Clinical trial results:
A Phase II/III, Double-Blind, Randomized, Placebo-Controlled, Multicenter, International Study Evaluating the Safety and Efficacy of Inhaled, Human, Alpha-1 Antitrypsin (AAT) in Alpha-1 Antitrypsin Deficient Patients with Emphysema

Summary

EudraCT number	2008-005326-36
Trial protocol	GB NL SE DK DE IE
Global end of trial date	11 December 2013

Results information

Result version number	v1 (current)
This version publication date	05 September 2019
First version publication date	05 September 2019

Trial information

Trial identification

Sponsor protocol code	Kamada-AAT(inhaled)-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01217671
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kamada Ltd
Sponsor organisation address	2 Holtzman Street, Weizmann Science Park, Rehovot, Israel, 7670402
Public contact	Sponsor, Kamada Limited, 00972 89406472,
Scientific contact	Sponsor, Kamada Limited, 00972 89406472,

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	26 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2013
Global end of trial reached?	Yes
Global end of trial date	11 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore rate and severity of exacerbations in AAT deficient patients when treated with inhaled AAT or placebo during a 50-week double-blind treatment period. The objective will be evaluated by the primary endpoint of the time from randomization to the first exacerbation with a severity of moderate or severe.

Protection of trial subjects:

Patients were trained in the operation and cleaning of the eFlow® inhalation device (PARI Pharma GmbH, Germany). Instructions included a demonstration of the nebuliser and training in the use of an electronic diary (eDiary, the LogPad (PHT Corporation, Switzerland)). This diary recorded the daily condition of the patient so that the physicians could be alerted if there was a change in the clinical condition of the patient and respond accordingly.

Background therapy:

Study patients were allowed free use of concomitant medications for the treatment of the underlying disease, including antibiotics, steroids (inhaled and systemic), as well as any additional therapy approved by the principal investigator of the study site

Evidence for comparator: -

Actual start date of recruitment	18 March 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 36
Country: Number of subjects enrolled	Sweden: 22
Country: Number of subjects enrolled	United Kingdom: 56
Country: Number of subjects enrolled	Denmark: 13
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Ireland: 15
Country: Number of subjects enrolled	Canada: 12
Worldwide total number of subjects	168
EEA total number of subjects	156

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)	135
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Men and women over the age of 18 with a diagnosis of emphysema confirmed by computed tomography (CT) scan and a record of inherited severe AATD (ZZ or other rare genotypes with a serum AAT level below 11 µM). Patients (168) were recruited between 18/March/2010 and 17/December/2012 in 12 sites in 7 countries. Randomization was 1:1 placebo or AAT.

Pre-assignment

Screening details:

The inclusion criteria included FEV1 percent predicted post-bronchodilator < 80%, and a history of two or more moderate or severe exacerbations requiring a change in treatment (antibiotics, systemic steroids, hospitalization) over the past 18 months, with at least one episode within the 12 months prior to screening.

Period 1

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

Blinding implementation details:

Eligible patients were randomized 1:1 to receive study drug or placebo by an IVRS system. Allocation of the study drug during the study was also regulated by the IVRS. Site staff telephoned IVRS prior to dispensing the study drug and were notified of the AAT kit labels to be dispensed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Kamada-AAT for Inhalation

Arm description:

Study Drug was administered by eFlow® nebulizer twice daily, each session lasting for approximately 10 to 15 minutes. If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the placebo. Kamada-AAT for Inhalation was supplied in sterile, single-use glass vials containing 4 mL of a ready-to-use solution.

Arm type	Experimental
Investigational medicinal product name	Kamada AAT for Inhalation
Investigational medicinal product code	EMEA/H/C/003934
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Treatment with study drug began at the baseline/randomization visit and continued for a period of 50 weeks. During this period, either Kamada-AAT for Inhalation 80 mg or placebo was administered by eFlow® nebulizer twice daily, each session lasting for approximately 10 to 15 minutes (i.e., a total daily dose of 160 mg of AAT or an equivalent volume of placebo). If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of study drug.

Arm title	Placebo for Inhalation

Arm description:

Placebo was administered by eFlow® twice daily, each session lasting for approximately 10 to 15 minutes. If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the placebo. The placebo was supplied in sterile, single-use glass vials containing 4 mL of a ready-to-use solution.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	EMEA/H/C/003934
Other name	Kamada-AAT for Inhalation
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Treatment with study drug began at the baseline/randomization visit and continued for a period of 50 weeks. During this period, either Kamada-AAT for Inhalation 80 mg or placebo was administered by eFlow® twice daily, each session lasting for approximately 10 to 15 minutes (i.e., a total daily dose of 160 mg of AAT or an equivalent volume of placebo). If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the AAT.

Number of subjects in period 1	Kamada-AAT for Inhalation	Placebo for Inhalation
Started	85	83
Completed	51	69
Not completed	34	14
Adverse event, serious fatal	1	-
Possible side effects	1	-
No confirmed AATD	-	1
Consent withdrawn by subject	12	4
Health and social circumstances	1	-
Adverse event, non-fatal	15	6
Patient moved to lung transplantation list	1	-
Family Circumstances	-	1
Lost to follow-up	2	2
Failure to attend visits	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Kamada-AAT for Inhalation

Reporting group description:

Study Drug was administered by eFlow® nebulizer twice daily, each session lasting for approximately 10 to 15 minutes. If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the placebo. Kamada-AAT for Inhalation was supplied in sterile, single-use glass vials containing 4 mL of a ready-to-use solution.

Reporting group title	Placebo for Inhalation

Reporting group description:

Placebo was administered by eFlow® twice daily, each session lasting for approximately 10 to 15 minutes. If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the placebo. The placebo was supplied in sterile, single-use glass vials containing 4 mL of a ready-to-use solution.

Reporting group values	Kamada-AAT for Inhalation	Placebo for Inhalation	Total
Number of subjects	85	83	168
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)	67	68	135
From 65-84 years	18	15	33
85 years and over	0	0	0
Age continuous Units: years			
median	57	53	
inter-quartile range (Q1-Q3)	48 to 63	46.5 to 61.5	-
Gender categorical Units: Subjects			
Female	34	34	68
Male	51	49	100

End points

End points reporting groups

Reporting group title	Kamada-AAT for Inhalation

Reporting group description:

Study Drug was administered by eFlow® nebulizer twice daily, each session lasting for approximately 10 to 15 minutes. If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the placebo. Kamada-AAT for Inhalation was supplied in sterile, single-use glass vials containing 4 mL of a ready-to-use solution.

Reporting group title	Placebo for Inhalation

Reporting group description:

Placebo was administered by eFlow® twice daily, each session lasting for approximately 10 to 15 minutes. If the subject was required to inhale a bronchodilator, this was administered prior to inhalation of the placebo. The placebo was supplied in sterile, single-use glass vials containing 4 mL of a ready-to-use solution.

Primary: The time from randomization to the first event-based exacerbation with a severity of moderate or severe

End point title	The time from randomization to the first event-based exacerbation with a severity of moderate or severe

End point description:

A moderate event-based exacerbation was defined as a course of treatment with antibiotics and/or systemic corticosteroids and severe exacerbation as an episode requiring hospitalisation. For patients taking routine antibiotics, any increase in the current dose of antibiotics or change of type of antibiotics was deemed to indicate a moderate exacerbation. The time to first moderate/severe and mild/moderate/severe exacerbation was derived from the subject's eDiary and updated after a blind review by two experts in the field. They reconciled the eDiary data with the concomitant medications and reports of treatment emergent adverse events in order to determine the start date and severity of the symptom-based exacerbation.

End point type	Primary

End point timeframe:

50 weeks

End point values	Kamada-AAT for Inhalation	Placebo for Inhalation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	60		
Units: Days	112	140		

Statistical analyses

Statistical analysis title	Time to first serious or moderate exacerbation

Statistical analysis description:

Median days to first serious or moderate exacerbation

Comparison groups	Kamada-AAT for Inhalation v Placebo for Inhalation

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0952 [2]
Method	Logrank

Notes:

[1] - Analysis of ITT population

[2] - p Value from Log Rank comparison between treatments adjusted for country

Post-hoc: Improvement in lung function measures

End point title	Improvement in lung function measures

End point description:

Overall change of FEV1 from baseline to 50 weeks

End point type	Post-hoc

End point timeframe:

Change from baseline to 50 weeks

End point values	Kamada-AAT for Inhalation	Placebo for Inhalation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85[3]	83[4]		
Units: ml				
number (not applicable)	18.6	-29.4		

Notes:

[3] - The parameter is calculated as the overall change so all the patients contribute to the final value

[4] - The parameter is calculated as the overall change so all the patients contribute to the final value

Attachments (see zip file)	Overall Change in FEV1.pdf

Statistical analyses

Statistical analysis title	Change in FEV1

Statistical analysis description:

Overall change of FEV1 from baseline to 50 weeks

Comparison groups	Kamada-AAT for Inhalation v Placebo for Inhalation
Number of subjects included in analysis	168
Analysis specification	Post-hoc
Analysis type	superiority[5]
P-value	= 0.0124 [6]
Method	Mixed models analysis
Parameter estimate	LS Mean overall change from baseline
Point estimate	48
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.5
upper limit	82.43
Variability estimate	Standard error of the mean

Notes:

[5] - The results along the DB period were analyzed by Mixed Model For Repeated Measures (MMRM) comparing the least squares means for the changes from baseline at week 50 and the overall effect in the two cohorts

[6] - The same pattern of statistical significant favourable response in the AAT-treated patients group was observed, regardless of the imputation method used to deal with missing data.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
54 weeks	
Adverse event reporting additional description:	
50 weeks of treatment and 4 weeks follow-up. Events were reported by the patient	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	Safety Population AAT
Reporting group description:	
All patients who were exposed to study drug	
Reporting group title	Safety Population Placebo
Reporting group description:	
All patients who were not exposed to study drug	

Serious adverse events	Safety Population AAT	Safety Population Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 87 (34.48%)	15 / 81 (18.52%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Investigations			
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lung			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyosarcoma			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial haemorrhage			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Facial palsy			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Idiopathic thrombocytopenia purpura			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Food poisoning			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 87 (4.60%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	7 / 87 (8.05%)	6 / 81 (7.41%)	
occurrences causally related to treatment / all	1 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 87 (1.15%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranasal cyst			
subjects affected / exposed	0 / 87 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 87 (1.15%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Bronchiectasis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 87 (2.30%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 87 (1.15%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	4 / 87 (4.60%)	2 / 81 (2.47%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 87 (4.60%)	3 / 81 (3.70%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 87 (1.15%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sputum purulent			
subjects affected / exposed	1 / 87 (1.15%)	0 / 81 (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: 3 %

Non-serious adverse events	Safety Population AAT	Safety Population Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 87 (98.85%)	78 / 81 (96.30%)	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 87 (10.34%)	10 / 81 (12.35%)	
occurrences (all)	12	13	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 87 (10.34%)	9 / 81 (11.11%)	
occurrences (all)	16	10	
Influenza like illness			
subjects affected / exposed	8 / 87 (9.20%)	7 / 81 (8.64%)	
occurrences (all)	21	16	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 87 (9.20%)	10 / 81 (12.35%)	
occurrences (all)	10	12	
Dry mouth			
subjects affected / exposed	7 / 87 (8.05%)	4 / 81 (4.94%)	
occurrences (all)	7	5	
Nausea			
subjects affected / exposed	10 / 87 (11.49%)	5 / 81 (6.17%)	
occurrences (all)	14	6	
Vomiting			
subjects affected / exposed	4 / 87 (4.60%)	5 / 81 (6.17%)	
occurrences (all)	4	5	
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
subjects affected / exposed	41 / 87 (47.13%)	38 / 81 (46.91%)	
occurrences (all)	92	84	
Cough			
subjects affected / exposed	17 / 87 (19.54%)	16 / 81 (19.75%)	
occurrences (all)	24	20	
Dysphonia			
subjects affected / exposed	5 / 87 (5.75%)	7 / 81 (8.64%)	
occurrences (all)	5	8	
Dyspnoea			
subjects affected / exposed	37 / 87 (42.53%)	33 / 81 (40.74%)	
occurrences (all)	70	69	
Haemoptysis			
subjects affected / exposed	5 / 87 (5.75%)	2 / 81 (2.47%)	
occurrences (all)	7	2	
Nasal congestion			
subjects affected / exposed	1 / 87 (1.15%)	5 / 81 (6.17%)	
occurrences (all)	1	7	
Oropharyngeal pain			
subjects affected / exposed	10 / 87 (11.49%)	5 / 81 (6.17%)	
occurrences (all)	13	7	
Productive cough			
subjects affected / exposed	14 / 87 (16.09%)	8 / 81 (9.88%)	
occurrences (all)	21	13	
Sputum discoloured			
subjects affected / exposed	9 / 87 (10.34%)	2 / 81 (2.47%)	
occurrences (all)	11	2	
Sputum increased			
subjects affected / exposed	7 / 87 (8.05%)	4 / 81 (4.94%)	
occurrences (all)	9	8	
Wheezing			
subjects affected / exposed	2 / 87 (2.30%)	6 / 81 (7.41%)	
occurrences (all)	2	6	
Musculoskeletal and connective tissue disorders			

Musculoskeletal chest pain			
subjects affected / exposed	5 / 87 (5.75%)	6 / 81 (7.41%)	
occurrences (all)	8	6	
Infections and infestations			
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	7 / 87 (8.05%)	3 / 81 (3.70%)	
occurrences (all)	13	13	
Influenza			
subjects affected / exposed	6 / 87 (6.90%)	2 / 81 (2.47%)	
occurrences (all)	9	5	
Lower respiratory tract infection			
subjects affected / exposed	17 / 87 (19.54%)	14 / 81 (17.28%)	
occurrences (all)	44	29	
Nasopharyngitis			
subjects affected / exposed	12 / 87 (13.79%)	12 / 81 (14.81%)	
occurrences (all)	17	14	
Oral candidiasis			
subjects affected / exposed	7 / 87 (8.05%)	1 / 81 (1.23%)	
occurrences (all)	9	1	
Rhinitis			
subjects affected / exposed	5 / 87 (5.75%)	3 / 81 (3.70%)	
occurrences (all)	7	4	
Sinusitis			
subjects affected / exposed	8 / 87 (9.20%)	2 / 81 (2.47%)	
occurrences (all)	8	3	
Upper respiratory tract infection			
subjects affected / exposed	8 / 87 (9.20%)	9 / 81 (11.11%)	
occurrences (all)	12	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

While the study did not meet the primary endpoint of time to first moderate or severe exacerbation, post hoc analysis showed that treatment with Kamada- AAT for Inhalation improved pulmonary function

Notes: