Clinical trial results:
An Open-Label Safety Extension Study to a Multicenter Study of Liposomal Amikacin for Inhalation (LAI) in Adult Patients with Nontuberculous Mycobacterial (NTM) Lung Infections Caused By Mycobacterium Avium Complex (MAC) That are Refractory to Treatment

Summary

EudraCT number	2015-003170-33
Trial protocol	DE GB AT ES PL NL SE IT
Global end of trial date	17 October 2018

Results information

Result version number	v1
This version publication date	31 October 2019
First version publication date	31 October 2019

Trial information

Trial identification

Sponsor protocol code	INS-312

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02628600
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Insmed Incorporated
Sponsor organisation address	10 Finderne Avenue, Building 10, Bridgewater, NJ, United States, 08807-3365
Public contact	Tom Vanthienen, Insmed Incorporated, +41 795432860, tom.vanthienen@insmed.com
Scientific contact	Tom Vanthienen, Insmed Incorporated, +41 795432860, tom.vanthienen@insmed.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate long term safety and tolerability of LAI (590 mg) administered once daily (QD) for up to 12 months in participants who were refractory to standard multi-drug treatment and failed to convert in Study INS-212.

Protection of trial subjects:

This study was performed in compliance with Good Clinical Practices (GCP), including the archiving of essential documents, the International Council for Harmonisation (ICH) Guidelines, and is consistent with the ethical principles in the Declaration of Helsinki.

Background therapy:

This was a single arm open-label study in which all participants received background multidrug regimen (MDR) composed of an antimycobacterial regimen of at least 2 antibiotics based on the 2007 American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines or respective local guidelines.

Evidence for comparator:

Not applicable

Actual start date of recruitment	05 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Japan: 30
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Thailand: 1

Country: Number of subjects enrolled	United States: 68
Worldwide total number of subjects	163
EEA total number of subjects	31

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	75
From 65 to 84 years	86
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 77 sites in 16 countries.

Pre-assignment

Screening details:

Since this study was an open-label extension study to Study INS-212, no pre-specified number of participants was planned. A total of 163 participants (Safety population) were included for the analysis.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Prior LAI + Multidrug Regimen

Arm description:

Participants in the prior Study INS-212 who received LAI+MDR. All participants in this safety extension study received LAI+MDR.

Arm type	Experimental
Investigational medicinal product name	Liposomal Amikacin for Inhalation
Investigational medicinal product code	
Other name	Amikacin Liposome Inhalation Suspension (ALIS), ARIKAYCE
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

LAI 590 mg QD, administered by inhaling drug product that had been aerosolised in an investigational eFlow nebuliser over approximately 14 minutes.

Arm title	Prior Multidrug Regimen Alone

Arm description:

Participants in the prior Study INS-212 who received MDR alone. All participants in this safety extension study received LAI+MDR.

Arm type	Experimental
Investigational medicinal product name	Liposomal Amikacin for Inhalation
Investigational medicinal product code	
Other name	Amikacin Liposome Inhalation Suspension (ALIS), ARIKAYCE
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

LAI 590 mg QD, administered by inhaling drug product that had been aerosolised in an investigational eFlow nebulizer over approximately 14 minutes.

Number of subjects in period 1	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone
Started	73	90
Completed	49	58
Not completed	24	32
Adverse event, serious fatal	2	1
Consent withdrawn by subject	13	8
Physician decision	2	2
Adverse event, non-fatal	3	20
Lost to follow-up	1	-
Lack of efficacy	2	-
Other not specified	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	Prior LAI + Multidrug Regimen

Reporting group description:

Participants in the prior Study INS-212 who received LAI+MDR. All participants in this safety extension study received LAI+MDR.

Reporting group title	Prior Multidrug Regimen Alone

Reporting group description:

Participants in the prior Study INS-212 who received MDR alone. All participants in this safety extension study received LAI+MDR.

Reporting group values	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone	Total
Number of subjects	73	90	163
Age categorical Units: Subjects			
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
geometric mean	64.9	64.8	
standard deviation	± 9.12	± 10.33	-
Gender categorical Units: Subjects			
Female	51	54	105
Male	22	36	58

End points

End points reporting groups

Reporting group title	Prior LAI + Multidrug Regimen

Reporting group description:

Participants in the prior Study INS-212 who received LAI+MDR. All participants in this safety extension study received LAI+MDR.

Reporting group title	Prior Multidrug Regimen Alone

Reporting group description:

Participants in the prior Study INS-212 who received MDR alone. All participants in this safety extension study received LAI+MDR.

Primary: Treatment-Emergent Adverse Events (TEAEs)

End point title	Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

TEAEs are defined as those AEs that occurred on or after the date of first dose of study medication in INS-312 and within 28 days after the last dose. If it couldn't be determined whether the AE is treatment emergent due to a partial onset date, then it was classified as treatment emergent.

End point type	Primary

End point timeframe:

Throughout the trial, up to 13 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics are reported.

End point values	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	90		
Units: Participants				
number (not applicable)				
>=1 TEAE	68	90		
>=1 Serious TEAE (sTEAE)	20	32		
>=1 TEAE leading to study drug withdrawn	8	24		
>=1 TEAE leading to LAI withdrawn	6	22		
>=1 TEAE leading to MDR for NTM withdrawn	4	8		
>=1 TEAE leading to LAI and MDR for NTM withdrawn	1	5		
>=1 sTEAE leading to LAI withdrawn	3	9		
>=1 TEAE leading to death	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving Culture Conversion by Month 6 and Month 12

End point title	Number of Participants Achieving Culture Conversion by Month 6 and Month 12

End point description:

6 months: converters are defined as participants who had 3 consecutive monthly MAC-negative sputum cultures by Month 6 (last opportunity to convert was at Month 4)
12 months: converters are defined as participants who had 3 consecutive monthly MAC-negative sputum cultures by Month 12 (last opportunity to convert was at Month 10)

End point type	Secondary

End point timeframe:

6 months, 12 months

End point values	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	90		
Units: Participants				
number (not applicable)				
6 months	7	24		
12 months	10	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 1) to Month 6 and Month 12 in the 6MWT Distance

End point title	Change from Baseline (Day 1) to Month 6 and Month 12 in the 6MWT Distance

End point description:

A 6-minute walk assessment of exertional capability was performed as Baseline (Day 1) and Month 6 and Month 12/EOT. The standard protocol based on ATS guidelines was used. After assessments were performed for heart rate, blood pressure, pulse oximetry (SpO2), dyspnoea, and overall fatigue using the Borg scale, participants were instructed to walk on a prescribed course as far as they could in 6 minutes. Pre-test assessment parameters were repeated after exertion. The maximum distance achieved and post exertion heart rate and SpO2 were compared to pre-test values. The maximum distance achieved was recorded in the eCRF.

End point type	Secondary

End point timeframe:

6 months, 12 months

End point values	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	90		
Units: Meters				
arithmetic mean (standard deviation)				
Baseline	435.9 (± 132.33)	449.0 (± 122.64)		
Change from Baseline to Month 6	-10.4 (± 69.77)	-20.8 (± 51.57)		
Change from Baseline to Month 12	-10.1 (± 79.23)	-42.2 (± 72.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Culture Conversion

End point title	Time to Culture Conversion

End point description:

The time to culture conversion is defined as the date of the first of 3-consecutive monthly negative sputum cultures. Then, the number of days to culture conversion is defined as the difference between the date of conversion and the date of the first dose of LAI. Data were not estimable at 6 and 12 Months due to the proportion of participants achieving conversion.

End point type	Secondary

End point timeframe:

6 months, 12 months

End point values	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	90		
Units: Months				
median (confidence interval 95%)				
6 Months	0 (0 to 0)	0 (0 to 0)		
12 Months	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout trial, up to 13 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Prior LAI + Multidrug Regimen
Reporting group description:	
Participants in the prior Study INS-212 who received LAI+MDR. All participants in this safety extension study received LAI+MDR.	
Reporting group title	Prior Multidrug Regimen Alone
Reporting group description:	
Participants in the prior Study INS-212 who received MDR alone. All participants in this safety extension study received LAI+MDR.	

Serious adverse events	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 73 (27.40%)	32 / 90 (35.56%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events	2	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	2 / 73 (2.74%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Radius fracture			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 73 (1.37%)	2 / 90 (2.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			

subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 73 (2.74%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Alveolitis allergic			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	2 / 73 (2.74%)	4 / 90 (4.44%)	
occurrences causally related to treatment / all	0 / 2	5 / 7	
deaths causally related to treatment / all	0 / 1	1 / 1	
Dyspnoea			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea at rest			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 73 (1.37%)	2 / 90 (2.22%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 73 (0.00%)	2 / 90 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			

subjects affected / exposed	0 / 73 (0.00%)	2 / 90 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	0 / 73 (0.00%)	2 / 90 (2.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (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			
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	1 / 73 (1.37%)	3 / 90 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			

subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Mycobacterium abscessus infection			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium avium complex infection			
subjects affected / exposed	2 / 73 (2.74%)	5 / 90 (5.56%)	
occurrences causally related to treatment / all	0 / 2	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 73 (4.11%)	4 / 90 (4.44%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pneumonia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinobronchitis			

subjects affected / exposed	0 / 73 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 73 (1.37%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Prior LAI + Multidrug Regimen	Prior Multidrug Regimen Alone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 73 (87.67%)	89 / 90 (98.89%)	
Investigations			
Weight decreased			
subjects affected / exposed	7 / 73 (9.59%)	8 / 90 (8.89%)	
occurrences (all)	7	8	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 73 (4.11%)	13 / 90 (14.44%)	
occurrences (all)	3	13	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 73 (5.48%)	9 / 90 (10.00%)	
occurrences (all)	5	11	
Nausea			
subjects affected / exposed	5 / 73 (6.85%)	9 / 90 (10.00%)	
occurrences (all)	6	10	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	5 / 73 (6.85%)	39 / 90 (43.33%)	
occurrences (all)	6	54	
Cough			

subjects affected / exposed	9 / 73 (12.33%)	32 / 90 (35.56%)	
occurrences (all)	10	37	
Dyspnoea			
subjects affected / exposed	9 / 73 (12.33%)	16 / 90 (17.78%)	
occurrences (all)	10	17	
Haemoptysis			
subjects affected / exposed	10 / 73 (13.70%)	9 / 90 (10.00%)	
occurrences (all)	10	10	
Productive cough			
subjects affected / exposed	4 / 73 (5.48%)	6 / 90 (6.67%)	
occurrences (all)	5	6	
Oropharyngeal pain			
subjects affected / exposed	2 / 73 (2.74%)	7 / 90 (7.78%)	
occurrences (all)	2	8	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	4 / 73 (5.48%)	5 / 90 (5.56%)	
occurrences (all)	4	6	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 73 (13.70%)	7 / 90 (7.78%)	
occurrences (all)	11	10	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	6 / 73 (8.22%)	10 / 90 (11.11%)	
occurrences (all)	7	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2017	The protocol was amended to allow for additional time to analyse primary endpoints due to a longer than anticipated recruitment period and to update administrative and general details.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported