Clinical trial results:
High dose antioxidant treatment of patients with cystic fibrosis evaluated by measuring desmosine/isodesmosine in urine

Summary

EudraCT number	2016-000354-35
Trial protocol	DK
Global end of trial date	01 March 2017

Results information

Result version number	v1 (current)
This version publication date	29 October 2017
First version publication date	29 October 2017

Trial information

Trial identification

Sponsor protocol code	2016-01

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	Palle Juul Jensens Blv 100, Aarhus, Denmark, 8200
Public contact	Paediatric Department, Aarhus University Hospital, +45 78451471, anjor@clin.au.dk
Scientific contact	Paediatric Department, Aarhus University Hospital, +45 78451471, anjor@clin.au.dk
Sponsor organisation name	Aarhus University Hospital
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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	25 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 February 2017
Global end of trial reached?	Yes
Global end of trial date	01 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to evalutate if high dose antioxidant treatment (per oral) of cystic fibrosis patients can inhibit the oxaditive stress mediated inflammation in their lungs-Measured by concentration of desmosine/isodesmosine in the urine

Protection of trial subjects:

To minimize pain in relation to blood sampling the patients were offered local anestestics or inhalation with 50% N2O +50% O2. No other measures were taken

Background therapy:

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

Evidence for comparator: -

Actual start date of recruitment	01 April 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	26

Adolescents (12-17 years)	14
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 rutine control visits in the outpatient Clinic an asked if they wanted to participate.Recruitement period June 2016-October 2016

Pre-assignment

Screening details:

41 patients were screened. One produced pseudomonas aeruginosa positive sputum culture during the investigation period and had to be excluded.

Period 1

Period 1 title	baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Baseline

Arm description:

7 days without any antiinflammatory treatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	medical intervention

Arm description:

Pts. recieved 7 days N-acetyl cysteine 100 mg/kg/ in 3 doses + after that 7 days N-acetylcysteine 200mg/kg/in 3 doses.

Arm type	Experimental
Investigational medicinal product name	N-acetylcysteine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

7 days with 100mg/kg/ 24 hrs in 3 divided doses followed by 7 days with 200 mg /kg/24 hrs in 3 divided doses

Number of subjects in period 1	Baseline	medical intervention
Started	20	20
Completed	20	20

Period 2	
Period 2 title	medical intervention
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Arm title	baseline
Arm description: 7 days with no antiinflammatory treatment	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	baseline
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	Baseline
Reporting group description:	
7 days without any antiinflammatory treatment	
Reporting group title	medical intervention
Reporting group description:	
Pts. recieved 7 days N-acetyl cysteine 100 mg/kg/ in 3 doses + after that 7 days N-acetylcysteine 200mg/kg/in 3 doses.	

Reporting group values	Baseline	medical intervention	Total
Number of subjects	20	20	40
Age categorical			
children 2-11: 13 adolescents 12-17: 7			
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)	13	13	26
Adolescents (12-17 years)	7	7	14
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
children	0	0	0
adolescents	0	0	0
Gender categorical			
female:9 Male: 11			
Units: Subjects			
Female	9	9	18
Male	11	11	22

Subject analysis sets	
Subject analysis set title	Pre treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
A spot urine was taken at day 7 and 21 - and analyses for desmosine/isodesmosine was carried out and related to urine creatinin values	
Subject analysis set title	Post treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
A spot urine was taken at day 7 and 21 - and analyses for desmosine/isodesmosine was carried out and related to urine creatinin values	

Reporting group values	Pre treatment	Post treatment	
Number of subjects	20	20	
Age categorical			
children 2-11: 13 adolescents 12-17: 7			
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)	13	13	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
children	0	0	
adolescents	0	0	
Gender categorical			
female:9 Male: 11			
Units: Subjects			
Female	9	9	
Male	11	11	

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description:	
7 days without any antiinflammatory treatment	
Reporting group title	medical intervention
Reporting group description:	
Pts. recieved 7 days N-acetyl cysteine 100 mg/kg/ in 3 doses + after that 7 days N-acetylcysteine 200mg/kg/in 3 doses.	
Reporting group title	baseline
Reporting group description:	
7 days with no antiinflammatory treatment	
Subject analysis set title	Pre treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
A spot urine was taken at day 7 and 21 - and analyses for desmosine/isodesmosine was carried out and related to urine creatinin values	
Subject analysis set title	Post treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
A spot urine was taken at day 7 and 21 - and analyses for desmosine/isodesmosine was carried out and related to urine creatinin values	

Primary: change in urine desmosine/isodesmosine excretion

End point title	change in urine desmosine/isodesmosine excretion
End point description:	
Spot Urine samples were analysed for desmosine/isodesmosine in ng /ml and related to urine creatinine in mg/ml - making values in ng/mg	
End point type	Primary
End point timeframe:	
Measurements were made day 7 and 14	

End point values	Baseline	medical intervention	Pre treatment	Post treatment
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: ng/mg				
median (full range (min-max))	52.4 (32.9 to 100.6)	50.15 (16.3 to 82.7)	52.4 (32.9 to 100.6)	50.15 (16.3 to 82.7)

Statistical analyses

Statistical analysis title	Wilcoxon signed rank test
Statistical analysis description:	
Median and range for values from day 7- and day 14 were calculated and a Wilcoxon signed rank test was calculated between day 7 values and day 14 values	

Comparison groups	Pre treatment v Post treatment
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.95
Variability estimate	Standard error of the mean

Notes:

[1] - values from 20 patients at day 7 are compared to 20 treated patients values at day 14

[2] - No significant differences were found

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
28 days	
Adverse event reporting additional description:	
clinical examination and anamnestic review at all 4 clinical visits,blood tests	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse effects were observed

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.

None

Notes: