BRONCHOSPASM			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DYSPHONIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NASAL INFLAMMATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PAINFUL RESPIRATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PULMONARY CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
SPUTUM INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HICCUPS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NASAL DRYNESS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL OEDEMA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PLEURISY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PULMONARY PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
INSOMNIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
MOOD SWINGS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Abnormal dreams			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Investigations			
BLOOD GLUCOSE INCREASED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 21 (4.76%) 1	0 / 23 (0.00%) 0
C-REACTIVE PROTEIN INCREASED subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 21 (0.00%) 0	1 / 23 (4.35%) 1
GLUCOSE URINE PRESENT subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
LIVER FUNCTION TEST ABNORMAL subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	2 / 23 (8.70%) 2
PROTHROMBIN TIME PROLONGED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
PULMONARY FUNCTION TEST DECREASED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
ALANINE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
BLOOD IMMUNOGLOBULIN E INCREASED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
BLOOD SODIUM DECREASED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
BLOOD URINE PRESENT			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Sputum abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood immunoglobulin G increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Protein total increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
BACTERIA URINE IDENTIFIED			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
BLOOD PHOSPHORUS DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
CULTURE THROAT POSITIVE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
FUNGUS SPUTUM TEST POSITIVE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
PROTEIN URINE PRESENT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
URINE KETONE BODY PRESENT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
EXCORIATION			



subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
LIMB INJURY			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
MUSCLE STRAIN			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
THERMAL BURN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
JOINT INJURY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
SUNBURN			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	1 / 23 (4.35%) 1
VERTEBRAL INJURY subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Animal bite subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
ARTHROPOD BITE subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Congenital, familial and genetic disorders CYSTIC FIBROSIS LUNG subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 21 (4.76%) 1	0 / 23 (0.00%) 0
Cystic fibrosis related diabetes subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Cardiac disorders SINUS BRADYCARDIA subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
SINUS HEADACHE subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
MIGRAINE subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
TREMOR			

subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
TUNNEL VISION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	4 / 21 (19.05%)	5 / 21 (23.81%)	1 / 23 (4.35%)
occurrences (all)	5	7	1
NEURALGIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PRESYNCOPE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
LETHARGY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
LYMPHADENOPATHY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
EAR DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
EAR DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
TINNITUS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
EYELID OEDEMA			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
CONJUNCTIVITIS (EYE)			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	2 / 23 (8.70%)
occurrences (all)	0	1	2
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
ABDOMINAL PAIN			

subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
NAUSEA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN LOWER			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
FLATULENCE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DISTAL ILEAL OBSTRUCTION SYNDROME			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DRY MOUTH			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
DYSPEPSIA			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
FAECAL VOLUME INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
LIP SWELLING			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
POST-TUSSIVE VOMITING			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
STEATORRHOEA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
RASH MACULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
RASH PAPULAR			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
ACNE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HYPOAESTHESIA FACIAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
PRURITUS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
RASH FOLLICULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash generalised			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
RASH			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	2 / 23 (8.70%) 2
ALOPECIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
ECCHYMOSIS			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Renal and urinary disorders			
PYURIA			
subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Chromaturia			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Renal failure acute			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
PROTEINURIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
DYSURIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 21 (4.76%) 1	0 / 23 (0.00%) 0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
PAIN IN EXTREMITY			



subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Clubbing			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
COSTOCHONDRITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
MEDIAL TIBIAL STRESS SYNDROME			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
TORTICOLLIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
VIRAL INFECTION			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
RHINITIS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	5 / 23 (21.74%)
occurrences (all)	0	0	5
BACTERIAL DISEASE CARRIER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
CANDIDIASIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
ORAL HERPES			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Kidney infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
SINUSITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
FUNGAL INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
HERPES SIMPLEX			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
LARYNGITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
OTITIS MEDIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
VIRAL RASH			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	2 / 21 (9.52%) 3	0 / 23 (0.00%) 0
DEHYDRATION			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 21 (4.76%) 1	0 / 23 (0.00%) 0
Decreased appetite			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
ANOREXIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
HYPERCALCAEMIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0
HYPERGLYCAEMIA			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 21 (0.00%) 0	0 / 23 (0.00%) 0

<b>Non-serious adverse events</b>	Cohort 2: LUM 400 mg qd – Period 1	Cohort 2: LUM 600 mg qd – Period 1	Cohort 3: LUM 400 mg q12h – Period 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 21 (85.71%)	37 / 42 (88.10%)	6 / 11 (54.55%)
Vascular disorders			
Hot flush			
subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	3 / 42 (7.14%) 4	0 / 11 (0.00%) 0

PYREXIA			
subjects affected / exposed	0 / 21 (0.00%)	6 / 42 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	7	0
PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
APPLICATION SITE PRURITUS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CATHETER SITE HAEMORRHAGE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CATHETER SITE PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
FEELING HOT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
INJECTION SITE HAEMORRHAGE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Vessel puncture site bruise subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
NON-CARDIAC CHEST PAIN subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
APPLICATION SITE IRRITATION subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
FEELING OF BODY TEMPERATURE CHANGE subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
INFLUENZA LIKE ILLNESS subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
Reproductive system and breast disorders MENSTRUATION DELAYED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
BREAST TENDERNESS subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
MENOMETRORRHAGIA subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
MENORRHAGIA subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	1 / 11 (9.09%) 1
MENSTRUAL DISORDER subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
Dysmenorrhoea			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	8 / 21 (38.10%)	12 / 42 (28.57%)	1 / 11 (9.09%)
occurrences (all)	8	13	1
PRODUCTIVE COUGH			
subjects affected / exposed	2 / 21 (9.52%)	6 / 42 (14.29%)	2 / 11 (18.18%)
occurrences (all)	2	7	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
NASAL CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA			
subjects affected / exposed	1 / 21 (4.76%)	10 / 42 (23.81%)	0 / 11 (0.00%)
occurrences (all)	1	10	0
RALES			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RESPIRATION ABNORMAL			
subjects affected / exposed	2 / 21 (9.52%)	7 / 42 (16.67%)	2 / 11 (18.18%)
occurrences (all)	2	8	2
WHEEZING			



subjects affected / exposed	2 / 21 (9.52%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
LUNG HYPERINFLATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
BRONCHIAL SECRETION RETENTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HYPOVENTILATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
INCREASED VISCOSITY OF BRONCHIAL SECRETION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NASAL MUCOSAL DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NASAL OEDEMA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PROLONGED EXPIRATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RHONCHI			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	3 / 42 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	3	0

SINUS DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SNEEZING			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HAEMOPTYSIS			
subjects affected / exposed	3 / 21 (14.29%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	3	2	0
PLEURITIC PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SPUTUM DISCOLOURED			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BRONCHOSPASM			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
DYSPHONIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
NASAL INFLAMMATION			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PAINFUL RESPIRATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PULMONARY CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SPUTUM INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HICCUPS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NASAL DRYNESS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL OEDEMA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PLEURISY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PULMONARY PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

INSOMNIA			
subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
MOOD SWINGS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Abnormal dreams			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	5 / 42 (11.90%)	0 / 11 (0.00%)
occurrences (all)	0	5	0
GLUCOSE URINE PRESENT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
LIVER FUNCTION TEST ABNORMAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PULMONARY FUNCTION TEST DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ALANINE AMINOTRANSFERASE			

INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
BLOOD IMMUNOGLOBULIN E INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD SODIUM DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Sputum abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Blood creatinine decreased			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood immunoglobulin G increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Protein total increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
WHITE BLOOD CELL COUNT INCREASED			

subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
BACTERIA URINE IDENTIFIED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD PHOSPHORUS DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
CULTURE THROAT POSITIVE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
FUNGUS SPUTUM TEST POSITIVE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PROTEIN URINE PRESENT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
URINE KETONE BODY PRESENT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
EXCORIATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Arthropod sting			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
JOINT INJURY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Contusion			



subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SUNBURN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
VERTEBRAL INJURY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Animal bite			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ARTHROPOD BITE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	2 / 21 (9.52%)	7 / 42 (16.67%)	1 / 11 (9.09%)
occurrences (all)	2	7	1
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

<b>DIZZINESS</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	2 / 42 (4.76%) 2	0 / 11 (0.00%) 0
<b>SINUS HEADACHE</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
<b>MIGRAINE</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>TREMOR</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>TUNNEL VISION</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>HEADACHE</b> subjects affected / exposed occurrences (all)	4 / 21 (19.05%) 4	4 / 42 (9.52%) 7	1 / 11 (9.09%) 2
<b>NEURALGIA</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>PRESYNCOPE</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>LETHARGY</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>DYSGEUSIA</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
<b>Blood and lymphatic system disorders</b> <b>LYMPHADENOPATHY</b> subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
<b>Eosinophilia</b>			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
Increased tendency to bruise subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
Ear and labyrinth disorders			
EAR PAIN subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
EAR DISCOMFORT subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
EAR DISORDER subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
TINNITUS subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
Eye disorders			
EYELID OEDEMA subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 42 (0.00%) 0	0 / 11 (0.00%) 0
CONJUNCTIVITIS (EYE) subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
VISION BLURRED subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 42 (2.38%) 1	0 / 11 (0.00%) 0
Gastrointestinal disorders			

DIARRHOEA			
subjects affected / exposed	3 / 21 (14.29%)	5 / 42 (11.90%)	0 / 11 (0.00%)
occurrences (all)	3	5	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 21 (9.52%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
NAUSEA			
subjects affected / exposed	1 / 21 (4.76%)	8 / 42 (19.05%)	1 / 11 (9.09%)
occurrences (all)	3	8	1
VOMITING			
subjects affected / exposed	1 / 21 (4.76%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	3 / 21 (14.29%)	3 / 42 (7.14%)	0 / 11 (0.00%)
occurrences (all)	3	3	0
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			

subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
DISTAL ILEAL OBSTRUCTION SYNDROME			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DRY MOUTH			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
FAECAL VOLUME INCREASED			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
LIP SWELLING			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
POST-TUSSIVE VOMITING			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
STEATORRHOEA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
RASH MACULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RASH PAPULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ACNE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
HYPOAESTHESIA FACIAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
PRURITUS			
subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
RASH FOLLICULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
URTICARIA			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>Dermatitis atopic</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>Erythema</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>Rash generalised</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>RASH</b>			
subjects affected / exposed	1 / 21 (4.76%)	3 / 42 (7.14%)	0 / 11 (0.00%)
occurrences (all)	1	3	0
<b>ALOPECIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
<b>ECCHYMOSIS</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>Renal and urinary disorders</b>			
<b>PYURIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>Chromaturia</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>Renal failure acute</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
<b>PROTEINURIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
<b>DYSURIA</b>			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 21 (4.76%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
MUSCLE SPASMS			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
MYALGIA			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Arthritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Clubbing			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Osteopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
COSTOCHONDRITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
MEDIAL TIBIAL STRESS SYNDROME			



subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
TORTICOLLIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
VIRAL INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 21 (4.76%)	2 / 42 (4.76%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
BACTERIAL DISEASE CARRIER			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CANDIDIASIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ORAL HERPES			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Kidney infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	1 / 21 (4.76%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
FUNGAL INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HERPES SIMPLEX			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
LARYNGITIS			

subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
VIRAL RASH			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DEHYDRATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
ANOREXIA			
subjects affected / exposed	0 / 21 (0.00%)	1 / 42 (2.38%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
HYPERCALCAEMIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 42 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Cohort 2 and 3: Placebo (HO and HE) – Period 1	Cohort 2: LUM 200 mg qd+IVA 250 mg q12h (HO) – Period 2	Cohort 2: LUM 400 mg qd+IVA 250 mg q12h (HO) – Period 2
Total subjects affected by non-serious adverse events subjects affected / exposed	23 / 27 (85.19%)	12 / 21 (57.14%)	15 / 20 (75.00%)
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all)  PYREXIA subjects affected / exposed occurrences (all)  PAIN subjects affected / exposed occurrences (all)  APPLICATION SITE PRURITUS subjects affected / exposed occurrences (all)  CATHETER SITE HAEMORRHAGE subjects affected / exposed occurrences (all)  CATHETER SITE PAIN subjects affected / exposed occurrences (all)  CHEST DISCOMFORT subjects affected / exposed occurrences (all)  CHILLS subjects affected / exposed occurrences (all)  FEELING HOT	1 / 27 (3.70%) 1  3 / 27 (11.11%) 4  0 / 27 (0.00%) 0  1 / 27 (3.70%) 1  0 / 27 (0.00%) 0  0 / 27 (0.00%) 0  1 / 27 (3.70%) 1	0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0	1 / 20 (5.00%) 1  1 / 20 (5.00%) 1  0 / 20 (0.00%) 0  0 / 20 (0.00%) 0  0 / 20 (0.00%) 0  0 / 20 (0.00%) 0  0 / 20 (0.00%) 0

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INJECTION SITE HAEMORRHAGE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
APPLICATION SITE IRRITATION			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
FEELING OF BODY TEMPERATURE CHANGE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

MENSTRUATION DELAYED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BREAST TENDERNESS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MENORRHAGIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MENSTRUAL DISORDER			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 27 (22.22%)	3 / 21 (14.29%)	5 / 20 (25.00%)
occurrences (all)	6	5	5
PRODUCTIVE COUGH			
subjects affected / exposed	5 / 27 (18.52%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	5	3	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 27 (3.70%)	1 / 21 (4.76%)	4 / 20 (20.00%)
occurrences (all)	1	1	5
NASAL CONGESTION			

subjects affected / exposed	3 / 27 (11.11%)	2 / 21 (9.52%)	3 / 20 (15.00%)
occurrences (all)	3	2	3
RHINORRHOEA			
subjects affected / exposed	3 / 27 (11.11%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
DYSпноEA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RALES			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
RESPIRATION ABNORMAL			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
WHEEZING			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
LUNG HYPERINFLATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	2 / 27 (7.41%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
BRONCHIAL SECRETION RETENTION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HYPOVENTILATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INCREASED VISCOSITY OF BRONCHIAL SECRETION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASAL MUCOSAL DISORDER			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0



NASAL OEDEMA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PROLONGED EXPIRATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
RHONCHI			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	2 / 27 (7.41%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	2
SINUS DISORDER			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SNEEZING			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HAEMOPTYSIS			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
PLEURITIC PAIN			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
EPISTAXIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SPUTUM DISCOLOURED			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BRONCHOSPASM			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPHONIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASAL INFLAMMATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PAINFUL RESPIRATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PULMONARY CONGESTION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SPUTUM INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HICCUPS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASAL DRYNESS			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
PHARYNGEAL OEDEMA subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
PLEURISY subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
PULMONARY PAIN subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Psychiatric disorders ANXIETY subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
INSOMNIA subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	2 / 21 (9.52%) 2	0 / 20 (0.00%) 0
MOOD SWINGS subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
DEPRESSED MOOD subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Abnormal dreams subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Investigations BLOOD GLUCOSE INCREASED subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
C-REACTIVE PROTEIN INCREASED subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
GLUCOSE URINE PRESENT			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
LIVER FUNCTION TEST ABNORMAL			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
PULMONARY FUNCTION TEST DECREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD IMMUNOGLOBULIN E INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD SODIUM DECREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Sputum abnormal			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood immunoglobulin G increased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			
subjects affected / exposed	2 / 27 (7.41%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Protein total increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BACTERIA URINE IDENTIFIED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD PHOSPHORUS DECREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
CULTURE THROAT POSITIVE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FUNGUS SPUTUM TEST POSITIVE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PROTEIN URINE PRESENT			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
URINE KETONE BODY PRESENT			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
EXCORIATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
JOINT INJURY			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SUNBURN			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
VERTEBRAL INJURY			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Animal bite			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ARTHROPOD BITE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Congenital, familial and genetic			



disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	2 / 27 (7.41%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	2	1	1
Cystic fibrosis related diabetes			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SINUS HEADACHE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
MIGRAINE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
TREMOR			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
TUNNEL VISION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	5 / 27 (18.52%)	0 / 21 (0.00%)	2 / 20 (10.00%)
occurrences (all)	9	0	2
NEURALGIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PRESYNCOPE			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
LETHARGY			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
DYSGEUSIA			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Blood and lymphatic system disorders			
LYMPHADENOPATHY			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Eosinophilia			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Increased tendency to bruise			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Leukopenia			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
EAR DISCOMFORT			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
EAR DISORDER			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
TINNITUS			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	1 / 20 (5.00%) 2
Vertigo			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Eye disorders			
EYELID OEDEMA			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
CONJUNCTIVITIS (EYE)			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
VISION BLURRED			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 21 (0.00%) 0	2 / 20 (10.00%) 2
ABDOMINAL PAIN UPPER			
subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	0 / 21 (0.00%) 0	1 / 20 (5.00%) 1
ABDOMINAL DISCOMFORT			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
ABDOMINAL PAIN			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	1 / 21 (4.76%) 1	1 / 20 (5.00%) 1
NAUSEA			
subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3	0 / 21 (0.00%) 0	1 / 20 (5.00%) 2
VOMITING			
subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 21 (0.00%) 0	2 / 20 (10.00%) 2
ABDOMINAL DISTENSION			
subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
ABDOMINAL PAIN LOWER			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	2 / 27 (7.41%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
DISTAL ILEAL OBSTRUCTION SYNDROME			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
DRY MOUTH			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
TOOTHACHE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
FAECAL VOLUME INCREASED			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
LIP SWELLING			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
POST-TUSSIVE VOMITING			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
STEATORRHOEA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
RASH MACULAR			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RASH PAPULAR			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ACNE			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
HYPOAESTHESIA FACIAL			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RASH FOLLICULAR			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
ALOPECIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ECCHYMOSIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			

PYURIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chromaturia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
DYSURIA			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	2 / 27 (7.41%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
MYALGIA			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Clubbing			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
COSTOCHONDRITIS			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
MEDIAL TIBIAL STRESS SYNDROME			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
NECK PAIN			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
TORTICOLLIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
VIRAL INFECTION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0



RHINITIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 27 (0.00%)	3 / 21 (14.29%)	2 / 20 (10.00%)
occurrences (all)	0	3	2
BACTERIAL DISEASE CARRIER			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
CANDIDIASIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
ORAL HERPES			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 27 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Kidney infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			

subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	1 / 27 (3.70%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
FUNGAL INFECTION			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
HERPES SIMPLEX			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
LARYNGITIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 27 (3.70%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
VIRAL RASH			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 27 (3.70%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
DEHYDRATION			
subjects affected / exposed	0 / 27 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Decreased appetite subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
ANOREXIA subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
HYPERCALCAEMIA subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0
HYPERGLYCAEMIA subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 21 (0.00%) 0	0 / 20 (0.00%) 0

<b>Non-serious adverse events</b>	Cohort 2: LUM 600 mg qd+IVA 250 mg q12h (HO&HE) – Period 2	Cohort 3: LUM 400 mg q12h+IVA 250 mg q12h (HO) – Period 2	Cohort 2 and 3: Placebo (HO and HE) – Period 2
Total subjects affected by non-serious adverse events subjects affected / exposed	26 / 38 (68.42%)	10 / 11 (90.91%)	20 / 27 (74.07%)
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	1 / 27 (3.70%) 1
PYREXIA subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	1 / 27 (3.70%) 1
PAIN subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
APPLICATION SITE PRURITUS subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
CATHETER SITE HAEMORRHAGE			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
CATHETER SITE PAIN			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
CHEST DISCOMFORT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
FEELING HOT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
INJECTION SITE HAEMORRHAGE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
APPLICATION SITE IRRITATION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
FEELING OF BODY TEMPERATURE			

CHANGE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
MENSTRUATION DELAYED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
BREAST TENDERNESS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MENORRHAGIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MENSTRUAL DISORDER			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

COUGH			
subjects affected / exposed	5 / 38 (13.16%)	3 / 11 (27.27%)	6 / 27 (22.22%)
occurrences (all)	6	4	6
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 38 (2.63%)	2 / 11 (18.18%)	1 / 27 (3.70%)
occurrences (all)	1	2	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 38 (0.00%)	2 / 11 (18.18%)	1 / 27 (3.70%)
occurrences (all)	0	2	1
NASAL CONGESTION			
subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
RHINORRHOEA			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
DYSPNOEA			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
RALES			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
RESPIRATION ABNORMAL			
subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
WHEEZING			
subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
LUNG HYPERINFLATION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 38 (2.63%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
BRONCHIAL SECRETION RETENTION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

HYPOVENTILATION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
INCREASED VISCOSITY OF BRONCHIAL SECRETION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NASAL MUCOSAL DISORDER			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NASAL OEDEMA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PROLONGED EXPIRATION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
RHONCHI			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	0 / 38 (0.00%)	2 / 11 (18.18%)	2 / 27 (7.41%)
occurrences (all)	0	2	2
SINUS DISORDER			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
SNEEZING			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
HAEMOPTYSIS			
subjects affected / exposed	3 / 38 (7.89%)	0 / 11 (0.00%)	2 / 27 (7.41%)
occurrences (all)	3	0	2
PLEURITIC PAIN			



subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3
EPISTAXIS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
SPUTUM DISCOLOURED			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
BRONCHOSPASM			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DYSPHONIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NASAL INFLAMMATION			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
PAINFUL RESPIRATION			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
PULMONARY CONGESTION			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
SPUTUM INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
HICCUPS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NASAL DRYNESS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL OEDEMA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PLEURISY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PULMONARY PAIN			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MOOD SWINGS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Abnormal dreams			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Investigations			
BLOOD GLUCOSE INCREASED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 11 (9.09%) 1	0 / 27 (0.00%) 0
C-REACTIVE PROTEIN INCREASED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
GLUCOSE URINE PRESENT subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
LIVER FUNCTION TEST ABNORMAL subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
PROTHROMBIN TIME PROLONGED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
PULMONARY FUNCTION TEST DECREASED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 11 (18.18%) 2	0 / 27 (0.00%) 0
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
ALANINE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
BLOOD IMMUNOGLOBULIN E INCREASED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
BLOOD SODIUM DECREASED subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
BLOOD URINE PRESENT			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Forced expiratory volume decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 38 (5.26%)	1 / 11 (9.09%)	1 / 27 (3.70%)
occurrences (all)	2	1	1
Sputum abnormal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Blood immunoglobulin G increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Protein total increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
BACTERIA URINE IDENTIFIED			

subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
BLOOD PHOSPHORUS DECREASED			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
CULTURE THROAT POSITIVE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
FUNGUS SPUTUM TEST POSITIVE			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PROTEIN URINE PRESENT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
URINE KETONE BODY PRESENT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
EXCORIATION			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
JOINT INJURY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Rib fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
SUNBURN			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
VERTEBRAL INJURY			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Animal bite			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	1 / 27 (3.70%) 1
ARTHROPOD BITE			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	1 / 11 (9.09%) 1	4 / 27 (14.81%) 4
Cystic fibrosis related diabetes			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Cardiac disorders			
SINUS BRADYCARDIA			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Tachycardia			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
SINUS HEADACHE			
subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
MIGRAINE			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	1 / 27 (3.70%) 3
TREMOR			



subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
TUNNEL VISION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	7 / 38 (18.42%)	2 / 11 (18.18%)	5 / 27 (18.52%)
occurrences (all)	10	3	7
NEURALGIA			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
PRESYNCOPE			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
LETHARGY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
LYMPHADENOPATHY			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			

subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
EAR DISCOMFORT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
EAR DISORDER			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
TINNITUS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
EYELID OEDEMA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS (EYE)			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
VISION BLURRED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
ABDOMINAL PAIN			

subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
NAUSEA			
subjects affected / exposed	3 / 38 (7.89%)	0 / 11 (0.00%)	2 / 27 (7.41%)
occurrences (all)	3	0	2
VOMITING			
subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
FLATULENCE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	2 / 38 (5.26%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
DISTAL ILEAL OBSTRUCTION SYNDROME			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DRY MOUTH			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
FAECAL VOLUME INCREASED			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
LIP SWELLING			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
POST-TUSSIVE VOMITING			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
STEATORRHOEA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
RASH MACULAR			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
RASH PAPULAR			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
ACNE			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
HYPOAESTHESIA FACIAL			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	1 / 38 (2.63%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
RASH FOLLICULAR			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Dermatitis atopic			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rash generalised			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
RASH			
subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	1 / 11 (9.09%) 1	0 / 27 (0.00%) 0
ALOPECIA			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
ECCHYMOSIS			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Renal and urinary disorders			
PYURIA			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Chromaturia			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Renal failure acute			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
PROTEINURIA			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
DYSURIA			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 11 (9.09%) 1	0 / 27 (0.00%) 0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 6	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
PAIN IN EXTREMITY			

subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 38 (0.00%)	1 / 11 (9.09%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Arthritis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Clubbing			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
COSTOCHONDRITIS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MEDIAL TIBIAL STRESS SYNDROME			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>TORTICOLLIS</b>			
subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>Back pain</b>			
subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 11 (0.00%) 0	1 / 27 (3.70%) 1
<b>Infections and infestations</b>			
<b>VIRAL INFECTION</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>RHINITIS</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>UPPER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	1 / 11 (9.09%) 1	4 / 27 (14.81%) 4
<b>BACTERIAL DISEASE CARRIER</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>CANDIDIASIS</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>ORAL HERPES</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>VIRAL UPPER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>Infective pulmonary exacerbation of cystic fibrosis</b>			
subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
<b>NASOPHARYNGITIS</b>			



subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Kidney infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
FUNGAL INFECTION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
HERPES SIMPLEX			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
LARYNGITIS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	1 / 38 (2.63%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 38 (0.00%)	0 / 11 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
VIRAL RASH subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Metabolism and nutrition disorders HYPOGLYCAEMIA subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
DEHYDRATION subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
Decreased appetite subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 11 (18.18%) 2	0 / 27 (0.00%) 0
ANOREXIA subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
HYPERCALCAEMIA subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0
HYPERGLYCAEMIA subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 11 (0.00%) 0	0 / 27 (0.00%) 0

<b>Non-serious adverse events</b>	Cohort 4: Placebo	Cohort 4: LUM 400 mg q12h+IVA 250 mg q12h	
Total subjects affected by non-serious adverse events subjects affected / exposed	53 / 63 (84.13%)	51 / 62 (82.26%)	
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 62 (1.61%) 1	
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all)	6 / 63 (9.52%) 6	4 / 62 (6.45%) 6	

PYREXIA		
subjects affected / exposed	9 / 63 (14.29%)	7 / 62 (11.29%)
occurrences (all)	10	7
PAIN		
subjects affected / exposed	3 / 63 (4.76%)	0 / 62 (0.00%)
occurrences (all)	3	0
APPLICATION SITE PRURITUS		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
CATHETER SITE HAEMORRHAGE		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
CATHETER SITE PAIN		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
CHEST DISCOMFORT		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
CHILLS		
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)
occurrences (all)	3	0
FEELING HOT		
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)
occurrences (all)	4	0
INJECTION SITE HAEMORRHAGE		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
Chest pain		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Exercise tolerance decreased		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Malaise		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0

Vessel puncture site bruise subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 62 (0.00%) 0	
NON-CARDIAC CHEST PAIN subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
APPLICATION SITE IRRITATION subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
FEELING OF BODY TEMPERATURE CHANGE subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
INFLUENZA LIKE ILLNESS subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 62 (0.00%) 0	
Reproductive system and breast disorders MENSTRUATION DELAYED subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
BREAST TENDERNESS subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
MENOMETRORRHAGIA subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
MENORRHAGIA subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
MENSTRUAL DISORDER subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
Dysmenorrhoea			

subjects affected / exposed	2 / 63 (3.17%)	1 / 62 (1.61%)	
occurrences (all)	2	1	
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
Vulvovaginal discomfort			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	12 / 63 (19.05%)	13 / 62 (20.97%)	
occurrences (all)	15	16	
PRODUCTIVE COUGH			
subjects affected / exposed	3 / 63 (4.76%)	3 / 62 (4.84%)	
occurrences (all)	4	3	
OROPHARYNGEAL PAIN			
subjects affected / exposed	5 / 63 (7.94%)	3 / 62 (4.84%)	
occurrences (all)	6	3	
NASAL CONGESTION			
subjects affected / exposed	4 / 63 (6.35%)	5 / 62 (8.06%)	
occurrences (all)	5	7	
RHINORRHOEA			
subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	
occurrences (all)	4	4	
DYSPNOEA			
subjects affected / exposed	4 / 63 (6.35%)	9 / 62 (14.52%)	
occurrences (all)	5	10	
RALES			
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)	
occurrences (all)	2	2	
RESPIRATION ABNORMAL			
subjects affected / exposed	9 / 63 (14.29%)	17 / 62 (27.42%)	
occurrences (all)	9	20	
WHEEZING			

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
LUNG HYPERINFLATION		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
RESPIRATORY TRACT CONGESTION		
subjects affected / exposed	6 / 63 (9.52%)	5 / 62 (8.06%)
occurrences (all)	6	6
BRONCHIAL SECRETION RETENTION		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
HYPOVENTILATION		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
INCREASED VISCOSITY OF BRONCHIAL SECRETION		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
NASAL MUCOSAL DISORDER		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
NASAL OEDEMA		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
PROLONGED EXPIRATION		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
RHINITIS ALLERGIC		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
RHONCHI		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
SINUS CONGESTION		
subjects affected / exposed	4 / 63 (6.35%)	0 / 62 (0.00%)
occurrences (all)	4	0

SINUS DISORDER		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
SNEEZING		
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)
occurrences (all)	1	1
HAEMOPTYSIS		
subjects affected / exposed	7 / 63 (11.11%)	5 / 62 (8.06%)
occurrences (all)	10	5
PLEURITIC PAIN		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
EPISTAXIS		
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)
occurrences (all)	1	1
PARANASAL SINUS HYPERSECRETION		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
SPUTUM DISCOLOURED		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
OBSTRUCTIVE AIRWAYS DISORDER		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
BRONCHOSPASM		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
DYSPHONIA		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
DYSPNOEA EXERTIONAL		
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)
occurrences (all)	1	1
NASAL INFLAMMATION		



subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
PAINFUL RESPIRATION			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
PULMONARY CONGESTION			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
SPUTUM INCREASED			
subjects affected / exposed	12 / 63 (19.05%)	10 / 62 (16.13%)	
occurrences (all)	12	10	
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 63 (0.00%)	3 / 62 (4.84%)	
occurrences (all)	0	3	
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
HICCUPS			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
NASAL DRYNESS			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
PHARYNGEAL OEDEMA			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
PLEURISY			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
PULMONARY PAIN			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences (all)	1	1	

INSOMNIA			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
MOOD SWINGS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
DEPRESSED MOOD			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Abnormal dreams			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	2	
Investigations			
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	5 / 63 (7.94%)	2 / 62 (3.23%)	
occurrences (all)	6	2	
GLUCOSE URINE PRESENT			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
LIVER FUNCTION TEST ABNORMAL			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
PULMONARY FUNCTION TEST DECREASED			
subjects affected / exposed	2 / 63 (3.17%)	2 / 62 (3.23%)	
occurrences (all)	2	3	
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
ALANINE AMINOTRANSFERASE			

INCREASED		
subjects affected / exposed	1 / 63 (1.59%)	4 / 62 (6.45%)
occurrences (all)	1	4
BLOOD IMMUNOGLOBULIN E INCREASED		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
BLOOD SODIUM DECREASED		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
BLOOD URINE PRESENT		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
HEPATIC ENZYME INCREASED		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
INTERNATIONAL NORMALISED RATIO INCREASED		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Forced expiratory volume decreased		
subjects affected / exposed	4 / 63 (6.35%)	4 / 62 (6.45%)
occurrences (all)	4	4
Aspartate aminotransferase increased		
subjects affected / exposed	1 / 63 (1.59%)	4 / 62 (6.45%)
occurrences (all)	1	4
Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 63 (0.00%)	3 / 62 (4.84%)
occurrences (all)	0	3
Sputum abnormal		
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)
occurrences (all)	1	1
Blood alkaline phosphatase increased		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Blood creatinine decreased		

subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Blood creatinine increased		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Blood immunoglobulin G increased		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Chest X-ray abnormal		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Eosinophil count increased		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Gamma-glutamyltransferase increased		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Interleukin level increased		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Protein total increased		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Transaminases increased		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Weight decreased		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
WHITE BLOOD CELL COUNT INCREASED		

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>BLOOD GLUCOSE DECREASED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>NEUTROPHIL COUNT INCREASED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>BACTERIA URINE IDENTIFIED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>BLOOD PHOSPHORUS DECREASED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>BLOOD POTASSIUM INCREASED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>CULTURE THROAT POSITIVE</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>ELECTROCARDIOGRAM QT PROLONGED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>FUNGUS SPUTUM TEST POSITIVE</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>PLATELET COUNT DECREASED</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>PROTEIN URINE PRESENT</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
<b>URINE KETONE BODY PRESENT</b>		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0

WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
CHEST INJURY			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
EXCORIATION			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
JOINT SPRAIN			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
LIMB INJURY			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
MUSCLE STRAIN			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
THERMAL BURN			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)	
occurrences (all)	2	0	
Procedural pain			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Arthropod sting			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
JOINT INJURY			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Contusion			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Road traffic accident			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
SUNBURN			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
VERTEBRAL INJURY			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Animal bite			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
ARTHROPOD BITE			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Cystic fibrosis related diabetes			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

<b>DIZZINESS</b> subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	2 / 62 (3.23%) 2	
<b>SINUS HEADACHE</b> subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	1 / 62 (1.61%) 1	
<b>MIGRAINE</b> subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
<b>TREMOR</b> subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
<b>TUNNEL VISION</b> subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
<b>HEADACHE</b> subjects affected / exposed occurrences (all)	11 / 63 (17.46%) 18	3 / 62 (4.84%) 4	
<b>NEURALGIA</b> subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
<b>PRESYNCOPE</b> subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 62 (0.00%) 0	
<b>LETHARGY</b> subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 2	0 / 62 (0.00%) 0	
<b>DYSGEUSIA</b> subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
<b>Blood and lymphatic system disorders</b> <b>LYMPHADENOPATHY</b> subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
<b>Eosinophilia</b>			



subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 62 (1.61%) 1	
Increased tendency to bruise subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 62 (1.61%) 1	
Leukopenia subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 62 (0.00%) 0	
Ear and labyrinth disorders			
EAR PAIN subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
EAR DISCOMFORT subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
EAR DISORDER subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
TINNITUS subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 3	0 / 62 (0.00%) 0	
Eye disorders			
EYELID OEDEMA subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
CONJUNCTIVITIS (EYE) subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
VISION BLURRED subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 62 (0.00%) 0	
Gastrointestinal disorders			

DIARRHOEA		
subjects affected / exposed	5 / 63 (7.94%)	7 / 62 (11.29%)
occurrences (all)	9	7
ABDOMINAL PAIN UPPER		
subjects affected / exposed	7 / 63 (11.11%)	5 / 62 (8.06%)
occurrences (all)	10	5
ABDOMINAL DISCOMFORT		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
ABDOMINAL PAIN		
subjects affected / exposed	3 / 63 (4.76%)	1 / 62 (1.61%)
occurrences (all)	5	1
NAUSEA		
subjects affected / exposed	7 / 63 (11.11%)	7 / 62 (11.29%)
occurrences (all)	9	7
VOMITING		
subjects affected / exposed	2 / 63 (3.17%)	4 / 62 (6.45%)
occurrences (all)	2	4
ABDOMINAL DISTENSION		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
ABDOMINAL PAIN LOWER		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
FLATULENCE		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
GASTROOESOPHAGEAL REFLUX DISEASE		
subjects affected / exposed	0 / 63 (0.00%)	5 / 62 (8.06%)
occurrences (all)	0	7
HYPOAESTHESIA ORAL		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
CONSTIPATION		

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
DISTAL ILEAL OBSTRUCTION SYNDROME		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
DRY MOUTH		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
DYSPEPSIA		
subjects affected / exposed	0 / 63 (0.00%)	3 / 62 (4.84%)
occurrences (all)	0	3
RECTAL HAEMORRHAGE		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
TOOTHACHE		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
FREQUENT BOWEL MOVEMENTS		
subjects affected / exposed	1 / 63 (1.59%)	2 / 62 (3.23%)
occurrences (all)	1	3
FAECAL VOLUME INCREASED		
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)
occurrences (all)	1	1
DYSPHAGIA		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
LIP SWELLING		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
POST-TUSSIVE VOMITING		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
STEATORRHOEA		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1

Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
RASH MACULAR			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
RASH PAPULAR			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
ACNE			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
DERMATITIS CONTACT			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
HYPERHIDROSIS			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
HYPOAESTHESIA FACIAL			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
NIGHT SWEATS			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
PRURITUS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
RASH FOLLICULAR			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
URTICARIA			

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Dermatitis atopic			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Rash generalised			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
RASH			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
ALOPECIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
ECCHYMOSIS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
PYURIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Chromaturia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Renal failure acute			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
PROTEINURIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
DYSURIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	

Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 63 (1.59%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
MUSCLE SPASMS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
MYALGIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Arthritis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	3	
Clubbing			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
Osteopenia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
COSTOCHONDRITIS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
MEDIAL TIBIAL STRESS SYNDROME			

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>MUSCLE TIGHTNESS</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>MUSCULOSKELETAL STIFFNESS</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>NECK PAIN</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>TORTICOLLIS</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>Back pain</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>Infections and infestations</b>			
<b>VIRAL INFECTION</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>RHINITIS</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>UPPER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed	3 / 63 (4.76%)	3 / 62 (4.84%)	
occurrences (all)	4	3	
<b>BACTERIAL DISEASE CARRIER</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>CANDIDIASIS</b>			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
<b>ORAL HERPES</b>			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
VIRAL UPPER RESPIRATORY TRACT INFECTION		
subjects affected / exposed	4 / 63 (6.35%)	2 / 62 (3.23%)
occurrences (all)	4	2
Infective pulmonary exacerbation of cystic fibrosis		
subjects affected / exposed	10 / 63 (15.87%)	7 / 62 (11.29%)
occurrences (all)	11	8
NASOPHARYNGITIS		
subjects affected / exposed	6 / 63 (9.52%)	2 / 62 (3.23%)
occurrences (all)	6	2
ORAL CANDIDIASIS		
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)
occurrences (all)	0	2
PHARYNGITIS STREPTOCOCCAL		
subjects affected / exposed	2 / 63 (3.17%)	0 / 62 (0.00%)
occurrences (all)	2	0
Rash pustular		
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)
occurrences (all)	0	2
Acute sinusitis		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Bronchitis		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Bronchopulmonary aspergillosis allergic		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
INFLUENZA		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Conjunctivitis		



subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Gastroenteritis		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Gastroenteritis viral		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Kidney infection		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Lower respiratory tract infection bacterial		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Lung infection		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
Upper respiratory tract infection bacterial		
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)
occurrences (all)	1	0
Vulvovaginal mycotic infection		
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)
occurrences (all)	0	1
SINUSITIS		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
FUNGAL INFECTION		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
HERPES SIMPLEX		
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)
occurrences (all)	0	0
LARYNGITIS		

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
OTITIS MEDIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
PHARYNGITIS			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
VIRAL RASH			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
DEHYDRATION			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
Decreased appetite			
subjects affected / exposed	4 / 63 (6.35%)	0 / 62 (0.00%)	
occurrences (all)	4	0	
ANOREXIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
HYPERCALCAEMIA			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	
occurrences (all)	0	0	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 August 2011	Study design for cohort 2 was modified.
01 June 2012	Study design was modified to include an additional cohort, Cohort 3.
17 June 2013	Study design was modified to remove the q8h lumacaftor dose regimen in Cohort 3 based on available preliminary data obtained from the q12h lumacaftor dose regimen. In addition, Cohort 4 was included.
22 April 2014	The order of the primary and key secondary endpoints in Cohort 4 was switched.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported