Clinical trial results:
A double-blind, randomized, placebo-controlled cross-over study of inhaled alginate oligosaccharide (OligoG) administered for 28 days in subjects with Cystic Fibrosis.

Summary

EudraCT number	2014-000844-13
Trial protocol	DK SE DE
Global end of trial date	05 May 2017

Results information

Result version number	v1 (current)
This version publication date	23 July 2020
First version publication date	23 July 2020
Summary attachment (see zip file)	Study synopsis (SMR2984_CSR OligoG FINAL v1.0-synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	SMR-2984

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02157922
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Algipharma AS
Sponsor organisation address	Industrivn. 33, Sandvika, Norway, 1337
Public contact	Yngvar Berg, CEO, Algipharma AS, +47 90044903, yngvar.berg@algipharma.com
Scientific contact	Anne M Graver, Clinical Trial Manager, Algipharma AS, +47 93041021, anne.graver@algipharma.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	12 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2016
Global end of trial reached?	Yes
Global end of trial date	05 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate efficacy of inhaled OligoG measured by FEV-1 and supported by secondary endpoints including Mucociliary Clearance, rheology, microbiology, Quality-of-Life (CF-QR), and Lung Clearance Index (LCI)

Protection of trial subjects:

A Drug Safety Monitoring Board assessed unblinded data throughout the study to ensure prompt action in case of safety concerns.

Background therapy:

Standard of Care. The patient are allowed to continue other CF treatment as long as this has been ongoing in a stable fashion the past 21 days prior to randomization.

Evidence for comparator:

The use of placebo as a comparator is a naturally design in order to evaluate safety, tolerability and preliminary efficacy in patients with cystic fibrosis (CF).
Matching placebo DPI, where the OligoG is replaced with lactose, approx. 48 mg in HPMC capsules. The placebo DPI capsules will be indistinguishable from OligoG in appearance, smell, taste and packaging.

Actual start date of recruitment	30 December 2014
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	Sweden: 5
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Norway: 2
Worldwide total number of subjects	65
EEA total number of subjects	65

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

Subject disposition

Recruitment

Recruitment details:

Ninety patients were screened and 65 were randomised. Of the randomised patients, 56 completed two 28 day treatment periods separated by a 28-day washout period. 33 patients completed the OligoG-Placebo period, and 32 completed the placebo-OligoG period. Nine patients withdrew, 8 due to non-fatal AEs, and 1 is lost to follow-up.

Pre-assignment

Screening details:

Ability to inhale the IMP

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, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The IMP (OligoG DPI or placebo DPI) in identical capsules

Arms

Are arms mutually exclusive?	No
Arm title	OligoG-Placebo DPI

Arm description:

OligoG for 28 days, then 4 weeks wash-out, then Placebo DPI for 28 days

Arm type	Active comparator
Investigational medicinal product name	OligoG-PlaceboDPI (Cross-over)
Investigational medicinal product code	OligoG-Placebo DPI (cross-over)
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Ten capsules were taken by the study subjects three times daily to deliver a total daily dose of 1050 mg OligoG/Placebo DPI.

Arm title	Placebo DPI-OligoG

Arm description:

Placebo DPI for 28 days, then 4 weeks wash-out, and then OligoG for 28 days.

Arm type	Placebo
Investigational medicinal product name	Placebo DPI-OligoG (cross-over)
Investigational medicinal product code	Placebo DPI-OligoG (cross-over)
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Ten capsules were taken by the study subjects three times daily to deliver a total daily dose of equivalent to 1050 mg OligoG/Placebo DPI.

Number of subjects in period 1	OligoG-Placebo DPI	Placebo DPI-OligoG
Started	32	33
Completed	27	29
Not completed	5	4
Adverse event, non-fatal	4	4
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	Overall study

Reporting group description:

These are all patients together in both groups prior to wash-out, i.e OligoG and Palcebo combined.

Reporting group values	Overall study	Total	
Number of subjects	65	65	
Age categorical			
All 65 patients were in adult age category (age 18 - 64)			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	65	65	
From 65-84 years	0	0	
85 years and over	0	0	
adults	0	0	
Gender categorical Units: Subjects			
Female	34	34	
Male	31	31	

Subject analysis sets

Subject analysis set title	All patients
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects caucasian
Mean age 33,5 years. Range 19 - 59
31 male, 34 female

Reporting group values	All patients		
Number of subjects	65		
Age categorical			
All 65 patients were in adult age category (age 18 - 64)			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	65		
From 65-84 years	0		
85 years and over	0		
adults	0		
Gender categorical Units: Subjects			
Female	34		
Male	31		

End points

End points reporting groups

Reporting group title	OligoG-Placebo DPI
Reporting group description:	
OligoG for 28 days, then 4 weeks wash-out, then Placebo DPI for 28 days	
Reporting group title	Placebo DPI-OligoG
Reporting group description:	
Placebo DPI for 28 days, then 4 weeks wash-out, and then OligoG for 28 days.	
Subject analysis set title	All patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects caucasian Mean age 33,5 years. Range 19 - 59 31 male, 34 female	

Primary: The treatment difference OligoG – Placebo in FEV1

End point title	The treatment difference OligoG – Placebo in FEV1
End point description:	
The FEV1 values at the end of each treatment period will be examined with analysis of covariance (ANCOVA), using treatment, treatment period and treatment sequence as fixed effects, patient as random effect and the baseline FEV1 values in each period as covariates. Of the 56 patients who completed the study, one patient is withdrawn for the analysis due to missing data.	
End point type	Primary
End point timeframe:	
Change in FEV1 from start of each treatment period to Day 28 of treatment	

End point values	OligoG-Placebo DPI	Placebo DPI-OligoG	All patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	27[1]	29[2]	56[3]	
Units: % improvement				
number (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)	-0.013 (-0.038 to 0.012)	

Notes:

[1] - Number of patients who completed treatment sequence OligoG-Placebo DPI

[2] - Number of patients who completed treatment sequence Placebo DPI-OligoG

[3] - Of the 56 patients who completed the study, one patient is withdrawn due to missing data.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
The primary efficacy variable for the study was forced expiratory volume in one second (FEV1). The primary analysis was performed on the ITT population. Forthe FEV1 values at the end of each treatment period, a linear model was constructed using SAS PROC MIXED, with treatment, treatment sequence and treatment period as fixed effects, patients as random effects and the baseline value in each treatment period as a covariate.	

Comparison groups	OligoG-Placebo DPI v Placebo DPI-OligoG
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31 [4]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.038
upper limit	0.012

Notes:

[4] - The treatment difference was found to be 1.3% units in favour of placebo, and the difference was not statistically significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected and reported throughout the study; sequence 1, washout, and sequence 2.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	OligoG

Reporting group description:

Number of patients combined receiving OligoG either in the first treatment period or second treatment period.

Reporting group title	Placebo DPI

Reporting group description:

Number of patients combined receiving placebo either in the first treatment period or second treatment period.

Serious adverse events	OligoG	Placebo DPI	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 63 (11.11%)	8 / 61 (13.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood potassium increased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (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			
Pulmonary haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rales			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (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			
Pulmonary exacerbation			
subjects affected / exposed	4 / 63 (6.35%)	4 / 61 (6.56%)	
occurrences causally related to treatment / all	1 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	OligoG	Placebo DPI	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 63 (82.54%)	51 / 61 (83.61%)	
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	

Chest discomfort			
subjects affected / exposed	3 / 63 (4.76%)	2 / 61 (3.28%)	
occurrences (all)	3	2	
Chest pain			
subjects affected / exposed	2 / 63 (3.17%)	4 / 61 (6.56%)	
occurrences (all)	2	5	
Chills			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Crepitations			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Energy increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Influenza like illness			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 63 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	2 / 63 (3.17%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
Secretion discharge			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	0 / 63 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
Menstruation irregular			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 63 (1.59%)	2 / 61 (3.28%)	
occurrences (all)	1	3	
Bronchial obstruction			
subjects affected / exposed	4 / 63 (6.35%)	2 / 61 (3.28%)	
occurrences (all)	4	2	
Bronchial secretion retention			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Bronchospasm			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	3	0	
Cough			
subjects affected / exposed	8 / 63 (12.70%)	10 / 61 (16.39%)	
occurrences (all)	9	12	
Dysphonia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	10 / 63 (15.87%)	3 / 61 (4.92%)	
occurrences (all)	12	4	
Haemoptysis			
subjects affected / exposed	5 / 63 (7.94%)	8 / 61 (13.11%)	
occurrences (all)	5	8	
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 63 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
Increased viscosity of nasal secretion			

subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Nasal mucosal disorder			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Nasal polyps			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	4 / 63 (6.35%)	1 / 61 (1.64%)	
occurrences (all)	4	1	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	2	
Rales			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Sinus congestion			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
Sputum decreased			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
Sputum discoloured			
subjects affected / exposed	0 / 63 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
Sputum increased			
subjects affected / exposed	6 / 63 (9.52%)	5 / 61 (8.20%)	
occurrences (all)	6	5	
Sputum retention			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Upper-airway cough syndrome			

subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	4 / 63 (6.35%)	2 / 61 (3.28%)	
occurrences (all)	4	2	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Investigations			
Bacterial test positive			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Blood glucose increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus increased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Blood potassium increased			
subjects affected / exposed	3 / 63 (4.76%)	5 / 61 (8.20%)	
occurrences (all)	3	5	
Blood uric acid increased			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
Body temperature increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			

subjects affected / exposed	3 / 63 (4.76%)	0 / 61 (0.00%)	
occurrences (all)	3	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Haemoglobin increased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Liver function test abnormal			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Pulmonary function test decreased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Red blood cell count increased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Sputum abnormal			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
Sputum culture positive			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Urine leukocyte esterase			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
White blood cell count increased			
subjects affected / exposed	4 / 63 (6.35%)	1 / 61 (1.64%)	
occurrences (all)	4	1	
Injury, poisoning and procedural complications			

Accident			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Arthropod bite			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
Excoriation			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Animal bite			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Cystic fibrosis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Sinus arrhythmia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	2 / 63 (3.17%)	7 / 61 (11.48%)	
occurrences (all)	2	10	
Lethargy			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	1	

Speech disorder			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	3 / 63 (4.76%)	0 / 61 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Eye disorders			
Corneal opacity			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Abdominal pain			
subjects affected / exposed	1 / 63 (1.59%)	2 / 61 (3.28%)	
occurrences (all)	1	2	
Abdominal pain upper			
subjects affected / exposed	1 / 63 (1.59%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	4 / 63 (6.35%)	0 / 61 (0.00%)	
occurrences (all)	4	0	

Flatulence			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	3 / 63 (4.76%)	2 / 61 (3.28%)	
occurrences (all)	3	2	
Vomiting			
subjects affected / exposed	3 / 63 (4.76%)	1 / 61 (1.64%)	
occurrences (all)	3	2	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 63 (4.76%)	2 / 61 (3.28%)	
occurrences (all)	3	2	
Back pain			
subjects affected / exposed	2 / 63 (3.17%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Flank pain			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Mobility decreased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	2 / 63 (3.17%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			

subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Polyarthritis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	3	0	
Appendicitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Bacterial infection			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Burkholderia gladioli infection			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	

Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	8 / 63 (12.70%)	7 / 61 (11.48%)	
occurrences (all)	8	7	
Lower respiratory tract infection			
subjects affected / exposed	2 / 63 (3.17%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
Lower respiratory tract infection fungal			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	12 / 63 (19.05%)	10 / 61 (16.39%)	
occurrences (all)	14	11	
Otosalpingitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	4 / 63 (6.35%)	5 / 61 (8.20%)	
occurrences (all)	5	5	
Sputum purulent			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis viral			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 March 2015	It is added in inclusion criterion # 5 that patients with Gamma Glutamyl Transferase (GGT) values above 3 x ULN (upper limit of normal) can be included. In Exclusion Criterion # 14, which states that patients with blood values > 3 upper normal value should excluded, exceptions are made for exclusion if the GGT value is above 3x upper normal value. Specialists have confirmed that CF patients often have elevated Gamma Glutamyl Transferase (GGT), without changes in other liver function tests, such as ALT, AST, alkaline phosphatase and bilirubin. Studies have shown that interpretation of adverse events in clinical trials is complicated by the underlying high incidence of abnormal lab values in CF patients. Excluding patients with normal abnormalities can lead to a selected CF population in the study, which is not desirable.
29 August 2016	Amendment 2: This amendment was implemented to allow for retrospective data collection from pre and post study patient visits. The data to be collected included information on FEV1, FVC, FEF25-75, pulmonary exacerbations, antibiotic treatment (i.v.) and hospitalisations. Pulmonary exacerbations are critical events in the disease progression of patients with Cystic Fibrosis, causing acute morbidity with implications for long term morbidity and mortality. For improvement of a pivotal phase III study design, this protocol amendment was implemented to collect further long-term data regarding potential pulmonary exacerbation and hospitalisation rates before and after OligoG treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The protocol aimed for recruitment of 76 patients. Due to low recruitment rate the study was stopped after recruitment of 65 patients.

Notes: