



## Clinical trial results: High Dose Antioxidant Treatment for Patients with Cystic Fibrosis Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2013-005481-19    |
| Trial protocol           | DK                |
| Global end of trial date | 30 September 2015 |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 22 June 2016 |
| First version publication date | 22 June 2016 |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | 2013-01 |
|-----------------------|---------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Aarhus University Hospital  |
| Sponsor organisation address | Brendstrupsgaardvej 100, Aarhus N, Denmark, 8200                    |
| Public contact               | Pediatric Department A, Aarhus University Hospital,<br>peschi@rm.dk |
| Scientific contact           | Pediatric Department A, Aarhus University Hospital,<br>peschi@rm.dk |

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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 30 September 2015 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 30 September 2015 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 30 September 2015 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

To evaluate if high dose antioxidant treatment (per oral and inhalation) can inhibit the oxidative stress mediated inflammation in cystic fibrosis patients lung. The inflammation with neutrophil leucocytes is monitored by PET/CT scan

Protection of trial subjects:

To minimize pain in relation to blood sampling the patients were offered local anesthetics. No other measures were taken

Background therapy:

Pancreatic enzymes - vitamin supplementation- PEP mask therapy- pulmozyme inhalation

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 01 May 2014 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 11 |
| Worldwide total number of subjects   | 11          |
| EEA total number of subjects         | 11          |

Notes:

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**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)                     | 3 |
| Adolescents (12-17 years)                 | 8 |
| Adults (18-64 years)                      | 0 |
| From 65 to 84 years                       | 0 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patients were contacted during routine control visits in the outpatient Clinic and asked if they wanted to participate. Recruitment period August 2014 - April 2015

### Pre-assignment

Screening details:

14 pts. were screened. 2 did not want to participate and one suffered from liver disease and had to be excluded.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | medical intervention |
|------------------|----------------------|

Arm description:

All patients had the same run in period where they should be clinically stable and with out anti inflammatory treatment , then scan and tests were performed and there after they recieved Medical intervention (N acetylcysteine) for 14 dys. All tests were then repeated and the trial was over.

|  |                             |
|--|-----------------------------|
| Arm type                               | Experimental                |
| Investigational medicinal product name | Mucomyst or ACC             |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Effervescent tablet, Tablet |
| Routes of administration               | Oral use                    |

Dosage and administration details:

100 mg/kg/24hrs in 3 divided doses given per oral. The patients decided themselves whether they wanted mucomyst or ACC

|  |                             |
|--|-----------------------------|
| Investigational medicinal product name | Glutathione (TAD)           |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Inhalation vapour, solution |
| Routes of administration               | Intrapulmonary use          |

Dosage and administration details:

Inhalations were given 2 times daily 600 mg x2

|                                       |                      |
|---------------------------------------|----------------------|
| <b>Number of subjects in period 1</b> | medical intervention |
| Started                               | 11                   |
| Completed                             | 11                   |



## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values                                | Overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 11            | 11    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 3             | 3     |  |
| Adolescents (12-17 years)                             | 8             | 8     |  |
| Adults (18-64 years)                                  | 0             | 0     |  |
| From 65-84 years                                      | 0             | 0     |  |
| 85 years and over                                     | 0             | 0     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 6             | 6     |  |
| Male  | 5             | 5     |  |
| Genotypic verified cystic fibrosis                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| CF Genotype   | 11            | 11    |  |
| Pulmonary status                                      |               |       |  |
| Units: Subjects                                       |               |       |  |
| Forced vital capacity > 75%                           | 11            | 11    |  |
| clinical status                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| clinically stable                                     | 11            | 11    |  |

## End points

### End points reporting groups

|   |                      |
|---|----------------------|
| Reporting group title   | medical intervention |
| Reporting group description:<br>All patients had the same run in period where they should be clinically stable and with out anti inflammatory treatment , then scan and tests were performed and there after they recieved Medical intervention (N acetylcysteine) for 14 dys. All tests were then repeated and the trial was over. |                      |
| Subject analysis set title  | Post treatment       |
| Subject analysis set type   | Per protocol         |
| Subject analysis set description:<br>Post treatment   |                      |

### Primary: neutrophil metabolic activity

|  |                               |
|--|-------------------------------|
| End point title  | neutrophil metabolic activity |
| End point description:<br>PET-CT scan was carried out 60 minutes after iv injection of 18 F-FDG injection and patient was scanned 6 mins over parts of the lung of interest. |                               |
| End point type   | Primary                       |
| End point timeframe:<br>Pet CT scan was performed early on the day when antioxidant therapy was begun and Again 14 days later.   |                               |

| End point values                    | medical intervention | Post treatment       |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Reporting group      | Subject analysis set |  |  |
| Number of subjects analysed         | 7 <sup>[1]</sup>     | 7                    |  |  |
| Units: Standard uptake values (SUV) |                      |                      |  |  |
| median (full range (min-max))       | 0.33 (0.27 to 0.48)  | 0.36 (0.26 to 0.48)  |  |  |

Notes:

[1] - 4 patients did not complete the trial. Pre-post pairs are included.

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | Wilcoxon signed rank test             |
| Comparison groups                       | medical intervention v Post treatment |
| Number of subjects included in analysis | 14                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | < 0.001                               |
| Method                                  | Wilcoxon (Mann-Whitney)               |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

2 weeks.

Adverse event reporting additional description:

patients diaries, Anamnestic review at the final visit with investigator. Blood tests and physical examination.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | 1medical intervention |
|-----------------------|-----------------------|

Reporting group description:

All patients had the same run in period where they should be clinically stable and with out anti inflammatory treatment , then scan and tests were performed and there after they recieved Medical intervention (N acetylcysteine) for 14 dys. All tests were then repeated and the trial was over.

| Serious adverse events                            | 1medical intervention |  |  |
|---|-----------------------|--|--|
| Total subjects affected by serious adverse events |                       |  |  |
| subjects affected / exposed                       | 0 / 11 (0.00%)        |  |  |
| number of deaths (all causes)                     | 0                     |  |  |
| number of deaths resulting from adverse events    | 0                     |  |  |

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

| Non-serious adverse events                            | 1medical intervention                          |  |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events |  |  |  |
| subjects affected / exposed                           | 2 / 11 (18.18%)                                |  |  |
| Gastrointestinal disorders                            |  |  |  |
| Diarrhoea   | Additional description: One day with diarrhoea |  |  |
| subjects affected / exposed                           | 1 / 11 (9.09%)                                 |  |  |
| occurrences (all)                                     | 1  |  |  |
| Infections and infestations                           |  |  |  |
| common cold   |  |  |  |
| subjects affected / exposed                           | 1 / 11 (9.09%)                                 |  |  |
| occurrences (all)                                     | 1  |  |  |





## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported