



## Clinical trial results:

### Anti-inflammatory pulmonal therapy of CF-patients with Amitriptyline and Placebo - Randomised, double-blind, placebo-controlled cohort trial Summary

EudraCT number	2014-003581-25
Trial protocol	DE
Global end of trial date	14 June 2019

#### Results information

Result version number	v1 (current)
This version publication date	11 November 2021
First version publication date	11 November 2021
Summary attachment (see zip file)	Adverse Events information_APAIII (Adverse Events information_APAIII.pdf) Primary endpoint statistical analysis (Primary endpoint statistical analysis.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	APA-III
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	University Hospital Tübingen
Sponsor organisation address	Geissweg 3, Tübingen, Germany, 72076
Public contact	Dr.med. Andreas Hector, University Children's Hospital, CPCS, +49 70712981341, andreas.hector@med.uni-tuebingen.de
Scientific contact	Dr.med. Andreas Hector, University Children's Hospital, CPCS, +49 70712981341, andreas.hector@med.uni-tuebingen.de

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	12 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 May 2019
Global end of trial reached?	Yes
Global end of trial date	14 June 2019
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:

Difference in absolute FEV1 % predicted between verum and placebo at week 8 compared to baseline

Protection of trial subjects:

Patient's safety and well-being was taken in consideration during the whole procedure of the trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2015
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	Germany: 79
Worldwide total number of subjects	79
EEA total number of subjects	79

Notes:

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**Subjects enrolled per age group**

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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)	10
Adults (18-64 years)	66
From 65 to 84 years	3
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

According to study protocol recruitment was planned to start in March 2015 and to be done within 18 months.

Number of cases, statistical considerations, a total of 102 patients had to be included in this study (refer to study protocol chapter 9.1). The last follow-up included into this report took place on June 8th, 2018.

### Pre-assignment

Screening details:

As already mentioned hardly any data are documented concerning the pre-screening process and therefore the reasons, why patients could not be screened for the study.

### 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	Subject, Investigator

Blinding implementation details:

The study was done double blinded (patients and treating physicians) but due to the known side effects of amitriptyline it must be feared that physicians as well as patients knew which treatment they got.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Amitriptyline arm

Arm description:

Amitriptyline

Arm type	Experimental
Investigational medicinal product name	Amitriptyline
Investigational medicinal product code	549-18-8
Other name	Elavil
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Amitriptyline 2 x 12.5 mg oral (day 1-14), followed by 2x25mg twice daily (day 15-98).

<b>Arm title</b>	Placebo arm
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo (corn starch)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo (corn starch) 2 x 12.5 mg oral (day 1-14), followed by 2x25mg twice daily (day 15-98)

<b>Number of subjects in period 1</b>	Amitriptyline arm	Placebo arm
Started	42	37
Completed	36	34
Not completed	6	3
Lost to follow-up	2	1
Protocol deviation	4	2

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	79	79	
Age categorical			
The median age was 24 years. The minimum age was 13 years and the maximum was 68			
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)	19	19	
Adults (18-64 years)	59	59	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	34	34	
Male	45	45	

## End points

### End points reporting groups

Reporting group title	Amitriptyline arm
Reporting group description:	
Amitriptyline	
Reporting group title	Placebo arm
Reporting group description: -	

### Primary: Difference between baseline and week 8 in FEV1%

End point title	Difference between baseline and week 8 in FEV1% <sup>[1]</sup>
End point description:	
Difference in absolute FEV1 % predicted between verum and placebo at week 8 compared to baseline	
End point type	Primary
End point timeframe:	
8 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analyses can be found in the attached chart

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	37		
Units: 40				
arithmetic mean (standard deviation)	-2.23 (± 9.64)	-1.34 (± 6.85)		

<b>Attachments (see zip file)</b>	Primary endpoint statistical analysis/Primary endpoint statistical
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### Statistical analyses

No statistical analyses for this end point

### Secondary: Absolute and relative FEV1 as 2. Absolute and relative FEV1 as % predicted after 4, 8 and 16 weeks compared to baseline, if not primary

End point title	Absolute and relative FEV1 as 2. Absolute and relative FEV1 as % predicted after 4, 8 and 16 weeks compared to baseline, if not primary
End point description:	
Absolute and relative FEV1 as 2. Absolute and relative FEV1 as % predicted after 4, 8 and 16 weeks compared to baseline, if not primary	
End point type	Secondary
End point timeframe:	
between week 8 and week 16	

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	37		
Units: 40				
arithmetic mean (standard deviation)	66.71 ( $\pm$ 19.31)	64.67 ( $\pm$ 21.65)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: FEV1 [L]

End point title	FEV1 [L]
End point description: Absolute and relative FEV1 increase	
End point type	Secondary
End point timeframe: Until study termination (20 weeks)	

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	37		
Units: 40				
arithmetic mean (standard deviation)	2.37 ( $\pm$ 0.79)	2.42 ( $\pm$ 0.93)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Other lung function parameters (FVC) (%)

End point title	Other lung function parameters (FVC) (%)
End point description:	
End point type	Secondary
End point timeframe: 16 weeks	

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	37		
Units: 40				
arithmetic mean (standard deviation)	82.52 ( $\pm$ 18.23)	85.05 ( $\pm$ 18.10)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Other lung function parameters (FVC) (L)

End point title	Other lung function parameters (FVC) (L)
End point description:	
End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Amitriptyline arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	37		
Units: 40				
arithmetic mean (standard deviation)	3.39 ( $\pm$ 1.05)	3.73 ( $\pm$ 0.95)		

### Statistical analyses

No statistical analyses for this end point



## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

The trial duration and the follow up period

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	1
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Frequency threshold for reporting non-serious adverse events: 0 %

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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: Information regarding Adverse Events can be found in the attached documents

## 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