



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. For the 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 occurrences (all) | 3 / 63 (4.76%) 3 | 2 / 61 (3.28%) 2 | |
| Chest pain subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 4 / 61 (6.56%) 5 | |
| Chills subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Crepitations subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 1 / 61 (1.64%) 1 | |
| Energy increased subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Fatigue subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 1 / 61 (1.64%) 1 | |
| Influenza like illness subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 61 (1.64%) 1 | |
| Malaise subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 2 / 61 (3.28%) 2 | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 0 / 61 (0.00%) 0 | |
| Secretion discharge subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 61 (1.64%) 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 occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Arthropod bite subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 1 / 61 (1.64%) 1 | |
| Excoriation subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 61 (1.64%) 1 | |
| Animal bite subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 61 (1.64%) 1 | |
| Congenital, familial and genetic disorders Cystic fibrosis subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Sinus arrhythmia subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 61 (0.00%) 0 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 1 / 61 (1.64%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 7 / 61 (11.48%) 10 | |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 61 (1.64%) 1 | |
| Migraine subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 1 / 61 (1.64%) 1 | |

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 02 March 2015 | <p>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 be excluded, exceptions are made for exclusion if the GGT value is above 3x upper normal value.</p> <p>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.</p> |
| 29 August 2016 | <p>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.</p> <p>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.</p> |

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: