Clinical trial results:
Anti-inflammatory pulmonal therapy of CF-patients with Amitriptyline and Placebo

Summary

EudraCT number	2008-002673-13
Trial protocol	DE
Global end of trial date	01 October 2011

Results information

Result version number	v1 (current)
This version publication date	29 March 2022
First version publication date	29 March 2022

Trial information

Trial identification

Sponsor protocol code	APA-IIb

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01309178
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital Tübingen
Sponsor organisation address	Geissweg 3, Tübingen, Germany, 72076
Public contact	Prof. Dr. med. M. Bamberg, University Hospital Tübingen, +49 7071 29-88500 ,
Scientific contact	Dr. med. Joachim Riethmüller, University Hospital Tübingen, +49 (0)7071-2981391,

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	Interim
Date of interim/final analysis	01 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to assess the improvement of the lung function parameter FEV1 (absolute and relative to baseline) under verum and placebo in 4 weeks

Protection of trial subjects:

The written permission for use of the personal and study-related data and passing it on in pseudo-anonymous form will be done before the study starts. The patients' parents have to give their consent on behalf of their child for this data to be used within a scientific study. If no such consent is given, the data must not be used. Only those persons involved in the clinical trial will have access to the personal data and to the patient identification list.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 2009
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: 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)	0
Adolescents (12-17 years)	40
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study is scheduled to begin on November 1st 2008. The first patient should be treated not before spring 2009. The maximal duration of the study will be 12 months. The individual participation on the study will be at least 6 weeks.

Pre-assignment

Screening details:

95 patients were assessed for eligibility. 55 of them were excluded because they did not meet the inclusion and exclusion criteria. Therefore, 40 patients underwent randomization. Out of the 40 patients, 37 were included in the ITT analysis.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Amitriptyline arm

Arm description:

Patients were randomized to amitriptyline capsules, administered orally at a dosage of 25 mg amitriptyline per capsule, twice
daily for 4 weeks

Arm type	Experimental
Investigational medicinal product name	Amitriptyline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

25 mg amitriptyline per capsule, twice daily for 4 weeks

Arm title	Placebo arm

Arm description:

the placebo were corn starch capsules administered in the same frequency as the experimental drug

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Corn starch capsules twice daily during 4 weeks

Number of subjects in period 1	Amitriptyline arm	Placebo arm
Started	21	19
Completed	19	17
Not completed	2	2
High c-protein reactive values	1	-
high c-reactive protein levels	-	1
missing values	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
Adolescents (12-17 years)	15	15	
Adults (18-64 years)	25	25	
Age continuous Units: years			
arithmetic mean	25.5		
standard deviation	± 8.4	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	19	19	

End points

End points reporting groups

Reporting group title	Amitriptyline arm
Reporting group description:	
Patients were randomized to amitriptyline capsules, administered orally at a dosage of 25 mg amitriptyline per capsule, twice daily for 4 weeks	
Reporting group title	Placebo arm
Reporting group description:	
the placebo were corn starch capsules administered in the same frequency as the experimental drug	

Primary: The difference of forced expiratory volume in one second(FEV1) after 28 days

End point title	The difference of forced expiratory volume in one second(FEV1) after 28 days
End point description:	
Lung function was determined in the Intention to treat (ITT) and the per protocol (PP) population as forced expiratory volume in one second (FEV1) after 28 days of amitriptyline or placebo treatment	
End point type	Primary
End point timeframe:	
28 days	

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	19		
Units: 0-100				
geometric mean (standard deviation)	0.6 (± 5.7)	-3.8 (± 6.9)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Amitriptyline arm v Placebo arm
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.034
Method	t-test, 1-sided

Notes:

[1] - This endpoint results were analyzed from the ITT population of the study

Secondary: The relative fluorescence intensities for ceramide in epithelial cells

End point title	The relative fluorescence intensities for ceramide in epithelial

	cells

End point description:

The relative fluorescence intensities for ceramide in epithelial cells were scored by a blinded investigator with weak (1), mediate (2), strong (3) and very strong (4).

End point type	Secondary

End point timeframe:

28 days

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	19		
Units: 0-100	64	46		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The safety of amitriptyline was assessed after each treatment course of 28 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	1

Reporting groups	
Reporting group title	Amitriptyline arm
Reporting group description:	
Patients were randomized to amitriptyline capsules, administered orally at a dosage of 25 mg amitriptyline per capsule, twice daily for 4 weeks	
Reporting group title	Placebo arm
Reporting group description:	
the placebo were corn starch capsules administered in the same frequency as the experimental drug	

Serious adverse events	Amitriptyline arm	Placebo arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Amitriptyline arm	Placebo arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)	14 / 20 (70.00%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Tiredness			
subjects affected / exposed	17 / 20 (85.00%)	7 / 20 (35.00%)	
occurrences (all)	17	7	
Common cold			

subjects affected / exposed	11 / 20 (55.00%)	6 / 20 (30.00%)	
occurrences (all)	11	6	
Headache			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Sleep problems			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Xerostomia			
subjects affected / exposed	14 / 20 (70.00%)	3 / 20 (15.00%)	
occurrences (all)	14	3	
Gastroenteritis			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Exacerbation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2009	Unknown

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/23572075