



Clinical trial results:

An open-label, non-controlled, multicenter, pilot clinical trial of inhaled molgramostim in subjects with antibiotic-resistant non-tuberculosis mycobacterial (NTM) infection.

Summary

EudraCT number	2017-003374-14
Trial protocol	GB
Global end of trial date	13 January 2020

Results information

Result version number	v1
This version publication date	29 January 2021
First version publication date	29 January 2021

Trial information

Trial identification

Sponsor protocol code	SAV008-01
-----------------------	-----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03421743
WHO universal trial number (UTN)	-
Other trial identifiers	OPTIMA: OPTIMA

Notes:

Sponsors

Sponsor organisation name	Savara ApS
Sponsor organisation address	Slotsmarken 17, 1.th., Hørsholm, Denmark, DK-2970
Public contact	Cecilia Ganslandt, Savara ApS, +45 79301414, info@savarapharma.com
Scientific contact	Cecilia Ganslandt, Savara ApS, +45 79301414, info@savarapharma.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	13 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 January 2020
Global end of trial reached?	Yes
Global end of trial date	13 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective of the trial: To investigate efficacy of inhaled molgramostim on NTM sputum culture conversion to negative.

Protection of trial subjects:

Subjects could be discontinued from treatment and assessments at any time, if deemed necessary by the investigator.

Potential reasons for discontinuation of treatment included lack of efficacy/worsening of disease and unacceptable AE.

In case of worsening of NTM pulmonary disease, antimycobacterial treatment could be added or a dosage increase of antimycobacterial treatment could be applied as rescue treatment, according to investigator's discretion.

A safety interim analysis and data monitoring were conducted during the trial for the purpose of overseeing safety.

Background therapy:

Anti-mycobacterial therapy was continued, if ongoing.

Evidence for comparator: -

Actual start date of recruitment	01 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	32
EEA total number of subjects	2

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)	16
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adults with chronic pulmonary NTM infection and a positive sputum culture at Screening were recruited into 2 groups:

1: On multidrug NTM guideline based antimycobacterial regimen ongoing for ≥ 6 months prior to Baseline.

2: Had stopped multidrug NTM regimen ≥ 28 days prior to Screening (lack of response/intolerance)/never started such treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Group 1
------------------	---------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Molgramostim nebulizer solution 300 μ g
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Molgramostim nebulizer solution 300 μ g, administered once-daily by inhalation using an eFlow Nebulizer System.

Arm title	Group 2
------------------	---------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Molgramostim nebulizer solution 300 μ g
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Molgramostim nebulizer solution 300 μ g, administered once-daily by inhalation using an eFlow Nebulizer System.

Number of subjects in period 1	Group 1	Group 2
Started	14	18
Completed	11	16
Not completed	3	2
Adverse event, serious fatal	2	1
Consent withdrawn by subject	-	1
Lack of efficacy	1	-

Baseline characteristics

Reporting groups

Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2
Reporting group description: -	

Reporting group values	Group 1	Group 2	Total
Number of subjects	14	18	32
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	12	16
From 65-84 years	10	6	16
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	67.4	66.0	
standard deviation	± 9.9	± 9.0	-
Gender categorical Units: Subjects			
Female	12	10	22
Male	2	8	10

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2
Reporting group description: -	

Primary: Sputum culture conversion

End point title	Sputum culture conversion ^[1]
End point description: Sputum culture conversion defined as at least three consecutive negative sputum samples during the treatment period.	
End point type	Primary
End point timeframe: Baseline to week 48.	

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: This was an exploratory trial without hypothesis testing. Only descriptive statistics were used. The trial was open-label and non-controlled. The two groups represented separate cohorts, not intended for statistical comparison.

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: Subjects with sputum culture conversion	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Sputum smear conversion

End point title	Sputum smear conversion
End point description: Sputum smear conversion defined as at least three consecutive negative acid-fast bacilli (AFB) stained sputum smears on microscopy during the treatment period in subjects who were smear positive at Baseline.	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	16		
Units: Subjects with conversion	5	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Durability of sputum culture conversion

End point title	Durability of sputum culture conversion
End point description: Durability of sputum culture conversion (defined as conversion at or before Week 48 and culture still negative at 12-week Follow-up).	
End point type	Secondary
End point timeframe: Assessed at 12-week Follow-up.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: Subjects with durable conversion	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Durability of sputum smear conversion

End point title	Durability of sputum smear conversion
End point description: Durability of sputum smear conversion (defined as conversion at or before Week 48 and smear still negative at 12-week Follow-up). Includes 2 subjects who were culture positive but smear negative at baseline.	
End point type	Secondary
End point timeframe: Assessed at 12-week Follow-up.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: Subjects with durable conversion	5	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in sputum smear grade

End point title	Change in sputum smear grade
End point description: Change in grade of number of NTM on microscopy of AFB stained sputum smears. A grade between 0 and 4 was assigned (0 corresponding to no AFB on microscopy).	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	16		
Units: Smear grade				
arithmetic mean (standard deviation)	-0.8 (± 0.8)	-0.5 (± 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in sputum culture grade

End point title	Change in sputum culture grade
End point description: Change in grade of sputum cultures. A grade between 0 and 3 was assigned (0 corresponding to no growth).	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	10		
Units: culture grade				
arithmetic mean (standard deviation)	0.0 ($\pm$ 0.0)	0.1 ($\pm$ 1.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in symptom scores: LRTI total score

End point title	Change in symptom scores: LRTI total score
End point description: Change in symptom scores (assessed using Lower Respiratory Tract Infections – visual analogue scale [VAS]).	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	16		
Units: Units on VAS				
arithmetic mean (standard deviation)	2.48 ($\pm$ 9.13)	4.32 ($\pm$ 13.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in GRH

End point title	Change in GRH
End point description: Change in Global Rating of Health. GRH assesses global health on a scale from 1 to 4, 4 representing the best.	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	16		
Units: Units on GRH scale				
arithmetic mean (standard deviation)	-0.78 ($\pm$ 0.67)	-0.38 ($\pm$ 0.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight

End point title	Change in body weight
End point description: Change in body weight.	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	15		
Units: kilogram(s)				
arithmetic mean (standard deviation)	-1.77 ($\pm$ 2.51)	-1.44 ($\pm$ 3.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in 6MWD

End point title	Change in 6MWD
End point description: Change in 6-minute walking distance (6MWD) during a 6-minute walk test (6MWT).	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	15		
Units: meter				
arithmetic mean (standard deviation)	-17.1 (± 62.5)	12.5 (± 56.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in dyspnoea score

End point title	Change in dyspnoea score
End point description: Change in Borg CR10 scores during a 6-minute walk test (6MWT). The post-walk score is reported.	
End point type	Secondary
End point timeframe: Baseline to week 48.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	15		
Units: Borg CR10 score				
arithmetic mean (standard deviation)	0.79 (± 0.92)	1.43 (± 3.01)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to 12-week follow-up (60 weeks in total).

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	21.0
--------------------	------

Reporting groups

Reporting group title	Group 1
-----------------------	---------

Reporting group description: -

Reporting group title	Group 2
-----------------------	---------

Reporting group description: -

Serious adverse events	Group 1	Group 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 14 (57.14%)	6 / 18 (33.33%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Investigations			
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
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			
Fall			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose	Additional description: 1 case with PT Overdose was overdose with anxiolytics and alcohol (suicide).		
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Right ventricular failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 14 (7.14%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	3 / 14 (21.43%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 14 (0.00%)	2 / 18 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infective exacerbation of bronchiectasis			
subjects affected / exposed	4 / 14 (28.57%)	3 / 18 (16.67%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection pseudomonal			
subjects affected / exposed	0 / 14 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Group 1	Group 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	18 / 18 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 14 (7.14%)	2 / 18 (11.11%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 14 (28.57%)	4 / 18 (22.22%)	
occurrences (all)	4	7	
Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	4 / 18 (22.22%)	
occurrences (all)	4	5	
Chest pain			
subjects affected / exposed	2 / 14 (14.29%)	2 / 18 (11.11%)	
occurrences (all)	2	3	
Chest discomfort			
subjects affected / exposed	2 / 14 (14.29%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Malaise			

subjects affected / exposed	1 / 14 (7.14%)	2 / 18 (11.11%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 14 (64.29%)	13 / 18 (72.22%)	
occurrences (all)	15	24	
Dyspnoea			
subjects affected / exposed	9 / 14 (64.29%)	9 / 18 (50.00%)	
occurrences (all)	9	10	
Haemoptysis			
subjects affected / exposed	5 / 14 (35.71%)	3 / 18 (16.67%)	
occurrences (all)	12	8	
Sputum increased			
subjects affected / exposed	2 / 14 (14.29%)	4 / 18 (22.22%)	
occurrences (all)	3	4	
Bronchiectasis			
subjects affected / exposed	4 / 14 (28.57%)	1 / 18 (5.56%)	
occurrences (all)	5	1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 14 (7.14%)	2 / 18 (11.11%)	
occurrences (all)	1	3	
Oropharyngeal pain			
subjects affected / exposed	2 / 14 (14.29%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Asthma			
subjects affected / exposed	0 / 14 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	4	
Wheezing			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Dysphonia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Rhinorrhoea			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 18 (5.56%) 1	
Investigations			
Eosinophil count increased subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 4	6 / 18 (33.33%) 8	
C-reactive protein increased subjects affected / exposed occurrences (all)	6 / 14 (42.86%) 6	3 / 18 (16.67%) 3	
Weight decreased subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	3 / 18 (16.67%) 3	
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 3	2 / 18 (11.11%) 2	
Blood urine present subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 3	0 / 18 (0.00%) 0	
Haemoglobin decreased subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 18 (5.56%) 1	
Injury, poisoning and procedural complications			
Wrist fracture subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 18 (5.56%) 1	
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 3	4 / 18 (22.22%) 6	
Dizziness subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	2 / 18 (11.11%) 2	
Blood and lymphatic system disorders			
Eosinophilia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3	2 / 18 (11.11%) 2	

Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1	 3 / 18 (16.67%) 3 1 / 18 (5.56%) 1	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 5 / 14 (35.71%) 9 4 / 14 (28.57%) 5 2 / 14 (14.29%) 9 1 / 14 (7.14%) 1 2 / 14 (14.29%) 2	 7 / 18 (38.89%) 13 5 / 18 (27.78%) 7 3 / 18 (16.67%) 4 2 / 18 (11.11%) 2 1 / 18 (5.56%) 1	
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 3 2 / 14 (14.29%) 3 0 / 14 (0.00%) 0	 1 / 18 (5.56%) 1 0 / 18 (0.00%) 0 2 / 18 (11.11%) 2	
Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all)	 2 / 14 (14.29%) 3	 1 / 18 (5.56%) 1	

Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	2 / 14 (14.29%)	3 / 18 (16.67%)	
occurrences (all)	2	5	
Arthralgia			
subjects affected / exposed	3 / 14 (21.43%)	1 / 18 (5.56%)	
occurrences (all)	5	1	
Muscle spasms			
subjects affected / exposed	2 / 14 (14.29%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 18 (11.11%)	
occurrences (all)	1	2	
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	2	
Infections and infestations			
Infective exacerbation of bronchiectasis			
subjects affected / exposed	4 / 14 (28.57%)	5 / 18 (27.78%)	
occurrences (all)	5	9	
Upper respiratory tract infection			
subjects affected / exposed	3 / 14 (21.43%)	2 / 18 (11.11%)	
occurrences (all)	5	2	
Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 18 (5.56%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2017	The date reflects final amended protocol version 2.0. The changes were made before the protocol was submitted to any competent authority or independent ethics committee.
23 August 2018	The date reflects final amended protocol version 3.0. The number of sputum samples per visit was increased to strengthen the validity and robustness of the microbiological assessments. Definition of sexual abstinence was added.
04 October 2018	The date reflects final amended protocol version 4.0. Treatment period extended by 24 weeks to a total of 48 weeks. Dose modifications allowed after sponsor approval in case of intolerance in order to maintain subjects on treatment if deemed feasible by the investigator. CT scan added at week 48. CT scans should only be performed if this is already a part of local standard at the site. Safety laboratory sampling added at the 12-week Follow-up visit in order to assess the laboratory parameters.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported