



Clinical trial results:

A randomized double-blind, placebo-controlled cross-over study of inhaled alginate oligosaccharide (OligoG) for 28 days in subjects with Cystic Fibrosis using aztreonam due to chronic colonization with Burkholderia spp.

Summary

EudraCT number	2014-002125-35
Trial protocol	DE
Global end of trial date	10 May 2016

Results information

Result version number	v1 (current)
This version publication date	24 July 2020
First version publication date	24 July 2020
Summary attachment (see zip file)	SMR2591 clinical study report synopsis (SMR2591_CSR synopsis_OligoG_FINAL.pdf)

Trial information

Trial identification

Sponsor protocol code	SMR-2591
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02453789
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AlgiPharma AS
Sponsor organisation address	Industriveien 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	05 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 May 2016
Global end of trial reached?	Yes
Global end of trial date	10 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the efficacy of OligoG in reducing the microbial burden of Burkholderia spp. as measured in expectorated sputum samples.

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 14 days prior to treatment start and for the entire duration of the study (until Day 112).

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 (dry powder for inhalation), 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	01 February 2015
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	Germany: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	14
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 17 patients were screened across both sites in Germany. A total of 15 patients were randomised equally to the treatment sequence OligoG/placebo or placebo/OligoG.

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) in identical capsules

Arms

Are arms mutually exclusive?	Yes
Arm title	OligoG - Placebo

Arm description:

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

Arm type	Active comparator
Investigational medicinal product name	OligoG - Placebo (cross-over)
Investigational medicinal product code	OligoG - Placebo (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

Arm title	Placebo - OligoG
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Arm description:

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

Arm type	Placebo
Investigational medicinal product name	Placebo - OligoG (cross-over)
Investigational medicinal product code	Placebo - 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 equivalent to 1050 mg OligoG/Placebo

Number of subjects in period 1	OligoG - Placebo	Placebo - OligoG
Started	7	8
Completed	7	8

Baseline characteristics

Reporting groups

Reporting group title	Overall study (overall period)
Reporting group description:	
These are all patients together in both groups prior to wash-out, i.e OligoG and Placebo combined.	

Reporting group values	Overall study (overall period)	Total	
Number of subjects	15	15	
Age categorical			
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)	14	14	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	4	4	

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 35.1 years, Range 23 - 71	
4 male, 11 female	

Reporting group values	All patients		
Number of subjects	15		
Age categorical			
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)	14		
From 65-84 years	1		

85 years and over	0		
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Gender categorical			
Units: Subjects			
Female	11		
Male	4		

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End points

End points reporting groups

Reporting group title	OligoG - Placebo
Reporting group description: OligoG for 28 days, then 4 weeks wash-out, then Placebo for 28 days	
Reporting group title	Placebo - OligoG
Reporting group description: Placebo for 28 days, then 4 weeks wash-out, 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 35.1 years, Range 23 - 71 4 male, 11 female	

Primary: The treatment difference OligoG – Placebo in reducing the microbial burden of Burkholderia spp.

End point title	The treatment difference OligoG – Placebo in reducing the microbial burden of Burkholderia spp.
End point description: The log10 transformed Burkholderia rpoD gene copy number values at the end of each treatment period have been examined with analysis of covariance (ANCOVA), using treatment, treatment period and treatment sequence as fixed effects, patient as random effect and the baseline value in each period as a covariate. The 14 patients with data from both treatment periods are included in the analysis.	
End point type	Primary
End point timeframe: Changes in Burkholderia spp. from start of each treatment period to Day 28 of treatment.	

End point values	OligoG - Placebo	Placebo - OligoG	All patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	8	14	
Units: % reduction				
number (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)	0.94 (-0.0003 to 1.88)	

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: The primary variable was to explore the efficacy of OligoG in reducing the microbial burden of Burkholderia spp. as measured in expectorated sputum samples.	
Comparison groups	Placebo - OligoG v OligoG - Placebo

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0501 ^[1]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0003
upper limit	1.88

Notes:

[1] - The difference is not statistically significant on a 5% level but borderline significant in favour of placebo.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected and reported throughout the study; sequence 1, wash-out, and sequence 2.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17
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Reporting groups

Reporting group title	OligoG
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Reporting group description:

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

Reporting group title	Placebo
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Reporting group description:

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

Serious adverse events	OligoG	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 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	OligoG	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)	11 / 14 (78.57%)	
Investigations			
Eosinophil count increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

Forced expiratory volume decreased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Pulmonary function test abnormal subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 14 (0.00%) 0	
Surgical and medical procedures Hospitalisation subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 14 (0.00%) 0	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Exercise tolerance decreased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	1 / 14 (7.14%) 1	
Fatigue subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	1 / 14 (7.14%) 1	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Tinnitus			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	1 / 15 (6.67%)	4 / 14 (28.57%)	
occurrences (all)	1	5	
Dysphonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)	2 / 14 (14.29%)	
occurrences (all)	3	2	
Haemoptysis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Pulmonary haemorrhage			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Sputum discoloured subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Sputum increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Sputum retention subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	0 / 14 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Psoriasis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Rash subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 3	0 / 14 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Back pain subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Infections and infestations			
Clostridium difficile infection subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 14 (0.00%) 0	
Infective pulmonary exacerbation of cystic fibrosis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	1 / 14 (7.14%) 1	
Influenza subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 14 (7.14%) 1	
Nasopharyngitis			

subjects affected / exposed	2 / 15 (13.33%)	3 / 14 (21.43%)	
occurrences (all)	2	3	
Pertussis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pneumonia	Additional description: Bronchopneumonia		
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

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

None reported